UPDATED AS PER LATEST 2017 SYLLABUS

Pearson SUCCESS COMPANION

INCLUDES FULLY SOLVED GPAT 2017 QUESTION PAPER*

THIRD EDITION

THE PEARSON GUIDE TO THE GPAT

and Other Competitive Examinations in Pharmacy

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Ashish Patel

Pearson

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PREFACE

The Graduate Pharmacy Aptitude Test (GPAT) is an online national level examination for admission into all post graduate pharmacy programs approved and conducted by the All India Council for Technical Education (AICTE), New Delhi.

The GPAT is conducted annually for admission to the postgraduate courses in the affiliated institutes of AICTE and University Grants Commission (UGC). The GPAT score is also recommended for appearing in the National Institute of Pharmaceutical Education and Research (NIPER) examination and Ph.D. programmes in various universities.

The Pearson Guide to the GPAT and Other Competitive Examinations in Pharmacy in its third edition, is a sincere attempt to produce effective course material for the GPAT aspirants.

The book has six units, where the first four units are covering major sections of GPAT syllabus. Each chapter of the book covers important definitions; theoretical explanations and tabular data to help students learn effectively. Graded levels of MCQ (Multiple Choice questions) have been included in the chapter end exercise, which are in line with the previous year questions from GPAT, GATE, and NIPER JEE. This book is also useful for various entrance examinations such as Gujarat Public Service Commission (GPSC), Maharashtra CET (MH CET); Manipal University, and Union Public Service Commission (UPSC) examinations for Drug Inspector; government lectureship. Unit 5 of this title contains all important information regarding NIPER JEE examination syllabus, preparation guidelines, and 5 mock test papers. This book also contains a separate unit (Unit 6) with all previous years' solved papers from GPAT, GPSC and UPSC examination's Drug Inspector; government lecturer and pharmacist's examination. There is a special emphasis on GPAT 2017 question paper which is included in front matter of the book. Five new updated Mock-tests have been uploaded online for further practice.

We hope this book will help students understand the concepts and enable them to solve maximum questions in minimum time.

Finally, we wish all the very best to every student preparing for the GPAT examination.

Umang Shah
Ashok Akabari
Amit Baser
Ashish Patel

ACKNOWLEDGEMENTS

Writing a book is never one man effort, but it is often result of the invaluable contribution of a number of individuals in direct or indirect manner. This suitably applies to this title. Without help, encouragement & blessings from several persons, we would never have been able to finish this work.

Numerous people have been instrumental in enabling us to give a concrete shape to our book. I must mention the names of those people who have made a catalytic impact on the development of this book.

First and foremost, we pay reverence to the omniscient, omnipresent, omnipotent, The God who has perpetually patronized me with the contentiousness and love.

Words are an inadequate medium to express my deep sense of gratitude.

Motivation, encouragement and guidance keep person moving towards new endeavor.

I wholeheartedly express my sincere gratitude to Dr. Rajesh Maheshwari (Assistant Professor, Faculty of Pharmacy, Sumandeep Vidyapeeth), Dr. Sandip Patel, Mr. Dharmang Pandya, Ms. Kanan Gamit, Ms. Kunti Shah, Ms. Jagruti Prajapati, Ms. Avani Chokshi, and Ms. Mansi Paradkar (Assistant Professor, Ramanbhai Patel College of Pharmacy, CHARUSAT University) for helping us in reviewing of the book modules and MCQ's.

We wholeheartedly take this opportunity to place on record our profound gratitude to our respected Parents, who are always a source of strength and inspiration to us and sincerely aspired to see us pursue a higher education. We sincerely feel that all the credits should go to our family, for their consistent prayers, affectionate blessings, selfless care and endless confidence in us. We heartily believe that without support of our family, we would have never come to the stage of writing this acknowledgement.

Umang Shah
Ashok Akabari
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SYLLABUS FOR GPAT

PHARMACEUTICS

Introduction to physical pharmacy

Refer Unit 1: Chapter 1

- *Matter, Properties of Matter:*

  State of matter, change in the state of matter, latent heats and vapor pressure, sublimation critical point, eutectic mixtures, gases, aerosols-inhalers, relative humidity, liquid. Complexes, liquid crystals, glassy state, solids- crystalline, amorphous and polymorphism.

- *Micromeretics and Powder Rheology:*

  Particle size and distribution, average particle size, number and weight distribution, particle number, methods for determining particle volume, methods of determining particle size- optical microscopy, sieving, sedimentation; measurements of particle shape, specific surface area; methods for determining surface area; permeability, adsorption, derived properties of powders, porosity, packing arrangement, densities, bulkiness & flow properties.

- *Surface and Interfacial Phenomenon:*

  Liquid interface, surface and interfacial tensions, surface free energy, measurement of surface and interfacial tensions, spreading coefficient, adsorption at liquid interfaces, surface active agents, HLB classification, solubilization, detergency, adsorption at solid interfaces, solid-gas and solid- liquid interfaces, complex films, electrical properties of interface.

- *Viscosity and Rheology:*

  Newtonian systems, Law of flow, kinematic viscosity, effect of temperature; non-newtonian systems: pseudoplastic, dilatant, plastic; thixotropy, thixotropy in formulation, negative thixotropy, determination of viscosity, capillary, falling ball, rotational viscometers.

- *Dispersion Systems:*

  Colloidal dispersions: Definition, types, properties of colloids, protective colloids, applications of colloids in pharmacy; Suspensions and Emulsions: Interfacial properties of suspended particles, settling in suspensions, theory of sedimentation, effect of Brownian motion, sedimentation of flocculated particles, sedimentation parameters, wetting of particles, controlled flocculation, flocculation in structured vehicles, rheological considerations; Emulsions-types, theories, physical stability.

- *Complexation:*

  Classification of complexes, methods of preparation, analysis, & applications.

- *Kinetics and Drug Stability:*

  General considerations & concepts, half-life determination, Influence of temperature, light, solvent, catalytic species and other factors, Accelerated stability study, expiration dating.

Importance of microbiology in pharmacy

Refer Unit 1: Chapter 8

- *Structure of Bacterial Cell; Classification of microbes and their taxonomy:*

  Actinomycetes, bacteria, rickettsiae, spirochetes and viruses.
- *Identification of Microbes:*

  Stains and types of staining techniques, electron microscopy; Nutrition, cultivation, isolation of bacteria, actinomycetes, fungi, viruses, etc; microbial genetics and variation.
- *Control of Microbes by Physical and Chemical Methods:*

  Disinfection, factors influencing disinfectants, dynamics of disinfection, disinfectants and antiseptics and their evaluation.
- *Sterilization:*

  Different methods, validation of sterilization methods &equipments; Sterility testing of all pharmaceutical products. Microbial assays of antibiotics, vitamins & amino acids.
- *Immunology and Immunological Preparations:*

  Principles, antigens and heptans, immune system, cellular/humoral immunity, immunological tolerance, antigen-antibody reactions and their applications. Hypersensitivity, active and passive immunization. Vaccines and sera: their preparation, standardization and storage.
- *Genetic Recombination:*

  Transformation, conjugation, transduction, protoplast fusion and gene cloning and their applications. Development of hybridoma for monoclonal antibodies. Study of drugs produced by biotechnology such as Activase, Humulin, Humatrope, HB etc.
- *Antibiotics:*

  Historical development of antibiotics. Antimicrobial spectrum and methods used for their standardization. Screening of soil for organisms producing antibiotics, fermenter, its design, control of different parameters. Isolation of mutants, factors influencing rate of mutation. Design of fermentation process. Isolation of fermentation products with special reference to penicillins, streptomycins, tetracyclines and vitamin B12.

Introduction to pharmaceutical jurisprudence & ethics

Refer Unit 1: Chapter 6

- *Pharmaceutical Legislations:*

  A brief review; Drugs & Pharmaceutical Industry - A brief review; Pharmaceutical Education
- *An Elaborate Study of the Followings:*

  Pharmaceutical Ethics; Pharmacy Act 1948; Drugs and Cosmetics Act 1940 and Rules 1945; Medicinal & Toilet Preparations (Excise Duties) Act 1955; Narcotic Drugs & Psychotropic Substances Act 1985 & Rules; Drugs Price Control Order.
- *A Brief Study of the Following Acts with Special Reference to the Main Provisions and the Latest Amendments:*

  Poisons Act 1919; Drugs and Magic Remedies (Objectionable Advertisements) Act 1954; Medical Termination of Pregnancy Act 1970 & Rules 1975; Prevention of Cruelty to Animals Act 1960; States Shops & Establishments Act & Rules; Insecticides Act 1968; AICTE Act 1987; Factories Act 1948; Minimum Wages Act 1948; Patents Act 1970.

  A brief study of the various Prescription/Non-prescription Products. Medical/Surgical accessories, diagnostic aids, appliances available in the market.

Introduction to dispensing and community pharmacy

Refer Unit 1: Chapter 4

- *Prescription:*

  Handling of prescription, source of errors in prescription, care required in dispensing procedures including labeling of dispensed products. General dispensing procedures including labeling of dispensed products; Pharmaceutical

calculations: Posology, calculation of doses for infants, adults and elderly patients; Enlarging and reducing recipes percentage solutions, alligation, alcohol dilution, proof spirit, isotonic solutions, displacement value etc.

- *Principles Involved and Procedures Adopted in Dispensing of:*

  Typical prescriptions like mixtures, solutions, emulsions, creams, ointments, powders, capsules, pastes, jellies, suppositories, ophthalmic, pastilles, lozenges, pills, lotions, liniments, inhalations, paints, sprays, tablet triturates, etc.

- *Incompatibilities:*

  Physical and chemical incompatibilities, inorganic incompatibilities including incompatibilities of metals and their salts, non-metals, acids, alkalis, organic incompatibilities. Purine bases, alkaloids, pyrazolone derivatives, amino acids, quaternary ammonium compounds, carbohydrates, glycosides, anesthetics, dyes, surface active agents, correction of incompatibilities. Therapeutic incompatibilities.

- *Community Pharmacy:*

  Organization and structure of retail and whole sale drug store-types of drug store and design, legal requirements for establishment, maintenance and drug store-dispensing of proprietary products, maintenance of records of retail and wholesale, patient counseling, role of pharmacist in community health care and education (First aid, communicable diseases, nutrition, family planning).

- *Organization and Structure of Hospital Pharmacy:*

  Organization of a hospital and hospital pharmacy, Responsibilities of a hospital pharmacist, Pharmacy and therapeutic committee, Budget preparation and Implementation.

- *Hospital Formulary:*

  Contents, preparation and revision of hospital formulary.

- *Drug Store Management and Inventory Control:*

  Organization of drug store, Types of materials stocked, storage conditions; Purchase and Inventory Control principles, purchase procedures, Purchase order, Procurement and stocking.

- *Drug Distribution Systems in Hospitals:*

  Out-patient dispensing, methods adopted; Dispensing of drugs to in-patients. Types of drug distribution systems. Charging policy, labeling; Dispensing of drugs to ambulatory patients; Dispensing of controlled drugs, Dispensing of ancillary supplies.

- *Central Sterile Supply Unit and their Management:*

  Types of materials for sterilization, Packing of materials prior to sterilization, sterilization equipments, Supply of sterile materials.

- *Manufacture of Sterile and Non-sterile Products:*

  Policy making of manufacturable items, demand and costing, personnel requirements, manufacturing practice, Master formula Card, production control, Manufacturing records.

- *Drug Information Services:*

  Sources' of Information on drugs, disease, treatment schedules, procurement of information, Computerized services (e.g., MEDLINE), Retrieval of information, Medication error- types of medication errors, correction and reporting.

- *Records and Reports:*

  Prescription filling, drug profile, patient medication profile, cases on drug interaction and adverse reactions, idiosyncratic cases. Pharmacoeconomics: Introduction to pharmacoeconomics, different methods of pharmacoeconomics, application of pharmacoeconomics.

- *Pharmacoepidemiology:*

  Definition and scope, method to conduct pharmacoepidemiological studies, advantages & disadvantages of pharmacoepidemiological studies.

- *Nuclear Pharmacy:*

  Methods of handling radioisotopes, radioisotope committee.

Importance of unit operations in manufacturing, stoichiometry:

Refer Unit 1: Chapter 2

- *Unit Processes*

  Material and energy balances, molecular units, mole fraction, tie substance, gas laws, mole volume, primary and secondary quantities, equilibrium state, rate process, steady and unsteady states, dimensionless equations, dimensionless formulae, dimensionless groups, different types of graphic representation, mathematical problems.

- *Fluid Flow:*

  Types of flow, Reynold's number, Viscosity, Concept of boundary layer, basic equations of fluid flow, valves, flow meters, manometers and measurement of flow and pressure.

- *Evaporation:*

  Basic concept of phase equilibria, factor affecting evaporation, evaporators, film evaporators, single effect and multiple effect evaporators, Mathematical problems on evaporation.

- *Distillation:*

  Roult's law, phase diagrams, volatility; simple steam and flash distillations, principles of rectification, Mc-Cabe Thiele method for calculations of number of theoretical plates, Azeotropic and extractive distillation.

- *Drying:*

  Moisture content and mechanism of drying, rate of drying and time of drying calculations; classification and types of dryers, dryers used in pharmaceutical industries and special drying methods.

- *Size Reduction:*

  Definition, objectives of size reduction, mechanisms of size reduction, factors affecting size reduction, laws governing energy and power requirements of a mills including ball mill, hammer mill, fluid energy mill. Size separation: Different techniques of size separation, sieves, sieve shakers, sedimentation tank, cyclone separators, bag fillers Etc.

- *Mixing:*

  Theory of mixing, solid-solid, solid-liquid and liquid-liquid mixing equipments.

- *Filtration and Centrifugation:*

  Theory of filtration, continuous and batch filters, filter aids, filter media, industrial filters including filter press, rotary filter, edge filter, Etc. Factors affecting filtration, filtration, optimum cleaning cycle in batch filters. Principles of centrifugation, industrial centrifugal filters, and centrifugal sedimenters.

- *Crystallization:*

  Characteristics of crystals like-purity, size, shape, geometry, habit, forms size and factors affecting them, Solubility curves and calculation of yields. Material and heat balances around Swenson Walker Crystallizer. Supersaturation, theory and its limitations, Nucleation mechanisms, crystal growth.Study of various types of Crystallizers, tanks, agitated batch, Swenson Walker, Single vacuum, circulating magma and Krystal Crystallizer, Caking of crystals and its prevention. Numerical problems on yields;

- *Dehumidification and Humidity Control:*

  Basic concepts and definition, wet bulb and adiabatic saturation temperatures, Hygrometric chart and measurement of humidity, application of humidity measurement in pharmacy, equipments for Dehumidification operations;

- *Refrigeration and Air Conditioning:*

  Principle and applications of refrigeration and air conditioning;

- *Material of Construction:*

  General study of composition, corrosion, resistance, Properties and applications of the materials of construction with special reference to stainless steel and glass.

- *Material Handling Systems:*

  Liquid handling - Different types of pumps, Gas handling-Various types of fans, blowers and compressors, Solid handling-Bins, Bunkers, Conveyers, Air transport.
- *Corrosion:*

  Classification, mechanism of corrosion, factors affecting, prevention and control.
- *Plant Location:*

  Layout, utilities and services.
- *Industrial Hazards and Safety Precautions:*

  Mechanical, Chemical, Electrical, fire and dust hazards. Industrial dermatitis, Accident records Etc.
- *Automated Process Control Systems:*

  Process variables, temperature, pressure, flow, level and vacuum and their measurements; elements of automatic process control and introduction to automatic process control systems; elements of computer aided manufacturing (CAM). Reactors and fundamentals of reactors design for chemical reactions.

Dosages forms, designing & evaluation

Refer Unit 1: Chapter 3 and 8

- *Liquid Dosages Forms:*

  Introduction, types of additives used in formulations, vehicles, stabilizers, preservatives, suspending agents, emulsifying agents, solubilizers, colors, flavors and others, manufacturing packaging, labeling, evaluation of clear liquids, suspensions and emulsions official in pharmacopoeia;
- *Semisolid Dosage Forms:*

  Definitions, types, mechanisms of drug penetration, factors influencing penetration, semisolid bases and their selection. General formulation of semisolids, clear gels manufacturing procedure, evaluation and packaging;
- *Suppositories:*

  Ideal requirements, bases, displacement value, manufacturing procedure, packaging and evaluation;
- *Extraction and Galenical Products:*

  Principle and method of extraction, preparation of infusion, tinctures, dry and soft liquid extracts;
- *Blood Products and Plasma Substitutes:*

  Collection, processing and storage of whole human blood, concentrated human RBCs, dried human plasma, human fibrinogen, human thrombin, human normal immunoglobulin, human fibrin, foam plasma substitutes, -ideal requirements, PVP, dextran Etc. for control of blood pressure as per I.P.;
- *Pharmaceutical Aerosols:*

  Definition, propellants, general formulation, manufacturing' and packaging methods, pharmaceutical applications;
- *Ophthalmic Preparations:*

  Requirements, formulation, methods of preparation, labeling, containers, evaluation;
- *Cosmeticology and Cosmetic Preparations:*

  Fundamentals of cosmetic science, structure and functions of skin and hair. Formulation, preparation and packaging of cosmetics for skin, hair, dentifrice and manicure preparations like nail polish, nail polish remover, Lipsticks, eye lashes, baby care products Etc.
- *Capsules:*

  Advantages and disadvantages of capsule dosage form, material for production of hard gelatin capsules, size of capsules, formulation, method of capsule filling, soft gelatin, capsule shell and capsule content, importance of base absorption and minimum/gm factors in soft capsules, quality control, stability testing and storage of capsule dosage forms.

- *Micro-encapsulation:*

  Types of microcapsules, importance of microencapsulation in pharmacy, microencapsulation by phase separation, coacervation, multi-orifice, spray drying, spray congealing, polymerization complex emulsion, air suspension technique, coating pan and other techniques, evaluation of micro capsules.

- *Tablets:*

  Advantages and disadvantages of tablets, Application of different types of tablets, Formulation of different types of tablets, granulation, technology on large-scale by various techniques, different types of tablet compression machinery and the equipments employed, evaluation of tablets.

- *Coating of Tablets:*

  Types of coating, film forming materials, formulation of coating solution, equipments for coating, coating process, evaluation of coated tablets. Stabilityk inetics and quality assurance.

- *Parenteral Products:*

  Pre-formulation factors, routes of administration, water for injection, and sterile water for injection, pyrogenicity, non- aqueous vehicles, isotonicity and methods of its adjustment, Formulation details, Containers and closures and selection, labeling; Pre-filling treatment, washing of containers and closures, preparation of solution and suspensions, filling and closing of ampoules, vials, infusion fluids, lyophilization & preparation of sterile powders, equipment for large scale manufacture and evaluation of parenteral products; Aseptic Techniques-source of contamination and methods of prevention, Design of aseptic area, Laminar flow bench services and maintenance. Sterility testing of pharmaceuticals.

- *Surgical Products:*

  Definition, primary wound dressing, absorbents, surgical cotton, surgical gauzes etc., bandages, adhesive tape, protective cellulosic hemostastics, official dressings, absorbable and non- absorbable sutures, ligatures and catguts.

- *Packaging of Pharmaceutical Products:*

  Packaging components, types, specifications and methods of evaluation, stability aspects of packaging. Packaging equipments, factors influence choice of containers, legal and official requirements for containers, package testing.

- *Designing of Dosage Forms:*

  Pre-formulation studies, Study of physical properties of drug like physical form, particle size, shape, density, wetting, dielectric constant. Solubility, dissolution and organoleptic properties and their effect on formulation, stability and bioavailability. Study of chemical properties of drugs like hydrolysis, oxidation, reduction, racemization, polymerization etc., and their influence on formulation and stability of products. Study of pro-drugs in solving problems related to stability, bioavailability and elegancy of formulations. Design, development and process validation methods for pharmaceutical operations involved in the production of pharmaceutical products with special reference to tablets, suspensions. Stabilization and stability testing protocol for various pharmaceutical products. ICH Guidelines for stability testing of formulations.

- *Performance Evaluation Methods:*

  In-vitro dissolution studies for solid dosage forms methods, interpretation of dissolution data. Bioavailability studies and bioavailability testing protocol and procedures. In vivo methods of evaluation and statistical treatment. GMP and quality assurance, Quality audit. Design, development, production and evaluation of controlled/sustained/extended release formulations.

Biopharmaceutics & pharmacokinetics

Refer Unit 1: Chapter 5

- *Introduction to Biopharmaceutics:*

  Passage of drugs across biological barrier (passive diffusion, active transport, facilitated diffusion, ion-pair formation and pinocytosis); Factors influencing absorption- biological, physico-chemical, physiological and pharmaceutical; Drug distribution in the body, plasma protein binding.

- *Pharmacokinetics:*

  Significance of plasma drug concentration measurement. Compartment model- Definition and Scope. Pharmacokinetics of drug absorption - Zero order and first order absorption rate constant using Wagner-Nelson and residual methods. Volume of distribution and distribution coefficient. Compartment kinetics- One compartment and two compartment models. Determination of pharmacokinetic parameters from plasma and urine data after drug administration by intravascular and oral route. Clearance concept, mechanism of renal clearance, clearance ratio, determination of renal clearance. Extraction ratio, hepatic clearance, biliary excretion, extrahepatic circulation. Non-linear pharmacokinetics with special reference to one compartment model after I.V. drug administration.
- *Clinical Pharmacokinetics:*

  Definition and scope: Dosage adjustment in patients with and without renal and hepatic failure; Design of single dose bio-equivalence study and relevant statistics; Pharmacokinetic drug interactions and their significance in combination therapy.
- *Bioavailability and Bioequivalence:*

  Measures of bioavailability, Cmax, tmax, Keli and Area Under the Curve (AUC); Design of single dose bioequivalence study and relevant statistics; Review of regulatory requirements for conducting bioequivalent studies. Biopharmaceutical Classification System (BCS) of drugs.

PHARMACEUTICAL CHEMISTRY

Unit 3

Inorganic pharmaceutical & medicinal chemistry

Refer Unit 3: Chapter 6

- *Importance of Inorganic Compounds in Pharmacy and Medicine;*

  An outline of methods of preparation, uses, sources of impurities, tests for purity and identity, including limit tests for iron, arsenic, lead, heavy metals, chloride, sulphate and special tests if any, of the following classes of inorganic pharmaceuticals included in Indian Pharmacopoeia:
- *Gastrointestinal Agents:*

  Acidifying agents, Antacids, Protectives and Adsorbents, Cathartics;
- *Major Intra- and Extra-cellular Electrolytes:*

  Physiological ions. Electrolytes used for replacement therapy, acid-base balance and combination therapy;
- *Essential and Trace Elements:*

  Transition elements and their compounds of pharmaceutical importance, Iron and haematinics, mineral supplements; Cationic and anionic components of inorganic drugs useful for systemic effects;
- *Topical Agents:*

  Protectives, Astringents and Anti-infectives.
- *Gases and Vapors:*

  Oxygen, Anesthetics (inorganic) and Respiratory stimulants;
- *Dental Products:*

  Dentifrices, Anti-caries agents; Complexing and chelating agents used in therapy;
- *Miscellaneous Agents:*

  Sclerosing agents, Expectorants, Emetics, Inorganic poisons and antidotes.
- *Pharmaceutical Aids Used in Pharmaceutical Industry:*

  Anti-oxidants, Preservatives, Filter aids, Adsorbents, Diluents, Excipients, Suspending agents, Colorants;

- *Acids, Bases and Buffers:*

  Buffer equations and buffer capacity in general, buffers in pharmaceutical systems, preparation, stability, buffered isotonic solutions, measurements of tonicity, calculations and methods of adjusting isotonicity.

- *Inorganic Radiopharmaceuticals:*

  Nuclear reaction, radioisotopes, radiopharmaceuticals, Nomenclature, Methods of obtaining their standards and units of activity, half-life, measurement of activity, clinical applications, dosage, hazards and precautions.

Physical chemistry and its importance in pharmacy

Refer Unit 3: Chapter 1

- *Importance of Basic Fundamentals of Physical Chemistry in Pharmacy:*

  Behavior of Gases, Kinetic theory of gases, deviation from ideal behavior and explanation.

- *The Liquid State:*

  Physical properties (surface tension, parachor, viscosity, refractive index, dipole moment);

- *Solutions:*

  Ideal and real solutions, solutions of gases in liquids, colligative properties, partition coefficient, conductance and its measurement, Debye Huckel theory;

- *Thermodynamics:*

  First, Second and Third laws, Zeroth law, Concept of free energy, enthalpy and entropy, absolute temperature scale;

- *Thermochemical Equations; Phase Rule; Adsorption:*

  Freudlich and Gibbs adsorption, isotherms, La[illegible]s theory of adsorption.

- *Photochemistry:*

  Consequences of light absorption, Jabolenski diagram, Quantum efficiency; Chemical

- *Kinetics:*

  Zero, First and Second order reactions, complex reactions, theories of reaction kinetics, characteristics of homogeneous and heterogeneous catalysis, acid base and enzyme catalysis;

- *Quantum Mechanics:*

  Postulates of quantum mechanics, operators in quantum mechanics, the Schrodinger wave equation.

Organic Chemistry and its importance in pharmacy

Refer Unit 3: Chapter 2

- *Importance of Fundamentals of Organic Chemistry in Pharmaceutical Sciences; Structure and Properties:*

  Atomic structure, Atomic orbitals, Molecular orbital theory, wave equation, Molecular orbitals, Bonding and Anti-bonding orbitals, Covalent bond, Hybrid orbitals, Intramolecular forces, Bond dissociation energy, Polarity of bonds, Polarity of molecules, Structure and physical properties, Intermolecular forces, Acids and bases;

- *Stereochemistry:*

  Nomenclature, isomerism, stereoisomerism, conformational and configurational isomerism, optical activity, specification of configuration, Reactions involving stereoisomers, chirality, conformations;

- *Stereoselective and Stereospecific Reactions; Structure, Nomenclature, Preparation and Reactions of:*

  Alkanes, Alkenes, Alkynes, Cyclic analogs, Dienes, Benzene, Polynuclear aromatic compounds, Arenes, Alkyl halides, Alcohols, Ethers, Epoxides, Amines, Phenols, Aldehydes and ketones, Carboxylic acids, Functional derivatives of carboxylic acids, a,ß-Unsaturated carbonyl compounds, Reactive intermediates- carbocations, carbanions, carbenes and nitrenes;

- *Nucleophilic and Electrophilic Aromatic Substitution Reactions:*

  Reactivity and orientation; Electrophilic and Nucleophilic Addition Reactions; Rearrangements (Beckman, Hoffman, Benzilic acid, pinacole-pinacolone and Bayer-Villager).

- *Elimination Reactions; Conservation of Orbital Symmetry and Rules:*

  Electrocyclic, Cycloaddition and Sigmatropic reactions;
- *Neighboring Group Effects; Catalysis by Transition Metal Complexes; Heterocyclic Compounds:*

  Nomenclature, preparation, properties and reactions of 3, 4, 5, 6 & 7-membered heterocycles with one or two heteroatoms like 0, N, S. Chemistry of lipids, Carbohydrates and Proteins.

Biochemistry

Refer Unit 3: Chapter 4

- *Biochemistry in Pharmaceutical Sciences:*

  The concept of free energy, Determination of change in free energy - from equilibrium constant and reduction potential, bioenergetics, production of ATP and its biological significance;
- *Enzymes:*

  Nomenclature, enzyme kinetics and their mechanism of action, mechanism of inhibition, enzymes and iso-enzymes in clinical diagnosis.
- *Co-enzymes:*

  Vitamins as co-enzymes and their significance. Metals as cofactors and their significance; Carbohydrate Metabolism: Conversion of polysaccharides to glucose-1-phosphate, Glycolysis, fermentation and their regulation, Gluconeogenesis and glycogenolysis, Metabolism of galactose and galactosemia, Role of sugar nucleotides in biosynthesis, and Pentose phosphate pathway;
- *The Citric Acid Cycle:*

  Significance, reactions and energetics of the cycle, Amphibolic role of the cycle, and Glyoxalic acid cycle;
- *Lipids Metabolism:*

  Oxidation of fatty acids, ß-oxidation & energetics, biosynthesis of ketone bodies and their utilization, biosynthesis of saturated and unsaturated fatty acids, Control of lipid metabolism, Essential fatty acids & eicosanoids (prostaglandins, thromboxanes and leukotrienes), phospholipids, and sphingolipids, Biosynthesis of eicosanoids, cholesterol, androgens, progesterone, estrogens corticosteroids and bile acids.
- *Biological Oxidation:*

  Redox-potential, enzymes and co-enzymes involved in oxidation reduction & its control, The respiratory chain, its role in energy capture and its control, energetics of oxidative phosphorylation. Inhibitors of respiratory chain and oxidative phosphorylation, Mechanism of oxidative phosphorylation.
- *Metabolism of Ammonia and Nitrogen Containing Monomers:*

  Nitrogen balance, Biosynthesis of amino acids, Catabolism of amino acids, Conversion of amino acids to specialized products, Assimilation of ammonia, Urea cycle, metabolic disorders of urea cycle, Metabolism of sulphur containing amino acids.
- *Purine Biosynthesis:*

  Purine nucleotide inter-conversions. Pyrimidine biosynthesis and formation of deoxyribounucleotides.
- *Biosynthesis of Nucleic Acids:*

  Brief introduction of genetic organization of the mammalian genome, alteration and rearrangements of genetic material, Biosynthesis of DNA and its replications.
- *Mutation:*

  Physical & chemical mutagenesis/carcinogenesis, DNA repair mechanism. Biosynthesis of RNA;
- *Genetic Code and Protein Synthesis:*

  Genetic code, Components of protein synthesis and Inhibition of protein synthesis.

Medicinal chemistry

Refer Unit 3: Chapter 5

- *Basic Principles:*

  Physico-chemical and stereoisomeric (Optical, geometrical) aspects of drug molecules and biological action, Bioisosterism, Drug-receptor interactions including transduction mechanisms;

- *Drug Metabolism and Concept of Prodrugs; Principles of Drug Design (Theoretical Aspects):*

  Traditional analog and mechanism based approaches, QSAR approaches, Applications of quantum mechanics, Computer Aided Drug Designing (CADD) and molecular modeling.

- *Synthetic Procedures, Mode of Action, Uses, Structure Activity Relationships including Physicochemical Properties of the Following Classes of Drugs:*

  Drugs acting at synaptic and neuro-effector junction sites: Cholinergics, anti-cholinergics and cholinesterase inhibitors, Adrenergic drugs, Antispasmodic and anti-ulcer drugs, Local Anesthetics, Neuromuscular blocking agents.

- *Autacoids:*

  Antihistamines, Eicosanoids, Analgesic-antipyretics, Anti-inflammatory (non-steroidal) agents.

- *Steroidal Drugs:*

  Steroidal nomenclature (IUPAC) and stereochemistry, Androgens and anabolic agents, Estrogens and Progestational agents, Oral contraceptives, Adrenocorticoids;

- *Drugs Acting on the Central Nervous System:*

  General Anesthetics, Hypnotics and Sedatives, Anticonvulsants, Anti-Parkinsonian drugs, Psychopharmacological agents (Neuroleptics, Anti-depressants, Anxiolytics), Opioid analgesics, Anti-tussives, CNS stimulants.

- *Diuretics; Cardiovascular Drugs:*

  Anti-hypertensives, Anti-arrythmic agents, anti-anginal agents, Cardiotonics, Anti-hyperlipedemic agents, Anticoagulants and Anti-platelet drugs.

- *Thyroid and Anti Thyroid Drugs; Insulin and Oral Hypoglycemic Agents:*

  Chemotherapeutic Agents used in bacterial, fungal, viral, protozoal, parasitic and other infections, Antibiotics: ß-Lactam, macrolides, tetracyclines, aminoglycosides, polypeptide antibiotics, fluoroquinolones, Anti-metabolites (including sulfonamides); Anti-neoplastic agents; Anti-viral agents (including anti–HIV); Immunosuppressives and immunostimulants; Diagnostic agents; Pharmaceutical Aids.

- *Microbial Transformations:*

  Introduction, types of reactions mediated by micro-organisms, design of biotransformation processes, selection of organisms, biotransformation process and its improvements with special reference to steroids.

- *Enzyme Immobilization:*

  Techniques of immobilization, factors affecting enzyme kinetics, Study of enzymes such as hyaluronidase, penicillinase, streptokinase, amylases and proteases, Immobilization of bacteria and plant cells.

Pharmaceutical analysis

Refer Unit 3: Chapter 3

- *Different Techniques of Pharmaceutical analysis, Preliminaries and definitions:*

  Significant figures, Rules for retaining significant digits, Types of errors, Mean deviation, Standard deviation, Statistical treatment of small data sets, Selection of sample, Precision and accuracy.

- *Fundamentals of Volumetric Analysis:*

  Methods of expressing concentration, primary and secondary standards:

- *Acid Base Titrations:*

  Acid base concepts, Role of solvents, Relative strengths of acids and bases, Ionization, Law of mass action, Common ion effect, Ionic product of water, pH, Hydrolysis of salts, HendersonHasselbach equation, Buffer solutions,

Neutralization curves, Acid-base indicators, Theory of indicators, Choice of indicators, Mixed indicators, Polyprotic systems, Polyamine and amino acid systems, Amino acid titrations.

- *Oxidation Reduction Titrations:*

  Concepts of oxidation and reduction, Redox reactions, Strengths and equivalent weights of oxidizing and reducing agents, Theory of redox titrations, Redox indicators, Cell representations, Measurement of electrode potential, Oxidation-reduction curves, Iodimetry and Iodometry, Titrations involving cerric ammonium sulphate, potassium iodate, potassium bromate, potassium permanganate; titanous chloride, stannous chloride and Sodium 2,6-dichlorophenolindophenol.

- *Precipitation Titrations:*

  Precipitation reactions, Solubility product, Effect of acids, temperature and solvent upon the solubility of a precipitate, Argentometric titrations and titrations involving ammonium or potassium thiocyanate, mercuric nitrate, and barium sulphate, indicators, Methods of end point determination (GayLussac method, MohŶs method, Volhard's method and Fajan's method).

- *Gravimetric Analysis:*

  Precipitation techniques, The colloidal state, Supersaturation, Co-precipitation, Postprecipitation, Digestion, washing of the precipitate, Filtration, Filter papers and crucibles, Ignition, Thermogravimetric curves, Specific examples like barium sulphate, aluminium as aluminium oxide, calcium as calcium oxalate and magnesium as magnesium pyrophosphate, Organic precipitants.

- *Non-Aqueous Titrations:*

  Acidic and basic drugs, Solvents used, Indicators.

- *Complexometric Titrations:*

  Complexing agents used as titrants, Indicators, Masking and demasking;

- *Miscellaneous Methods of Analysis:*

  Diazotization titrations, Kjeldahl method of nitrogen estimation, Karl-Fischer aquametry, Oxygen flask combustion method, Gasometry.

- *Extraction Procedures including Separation of Drugs from Excipients; Potentiometry:*

  Standard redox potential, Nernst equation, Half-cell potential, Standard and indicating electrodes, potentiometric titrations;

- *Conductometry:*

  Specific and equivalent conductance, conductometric titrations.

- *Coulometry:*

  Coulowd's law, Coulometric titrations at fixed potential/current.

- *Polarography:*

  Decomposition potential, Half-wave potential, Diffision/migration/migration current, Ilkovic equation, Cathodic/anodic polarography, Dropping mercury electrode, Graphite electrode, Organic polarography.

- *Amperometry:*

  Rotating platinum electrode, Amperometric titrations.

- *Chromatography:*

  Theory of chromatography, plate theory, Factors affecting resolution, van Deemter equation. The following chromatographic techniques (including instrumentation) with relevant examples of Pharmacopoeial products: TLC, HPLC, GLC, HPTLC, Paper Chromatography and Column Chromatography.

- *The Theoretical Aspects, Basic Instrumentation, Elements of Interpretation of Spectra, and Applications (quantitative and qualitative) of the Following Analytical Techniques:*

Ultraviolet and visible spectrophotometry, Fluorimetry, Infrared spectrophotometry, Nuclear Magnetic Resonance spectroscopy [proton technique only], Mass Spectrometry (EI & CI only), Flame Photometry, Atomic Absorption Spectroscopy, X-ray Diffraction Analysis, Radioimmunoassay.

- *Quality Assurance:*

  GLP, ISO 9000, TQM, Quality Review and Quality documentation, Regulatory control, regulatory drug analysis, interpretation of analytical data, Validation, quality audit: quality of equipment, validation of equipment, validation of analytical procedures.

PHARMACOLOGY

Unit 2

- *Pathophysiology of Common Diseases; Basic Principles of Cell Injury and Adaptations:*

  Causes of Cellular injury, pathogenesis, morphology of cell injury, adaptations and cell death.

- *Basic Mechanisms Involved in the Process of Inflammation and Repair:*

  Vascular and cellular events of acute inflammation, chemical mediators of inflammation, pathogenesis of chronic inflammation, brief outline of the process of repair.

- *Immunopathophysiology:*

  T and B cells, MHC proteins, antigen presenting cells, immune tolerance, pathogenesis of hypersensitivity reactions, autoimmune diseases, AIDS, Amyloidosis.

- *Pathophysiology of Common Diseases:*

  Asthma, diabetes, rheumatoid arthritis, gout, ulcerative colitis, neoplasia, psychosis, depression, mania, epilepsy, acute and chronic renal failure, hypertension, angina, congestive heart failure, atherosclerosis, myocardial infarction, congestive heart failure, peptic ulcer, anemias, hepatic disorders, tuberculosis, urinary tract infections and sexually transmitted diseases. Wherever applicable the molecular basis should be discussed.

- *Fundamentals of General Pharmacology:* Refer Unit 2: Chapter 1

  Dosage forms and routes of administration, mechanism of action, combined effect of drugs, factors modifying drug action, tolerance and dependence; Pharmacogenetics; Principles of Basic and Clinical pharmacokinetics, absorption, Distribution, Metabolism and Excretion of drugs, Adverse Drug Reactions; Bioassay of Drugs and Biological Standardization; Discovery and development of new drugs, Bioavailability and bioequivalence studies;

- *Pharmacology of Peripheral Nervous System:* Refer Unit 2: Chapter 2

  Neurohumoral transmission (autonomic and somatic), Parasympathomimetics, Parasympatholytics, Sympathomimetics, Adrenergic receptor and neuron blocking agents, Ganglion stimulants and blocking agents, Neuromuscular blocking Agents, Local anesthetic Agents.

- *Pharmacology of Central Nervous System:* Refer Unit 2: Chapter 4

  Neurohumoral transmission in the C.N.S., General Anesthetics, Alcohols and disulfiram, Sedatives, Hypnotics, Anti-anxiety agents and Centrally acting muscle relaxants, Psychopharmacological agents (anti-psychotics), anti-maniacs, and hallucinogens, Antidepressants, Anti-epileptics drugs, Anti-Parkinsonian drugs, Analgesics, Antipyretics, Narcotic analgesics and antagonists, C.N.S. stimulants, Drug Addiction and Drug Abuse.

- *Pharmacology of Cardiovascular System:* Refer Unit 2: Chapter 7

  Drugs used in the management of congestive cardiac failure, Antihypertensive drugs, Anti-anginal and Vasodilator drugs, including calcium channel blockers and beta adrenergic antagonists, Anti- arrhythmic drugs, Anti-hyperlipedemic drugs, Drugs used in the therapy of shock.

- *Drugs Acting on the Hemopoietic System:*

  Hematinics, Anticoagulants, Vitamin K and hemostatic agents, Fibrinolytic and anti-platelet drugs, Blood and plasma volume expanders.

- *Drugs Acting on Urinary System:*

  Fluid and electrolyte balance, Diuretics. Refer Unit 2: Chapter 7

- *Autacoids:* Refer Unit 2: Chapter 6

  Histamine, Antihistaminic drugs, 5-HT- its agonists and antagonists, Prostaglandins, thromboxanes and leukotrienes, Angiotensin, Bradykinin and Substance P and other vasoactive peptides, non- steroidal anti-inflammatory and anti-gout agents.

- *Drugs Acting on the Respiratory System:* Refer Unit 2: Chapter 6

  Anti-asthmatic drugs including bronchodilators, Anti-tussives and expectorants, Respiratory stimulants.

- *Drugs Acting on the Gastrointestinal Tract:*

  Antacids, Anti-secretory and Anti-ulcer drugs, Laxatives and anti-diarrhoeal drugs, Appetite Stimulants and Suppressants, Emetics and anti-emetics, Miscellaneous: Carminatives, demulcents, protectives, adsorbents, astringents, digestants, enzymes and mucolytics.

- *Pharmacology of Endocrine System:* Refer Unit 2: Chapter 3

  Hypothalamic and pituitary hormones, Thyroid hormones and anti-thyroid drugs, parathormone, calcitonin and Vitamin D, Insulin, glucagons, incretins, oral hypoglycemic agents and insulin analogs, ACTH and corticosteroids, Androgens and anabolic steroids, Estrogens, progesterone and oral contraceptives, Drugs acting on the uterus.

- *Chemotherapy:* Refer Unit 2: Chapter 5

  General Principles of Chemotherapy, Bacterial resistance; Sulfonamides and cotrimoxazole, Antibiotics- Penicillins, Cephalosporins, Aminoglycosides, Chloramphenicol,Macrolides, Tetracyclines, Quinolones, fluoroquinolones and Miscellaneous antibiotics; Chemotherapy of tuberculosis, leprosy, fungal diseases, viral diseases, HIV and AIDS, urinary tract infections and sexually transmitted diseases, malaria, amoebiasis and other protozoal infections and Anthelmentics. Chemotherapy of malignancy and immunosuppressive agents.

- *Principles of Toxicology:*

  Definition of poison, general principles of treatment of poisoning with particular reference to barbiturates, opioids, organophosphorous and atropine poisoning, Heavy metals and heavy metal antagonists.

- *Basic Concepts of Pharmacotherapy:*

  Clinical Pharmacokinetics and individualization of Drug therapy, Drug delivery systems and their Biopharmaceutic s & Therapeutic considerations, Drugs used during infancy and in the elderly persons (Pediatrics & Geriatrics), Drugs used during pregnancy, Drug induced diseases, The basics of drug interactions, General principles of clinical toxicology, Common clinical laboratory tests and their interpretation.

- *Important Disorders of Organs, Systems and their Management:*

  Cardio-vascular disorders- Hypertension, Congestive heart failure, Angina, Acute myocardial infarction, Cardiac arrhythmias.

- *CNS Disorders:*

  Epilepsy, Parkinsonism, Schizophrenia, Depression.

- *Respiratory Disease-*

  Asthma.

- *Gastrointestinal Disorders-*

  Peptic ulcer, Ulcerative colitis, Hepatitis, Cirrhosis.

- *Endocrine Disorders-*

  Diabetes mellitus and Thyroid disorders.

- *Infectious Diseases-*

  Tuberculosis, Urinary tract infections, Enteric infections, Upper respiratory infections. Hematopoietic Disorders- Anemias,

- *Joint and Connective Tissue Disorders-*

  Rheumatic diseases, Gout and Hyperuricemia.

- *Neoplastic Diseases-*

  Acute Leukaemias, Hodgkin's disease. Therapeutic Drug Monitoring, Concept of Essential Drugs and Rational Drug use.

PHARMACOGNOSY

Refer Unit 4: Chapter 1

- *Sources of Drugs:*

  Biological, marine, mineral and plant tissue cultures as sources of drugs;
- *Classification of Drugs:*

  Morphological, taxonomical, chemical and pharmacological classification of drugs;
- *Study of Medicinally Important Plants Belonging to the Families with Special Reference to:*

  Apocynacae, Solanaceae, Rutaceae, Umbelliferae, Leguminosae, Rubiaceae, Liliaceae, Graminae, Labiatae, Cruciferae, Papaveraceae.
- *Cultivation, Collection, Processing and Storage of Crude Drugs:*

  Factors influencing cultivation of medicinal plants, Types of soils and fertilizers of common use. Pest management and natural pest control agents, Plant hormones and their applications, Polyploidy, mutation and hybridization with reference to medicinal plants.
- *Quality Control of Crude Drugs:*

  Adulteration of crude drugs and their detection by organoleptic, microscopic, physical, chemical and biological methods and properties.
- *Introduction to Active Constituents of Drugs:*

  Their isolation, classification and properties.

Systematic pharmacognostic study of the followings:

- *Carbohydrates and Derived Products:*

  Refer Unit 4: Chapter 5

  agar, guar gum acacia, Honey, Isabagol, pectin, Starch, sterculia and Tragacanth.
- *Lipids:*

  Bees wax, Castor oil, Cocoa butter, Codliver oil, Hydnocarpus oil, Kokum butter, Lard, Linseed oil, Rice Bran oil, Shark liver oil and Wool fat.
- *Resins:*

  Refer Unit 4: Chapter 5

  Study of Drugs Containing Resins and Resin Combinations like Colophony, podophyllum, jalap, cannabis, capsicum, myrrh, asafoetida, balsam of Tolu, balsam of Peru, benzoin, turmeric, ginger.
- *Tannins:*

  Refer Unit 4: Chapter 5

  Study of tannins and tannin containing drugs like Gambier, black catechu, gall and myrobalan.
- *Volatile Oils:*

  Refer Unit 4: Chapter 4

  General methods of obtaining volatile oils from plants, Study of volatile oils of Mentha, Coriander, Cinnamon, Cassia, Lemon peel, Orange peel, Lemon grass, Citronella, Caraway, Dill, Spearmint, Clove, Fennel, Nutmeg, Eucalyptus, Chenopodium, Cardamom, Valerian, Musk, Palmarosa, Gaultheria, Sandal wood;
- *Phytochemical Screening:*

  Preparation of extracts, Screening of alkaloids, saponins, cardenolides and bufadienolides, flavonoids and leucoanthocyanidins, tannins and polyphenols, anthraquinones, cynogenetic glycosides, amino acids in plant extracts.
- *Fibers:*

  Study of fibers used in pharmacy such as cotton, silk, wool, nylon, glass-wool, polyester and asbestos.

Study of the biological sources, cultivation, collection, commercial varieties, chemical constituents, substitutes, adulterants, uses, diagnostic macroscopic and microscopic features and specific chemical tests of following groups of drugs.

Glycoside containing drugs:

Refer Unit 4: Chapter 3

- *Saponins :*
  Liquorice, Ginseng, Dioscorea, Sarsaparilla, and Senega.
- *Cardioactive Glycosides:*
  Digitalis, squill, strophanthus and thevetia,
- *Anthraquinone Cathartics:*
  Aloe, senna, rhubarb and cascara,
- *Others:*
  Psoralea, gentian, saffron, chirata, quassia.

Alkaloid containing drugs:

Refer Unit 4: Chapter 2

- *Pyridine-Piperidine:*
  Tobacco, areca and lobelia.
- *Tropane:*
  Belladonna, hyoscyamus, datura, duboisia, coca and withania.
- *Quinoline and Isoquinoline:*
  Cinchona, ipecac, opium.
- *Indole:*
  Ergot, rauwolfia, catharanthus, nux-vomica and physostigma.
- *Imidazole:*
  Pilocarpus.
- *Steroidal:*
  Veratrum and kurchi.
- *Alkaloidal Amine:*
  Ephedra and colchicum.
- *Glycoalkaloid:*
  Solanum.
- *Purines:*
  Coffee, tea and cola. Biological sources, preparation, identification tests and uses of the following enzymes: Diastase, papain, pepsin, trypsin, pancreatin.

Studies of traditional drugs:

Refer Unit 4: Chapter 1

Common vernacular names, botanical sources, morphology, chemical nature of chief constituents, pharmacology, categories and common uses and marketed formulations of following indigenous drugs: Amla, Kantkari, Satavari, Tylophora, Bhilawa, Kalijiri, Bach, Rasna, Punamava, Chitrack, Apamarg, Gokhru, Shankhapushpi, Brahmi, Adusa, Atjuna, Ashoka, Methi, Lahsun, Palash, Guggal, Gymnema, Shilajit, Nagarmotha and Neem. The holistic concept of drug administration in traditional systems of medicine.Introduction to ayurvedic preparations like Arishtas, Asvas, Gutikas, Tailas, Chumas, Lehyas and Bhasmas.

General Techniques of Biosynthetic Studies and Basic Metabolic Pathways/ Biogenesis:

Brief introduction to biogenesis of secondary metabolites of pharmaceutical importance.

Refer Unit 4: Chapter 1

- *Terpenes:*

  monoterpenes, sesquiterpenes, diterpenes, and triterpenoids.
- *Carotenoids:*

  a-carotenoids, ß-carotenes, vitamin A, Xanthophylls of medicinal importance.
- *Glycosides:*

  Digitoxin, digoxin, hecogenin, sennosides, diosgenin and sarasapogenin.
- *Alkaloids:*

  Atropine and related compounds, Quinine, Reserpine, Morphine, Papaverine, Ephedrine, Ergot and Vinca alkaloids.
- *Lignans, Quassanoids and Flavonoids. Role of Plant-Based Drugs on National Economy:*

  A brief account of plant based industries and institutions involved in work on medicinal and aromatic plants in India. Utilization and production of phyto-constituents such as quinine, calcium sennosides, podophyllotoxin, diosgenin, solasodine, and tropane alkaloids. Utilization of aromatic plants and derived products with special reference to sandalwood oil, mentha oil, lemon grass oil, vetiver oil, geranium oil and eucalyptus oil. World-wide trade in medicinal plants and derived products with special reference to diosgenin (disocorea), taxol (Taxussps) digitalis, tropane alkaloid containing plants, Papain, cinchona, Ipecac, Liquorice, Ginseng, Aloe, Valerian, Rauwolfia and plants containing laxatives. Plant bitters and sweeteners.
- *Plant Tissue Culture:*

  Refer Unit 4: Chapter 1

  Historical development of plant tissue culture, types of cultures, nutritional requirements, growth and their maintenance. Applications of plant tissue culture in pharmacognosy.
- *Marine pharmacognosy:*

  Novel medicinal agents from marine sources.

Natural allergens and photosensitizing agents and fungal toxins. Herbs as health foods. Herbal cosmetics. Standardization and quality control of herbal drugs, WHO guidelines for the standardization of herbal drugs.

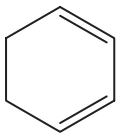
TIME MANAGEMENT STRATEGIES DURING GPAT EXAMINATION

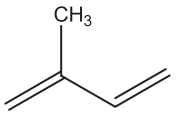
Time	Planned strategies to Crack GPAT
0 to 30 minute	• Preview the all 125 questions quickly • Mark the number of questions that you will answer easily in paper provided to you
31 to 60 Minute	Go to the marked questions you can readily answer and select proper answer
61 to 140 Minute	**Read each unattempted questions carefully** • **Identify key words -** Circle or underline key words, such as "all," "always," "never," "none," "not," "few," "many," some," and "sometimes." • **Identify subject area -** Identifying what lecture, reading, or laboratory exercise the question is from might help you narrow the choice of possible responses. • **Identify what is being asked** • **The "cover up" strategy -** Some students find it helpful to read the question and try to recall the answer from memory before looking at each of the possible responses • **If two responses appear to be equally correct -** You should eliminate the response that appears to be least related to the question being asked. Remember, you are looking for the best answer, not only a correct one. Some responses may be correct but are not directly related to the question
141 to 180 minute	• Review all answered questions carefully • Don't try to answer all questions because there is a negative marking of each wrong answer • You should know about the score of student who secured 1st rank in last year GPAT examination • e.g. In GPAT 2017 examination the student secured 1st rank has 261 Marks out of 500 (means he/ she was attempted around 53 Questions correctly) • You should also know about the Cutoff marks for qualified students. E.g. Last year cutoff marks was 115 out of 500

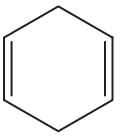
QUESTIONS FROM GPAT 2017 (MEMORY BASED)

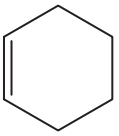
1. In a free radical reaction, free radicals are formed at:-
(a) Initiation step
(b) Propagation step
(c) Termination step
(d) Both (a) and (b)

2. Which of the following dienes can undergo Diels-Alder reaction most readily?

(a) 

(b) 

(c) 

(d) 

3. Separating techniques such as gas chromatography and liquid chromatography are not appropriate for separation of amino acids. Select correct reason from the following:-
(a) Amino acids high polarity substances
(b) Amino acids are low polarity substances
(c) Amino acids are non-polar substances
(d) Amino acids lowly charges substances

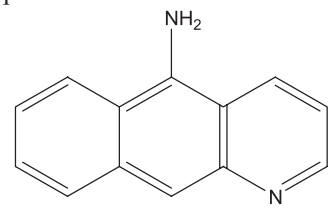
4. When trans-2-butene is treated with bromine an anti-addition of bromine yields meso- 2, 3-dibromobutane. Select the correct statement regarding the reaction from the following:-
(a) The reaction is stereo-selective as well as stereo-specific
(b) The reaction is stereoselective and not stereospecific
(c) The reaction is non stereos elective as well as non-stereospecific
(d) The reaction is stereospecific and not stereo-selective

5. In the reaction of 2-nitrotoluene with bromine in presence of iron, which of the product shown below is the most abundant (major) product?
(a) The product will not have a stereo center
(b) The product will have R configuration
(c) The product will not have S configuration
(d) The reaction will happen with racemization

6. Which of the following cannot react as a nucleophile?
(a) $(CH_3)_4N+$ (b) CH_3NH_2
(c) $(CH_3)_2NH$ (d) $(CH_3)_3N$

7. Which of the following compounds will be oxidized by CrO3 in acid?
(a) 4,4-Dimethyl-1- methyl-1,3- cyclohexandiol
(b) 3-Methyl 3-hydroxyclohexanone
(c) 4-Methylcyclohexene
(d) 2-Methylcyclohexanone

8. Choose the correct name for the following heterocyclic Compound:-

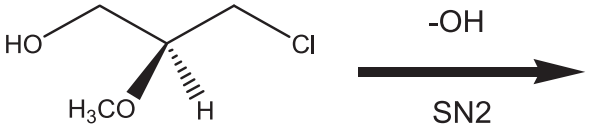


(a) Benzo[g]quinolin-5-ylamine
(b) 1-Aminonaphtho[b]pyridine
(c) 1-Aminonaphtho[e]pyridine
(d) Benzo[h]quinolin-5-ylamine

9. Which of the following reagents will reduce a disubstituted alkyne to trans-alkene?

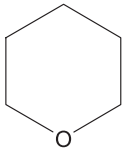
(a) Na and NH_3 (b) $LiAlH_4$
(c) B_2H_6 (d) Pd and H_2

10. Which of the following statement is true about following reaction?



(a) The product will not have a stereo center
(b) The product will have R configuration
(c) The product will not have S configuration
(d) The reaction will happen with racemization

11. Which functional group is present in the molecule shown below?



(a) Ether (b) Alcohol
(c) Ester (d) Amide

12. Match the following agents that cause cancer with the preferable sites for where it might cause:-

1. Arsenic	(a) Prostate
2. Benzene	(b) Angiosarcoma
3. Cadmium Compounds	(c) Leukemia
4. Vinyl chloride	(d) Hemangiosarcoma

(a) 1 - d; 2 - c; 3 - a; 4 -b
(b) 1 - b; 2 - a; 3 - c; 4- d
(c) 1 - c; 2 - d; 3 - b;4 - a
(d) 1 - a; 2 - b; 3 -d; 4 - c

13. If the pKa of lidocaine is 7.9 and pH of the infected tissue is 8.9, the fraction of drug in the ionized form will be _____.

(a) 90% (b) 1%
(c) 10% (d) 99%

14. Which among the following are the salient features of Glucocorticoids?

(a) Gets combined with highly specific cytosolic Glucocorticoids
(b) They promote phagocytosis by macrophages
(c) Releases of lytic enzymes
(d) Increases lipid eicosanoids and prostaglandin gene

15. The most commonly used test of sensitivity to antimicrobial agent is:-

(a) Kirby- Bauer techniques
(b) Immunodiffusion techniques
(c) Qudin procedure
(d) Ouchter- Ion procedure

16. Bulk product is defined as:-

(a) Product completing all processing stages but not necessarily final packing
(b) A product ready for final dispatch
(c) Raw material used for making final dosage form
(d) A defined quantity of raw material from the same batch

17. Product, _____, _____, and Promotion are four 'P's of marketing.

(a) Price and Place
(b) Place and Process
(c) Production and Process
(d) Price and Production

18. Insulin and thyroxin arrive at an organ / tissue / cell at the same time. Thyroxine causes an effect on the organ but insulin does not because

(a) The organ cell have receptors for thyroxine but not for insulin
(b) Thyroxin is a lipid -soluble hormone and insulin
(c) The target cell in the organ have up-regulated for receptors
(d) Thyroxin is local hormone and insulin is a circulating hormone

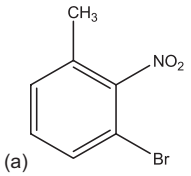
19. Which among the following is an incorrect statement with regard to the drug Dantrolene?

(a) It is a pyrazoline derivative
(b) It is an imidazoline analogue
(c) It is a nitrophenyl furfurylidene derivative
(d) It is a skeletal muscle relaxant

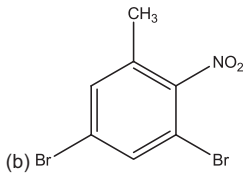
20. Diazepam is not suitable for peroral sustained release form since:-

(a) It is not absorbed in lower intestine
(b) It has biological half life less than one hour
(c) It has undesirable side effects
(d) It has biological half-life greater than twelve hours

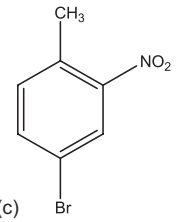
21. In the reaction of 2-nitrotoluene with bromine in presence of iron, which of the product shown below is the most abundant (major) product?



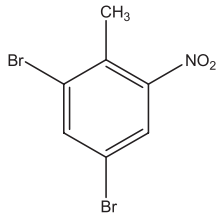
(a)



(b)



(c)



(d)

22. Antioxidant used as blocking agent in sterile product is:-
(a) Ascorbic acid esters
(b) Sodium bisulphate
(c) Ascorbic acid
(d) EDTA

23. Many mediators have been implicated in the asthmatic response. The clinical efficacy of pharmacologic intervention with inhibitors or antagonist of the mediators involves following category: except:-
(a) Platelet activating factors
(b) Anticholinergics
(c) Antihistaminics
(d) Cytokine inhibitors

24. Match the following adrenergic drugs with their receptor affinity:-

1. Epinephrine	(a) More alphla l, no beta 1, beta 2 & dopamine
2. Noradrenaline	(b) More alphla l & beta 1, less beta 2, no dopamine
3. Phenylephrine	(c) More beta l & beta 2, no alpha 1 and dopamine
4. Dobutamine	(d) More alphla l & beta 1, no beta 2 & dopamine

(a) 1 - b; 2 - d; 3 - a; 4 - c
(b) 1 - a; 2 - c; 3 - d; 4- b
(c) 1 - c; 2 - a; 3 - b; 4 - d
(d) 1 - d; 2 - b; 3 -c; 4 - a

25. If the drug substance has been substituted wholly or in part by another drug or substance, it is called as _____.
(a) Spurious drug (b) Adulterated drug
(c) Misbranded drug (d) Mixed drug

26. One of the principle upon which HPLC detector functions is:-
(a) Redox property of solute is the basis for functioning of Electrochemical detectors
(b) Fluorimetric detector has high selectivity and low sensitivity
(c) Small difference in Refractive Index of mobile phase permit precise measurements in Refractive index detectors
(d) UV detector function based on its ability to detector

27. Methanolic extract of a crude drug powder when treated with magensium turnings and concentrated hydrochloric acid turned the solution magenta coloured. The test is termed as:-
(a) Shinoda test (b) Van Urk's Test
(c) Keller Killiani test (d) Vitali Morin Test

28. Etoposide and Teniposide are the semisynthetic derivatives of:-
(a) Podophyllotoxin (b) Myrrhabolic acid
(c) Abietic acid (d) Umbelliferone

29. The thymus secretes several hormones related to the immunity. These hormones promote the maturation of T lymphocyte cells. These hormones are:-
1. Thymosin
2. Thymic humoral factor
3. Thymic factor
4. Interleukins
(a) 1, 2 and 3 (b) Only 1, 2
(c) Only 3 (d) Only 4

30. For the measurement of particle size of powders, the distance measured between two tangents on opposite sides of the particle parallel to some fixed direction is called:-
(a) Feret diameter
(b) Martin diameter
(c) Projected area diameter
(d) Edmundson diameter

31. Beta oxidation of fatty acids takes place in:-
(a) Mitochondria (b) Cytoplasm
(c) Nucleus (d) Choroplast

32. Which of the following genera is not the source for tropane alkaloids?
(a) Nicotiana (b) Duboisia
(c) Datura (d) Atropa

33. In humans end product of purine catabolism is:-
(a) Uric acid (b) Urea
(c) Purine oxide (d) Xanthine

34. In respect of female reproductive cycle, which of the following statements are correct:-
1. The female reproductive cycle consists of menstrual phase, a pre-ovulatory phase, Ovulation and a post ovulatory phase.
2. During the menstrual phase, small secondary follicles in the ovary begin to enlarge while the uterus is shedding its lining.
3. During the pre-ovulatory phase, a dominant follicle continues to grow and begins to secret estrogen and inhibin while the uterine lining begins to rebuild.
4. Ovulation results in the release of an ovum and the shedding of the uterus lining to nourish and support the release ovum.
5. After ovulation, a corpus luteum forms the ruptured follicles and begins to secrete progesterone and estrogen, which it will continue to do throughout pregnancy if the egg is fertilized.
6. If pregnancy does not occur, then the corpus luteum degenerates into a scar known as corpus albicans and uterine lining is prepared to be shed again.

(a) 1, 2, 3 and 6 (b) 2, 3, 4 and 6
(c) 1, 2, 4 and 5 (d) 1, 4, 5 and 6

35. Apparent volume of distribution will be highest in case of the drug with % plasma protein binding:-
(a) 89 (b) 10
(c) 50 (d) 68

36. To rule out the probability of dose dumping from an oral CR dosage form, USP has included which sampling time point for in vitro dissolution test where D is normal dosing interval
(a) 0.25D (b) 0.50D
(c) 0.5 - 1.0D (d) 1.0 - 2.0D

37. Which of the following statement regarding cerebral hemisphere is true?
(a) The right and left hemisphere are symmetrical.
(b) This right more important for spoken and written language.
(c) The left hemisphere is more important for musical and artistic awareness.
(d) Hemispheric lateralization is more pronounced in male than in female.

38. Which among the following is a Class-I method, used for rendering a solution of drug isotonic with body fluids?
(a) Cryoscopic method
(b) White-Vincent method
(c) Sprowls method
(d) Hammarlund method

39. (Weight in pounds/150)*Adult Dose = Child dose
The above formula is known as _____ in Posology.
(a) Clarkes formula (b) Dillings formula
(c) Youngs formula (d) Frieds formula

40. Type of particle diameter obtained by microscopic method of evaluation is:-
(a) Projected diameter
(b) Surface -volume diameter
(c) Volume - surface diameter
(d) Stokes diameter

41. Naphazoline:-
(a) Is used for relief of nasal congestion
(b) Exhibits peripheral beta-adrenoceptor stimulant
(c) Is a pyrazoline derivative
(d) Chemically, is 1H - Imidazole, 3, 4 - dihydro- 2 - (3-naphthylmethyl) monohydrochloride

42. A patient receiving warfarin develops rheumatoid arthritis. Which one of the following drugs would be contraindicated?
(a) Asprin (b) Tolmetin
(c) Aurothioglucose (d) Ibuprofen

43. A crude drug powder was heated with ferric chloride, water and concentrated hydrochloric acid followed by extraction with chloroform. The chloroform layer was treated with ammonia, the ammonical layer turned pink. The test indicates presence of _____ phyto constitutent.
(a) Anthraquinone-C- glycosides
(b) Flavanones
(c) Cardiac glycosides
(d) Saponin glycosides

44. The first vaccine was discovered by:-
(a) Edward Jenner (b) Paul Ehrlich
(c) Robert Koch (d) DeBary

45. Type IV dissolution apparatus as per USP is:-
(a) Flow through cell,
(b) Paddle type apparatus
(c) Reciprocating cylinder
(d) Paddle over disk apparatus

46. Hoeppler viscometer is a type of:-
(a) Falling sphere viscometer
(b) Capillary viscometer
(c) Cup and Bob viscometer
(d) Cone and plate viscometer

47. Following are the list of various inherited metabolic disorders that can affect functioning of liver:-
1. Primary biliarycirrhosis
2. Glycogen storage disease
3. Gilbert's syndrome
4. Haemochromatosis
5. Wilson's disease

(a) 2, 2, 4, 5 (b) 1, 2, 3, 4
(c) 1, 3, 4, 5 (d) 1, 2, 4, 5

48. In relation to buccal and sublingual route of administration which of the following statement is incorrect?
(a) Absorption through epithelium is not affected by partition coefficient of the drug
(b) Drug absorption by these routes by pass first pass metabolism
(c) There is an optimum log P for sublingual absorption
(d) These are preferred routes for anti-anginal drug

49. Which among the following statements describing surface activity for surfactants is incorrect?
(a) Increase in length of hydrocarbon chain decreases surface activity.
(b) Increase in ethylene oxide chain of polyoxy ethyl-alcohol Increase in surface activity
(c) Increase in surface activity results in decrease length of hydrocarbon chain
(d) Relationship between hydrocarbon chain length and hydrphobicity

50. Surface tension is categorized as a/an _____ factor.
(a) Intensive (b) Capacity
(c) Extensive (d) Tolerance

51. Which of the following gums is obtained from endosperm?
(a) Guar gum (b) Acacia gum
(c) Tragacanth gum (d) Sterculia gum

52. High lightening differences among brands within the same product category is _____.
(a) Product differentiation
(b) Brand launch
(c) Product brand
(d) Branding

53. Hot stage microscopy is an important tool in pre formulation studies for the study of:-
(a) Pseudopolymorphism
(b) Paricle size measurement
(c) Microbial contamination
(d) Compaction behavior

54. In Bismuth subgallate suppositories B.P.C, when no strength of the drug is specified, B.P.C directs bismuth subgallate per suppository.
(a) 100 mg (b) 200 mg
(c) 300 mg (d) 400 mg

55. A reporting relationship in which an employee receives orders from, and reports to, only one supervisor is known as _____.
(a) Unity of command
(b) Centralisation
(c) Decentralisation
(d) Line of authority

56. The largest gene in human is _____.
(a) Dystrophin (b) Titin
(c) Insulin (d) Phosphofructokinase

57. Which of the following techniques is not useful to detect polymorphs?
(a) HPLC
(b) DSC
(c) PXRD
(d) Melting point determination

58. Which of the following constituents is responsible for colour of shellac?
(a) Laccaic acid (b) Shelloic acid
(c) Aleurotic acid (d) All of the above

59. Match the following drugs with alteration they produces in structural-functional of kidney:-

1. Aminoglycoside antibiotics	(a) Glomerular abnormality
2. ACE inhibitors	(b) Tubular epithelial cell damage
3. Methotrexate	(c) Hemodynamic mediated kidney injury
4. NSAIDs	(d) Obstructive nephropathy

(a) 1 - b; 2 - c; 3 - d; 4 - a
(b) 1 - a; 2 - b; 3 - c; 4 - d
(c) 1 - c; 2 - d; 3 - a; 4 - b
(d) 1 - d; 2 - a; 3 - b; 4 - c

60. Hixon Crowell's cube root law of dissolution states that:-
(a) There is a change in particle size and surface area during dissolution of drug
(b) Dissolution process is controlled by diffusion of molecules/ions
(c) High free energy of activation is required for solution
(d) Renewal of surface fluid layer around drug particle

61. All of the following statements regarding estrogen therapy in postmenopausal women are true EXCEPT:-
(a) It restores the loss of bone mass due to osteoporosis
(b) It may be useful to treat vasomotor symptoms
(c) Administration in a regimen including a progestin
(d) It is useful in the treatment of atrophic vaginities

62. Chapter IV of which law states that experiments on animals are avoided wherever it is possible to do so; as for example; in medical schools, hospitals, colleges and the like, if other teaching devices such as books, models, films and the. like, may equally suffice. Also, that experiments on larger animals are avoided when it is possible to achieve the same results by experiments upon small laboratory animals like guinea- 'pigs, rabbits, frogs and rats.
(a) The prevention of cruelty to animal act, 1960
(b) The Pharmacy Act, 1948
(c) Drugs and Cosmetics Act, 1940
(d) Medicinal and Toilet Preparations Act, 1955

63. Which among the following rules about spin - spin coupling and bond multiplicities are correct with regard to NMR spectra?
(a) Coupling constant rarely exceeds 20 cps while chemical shifts are over 1000 cps
(b) Spin - Spin interactions are dependent of strength of the applied field
(c) Coupling constants increase with distance
(d) Equivalent nuclei interact with each other to show interaction

64. Most accepted mechanism for developing bacterial resistance to sulphonamides is:-
(a) An alternative metabolic pathway for synthesis of essential metabolite
(b) An increasing capacity to metabolize the drug
(c) Increased antagonism of drug
(d) An alteration in enzyme that utilizes PABA

65. All the dopaminergic agonists having affinity for D2 receptors are clinically used in following conditions except _____.
(a) Obsessive-compulsive disorder
(b) Hyperprolactinemia
(c) Acromegaly
(d) Parkinsonism

66. The labelling instruction "To be diluted 20 times its volume with water" indicates the dispensed product is a:-
(a) Mouthwash (b) Elixir
(c) Linctus (d) Mixture

67. Which among the following is a structural variant of GABA and is used as a muscle relaxant?
(a) Baclofen
(b) Tybamate
(c) Metocurine
(d) Cyclobenzaprine

68. A steroidal phyto constituent lowering blood sugar is obtained from:-
(a) Momordica charantia
(b) Quillaja saponaria
(c) Dioscorea deltoidea
(d) Glycyrrhiza glabra

69. Which of the following drug is associated with the reaction of extreme photosensitivity?
(a) Tetracycline
(b) Fluoroquinolones
(c) Niacin
(d) (a) and (b)

70. Which among the following statements related to Ceric sulphate as oxidizing agent, as titrant are correct?
(a) Ce (IV) during reaction exists as an anionic complex in media of sulphuric acid
(b) Ionic equation is $Ce^{3+} \longrightarrow Ce^{2+} + e^-$
(c) Formal potential of Ce (III) Ce (II) couple is 1
(d) Ce (IV) does not permit use of HCl as reducing media

71. Which of the following conditions is treated with benztropine?
(a) Parkinsonian disorders
(b) Manic depressive disorders
(c) Huntington's disease
(d) Tardive dyskinesia

72. A labeled piece of DNA that is complementary to the sequence of DNA you are interested in, say the gene you are trying to put into cells, is called as _____.
(a) A probe
(b) A receptor
(c) A epitope
(d) A target

73. As per first schedule of Drugs and Cosmetics Act, 1940, following is name of the book under Siddha system of medicine:-
(a) Arka Prakasha
(b) Yog Ratnakar
(c) Nagamuni
(d) Vrinda Chikitsa

74. Amantadine is helpful in Parkinson's disease because:-
(a) It liberates dopamine from nerve endings
(b) It decreases cholinergic Activity
(c) It is metabolized into Dopamine
(d) It increases adrenergic activity

75. An intermediate 3- Chloroaniline 4, 6 - disulphonamide on heating with formic acid yields a compound:-
(a) 6 chloro 2H -1, 2, 4 benzothiadiazine 7 sulphonamide
(b) 3 chloro-2H-1, 2, 4-benzothiadiazine 7 sulphonamide
(c) Used in treatment of urinary tract infections
(d) Used as antibacterial

76. Rubella virus is associated with disease:-
(a) Progressive encephalitis
(b) Enterovirus infection
(c) Yellow fever
(d) Brucellosis

77. Which among the following electronic systems are not involved in the origin of UV Spectrum?
(a) s and p shell electrons
(b) sigma and pi electrons
(c) Charge transfer electrons
(d) d and f shell electrons

78. Which of the following is not a thermoplastic resin?
(a) Phenolic plastic resin
(b) Polystyrene
(c) Polyethylene
(d) Polypropylene

79. Choose the right combination from the following:-

Types of Stomata and Trichome	Crude Drugs
1. Diacytic stomata and sessile glandular trichome	(a) Datuar
2. Paracytic stomata and unicellular warty covering trichome	(b) Vasaka
3. Anomocytic stomata and unicellular and multi cellular trichome	(c) Senna
4. Anisocytic stomata and multicellular covering trichome	(d) Digitalis

(a) 1 - b, 2 - c, 3 - d, 4 - a
(b) 1 - c, 2 - d, 3 - a, 4 - b
(c) 1 - a, 2 - d, 3 - b, 4 - c
(d) 1 - d, 2 - b, 3 - a, 4 - c

80. Pharmaceutical alternatives possess:-
(a) Indentical therapeutic moiety/precursor but not in the same amount/dosage form
(b) Same amount of therapeutic moiety
(c) Same dosage form
(d) Same formulation ingredients in exactly same amount of dose

81. Topical application of timolol to the eye would be expected to induce which of the following?
(a) Decreased formation of aqueous humor
(b) Miosis
(c) Mydriasis
(d) Increased outflow of aqueous humor

82. The major component of liquid glucose is _____ and is prepared from _____.
(a) Dextrose, Starch (b) Dextrin, Starch
(c) Maltose, Pectin (d) Glucose, Starch

83. Which of the following formulations under ASU system are offered infinite period of shelf life in D and C Act?
(a) Asava & Arishta
(b) Churna
(c) Ghutika
(d) Kwatha

84. Which of the following is an example of hemiesters anionic surfactant for pharmaceutrical emulsions?
(a) Sulfosuccinates (b) Sarcosinates
(c) Taurates (d) Lactylates

85. The major differences between the prokaryotic and eukaryotic protein synthesis mechanisms are in which part of the process?
(a) The initiation of synthesis
(b) The chain elongation process
(c) The chain termination Process
(d) None of the above

86. In DNA replication the newly added nucleotide is joined to the growing DNA strand by an enzyme.
(a) DNA polymerase
(b) DNA ligase
(c) Restriction endonuclease
(d) Reverse transcriptase

87. Which of the following adverse effects is caused by thioridazine?
(a) Constipation
(b) Orthostatic hypotension
(c) Tardive dyskinesia
(d) All of the above

88. Which of the following dosage form of digoxin will provide greater bioavailability based on value of F?
(a) F equals 1.0 (b) F equals 0.32
(c) F equals 0.62 (d) F equals 0.77

89. The process by which the formed elements of blood develop is call as hemopoiesis. In the process of hemopoiesis the stem cells are converted in to myeloid stem cell and subsequently differentiated and are developed into precursor cells.

Match the following precursor cells with the formed elements of blood from which they are formed:-

1. Reticulocyte	(a) Platelets
2. Megakaryoblast	(b) Macrophages
3. Myeloblast	(c) Erythrocytes
4. Monoblast	(d) Neutrophils

(a) 1 - c; 2 - a; 3 - d; 4 - b
(b) 1 - a; 2 - c; 3 - b; 4 - d
(c) 1 - b; 2 - d; 3 - c; 4 - a
(d) 1 - d; 2 - b; 3 - a; 4 - c

90. Using Young's rule, calculate the dose for a 5 year old child if the adult dose is 340 mg.
(a) 100 mg (b) 200 mg
(c) 400 Mg (d) 800 mg

91. Which among the following statements on electro analytical methods are correct?
(a) Measures conductance between two electrodes with AC powered Wheatstone bridge
(b) Polarography involves plotting of conductance - voltage
(c) Potentiometry involves application of Ilkovic equation
(d) Coulometry involving application of Nernst law relating equivalence between quantity of electricity passed and amount of compound generated at electrodes

92. Chemical interferences are common than spectral interferences due to:-
(a) Formation of compounds of low volatility
(b) Ionization in flames
(c) Increase in rate of atomization
(d) No shift in ionization equilibrium

93. Phase 0 studies means:-
(a) First in human micro dosing studies
(b) Part of phase I studies of clinical trials
(c) in vitro studies
(d) Studies carried out on small number of animals

94. Condensation product of Ethyl isopentyl ester of diethyl malonic acid with urea and sodium ethoxide yields:-
(a) Amylobarbitone (b) Phenobarbitone
(c) Pentobarbitone (d) Quinobarbitone

95. Clavulanic acid is:-
(a) Inactivates bacterial ß–lactamase
(b) Potent inhibitor of peptidoglycan synthesis
(c) Specific for gram negative bacteria
(d) Inhibitor of 50S ribosomal subunit

96. The method by which different constituents of a liquid mixture can be separated without decomposition of the constituents is:-
(a) Molecular distillation
(b) Distillation under reduced pressure
(c) Steam distillation
(d) Fractional distillaton

97. The preferred rheological behavior of Pharmaceutical suspensions is that of:-
(a) Pseudoplasticity and thixotrophy
(b) Pseudoplasticity
(c) Dilatancy and thixotrophy
(d) Pseudoplasticity and rheopexy

98. An inventory turnover of _____ a year is considered satisfactory.
(a) Four to six times (b) Six to eight times
(c) One to two times (d) None of the above

99. The number of glucopyranose units in the structure of alpha cyclodextrins are:-
(a) 6
(b) 8
(c) 9
(d) 7

100. The compound 2 - (Diethylamino) ethyl [bicyclohexyl] - 1-carboxylate hydrochloride is:-
(a) Dicycloverine
(b) Diphenhydramine
(c) Both nicotinic and specific antispasmodic
(d) Diagonistic agent for diagnosis of thyroid gland

101. In new product development process, after analysis of business next step to be taken is _____.
(a) Test marketing
(b) Penetration marketing
(c) Brand marketing
(d) Individual marketing

102. Which of the following alkaloid (form) is used to treat migrane?
(a) Ergot (b) Coca
(c) Vinca (d) Belladonna

103. Free flowing powders show a flatter cone and have _____.
(a) Smaller angle of repose
(b) Larger angle of repose
(c) Intermediate angle of repose
(d) None of the above

104. The WIPO is the specialized agency of the United Nations. It promotes protection of _____ throughout the world.
(a) Intellectual properties
(b) World properties
(c) Pharmaceutical organizations
(d) Finace companies

105. Herpesviruses are large encapsulated viruses that have double stranded DNA genome that encodes approximately 70 proteins. It causes acute infection followed by latent infection in which virus persist in noninfectious form with periodic reactivation and shedding of infectious virus. Following are the examples of such herpesvirus – except:-
(a) Epstein-Barr Virus
(b) Herpes simplex
(c) Varicella Zoster
(d) Cytomegalovirus

106. A fatty acid not synthesized in human body and has to be supplied in diet is:-
(a) linolenic acid
(b) Oleic acid
(c) Palmitic acid
(d) Stearic acid

107. Chemical class of drugs that are susceptible to oxidation are:-
(a) Sterols (b) Lactam
(c) Esters (d) Carbamates

108. The only analgesic acting centrally is _____.
(a) Tramadol
(b) Methadone
(c) Naloxane Congeners
(d) (a) and (b)

109. Neuropathy is adverse effect of:-
(a) Isoniazid (b) Ethambutol
(c) Pyrazinamide (d) Dapsone

110. As per I.P. if the solubility range of a solute is 30 to 100 parts, it will be:-
(a) Soluble
(b) Freely soluble
(c) Sparingly soluble
(d) Slightly soluble

111. SDS is used in PAGE of a mixture of proteins for their efficient separation on the gel. SDS, in the experiment is used to _____.
(a) Have uniform charge density on the proteins
(b) Stabilize the proteins
(c) Decrease the surface tension of buffer
(d) Solubilize the proteins

112. Indicate which of the following statements is true:-
(a) A weakly acidic drug is unionised when pH of the solution is at least 2 pH units below its pKa
(b) Acidic drugs are noninonized at pH 9
(c) Acidic drugs are less soluble in alkaline solution
(d) The higher the pKa of a weak acid, The stronger is acid

113. Dissemination of cancer occurs through one of the following pathway - except:-
(a) Migration
(b) Direct seeding
(c) Lymphatic spread
(d) Hematogenous spread

114. Which of the following alkaloids has hypotensive activity?

(a) Reserpine (b) Quinine
(c) Emetine (d) Papaverine

115. Which of the following is a characteristic of cytochrome P-450?

(a) Catalyzes aromatic and aliphatic hydroxylations
(b) Located in the lipophilic environment of mitochondrial membrane
(c) Catalyzes O-, S-, N-methylation reactions
(d) Catalyzes conjugation reactions

116. Which of the following statements about Michaelis-Menten kinetics is correct?

(a) Km the Michaelis constant, is a measure of the affinity the enzymehas for its substrate.
(b) Km the Michaelis constant, is defined as the concentration of substrate required for the reaction to reach maximum velocity.
(c) Km, the Michaelis constant, is defined as the dissociation of the substrate from the enzyme
(d) None of above

117. Which among the following describe the characteristic features of Tetracyline?

(a) Undergoes epimerization in solutions having intermediate pH range
(b) Forms Anhydroustetracycline in presence of acidic
(c) Forms Minocycline in basic medium
(d) Forms stable chelate complexes with potassium ions

118. Cells that contribute for immune system are:-

1. T Lymphocytes
2. Eosinophil
3. B Lymphocytes
4. Dendritic cells
5. Erythrocytes
6. Natural killer cells

(a) 1, 3, 4, 6 (b) 1, 2, 4, 6
(c) 1, 3, 5 ,6 (d) 1, 2, 5 , 6

119. Dielectric constant of Ethanol at room temperature is almost equal to:-

(a) 24 (b) 48
(c) 54 (d) 72

120. Foaming during liquid filling can be reduced by following ways, except:-

(a) Increase in speed of the filling line
(b) Minimised product turbulence
(c) Closed system filling
(d) Defoaming device

121. If the excitation energy of the resonance level is 2.10 eV (when hc = 12,330) then the wavelength of resonance line of sodium atoms is _____.

(a) 587.2 nm (b) 577.2 nm
(c) 567.2 nm (d) 597.2 nm

122. After vascular injury, platelets encounter extracellular matrix constituents such as collagen and adhesive glycoprotein. On contact with these proteins platelets undergo:-

1. Adhesion
2. Secretion
3. Aggregation
4. Degradation

(a) 1, 2 and 3
(b) 1, 2 and 4
(c) 1, 2, 3 and 4
(d) 1 and 2

123. The useful variable from in vitro dissolution test data for IVIVC includes:-

(a) Sampling interval
(b) Sample volume
(c) Volume of dissolution fluid
(d) None of above

124. What is the specific rotation of a compound 'X' when the concentration is 0.5% w/v, angle of rotation is 1.3 and tube-length is 25 cm?

(a) 0.104^0 (b) 1.04^0
(c) 10.4^0 (d) 104^0

125. The Michaelis-Menten equation for saturated active transport system is:-

(a) $V_{max} = k_{cat}[E_0]$
(b) $V_{max} = k_m$
(c) $V_{max} = k_m[S]$
(d) None of above

ANSWER KEYS

1. (d)	**2.** (a)	**3.** (a)	**4.** (a)	**5.** (a)	**6.** (a)	**7.** (a)	**8.** (a)	**9.** (a)	**10.** (a)
11. (a)	**12.** (a)	**13.** (a)	**14.** (a)	**15.** (a)	**16.** (a)	**17.** (a)	**18.** (a)	**19.** (a)	**20.** (d)
21. (c)	**22.** (a)	**23.** (a)	**24.** (a)	**25.** (a)	**26.** (a)	**27.** (a)	**28.** (a)	**29.** (a)	**30.** (a)
31. (a)	**32.** (a)	**33.** (a)	**34.** (a)	**35.** (a)	**36.** (a)	**37.** (d)	**38.** (a)	**39.** (a)	**40.** (a)
41. (a)	**42.** (a)	**43.** (a)	**44.** (a)	**45.** (a)	**46.** (a)	**47.** (a)	**48.** (a)	**49.** (a)	**50.** (a)
51. (a)	**52.** (a)	**53.** (a)	**54.** (a)	**55.** (b)	**56.** (a)	**57.** (a)	**58.** (a)	**59.** (a)	**60.** (a)
31. (c)	**32.** (c)	**33.** (d)	**34.** (d)	**35.** (a)	**36.** (a)	**37.** (c)	**38.** (d)	**39.** (a)	**40.** (c)
41. (c)	**42.** (a)	**43.** (a)	**44.** (a)	**45.** (a)	**46.** (a)	**47.** (a)	**48.** (a)	**49.** (a)	**50.** (a)
51. (a)	**52.** (a)	**53.** (a)	**54.** (c)	**55.** (a)	**56.** (a)	**57.** (a)	**58.** (a)	**59.** (a)	**60.** (a)
61. (a)	**62.** (a)	**63.** (a)	**64.** (a)	**65.** (a)	**66.** (a)	**67.** (a)	**68.** (a)	**69.** (d)	**70.** (a)
71. (a)	**72.** (a)	**73.** (c)	**74.** (a)	**75.** (a)	**76.** (a)	**77.** (a)	**78.** (a)	**79.** (a)	**80.** (a)
81. (a)	**82.** (a)	**83.** (a)	**84.** (a)	**85.** (a)	**86.** (a)	**87.** (d)	**88.** (a)	**89.** (a)	**90.** (a)
91. (a)	**92.** (a)	**93.** (a)	**94.** (a)	**95.** (a)	**96.** (a)	**97.** (a)	**98.** (a)	**99.** (a)	**100.** (a)
101. (a)	**102.** (a)	**103.** (a)	**104.** (a)	**105.** (a)	**106.** (a)	**107.** (a)	**108.** (d)	**109.** (a)	**110.** (c)
111. (a)	**112.** (a)	**113.** (a)	**114.** (a)	**115.** (a)	**116.** (a)	**117.** (a)	**118.** (a)	**119.** (a)	**120.** (a)
121. (a)	**122.** (a)	**123.** (d)	**124.** (c)	**125.** (a)					

UNIT 1

PHARMACEUTICS

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CHAPTER 1

PHYSICAL PHARMACEUTICS

MICROMERITICS AND POWDER RHEOLOGY

Micromeritics is the science and technology which deals with small particles. There are two types of properties for a particle to characterize.

Fundamental Properties

Surface area, particle size and distribution, particle number, particle volume, particle shape.

Derived Properties

Porosity, density, bulkiness, flow ability (Flow property).

Particle Size and Particle Size Distribution

- Particle size is quoted as the diameter of the sphere that has same weight (Weight based diameter) or same volume (Volume based diameter) or same surface (area based diameter) or same drag coefficient /sedimentation velocity (Hydrodynamic or Aerodynamic based diameter), to the given particle.

Types of powders according to particle size

Monodisperse powder All particles are of same size.

Polydispersed powder Particles of different size.

Generally, powder sample contains number of irregular shaped three dimensional particles so we generally consider average particle size.

Average particle size Average size of the particles which are distributed in the system.

$$d_{mean} = (\sum nd^{p+f}/\sum nd^{f})^{1/p}$$

p = 1 – particle length, p = 2 – surface

p = 3 – expression of volume,

p = +ve –arithmetic mean

p = –ve – harmonic mean,

p = zero – geometric mean

Methods for Particle Size Determination

Method	Size range	Instrument	Comment
Microscopy	0.2 to 100 micron	Optical microscope	Ferret, Martin and projected diameter measured
Sieving	50 to 1500 micron	Mechanical shaker	
Sedimentation	1 to 200 micron	Anderson Pipette (Gravity sedimentation based)	Stoke diameter measured
Conductivity	0.5 to 500 micron	Coulter-Current or Royco/HIAC	Equivalent volume diameter measured

1. Microscopy

Range of analysis

- By transmission electron microscope 0.001–0.1 micron.
- By scanning electron microscope 0.01–1000 micron.
- By light microscope 1–1000 micron.

Advantages

- Easy and convenient
- A size-frequency distribution curve can be plotted by counting the number of particles in a size range.
- Can detect the presence of agglomerates and particles of more than one component.

Disadvantages

- Diameter is obtained from only two dimensions—length and breadth.
- No estimation of the depth (thickness) of particle is available.

- The number of particles that must be counted to get a good estimate of the distribution makes the method slow and tedious.

2. Sieving

- This method utilizes a series of standard sieves calibrated by the National Bureau of Standards.

Range of analysis

We obtain particle size range 5–12000 μm.

Air jet sieving method

Another type of sieve analysis called air jet sieving, uses individual sieves rather than a complete nest of sieves. A reverser air jet circulator beneath the sieve mesh, blowing oversize particles away from the mesh to blocking. It is better than mechanically vibrated sieve analysis, although with finer particles agglomeration can become a problem.

3. Sedimentation

- Particle size may be indirectly determined by measurement of rate of sedimentation in a Gravitational field (Figure 1.1).

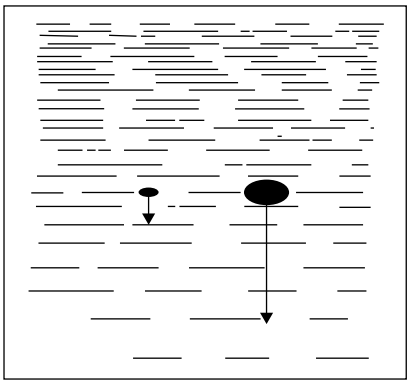


Figure 1.1 Sedimentation

- A number of classical techniques based on sedimentation methods, utilizing devices such as the Anderson pipette or recording balances.
- Stokes gave a theoretical description of the motion of falling under the influence of gravity.

$$d_{st} = [18\ \eta\mu/(P_p - P_L)\ g\ ]^{1/2}$$

Stokes law of sedimentation

- Rate of settling = $d^2 (\eta - \eta')\ g/18\ \eta$
  where d is diameter of particle; η is density of particle; η' is density of liquid and ηis viscosity of liquid.
- Used only for dilute suspension (less than 2% dispersed particles)

4. Elutriation

- Elutriation is a procedure in which the fluid moves in the direction opposite to sedimentation movement so that in the gravitational force, the particle will move vertically downwards and fluid moves vertically upwards (Figure 1.2).
- If velocity of fluid is higher than the particle are carried upwards and vice versa.

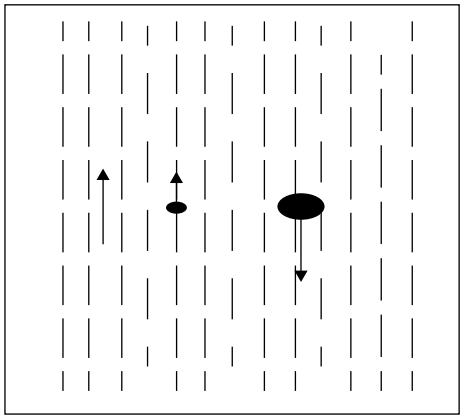


Figure 1.2 Elutriation

5. Electronic scanning zone (coulter counter)

Particles are suspended in electrically conductive fluid. The suspension flows through suitable aperture with an immersed electrode on either side and particle concentration is arranged so that one particle travels at a time. When the particle passes, some resistance is seen and that change is measured as particle.

Coulter-Current When a suspended particle travels across the orifice, it displaces its own volume of electrolyte. This causes change in electrical resistance.

- Its main advantages are:
  1. Fastest counting.
  2. 1000 particles counted in one second.
  3. More reliable since number of particles are counted.
  4. To study particle growth and dissolution and the effect of anti-bacterial agent on the growth of microorganism.

6. Surface method

Take some powder and add air and liquid to it. Powder absorbs liquid and air's mono-molecular layer on its surface. This absorbed volume can give mean of powder's particle size.

7. Fluid classification method

A number of size analysis methods for powder in the sub sieve depend on the movement of the particle in a fluid. The behaviour of sphere in a fluid can be expressed by Stroke's law. There are several cumulative methods:

1. Pipette method
2. Hydro meter method
3. Pressure method
4. Turbidimetric method

8. Laser light scattering methods

- In this method, the particle can be presented either in liquid or in air suspension.
- Both the large particle and small particle analysers are based on the interaction of laser light with particles.
- **Royco/HIAC**–based on light blockage principle.

9. X-ray diffraction method

Principle

- An x-ray irradiation produces a highly specific diffraction pattern from a crystal of material.
- An X-ray diffraction pattern from the crystal is formed and a series of dots of varying intensity with fixed angular and is recorded on photographic film.
- It is a powerful tool for particle size analysis.

Advatages

Very sensitive and used in identification of polymorphs.

Disadvantages

Very expensive

10. Cascade impaction

Size Range 0.1-80 microns

Material Particles of all kind

- It can be used to obtain the size distribution of an aerosol.
- Air samples are withdrawn through device which consists of several stages on which particles are deposited on impaction plate.
- Particles will impact on certain stage depending on their size.

Conclusion

This method is suitable **to determine the distribution of particles of respirable size.**

11. Rotating drum method

Material Dry powder, Granulates, Friable products.

Size Range 0.5–10000 microns

- This method is suitable to determine the distribution of particle of respirable or inhalable size.

Properties of drug that are affected by particle size and particle size distribution

- Surface area
- Density, porosity and compressibility
- Angle of repose and flow property
- Bulkiness and packaging criteria
- Hygroscopicity
- Electrostatic charge

Surface area

- As the particle size decreases, the surface area of the particle increases.
- Surface area is important for drug absorption, dissolution, solubility and bioavailability.
- The particle size and surface area of drug exposed to the medium can affect actual solubility.

$$\text{Log } (S/S_0) = [2\gamma V/2.303 + RT\, r\,]$$

S = Solubility of small particle

S_0 = Solubility of large particle

Y = Surface tension

V = Molar volume

R = Gas volume

T = Absolute temperature

r = Radius of small particle

The equation is used to estimate the decrease in particle size required to increase in solubility.

Noyes Whitney equation $dC/dt = KS(C_s - C_f)$

dc/dt = rate of dissolution

K = dissolution rate constant

S = surface area

C_s = concentration of drug in immediate proximity of dissolving particle, that is, solubility of drug

C_f = concentration of drug in bulk fluid

- According to Noyes Whitney equation, increase in the total surface area of drug in contact with GIF will cause increase in dissolution rate because of particles initially wetted by GIF. The effective surface area exhibited by drug is directly proportional to the particle size.
- Hence smaller the particle size, greater will be effective surface area and higher dissolution rate and it will result in higher bioavailability.

- Drugs which increase the bioavailability by particle reduction are:

  Sulphadiazine
  Phenothiazine
  Tolbutamide
  Nitrofurantoin

Surface Area Determination

1. Adsorption method

- Amount of the gas (Nitrogen or Argon gas) or liquid solute that is adsorbed onto sample of powder to form a monolayer is directly the function of surface area.
- Quantasorb instrument is used.

2. Air permeability method

- The rate at which gas or liquid permeates a bed of powder is calculated. Resistance to flow of a fluid through a plug of compact powder is the surface area of powder.

Porosity

True volume–Volume of powder itself.

Granule volume–Volume of powder itself plus the volume of intra-particle space/pore.

Bulk volume–Volume of powder itself plus the volume of intra-particle space/pore plus volume of inter-particle space (Void).

$$\text{Void Volume } (V_v) = \text{Bulk Volume } (V_b) - \text{True Volume } (V_t)$$

$$\text{Porosity } (E) = V_v/V_b = (V_b - V_t)/V_b = (1 - V_t/V_b) \times 100$$

Types of Density

True density	Helium pycnometer (Porous solid) Liquid displacement (Non-porous solid)	M/V_t
Granule density	Mercury displacement method	M/V_g
Bulk density	Graduated cylinder method based on tapping the powder from 1 inch height thrice in 2 min interval	M/V_b

Bulkiness and packaging

- As the particle size increases, the bulkiness decreases. It is a reciprocal of bulk density. Uniformity of powder blend is important.
- If not, then smaller particle takes place in space between larger particles that decreases bulkiness.
- Bulk property also important for packing criteria for powder.

Powder Flow Property Measurement

1. Per cent compressibility

Compressibility is the ability of powder to decrease volume under pressure. Compressibility is a measure that is obtained from density determinations.

% Compressibility = (Tapped bulk density–poured or untapped or aerated Bulk density/Tapped bulk density)*100

Compressibility measure gives idea about flow property of the granules as per CARR'S index which is as follows:

Carrs'Index (% compressibility)	Flow description
5–15	Excellent–free flowing granules
12–16	Good–free flowing powder granules
18–21	Fair powder granules
23–28	Poor–very fluid powders
28–35	Poor–fluid cohesive powder
35–38	Very poor–fluid cohesive
>40	Extremely poor–cohesive powder

2. Hausner ratio

It is a very important parameter to be measured since it affects the mass of uniformity of the dose. It is usually predicted from Hausner Ratio and Angle of Repose Measurement.

Hausner Ratio = Tapped Density/Bulk Density

Hausner ratio

Hausner Ratio	Type of Flow
Less than 1.25	Good Flow
1.25–1.5	Moderate
More than 1.5	Poor Flow

Note

Key points about density

- Light powder means low bulk density or large bulk volume.
- Heavy powder means high bulk density or low bulk volume.
- True density = or > Granule density > Bulk density

3. Angle of repose

Angle of Repose (Φ) is the maximum angle between the surface of a pile of powder and horizontal plane. It is usually determined by Fixed Funnel Method and is the measure of the flowability of powder/granules.

$$\Phi = \tan^{-1}(h/r)$$ where,

h = height of heap of pile

r = radius of base of pile

Measurement methods

1. Rotating Cylinder method
2. Tilted Box method
3. Fixed Cone Method

Relation between angle of repose and type of flow and type of powder

Angle of repose	Type of flow	Type of powder
<25	Excellent	Non cohesive
25–30	Good	
30–40	Passable	Cohesive
>40	Very poor	Very cohesive

Grades of powder

Grade of powder	Sieve through which all particles must pass	Sieve through which not more than 40% of particles pass	Relative
Coarse	10	44	01
Moderately coarse	22	60	1/6
Moderately fine	44	85	1/24
Fine	85	120	1/90
Very fine	120	-	1/120
Micro fine	90% pass through 350 mesh	-	-
Super fine	90% pass through 10μm	-	-

Factors Affecting Flowability

Particle size and particle size distribution

- Addition of small particle to larger particle which fill the void space reduce inter particles cohesive force and reduces surface rugosity and acts as lubricant.
- Presence of particle of size smaller than 10 micron gives stickiness to material.

Particle shape and surface roughness

- Spherical shape is the best shape which gives the maximum flow rate.
- Irregular shape of particle in material causes the bridging in hopper.
- Roughness on the surface can cause mechanical hindrance to the flow of material.

Example: Spray-dried lactose has good flowability because of the produced near spherical shape.

Density and porosity

- More density and less porosity give better flow.

Hygroscopicity

It reduces flow rate, because it increases adhesive and cohesive forces between particles.

Electrostatic charge

- More electrostatic charge so reduced flowability.

Methods of Improvement of Flowability

(a) By addition of glidant

- Flow can be improved by **reducing adhesion and cohesion.**
- Effectiveness of glidant is found to be dependent on particle size of material to which it is added.
- E.g., **corn starch** is more effective in coarser particle.

Talc, silicon dioxide and Mg-stearate are effective in finer particles. There are two types of silicon dioxide: (i) Hydrophilic (ii) Hydrophobic–more effective as glidant independent of mixing condition.

(b) By size reduction or by addition of fine particles

- Both should be up to optimum limit
- Addition of fine particles to certain level improves flow.

(c) By wet granulation

- Gives regular shape and also removes the static charge of powder surface, thus improves the flow.

(d) By removing static charge.

(e) By densification with the help of slugging.

(f) By using auger feed equipment.

(g) By addition of flow activator

Powder flow property is impaired through increased moisture content of very fine MgO and may be used as a

flow activator. MgO adsorbs water surrounding the moist particle.

(h) For hygroscopic and moist powder

- **Use of silicon treated powder** such as silicon coated talc or Na-bicarbonate may also be beneficial in improving the flowability of moist and hygroscopic powder.

(i) By alterations of process condition

- Used vibration assisted hopper
- Used force feeder

(j) By use of spray drying

- Advantose 100 maltose powder has improved flow property and compressibility than MCC by using this process.

Importance of PS and PSD

1. Particle size affects many physical properties of drug like surface area, density, porosity, compressibility, and moisture absorption, surface properties like solubility, absorption, dissolution and bioavailability.
2. **Tablet:** PS and PSD is important for selecting granulation process. It also affects average tablet weight variation, granules properties like uniformity of colour, size uniformity, also uniformity of dose, absorption, dissolution and finally bioavailability.
3. **Suspension:** Sedimentation rate, suspendibility, redispersibility, coalescence and agglomeration.
4. **Aerosol:** Affects site of absorption in the bronchopulmonary tract.
5. **Bioavailability:** Drugs whose BA is increased by PS reduction are Sulphadiazine, Phenothiazen, Tolbutamide, Spironolactone, Aspirin, Nitrofurantoin.
   - But in case of Nitrofurantoin, increase in bioavailability may result in increase in its side effects.
   - Penicillin-G and Erythromycin, if PS decreases, surface area increases; if remain more time in contact with GIF, so degradation increases.
   - Greseofulvin: If micronized the increases rate of absorption and finally the dissolution.
   - Poorly soluble hydrophobic drug: If PS decreases then there is increased chance of formation of agglomerates.
   - PS and PSD also affects the porosity and bulkiness so affects packing.

Compaction, Compression and Consolidation

Compaction: Compaction of powder is the term used to describe the situation in which materials are subjected to same level of mechanical force.

Compression: Compression is the reduction in the bulk volume of the material particle displacement of gaseous phase.

Consolidation: Consolidation is the increase in mechanical strength of material resulting from particle–particle interactions.

Evalution of compaction

1. Strain index (SI): Measures internal strain associated with a powder when compacted.
2. Bonding index (BI): Ability of material to the bonds.
3. Brittle fracture index (BFI): Measures brittleness of material.
   Higher is the BI index, stronger is the tablet.
   Higher is the SI index, softer is the tablet.

Effect of compaction on different factors

Compression force affects surface area, granule density, porosity and hardness and disintegration time of the pharmaceutical tablets.

- Surface area is increased to a maximum and then decreased.
- The initial increase in surface area can be attributed to the formulation of new surface as the primary crystalline material is fragmented while the decrease in specific surface is due to cold bonding between the unit particles.
- Porosity is decreased and density is increased as a linear function of the logarithm of the compression force.
- As the compression increases, the tablet hardness and fracture resistance also rises.

Moisture and compression

- Moisture is essential for the formation of the tablet.
- Moisture increases the tensile strength of the tablet by increasing contact area for bonding
- Moisture decreases particle surface energy and thus decreases adhesion of the tablet to the die wall.
- In case of MCC, the moisture present within the pores facilitated the flow during the compaction.
- Lack of moisture leads to lamination because of elastic recovery.
- Excessive moisture produces capillary state of powder aggregation and thus surface tension effects are insignificant to have better compaction.

Sieve

A sieve consists of a pan with a bottom of wire cloth with square opening. In the US, two standards of sieve are used.

1. Tyler Standard scale–Ratio of the width of opening in successive sieves is $2^{1/2}$. Tyler scale is based on size of

opening in a wire cloth having 200 openings per linear inch i.e., 200-mesh.

2. National Bureau of Standard also uses the ratio $2^{1/2}$ but it is based on an opening of 1 mm (18 mesh).

Special terminology used in powder mixing

1. Trituration

Reducing the particle size by rubbing them in pestle–mortar.

2. Pulverization by intervention

Powder is mixed with volatile solvent that can be easily removed after size reduction.

Example–Camphor plus alcohol

3. Levigation

Powder is mixed with a non-solvent and a paste is prepared, then it is rubbed to reduce the size. This method is particularly used when solute is incorporated into dermatological preparations. Mostly used non-solvent is mineral oil.

4. Geometric dilution

It is used when potent substances must be mixed with a large amount of diluents.

(a) First, a potent drug and an approximately equal volume of diluents are placed in mortar and thoroughly mixed by trituration.

(b) A second portion of diluents, equal in volume to the powder mixture in the mortar, is added and trituration is repeated. The process is continued; equal volume of diluents are added to the powder mixture in the mortar until all of the diluents are incorporated.

5. Hygroscopicity

- **Hygroscopicity:** It is the tendency of material to absorb moisture from atmosphere and be in dynamic equilibrium with water in the atmosphere.
- **Deliquescent:** It is the hygroscopic substance which absorbs moisture from air to the extent that they liquefy by partially or wholly forming solution.
- **Efflorescent:** A substance which loses water to form a lower hydrate or becomes anhydrous is termed as efflorescent.
- **Examples:**

Hygroscopic material and Deliquescent	Efflorescent
Ephedrine	Atropine
Hyoscymine	Cocaine
Phenobarbital	Codeine
Pilocarpine	Scopolamine
Physostigmine	Caffeine

Glycerinated gelatin and PEG base of suppository are hygroscopic in nature.

- Moisture content can be determined by **Thermo gravimetric analysis or by Karl Fisher titration or by gas chromatography.**

Important Points

Key points related to hygroscopicity

- It affects the flow property. Hygroscopic materials have poor flow property.
- It affects **compression** characteristic of powder, also affects **hardness** of final tablet and granulation.
- Moisture in cohesive material causes solid bridge and liquid bridge formation between the particles which ultimately form hard cake.
- Hygroscopic compounds are generally sticky, so this also affect the **compaction**.
- It is important for **aerosol** containing powder; moisture content should be below 300 ppm. Higher moisture level generally results into particle agglomeration.
- It also affects **chemical stability** of hydrolysable drug.

SURFACE AND INTERFACIAL PHENOMENON

Surface Tension (ST)

- Force per unit length acting at surface at right angle (N/meter) or (Dyne/cm)
- Indicate strength of Cohesive force (force between like molecules)
- Examples:
  - Formation of spherical globules in emulsion
  - Shape of falling water drop
  - Shape of mercury drop on flat surface
  - Rise in capillary tube

Interfacial Tension (IT)

- Force per unit length acting at interface at right angle (N/m)
- Indicates strength of adhesive force (force between unlike molecules)

Note

In general, surface tension is greater than interfacial tension because cohesive force between two liquids at interface is greater than adhesive force between the liquid and the gas.

Factors affecting ST and IT

- Temperature–T increases → Kinetic Energy increases → weakening of cohesive forces, hence ST decreases.
- Electrolytes
- Surface Active agents

Determination of ST and IT

1. Capillary rise method–Only ST can be determined.
2. DuNouy Tensiometer–Both ST and IT can be determined.
3. Bubble pressure
4. Drop weight or Drop count method–Both ST and IT can be determined.

Capillary rise method–Based on Young–Laplace Equation

$$P = 2\gamma/r$$

$$P = h\rho g$$

$$\text{So } \gamma = h \rho g \times r/2$$

Where γ is surface tension, ρ is density of liquid, h is height occupied by liquid, r is inside radius of capillary tube.

Drop weight method–Instrument used: Stalagmometer

$$Mg = 2 \pi r \times \gamma$$

Surface Free energy–It is the work required to increase the area of liquid by 1 cm^2.

$$\text{Work done} = \gamma \times 2L \times d$$

Surface Free energy $\Delta G = \gamma \times \Delta A$

Spreading coefficient

Spreading coefficient (S) = Work of adhesion (W_a) –Work of cohesion (W_b)

Work of adhesion Work required breaking the attraction between unlike molecules

$$(W_a) = \gamma_L + \gamma_S - \gamma_{LS}$$

Work of cohesion Work required to separate the molecule of spreading liquid $(W_b) = 2\gamma_L$

$$S = W_a - W_b$$

$$S = (\gamma_L + \gamma_S - \gamma_{LS}) - 2\gamma_L$$

$$S = \gamma_S - (\gamma_L + \gamma_{LS})$$

- Spreading occurs when S is positive, that is, Surface tension of sub-layer liquid is greater than sum of surface tension of spreading liquid and IT between sub-layer liquid and spreading liquid.
- Initially, spreading coefficient may be positive or negative, but finally, it is always negative.

Adsorption

Adsorption is the process in which matter is extracted from one phase and concentrated at the surface of a second phase. (Interface accumulation). This is a surface phenomenon as opposed to absorption where matter changes solution phase.

- **Adsorbate:** material being adsorbed.
- **Adsorbent:** material doing the adsorbing. Examples are activated carbon or ion-exchange resin.
- **Surface excess** can be defined as:

$$\Gamma = \frac{(C_{initial} - C_{after\ adsorption}) \cdot Volume}{surface\ area}$$

Where *Volume* is the volume of the solution from which the adsorption is occurring onto the surface with total surface area = *surface area*.

Surface excess is defined as the mass adsorbed per surface area. A more fundamental definition is given by the **Gibbs relationship.**

$$d\gamma = -\sum_i \Gamma_i d\mu_i$$

Where: μ_i = the molar free energy of solute i. C_i is the bulk concentration of this solute.

The Gibb's expression simply uses Γ as a proportionality constant to relate the change in solute molar free energy to surface tension (y) during adsorption.

The underlying principle here is that for the adsorption process, changes in the sum of all solute free energy must be accounted for in changes in the surface tension during the adsorption process.

For a single solute:

$$d\gamma = -\Gamma d(\mu^0 + RT \ln C)$$

$$d\gamma = -\Gamma RT \frac{dC}{C}$$

$$\frac{d\gamma}{dC} = \frac{R \cdot T \cdot \Gamma}{C}$$

Therefore,

Results in increases in Γ (surface concentration) $\frac{d\gamma}{dC} < 0$

Results in decrease in Γ $\frac{d\gamma}{dC} > 0$

Types of adsorption

- **Exchange adsorption (ion exchange)**–Electrostatic due to charged sites on the surface. Adsorption goes up as ionic charge goes up and as hydrated radius goes down.
- **Physical adsorption:** Van der Waals attraction between adsorbate and adsorbent. The attraction is not fixed to a specific site and the adsorbate is relatively free to move on the surface. This is relatively weak, reversible adsorption, capable of multilayer adsorption.
- **Chemical adsorption:** Some degree of chemical bonding between adsorbate and adsorbent characterized by strong attractiveness. Adsorbed molecules are not free to move on the surface. There is a high degree of specificity and typically, a monolayer is formed. The process is seldom reversible.

Generally, some combination of physical and chemical adsorption is responsible for activated carbon adsorption in water and waste water.

Adsorption Equilibria

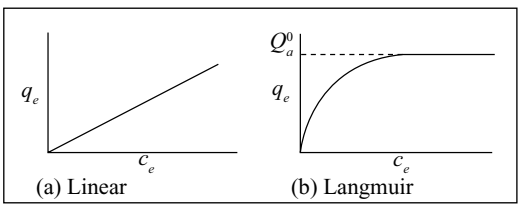
If the adsorbent and adsorbate are contacted long enough, an equilibrium will be established between the amount of adsorbate adsorbed and the amount of adsorbate in solution. The equilibrium relationship is described by isotherms.

q_e = mass of material adsorbed (at equilibrium) per mass of adsorbent.

C_e = equilibrium concentration in solution when amount adsorbed equals q_e.

q_e/C_e relationships depend on the type of adsorption that occurs, multi-layer, chemical, physical adsorption, etc.

Isotherm models



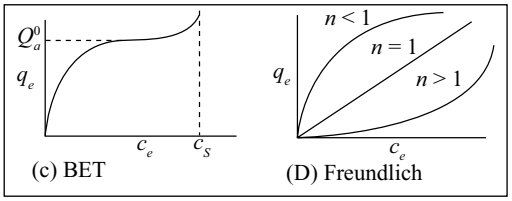


Figure 1.3 Adsorption Isotherm models

1. Langmuir isotherm

This model assumes monolayer coverage and constant binding energy between the surface and adsorbate. The model is:

$$q_e = \frac{K \cdot Q_a^0 \cdot C_e}{1 + K \cdot C_e}$$

Q_a^0 represents the maximum adsorption capacity (monolayer coverage) (g solute/g adsorbent).
C_e has units of mg/L.
K has units of L/mg
For the Langmuir model, linearization gives:

$$\frac{C_e}{q_e} = \frac{1}{K \cdot Q_a^0} + \frac{C_e}{Q_a^0}$$

A plot of C_e/q_e versus C_e should give a straight line with intercept: $\frac{1}{K \cdot Q_a^0}$ and slope: $\frac{1}{Q_a^0}$

2. BET (Brunauer, Emmett and Teller) isotherm

This is a more general, multi-layer model. It assumes that a Langmuir isotherm applies to each layer and that no transmigration occurs between layers. It also assumes that there is equal energy of adsorption for each layer except for the first layer.

$$q_e = \frac{K_B \cdot C_e \cdot Q_a^0}{(C_S - C_e)\{1 + (K_B - 1)(C_e / C_S)\}}$$

C_S = saturation (solubility limit) concentration of the solute. (mg/litre)

K_B = a parameter related to the binding intensity for all layers.

NOTE

when $C_e << C_S$ and $K_B >> 1$ and $K = K_B/C_s$ BET isotherm approaches Langmuir isotherm.

3. Freundlich isotherm

For the special case of heterogeneous surface energies (particularly good for mixed wastes) in which the energy term, K_F, varies as a function of surface coverage, we use the Freundlich model.

$$q_e = K_F C_e^{1/n}$$

n and K_F are system specific constants.

For the Freundlich isotherm, use the log-log version:

$$\log q_e = \log K_F + \frac{1}{n} \log C$$

A log-log plot should yield an intercept of log K_F and a slope of 1/n.

Factors which affect adsorption extent (and therefore affect isotherm) are:

1. Adsorbate

In general, as solubility of solute increases the extent of adsorption decreases. This is known as the "Lundelius' Rule". Solute-solid surface binding competes with solute-solvent attraction.

Factors which affect solubility include molecular size (high MW-low solubility), ionization (solubility is minimum when compounds are uncharged), polarity (as polarity increases get higher solubility because water is a polar solvent).

2. pH

pH often affects the surface charge on the adsorbent as well as the charge on the solute. Generally, for organic material, as the pH goes down, adsorption goes up.

3. Temperature

Adsorption reactions are typically exothermic i.e., ηH_{rxn} is generally negative. Here heat is given off by the reaction therefore as **T increases extent of adsorption decreases.**

4. Presence of other solutes

In general, get competition for a limited number of sites therefore get reduced extent of adsorption or a specific material.

Wetting

Intimate contact between solid and liquid or liquid and liquid.

Application

- Initial step in preparation of emulsion and suspension
- In granulation process
- Film coating requires wetting and spreading of liquid over tablet surface

Surfactant used for wetting of powder

- Has HLB 7 to 9
- Function Via
  1. Lowering Interfacial tension
  2. Lowering of Contact angle between solid and liquid
  3. Dispersing air and permit intimate contact

Contact angle

- Angle between liquid droplet and surface over which it spreads
- Indicator of evaluating the efficiency of a wetting agent
- Normally lies between 0 to 180 degree
- Zero(0) degree means complete (Significant) wetting so Cos $\theta = 1$
- 180 degree means insignificant wetting

Efficiency of wetting agent is measured by

1. Contact angle method
2. Draves test

- **Draves test** Time for weighed skin of cotton yarn to sink in wetting solution contained in 500 ml graduate.

Critical surface tension Surface tension obtained at Cos $\eta = 1$

Critical Temperature at which surface tension is zero.

Detergency

- It is a complex process used to remove dirt from substrates such as glass, fabric, skin etc., and maintain hygiene.
- HLB value lies between 13 to 16
- Cationic type–Cetrimide (cetyl trimethyl ammonium chloride)
- Anionic type–Soaps, Sodium lauryl sulphate

Surfactant (Surface Active Agent)

Amphiphilic molecules that are partitioned at interface and decrease interfacial tension of solution.

- Polar head group orient towards polar region of solution.
- Non-polar group orient towards non-polar region.
- Polar group or hydrophilic part of surfactant provides much greater barrier than non-polar (hydrophobic) portion.

HLB scale

- Arbitary scale devised by Griffin

- Indicates extent of hydrophilic-lipophilic balance
- Range 1(Oleic acid) to 40 (Sodium Lauryl Sulphate)
- Higher the HLB, more will be the hydrophilicity of compound

HLB scale

Lipophilic portion (0 to 8) Hydrophilic portion (8–16)	Category
1–3	Anti-foaming agent
3–8	w/o emulsifier
7–9	Wetting and spreading agent
8	Foaming agent
8–16	o/w emulsifier
13–16	Detergent
16–18	Solubilizing agent

Method for HLB value determination

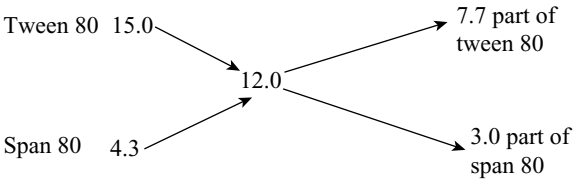
1. HLB = η(Hydrophilic group number)–n (Lipophilic group number) + 7
2. HLB = (E + P)/5
   Where E is per cent by weight of ethylene oxide chain and P is per cent by weight of polyhydric alcohol
3. HLB = 20 (1–S/A)
   Where S is Saponification Value of ester and A is Acid value of fatty acid.
4. Required $HLB_{mixture}$ value = $F.HLB_a + (1–F)\ HLB_b$

Question 1. Calculate the HLB of mixture of 40% of span 60 and 60% of tween 60. HLB of span 60 = 4.7 and HLB of tween 60 = 14.9

Ans. $HLB_{mixture}$ value = $F.HLB_a + (1–F)\ HLB_b$
$HLB_{mixture}$ value = $0.4 \times 4.7 + 0.6 \times 14.9$
$HLB_{mixture}$ value = $1.9 + 8.9 = 10.8$

Question 2. In what proportion should tween 80 and span 80 should be blended to obtain a required HLB of 12.0.HLB of span 80 = 4.3 and HLb of tween 80 15.0?

Ans. Apply Alligation Method



Per cent of tween 80 required will be =7.7/7.7 + 3.0 = 72%
Per cent of span 80 required will be =3.0/7.7 + 3.0 = 28%

NOTE

Common brand names of surfactants

1. Polysorbate means tween and polysorbate ester means Span.
2. Brij is polyoxyethylene lauryl ether
3. Myrj is poly oxyethylene monostearate
4. Tween are poly oxyethylene derivatives of sorbitan esters

poly oxyethylene mono oleate	Tween 80
poly oxyethylene monpalmitate	Tween 60
poly oxyethylene monolaurate	Tween 20
poly oxyethylene monomyristate	Tween 40

RHEOLOGY

Rheology is the science which deals with flow of liquid and deformation of solid.

Flow of Liquid

1. **Non-Newtonian flow**
2. **Newtonian flow**
   a. Plastic flow
   b. Pseudoplastic flow
   c. Dialatent flow

Deformation of Solid

1. Plastic–permanent and irreversible
2. Elastic–spontaneous and reversible

Newtonian law of viscosity

Shearing stress is directly proportional to Shearing Rate

$$F \alpha dv/dr$$

$$F = \eta\, dv/dr$$

Where,

F is Shearing stress = f/A force per unit area

Unit = newton per meter^2

G = dv/dr = Shearing rate = change in velocity/change in distance

Unit = sec^{-1}

Rheogram

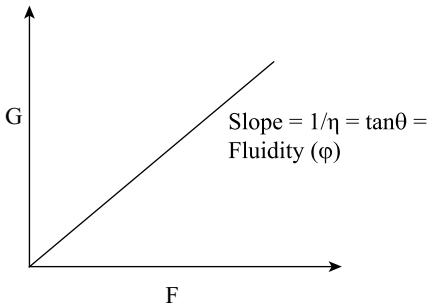


Figure 1.4 Rheogram of Newtonian flow

Where G = dv/dr = Shearing rate = change in velocity/change in distance

F = Shearing Stress = f/A force per unit area

Viscosity-Property of a liquid which show index of resistance to flow.

Basic unit of viscosity–**Poise** (C.G.S.System)

Convenient unit of viscosity–centi **poise (cp)**

Dimension dyne × sec/cm^2 or M L^{-1} T^{-1}

Fluidity (ϕ) = Reciprocal of viscosity

Unit is poise^{-1}

$\Phi = 1/\eta$

Viscosity coefficient (η) = F/G = (f/a)/(dv/dr)

Kinematic viscosity–Viscosity is officially (IP) expressed as Kinematic viscosity.

Kinematic viscosity = η/ρ = Absolute viscosity of liquid/density of liquid

Unit–stoke or centistoke

Generally, non-Newtonian fluids are expressed as apparent viscosity.

Temperature and viscosity

On increasing T, viscosity of gas increases due to increased collision while viscosity of liquid is decreased.

Arrhenius Equation

$$\eta = A\, e^{-E/RT}$$

A is constant and depends upon mol.wt. and molar volume

E is activation energy
R is gas constant
T is temperature in Kelvin

Non-Newtonian flow

- Where there **no direct relation** between shear stress and shear rate.

These are of three types:

1. Plastic flow

- It is the Newtonian system at shear stress above **yield value**.
- Material does not begin to flow until a shearing stress corresponding to yield value exceeds.
- Associated with presence of **flocculated particle in concentrated suspension and emulsion**.

2. Pseudoplastic flow

- Here, yield value not associated .As applies shear stress increasing, viscosity decreases and disarranged molecules begin to align their long axes inline of molecules.
- Exhibits by natural and synthetic gum. **E.g., tragacanth, CMC, Na-CMC**.

3. Dilatant flow

- Opposite to pseudoplastic flow
- Increase in the shear rate, increase in resistance to flow as viscosity increases.
- **E.g., deflocculated suspension of Mg magma**

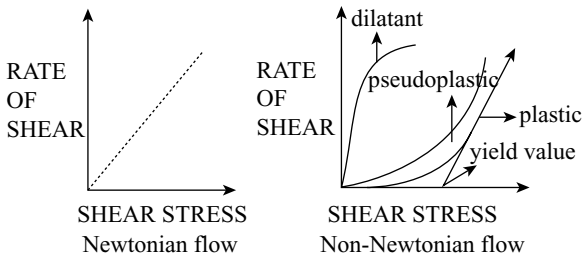


Figure 1.5 Newtonian flow and non-Newtonian flow

Type of Flow

Type of flow	Example
Newtonian	Water, Glycerine, Benzene, Alcohol, Syrup solution, very dilute colloid solution
Plastic (Bingham body)	Suspension of ZnO in mineral oil Paint, Printing Inks and Firm jellies Flocculated suspension (1-10% solid content)
Psuedoplastic	Natural and synthetic gums , Polymers such as MC, CMC, Tragacanth, Sodium alginate, gelatin
Dilatant	De-flocculated suspension (more than 50% solid content) E.g., Concentrated titanium dioxide suspension

Methods of viscosity determination

Viscosity measurement	Method of determination
Newtonian fluid	Capillary viscometer (Ostwald viscometer) Falling and Rising body (Sphere)
Non-Newtonian fluid	Cup and bob viscometer Cone and Plate viscometer

Ultrasonic Shear Rheometer It is used for analysing protein solution Rheology.

Instron Capillary Rheometer It measures viscosity as a function of shear rate and temperature, particularly at a high shear rate.

Shear dependent and time-dependent viscosity

Shear dependent viscosity involves either increase in apparent viscosity (i.e., **Shear thickening; or dilatancy**) or decrease in apparent viscosity (i.e., **Shear thinning; or Pseudoplasticity**) with an increase in rate of shear.

Shear thickening is displayed by suspension have a high solid content of small deflocculated particles**. Shear thickening** is displayed by polymer or macromolecule solution (Figure 1.6).

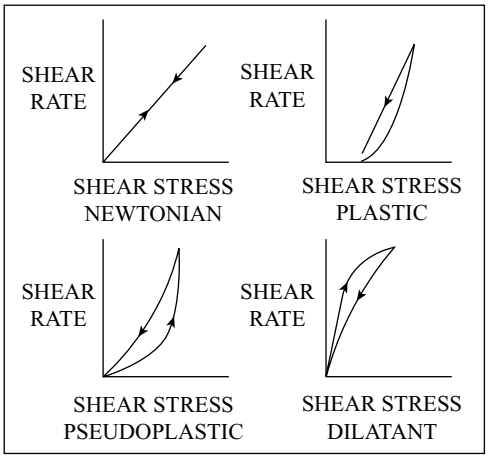


Figure 1.6 Shear thickening

Time-dependent viscosity

Thixotropy (Gel-Sol transformation)	Gel----Sol----Gel Plastic system–Bentonite (Magma)gel, petrolatum Pseudoplastic system–dispersion of synthetic suspending agent
Anti-Thixotropy (Negative thixotropy) or Rheopexy (Sol-Gel transformation)	Sol----Gel----Sol E.g., magnesia magma, Flocculated suspension (1–10% solid content)

NOTE

Key point to remember

Plastic or Bingham bodies may show both time and shear dependent viscosity.

Capillary Viscometer

Relative viscosity

$$\eta_a/\eta_b = \rho_1 \times t_1/\rho_2 \times t_2$$

where ρ is density of liquid, η is viscosity, t is time taken by liquid to reach from A mark to B mark.

Time taken to flow of liquid from one mark to another mark under gravity is measured.

Poiseuilli equation

$$\eta = \pi r^4 t \Delta p / 8LV$$

where r is radius of inside capillary; Δp is pressure drop; L is length of capillary and V is volume of the flowing liquid.

Plug flow

It occurs during analysis of plastic material. When bob is rotated at lower speed, the stress closer to rotating bob may be higher than the yield value but at inner wall of cup, the stress may be below the yield value.

Important Points

Key points to remember

- Ostwald viscometer determines kinematic viscosity.
- Paste mostly shows dilatant flow and some show psudoplastic.
- Ointment, gel, cream (semi-solid) show plastic flow.
- Suspension-Flocculated show plastic while de-flocculated show dilatant.
- Brookfield viscometer (Rotating Spindle T viscometer) used to evaluate rheological properties of suspension.

Phase volume Ratio (Volume of Dispersed phase to total Volume)	Type of Flow
5%	Newtonian
50%	Pseudo plastic
74% (50 to 74%)	Plastic

STATE OF MATTER

Gibbs' Phase Rule

$$F + P = C + 2$$

P (Alternatively π or Φ) is the number of phases in thermodynamic equilibrium with each other

C is the number of components. Typical phases are solids, liquids and gases. A system involving one pure chemical is an example of a one-component system. Two-component systems, such as mixtures of water and ethanol, have two chemically independent components.

F is the number of degrees of freedom, which means the number of intensive properties such as temperature or pressure, which are independent of other intensive variables. This version of the Gibbs' phase rule is only valid for non-reacting systems.

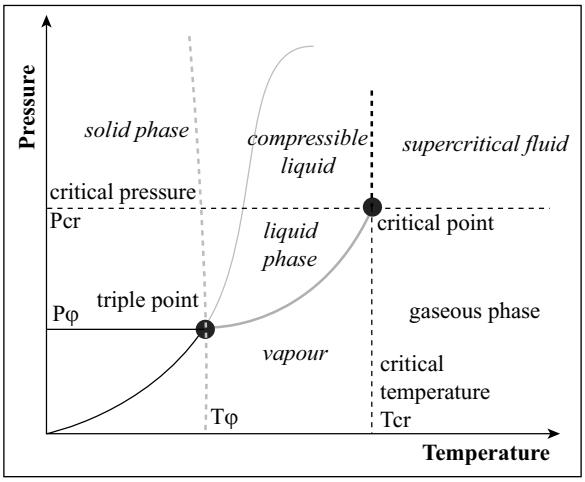


Figure 1.7 Typical phase diagram of water

Note

Triple point It is a condition at which three different phases can coexist.

- Triple point of water corresponding to the single temperature and pressure at which solid, liquid, and gaseous water can coexist in a stable equilibrium. The single combination of pressure and temperature at which liquid water, solid ice, and water vapour can coexist in a stable equilibrium occurs at exactly 273.16 K (0.01 °C) and a partial vapour pressure of 611.73 Pascal.

One-Component Example

- The system is entirely composed of H_2O, so there is only one component present.
- The phases present represents three states of matter: liquid (water), solid (ice), and vapour (steam). All have distinct physical properties (E.g., density,

structure-or lack of, etc.) and chemical properties (E.g., ΔG formation, molar volume etc.) so they must be considered distinct phases.

- Note that there is only one point on this diagram where all three phases coexist in equilibrium–this "triple point" is also referred to as an *invariant point*; because P and T are uniquely specified, there are zero degrees of freedom.
- Each of the curves represents a chemical reaction that describes a phase transformation: solid to liquid (melt/crystallization), liquid to vapour (boiling/condensation), solid to vapour (sublimation/deposition).
- There are three distinct areas where only ice, liquid, or vapour exit. These are *divariant* fields. T and P are both free to change within these fields and you will still have only one phase (a bit hotter or colder, or compressed or expanded, but nonetheless the same phase).
- The end of the "boiling curve", separating the liquid to vapour transition, is called the "critical point". This is a particularly interesting part of the phase diagram because beyond this region the physico-chemical properties of water and steam converge to the point where they are identical. Thus, beyond the critical point, we refer to this single phase as a "supercritical fluid".

COLLOIDS

Dispersion

1. Molecular (less than 0.1nm)
2. Colloidal (particle size 0.5 to 1 nm and show Tyndall effect, scattering of light)
3. Coarse dispersion (>0.5 micron)

Dispersions are also thermodynamically unstable because dispersed particles aggregate and settle.

- **Peptization**–Breakdown of aggregates into particles of colloidal size.
- **Amphiphiles**–Molecules or ions which have affinity for both polar and non-polar solvents.
- **Critical micelle concentration** (CMC)–Concentration of surfactant at which micelle formation starts.
- **Krafft point (K_t)-**Temp at which the solubility of the surfactants is equal to the CMC and above which sudden rise in solubility results.
- **Electrodialysis**–Diffusion of ions or molecules is enhanced by applying a potential difference across the membrane.

Type of Colloids

- **Lyophilic colloid (Solvent Loving)-**Hydrophilic and lipophilic colloids
- Lyophobic colloid (Solvent Hating)

Lyophilic colloid	Lyophobic colloid
Stable towards prolong dialysis	Not stable
Weak Tyndall effect	Strong Tyndall effect
Act as protective colloid	Do not act as protective colloid
Easy to prepare due to affinity towards solvent	Difficult to prepare due to lower affinity towards solvent

- Association Colloid (Amphiphilic colloid/Aggregation colloid)

Cationic type	Sodium lauryl sulphate	Counter ion – Sodium ion
Anoinic type	Cetyl trimethyl ammonium bromide (Cetrimide)	Counter ion – Bromide ion
Non-ionic type	Poly oxyethylene lauryl ether	-
Ampholytic (Zwitter ionic)	Lecithin	-

Micelle

- Association of amphipathic molecule or ions into aggregates of colloidal dimension.
- Usually size order of 50 Å.
- **Aggregation Number**–Number of surfactant molecules which undergo aggregation to form micelle or number of monomers per micelle (usually 50 or more)
- Below CMC, surfactant molecules adsorb at interface. Above CMC, surfactant molecules undergo aggregation in Bulk phase to form micelle.

Micelle structure type

1. Spherical micelle Exists at CMC and above CMC

2. Laminar micelle Exists only above CMC at high concentration of surfactant

DLVO Theory (Derijaguin, Landau, Verwey and Overbeek Theory)

- It describes stability of Lyophobic colloid. Two forces act on the particle:
  1. Attraction force due to Van der Waal force
  2. Repulsive force due to electric double layer

Stability of colloid

1. Lyophobic colloid mainly depends on the presence of charge (Electrical double layer)
2. Lyophilic colloid mainly depends on presence of hydration sheath around particle and on presence of charge (Electric double layer).

Schulze-Hardy rule (For hydrophobic colloid)

- Precipitation power of an ion on a dispersed phase of opposite charge increases with the increases in the valance or charge of the ion.
- Higher the valency ----- greater the precipitation power.

Cations ------ $Al^{+3} > Ba^{+2} > Na^{+1}$

Anions ------- $[Fe(CN)_6]^{-3} > So^{-2} > Cl^{-1}$

Hofmeister or lyotropic series (For hydrophilic colloid)

- It arranges the anions and cations in their precipitating power of hydrophilic colloids by removing hydration sheath from dispersed phase.

Citrate> Tartarate > Sulphate> Acetate >Chloride> Nitrate >Bromide

Interaction of Colloids

Mutual precipitation Two oppositely charged hydrophobic colloid mixed, result in precipitation due to neutralization of charge.

Coacervation Two oppositely charged hydrophilic colloid mixed, result in a colloid rich layer separate called Coacervate.

Example Acacia (–ve charged) and gelatin (+ve charged)

Sensitization Presence of very small amount of hydrophilic colloid, make the hydrophobic colloid to more susceptible to precipitation by electrolyte.

Protection High amount of hydrophilic colloid, make the hydrophobic colloid more stable towards electrolytes.

Gold number

- Number of hydrophilic colloid which when added to 10 ml of red gold solution to prevent colour change (red to violet) on addition of 1 ml of 10 5 NaCl solution.
- Gold number is used to measure protective ability of hydrophilic colloid.
- Lower the Gold Number, higher the protective ability.

Example–Gelatin – 0.01, Albumin – 0.1

Tyndall effect

When an intense, narrow beam of light is passed through the dispersion of colloids. Its path is visible due to scattered light.

Turbidity

- Used to estimate the concentration of dispersed particles and MW of the solute.
- It is determined by spectroscopy and nephelometer.

Electrokinetic Phenomenon

Electrophoresis Zeta potential ş = (V/E × 4ππη/k) 9 × 10^4 volt	Movement of charged dispersed phase through a liquid medium upon applying potential difference.
Electro-osmosis	Movement of liquid relative to a fixed solid under influence of field.
Streaming Potential	Potential difference is set-up when liquid flow through a fixed solid. It is the opposite process of electro-osmosis.
Sedimentation Potential	Potential difference is set-up when movement of suspended particle takes place in liquid medium. It is opposite to the process of electrophoresis.

Donnan membrane effect

Diffusion of small ions through a membrane will be affected by the presence of a charged macromolecule that is unable to penetrate the membrane because of its size.

Electrical double layer

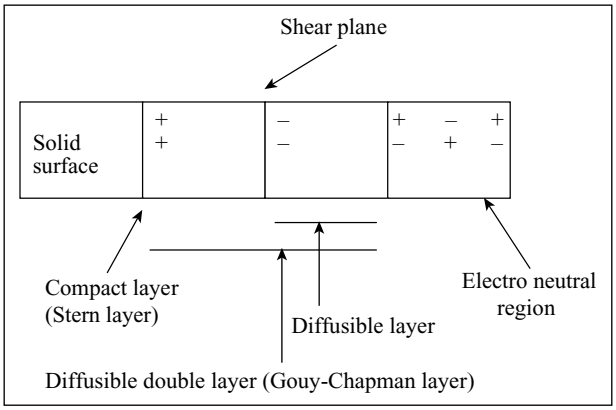


Figure 1.8 Electrical double layer: Adjacent Environment of a solid particle

Nernst potential (Electro thermodynamic potential)

- Potential at the interface (Solid surface) or actual surface
- Defined as the difference in potential between actual surface and electro neutral region.

Zeta potential (Electro kinetic potential)

- Potential at the shear plane.
- Defined as the difference in potential between surface of tightly bound layer (Shear plane) and electro neutral region.

  May be + or – or zero
- Velocity of migration ηPotential gradient across surface

  $V =$ zeta potential $\times E$

DIFFUSION

Diffusion is the random movement of molecules but has a net direction towards regions of lower concentration in order to reach equilibrium.

- Simple passive diffusion occurs when small molecules pass through the lipid bilayer of a cell membrane.
- Facilitated diffusion depends on carrier proteins imbedded in the membrane to allow specific substances to pass through, that might not be able to diffuse through the cell membrane.

Simple Diffusion

Rate of diffusion is directly proportional to the concentration gradient by the Fick's equation:

$$\frac{dn}{dt} = P \times A \times \left(\frac{dC}{dx}\right)$$

Where A is the membrane surface area and P is the permeability constant. P is a constant relating the ease of entry of a molecule into the cell depending on the molecule's size and lipid solubility. C is concentration of diffusing molecules (mol/cm^3), x is thickness or width of membrane (cm) and t is time (sec).

When A and P are constants, this equation simply describes a line where dn/dt is a function of dC/dx. If we graph the rate of diffusion as a function of the concentration gradient, we get a simple linear function.

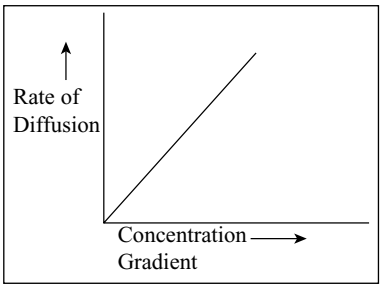


Figure 1.9 Graphical Representation–Simple diffusion

Facilitated Diffusion

Facilitated diffusion involves a limited number of carrier proteins. At low concentrations, molecules pass through the carrier proteins in a way similar to that of simple diffusion. At high solute concentrations, however, all the proteins are occupied with the diffusing molecules.

Increasing the solute concentration further will not change the rate of diffusion. In other words, there is some maximum rate of diffusion (V_{max}) when the entire carrier proteins are saturated.

The carrier proteins become saturated and can be described by the variable K, the concentration gradient at which the rate of diffusion is 1/2 V_{max}. K and V_{max} depend on properties of the diffusing molecule, such as its permeability (P), as well as the surface area (A) of the cell, but for simplification we give the equation as:

$$\frac{dn}{dt} = \frac{V_{Max}}{1 + K/\left(dc/dx\right)}$$

We can graph this equation, dn/dt as a function of dC/dx, to see how the rate of diffusion changes with increasing solute concentration outside the cell.

V_{max} is saturation constant (mol/cm^3/sec) and K is constant determining speed of saturation (mol/cm^3).

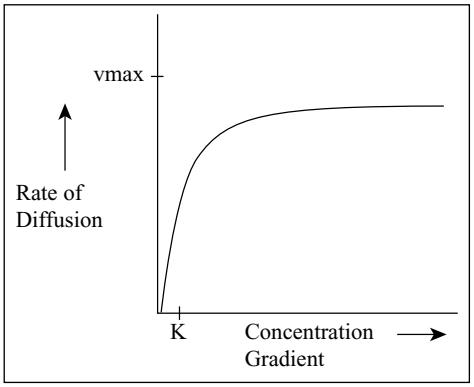


Figure 1.10 Graphical Representation–Facilitated diffusion

Fick's First Law

Fick's first law states:

$$J = -D\,(\partial C(x,t)/\partial x)$$

Where J is the flux, D is the diffusion constant for the material that is diffusing in the specific solvent, and $\partial C(x, t)/\partial x$ is the concentration gradient. The diffusion constant of a material is also referred to as 'diffusion coefficient' or simply 'diffusivity.' It is expressed in units of length^2/time, such as μm^2/hour. The negative sign of the right side of the equation indicates that the solute molecules are flowing in the direction of lower concentration.

Where

- *J* is the "diffusion flux" [(amount of substance) per unit area per unit time], $\left(\frac{\text{mol}}{\text{m}^2 \cdot \text{s}}\right)$

  J measures the amount of substance that will flow through a small area during a small time interval.
- *D* is the **diffusion coefficient** or **diffusivity** in dimensions of [length^2 time^{-1}], $\left(\frac{\text{m}^2}{\text{s}}\right)$
- ϕ (for ideal mixtures) is the concentration in dimensions of [(amount of substance) length^{-3}], $\left(\frac{\text{mol}}{\text{m}^3}\right)$
- *x* is the position [length],(m)

Fick's Second Law

Fick's first law does not consider the fact that the gradient and local concentration of the solute molecules in a material decreases with an increase in time, an aspect that's important to diffusion processes.

This is Fick's second law, which states that the change in solute concentration over time is equal to the change in local diffusion flux, or

$$\partial C(x, t)/\partial t = -\partial J/\partial x$$

Or, from Fick's First Law,

$$\partial C(x, t)/\partial t = \partial(D\partial C(x, t)/\partial x)/\partial x.$$

If the diffusion coefficient is independent of position, such as when the solute concentration is low, then Fick's second law may be further simplified into the following equation:

$$\partial C(x,t)/\partial t = D\,\partial^2 C(x, t)/\partial x^2.$$

Diffusion Cell

1. Vertical diffusion cell (Franz diffusion cell)
2. Horizontal diffusion cell

A diffusion cell consists of a donor chamber and receptor chamber (2 chambers) with a membrane clamped in between.

The diffusion cell donor chamber contains a known concentration of a solute. This solution is referred to as the donor solution. The receptor solution is contained in the receptor chamber on the other side of the membrane. When the diffusion experiment begins, the solute in the donor solution diffuses through the membrane and into the receptor solution. The receptor solution is periodically removed for analysis in order to determine the concentration of the diffusing solute from the donor solution in the receptor solution. The sampled receptor solution is replaced with new receptor solution. The results of the analysis can be used to calculate the diffusion coefficient.

Multiple Choice Questions

1. Following are used for particle size analysis

P. Coulter counter Q. BET N2 adsorption
R. XRPD S. HIAC counter
(a) Q and S (b) P and S
(c) Q, R and S (d) R and S

2. Which instrument is used for the determination of shear rate/shear stress?

(a) Ultrasonifier (b) Rotational viscometer
(c) Accela cota (d) Chilsonator

3. Colloid particle have …… type of rheology.

(a) Newtonian flow
(b) Pseudoplastic flow
(c) Non-Newtonian flow
(d) Dilatant

4. Wetting agent has …… HLB value.

(a) 1 to 3 (b) 3 to 6
(c) 7 to 9 (d) 8 to 18

5. Carr's compressibility index gives an idea about

(a) Flow property of powders
(b) Cohesiveness of powders
(c) Both
(d) None

6. Following is not a derived property of powder:
(a) Surface area (b) Particle size
(c) Bulk density (d) None

7. Following is not the method for determining the surface area of particles:
(a) Adsorption method
(b) Mercury displacement method
(c) BET method
(d) Air permeability method

8. Following is related to the air permeability method:
(a) Kozeny Carman equation
(b) BET equation
(c) Kelvin equation
(d) Stocks' equation

9. Kelvin equation is related to the
(a) Particle size analysis
(b) Pore size analysis
(c) Surface area analysis
(d) Sedimentation

10. Following is not used as a measure of flow property of powder:
(a) Compressibility index
(b) Hausner's ratio
(c) Angle of repose
(d) Bulk density

11. _____ is a zwitterionic surfactant.
(a) SLS
(b) Lecithin
(c) Tween
(d) Benzalkonium chloride

12. Following gel shows a thixotropic behavior
(a) Bentonite (b) Starch
(c) Pectin (d) Silica

13. Sorbitan esters, used as nonionic surfactants, are
(a) Tweens (b) Spans
(c) Polawaxes (d) Poloxalkols

14. A surfactant X forming poor/no dispersion in water at room temperature will be having an HLB value _____
(a) < 5 (b) 7–10
(c) 12–15 (d) 15

15. Phase inversion temperature is also called _____
(a) Fusion temperature
(b) Collapse temp.
(c) Transition temperature
(d) HLB temperature

16. First-order half-life is equal to
(a) $1/k$ (b) k
(c) $0.693/k$ (d) $2k+1$

17. Which of the following property is the derived property of powder?
(a) Size distribution
(b) Surface area of powder
(c) Porosity
(d) None of above

18. The slope of rheogram of a plastic flow is called ____.
(a) Mobility (b) Fluidity
(c) Yield value (d) Yield stress

19. In case of colloids, particles in red gold sol increase in size, the colour of dispersion will become _____.
(a) Red (b) Blue
(c) Green (d) Yellow

20. Air permeability method is used to determine the _____ of powder.
(a) Volume (b) Density
(c) Weight (d) Specific surface area

21. Red blood cells are _____.
(a) Molecular dispersion
(b) Colloidal dispersion
(c) Coarse dispersion
(d) None of above

22. Which of the following method is used to determine the surface area of particles?
(a) Sedimentation (b) Hydrometer
(c) Coulter counter (d) Adsorption method

23. The reciprocal of bulk density is _____.
(a) Porosity (b) Bulkiness
(c) Both of above (d) None of above

24. Ordinarily, interfacial tensions are _____ than surface tension.
(a) Greater (b) Lesser
(c) Same (d) Cannot be determined

25. Kinematic viscosity is the absolute viscosity divided by the _____ at specific temperature.
(a) Weight of liquid (b) Density of liquid
(c) Unit time (d) None of above

26. What is the formula to find surface area of a spherical particle?
(a) $\pi d^3/6$ (b) πd^2
(c) πd (d) πd^3

27. Mac Michael viscometer is a type of _____ viscometer.
(a) Capillary viscometer
(b) Falling sphere viscometer
(c) Cup and bob viscometer
(d) Cone and plate viscometer

28. Shearing stress is _____.
(a) Force required to bring about flow
(b) Force per unit area required to bring about flow
(c) Force per unit time required to bring about flow
(d) None of above

29. Water is _____ fluid
(a) Newtonian (b) Non-newtonian
(c) Both (a) and (b) (d) None of above

30. Suspension follows _____ kinetics.
(a) Zero-order (b) Apparent zero-order
(c) First-order (d) Second-order

31. Higher the HLB value of surfactant, more _____ it is.
(a) Hydrophilc (b) Lipophilic
(c) Amphoteric (d) None of above

32. When one of the reactants is present in such great excess then its concentration may be considered constant or nearly so, the reaction is said to be _____
(a) Zero order (b) Apparent zero order
(c) First order (d) Second order

33. Bingham bodies show which type of flow?
(a) Newtonian flow (b) Plastic flow
(c) Pseudoplastic (d) Dilatant.

34. The instrument used for measuring the volume of particles is
(a) Hydrometer
(b) Balance
(c) Anderson pipette
(d) Coulter counter

35. The particle size range of colloidal dispersion is _____.
(a) 1 nm to 1 μm (b) 1 nm to 0.5 μm
(c) 1 nm to 100 nm (d) Greater than 100 nm

36. Inorganic particles such as gold and silver dispersed in water form _____?
(a) Lyophilic (b) Lyophobic
(c) Amphiphilic (d) None of above

37. The Du-Nouy ring method (Du-Nouy tensiometer) determines _____
(a) Surface tension
(b) Interfacial tension
(c) Both (a) and (b)
(d) None of above

38. _____-shaped particles have the minimum surface area per unit volume.
(a) Square (b) Rectangular
(c) Spherical (d) Oblong

39. Roto viscometer is a type of _____ viscometer.
(a) Couette type
(b) Cup and bob
(c) Searle-type cup and bob
(d) None

40. Bulkiness (specific bulk volume) _____ with a decrease in particle size.
(a) Increases
(b) Decreases
(c) Cannot be determined
(d) None of above

41. With increasing departure from spherical, the flowability _____.
(a) Increases
(b) Decreases
(c) Can either increase or decrease
(d) None of above

42. A sample of a powder with true density of 3 g/cm^3 and weighing 100 g was found to have bulk volume of 80.33 cm^3 when placed in a 100-ml graduated cylinder. Calculate the porosity.
(a) 0.41 (b) 0.58
(c) 0.31 (d) 0.25

43. Thixotropy phenomenon can be applied to _____ system.
(a) Shear thinning system
(b) Shear thickening system
(c) Both of above
(d) None of above.

44. Faraday Tyndall effect in colloids occurs due to _____?
(a) Reflection of light by colloidal particles
(b) Brownian motion of colloidal particles
(c) Scattering of light by colloidal particles
(d) Diffusion of particles

45. Which of the following surfactant also possess antibacterial activity?
(a) Glyceryl monostearate
(b) Quaternary ammonium compounds
(c) Sodium oleate
(d) Sodium lauryl sulphate

46. A solvent sheath is formed around the particles of dispersed phase in _____ type of colloidal system.
(a) Lyophilic (b) Lyophobic
(c) Amphiphilic (d) None of above

47. Pseudoplastic flow is typically exhibited by
(a) Emulsion (b) Polymer solution
(c) Suspension (d) Ointment

48. Which of the following method is used to obtain surface tension?
(a) X-ray diffraction
(b) Karl Fischer method
(c) Capillary rise method
(d) Sedimentation method

49. If the Carr's index of a powder is 10% then the type of powder flow is
(a) Poor (b) Excellent
(c) Very poor (d) Good

50. One of the following ingredients improves the flow property of granules in
(a) Glidant (b) Emollient
(c) Lubricant (d) Surfactant

ANSWER KEYS

1. (b)	**2.** (b)	**3.** (c)	**4.** (c)	**5.** (c)	**6.** (c)	**7.** (d)	**8.** (a)	**9.** (b)	**10.** (d)
11. (b)	**12.** (a)	**13.** (b)	**14.** (a)	**15.** (d)	**16.** (c)	**17.** (c)	**18.** (a)	**19.** (b)	**20.** (d)
21. (c)	**22.** (d)	**23.** (b)	**24.** (b)	**25.** (b)	**26.** (b)	**27.** (c)	**28.** (b)	**29.** (a)	**30.** (b)
31. (a)	**32.** (b)	**33.** (b)	**34.** (d)	**35.** (b)	**36.** (b)	**37.** (b)	**38.** (c)	**39.** (c)	**40.** (a)
41. (b)	**42.** (b)	**43.** (a)	**44.** (c)	**45.** (b)	**46.** (a)	**47.** (b)	**48.** (c)	**49.** (b)	**50.** (a)

CHAPTER 2

PHARMACEUTICAL ENGINEERING (UNIT OPERATION)

SIZE REDUCTION

Definition: It is a unit operation in which reduction of materials to coarse particle or to fine powder before formulate into suitable dosage form.

Comminution, grinding, milling, pulverizing are other terms used for size reduction.

Specific Objectives

1. It increases surface area of the particle, hence increases rate of dissolution and absorption and bioavailability, and therefore increases therapeutic efficacy.
2. It facilitates mixing and drying by milling by increase surface area.
3. In ophthalmic, aerosol, inhalation and parenteral preparation where controlled particle size is required which facilitate by size reduction.

Factors affecting size reduction

1. **Hardness:** Harder the material, more difficult to reduce its size.
2. **Toughness:** Soft but tough material creates problem in size reduction and its toughness is reduced by decrease temperature.
3. **Stickness:** Gum and resinous substances cause problem in size reduction.
4. **Moisture content:** <5% moisture suitable for dry grinding and >50% for wet grinding.

Mechanism of Size Reduction

Method/ Principle	Common equipment	Approx particle Size (micron)
Cutting	Cutter mill	100–80000
Compression	Roller mill	50–10000
Impact	Hammer mill	50–8000
Attrition	Colloid mill, Roller mill	1–50
Impact and Attrition	Ball mill, Fluid energy mill	1–2000

Size Reduction Equipment

Mill	Action	Product size	Used for	Not used for
Cutter mill	Cutting	0.5 to 0.01 cm	Fibrous, tough and soft material.	Friable material
Roller mill	Compression	0.5 to 0.01 cm	Soft material, cracking seeds before extraction	Abrasive material
Hammer mill	Impact	0.5 to 0.01 cm	For all types of material	Abrasive material
Fluid energy mill (jet mill) or micronized	Impact and Attrition	1–30 micron	Hard, Friable and them labile substance like vitamin, antibiotics, enzyme, hormone.	Soft, Sticky material

Mill	Action	Product size	Used for	Not used for
Ball mill	Impact and Attrition	0.01 cm	Soft, fibrous material and serial grinding	Hard and Abrasive
End and Edge runner mill	Crushing and shearing	0.5 to 0.01 cm	Fibrous, tough, sticky material	

SIZE SEPARATION

Particle Size Separation by Different Method

Size separation method	Particle diameter (micron)
Sieving	5–10000
Sedimentation	
A. Gravitational	5–1000
B. Centrifugal	0.1–5
Elutriation	
A. Water and Air gravitational	10–500
B. Centrifugal	0.5–50
Cyclone separation	2–50

Standards of Powder

Grade of powder	Sieve through which all particle must pass	Sieve through <40% particle pass
Coarse	10	44
Moderately coarse	22	60
Moderately fine	44	85
Fine	85	120
Very fine	120	–
Microfine	350 (90% pass)	–
Superfine	90% pass through 10 micron	–

DRYING

Definition: It is process of removal of small amount of water or any liquids from material by application of heat.

Psychrometry

Psychrometry is the science of studying the thermodynamic properties of moist air and the use of these properties to analyse conditions and processes involving moist air.

The **Dry Bulb**, **Wet Bulb** and **Dew Point** temperatures are important to determine the state of humid air. The knowledge of only two of these values is enough to determine the state—including the content of water vapour and the sensible and latent energy (enthalpy).

Thermodynamic Properties of Air

1. Dry bulb temperature – T_{db}

The dry bulb temperature, usually referred to as air temperature, is the air property that is most common used. When people refer to the temperature of the air, they are normally referring to its dry bulb temperature.

The dry bulb temperature refers basically to the ambient air temperature. It is called "Dry Bulb" because the air temperature is indicated by a thermometer not affected by the moisture of the air.

Dry-bulb temperature–T_{db}, can be measured using a normal thermometer freely exposed to the air but shielded from radiation and moisture. The temperature is usually given in degrees Celsius (°C) or degrees Fahrenheit (°F). The SI unit is Kelvin (K). Zero Kelvin equals to –273°C.

The dry-bulb temperature is an indicator of heat content and is shown along the bottom axis of the psychrometric chart. Constant dry bulb temperatures appear as vertical lines in the psychrometric chart.

2. Wet bulb temperature – T_{wb}

The **Wet Bulb** temperature is the temperature of adiabatic saturation. This is the temperature indicated by a moistened thermometer bulb exposed to the air flow.Wet Bulb temperature can be measured by using a thermometer with the bulb wrapped in wet muslin. The adiabatic evaporation of water from the thermometer and the cooling effect is indicated by a "wet bulb temperature" lower than the "dry bulb temperature" in the air.

The rate of evaporation from the wet bandage on the bulb, and the temperature difference between the dry bulb and

wet bulb, depends on the humidity of the air. The evaporation is reduced when the air contains more water vapour.

The wet bulb temperature is always lower than the dry bulb temperature but will be identical with 100% relative humidity (the air is at the saturation line).

Combining the dry bulb and wet bulb temperature in a psychrometric diagram or Mollier chart, gives the state of the humid air. Lines of constant wet bulb temperatures run diagonally from the upper left to the lower right in the psychrometric chart.

3. Dew point temperature – T_{dp}

The **dew point** is the temperature at which water vapour starts to condense out of the air (the temperature at which air becomes completely saturated). Above this temperature, the moisture will stay in the air.

- If the dew-point temperature is close to the dry air temperature-the relative humidity is high
- If the dew point is well below the dry air temperature-the relative humidity is low

If moisture condensates on a cold bottle taken from the refrigerator, the dew-point temperature of the air is above the temperature in the refrigerator.

The Dew Point temperature can be measured by filling a metal can with water and some ice cubes. Stir by a thermometer and watch the outside of the can. When the vapour in the air starts to condensate on the outside of the can, the temperature on the thermometer is pretty close to the dew point of the actual air.

The Dew Point is given by the saturation line in the psychrometric chart.

The typical psychrometric chart is shown below:

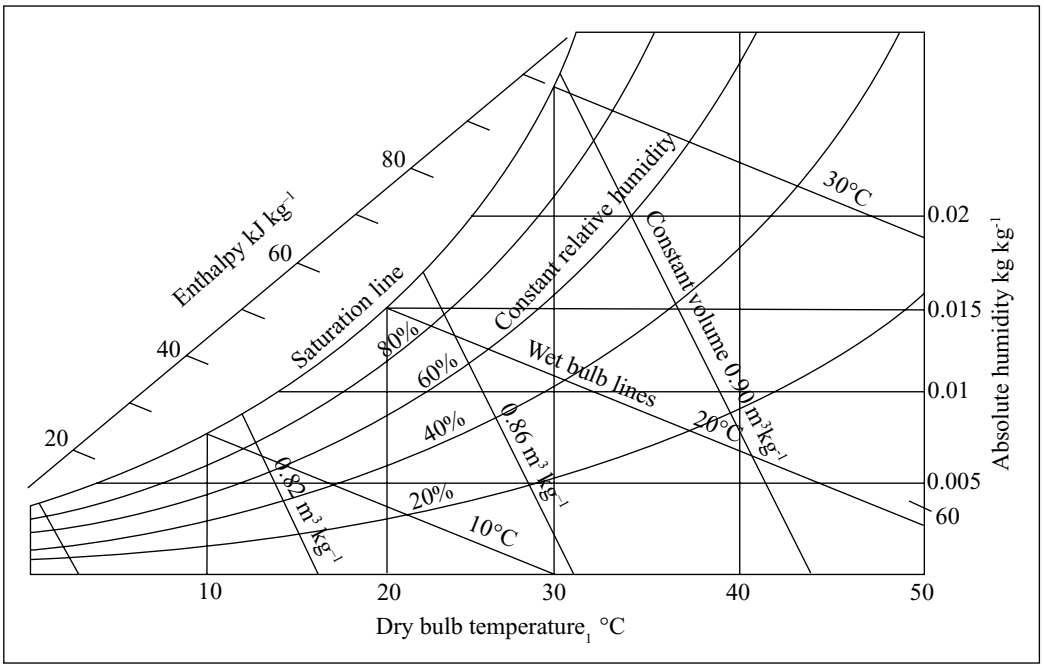


Figure 2.1 Psychrometric chart

4. Humidity ratio/moisture content

Humidity ratio w (kg/kg) of a given moist air sample is defined as the ratio of the mass of water vapour (mw) to the mass of dry air (ma) contained in the sample.

$$m = m_w/m_a \quad \ldots\ldots\ldots 1.$$

When the dry air and water vapour occupy the same volume and temperature, by applying the characteristic equation of state for perfect gas, Eqn. 1. becomes:

$$W = 0.622\ P_w/P_{at} - P_w \quad \ldots\ldots\ldots 2.$$

Where

P_w = partial pressure of water vapour in moist air

P_{at} = atmospheric pressure of moist air

5. Relative humidity (RH)

Relative humidity (RH) is defined as the ratio of the mole fraction of the water vapour (X_w) in a given moist air sample to the mole fraction of water vapour in an air sample

of saturated moist air (X_{ws}) at the same temperature and pressure.

$$RH = X_w/X_{ws} \quad \text{…….. 3.}$$

By definition, the mole fraction of the water vapour (xw) is the ratio of the number of mole of water vapour in a given moist air sample to the total number of dry air and water vapour.

$$X_w = N_w/N_w + N_a \quad \text{…… 4.}$$

When the dry air and water vapour occupy the same volume and temperature, by applying the characteristic equation of state for perfect gas, Eqn. 3. becomes:

$$RH = P_w/P_{ws} \quad \text{…… (5)}$$

Where P_w = partial pressure of water vapour in moist air

P_{ws} = partial pressure of water vapour in saturated moist air

Relative humidity is usually expressed as percentage (%).

6. Degree of saturation/percentage saturation

Degree of saturation (m) is the ratio of the humidity ratio of moist air (w) to the humidity ratio of saturated moist air (w_s) at the same temperature and pressure.

$$\mu = w/w_s \quad \text{…… (6)}$$

From Eqn. 2., Eqn. (6) becomes

$$\mu = \varphi (P_w - P_{ws})/(P_{at} - P_w) \quad \text{……(7)}$$

The difference between relative humidity RH and degree of saturation m is usually less than 2%.

Percentage saturation is degree of saturation when expressed in percentage.

7. Specific volume/moist volume

Specific volume v (m^3/kg) is defined as the total volume V (m^3) of the dry air and water vapour mixture per kg of dry air.

$$v = V/m_a \quad \text{…… (8)}$$

Where m_a = mass of dry air, kg

8. Specific enthalpy

The enthalpy of moist air is defined as the sum of its internal energy and the product of its pressure and volume. Specific enthalpy h (kJ/kg) of moist air is defined as the total enthalpy of the dry air and water vapour mixture per kg of moist air.

$$h = h_a + w\, h_w \quad \text{…… (9)}$$

Where

h_a specific enthalpy of dry air, kJ/kg

h_w specific enthalpy of water vapour, kJ/kg

w = moisture content, kg/kg

Humidity Measurement

1. **Gravimetric Method–**It is the most accurate mean for humidity measurement. But it is slow and cumbersome. **Procedure**–A known amount of air is passed over a previously weighed moisture-absorbing chemical such as Phosphorous Pentaoxide and the resultant increase in weight of chemical is measured.
2. **Temperature Based**–These methods are rapid comparative to Gravimetric method.
   A. Wet-bulb temperature determination method–Instrument used is Sling Psychrometer.
   B. Dew point temperature determination method
3. **Hygrometer**–It uses certain materials whose properties changes on contact with air of different relative humidities.
   - Loss on Drying (LOD)–It is a method of expressing water content in solids on wet weight basis.
     % LOD = (Weight of water in sample/Total weight of wet sample) × 100
     LOD of wet sample is often determined by moisture balance.
   - Moisture Content (MC)-
     % MC = (Weight of water in sample/weight of Dry sample) × 100

LOD values can vary in any solid-fluid mixture from slightly above 0% to slightly below 100% but MC values can change from slightly above 0% and approach infinity.

Theory of Drying

1. Equilibrium moisture content (E.M.C.)

It is the number of pounds of water per pound of dry solid at any given temperature and humidity.

This E.M.C. is low for non-porous solids and zero for sand, china clay and higher for fibrous and colloidal organic substances.

2. Bound moisture (bound water)

It is present as liquid in solids which exert vapour pressure less than of pure liquid at same temperature.

The substance containing bound water is called **Hydroscopic.**

3. Free moisture content

It is amount of water removed from wet solid under given condition.

Free moisture content = Total pound of water of dry solid–E.M.C.

4. Unbound moisture

It exerts its full vapour pressure and held in voids of solid. Bound and Unbound water depend on property of material itself while E.M.C depend on particular conditions.

Dryer Equipments (According to its principle)

A. Convection dryer

Name of dryer	Characteristics and Used for	Not used for
Tray dryer (shelf dryer)	Drying of chemical, powder, crude drugs, equipments, tablet granules.	Continuous process only batch process.
Fluidized Bed dryer (FBD)	Short Drying time (30 min), drying of tablet granules, plastic material, coal, inorganic salt, in fertilizer also.	It produces explosion and attrition. Only for batch process.
Tunnel dryer (belt or conveyor dryer)	Drying of paraffin wax, gelatin, soap	Not for Batch process.
Rotary dryer (modified tunnel)	Drying of powder and granular solid.	Not for Batch process.

B. Conduction dryer

1. **Freeze dryer (Sublimation drying, Lyophilization, desiccation):**
   It based on the phenomenon of sublimation at temperature and pressure below triple point.
   Sublimation pressure is 0.1 to 0.3 mm-Hg and temperature is –10 to –30°C and after sublimation honeycomb structure is formed.
   Application: For drying of biological products like antibiotics, blood products, vaccines (B.C.G, yellow fever, small pox) and in enzyme preparation like Hyaluronidase, Microbiological culture, Hormones.
2. **Spray dryer:** It based on atomization of liquid to small droplets which dried to solid particles.
   Application: For drying of solution, suspension, milk products, thermo labile materials, Plasma, soap, starch, vitamin-C, Adrenaline, anti-A and anti-B agglutinins of human sera.
3. **Vacuum dryer:** It gives friable and porous material so easy to tableting.
   - Drying of thermo labile like penicillin and oxidisable materials.
   - Recovery of solvent like ethanol extractive.
4. **Pneumatic dryer:**
   - Pneumatic dryers are those in which powders or granular materials are dried while suspended in a stream of heated air.
   - Powders or particulate foods are continuously dried in vertical or horizontal metal ducts. A cyclone separator is used to remove the dried product.
   - A pneumatic conveying dryer is often integrated with a spray dryer to provide a second stage of drying, for example to produce sufficiently dry egg or milk powder.
   - Pneumatic dryers have relatively low capital costs, high drying rates and thermal efficiencies, and close control over drying conditions. They are often used after spray drying to produce foods, which have lower moisture content than normal (e.g. special milk or egg powders and potato granule).
5. **Drum dryer:**
   - Dryers may have a single drum, or double drums or twin drums.
   - Materials ranging from dilute solutions to heavy pastes can be effectively dried in double -drum dryers.
   - Food products dried by this method include heat-sensitive liquids and pastes, which can be quickly rehydrated from the resulting flakes or powders.
   - Applesauce, fruit purees, bananas, pre-cooked breakfast cereals, and dry soup materials are manufactured in double-drum dryers.
6. **Pan dryer:**
   - It is widely used for batch drying of slurries, solutions, filter cakes, damp powder and crystalline powder.

C. Radiant heat dryer

The I.R. lamp is used for drying of granules and paint films.

D. Modern dryer

Microwave-Vacuum dryer: The microwave energy is used which is similar to radio wave.

Frequency range: 300–3000 MHZ, but pharmaceutical processor uses 2450 MHZ.

In this dryer, polypropylene plastic is present between two chambers through which microwave energy is passing.

Application: For drying of thermo labile material.

For solids (granules)	For solution	For Paste or sludges
Tray dryer (Batch Process)	Rotary dryer	Vacuum dryer
FBD (Batch Process)	Tunnel dryer	Agitator dryer
Tunnel/belt/conveyor dryer (continuous Process)	Pan dryer	
Rotary dryer (continuous Process)	Spray dryer	
Turbo dryer (continuous Process)	Drum dryer	
Freeze dryer (batch Process)		
Pneumatic dryer (continuous Process)		
Vacuum dryer (batch Process)		

CRYSTALLIZATION

Crystallization is the (natural or artificial) process of formation of solid crystals from a uniform solution. Crystallization is also a chemical solid-liquid separation technique, in which mass transfer of a solute from the liquid solution to a pure solid crystalline phase occurs.

The crystallization process consists of two major events: nucleation and crystal growth.

Nucleation

It is the step where the solute molecules dispersed in the solvent start to gather into clusters, on the nanometer scale (elevating solute concentration in a small region), that becomes stable under the current operating conditions. These stable clusters constitute the nuclei. Nucleation can occur spontaneously or induce artificially by any foreign surface. These two cases are referred as homogenous and heterogeneous nucleation respectively.

Crystal growth

It is the subsequent growth of the nuclei that succeed in achieving the critical cluster size. It occurs through four stages:

1. Transport through or from the bulk solution to an impingement site, which is not necessarily final site.
2. Adsorption at impingement site, where precursors may shed solvent molecules. Hence solvent must be transported back in soln.
3. Diffusion of growth units of precursors from site of impingement to growth site.
4. Incorporation into lattice; for precursors, after desolvation. Thus, the growth site may also be a source of solvent that has possibility of, again, being adsorbed before escaping into the solution.

Nucleation and growth continue to occur simultaneously while the supersaturation exists. *Super saturation* is the driving force of the crystallization; hence the rate of nucleation and growth is driven by the existing super saturation in the solution. Depending upon the conditions, crystals with different sizes and shapes are obtained. Once the super saturation is exhausted, the solid-liquid system reaches equilibrium and the crystallization is complete, unless the operating conditions are modified from equilibrium so as to supersaturate the solution again.

Theory of Crystallization (The Miers Super Saturation Theory)

It is well defined curve for any defined condition of heterogeneous nucleation can be established in super saturation zone which is parallel to solubility curve.

Methods to Achieve Super Saturation

1. ***By cooling:*** It is applicable when solubility depend on temperature like inorganic salt, organic substance. At higher temperature, solution is saturated and at lower temperature solution is supersaturated.
2. ***By evaporation of solvent:*** It is applicable to those whose solubility independent to temperature like NaCl.
3. ***By addition of third component:***
   A. **Salting out:** It is applied when solubility of substance is very high so super saturation is difficult by method 1. and 2.
   B. **Precipitation**
   C. **pH change**

Crystallization equipment: According to super saturation method

Crystallizer	Method	Uses and characteristics
Tank Crystallizer	Cooling	Globar salts, synthetic sponge, for only batch process
Swenson-Walker Crystallizer	Cooling	It has spiral agitator run at 7 rpm for to prevent accumulation of crystal.

Crystallizer	Method	Uses and characteristics
Krystal crystallizer	Cooling	
Krystal evaporator/ OLSO crystallizer	Evaporation	
Magma crystallizer	Evaporation	Propeller agitator used to lift magma. Not used when refrigeration temperature required to obtain good yield or solution has large B.P elevation and not used for salt which has flat solubility curve.

EVAPORATION

It is simply vaporization from surface of liquid. Means the removal of liquid from solution by boiling the liquor in suitable vessel and withdrawing vapour, leaving concentrate liquid residue and heat supply is latent heat of vaporization.

Factors Affecting Evaporation

1. ***Surface area of liquid***: Greater the surface exposed to evaporation higher will be the rate of evaporation like in film evaporator.
2. ***Temperature:*** Higher the temperature, higher will be evaporation.
3. ***Agitation:*** It breaks scum or layer and increase rate of evaporation.

Evaporation equipments (Evaporator)

Evaporator	Principle	Characteristic and use
Evaporating pan	Natural circulation	It contain liner as pan and use for aqueous and thermo-stable liquor
Vacuum pan	Natural circulation	Use for thermo labile materials
Evaporating stills	Natural circulation	Use for thermo labile materials
Horizontal tube evaporator	Natural circulation	Use for liquor that do not crystallize and not form scale and non viscous.
Vertical tube evaporator (CALENDRIA)	Natural circulation	Use in sugar industry, concentrate cascara extract and not for foamy liquid.
Vertical tube (basket type) evaporator.	Natural circulation	Use for sugar, salts and heavy chemical.
Climbing film (kestner Tube) evaporator	Natural circulation	Use for Insulin, Vitamin, Blood plasma, Liver extract like thermo labile material and for foamy, corrosive liquid. Not for Viscous liquids.
Falling film evaporator	Natural circulation	Use for viscous liquid and when high percentage of evaporation is required.
Wiped/Rotary film evaporator (AHSO LUWA)	Natural circulation	Its modified falling film evaporator Use for highly viscous liquid.

MIXING

Definition

It is a unit operation in which two or more than two components in separately or roughly mixed. So each particle lies as nearly as possible.

Objectives

1. For homogeneity
2. To increase diffusion and dissolution
3. To facilitate dispersion
4. To ensure stability and uniformity
5. To promote chemical reaction

Types of Mixtures

1. Positive mixture (Miscible mixing) It is irreversible mixing and formed from gases and miscible liquid by diffusion process.

E.g., Sugar in water.

2. Negative mixture It requires energy for mixing and difficult to prepare.

E.g., Two immiscible liquids are mixed to form emulsion.

3. Neutral mixture It is neither mixing nor de-mixing means no tendency to mix spontaneously or to segregate when mixed.

Mechanism of Mixing

1. For liquid mixing It requires localized mixing and general movement.

2. For powder mixing It is a neutral mixture.

Three mechanisms may be involved:

- Convective mixing (Macro mixing): It occurs by tilting material so gravitational force causes upper layer to slip.
- Diffusion mixing (Micro mixing): In this, all particles are distributed over interface.
- Shear mixing: It involves thorough incorporation of material passing along forced slip planes in a mixer.

E.g., Ribbon mixer gives only convective mixing while Barrel mixer gives diffusion mixing.

3. Semi-solid mixing The dilatants plastic or materials are difficult to mix than Newtonian liquids.

Mixing Equipment

1. Liquid mixers

Mixer	Characteristic and use
Propeller mixer	Used for low viscous liquid and rotate at < 8000 R.P.M Not used for glycerin, liquid paraffin, castor oil. Various offset, angled, push-pull, baffled type propeller is use for liquid mixing.
Turbine mixer	It contains impeller and is used for viscous liquid like liquid glucose and due to high shear force use in emulsification. And not for suspension. Various flat and curved blade, pitched vane and tilted type turbine is for mixing.
Paddle mixer	Agitator used foe mixing and rotate at 100 R.P.M

2. Solid mixers (Powder mixers)

Mixer	Characteristic and Uses
Ribbon blender mixer (Dry mixer)	It is convective mixing. Used for blending free flow material of uniform size and density.
Tumbling-mixer	It is shear and diffusion mixing. Rotation speed is 30–100 RPM. Various twin V-shape, double cone, cubicle, Y-shaped and cylindrical type tumbler is used for mixing.

3. Semi solid mixers

A. Agitator mixer

Mixer	Characteristics and uses
Planetary motion mixer	It contains anchor type paddle which provides pulling and kneading action. Used for paste, ointment, pill mass, tablet granulation mass and viscous material.
Sigma blade mixer (z-blade/double cone mixer)	It is kneading machine which contains open trough and blade. Used for pill mass, ointment and tablet granulation mass Banbury mixer is modified sigma blade mixer

B. Shear mixer

Mixer	Characteristics and uses
Triple roller mixer	3 to 5 rollers are used for cream and ointment.
Colloid mill	It reduces particle to 1 micron by grinding. It contains stator and rotor (moving). The rotor speed is 3000–20000 R.P.M Use for lotion, emulsion, suspension, ointment, cream.

Homogenizer

1. Q.P Emulsifier
2. Silversion-mixer-emulsifier
3. Ultrasonic mixers

FILTRATION

It is process of separation of solids from fluid by passing the same through porous medium that retain the solids, but allows the fluid to pass through.

Mechanism of Filtration

1. Straining: It is similar to sieving, means the particles of larger size cannot pass through the smaller pore size of filter medium.
2. Impingement: Solids move with streamline flow and strike the filter medium.
3. Entanglement: Particle becomes entangled in mass of fiber due to small size of particle than pore size.
4. Attractive force: Solids are retaining due to attractive forces between particles and filter medium.

Types of Filtration

1. Surface filtration (Screen filtration): E.g., Membrane filter
2. Depth filtration: E.g., Ceramic filter, sintered filter
3. Cake filtration: E.g., Filter cake made from diatomite

Filtration Equipment

A. Pressure filters

Name	Principle	Characteristic and Use
Plate and Frame filter press	Surface filtration	Used for sterile filtration, collection of antitoxin. Use for slurries contain less than 5%
Meta filter (Edge filter)	Surface filtration	It contain S.S. metal ring. Used for clarification of syrup, insulin liquors, injection.

B. Vacuum filter

Name	Principle	Characteristic and Use
Filter leaf	Surface filtration	Used for 5% solids containing slurries

C. Sieve filters

Name	Principle	Characteristic and Use
Cartridge filter	Sieving	Contains two membrane filter made of polypropylene. Used for preparation of free solution for parenteral and ophthalmic use.
Drum filter (Rotary filter)	Sieving	Used for slurries contain 30% solids and in production of penicillin.

D. Centrifugal filter

Discussed in centrifugation.

CENTRIFUGATION

It is a unit operation employed for separating the constituents present in dispersion with aid of centrifugal force.

Classification of centrifuge

Type	Characteristic and Use
Sedimentation centrifuge	Used for blood plasma separation, preparation of bacterial enzyme, manufacturing of insulin. Used for clarification of olive and fish liver oil
Filtration centrifuge	Used for obtained anhydrous product.
Ultracentrifuge	Used in colloidal research for separate solid from liquid. r.p.m-85000
Angle centrifuge	45–50 angle
High speed centrifuge	r.p.m-10000

Equipment

Name	Principle	Characteristics and Uses
Perforated basket type	Filtration	Used for separating crystalline drug like aspirin.
Non-Perforated basket type	Sedimentation	Used when deposited solids offer high resistance to flow.
Short cycle automated batch centrifuge	Filtration	Semi-continuous type.
Horizontal centrifuge	Sedimentation	Used for slurries contains 0.5 to 50% solids.
Super centrifuge	Sedimentation	Used for separating liquid phase of emulsion.
De Laval Clarifier	Sedimentation	Used in manufacture of antibiotics Separation of cream from milk, concentration of rubber wax removing solids from oils, inks.

HEAT AND MASS TRANSFER

Heat flow from high region temperature to lower region temperature. According to principle of thermodynamic, whenever physical or chemical transformation occurs, heat flows into or leaves the system.

Mechanism

1. Conduction

When heat flow in body is achieved by transfer of momentum of individual atoms or molecule without mixing. This mechanism is based on Fourier's law.

Fourier's law

It states that the rate of heat flow through a uniform material is proportional to the area and temperature drop and inversely proportional to length of path of flow.

2. Convection

A. Forced convection

When mixing of fluid is achieved by use of agitator or stirrer or pumping the fluid for recirculation, such process in heat transfer is called forced convection.

In force convection, the stagnant films (film or surface coefficients) are of great importance in determining rate of heat transfer.

Film coefficient is the quantity of heat flowing through unit area of film for unit drop in temperature.

Factor affecting film coefficients

- Thermal conductivity of the liquid
- Specific heat of the film
- Density of the liquid
- Turbulence of the liquid
- Thickness of the film

B. Natural convection

Mixing of fluid is accomplished by the currents set up, when body of fluid is heated. Such process is known as natural convection.

Fluid circulation caused by change in the density due to temperature difference in the fluid which depends on:

- Geometry of the system (size, shape and arrangement of heating surface).
- Shape of vessel in which the fluid is enclosed.
  - This natural convection is observed when extracts are evaporated in open pans.

3. Radiation

Radiation is a process in which heat flows through space by means of electromagnetic waves.

Thermal radiation Heat transfer by radiation is known as thermal radiation.

Various forms of emitters used for the supply of radiant energy are given below:

Radiation source	Wave-length	Application
IR lamp	1 μm	High intensity radiation
Ceramic rods and panels Heated by gas or electricity	2 to 4 μm	Pharmaceutical purpose, thermo labile substance.

Black body It is defined as a body that radiates maximum possible amount of energy at given temperature.

Normally, hot bodies emit radiation. Stephen-Boltzmann law gives the total amount of radiation emitted by black body.

$$q = bAT^4$$

q = energy radiated per second

A = area of radiating surface

T = absolute temperature of radiating surface

b = constant

The actual bodies do not radiate as much as black body, so for actual bodies, the equation is

$$q = bAT^4$$

= emissivity of the actual body.

When emissivity is equal to absorptivity then substance is considered as **black body.**

Grey body It is defined as that body whose absorptivity is constant at all wavelength of radiation, at given temperature.

DISTILLATION

It is defined as the separation of the components of the liquid mixture by process involving vaporization and subsequent condensation at another place.

Ideal (Perfect) solutions: It is defined as the one in which there is no change in the properties of the components other than dilution, when they are mixed to form a solution.

Example is methanol and water.

Raoult's law It states that partial vapour pressure of each volatile constituent is equal to the vapour pressure of the

pure constituent multiplied by its mole fraction in the solution at given temperature.

Ideal solution obeys Raoult's law. Raoult's law is obeyed by only a few solution of liquid in liquids.

Examples are benzene, toluene, n-hexane, n-heptane, ethyl bromide, ethyl iodide.

Dalton's law It states that the total pressure exerted by a mixture of ideal gases may be considered as sum of the partial vapour pressure exerted by each gas, if alone were present and occupied the total volume.

Application According to the ideal solution, the component having relatively greater vapour pressure will be distilled first.

Real solutions Most systems show varying degree of deviation from Raoult's law, depending on nature of liquids and temperature. These solutions are known as real solutions.

Examples are carbon tetrachloride, cyclohexane, chloroform, and acetone.

Volatility It may be defined as the equilibrium partial pressure of the substance in the vapour phase divided by the mole fraction of the substance in the solution.

Classification of Distillation Methods

Distillation method	Characteristics and Uses
Simple distillation (Differential type)	It is used for preparation of distilled water and water for injection.
Flash distillation	It vapourizes liquid by passing feed from high pressure zone to low pressure zone. It is used in petroleum ether separation.
Fractional distillation (Rectification)	It vapourizes liquid mixture by giving rise to mixture of constituents from which desired one is separated in pure form. It based on counter-current diffusion principle. It is used for separation of miscible liquid like acetone and water. It can't separate miscible liquid which form azeotropic mixture.
Azeotropic distillation (constant boiling type)	It is a method in which azeotropic mixture is broken by addition of third substance. Absolute alcohol is prepared by this method. It is used for determination of water content in substance using toluene (I.P-1996)
Extractive distillation	In this, third added to azeotropic mixture is relatively non-volatile liquid compared to components to be separated.
Steam distillation (Differential type)	Steam is used for separation of high-boiling substance from non-volatile impurities. Used for separation of immiscible liquids. Used for camphor distillation and extraction of volatile oil like clove, eucalyptus.
Molecular distillation (Evaporative or short path distillation)	It is a process in which vapour phase molecule get condensed individually without intermolecular collisions on appled vacuum. Used for separation of Vitamin-A and E, steroids, free fatty acid, triglyceride. It is used in the refining of fixed oil.
Destructive distillation (Dry distillation)	It is a method in which distillate is the decomposed product of constituents of organic matter burnt in absence of air.
Compression distillation	Use for obtaining fresh water from sea-water which is pyrogen free.

FLOW OF FLUIDS

It is the flow of substance that does not permanently resist distortion.

Manometers These are the devices which are use for measuring the pressure difference.

1. Simple manometer: It helps in measuring the consumption of gases in the chemical reaction.
2. Differential manometer (two-fluid U-tube manometer): It useful for measuring small gas pressure.

Critical velocity It is defined as average velocity of any fluid at which viscous flow changes into turbulent flow.

Reynolds number It is used for measurement and type of flow determination.

$$Re = D \times u \times \text{density of liquid/Viscosity of fluid}$$

D = diameter of pipe, u = Average velocity

When Re<2000 then flow is laminar or viscous or streamline
Re>4000 then flow is turbulent
Re is 2000–4000 then flow is laminar or turbulent

Bernoulli's Theorem When principle of conservation of energy is applied to the flow of fluids, the resulting is called as Bernoulli's Theorem.

Measurement of rate of flow of fluids

1. Direct weighing or measuring
2. Hydrodynamic methods

Name	Characteristic and Use
Orifice meter (variable head meter)	Normally used for testing purpose like for steam, lines.
Venturi meter (variable head meter)	Used in on-line installation and for measurement of gases.
Pitot tube (insertion meter)	It measures the velocity at one point only.
Rotameter (area meter)	It use in bulk drugs chemical industries and in fermenters for control of air supply.

Valves These are used to control the rate of flow of fluids in a pipeline.

Name	Characteristic and Use
Plug Cocks valve	Use for handling compressed air
Globe valve	It contain seat ring and used in <50 mm pipes.
Gate valve	It contains inclined seat type of gate.
Diaphragm valve	The rubber diaphragm coated with PTFE (polytetra fluoroethylene) is used. Used for fluid containing suspended solids and in production of sterile product.

Pumps These are mechanical devices use to increase the pressure energy of a liquid.

A. Reciprocating pumps These are used for injection of inhibitors in polymerization units and corrosion inhibitors to high pressure system.

Name	Characteristic and Use
Piston pump	Used in peristaltic and HPLC pumps and for spray system in sugar coating and film coating operations.
Plunger pump	Used for handling liquids at high pressure. Used for transport viscous liquid and liquid contain suspended solids.
Diaphragm pump	Used in transporting liquid containing solids. Hazardous, toxic and corrosive liquids can also handle.

B. Rotary pumps

Name	Characteristics and Uses
Gear pump	Used for handling viscous or heavy liquid like vegetable oil, animal oil, waxes. Used in aqueous film coating
Centrifugal pump A. Volute pump B. Turbine pump Deep well pump	Used for viscous liquid Used for non-viscous and non-corrosive liquids Used for handling organic solvents.

C. Miscellaneous pumps

Peristaltic pump: It contains silicone rubber tube in a U-shape against roller is clamped.

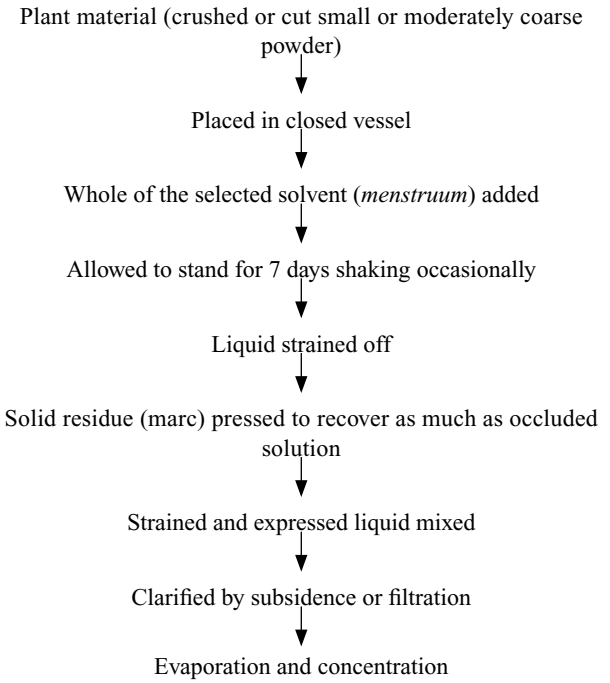
Use: It is used for pumping emulsions, creams in pharmaceutical industry and pumping parenteral nutrition infusions to patient and blood pumping for surgical operation.

EXTRACTION

The purpose of extraction process for crude drugs are to obtain therapeutically desirable portion and eliminate the inert material by treatment with a selective solvent known as *menstruum*.

1. Maceration

General Process-



Maceration Process		
Sr. no.	Organized drugs (e.g bark & root)	Un-Organized drugs (e.g Gum-resin)
1.	Drug + whole of *menstruum*	Drug + 4/5 th of *menstruum* in most cases
2.	Shake occasionally during 7 days	Shake occasionally during 2 to 7 days as specified
3.	Strain of liquid and press the marc	Decant the liquid and marc is not pressed
4.	Mix the liquid and clarify by filtration Filtrate is not adjusted to volume	Filter the liquid and passed more *menstruum* through filter to volume
Sr. no.	Organized drugs (e.g bark & root)	Un-Organized drugs (e.g Gum-resin)
5.	The direction to press the marc because there is a considerable proportion of liquid adherent to it which could not otherwise be separated.	The omission of directions to press the marc because it is neither practicable nor necessary.
6.	The omission of directions to adjust to volume because a variable amount of liquid is left in the mark. This liquid contains soluble matter. If adjustment to volume were made, a weak product would result from defective expression. Omitting adjustment, the volume of liquid expressed influences the yield of product, but not its strength.	The direction to adjust to volume because the clear upper layer. (i) Is easily separable by filtration from the lower. (ii) Contains practically all the soluble matter of the drug, the small amount adherent to the gummy matter being washed there from the *menstruum* passed through the filter. Hence adjustment to volume leads to uniformity.
7.	Preparation made by this procedure - Vinegar of squill, B.P.C Oxymel of Squill, B.P.C Tincture of Orange I.P Tincture of Capsicum, B.P.C Compound Tincture of Gentian Tincture of Lemon Tincture of Squill, B.P.C	Preparation made by this procedure - Compound Tincture of Benzoin Tincture of Myrrh, B.P.C Tincture of Tolu, B.P.C

2. Percolation (Exhaustive extraction)

Process –

- Organized vegetable drug in a suitably powdered form.
- Uniform moistening of the powdered vegetable drugs with *menstruum* for a period of 4 hours in a separable vessel (Imbibition).
- Packed evenly into the percolator.
- A piece of filter paper is placed on surface followed by a layer of clean sand so that top layers of drugs are not disturbed.
- Sufficient *menstruum* is poured over the drug slowly and evenly to saturate it, keeping the tap at bottom open for passing of occluded gas to pass out.
- Sufficient *menstruum* is also added to maintain a small layer above the drug and allowed to stand for 24 hours.
- After maceration, the outlet is opened and solvent is percolated at a control rate with continuous addition of fresh volume.
- 75% of the volume of the finished product is collected.
- Marc is pressed and expressed liquid is added to the percolate giving 80% to 90% of the final volume.
- Volume is adjusted with calculated quantities of fresh *menstruum*.

- Evaporation and concentration to get finished products by applying suitable techniques and apparatus

Small scale extraction by Percolator (Soxhlet Apparatus)

- On the laboratory scale, the apparatus consists of a flask, a soxhlet extractor and a reflux condenser.
- The raw material is usually placed in a thimble made of filter paper and inserted into the wide central tube of the extractor.
- Alternatively the drug, after imbibition with the *menstruum* may be packed into the extractor taking care to see that the bottom outlet for the extract is not blocked.
- Solvent is placed in the flask and brought to its boiling point.
- Its vapor passes up the larger right hand tube into the upper part of the drug and then to the condenser where it condenses and drops back on to the drug.
- During its percolation, it extracts the soluble constituents.
- When the level of the extracts reaches the top level of syphon tube, the whole of the percolates syphon over into the flask.
- The process is continued until the drug is completely extracted and the extract in the flask is then processed.
- This extraction is series of short maceration.

3. Infusion

General Consideration

- Infusions are dilute solutions containing the readily-soluble constituents of crude drugs.
- Formerly, fresh infusions, prepared by macerating the drug for a short period in cold water or boiling water were used.
- Now, infusions are usually prepared by diluting one volume of a concentrated infusion to ten volumes with water.
- Concentrated infusions are prepared by modified percolation or maceration process, which after dilution with water, resemble in potency and aroma the corresponding fresh infusion.
- Infusions are liable to fungus and bacterial growth, and it is necessary to dispense them within twelve hours of their preparation.

General Method for Preparing Fresh Infusion

- The drug is usually coarsely powdered, **very fine powder being avoided** (50 gm).
- Moisten the drug in a suitable vessel, provided with a cover, with 50 ml of cold water. Allow to stand for 15 minutes.
- Then add 900 ml of boiling water, cover the vessel tightly.
- Allow it to stand for 30 minutes.
- Then strain the mixture, pass enough water to make the infusion measure 1000 ml
- Some drugs are supplied in accurately weighed in muslin bags for preparing specific amounts of infusion.
- If the activity of the infusion is affected by the temperature of boiling water, cold water should be used.
- As the fresh infusions do not keep well, they should be made **extemporaneously and in small quantities.**

Preparation of Concentrated Infusions

- The official monographs also recognize certain "concentrated infusions" in which 25% alcohol is added during or subsequent to the infusion process.
- Concentrated infusions are especially prepared in which the active and desirable principles of drug are equally soluble in water or in the *menstruum* used for both concentrate and infusions.

4. Evaporations

- One of the quality- relevant parameter is the evaporation of the eluate to the soft extract.
- The state of art are cautious vacuum evaporation apparatus and evaporation temperatures not exceeding 55 0C.
- The temperature in correlation with the evaporation time is of special importance for quality of this step of manufacture, if the extract contains easily volatile or thermo- labile constituents.

Factors Affecting Choice of Extraction Process

The final choice of the process to be used for the extraction of a drug will depend on a number of factors, including:

1. Character of Drug

- If hard and tough (such as nux vomica) use percolation.
- If soft and parenchymatous (such as gentian) use maceration.
- If 'unpowderable' (such as squill) use maceration.
- If an 'unorganized drug (such as benzoin) use maceration.
- If preferable to avoid powdering (such as senna fruits) use maceration.
- Thus, knowledge of the pharmacognosy of the drug is essential to selection of the extraction process that will give the best results.

2. Therapeutic Value of the Drug

When the drug has considerable therapeutic value, the maximum extraction is required, so that percolation is used, as in belladonna. If the drug has little therapeutic value, however, the efficiency of extraction is unimportant and maceration is adequate; for example, "flavours" (lemon), or "bitters", (gentian).

3. Stability of Drug

Continuous extraction should be avoided when the constituents of the drug are thermo-labile.

4. Cost of Drug

- From the economic point of view, it is desirable to obtain complete extraction of an expensive drug, so that percolation should be used; Ginger is an example of this type.
- For cheap drugs, the reduced efficiency of maceration is acceptable in view of the lower cost of the process. In particular, the cost of size reduction to a powdered state is avoided, whereas this is a significant part of the percolation process.

5. Solvent

If the desired constituents demand a solvent other than a pure boiling solvent or an azeotrope, continuous extraction should be used.

6. Concentration of Product

- Dilute products such as tincture can be made by maceration or percolation, depending on the previous factors.
- For semi-concentrated preparations (concentrated infusions, for e.g.) the more efficient percolation process is used) unless the drug cannot be powdered or is not worth powdering, when double or triple maceration is chosen.
- Concentrated preparations, of which liquid extracts or dry extracts are example, are made exclusively by percolation, with the exception that continuous extraction can be used if the solvent is suitable and the constituents are thermo-stable.

7. Recovery of Solvent from the Marc

The residue of the drug after extraction (often known as the marc) is saturated with solvent and if economic the latter is recovered.

Multiple Choice Questions

1. Following mixture(s) is/are of the irreversible nature:
(a) Positive mixtures (b) Negative mixtures
(c) Neutral mixtures (d) None

2. Saturated solution left behind the process of crystallization is called
(a) Final solution (b) Daughter liquor
(c) Mother liquor (d) Parent liquor

3. Following is the same for all crystals of the same material
(a) Sizes of the faces of crystal
(b) Size of the edge of the crystals
(c) Angles made by the faces of crystals
(d) All

4. Swenson–Walker crystallizer is a type of
(a) Scrapped surface crystallizer
(b) Agitated batch crytallizer
(c) Static tank crystallizer
(d) Evaporator crystallizer

5. Chose a method to achieve supersaturation for a substance whose solubility is independent of temperature (substance with flat solubility).
(a) Cooling (b) Evaporation
(c) Precipitation (d) None

6. Following uses the evaporation technique to achieve supersaturatoin:
(a) Circulation magma crystallizer
(b) Sternson–Walker crystallizer
(c) Static tank crystallizer
(d) All

7. McCabe and Thiele method represents
(a) Graphical method for determining the number of theoretical plates of a fractionating column
(b) Graphical relation between vapour pressure and temperature of component liquids of a mixture
(c) Relationship between the vapour pressure and mole fraction of component of a mixture
(d) None

8. Florentine receiver works on the principle of separation of component liquids of a mixture based on
(a) Molecular weight difference
(b) Density difference
(c) Volume difference
(d) All

9. Following is not true for an azeotropic mixture:
(a) Volatility of each component becomes equal
(b) Relative volatility of mixture is 1
(c) Components of such mixture cannot be fractionated
(d) None

10. Following is most widely used for extraction of volatile oils
(a) Steam distillation
(b) Azeotropic distillation
(c) Molecular distillation
(d) Destructive distillation

11. Fixed oils can be extracted using
(a) Vacuum still (b) Molecular still
(c) Water still (d) Fractional distillation

12. A material is termed bone dry if the moisture content is reduced to
(a) EMC (equilibrium moisture content)
(b) Zero moisture
(c) CFMC (critical free moisture content)
(d) None

13. Ideally the drying should be done to a level of
(a) EMC. (b) CMC
(c) CFMC (d) Zero moisture content

14. Gelsication is the term used for
(a) Freeze drying (b) Turbo drying
(c) Vacuum drying (d) Rotary drying

15. Freeze drying works on the principle of
(a) Evaporation of water
(b) Sublimation of water from ice phase to gas phase
(c) Liquefaction of ice to water
(d) Heating at the freezing temperature of water

16. Dewar flasks are used in
(a) Vacuum drying (b) Microwave drying
(c) Freeze drying (d) Rotary drying

17. The most efficient heat exchange between the particles and flowing air occurs in the
(a) Tray dryer
(b) Spray dryer
(c) Fluidized bed dryer
(d) Rotary dryer

18. Following light is mostly used in radiant heat dryer:
(a) Radio waves (b) Sunlight
(c) UV rays (d) Infrared rays

19. Reynold's number (Re) for streamline flow of a fluid is
(a) <0.2 (b) >0.2
(c) <0.8 (d) >0.8

20. Following is not the mechanism of size reduction
(a) Impact and attrition
(b) Cutting
(c) Bruising
(d) Elutriation

21. In dry milling the moisture content should be
(a) <2% (b) <4%
(c) <6% (d) <8%

22. For effective operation of ball mill the ball charge (% volume of mill filled by the balls) should be
(a) 60–70% (b) 30–50%
(c) <30% (d) >50%

23. Critical speed of the ball mill is the speed at which
(a) Balls begin to centrifuge with the mill
(b) Balls cascade over one another
(c) Balls are carried up the sides and fall freely onto material
(d) Balls start tumbling

24. Rouwolfia and *Glycirriza* can be size reduced the best way by of
(a) Roller mill (b) Ball mill
(c) Cutter mill (d) Colloid mill

25. Select a mill for a low melting drug.
(a) Hammer mill (b) Roller mill
(c) Ball mill (d) Fluid energy mill.

26. According to IP/BP very fine powder is one of which
(a) All particles pass through 120# sieve
(b) 90% particles pass through 350# sieve
(c) All particles pass through 350 # sieve
(d) 90% particles are of size <10μm

27. Total 100 squares in a 1 $inch^2$ area is termed
(a) 100 mesh sieve (b) 10 mesh sieve
(c) 20 mesh sieve (d) 25 mesh sieve

28. Following is not a filter aid:
(a) Diatomite (b) Carbon
(c) Gelatin (d) Asbestos

29. Filter aids may be applied by
(a) Precoating technique
(b) Body-mix technique
(c) Both
(d) None

30. Integrity tests are intended for following filters:
(a) Leaf filters
(b) Drum filters
(c) Membrane filters
(d) Edge filters

31. The equation describing the factors affecting the rate of filtration is
(a) Darcy's equation (b) Dalton's equation
(c) Stokes' equation (d) None

32. For effective screening of all bacteria for sterilization of liquids the membrane pore size is
(a) 0.2μm (b) 0.45μm
(c) 0.8μm (d) 1.2μm

33. Duhring's rule is related to
(a) Crystallization (b) Distillation
(c) Filtration (d) Size reduction

34. Filters function by the following mechanism(s)
(a) Sieving or screening
(b) Entrapment or impaction
(c) Electrostatic attraction
(d) All

35. Clarification is the term used when the solid content of the product
(a) Doesn't exceed 1%
(b) Doesn't exceed 10%
(c) Doesn't exceed 5%
(d) All are true

36. Hammer mill works by following principle:
(a) Impact (b) Attrition
(c) Compression (d) None

37. Following laws are used to predict energy requirements for comminuting process.
(a) Rittinger's law (b) Kick's law
(c) Bond's law (d) All

38. Following is/are dimensionless number(s)
(a) Reynold's number
(b) Power number
(c) Mass transfer number
(d) All

39. Sweet land filter is a modified type of
(a) Leaf filter (b) Edge filter
(c) Cartridge filter (d) Rotary drum filter

40. One of the following mills works on both the principles of interparticulate attrition and impact
(a) Cutter mill
(b) Hammer mill
(c) Roller mill
(d) Fluid energy mill

ANSWER KEYS

1. (b)	**2.** (c)	**3.** (c)	**4.** (a)	**5.** (b)	**6.** (a)	**7.** (a)	**8.** (b)	**9.** (d)	**10.** (a)
11. (b)	**12.** (b)	**13.** (a)	**14.** (a)	**15.** (b)	**16.** (c)	**17.** (c)	**18.** (d)	**19.** (a)	**20.** (d)
21. (a)	**22.** (b)	**23.** (a)	**24.** (c)	**25.** (d)	**26.** (a)	**27.** (b)	**28.** (c)	**29.** (c)	**30.** (c)
31. (c)	**32.** (a)	**33.** (b)	**34.** (d)	**35.** (a)	**36.** (a)	**37.** (d)	**38.** (d)	**39.** (a)	**40.** (d)

CHAPTER 3

PHARMACEUTICAL TECHNOLOGY AND MODERN PHARMACEUTICS

PREFORMULATION

- **Preformulation** is a link between drug discovery and drug development. It is the fundamental step in the rational development of dosage form.
- It can also be **defined as** an investigation of physical and chemical properties of drug substance alone and when combined with excipients.

Goal of preformulation

- To formulate an elegant, safe, efficacious dosage form with good bioavailability.
- To formulate new dosage form of an already existing drug.
- Determination of all the properties of drug and the best suitable dosage form for the drug molecule.

Physical Characteristics

A. Bulk characteristics

Particle Size and Surface Area	Polymorphism
Crystallinity	Hygroscopicity
Flow properties and Bulk density	Compressibility
Drug-Excipient Compactibility	Electrostatic charge
Osmolarity	Rheology
Wettability	

B. Solubility analysis

Aqueous Solubility a) Intrinsic Solubility b) Dissociation Constant	Solubilization
Partition Coefficient	Thermal effect
Common ion effect	Dissolution

C. Stability analysis

Solid State Stability	Solution state stability

Chemical Characteristics

Oxidation	Hydrolysis
Photolysis	Racemization
Polymerization	Isomerization
Decarboxylation	Enzyme decomposition

Polymorphism It is the ability of any compound or element to crystallize as one or more distinct crystal species with different internal lattice.

- Example: Carbon—Cubic: diamond
  —Hexagonal: graphite

Class	% of Polymorphism
Barbiturates	63
Steroids	67
Sulphonamides	40

The effect of polymorphism on bioavailability is the most important consequence for drug substances if the bioavailability is mediated via dissolution. The oldest known example is chloramphenicol palmitate.

Types of polymorphism

Phase transition: The process of transformation of one polymorph into another, which may also occur on storage or during processing, is called phase transition.

- Enantiotrophic Polymorphs: Phase trantsition is reversible that means metastable stable. E.g., sulphur
- Monotrophic Polymorphs: Phase transition occurs only in one direction
  metastable→stable. E.g., glyceryl stearate.

Solvates (Pseudopolymorphism)

Solvates are molecular complexes that have incorporated the crystallizing solvent molecule in their specific lattice position and in fixed stoichiometry. When the solvent incorporated in the solvate is water, it is called a hydrate.

A classical method for distinguishing solvates from polymorphs involves observation of the melting behaviour of crystals embedded in silicon oil, where upon heating, bubbles of solvent are generated by solvates. In case of polymorphs, no such generation occurs.

Methods to identify polymorphism

- Optical crystallography
- Hot stage microscopy → Using this technique, fluid phase transformation as a function of temperature is observed. Generally, silicon oil hot stage microscopy is used for detection of pseudo polymorphs.
- X-ray diffraction method–Using Bragg's equation:

$$N\lambda = 2d\sin\theta$$

Where d = distance for different planes of crystal, λ = wavelength of x-ray used, θ = angle of incoming beam, n = order of spectrum

- X-ray diffraction-(a) powder x-ray diffraction → Basically focusing on packing pattern of the atom. (b) exact relative location of atom in crystal is determined.
- NMR technique → In this technique, powder sample must be rotated at a special angle with respect to magnetic field.
- FTIR technique → It has been used to quantify binary mixtures of polymorphs.
- Dilatometry → Measure change in volume caused by thermal or chemical effect.
- Microcalorimetry → Used to characterize thermodynamic properties of different molecules.
- Thermal methods → (a) DSC[Differential scanning calorimetry] (b) DTA[Differential thermal analysis] (c) TGA [thermal gravimetric analysis]
- Melting point determination

Properties of polymorphs

- Polymorphs show the same properties in liquid or gaseous state but they behave differently in solid state.
- Polymorphs differ from each other with respect to physical properties like

☐ Melting and sublimation temperature		Vapour pressure
☐ Solubility and dissolution rate		Stability
☐ Optical and electrical properties		Crystal habit
☐ Hygroscopicity	Heat capacity	Solid–state reactions
☐ Conductivity		Compression characteristics

Crystal

A crystal is a solid in which the constituent atoms, molecules, or ions are packed in a regularly ordered, repeating pattern extending in all three spatial dimensions.

Classification of chemical compound

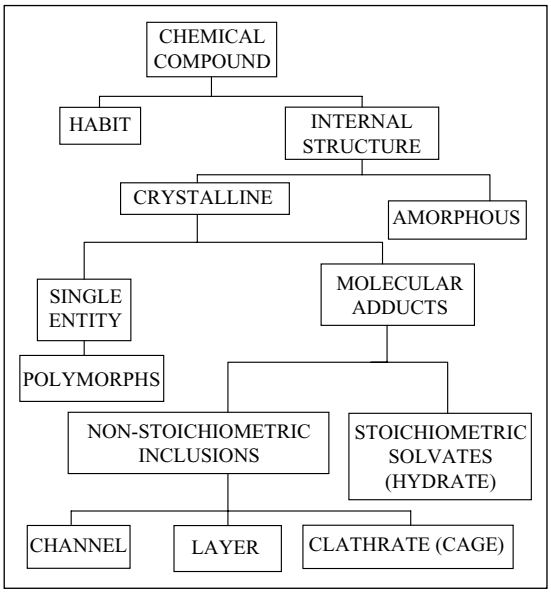


Figure 3.1 Classification of chemical compound

Amorphous Compound

Amorphous forms are usually of higher thermodynamic energy than corresponding crystalline forms, so solubilities as well as dissolution rates are generally greater but due to high energy, they are unstable and tend to revert back to a stable form. This is particularly true for formulations like aqueous suspensions.

In case of amorphous novobiocin suspension, it slowly converts to a crystalline form and thus becomes less and less absorbable and finally loses therapeutic effect. Thus a search for additives was begun to prevent such condition.

Characterization of amorphous solids

The only positive way to differentiate amorphous from crystalline solids is by means of **X-ray powder diffraction**. This technique gives very diffuse reflections of amorphous

compounds, where the *d* distances, the distance between parallel planes in which the atoms of the crystal line cannot be determined as is done with crystalline solids.

Clathrates

A clathrate is a single-phased solid with two distinct components: the host and the guest. The guest is retained in the closed cavities provided by the crystalline structure of the host. Thus it is a non-stoichiometric molecular adduct. The major classes of clathrates are hydroquinone clathrates, water clathrates, phenol clathrates etc.

Pharmaceutical applications of clathrates

Purification Benzene was purified of one of its usual contaminants thiophene by clathrate formation. Although both form clathrates with monoamine nickel cyanide, benzene is more firmly held in cage structure, so it is preferentially clathrated and separated from solution by filtration.

Separation of rare gases Argon is separated from neon by adjusting the pressure conditions in which hydroquinone-argon clathrate is formed, while neon does not form clathrate.

Separation of optical isomers Inclusion complexing substance that will separate optical isomers is tri-o-thymotide.

Storage of inert gases They are used for convenient storage of inert gases like hydroquinone or to introduce such gases into fairly inaccessible locations. The gas can be released by heating or dissolving the clathrates.

Mode of action of anesthetics Non-hydrogen bonding anesthetics work primarily due to clathrate formation of molecules of anesthetic agent with water contained in the neurons and around the neural network.

Comparison of Crystalline and Amorphous Forms

Amorphous form	Crystalline form
Least ductile (highest indentation hardness value)	More ductile (low indentation hardness value)
Form compacts with lowest tensile strength	Form compacts with high tensile strength
Compacts have high brittleness value	Compacts have low brittleness value
Require lower compression stress to form compacts	Higher compression stress required
Randomly arranged molecules	Fixed molecular order
No melting points	A distinct melting point
Isotropicity (i.e., properties are same in all directions)	Anisotropicity (i.e., their properties are not same in all directions except cubic crystal)

Comparison of solubility of crystal, solvate and hydrate

- Amorphous form is always more soluble than a corresponding crystalline form.
- The dissolution rates of hydrates are less than corresponding anhydrous crystalline form. E.g., gluthethimide, theophylline, caffeine, succinyl sulphathiazole, Phenobarbital.
- The dissolution rates for organic solvates are higher than corresponding pure crystalline forms. E.g., 1, 4-dioxane solvate of Nifedipine shows better solubility than di-hydrate form.

Importance of Crystallinity in Preformulation Studies

Effect on solubility and bioavailability

- The antibiotic, novobiocin is essentially inactive when administered in crystalline form, but in amorphous form, absorption from G.I.T proceeds rapidly with good therapeutic response. Thus due to difference in solubility amorphous novobiocin is 10 times more bioavailable.
- The hormone insulin presents another striking example of different degree of activity that may result from use of different physical forms of it.

Insulin is a protein that forms an extremely insoluble zinc-insulin complex when combined with zinc in presence of acetate buffer. Depending upon the pH of acetate buffer sol, the complex may be an amorphous ppt or crystalline material.

Type of insulin	Form of insulin	Onset of action	Duration of action
Prompt insulin-zinc suspension (semilente)	Amorphous	fast	Short
Extended insulin-zinc suspension (ultralente)	Crystalline	slow	Long
Insulin-zinc suspension (lente)	30% amorphous + 70% crystalline	fast	Intermediate

- The more soluble form of chloramphenicol palmitate, form B shows greater bioavailability after oral administration than least soluble form A.
- Similarly in chloro tetracycline hydrochloride, βform is more soluble and bioavailable than corresponding α form.

Chemical stability

- In other instances, crystalline forms of drugs may be used because of greater stability than corresponding amorphous forms.

E.g., crystalline forms of penicillin G as potassium or sodium salt are more stable.

Solubility Analysis

Aqueous solubility

- A drug must possess aqueous solubility for therapeutic efficacy in physiological pH range of 1 to 8 at 37 ºC.
- Poor solubility (<10mg/ml) may result into bioabsorption problems.
- If solubility of drug is less than 1 mg/ml, it indicates the need for a salt, particularly if the drug will be formulated as a tablet or capsule.
- In the range 1–10 mg/ml, serious consideration should be given to salt formation.

There are **two fundamental properties** mandatory for a new compound.

(a) Intrinsic Solubility (C_o).
(b) Ionization Constant (pK_a).

Intrinsic solubility (C_o)

The solubility of weakly acidic and weakly basic drug as a function of pH can be predicted with the help of eqn.

$$S=S_o\{1 + (K_1/[H^+])\}$$ ---------- for weak acids.

$$S=S_o\{1 + ([H^+]/K_2)\}$$ ---------- for weak bases.

Where, S = Solubility at given pH

S_o = Intrinsic solubility of the neutral form.

K_1 = Dissociation constant of weak acid.

K_2= Dissociation constant of weak base.

The intrinsic solubility should ideally be measured at 2 temperatures:

(a) 4ºC → to ensure physical and chemical stability.
(b) 37ºC → to support biopharmaceutical evaluation.

Method to determine solubility

1. Equilibrium solubility method.
   - An excess of drug is placed in solvent and shaken at constant temperature over a prolonged time (24–72 h.) till equilibrium is attained.
     ↓
   - Filtration is done.
     ↓
   - Analyse the supernant via HPLC to determine degree of solubility.
2. Turbidometric solubility method.
3. Nephlometric solubility method.
4. Ultra-filtration LC/MS solubility method.
5. Direct solubility method.

Ionization constant (pK_a)

The unionized forms are more lipids soluble and more rapidly absorbed from G.I.T.

The relative conc. of unionized and ionized form of weakly acidic or basic drug in a solution at a given pH can be calculated using the **Henderson-Hasselbalch equation.**

$pH = pK_a + \log$ [unionized form]/[ionized form] —for weak bases.

$pH = pK_a + \log$ [ionized form]/[unionized form] —for weak acids**.**

Uses of these equations

1. To determine pK_a.
2. To predict solubility at any pH provided that C_o and pK_a are known.
3. To facilitate the selection of suitable salt forming compounds.
4. It predicts the solubility and pH properties of the salts.

Limitation

To fail outside the pH limits of 4-10 or when the solution is very dilute.

Method to determine pK_a

1. Potentiometric method.
2. Conductivity method.
3. Dissolution rate method.
4. Liquid–Liquid partition method.
5. Spectrophotometric method.

Note

75% of all drugs are weak bases, 25% are weak acids and only, 5% are non-ionic Amphoteric.

SOLUBILIZATION

Many different approaches have been developed to improve drug solubility:

1. Micronization

E.g., Griseofulvin shows increased solubility by reducing particle size.

2. Change in pH

E.g., Solubility of nimesulide increases as pH is increased.

E.g., Etoposide formulation is difficult because of its poor solubility and labile chemical stability so its most stable formulation is Etoposide loaded emulsion (ELE) at pH 4–5.

3. Cosolvency

Addition of a water miscible solvent can often improve the solubility of a weak electrolyte or non-polar compound in water by altering the polarity of the solvent.

The choice of suitable cosolvent is limited for pharmaceutical use because of possible toxicity and irritancy.

Ideally, suitable blends should possess values of dielectric constant between 25–80.

Commonly used cosolvents are ethanol, sorbitol, glycerin, propylene glycol, dimethylacetamide (DMA), DMSO, etc.

4. Solubilization by surfactant

E.g., Gelucire 44/14 is a surface active excipient that can solubilize poorly soluble drugs.

E.g., Anionic and cationic surfactants exhibited dramatically higher solubilization for gliclazide, while nonionic surfactants showed significantly lower solubilizing ability.

5. Complexation

E.g., The complexation of iodine with 10-15% polyvinylpyrolidone (PVP) can improve aqueous solubility of active agent.

6. Formation of inclusion compound

E.g., The aqueous solubility and chemical stability of Quercetin can be improved via Complexation with β-cyclodextrin.

E.g., The enhancement of solubilization increased 300 fold for Nimodipine at a polymer concentration 10% by use of water soluble dendrimer based on polyglycerol.

7. Chemical modification

Many poorly soluble drugs are modified into salt form (water soluble).

(8) Use of metastable polymorphs

E.g., B form of Chloramphenicol palmitate is more water soluble than A and C forms.

Partition coefficient

A measurement of drug lipophilicity and indication of its ability to cross cell membranes is oil/water partition coefficient in systems such as octanol/water and chloroform/water.

It is defined as ratio of un-ionized drug distributed between the organic and aqueous phases at equilibrium.

$$P_{0/w} = (C_{oil}/C_{water})_{equilibrium}$$

- When a solute is added to two immiscible liquids it will distribute itself between the two phases in a fixed ratio, which is referred to as partition or distribution coefficient.
- It is independent of concentration of dilute solution of given solute species.
- Various organic solvents used in determination of partition coefficient include chloroform, ether, amyl acetate, etc.
- Solubility parameter of n-octanol ($\delta = 10.24$) lies mid-

way in the range for major drugs (δ = 8–12). Thus in formulation development the n-octanol-water partition coefficient is commonly used.

- P= (Conc. of drug in octanol)/(Conc. of drug in water)—For unionizable drugs.
- P= (Conc. of drug in octanol)/(1-α)*(Conc. of drug in water)—For ionizable drugs.

  Where

  α = degree of ionization.
- P > 1 ⇨ Lipophilic drug.
- P < 1 ⇨ Hydrophilic drug.
- The value of P at which maximum activity of controlled release dosage forms is observed is approximately 1000:1 in octanol/water.

Methods to determine P

(a) Shake Flask Method.
(b) Chromatographic Method (TLC, HPLC).
(c) Counter Current and Filter Probe method.

Thermal effect

- Effect of temperature on the solubility of drug can be determined by measuring heat of solution. (ΔH_s).

$$\ln S = -\Delta H_s/R*T + C.$$

Where,

S = Molar solubility at temperature T (ºK).

R = Gas constant.

- Heat of solution represents the heat released or absorbed when a mole of solute is dissolved in a large quantity of solvent.
- Mostly solution process is endothermic (ΔH_s = +ve) and thus increasing the solution temperature increase the drug solubility.
- Typical temperature range should include 5ºC, 25ºC, 37ºC and 50ºC.

- **Importance:** Determination of temperature effect on solubility helps in predicting storage condition and dosage form designing.

Common ion effect

- Addition of common ion reduces the solubility of slightly soluble electrolyte.
- The "salting out" results from the removal of water molecules as solvent due to the competing hydration of other ions.
- So weakly basic drug which are given as HCl salts have decreased solubility in acidic solution.

E.g., Chlortetracycline, Papaverine, Bromhexine, Triamterene, etc.

The reverse process "**salting in"** arises with larger anions. (E.g., Benzoate, salicylate) which can open the water structure.

These hydrotropes increase the solubility of poorly water soluble compounds.

To identify a common ion interaction, the IDR (Intrinsic dissolution rate) of HCl salt should be compared between

(a) Water and water containing 1.2% W/V NaCl.
(b) 0.05 M HCl and 0.9% NaCl in 0.05 M HCl.

Both saline media contains 0.2 M Cl^- which is typically encountered in fluids *in vivo.*

Dissolution

- The absorption of solid drugs administered orally can be understood by following flowchart.

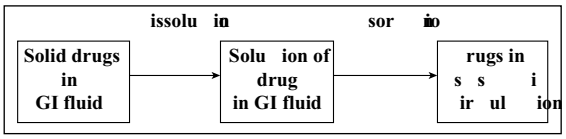


Figure 3.2 Dissolution and absorption process after oral administration

- In many instances, dissolution rate in the fluids at the absorption site is the rate limiting step in the absorption process.
- Dissolution rate can affect
  - Onset of action
  - Intensity of action
  - Duration of response
  - Control the overall Bioavailability of drug form
- Dissolution is considered to be of two types:

Intrinsic dissolution

- The dissolution rate of solid in its own solution is adequately described by **Noyes-Whitney equation:**

$$dC/dt = AD (C_s - C)/hv$$

Where,

dC/dt = Dissolution rate

A = Surface area of dissolving solid

D = Diffusion coefficient

C = Concentration of drug in solution

h = Thickness of diffusion layer (at the solid-liquid interface)

v = Volume of dissolution medium

C_s = Solute concentration in the diffusion layer

- This equation helps to the preformulation scientist in predicting if absorption would be dissolution rate limited or not.
- Method to determine intrinsic dissolution

Rotating disk method or Wood's apparatus

This method allows for the determination of dissolution from constant surface area, obtained by compressing powder into a disc of known area with a die-punch apparatus.

Particulate dissolution

- This method determines the dissolution of solids at different surface area.
- A weighed amount of powder sample from a particular sieve fraction is introduced in the dissolution medium. Agitation is usually provided by a constant speed propeller.
- It is used to study the influence on dissolution of particle size, surface area and mixing with excipients.

Stability Analysis

Development of a drug substance into a suitable dosage form requires the Preformulation stability studies of drug under the following categories:

1. Solid state stability
2. Solution state stability

Solid state stability

Solid state reactions are much slower and more difficult to interpret than solution state reactions because of reduced number of molecular contacts between drug and excipient molecules and occurrence of multiple reactions.

Techniques for solid state stability studies

- Solid State NMR Spectroscopy (SSNMR)
- Powder X-ray diffraction (PXRD)
- Fourier Transform IR (FTIR)
- Raman Spectroscopy
- Differential Scanning Calorimetry (DSC)
- Thermo gravimetric Analysis (TGA)
- Dynamic Vapour Sorption (DVS)

Solution state stability

The primary objective is the identification of conditions necessary to form a solution.

These studies include the effects of

- pH
- Temperature
- Light
- Oxygen
- Cosolvent
- Ionic strength

Stress conditions used in preformulation stability assessment

Test	Condition
SOLID	
Heat (°C)	4, 20, 30, 40, 40/75% RH, 50 and 75.
Moisture uptake	30,40,60,75 and 90% RH at RT.
Physical stress	Ball milling.
Aqueous Solution	
pH	1,3,7,9 and 11 at RT and 37°C. Reflux in 1M HCl and 1M NaOH.
Light	UV (254 and 366 nm) and Visible (south facing window) at RT.
Oxidation	Sparing with oxygen at RT, UV may accelerate breakdown.

Chemical Characteristics

Oxidation

- It is a very common pathway for drug degradation in liquid and solid formulation.

  Oxidation occurs in two ways:

1. Auto oxidation
2. Free radical chain process

Auto oxidation

- It is defined as a reaction of any material with molecular oxygen which produces free radicals by hemolytic bond fission of a covalent bond.
- These radicals are highly unsaturated and readily take electron from other substance causing oxidation.
- For auto oxidation to occur in solid molecular oxygen must be able to diffuse through the crystal lattice to liable sites. Hence crystal morphology and packing are important parameters for determining oxidation kinetics.

Free radical chain process

(a) **Initiation**

$$RH \xrightarrow[\text{Light, Heat}]{\text{Activation}} R^{\bullet} + H^{\bullet}$$

(b) **Propagation**

$$R^{\bullet} + O_2 \rightarrow RO_2^{\bullet}$$

$$RO_2^{\bullet} + RH \rightarrow RCOOH + R^{\bullet}$$

(c) **Hydroperoxide decomposition**

$$RCOOH \rightarrow RO^{\bullet} + OH^{\bullet}$$

(d) **Termination**

$$RO_2^{\bullet} + X \rightarrow \text{Inactive product}$$

$$RO_2 + RO_2 \rightarrow \text{Inactive product}$$

Factors affecting oxidation process

1. Oxygen concentration
2. Light
3. Heavy metals particularly those having two or more valence state. (E.g., Copper, iron, nickel, cobalt)
4. Hydrogen and hydroxyl ion
5. Temperature

Antioxidant

(a) Reducing agent
(b) Chain inhibitors of radical induced decomposition

Antioxidant	
↓ **Oil Soluble** ↓	↓ **Water Soluble** ↓
• Free radical acceptor and inhibit free radical chain process.	• Oxidized itself and prevent oxidation of drug.
Examples	
Hydroquinone	Sodium metabisulphate
Propyl gallate	Sodium bisulphite
Butylated Hydroxy Anisole (BHA)	Acetyl cysteine, Ascorbic acid
Butylated Hydroxy Toluene (BHT)	Sodium thiosulfate, Sulphur dioxide
Lecithin	Thioglycolic acid
α–Tocopherol	Thioglycerol

Chelating agent

- It forms complexes with trace amount of heavy metal ion and inactivate their catalysing activity.
  E.g., EDTA, Citric acid,Tartaric acid.

Hydrolysis

- It involves nucleophilic attack of labile groups. Lactam > Ester > Amide > Imide.
- When this attack is by a solvent other than water then it is known as **solvolysis.**

Photolysis

Mechanism of photodecomposition

- Electronic configuration of drug overlaps with spectrum of sunlight or any artificial light, and thereby, energy is absorbed by electron and it goes to the excited state.
- They are unstable and release the acquired energy and come to the ground state and decompose the drug.
- **Photosensitization** means molecule or excipient which absorbs energy but do not participate themselves directly in the reaction but pass the energy to other that will cause cellular damage by inducing radical formation.

Photosensitizer	
↓ **Energy transfer** ↓	↓ **Electron transfer** ↓
Convert oxygen from its ground state to singlet excited state.	Generate superoxide molecule, which is an anion radical and acts as a powerful oxidizing agent.

Photodecomposition pathway

1. **N-Dealkylation**
   E.g., Diphenhydramine, Chloroquine, Methotrexate.
2. **Dehalogenation**
   E.g., Chlorpropamide, Furosemide.
3. **Dehydrogenation of Ca^{++} channel blocker**
   E.g., Solution of Nifedipine → Nitrosophenylpyridine (with loss of water)
   Rapidly yellow colour → Brown
4. **Decarboxylation in anti-inflammatory agents**
   E.g., Naproxen, Flurbiprofen, Benzoxaprofen.
5. **Oxidation**
   E.g., Chlorpromazine and other phenothiazines give N- and S-oxides in the presence of sunlight.
6. **Isomerization and cyclization**
   E.g., Noradrenaline, Doxepine
7. **Rearrangement**
   E.g., Metronidazole → Oxidiazine → Yellow colour

Racemization

- The interconversion from one isomer to another can lead to different Pharmacokinetic properties (ADME) as well as different Pharmacological and toxicological effect.

- E.g., L-epinephrine is 15 to 20 times more active than D-form, while activity of racemic mixture is just one half of the L-form.
- It follows first order kinetics.
- It depends on temperature, solvent, catalyst and presence or absence of light.

Polymerization

- It is a continuous reaction between molecules.
- More than one monomer reacts to form a polymer.
- E.g., Darkening of glucose solution is attributed to polymerization of breakdown product [5- (hydroxyl methyl) furfural].
- E.g., Polymerization of HCHO to Para-HCHO which crystallizes out from the solution.

Isomerization

- It is the process involving change of one structure to another having same empirical formula but different properties in one or more respects.
- Its occurrence is rare.

Examples

1. Tetracycline and its derivatives can undergo reversible isomerization at pH range 2–6.
2. Trans-cis Isomerization of Amphotericin B.
3. Isomerization of tetrahydrouridine.

Decarboxylation

- Evolution of CO_2 gas from –COOH group containing drugs.
- E.g., Solid PAS undergoes pyrolytic degradation to m-aminophenol and CO_2.
- The reaction which follows 1st order kinetics is highly pH dependent and is catalysed by hydronium ions.

TABLET

Types of Tablets

According to drug release rate from the tablet (USP classification):

A. Immediate-Release Tablet

The tablet is intended to be released rapidly after administration, or the tablet is dissolved and administered as solution. It is the most common type and includes:

1. Disintegrating tablet (conventional or plain tablet)
2. Chewable tablets
3. Effervescent tablets
4. Sublingual and Buccal tablets
5. Lozenges

B. Modified-Release Tablet

They have release features based on; time, course or location. They must be swallowed intact.

Disintegrating tablet (conventional or plain tablet)

Disintegrating tablet is the most common type of tablet that is intended to be swallowed and to release the drug in a relatively short time thereafter, by disintegration and dissolution (fast and complete drug release in vivo).

It includes normally the following type of excipients: filler (with low dose drug), disintegrant, binder, glidant, lubricant and anti-adherent.

Chewable tablets

Chewable tablets are to be chewed and thus mechanically disintegrated in the mouth, so that **no disintegrant is included in its composition**. Flavouring, sweetening and colouring agents are important.

Sorbitol and **mannitol** are common examples of fillers in chewable tablets, (mannitol has negative heat of solution which results in cooling effect and also has sweetening action as previously mentioned under mannitol as a filler).

Advantages of chewable tablets

- Provide quick and complete disintegration of the tablet and thus obtain a rapid drug effect after swallowing and dissolution.
- Easy administration, especially for infants and elderly people.
- Could be administered when water is not available.

Examples for chewable tablets are:

1. Chewable Aspirin tablets
2. Chewable Antacid tablets

Effervescent tablets

Effervescent tablets are dropped into a glass of water before administration during which CO_2 is liberated. This facilitates tablet disintegration and drug dissolution; the tablet disintegration should be complete within few minutes. (Effervescence is a special mechanism for disintegration).

CO_2 is created by the reaction between carbonate or bicarbonate and a weak acid such as citric acid or tartaric acid.

Advantages of effervescent tablets

- To obtain rapid drug action, for example, analgesics and antacids.
  Effervescent Paracetamol tablet (analgesic) and effervescent antacid tablets
- To facilitate drug intake, for example, Vitamin C effervescent tablets

Effervescent tablets often include a flavour and a colourant. Effervescent tablets are prepared by direct compression or dry granulation. Effervescent tablets should be protected from moisture, so that a special package is needed; each tablet is completely covered with aluminum foil and kept in a water-proof container, often including a desiccant. Effervescent tablets may be packed in blister packs.

Sublingual and buccal tablets

They are used for drug release in mouth followed by systemic uptake of the drug. A rapid systemic drug effect can thus be obtained without first-path liver metabolism, because the drug diffuses into the blood, directly through tissues under the tongue in case of sublingual tablets and through oral mucosa in case of buccal tablets. Sublingual tablets are placed under the tongue.

- Examples
  1. Nitroglycerin sublingual tablet; it exerts its action within two minutes for rapid relief of "Angina pectoris" attack, because the sublingual area is rich in blood supply. Nitroglycerine suffers from first-pass metabolism if taken orally.
  2. Vitamin B12 Sublingual tablet

Buccal tablets are placed in the side of the cheek for absorption through oral mucosa.

Lozenges

They are tablets that dissolve slowly in the mouth and so release the drug dissolved in the saliva.

Lozenges may be used for local medications in the mouth or throat, e.g., local anesthetics, antiseptics and antibiotics and systemic drug uptake.

Compressed lozenges are made by using tablet machines with large and flat punches, high pressure is applied to produce hard tablets, so that they dissolve slowly in the mouth.

No disintegrant is included in compressed lozenges composition. Other additives (binder and filler) must have pleasant taste or feeling during dissolution. Common binder used in compressed lozenges is gelatin; common fillers are (Sorbitol, mannitol and glucose). Bradoral® Compressed lozenges, for the treatment of sore throat.

FORMULATION OF TABLETS

Types of Excipients

Lubricants

- Lubricants are the agents that act by reducing friction by interposing an intermediate layer between the tablet constituents and the die wall during compression and ejection.
- Solid lubricants, act by boundary mechanism, results from the adherence of the polar portions of molecules with long carbon chains to the metal surfaces to the die wall. Magnesium stearate is an example of boundary lubricant.
- Other is hydrodynamic mechanism i.e., fluid lubrication where two moving surfaces are separated by a finite and continuous layer of fluid lubricant. Since adherence of solid lubricants to the die wall is more than that of fluid lubricants, solid lubricants are more effective and more frequently used.

Classification of Lubricants

List of insoluble lubricants

Insoluble Lubricants	Concentration	Comments
Stearate (Magnesium Stearate, Calcium Stearate, Sodium stearate)	0.25 – 1	Reduce tablet strength; prolong disintegration; widely used.
Talc	1 – 2	Insoluble but not hydrophobic; moderately effective.
Glyceryl di behenate (Compritol® 888)	1 – 5	Both lubricant and binder;
Liquid paraffin	Up to 5	Dispersion problem; inferior to stearate

List of soluble lubricants

Water Soluble Lubricants	Concentrationrange (%W/W)
Boric acid	1
Sodium benzoate	5
Sodium oleate	5
Sodium acetate	5
Sodium Lauryl sulfate (SLS)	1 – 5
Magnesium lauryl sulfate (MLS)	1 – 2

Antiadherents

- Anti adherents prevent sticking to punches and die walls.
- Talc, magnesium stearate and corn starch have excellent anti adherent properties. Vegan had suggested that silicon oil can be used as anti adherent.

List of antiadherents

Antiadherent	Range (%W/W)	Comment
Talc	1 – 5	Lubricant with excellent antiadherents properties
Cornstarch	3 – 10	Lubricant with excellent antiadherents properties
Colloidal silica	0.1 – 0.5	Does not give satisfactory results due to small surface area. Cab-O-Sil® and Syloid®
DL-Leucine	3 – 10	Water soluble lubricant; excellent anti-adherents properties
Sodium lauryl sulfate	<1	Antiadherents with water soluble lubricant
Stearates	<1	Antiadherents with water insoluble lubricant

Glidants

- Glidants are added to the formulation to improve the flow properties of the material which is to be fed into the die cavity and aid in particle rearrangement within the die during the early stages of compression.
- Starch is a popular glidant because it has additional value of disintegrant. Concentration of starch is common up to 10%.
- Talc is a glidant which is superior to starch; its concentration should be limited because it has retardant effect on dissolution-disintegration profile.
- Silaceous material like colloidal silica i.e., syloid, pyrogenic silica (0.25%), hydrated sodium silio aluminate (0.75%) are also successfully used to induce flow.
- Glidants act by interposing their particles between those of material and lower the overall inter-particulate friction of the system by virtue of their reduced adhesive tendencies. Similar to lubricants, they are required at the surface of feed particles and they should be in fine state of division and appropriately incorporated in the mixture.

Binders

- Binders or adhesives are the substances that promote cohesiveness. It is utilized for converting powder into granules through a process known as granulation.
- Flow property/fluidity is required to produce tablets of a consistent weight and uniform strength. Compressibility is required to form a stable, intact compact mass when pressure is applied.
- These two objectives are obtained by adding binder to tablet formulation and then proceeding for granulation process.

Classification of binders

Sugars	Natural Binders	Synthetic/Semisynthetic Polymer
Sucrose	Acacia	Methyl Cellulose
Liquid glucose	Tragacanth	Ethyl Cellulose
	Gelatin	Hydroxy Propyl Methyl Cellulose (HPMC)
	Starch Paste	Hydroxy Propyl Cellulose
	Pregelatinized Starch	Sodium Carboxy Methyl Cellulose
	Alginic Acid	Polyvinyl Pyrrolidone (PVP)
	Cellulose	Polyethylene Glycol (PEG)
		Polyvinyl Alcohols, Polymethacrylates

Characteristics of commonly used binders

Binder	Specified Concentration	Comments
Starch Paste	5–25%w/w	• Freshly prepared starch paste is used as a binder.
Pregelatinized Starch (PGS) [Partially and Fully PGS]	5–10%w/w (Direct Compression) 5–75%w/w (Wet Granulation)	• It contains 5% free amylose,15% free amylopectin and 80% unmodified starch. • Obtained from maize, potato or rice starch. • It is multifunctional excipient used as a tablet binder, diluent, disintegrant and flow aid.
Hydroxypropyl Methyl Cellulose (HPMC)	2–5%w/w	• Used as a binder in either wet or dry granulation processes.
Polyvinyl Pyrrolidone (PVP)	0.5–5%w/w	• Soluble in both water and alcohol. • Used in wet granulation process. • Valuable binder for chewable tablets.
Polyethylene Glycol (PEG) 6000	10–15%w/w	• Used as a meltable binder.

Direct Compression (DC) Binders

Commonly used dc binders

DC Binder	Class
Avicel (PH 101)	MCC[a]
SMCC (50)	SMCC[b]
UNI-PURE(DW)	Partially PGS[c]
UNI-PURE (LD)	Low density starch
DC Lactose	DC lactose anhydrous
DI TAB	DC-DCPD[d]

(a) Microcrystalline Cellulose, (b) Silicified Microcrystalline Cellulose, (c) Pregelatinized Starch, (d) Dibasic Calcium Phosphate Dihydrate)

Diluents (Filler)

1. To provide improved cohesion
2. To allow direct compression manufacturing
3. To enhance flow
4. To adjust weight of tablet as per die capacity

Classification of diluents

Tablet diluents or fillers can be divided into the following categories:

- Organic materials–Carbohydrate and modified carbohydrates.
- Inorganic materials–Calcium phosphates and others.
- Co-processed Diluents.

Insoluble Tablet Fillers or Diluents	Soluble Tablet Fillers or Diluents
Starch Powdered cellulose Microcrystalline cellulose Calcium phosphates, etc.	Lactose Sucrose Mannitol Sorbitol, etc.

α-Lactose monohydrate (hydrous)	• Lactose monohydrate is not directly compressible • Undergoes discolouration when formulated with amines and alkaline materials (i.e., **Browning or maillard reaction**).
Lactose spray dried	• It is directly compressible diluent. • It exhibits free flowing characteristics. • It is more prone to darkening in the presence of excess moisture, amines and other compounds due to the presence of a furfuraldehyde.
Lactose anhydrous	• Lactose anhydrous is directly compressible diluents. • It does not exhibit free flowing property. • It does not undergo a maillard reaction to the extent shown by spray dried lactose
Sucrose	• It is a calorie contributor and is carcinogenic.

Mannitol	• Mannitol a sugar alcohol is an optical isomer of Sorbitol. • It is widely used in chewable tablets because of its negative heat of solution, its slow solubility and its mild cooling sensation in mouth. • It can be used in vitamin formulation, where moisture sensitivity may create a problem. • It is comparatively non hygroscopic. • It possesses low caloric value and is non-carcinogenic.
Sorbitol	• It is highly compressible diluent and is water soluble. • It possesses low caloric value and is non-carcinogenic
Microcrystalline cellulose	• Microcrystalline cellulose (MCC) is highly compressible and is perhaps the most widely used direct-compression tablet diluent. • Its trade name is Avicel and available in 2 grades PH 101 (Powder form) and PH 102 (Granule form).
Calcium phosphates	• Dibasic calcium phosphate is available commercially under the trade name Di-Tab® and Emcompress®.

Co-processed diluents

Co-processing means combining two or more materials by an appropriate process. The products so formed are physically modified in such a special way that they do not lose their chemical structure and stability. The composite particles or co-processed excipients are introduced in order to provide better tableting properties than a single substance or the physical mixture.

List of co-processed excipients

Trade Name	Description
Fast Flo lactose®	• It is spray processed lactose which is a mixture of crystalline α-lactose monohydrate and amorphous lactose.
Microcellac®	• 75% lactose and 25% MCC (MicroCrystalline Cellulose)
Ludipress®	• 93% α-lactose monohydrate, 3.5% polyvinylpyrrolidone, and 3.5% crospovidone.
Nu-Tab®	• Sucrose 95–97%, invert sugar 3–4% and magnesium stearate 0.5%
Di-Pac®	• Sucrose 97% and modified dextrins 3%
Sugartab®	• Sucrose 90–93% and invert sugar 7–10%.
Emdex®	• Dextrose 93–99% and maltose 1–7%
Cal-Tab®	• Calcium sulfate 93% and vegetable gum 7%
Cal-Carb®	• Calcium carbonate 95% and maltodextrins 5%

Disintegrants

The objectives behind addition of disintegrants are to increase surface area of the tablet fragments and to overcome cohesive forces that keep particles together in a tablet.

Mechanism of tablet disintegration

The tablet breaks to primary particles by one or more of the mechanisms listed below:

I. Capillary action
II. Swelling
III. Heat of wetting
IV. Particle repulsive forces
V. Deformation
VI. Release of gases
VII. Enzymatic action

Disintegrants	Concentration In Granules (%W/W)	Special Comments
Starch USP	5–20	Higher amount is required, poorly compressible
Starch 1500	5–15	–
Avicel® (PH 101, PH 102)	10–20	Lubricant properties and directly compressible
Alginic acid	1–5	Acts by swelling
Na alginate	2.5–10	Acts by swelling
Explotab®	2–8	Sodium starch glycolate, superdisintegrant.
Polyplasdone® (XL)	0.5–5	Crosslinked PVP

Disintegrants	Concentration In Granules (%W/W)	Special Comments
Amberlite® (IPR 88)	0.5–5	Ion exchange resin
Methyl cellulose, Na CMC, HPMC	5–10	–
AC-Di-Sol® (crosscarmellose sodium)	1–3 % in Direct Compression	2-4% in Wet granulation
Carbon dioxide (CO_2)	_	Created in situ in effervescent tablet

Superdisintegrants

- Superdisintegrants which are effective at low concentration and have greater disintegrating efficiency and they are more effective intra-granularly. But have one drawback that it is hygroscopic therefore not used with moisture sensitive drugs.
- Superdisintegrants act by swelling and due to swelling pressure that is exerted causes the tablet to burst or the accelerated absorption of water leading to an enormous increase in the volume of granules to promote disintegration.

Crosscarmellose®	Ac-Di-Sol®	Primellose®	Solutab®
Crosspovidone	Vivasol®	Kollidon®	Polyplasdone®
Sodium starch glycolate	Explotab®	Primogel®	Alginic acid NF

Miscellaneous Excipients

Wetting agents

- Wetting agents in tablet formulation aid water uptake and thereby enhancing disintegration and assisting in drug dissolution.
- Incorporation of anionic surfactant like Sodium Lauryl Sulphate (SLS) is known to enhance the dissolution. It has been established that SLS improves permeation of drug through biological membrane since it destroys the path through which drug has to pass and thus minimizing the path length for the drug to travel.
- Wetting agents are mainly added when hydrophobic drug is to be formulated into tablet. SLS, Sodium di-isobutylsulfosuccinate are used as wetting agents in tablet formulation.

Dissolution retardants

- Dissolution retardants are incorporated into tablet formulation only when controlled release of drug is required.
- Waxy materials like stearic acid and their esters can be used as dissolution retardants.

Dissolution enhancers

- They are the agents that alter the molecular forces between ingredients to enhance the dissolution of solute in the solvent.
- Fructose, Povidone, Surfactants are used as dissolution enhancer.

Adsorbents

- Adsorbents are the agents that can retain large quantities of liquids.
- Most commonly used adsorbents in pharmaceuticals are anhydrous calcium phosphate, starch, magnesium carbonate, bentonite, kaolin, magnesium silicate, magnesium oxide and silicon dioxide. Generally, the liquid to be adsorbed is first mixed with the adsorbent prior to incorporation into the formulation.
- Silicon dioxide when added can play as both glidant and an adsorbent role in the formula.

Buffers

- Buffers are added to maintain a required pH since a change in pH may cause significant alteration in stability.
- Most commonly used buffering agent in tablet formulation includes sodium bicarbonate, calcium carbonate, and sodium citrate.

Coatings

- Tablet coatings protect tablet ingredients from deterioration by moisture in the air and make large or unpleasant-tasting tablets easier to swallow.
- For most coated tablets, a hydroxypropylmethylcellulose (HPMC) film coating is used which is free of sugar and potential allergens.
- Occasionally, other coating materials are used, for example synthetic polymers, shellac, corn protein zein or other polysaccharides.
- Capsules are coated with gelatin.

Types of flavours

Bitter	Mint, Cherry or Anise
Salty	Peach, Apricot or Liquorice
Sour	Raspberry or Liquorice
Excessively Sweet	Vanilla

Preservatives

- **Antioxidants** Like Vitamin A, Vitamin E, Vitamin C, Retinyl Palmitate
- **The Amino Acids** Cysteine And Methionine
- **Citric Acid And Sodium Citrate**
- **Synthetic Preservatives** like Methyl Paraben And Propyl Paraben

Chelating agents

- Chelating agents tend to form complexes with trace amount of heavy metal ions inactivating their catalytic activity in the oxidation of medicaments.
- Ethylene diamine tetra acetic acid and its salts, Dihydroxy Ethyl Glycine, Citric Acid and Tartaric Acid are most commonly used chelators.

Colourants

- Colourants neither contribute to therapeutic activity nor do they improve product bioavailability or stability but are incorporated into tablets for purposes like
- Most widely used colourants are dyes and lakes which are FD & C and D & C approved.
- Reflectance Spectrophotometry, Tristimulus Colourimetric Measurements and Micro reflectance Photometer used to measure the colour uniformity and gloss on a tablet surface.

Fd And C Colour	Common Name
Red 3	Erythrosine
Red 40	Allura red AC
Yellow 5	Tartrazine
Yellow 6	Sunset Yellow
Blue 1	Brilliant Blue
Blue 2	Indigotine
Green 3	Fast Green

Sweeteners

- Sweeteners are added primarily to chewable tablets.
- Saccharin has a bitter aftertaste and is carcinogenic. Cyclamate is carcinogenic.
- Aspartame has lack of stability in the presence of moisture.
- Sweetness order–Compared to Sucrose

Lactose (16 times), Dextrose (74 times) , Fructose (173 times), Mannitol(174), Aspartame (200), Saccharin (500).

Types of sweetners

Natural Sweeteners	Artificial Sweeteners
Mannitol Lactose Sucrose Dextrose	Saccharin Cyclamate Aspartame

Problems in Tablet Manufacturing

I. Tableting Process
II. Excipient
III. Machine

The defects related to tableting process are as follows:

1. **Capping:** It is due air-entrapment in the granular material.
2. **Lamination:** It is due air-entrapment in the granular material.
3. **Cracking:** It is due to rapid expansion of tablets when deep concave punches are used.

The defects related to excipient are as follows:

4. **Chipping:** It is due to very dry granules.
5. **Sticking**
6. **Picking**
7. **Binding**

These problems (5, 6, 7) are due to more amount of binder in the granules or wet granules.

The defect related to more than one factor:

8. **MOTTLING**: It is either due to any one or more of these factors: Due to a coloured drug, which has different colour than the rest of the granular material. (Excipient-related); improper mixing of granular material (Process-related); dirt in the granular material or on punch faces; oil spots by using oily lubricant.

The defect related to Machine:

9. **DOUBLE IMPRESSION**: It is due to free rotation of the punches which have some engraving on the punch faces.

Capping

- 'Capping' is the term used, when the upper or lower segment of the tablet separates horizontally, either partially or completely from the main body of a tablet and comes off as a cap, during ejection from the tablet press, or during subsequent handling.
- Reason: Capping is usually due to the air–entrapment in a compact during compression, and subsequent expansion of tablet on ejection of a tablet from a die.

Causes and remedies of capping related to machine (dies, punches and tablet press)

Causes	Remedies
Poorly finished dies	Polish dies properly. Investigate other steels or other materials.
Deep concave punches or beveled-edge faces of punches.	Use flat punches.
Lower punch remains below the face of die during ejection.	Make proper setting of lower punch during ejection.
Incorrect adjustment of sweep-off blade.	Adjust sweep-off blade correctly to facilitate proper ejection.
High turret speed.	Reduce speed of turret (Increase dwell time).

Lamination/Laminating

- 'Lamination' is the separation of a tablet into two or more distinct horizontal layers.
- Reason: Air–entrapment during compression and subsequent release on ejection.
- The condition is exaggerated by higher speed of turret.

Causes and remedies of lamination related to formulation (granulation)

Causes	Remedies
Oily or waxy materials in granules.	Modify mixing process. Add adsorbent or absorbent.
Too much of hydrophobic lubricant e.g., Magnesium-stearate.	Use a less amount of lubricant or change the type of lubricant.

Causes and remedies of lamination related to machine (dies, punches and tablet press)

Causes	Remedies
Rapid relaxation of the peripheral regions of a tablet, on ejection from a die.	Use tapered dies, i.e., upper part of the die bore has an outward taper of 3° to 5°.
Rapid decompression	Use pre-compression step. Reduce turret speed and reduce the final compression pressure.

Chipping

- 'Chipping' is defined as the breaking of tablet edges, while the tablet leaves the press or during subsequent handling and coating operations.
- Reason: Incorrect machine settings, specially mis-set ejection take-off.

Causes and remedies of chipping related to formulation (granulation)

Causes	Remedies
Sticking on punch faces	Dry the granules properly or increase lubrication.
Too dry granules.	Moisten the granules to plasticize. Add hygroscopic substances.
Too much binding causes chipping at bottom.	Optimize binding, or use dry binders.

Causes and remedies of chipping related to machine (dies, punches and tablet press)

Causes	Remedies
Groove of die worn at compression point.	Polish to open end, reverse or replace the die.
Barreled die (center of the die wider than ends)	Polish the die to make it cylindrical
Edge of punch face turned inside/inward.	Polish the punch edges
Concavity too deep to compress properly.	Reduce concavity of punch faces. Use flat punches.

Cracking

- Small, fine cracks observed on the upper and lower central surface of tablets, or very rarely on the sidewall are referred to as 'Cracks'.

- Reason: It is observed as a result of rapid expansion of tablets, especially when deep concave punches are used.

Causes and remedies of cracking related to formulation (granulation)

Causes	Remedies
Large size of granules.	Reduce granule size. Add fines.
Too dry granules.	Moisten the granules properly and add proper amount of binder.
Tablets expand.	Improve granulation. Add dry binders.
Granulation too cold.	Compress at room temperature.

Causes and remedies of cracking related to machine (dies, punches and tablet press)

Causes	Remedies
Tablet expands on ejection due to air entrapment.	Use tapered die.
Deep concavities cause cracking while removing tablets	Use special take-off.

Sticking/Filming

- 'Sticking' refers to the tablet material adhering to the die wall.
- Filming is a slow form of sticking and is largely due to excess moisture in the granulation.
- Reason: Improperly dried or improperly lubricated granules.

Causes and remedies of sticking related to formulation (granulation)

Causes	Remedies
Granules not dried properly.	Dry the granules properly. Make moisture analysis to determine limits.
Too little or improper lubrication.	Increase or change lubricant.
Too much binder	Reduce the amount of binder or use a different type of binder.
Hygroscopic granular material.	Modify granulation and compress under controlled humidity.
Oily or way materials	Modify mixing process. Add an absorbent.
Too soft or weak granules.	Optimize the amount of binder and granulation technique.

Causes and remedies of sticking related to machine (dies, punches and tablet press)

Causes	Remedies
Concavity too deep for granulation.	Reduce concavity to optimum.
Too little pressure.	Increase pressure.
Compressing too fast.	Reduce speed.

Picking

- 'Picking' is the term used when a small amount of material from a tablet is sticking to and being removed off from the tablet-surface by a punch face.
- The problem is more prevalent on the upper punch faces than on the lower ones. The problem worsens, if tablets are repeatedly manufactured in this station of tooling because of the more and more material getting added to the already stuck material on the punch face.
- Reason: Picking is of particular concern when punch tips have engraving or embossing letters, as well as the granular material is improperly dried.

Causes and remedies of picking related to formulation (granulation)

Causes	Remedies
Excessive moisture in granules.	Dry properly the granules, determine optimum limit.
Too little or improper lubrication.	Increase lubrication; use colloidal silica as a 'polishing agent', so that material does not cling to punch faces.
Low melting point substances, may soften from the heat of compression and lead to picking.	Add high melting-point materials. Use high meting point lubricants.
Low melting point medicament in high concentration.	Refrigerate granules and the entire tablet press.

Causes	Remedies
Too warm granules when compressing.	Compress at room temperature. Cool sufficiently before compression.
Too much amount of binder.	Reduce the amount of binder, change the type or use dry binders.

Causes and remedies of picking related to machine (dies, punches and tablet press)

Causes	Remedies
Rough or scratched punch faces.	Polish faces to high luster.
Embossing or engraving letters on punch faces such as B, A, O, R, P, Q, G.	Design lettering as large as possible. Plate the punch faces with chromium to produce a smooth and non-adherent face.
Bevels or dividing lines too deep.	Reduce depths and sharpness.
Pressure applied is not enough; too soft tablets.	Increase pressure to optimum.

Binding

- 'Binding' in the die, is the term used when the tablets adhere, seize or tear in the die. A film is formed in the die and ejection of tablet is hindered. With excessive binding, the tablet sides are cracked and it may crumble apart.
- Reason: Binding is usually due to excessive amount of moisture in granules, lack of lubrication and/or use of worn dies.

Causes and remedies of binding related to formulation (granulation)

Causes	Remedies
Too moist granules and extrudes around lower punch.	Dry the granules properly.
Insufficient or improper lubricant.	Increase the amount of lubricant or use a more effective lubricant.
Too coarse granules.	Reduce granular size, add more fines, and increase the quantity of lubricant.
Too hard granules for the lubricant to be effective.	Modify granulation. Reduce granular size.
Granular material very abrasive and cutting into dies.	If coarse granules, reduce its size. Use wear-resistant dies.
Granular material too warm, sticks to the die.	Reduce temperature. Increase clearance if it is extruding.

Causes and remedies of binding related to machine (dies, punches and tablet press)

Causes	Remedies
Poorly finished dies.	Polish the dies properly.
Rough dies due to abrasion, corrosion.	Investigate other steels or other materials or modify granulation.
Undersized dies. Too little clearance.	Rework to proper size. Increase clearance.
Too much pressure in the tablet press.	Reduce pressure. OR Modify granulation.

Mottling

- 'Mottling' is the term used to describe an unequal distribution of colour on a tablet, with light or dark spots standing out in an otherwise uniform surface.
- Reason: One cause of mottling may be a coloured drug, whose colour differs from the colour of excipients used for granulation of a tablet.

Causes and remedies of mottling

Causes	Remedies
A coloured drug used along with colourless or white-coloured excipients.	Use appropriate colourants.
A dye migrates to the surface of granulation while drying.	Change the solvent system, change the binder, Reduce drying temperature and Use a smaller particle size.
Improperly mixed dye, especially during 'Direct Compression'.	Mix properly and reduce size if it is of a larger size to prevent segregation.

Causes	Remedies
Improper mixing of a coloured binder solution.	Incorporate dry colour additive during powder blending step, then add fine powdered adhesives such as acacia and tragacanth and mix well and finally add granulating liquid.

Double impression

- 'Double Impression' involves only those punches, which have a monogram or other engraving on them.
- Reason: At the moment of compression, the tablet receives the imprint of the punch. Now, on some machines, the lower punch freely drops and travels uncontrolled for a short distance before riding up the ejection cam to push the tablet out of the die, now during this free travel, the punch rotates and at this point, the punch may make a new impression on the bottom of the tablet, resulting in 'Double Impression'.
- If the upper punch is uncontrolled, it can rotate during the short travel to the final compression stage and create a double impression.

Causes and remedies of double impression

Cause	Remedies
Free rotation of either upper punch or lower punch during ejection of a tablet.	Use keying in tooling, i.e., insert a key alongside of the punch, so that it fits the punch and prevents punch rotation. Newer presses have anti-turning devices, which prevent punch rotation.

Problems and Remedies for Tablet Coating

Blistering

- It is local detachment of film from the substrate forming blister.
- Reason: Entrapment of gases in or underneath the film due to overheating either during spraying or at the end of the coating run.

Cause and remedy of blistering

Cause	Remedy
Effect of temperature on the strength, elasticity and adhesion of the film.	Use mild drying condition.

Chipping

- It is defect where the film becomes chipped and dented, usually at the edges of the tablet.
- Reason: Decrease in fluidizing air or speed of rotation of the drum in pan coating.

Cause and remedy of chipping

Cause	Remedy
High degree of attrition associated with the coating process.	Increase hardness of the film by increasing the molecular weight grade of polymer.

Cratering

- It is the defect of the film coating whereby volcanic-like craters appears exposing the tablet surface.
- Reason: The coating solution penetrates the surface of the tablet, often at the crown where the surface is more porous, causing localized disintegration of the core and disruption of the coating.

Causes and remedies of cratering

Causes	Remedies
Inefficient drying.	Use efficient and optimum drying conditions.
Higher rate of application of coating solution.	Increase viscosity of coating solution to decrease spray application rate.

Picking

- It is the defect where isolated areas of film are pulled away from the surface when the tablet sticks together and then part.
- Reason: Conditions similar to cratering that produces an overly wet tablet bed where adjacent tablets can stick together and then break apart.

Causes and remedies of picking

Cause	Remedy
Inefficient drying.	Use optimum and efficient drying conditions or increase the inlet air temperature.
Higher rate of application of coating solution.	Decrease the rate of application of coating solution by increasing viscosity of coating solution.

Pitting

- It is the defect whereby pits occur in the surface of a tablet core without any visible disruption of the film coating.
- Reason: Temperature of the tablet core is greater than the melting point of the materials used in the tablet formulation.

Cause and remedy of pitting

Cause	Remedy
Inappropriate drying (inlet air) temperature	Dispensing with preheating procedures at the initiation of coating and modifying the drying (inlet air) temperature such that the temperature of the tablet core is not greater than the melting point of the batch of additives used.

Blooming

- It is the defect where coating becomes dull immediately or after prolonged storage at high temperatures.
- Reason: It is due to the collection on the surface of low molecular weight ingredients included in the coating formulation. In most circumstances, the ingredient will be a plasticizer.

Cause and remedy of blooming

Cause	Remedy
High concentration and low molecular weight of plasticizer.	Decrease plasticizer concentration and increase molecular weight of plasticizer.

Blushing

- It is the defect best described as whitish specks or haziness in the film.
- Reason: It is thought to be due to precipitated polymer exacerbated by the use of high coating temperature at or above the thermal gelation temperature of the polymers.

Causes and remedies of blushing

Causes	Remedies
High coating temperature	Decrease the drying air temperature
Use of sorbitol in formulation which causes largest fall in the thermal gelation temperature of the Hydroxy Propyl Cellulose, Hydroxy Propyl Methyl Cellulose, Methyl Cellulose and Cellulose ethers.	Avoid use of sorbitol with Hydroxy Propyl Cellulose, Hydroxy Propyl Methyl Cellulose, Methyl Cellulose and Cellulose ethers.

Colour variation

- A defect which involves variation in colour of the film.
- Reason: Alteration of the frequency and duration of appearance of tablets in the spray zone or the size/shape of the spray zone.

Cause and remedy of colour variation

Cause	Remedy
Improper mixing, uneven spray pattern, insufficient coating, migration of soluble dyes-plasticizers and other additives during drying.	Go for geometric mixing, reformulation with different plasticizers and additives or use mild drying conditions.

Orange peel/Roughness

It is surface defect resulting in the film being rough and non-glossy. Appearance is similar to that of an orange.

Reason Inadequate spreading of the coating solution before drying.

Causes and remedies of orange peel/roughness

Causes	Remedies
Rapid Drying	Use mild drying conditions
High solution viscosity	Use additional solvents to decrease viscosity of the solution.

Cracking/Splitting

- It is the defect in which the film either cracks across the crown of the tablet (cracking) or splits around the edges of the tablet (Splitting)
- Reason: Internal stress in the film exceeds tensile strength of the film.

Cause and remedy of cracking/splitting

Cause	Remedy
Use of higher molecular weight polymers or polymeric blends.	Use lower molecular weight polymers or polymeric blends. Also adjust plasticizer type and concentration.

Quality Control Tests for Tablets

Size and shape

- The thickness of individual tablets may be measured with a micrometer.
- Tablet thickness should be controlled within ±5% variation of a standard value.

Weight variation

- Twenty tablets are weighed individually and the average weight is calculated. The individual tablet weights are then compared to the average weight.
- Not more than two of the tablets must differ from the average weight by not more than the percentages stated in table.

Weight variation USP

Average weight	Per cent difference
130 mg or less	10
More than 130 mg through 324 mg	7.5
More than 324 mg	5

Weight variation IP/BP

Average weight	Per cent difference
80 mg or less	10
More than 80 mg through 250 mg	7.5
More than 250 mg	5

Organoleptic properties

- Reflectance Spectrophotometry, Tristimulus colourimetric measurements and micro reflectance photometer have been used to measure colour uniformity and gloss on a tablet surface.

Content uniformity

- Applicable to all coated and uncoated tablets and all capsules containing 50 mg or smaller sizes.
- Tablet monographs with a content uniformity requirement do not have weight variation requirements.
- For content uniformity test, representative samples of 30 tablets are selected and 10 are assayed individually. At least 9 must assay within ±15% of the declared potency and none may exceed ±25%.

Mechanical strength of the tablets

- The mechanical properties of pharmaceutical tablets are quantifiable by the friability, hardness or crushing strength, crushing strength-friability values, tensile strength and brittle fracture index.

Friability (Official in USP)

- It is usually measured by the use of the Roche friabilator.
- A number of tablets are weighed and placed in the apparatus where they are exposed to rolling and repeated shocks as they fall 6 inches in each turn within the apparatus.
- After 4 minutes of this treatment or 100 revolutions, the tablets are weighed and the weight compared with the initial weight. The loss due to abrasion is a measure of the tablet friability. The value is expressed as a percentage.
- A maximum weight loss of not more than 1% of the weight of the tablets being tested during the friability test is considered generally acceptable and any broken or smashed tablets are not picked up.

Hardness or crushing strength

- The resistance of tablets to capping, abrasion or breakage under conditions of storage, transportation and handling before usage depends on its hardness.
- The Monsanto or Stokes hardness tester measures the force required to break the tablet when the force generated by a coil spring is applied diametrically to the tablet.
- The Strong-Cobb Pfizer and Schleuniger apparatus which were later introduced, masure the diametrically applied force required to break the tablet.

Tensile strength

- A non-compendial method of measuring the mechanical strength of tablets that is now widely used is the tensile strength. This is the force required to break a tablet in a diametral compression test. The radial tensile strength, T, of the tablets can be calculated from the equation:

$$T = 2\,F/\pi\,d\,H$$

Where F is the load needed to break the tablet, and d and H are the diameter and thickness respectively. Several precautions must be taken when using the equation.

Brittle fracture index (BFI)

The brittle fracture index (BFI) of the tablets was calculated using the following equation:

$$BFI = (T/To) - 1$$

Where T is the tensile strength of the tablet without a hole and to the tensile strength of a tablet with a hole. The theoretical value of BFI range is 0 – 1 when the stress concentration factor is 3.

A high value of BFI is an indication of the tendency of the tablet to laminate during the compaction process. A low BFI value is desirable for minimal lamination and capping during production.

Disintegration

- The disintegration test is a measure of the time required under a given set of conditions for a group of tablets to disintegrate into particles which will pass through a **10 mesh** screen.
- The disintegration test is carried out using the disintegration tester which consists of a basket rack holding 6 plastic tubes, open at the top and bottom, the bottom of the tube is covered by a 10-mesh screen.
- The basket is immersed in a bath of suitable liquid held at 37°C, preferably in a 1L beaker. For compressed uncoated tablets, the testing fluid is usually water at 37°C but some monographs direct that simulated gastric fluid be used.
- If one or two tablets fail to disintegrate, the test is repeated using 12 tablets. For most uncoated tablets, the BP requires that the tablets disintegrate in 15 minutes (although it varies for some uncoated tablets) while for coated tablets, up to 2 hours may be required.

Disintegration time

Uncoated Tablet	15 minutes
Film and Sugar coated Tablet	60 minutes
Enteric Coated Tablet	3 hours
Hard Gelatin Capsule	30 minutes
Soft Gelatin Capsule	60 minutes

Dissolution

- Dissolution may be defined as the amount of drug substance that goes into solution per unit time under standardized conditions of liquid/solid interface, temperature and solvent composition.
- At least 75% of the drug should get dissolved in 45 min.

Dissolution Apparatus	Name
USP I	Basket type
USP II	Paddle Type
USP III	Reciprocating Cylinder
USP IV	Flow through Cell

Interpretation

Stage	Number Tested	Acceptance Crieteria
S_1	6	Each unit is not less than Q + 5%
S_2	6	Average of 12 units ($S_1 + S_2$) is equal to or greater than Q, and no unit is less than Q – 15%
S_3	12	Average of 24 units ($S_1 + S_2 + S_3$) is equal to or greater than Q, and not more than 2 units are less than Q – 15%, and no unit is less than Q – 25%

Where Q is the amount of dissolved active ingredient specified in monograph, expressed as label content

Tests for coated tablets

I. Water vapour permeability
II. Film tensile strength
III. Coated tablet evaluations

- Adhesion test with tensile-strength tester: Measures force required to peel the film from the tablet surface.
- Diametric crushing strength of coated tablet: Tablet hardness testers are used. This test gives information on the relative increase in crushing strength provided by the film and the contribution made by changes in the film composition.

In–process quality control test

I. Weight of tablet
II. Crushing strength
III. Tablet thickness
IV. Disintegration time
V. Friability

Granulation

1. Wet granulation
2. Direct compression
3. Dry granulation

- Slugging
- Roll compaction

Dry granulation is used when effective dose of drug is too high for direct compression and the drug is sensitive to heat or moisture or both.

The most commonly used equipment for dry granulation is **Roller compactor.**

Wet granulation

Wet granulation is manufactured using the following steps:

1. Sifting
2. Granule formation
3. Drying
4. Milling
5. Blending

Sifting Vibro-Sifter is used.

Wet granulation

High shear mixer/granulator includes

Littleford lodige mixer	Littleford MGT Granulator
Gral mixer/Granulator	Diosna mixer/Granulator

Granulator with dryer includes

Fludised bed Granulator	Day Nauta Mixer Processor
Double Core/Twin Shell Granulator	Topo Granulator

Most commonly used granulator is the Rapid Mixture Granulator (RMG).

Fluid Bed Spray Granulators

Fluidized bed drywer (FBD)

Principle

- When a gas is allowed to flow through a bed of particulate solids at a velocity greater than the settling velocity of the particles and less than the velocity for pneumatic conveyor, the solids are buoyed up and become partially suspended in the gas stream. The resultant mixer of solids and gas behaves like a liquid and solids are said to be fluidized.

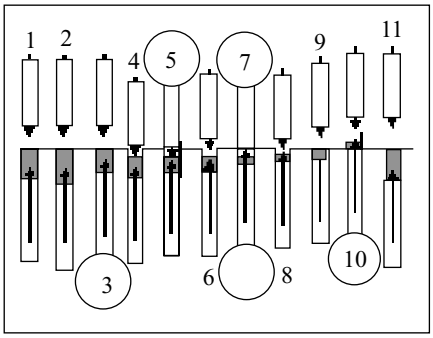
Compression machine

Tablet machine is regulated by

- Number of tooling sets–It consists of die, and upper and lower punch.

  BB tooling (most commonly used. 5.25 length, Barrel diameter 0.75 inches, head diameter 1 inches)
  B tooling
  D tooling
- Number of compression station
- Rotational speed of the press

Different stages of compression



1. Feeling of granules from hopper.
2. Excess lowering of lower punch.
3. Weight adjustment via weight adjustment knob.
4. Lowering of upper punch.
5. Precompression.
6. Relaxation.
7. Compression.
8. and
9. Lower and upper punch moves up.
10. Ejection of tablet and they get scrap via scrapper.
11. Same step as that of 1

Figure 3.3 Compression stages during Tabletting process

Tablet Coating Process

Objectives of coating

- To mask taste, odour, colour, of the drug.
- To provide physical and chemical protection to the drug.
- To control release of the drug from the tablet.
- To protect drug from gastric environment.
- To avoid chemical incompatibilities.
- To provide physical elegance.

Sugar coating It involves the following steps:

Seal coating

- To prevent moisture penetration into tablet core. Shellac is an effective sealant but tablet disintegration and dissolution times tend to lengthen on aging because of polymerization of the shellac. Zein is an

alcohol–soluble protein derivative from corn is also effective sealant.

Sub coating

- It is applied to round the edges and build up tablet size. Sugar coating can increase the tablet weight by 50 to 100%. The sub coating step involves alternately applying a sticky binder to the tablets followed by dusting of sub coating powders and then drying.

Syrup (smoothing/colour) coating

- The purpose of this step is to cover and fill in the imperfections in the tablet surface caused by the sub coating step, and to impart the desired colour to the tablet. This step perhaps requires the most skill.

Polishing

- Tablet can be polished in standard coating pans, or canvas lined polishing pans, by carefully applying powdered wax (beeswax or carnauba) or warm solution of these waxes in naphtha or other suitable volatile solvents.

Film coating method

1. Pan-Pour method
2. Pan Spray method

Film Formers

Non-enteric materials

HPMC	Methyl Hydroxy ethyl cellulose
Hydroxy propyl cellulose	Povidone
Polyethylene glycols	Acrylate polymers (Eudragit)
Ethyl cellulose (30% solution in ethanol known as Aqua coat)	Sodium CMC

Enteric materials

Cellulose acetate Phthalate (CAP)	Acrylate polymers (Eudragit L and S)
Poly vinyl acetate Phthalate (PVAP)	Hydroxy propyl methyl cellulose Phthalate

Plasticizers in film

- Recommended plasticizer levels of plasticizer ranges from 1% to 50% by weight of the film former.
- Castor Oil, Propylene Glycol, Low Molecular Weight Polyethylene Glycols of 200 and 400 Series, Surfactants such as Polysorbates (Tween) and Sorbitan Esters (Spans) are used as Plasticizers.

Opaquant-Extender

- These are very fine inorganic powders used in coating solution formulations to provide more pastel colours and increase film coverage.
- Most commonly used material for this purpose is titanium dioxide. Other materials are silicates (talc, Aluminium silicates), Carbonates (magnesium carbonates), Sulfates (Cacium Sulfates), Oxide (Magnesium Oxide) and Hydroxide (Aluminum hydroxide).

Coaters

Most coating processes use one of three general types of equipment.

Standardized coating pan

(a) Pellegrini pan
(b) Immersion sword system
(c) Immersion tube system

Perforated coating pan

(a) Accela cota and Hi coater system
(b) Driacoater
(c) Glatt coater

- It is the latest one. Drying air can be directed from inside the drum through the tablet bed and out an exhaust duct, alternatively with an optional split chambered plenum, drying air can be directed in the reverse manner up through the drum perforation for partial fluidization of the tablet bed.
- In all four types of these perforated pan systems, the coating solution is applied to the surface of the rotating tablets through spraying nozzles that are positioned inside the drum. Perforated pan coaters can be completely automated for sugar and film coatings.

Fluidized bed coater

- Fluidization of the tablet mass is achieved in a columnar chamber by the upward flow of drying air.
- The movement of tablets is upward in the center of the chamber and then fall toward the chamber wall, move downward to re-enter the air stream at the bottom of the chamber.

- Coating solution is continuously applied from a spray nozzle located at the bottom of the chamber or is sprayed onto the top of the cascading tablet bed by nozzles located in the upper region of the chamber.
- Different approaches of FB coater:
  1. Top spray
  2. Bottom Spray (Wurster Process)
  3. Tangential spray (Rotor process)

CAPSULE

Capsules are mainly of two types:

- Hard Gelatin Capsules
- Soft Gelatin Capsules

Hard Gelatin Capsule (Dry Filled Capsule)

The hard gelatin capsule consists of a base or body and a shorter cap, which fits firmly over the base of the capsule. It is mainly used for Powder, Granules, Pellets.

Physical Specification for HSG

Size	Actual Volume (ml)	Typical Fill Weights (mg) 0.70 Powder Density
000	1.37	960
00	0.95	665
0	0.68	475
1	0.50	350
2	0.37	260
3	0.30	210
4	0.21	145
5	0.13	90

Composition

Gelatin

- **Bloom Strength (Gel strength)**–It is measured in Bloom Gelometer. It indicates strength of cross-linked gelatin molecules. It should be **150 – 250 grams**.
- It is determined by measuring the weight required to remove a plastic plunger that is inserted 4 mm into 6.66% gelatin solution at 25°C for 17 hours.
- **Viscosity**–It indicates molecular chain length. It should be 25 to 45 millipoise.
- **Type A gelatin**–Derived from acid treated precursor. Isoelectric pH is 9.0 and obtained from pork skin. It imparts elasticity/plasticity and clarity to the shell.
- **Type B gelatin**–Derived from alkali treated precursor. Isoelectric pH is 4.7, obtained from the bone. It imparts toughness to the shell.
- **Acid-Bone gelatin**–Isoelectric pH is 5.5 to 6.0.
- Iron **Content**–Less than 15 ppm

Dark Spot on Shell indicates migration of iron sensitive ingredients from the filled capsule.

- **Water or Moisture content** (12–15%)
- Colourants
- Opacifier (TiO2 Dyes and Other)

Functions

1. Render the shell opaque
2. Protection against light
3. Conceal the content

Solubility limit for empty capsules

Water Resistance Fails to dissolve in water at 20° to 30° C in 15 min.

Acid Solubility Should get dissolved in less than 5 min in 0.5% aq. HCl at 36 to 38°C.

Steps of Manufacuring of Hard Gelatin Capsule Shell

1. Centrifugal Casting method
2. Dip-Pin method (Mostly used on commercial scale)

1. *Gelatin Solution*
   - Raw gelatin and water are mixed in the ratio of 1: 2 and processed at precise temperature in Safrroys melting systems.
   - After vacuum is applied, the solution is received in jacketed tanks.
   - Colours and preservatives are added before taking to the capsule machine.
2. Dipping
3. Setting/Spinning
4. Drying
5. *Stripping*
   Capsule halves are individually stripped from the pins using bronze jaw.
6. *Cutting*
   Caps and body halves are trimmed to narrow tolerance as per standards.
7. Joining

Filling of Capsule

Steps

1. **Rectification–**Empty capsule are oriented so that all point in same direction i.e., body end downward.
2. **Separation of Body and cap–**Vacuum applied body pull down into lower portion of split bushing or split filling rings.
2. **Dosing of Fill material**
3. **Joining and Ejection**–Capsule are joined by peg rings. it forces the capsule body against the closing plate. Filled capsules are ejected via compressed air.
4. **Collection**–Filled capsule are collected through Chute.

Dosing of Fill Material

Direct filling method

1. Auger filling method (Free flowing powder filled)
   Examples of Machine–Eli–Lilly, Parke–Devis, Perry
2. Vibration assisted filling
   Example of Machine-Osaka

Indirect filling method

1. Tamp-Filling Method (Dosing disk)–JKF or Bosch or Hoflinger-Karg,
2. Dosator Machine–Zanasi, Macofar, MG-2, Farmatic

Imprinting

- It is a method by which product or company identification information can be placed upon capsule.
- Imprinting of filled capsule can damage or contaminate the products. Hence empty capsule are printed.
- Harnett, Markem, Ackley are imprinting machines based on Off-Rotagravure principle.

Capsule weighing machine

1. **Roto weigh**–It is capsule weighing machine. It measures the reflected energy (backscatter) of low power X-ray beam.
2. **Vericap 1200**–It measures the change in dielectric constant or capacitance variation.

Finishing

1. **Pan Polishing**-Accelacota tablet coating pan using polyurethane cloth.
   Salt polishing using crystalline NaCl.
2. **Cloth dusting**–Cloth impregnated with inert oil
3. **Erweka kea**–Dedusting and polishing machine

Soft Gelatin Capsule (Soft gel/Soft Elastic Capsule/Wet Filled Capsule)

One piece hermetically sealed soft gelatin shell containing a liquid, a suspension or semisolid.

Note

- Accogel machine fills dry powder in soft gelatin capsule.
- Most widely used vehicles are oils e.g., Vegetable oils (Soyabean, castor oil), Mineral oil, SAA (Polysorbate 80), PEG 400 and 600.
- pH of encapsulated preparation should in between 2.5 to 7.5.because more acidic pH causes hydrolysis of gelatin shell. More alkaline pH cause tanning of gelatin shell (Reduce the solubility)
- Formulation of Suspension for SGC involves Base Adsorption consideration.

  Base Adsorption (BA) = weight of Base/Weight of Solid

  BA is number of grams of liquid base required to produce a capsutable mixture with 1 gram of solid.

  Minim per gram (M/G) = (BA + S) × V/w

- Base adsorption is used to determine minim per gram factor of solid.
- M/G is volume in minim that is occupied by one gram of solid(S) plus weight of liquid base requied to produce a capsutable mixture.
- Lower the BA of solid, higher the density of mixture and thus smaller the capsule size.
- Most widely used Suspending agents are-
  - For Oily base – Wax mixture
  - For Non-Oily base – PEG4000 and 6000

Composition of Soft Gelatin Capsule Shell

- Gelatin
- Plasticizer –glycerin, sorbitol, Propylene Glycol
- Water or Moisture Content **(6 to 10%)**

(Moisture Content is determined by Toluene Distillation Method or Azeotropic Distillation.)

- Preservatives-Methyl and Propyl Paraben **(4:1)**
- Colourants–FD and C, Certified Lakes
- Opacifier–Titanium Dioxide **(0.2 to 1.2%)**
- Flavouring Agent–Ethyl Vanillin **(0.1%)**
- Fumaric acid is added to aid solubility and to reduce aldehyde tanning of gelatin.While Formalin treatment reduces the solubility of shell.

Hardness of soft gelatin capsule shell

It is determined by weight ratio of dry plasticizer to dry gelatin.

Ratio (Dry Glycerin to Dry gelatin)	Hardness
0.4/1	Hard
0.6/1	Medium
0.8/1	Soft

Preparation

1. Plate Process
2. Rotary Process (Mostly used in large Scale)

Capsule washing

Immediately after the manufacturing, capsules are subjected to **"naptha**" wash to remove mineral oil form the outer surface of the capsule.

Important tests

1. Weight Variation test–20 Capsules

Weight	Allowed Variation
Less than 300 mg	10%
Equal or More than 300 mg	7.5%

2. Disintegration Test

Capsule Type	Time
Soft Gelatin Capsule	60 min
Hard Gelatin Capsule	30 min

3. Content Uniformity–Applicable to Potent drugs
4. Content of Active Ingredients–100 ± 10%

Rotoshort	A unfilled, loose capsule sorting machine
Rotofill	Fill Pellet in Hard Gelatin Capsule
Accofill	Fill Powder in Hard Gelatin Capsule
Accogel	Fill Powder in Soft Gelatin Capsule
Roto-weigh	A High speed Capsule Weighing Machine
Seidinader	Capsule Polishing machine

PARENTERALS

Sterile products are dosage forms of therapeutic agents that are free of living microorganisms. These may be—

- Injectable
- Ophthalmic
- Irrigating preparations

Definition

Parenterals are sterile preparations intended for administration under or through one or more layers of skin or mucous membranes.

Pharmacopeial storage conditions

Storage Condition	Meaning
Cold Storage or Under refrigeration	Any temperature not exceeding 8°C and usually 2 to 8°C
Cool Storage	Any temperature between 8 to 25°C (As per IP) and 8 to 15°C (As per USP)
Room temperature	The temperature prevailing in working area (20 to 25°C)
Warm	Any temperature between 30 to 40°C
Excessive Heat	Any temperature above 40°C
Freezer	Store between –5 and –20°C
Deep Freezer	Store below –18 °C
Controlled Room temperature (CRT) USP	store between 20–25°C

IP terminology for solubility

Descriptive term	Approximate volume of solvent in ml per gram of solute
Very soluble	Less than 1 part
Freely soluble	1 to 10 parts
Soluble	10 to 30 parts
Sparingly soluble	30 to 100 parts
Slightly soluble	100 to 1000 parts
Very slightly soluble	1000 to 10,000 parts
Practically insoluble	More than 10,000

Types of water–USP

Type	Method of preparation	Pyrogen Free	Comment
Purified water	Distillation and Ion exchange	No	Pharmaceutical solvent
WFI	Distillation or Reverse osmosis	Yes	Not sterile, must be used within 24 hours or stored below 5°C or at 80°C
Sterile WFI	Distillation or Reverse osmosis	Yes	Same as WFI, Single dose container also used to reconstitute sterile solids and dilute sterile solution
Bacteriostatic WFI	Distillation or Reverse osmosis	Yes	Multiple and Single Dose

- The limit of total solid content in WFI is 10 ppm but for sterile WFI it is 20 to 40 ppm.
- Conductivity of WFI should not more than 1 micromho (1 megohm, approximately 0.1 ppm NaCl)

Hypodermal Subcutaneous (S.C.) route	Injected under skin layer	Aqueous or oily suspension and oily solution can not be given SC. Insulin given by SC route
Intradermal/ intracutaneous	Injected into dermis Volume 0.1 to 0.2 ml	Used for Diagnostic purpose or drug sensitivity testing E.g., Tuberculin skin test
Intramuscular route	Injected into skeletal muscles Volume 2 to 4 ml	Aqueous or oily suspension and oily solution can be given IM.
Intravenous	Injected into vein Volume upto 500 ml or more Large volume known as Infusion fluid	Only aqueous preparation
Intra thecal	Injection into spinal cord Volume less than 20 ml	For spinal anaesthetic and antibiotics

Formulation additives for parenterals

Aqueous vehicle	Sodium chloride injection, Ringer solution Dextrose solution, Lactated-Ringer solution **WFI (Ideal for parenteral)**
Water miscible	Ethyl alcohol, **Propylene glycol PEG 300, 400, 600,** Glycerine
Non-aqueous	Fixed oils–Ethyl oleate, Isopropyl myristate, Peanut oil, Seasame oil, Corn oil, Cotton seed oil, **Soyabean oil**

Anti-microbacterial preservatives

Phenyl mercuric nitrate	0.001%
Phenyl mercuric acetate	0.002%
Methyl paraben	0.01 to 0.18%
Propyl paraben	0.005 to 0.035%
Thiomersal	0.001 to 0.02%
Benzyl alcohol	0.5 to 10.0%
Phenol	0.065 to 0.5%
Chlorobutanol	0.25 to 0.50%

Anti oxidants

1. **Anti oxidants** (Reducing agents)	Usual Concentration
Ascorbic acid	0.02 to 0.1%
Sodium bisulfite	0.1 to 0.15%
Sodium metabisulfite	0.1 to 0.15
Thiourea	0.005%
(All are used for aqueous system)	
2. **Anti oxigens** (Oxidation chain blockers by interacts with free radicals)	
Ascorbic acid esters	
Butyl hydroxy toluene (BHT)	
Butyl hydroxy Anisole (BHA)	0.01 to 0.015%
Nor dihydroguieretic acid (NDGA)	
Tocopherols	0.005 to 0.02%
(All are used for oily systems)	0.05 to 0.075%
3. **Synergists**	
Ascorbic acid	0.01 to 0.05%
Citric acid	0.005 to 0.01%
Tartaric Acid	0.01 to 0.02%
Phosphoric acid	0.005 to 0.01%
Chelating agents Ethylene diamine tetra acetic acid salts(EDTA)	0.01 to 0.075%

Note

- Ampoules are hermatically sealed (high temperature fusion). 1. Tip sealed 2. Pull sealed
- Vials or bottles are sealed and capped.
- Terminal sterilization method–Autoclave for aqueous solution and dry heat for oily solution used.
- CIP means clean in place and SIP means sterile in place.
- Defects are usually expressed in terms of acceptable quality Levels (AQL's); the more critical AQL's are less than 1.0
- Positive pressure is normally found in aseptic and sterile area (Class 100 area).
- Aseptic process validation: **Sterile media fill** ("broth fills")
- HVAC means Heating Ventilation and Air Conditioning

Types of operations to be carried out in the various grades for terminally sterilized products

Grade	Types of operations for terminally sterilized products
A	Filling of products, which are usually at risk
C	Placement of filling and sealing machines, preparation of solutions, when usually at risk. Filling of product when unusually at risk
D	Moulding, blowing (pre-forming) operations of plastic containers, preparation of solutions and components for subsequent filling.

Types of operations to be carried out in the various grades for aseptic preparation

Grade	Class	Types of operation
A	100	Aseptic preparation and filling
B	1000	Background room conditions for activities requiring Grade A
C	10,000	Preparation of solution to be filtered
D	1,00,000	Handling of components after washing

Small Volume Parenteral (SUV)	Volume < 100 ml or equal to 100 ml
Large Volume Parenteral (LUV)	Volume > 100 ml
Single Dose container	Size is limited to 1000 ml
Multiple dose Container	Size is limited to 30 ml

Types of glass: mainly composed of silicon dioxide

- Powdered glass test–Performed on ground, sized glass particles
- Water attack test–Performed on whole container

Type	Description	Test	0.02N H_2SO_4 (ml)	General use
I	Highly resistant, borosilicate glass	Powdered glass	**1**	Buffered and unbuffered aqueous solution
II	Treated soda lime glass	Water attack ≤100 ml size >100 ml size	 **0.7** **0.2**	Buffered aqueous solution with pH below 7.0, Dry powder and Oleaginous solution
III	Soda lime glass	Powdered glass	**8.5**	Dry powder and Oleaginous solution
NP	General purpose soda lime glass	Powdered glass	**15.0**	Not for parenteral, used for tablet, capsule, oral solution or suspensions

Evaluation of parenteral products

Leaker test (Packaging integrity test)	Applicable to only Ampoules (Not for vials and bottles) 1% Methylene Blue dye and vacuum used. Defective Ampoules becomes blue coloured
Clarity test (Particulate matter test)	**Instrument-**Light scattering (Nephelometer) Light absorption, Electrical resistance (Coulter counter) AS per light obscuration test(USP)- 1. Solutions for parenteral infusion or solutions for injection supplied in containers with a nominal content **of more than 100 mL.** The preparation complies with the test if the average number of particles present in the units tested does not exceed 25 per mL equal to or greater than 10 µm and does not exceed 3 per mL equal to or greater than 25 µm. 2. Solutions for parenteral infusion or solutions for injection supplied in containers with a nominal **content of less than 100 ml.** The preparation complies with the test if the average number of particles present in the units tested does n.ot exceed 6000 per container equal to or greater than 10 µm and does not exceed 600 per container equal to or greater than 25 µm.
Pyrogen test	Fever response in Rabbits (3 in number)–if pyrogens are present body temperature rises. Limulus test (LAL test)–based on gelling of pyrogenic preparation in presence of the lysate of the amebocytes of horseshoe crab (Limulus polyphemus)

Sterility test	Method – 1. Membrane filteration 2. Direct inoculation Medium used – 1. Nutrient broth for Aerobic 2. Fluid thioglycolate for Aerobic and Anaerobic 3. Soyabean casein digest for Fungi Aerobic Incubation–for 2 weeks at 30 to 35°C (For FTM) and 20 to 25°C (For SCD)

Selection of sample size in sterility testing

Preparation type	No. of items in batch	Minimum no. of items to be used
Injectable	NMT 100 container MT 100 but NMT 500 containers MT 500 containers	10% or 4 containers whichever is greater 10 containers 2% or 20 which ever is less
Ophthalamic	NMT 200 containers MT 200	5% or 2 containers whichever is greater 10 containers
Surgical Dressings	NMT 100 packages MT 100 but NMT 500 MT 500	10% or 4 whichever is greater 10 packages 2% 0r 20 packages whichever is less
Bulk solids	LT 4 containers 3 containers but NMT 50 MT 50 containers	Each container 20% 0r 4 containers whichever is greater 2% 0r 10 containers whichever is greater

Quantity in each container	Minimum to be used
For liquid– LT 1 ml 1ml or more but LT 4 ml 4ml or more but LT 20 ml 20ml or more but LT 100 ml 100 ml or more	Total content of container Half of the container 2ml 10% of the content NLT half of the container
For Solids – LT 50 mg 50 mg or More but LT 200 mg 200 mg or more	 Total content Half content 100 mg

Air control–HEPA filter

- High efficiency particulate air filter (HEPA) removes out particles of 0.3 microns and larger than this size with the efficiency of 99.97%. HEPA is the only means for achieving class 100 clean room.
- Air velocity – 100 ± 20 ft/min.

Class 100 area	Particle count in air is not more than 100 per cubic foot of 0.5 micron and larger size	Sterile and aseptic area
Class 10,000 area	Particle count in air is not more than 10,000 per cubic foot of 0.5 micron and larger size	Manufacturing area
Class 1,00,000 area	Particle count in air is not more than 1,00,000 per cubic foot of 0.5 micron and larger size	Packaging and storage area

Freeze–drying (Lyophilization)

- Used when drug is unstable in solution form or thermolabile.
- Freeze dried products normally contains less than 1% moisture.

Steps

- Freezing generally at – 50°C (It should be done below the product collapse temperature)

- Primary drying (Sublimation/Removal of frozen water)
- Secondary drying (Sublimation of bound water)
- Post heat

AEROSOLS

Aerosols are suspensions of small solid particles or droplets suspended in a gas or vapour.

Common perception Products that depend on the pressure of a compressed or liquefied gas to expel the contents from a container.

Advantages

- Dose can be removed without contamination.
- Stability enhancement for oxygen or moisture sensitive drugs.
- Sterility maintained up to administration.

Disadvantages

- Costlier.
- Aerosol packs must be store in a cool place.
- Propellant may cause toxic reaction.
- The refrigerant effect of propellant may cause discomfort.

Components of Aerosol

1. Container

The materials should withstand pressure as high as 140–180 psig at 130°C.

A. Metal

- **Tin plated steel**
- Aluminium
  They should not be used with pure ethanol or water as can cause corrosion.
- Stainless Steel

B. Glass

- Uncoated glass
- Plastic coated glass.

2. Valves

- Responsible for the delivery of the product in the desired form.

They are of two types:

- **Continuous Spray Valve:** Are used with topical aerosols
- **Metering valves:** Should accurately deliver a measured amount of the product

The amount delivered should be reproducible, not only for the dose delivered from the same container but from different containers of the batch as well.

Metering valve components

- **Ferrule or Mounting Cup**–It is used to attach valve properly to the container. It is made up of tin plated steel, although aluminum can be used.
- **Valve body or Housing**–Made up of Nylon or Delrin
  Stem–Made up of Nylon or Delrin
- **Gasket**–Buna-N and Neoprene Rubber
- **Spring**–Stainless steel
- **Dip Tube-**From Polyethylene or Poly propylene

3. Actuater

To ensure that the product is delivered in the proper and desired form, a specially design button or actuator is fitted to the valve system.

- Spray actuators
- Foam actuators
- Solid-stream actuators
- Special actuators

It also allows for easy opening and closing of the valve and is an integral part of almost every aerosol package.

Propellant

- The propellant is responsible for developing the proper pressure within the container, and it expels the product when the valve is opened and aids in the atomization or foam production of the product.
- Mainly two types of propellants are used:

  Hydrocarbon gas – Propane, Butane, Iso-Butane

  Compressed gas – Nitrogen, Carbon dioxide, Nitrous oxide

Fluorinated Hydrocarbons:

1. Propellant 12 (Dichloro di fluoro methane)
2. Propellant 11(tri chloro mono fluoro methane)
3. Propellant 114 (Dichloro tetra fluoro ethane)

Daltons Law Total pressure in any system is equal to the sum of the individual or partial pressure of various components.

$$P(\text{total Vapour pressure}) = P_a + P_b$$

Where $P_a + P_b$ are partial vapour pressure of component A and B respectively.

Raoults law Lowering in vapour pressure of liquid by the addition of another substance, states that depression of vapour pressure of a solvent upon addition of solute is proportional to the mole fraction of solute molecules in the solution.

$$P_a = (N_a/N_a + N_b) \times \text{vapour pressure of pure propellant } P^0(a)$$

Psia (pound per inch square Absolute) – 14.7 = psig (pound per inch square gauge)

Types of Inhalation Devices

- Metered dose inhalers
- Nebulizers
- Dry powder inhalers

Metered dose inhalers

- Mostly used to deliver suspension aerosols.
- Principle of operation is: a metering chamber fills with suspension as can is inverted.
- By, depressing valve stem, metering chamber is simultaneously closed to reservoir and opened to atmosphere by actuator jet.
- As atmospheric pressure is much lower than equilibrium vapour pressure in the can, propellant vapourises rapidly, which propels the suspended particles through jet to the patient.

Nebulizers

They are of two types:

1. Jet nebulizers
2. Ultrasonic nebulizers

Jet nebulizers

- Principle of operation is by passing air at high speed over the end of capillary tube, liquid may be drawn up the tube from reservoir in which it is immersed (Venturi or Bernoulli effect).
- When liquid reaches end of capillary it is drawn into air-stream and forms droplets that disperse to become an aerosol.

Ultrasonic nebulizers

- Principle of operation is that it uses piezoelectric transducer to induce waves in a reservoir of solution. Interference of these waves at reservoir surface leads to production of droplets in atmosphere above reservoir. An air-stream is passed through this atmosphere to transport droplets as an aerosol.

Dry powder inhalers

- Principle of operation is: Capsule is placed in **spinhaler** device. It pierces the capsule by a special mechanism. This **spinhaler** rotates the capsule under influence of patients breath, ejecting aerosol particles into air-stream.These particles pass through rotor blades and are collected or deaggregated to ensure that small particles is administered to patient.

Propellant filling method

Cold filling

- Prod. conc. is cooled to 0 to 10°F and then added to the containers
- Propellant is refrigerated (–20° to –40°F) and added to the container as cold liquid
- Moisture elimination is problematic

Pressure filling

- First prod. conc. is added
- Through valve opening propellant is added by pressuring propellant at temp. of filling area headspace air may compressed. Therefore headspace purging is necessary.

Leak testing and Burst testing

- It is done by passing filled and sealed aerosol product container through hot water tank for three minutes (accepted time).
- Containers should be heated at ~55°C (130°F) and observe for leakage or bursting.
- Temp. should not rise more than 60°C.
- Leakage is detected by visual inspection of fine bubbles.

Finished Product Specification

Flammability and combustibiliy

Flash point

- This is measured by use of the "Standard Tag Open Cup Apparatus" The aerosol product is chilled to a temperature of about –25°F and transferred to the test apparatus. The test liquid is allowed to increase slowly in temp. And the temp. At which the vapours ignite is taken as the Flash Point.

Flame projection

- This test indicates the effect of an aerosol formulation on the extension of an open flame. The product is sprayed for about 4 sec into a flame. Depending on the nature of the formulation, the flame is extended, the exact length of measured with a ruler.

Physicochemical characteristics

Vapour pressure

The pressure can be measured simply with a pressure gauge.

Density

The density of an aerosol system may be accurately determined through the use of a hydrometer or a pycnometer.

Moisture content

The Karl Fischer method has been accepted to a great extent. GAS chromatography may be used for this purpose.

Identification of propellants

GAS chromatography and Infra red spectophotometry have been used to identify the propellant and also indicate then proportion of each component in a blend.

Concentration-propellant ratio

Performance

Aerosol valve discharge rate

This is determined by taking an aerosol product of known weight and discharging the contents for a given period of time using standard apparatus. By re-weighing the container after the time limit has expired, the change in weight per time dispensed is the discharge rate, which can then be expressed as a gram per second.

Spray pattern

Spray pattern testing also based on the impingement spray on a piece of paper that has been treated with a DYE-TALC mixture. Depending on the nature of the aerosol, an oil-soluble or water soluble dye is used.

Dosage with metered valves

Net content

The tarred cans that have been placed onto the filling line are reweighed and the difference in weight is equal to the net contents.

Foam stability

The life of foam can range from a few seconds (for some quick breaking foams) to one hours or more depending on the formulation.

Particle size distribution

- Cascade impactor and light scatter decay methods have been used for determination of particle size distribution.
- Aerosol dynamic particle size (APS) is more appropriate for inhalation aerosol.

Leakage

Biological testing

Therapeutics activity

Toxicity Toxicity testing should include both topical and inhalation effects. Aerosols applied topically may be irritating to the affected area and/or may cause chilling effect.

STERILIZATION AND DISINFECTANTS

- **Sterilization**–It is a process in which all viable life forms are either killed or removed.
- **Aseptic Technique**–Procedure that excludes the access of viable microorganisms into the products.
- **Sterility**–Total absence of viable microorganisms. It is an Absolute term.
- **Disinfectant**–Chemical agent used to destroy harmful micro-organisms usually in inanimate objects.
- **Antiseptic**–Chemical agent usually applied to living tissues in humans or animals in order to destroy harmful microorganisms.
- **D-Value or Decimal reduction time**–Time (for heat or chemical exposure) or Dose (For radiation exposure) required for microbial population to decline by one decimal point (90%, one logarithmic unit, reduction).
- **Z-Value or Thermal destruction Value**–The degree of temperature required for 1 log reduction in D value.

Autoclaving Condition

Temperature Degree C	Pressure in excess of atmospheric (lb/sq.inch)	Holding time in min.
115 to 116	10	30
121 to 123	15	15
126 to 129	20	10
134 to 138	32	3

Mechanical Method of Sterilization

Bacteria proof Filters (Cold sterilization)	Material Sterilized	Composition
Ceramic filters (filter candle or Berkefeld filter)	Thermolabile aqueous solution	Kieselguhr, Unglazzed procelain
Seitz filter (Asbestos pads)	Viscous solutions	Asbestos fibre, wood cellulose
Sintered glass filters	Thermolabile solution	Borosilicate glass
Membrane filters	Aqueous and oily solution for parenteral use	Cellulose acetate, Cellulose nitrate, Nylon, Cellulose ester
HEPA Filters	Air free from greater than 0.3 micron particles	Asbestos

Various Method of Sterilization and its Principle and Application

Sterilization Method	Mechanism	Application
Dry Heat Hot air Oven (180°C for 2 hour or 45 min at 260°C)	Oxidation of protein	• Glassware • Scissors, Scalpels, Ointment tubes, Oil and powder in small container • Oily injection
Moist Heat AutoClave (115 to 117°C for 30 min.)	Denaturation and Coagulation of protein	• IV fluids • Rubber and Plastic items such as nylon and PVC bag
Tyndallization (Fractional sterilization) Heating the medium 80°C 1 hour on each of 3 successive days		• Surgical Dressings • Culture media
Pasteurization Holder method (62.8°C for 30 min.) Flash method (71–72°C for 15 second)		• Milk

Gaseous Method

Ethylene Oxide	Alkylation of sulphdryl (-SH), imino (-C=N-H), carboxyl (-COOH) and hydroxyl (-OH) groups of proteins	Thermolabile materials (Plastic and Rubber)
Formaldehyde	Alkylating agent	For Fumigation
Beta propiolactone		Sterilization of operation theatres and Aseptic rooms

Radiation Method

1. UV Mercury vapour lamp A dose of 2.5 M rads is generally used.	Nucleoprotein damage by UV of λ 253 nm	Thermo labile substances To maintain aseptic area in industry To prevent cross infection in hospitals
2. Ionizing Radiation Cobalt -60 (Gamma rays), cathode rays, beta rays	Denaturation of essential cell constituent such as enzyme, DNA etc by excitation, ionization and free radical formation	Plastic, Syringes, Hypodermic needles, Surgical blades, Adhesive dressings, Thermolabile medications, Catheters and Sutures

HEPA filter efficiency test

To check efficiency of HEPA for Air sterilization DOP (Dioctyl phthalate or DOP smoke test is performed. HEPA filter remove particles larger than 0.3 microns.

Validation of various methods of Sterilization

Method of Sterilization	Validation
Dry Heat method (Hot air oven)	Physical–Temperature recording charts Chemical–Brownes tubes, Browie-Dick heat sensitive taps Biological–Spores of Bacillus Subtilus ver. niger
Moist Heat method (Auto clave)	Biological–Spores of Bacillus Stearo thermophilus and Clostridium Sporogenes
Gaseous Method	**Chemical**–Royce Sachet **Biological**–spores of Bacillus Subtilus ver. niger
Radiation method	**Chemical**–Chemical dosimeters Biological–Bacillus pumilus and spheri-cus
Filteration	Pseudomonas diminuta or Serratia marsenence
Membrane Filter Integrity	**Bubble Point test**–based upon the fact that capillaries in filter are full of liquid, the liquid is held by surface tension. Minimum pressure required to force theliquid out of capillary must be sufficient to overcome the surface tension. **Forward flow test**–based upon the measurement of the diffusion rate of air through water in a wetted filter at a pressure below the bubble point pressure.

Chemical Anti-microbials

Surfactants	Various organic acids and bases
Heavy metals	Halogen-containing compounds
Alcohols	Phenol and phenol derivatives
Oxidizing agents	alkylating agents

Mechanisms of action of chemical agents

Protein denaturation	Membrane disruption
Nucleic acid damage	Inhibition of metabolism

Surfactants

- Surfactants are substances that are soluble in water but are able to dissolve lipids.
- In that way they are able to increase the solubility of lipids in water solutions.
- Surfactants additionally increase the ability to water solutions to wet, i.e., move along or penetrate, lipid surfaces.
- Examples of surfactants are soaps and detergents.

Soap

- Soaps are sodium or potassium salts of fatty acids
- Consequently, soaps are alkaline (pH greater than 7)
- Soaps exert their anti-microbial effects in two ways:
  - By harming bacteria that are sensitive to high pH's
  - By removing pathogens from surfaces by cleaning the surface

Detergent

- Detergents are synthetic surfactants.
- A detergent may be cationic (positively charged) or anionic (negatively charged).
- Cationic detergents are better at killing bacteria than anionic detergents.

Quaternary ammonium compounds (quats)

- One type of commonly employed cationic detergent disinfectants are quaternary ammonium compounds (quats).
- Problems with the use of quats as disinfectants include:
  - Their inactivation by soaps.
  - Their inhibition by divalent cations (calcium and magnesium ions).
  - Their inhibition by cotton and other porous organic substances.
  - Their inability to kill certain species of *Pseudomonas.*

Organic acids

- Various organic acids are employed especially as inhibitors of fungi and molds in foods.
- For example, benzoate of soda is a sodium salt of benzoic acid, an organic acid.

Heavy metals

- Various metals and metal salts are commonly employed to prevent microbial growth or kill microbes.
- For example, silver nitrate has been and increasingly is again used to treat the eyes of newborns to kill any *Neisseria gonorrhea* that may have been acquired during passage down the birth canal.

- A common example in Ohio is the treatment of ponds with copper sulfate (which is blue in water solution) as an anti-algal; note that though effective at inhibiting algal growth in ponds, it may be similarly disruptive of algal growth in down-stream ecosystems.
- Selenium compounds are effective anti-fungals.

Halogens

- Two halogens are regularly employed as anti-microbials: iodine and chloride.

Chlorine and hypochlorite ion

- Drinking water is commonly disinfected using hypochlorite.
- Hypochlorite may either be added directly (i.e., in the form of bleach) or created within water by bubbling chlorine gas through the water.
- Note that chlorine is less effective in the presence of significant organic compounds (basically because the hypochlorite ion interacts with–oxidizes–organic compounds indiscriminately and thus is used up in the presence off excess organic compounds).

Iodine

- Iodine is often employed as a tincture or as an iodophor.
- A tincture is an alcohol solution of a substance, in this case iodine.
- Iodine tinctures may be employed as antiseptics.

Iodophors

- Iodophors are organic compounds that slow the release of iodine.
- The iodophors additionally serve as surfactants, thus increasing penetration while simultaneously steadily supplying iodine over long periods.
- Betadine and Isodine are examples of iodophors.

Alcohols

- Alcohols work best as 70 to 99% mixtures with water.
- Alcohol-water mixtures are additionally more penetrating than pure alcohols.
- Either ethanol or isopropyl (rubbing) alcohol may be employed for disinfecting.
- Alcohols are especially appropriate for application to sites in which their propensity to evapourate away is convenient (e.g., to disinfect skin prior to injection).
- Alcohols should not be applied to wounds since they can cause tissue damage.

Phenol and phenol derivatives (phenolics)

- Phenol and their derivatives (called phenolics) are especially useful when disinfecting materials contaminated with organic materials.
- Lysol employs phenolics.
- Some phenolics are mild enough for use as antiseptics while others are too harsh or otherwise dangerous to be employed on living tissue.

Oxidizing agents (hydrogen peroxide)

- Hydrogen peroxide (HOOH) is a typical oxidizing agent.
- Note that hydrogen peroxide is actually not a terribly effective antiseptic or disinfectant.
- This is because bacteria and body tissues contain enzymes (catalase) that inactivate hydrogen peroxide.
- On the other hand, the oxygen released upon inactivation can help oxygenate deep wounds and thus kill strict-anaerobe contaminants.

Alkylating agents (formaldehyde, glutaraldehyde, ethylene oxide)

- Formaldehyde, glutaraldehyde, and ethylene oxides are alkylating agents they add carbon-containing functional groups to biological molecules.
- Formaldehyde is employed to inactivate viruses and toxins to produce whole-killed vaccines and toxoid vaccines [whole-killed vaccines].
- Glutaraldehyde is capable of sterilizing equipment, though to effect sterilization often requires many hours of exposure.
- Ethylene oxide is a gaseous chemosterilizer that is especially useful due to its extraordinary penetrating power; this allows it to penetrate all sorts of nooks and crannies.
- Ethylene oxide is employed to sterilize prepackaged laboratory equipment that is otherwise destroyed by heat (e.g., plastic petri dishes).

Assessing Antimicrobial Efficacy

Phenol coefficient

- Lister's disinfectant, phenol, is considered the disinfectant standard against which all other disinfectants are compared.
- These comparisons give rise to the phenol coefficient where a disinfectant that
  - is more efficacious than phenol is given a phenol coefficient that is greater than 1
  - one less efficacious than phenol is given a coefficient of less than 1
  - one of equal efficacy to phenol is given a phenol coefficient of 1 (i.e., efficacy of disinfectant divided by efficacy of phenol)
- Two organisms, *Salmonella typhi and Staphylococcus aureus* are commonly used to determine phenol coefficients.

The **Rideal-Walker or Phenol coefficient** is a figure expressing the disinfecting power of any substance and is obtained by dividing the figure indicating the degree of dilution of the disinfectant that kills a microorganism in a given time by that indicating the degree of dilution of phenol that kills the organism in the same space of time under similar conditions.

Filter paper method

- A method that requires less manipulation to judge the efficacy of disinfectants is the filter paper method.
- Here, filter paper is soaked with disinfectant and then simply placed on the agar surface of a petri dish that has been inoculated with a lawn of test organism.
- The clear area around the disk following incubation is used as an indication of disinfectant efficacy.

Use-dilution test

- A third method of determining disinfectant efficacy, and one that is especially useful for determining the ability of disinfectants to kill microorganisms dried onto a typical clinical surface (stainless steel) is the use-dilution test.
- Organism is air dried onto a stainless-steel surface and then exposed to disinfectant; following sterile-water rinsing the entire surface is then placed in broth; successful disinfection results in no bacterial growth in the broth.
- Disinfectants that completely kill (or otherwise remove) microbes at the lowest dilutions (of the disinfectant) are considered the most efficacious.

CONTROLLED DRUG DELIVERY SYSTEM

Conventional drug delivery systems like tablets, injections, suspensions, creams, ointments, liquids, aerosols etc., that require periodic doses of the therapeutic agent. These agents are formulated to produce maximum stability, activity and bioavailability. For most drugs, conventional methods of drug administration are effective, but some drugs are unstable or toxic and have narrow therapeutic ranges. Some drugs also possess solubility problems. In such cases, a method of continuous administration of therapeutic agent is desirable to maintain fixed plasma levels as shown in figure.

Various categories of these modulations of drug release or controlled drug release:

Sustained Release (SR)

Constitutes any dosage form that provides medication over an extended time.

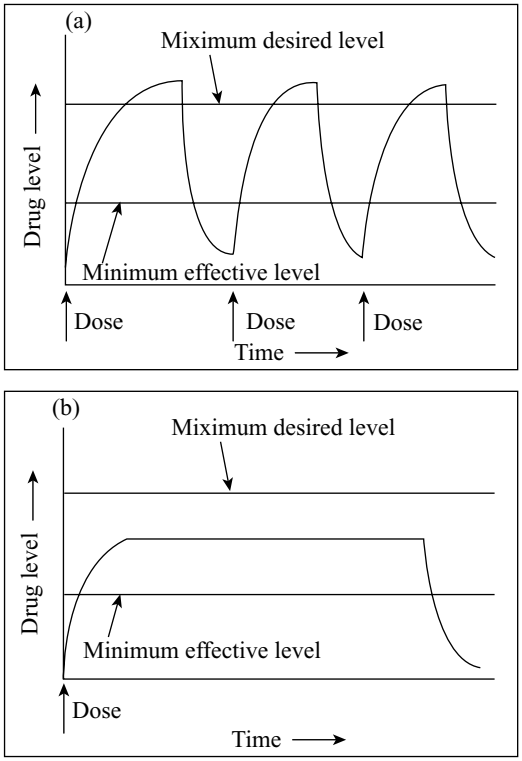


Figure 3.4 Drug levels in the blood with a) conventional drug delivery systems and (b) controlled drug delivery systems.

- Typical pharmacokinetics

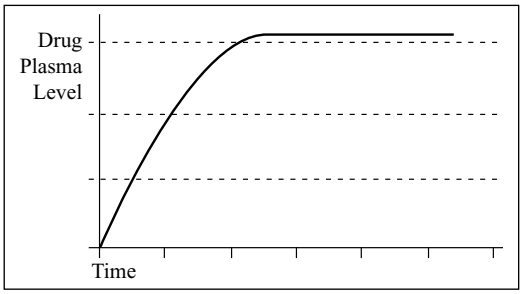


Figure 3.5 Sustain release drug profile–Graphical representation

Benefits of a sustained release profile include

- Maintenance of plasma drug levels within a defined therapeutic range
- Reduction in the number of doses taken by a patient
- Enhanced drug safety profiles
- Improved patient compliance

Modified Release

Different drug release profiles to be combined in a single dosage unit.

- Example of pharmacokinetics:

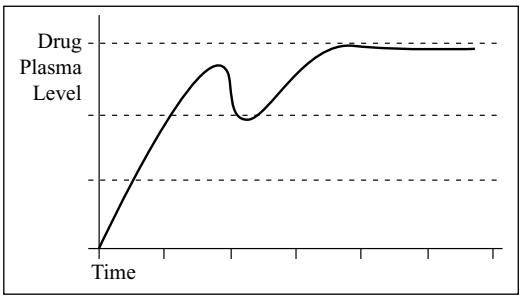


Figure 3.6 Modified drug release profile–Graphical representation

Benefits

- Optimize treatment in cases where different drug levels are required at different times
- Provide rapid onset of action and sustained release benefits within a single dose
- Provide controlled escalation of drug levels throughout a defined period of time

Chrono Release

Enables a drug to be released such that its effect takes advantage of the natural biorhythms of the human body. For example, many hormones have circadian rhythms, and gastric pH follows a daily pattern.

- Typical pharmacokinetics

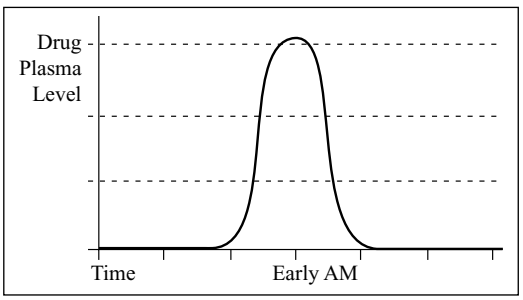


Figure 3.7 Chrono release profile–Graphical representation

- Drugs that substitute for endogenous compounds such as corticosteroids or anti-diuretic hormones can be dosed so that their release mimics that of the natural compound.
  - ☐ Pulsatile drug delivery systems are widely used to achieve this chrono release.

Advantages of CR

- Improve patient compliance
- Reduction in frequency of dosing
- Employ less total drug so reduce or eliminate local or systemic side effects.
- Improve efficiency in the treatment

  Increase controlled delivery at predetermined rate
  Reduced fluctuations
  More uniform effect

Disadvantages

- High cost
- Poor IVIVC
- Dose dumping

Drugs Unsuitable for CR

- Short elimination half-life (<1 hrs) ... Penicillin G, Furosemide
- Long elimination half-life (>12 hrs) ... Diazepam, Phenytoin
- Poor absorption
- Narrow therapeutic index ..... Digitoxin
- Extensive first pass metabolism
- Large doses (>1gm) ..... Sulfonamides

Factors Governing the Design of CR Dosage Forms

1. Drug related
2. Biological
3. Physiological
4. Pharmacokinetic
5. Pharmacological

Drug related

- Aqueous solubility
- Partition coefficient
- Molecular size
- Drug stability
- Protein binding

Biological

- ADME
- Duration of action
- Margin of safety
- Side effects
- Disease state

Physiological

- Prolonged drug absorption
- Variability on GI emptying and motility, GI blood flow

Pharmacokinetic

- Dose dumping
- First pass metabolism
- Variability of urinary pH and its effect on drug elimination

Pharmacological
- Changes in drug effect upon multiple dosing
- Sensitivity/tolerance

Various Controlled Release–Mechanisms

1. **Diffusion controlled**
   - Matrix and Reservoir
2. **Dissolution controlled**
   - Matrix and Encapsulation
3. **Diffusion and dissolution controlled**
4. **Chemically controlled**
   - Biodegradable system
5. **Ion exchange resins**
   - Cation exchange
   - Anion exchange
6. **Swelling controlled (Hydrogel)**
7. **Osmotically controlled**
8. **Magnetically controlled**

Diffusion Controlled Release System

It is broadly classified into two categories:
1. Matrix systems
2. Reservoir systems

In monolithic-matrix systems

- The therapeutic agent is dispersed in a polymer matrix and drug release is controlled by its diffusion from the matrix into the surrounding environment. Polymer and active agent are mixed to form a homogenous system.
- The drug molecules elute out of the matrix only by dissolution followed by diffusion through the polymer structure. Firstly, the drug particles present in the layer closer to the surface of the device elute and after complete depletion of this layer, the drug particles present in next layer starts depleting.

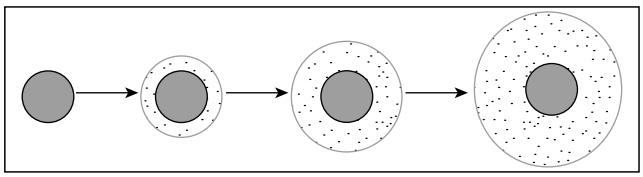


Figure 3.8 Diffusions controlled release process in matrix systems

Materials Used as Retardants in Matrix Tablet Formulations

Matrix Characteristics	Material
Hydrophobic carriers A. Insoluble, inert matrix	Polyethylene Polyvinyl acetate Polyvinyl chloride Ethyl cellulose
B. Insoluble, erodable	Carnauba wax Stearic acid Stearyl alcohol Fatty alcohol Fatty acids
Hydrophilic carriers	Methyl cellulose Hydroxyethylcellulose HPMC, CMC, NaCMC, PEGs Polyacrylic acids Galactomannose Sodium alginate Methacrylate hydrogels

In reservoir systems

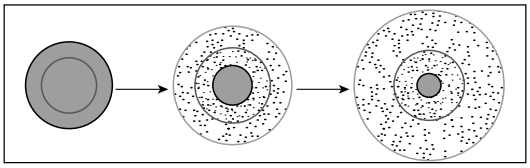


Figure 3.9 Diffusion controlled release process in reservoir systems

- The active agent is contained in a core surrounded by a thin polymer membrane and the active agent is released to the surrounding by diffusion process through the rate limiting membrane.
- The drug release limiting structure is the polymer layer surrounding the reservoir.
- The coating is uniform so the diffusion rate of the active agent is fairly stable throughout the lifetime of the delivery system.

Combined reservoir-monolithic systems

This type of system is designed into two phases:

Phase I – outer membrane layers
Phase II – reservoir matrix material

Initially, the release rate is the rate of diffusion through the membrane phase I. As the time progresses, a layer depleted from the active agent is generated in phase II matrix reservoir material immediately adjacent to the membrane layer.

Advantages and disadvantages of the systems

Matrix system	Reservoir system
• Achievement of zero order is difficult	• Achievement of zero order is easy
• Suitable for both degradable and non-degradable systems	• Degradable reservoir systems may be difficult to design
• No danger of dose dumping	• Rupture can result in dangerous dose dumping
• Not all drugs can be blended with a given polymeric matrix	• Drug inactivation by contact with the polymeric matrix can be avoided
• Can deliver high mol. wt compounds	• Difficult to deliver high mol. wt compounds

Dissolution Controlled Release Systems

It is classified into two categories:

- Matrix dissolution control
- Encapsulation dissolution control
  - In case of matrix dissolution control, drug is dispersed in slow dissolving matrix consisted of polymer. The rate of penetration of dissolution fluid in to the matrix determines the drug dissolution and subsequent release.
  - In case of encapsulation dissolution control, systems involve coating of individual particles of drug with a slow dissolving material and the coated particles can be compressed directly into tablets or placed in capsules.

By microencapsulation OR by altering layers of drug with rate-controlling coats OR other alternative is to prepare beads having different coating thickness so their release will occur in progressive manner. Thinner coat–initial dose, thicker coat–maintain drug levels at later time.

Diffusion and Dissolution Controlled Systems

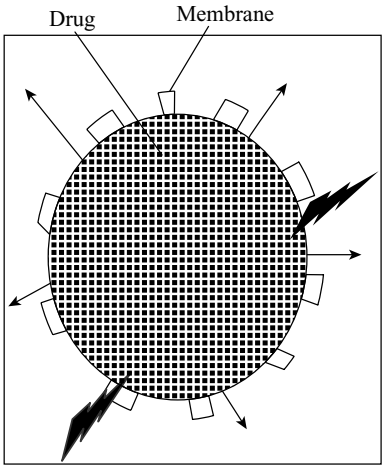


Figure 3.10 Diffusion and dissolution controlled release process

- Drug core is enclosed in partially soluble membrane. Dissolution of part of outer membrane leads to facilitated diffusion of the drug through pores in the coating.
- Release rate is dependent on
  - surface area
  - diffusion coefficient of drug though pore in coating
  - diffusion path length
  - conc. of drug in core
  - conc. of drug in dissolution media
- The fraction of soluble ingredient in the coating is a release rate controlling factor.

Ion-Exchange Resin

- Water insoluble, cross-linked polymer containing salt forming groups in repeating positions on the polymer chain.
- Drug is bound to resin by repeated exposure of resin to the drug in chromatographic column OR by prolonged contact of resin with drug solution. The drug-resin is then washed to remove contaminating ions and dried to form particles/beads.
- The drug is released by exchanging with appropriately charged ions in the GIT. The drug is then diffuse out of the resin.

- The rate of diffusion control by: the area of diffusion, diffusion path length and rigidity of resin.
- Thus, drug release depends on the ionic environment (pH, electrolyte conc.) and the properties of resin.
- **Advantage**-For those drugs which are highly susceptible to degradation by enzymatic processes since, it offers a protective mechanism by temporarily altering the substrate.
- **Limitation**-The release rate is proportional to the conc. of the ions present in the vicinity of administration site. So variable diet, water intake and intestinal contents affects the release rate of drug.
- They are mainly of two types: cation exchange resin and anion exchange resin.

Chemically Controlled Systems

- Delivery systems that change their chemical structure, when exposed to biological milieu. This system includes biodegradable polymer that degrade within body as a result of natural biological process, eliminating the need to remove the delivery system after exhausting of active agent from system.
- The polymers used in the formulation and fabrication of *biodegradable drug delivery devices,* erode (with or without changes to the chemical structure) or degrade (breakdown of the main chain bonds) as a result of the exposure to chemicals (water) or biologicals (enzymes).

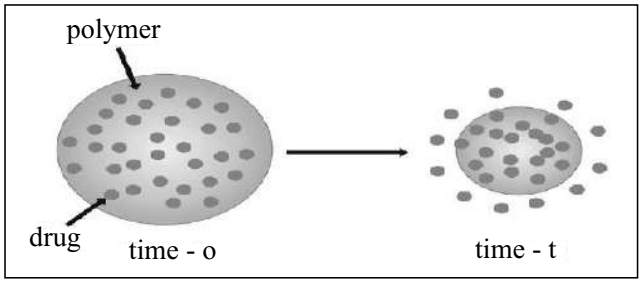


Figure 3.11 Chemically controlled release process from biodegradable system

Polymer degradation takes place by two ways

(a) Bulk erosion
(b) Surface erosion

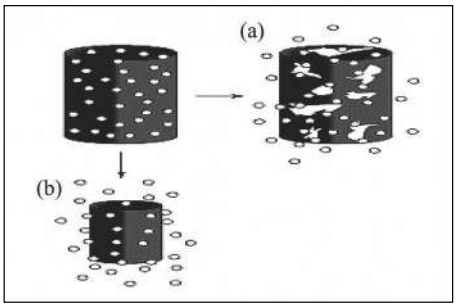


Figure 3.12 Chemical controlled release – via bulk & surface erosion

Mechanism of Polymer Erosion

Type I–Erosion mechanism

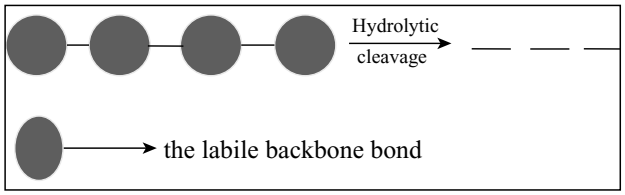


Figure 3.13 Polymer Erosion via Hydrolytic cleavage

Type II–Water insoluble macromolecules are converted into water soluble compounds by hydrolysis, ionization or protonation of a pendent group.

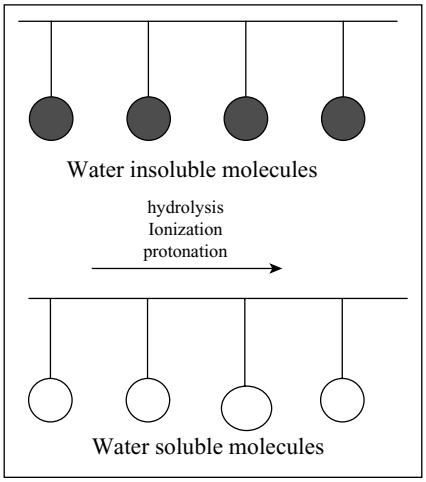


Figure 3.14 Polymer Erosion – via Hydrolysis, Ionization & protonation

Type III–Cleavage of cross links

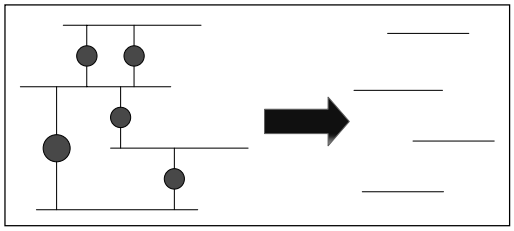


Figure 3.15 Polymer Erosion via cross links cleavage

Mechanism of Drug Release

Breakdown of the bonds connecting the drug to polymer backbone.

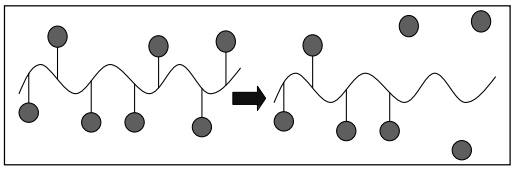


Figure 3.16 Drug release process via bond breaking from polymer system

List of biodegradable polymer

- Polylactides (PLA)
- Polyglycolides (PGA)
- Poly(lactide-co-glycolides) (PLGA)
- Polyanhydrides
- Polyorthoesters

A very different erosion pattern is the characteristic of polyorthoesters, which are surface-eroding polymers.

Magnetically controlled release system

- Small magnetic beads are uniformly dispersed within a polymer.
- When the unit is exposed to a biological system, normal diffusion of the drug due to a concentration gradient is seen. However, upon exposure to an external oscillating magnetic field, larger quantities of drug can be released quickly.
- Major advantage: possibility of manipulating the release kinetics of the drug by using external magnetic stimuli.

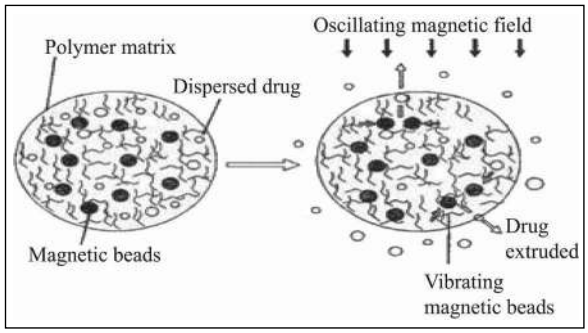


Figure 3.17 Magnetically controlled drug release process

MULTIPLE CHOICE QUESTIONS

1. NDA is filled at which of the following stage?
(a) Before Phase I
(b) After Phase III
(c) During preclinical stages
(d) After Phase II

2. Bolting of lubricant means
(a) Lubricant is passed through 150 mesh of nylon cloth
(b) Lubricant is passed through 100 mesh of nylon cloth
(c) Lubricant is completely dried before use
(d) Lubricant is thoroughly mixed with excipient before adding

3. Which of the following is a carbohydrate-based binder?
(a) Gelatin (b) PVP
(c) Both (d) None

4. Which of the following is a pH-sensitive bioerodible polymer?
(a) Polymethacrylate (b) HPMC
(c) NaCMC (d) None

5. From the point of view of dissolution, which of the following dosage forms is least absorbed?
(a) Coated tablets (b) Solution
(c) Suspension (d) Uncoated tablets

6. The rate-limiting step for the absorption of liquid-soluble drug from the immediate release tablet is the rate of:
(a) Blood flow to the intestinal tract
(b) Disintegration of tablet and release of drug
(c) Dissolution of drug
(d) Transport of the drug molecule across the intestinal mucosal tract

7. According to Noyes–Whitney's equation, the factor that affects the dissolution is
(a) Intrinsic solubility
(b) Surface area
(c) Temperature
(d) Viscosity

8. Ratio of dry glycerin/dry gelatin for hard gelatin capsules is
(a) 0.6 : 1 (b) 0.4 : 1
(c) 0.8 : 1 (d) 1 : 0.8

9. Which of the following properties is extensively applied for determining the molecular weight of polymers?
(a) Depression of freezing point
(b) Elevation of boiling point
(c) Lowering of vapour pressure
(d) Osmotic pressure

10. An unequal distribution of colour on the surface of the tablet is called
(a) Cracking (b) Chipping
(c) Picking (d) Mottling

11. The chemical nature of Eudragit is similar to
(a) Acrylic acid
(b) Methacrylate
(c) Lactate-co glycolide
(d) Methyl cellulose

12. In dissolution experiments, which one of the following coated basket is preferred, when acid medium is used?
(a) Chrome (b) Gold
(c) Teflon (d) Stainless steel

13. Major problem for the controlled release formulation is
(a) Occurrence of dose dumping
(b) To maintain therapeutic occupancy time
(c) a and b both
(d) To determine AUC

14. Which one of the following ingredients enhances the dissolution of a hydrophobic drug?
(a) Gum acacia (b) Ethyl cellulose
(c) Lactose (d) Magnesium Stearate

15. For *in vitro* or *in vivo* correlation, which one of the following dissolution parameters is extensively used?
(a) Mean amount of drug dissolved
(b) Percent of drug dissolved
(c) Rate of dissolution
(d) Time required for maximum dissolution

16. The abbreviated form of cGMP is
(a) Current Good Manufacturing Practices
(b) Clear Good Manufacturing Practices
(c) Certified Good Manufacturing Practices
(d) Concrete Good Manufacturing Practices

17. Schleuniger tester used for testing the hardness of tablet measures in which unit?
(a) g/cm^2 (b) kg/cm^2
(c) Strong Cobb (d) Both b and c

18. Chemically Veegum is
(a) Magnesium silicate
(b) Aluminium silicate
(c) Magnesium aluminosilicate
(d) Calcium oxide

19. The 000 size capsules can fill the volume of
(a) 0.13 ml (b) 0.95 ml
(c) 1.36 ml (d) 0.27 ml

20. Filling of pellets in capsules is done by
(a) Rotosort (b) Rotofil
(c) Accofil (d) Pelletofil

21. Filling of liquid in capsules is done by
(a) Rotofil (b) Qualiseal
(c) mG2 (d) Liquiseal

22. Which type of drug can be incorporated in liposome?
(a) Lipophilic (b) Hydrophilic
(c) Both (d) None

23. DNA is incorporated with which type of polymer?
(a) Positively charged polymer
(b) Chitosan
(c) Both a and b
(d) Negatively charged

24. Which of the following polymer is used in a micro-adhesive system as a bioadhesive polymer?
(a) Polymethacrylate (b) Polyacrylic acid
(c) PEG (d) Polyactate

25. Separation of the tablet into two or more distinct layers is
(a) Picking (b) Capping
(c) Lamination (d) Broken

26. Tablets that are placed under the skin are
(a) Electric-coated tablets
(b) Film-coated tablet
(c) Implants
(d) Sublingual

27. Tablets that after oral administration release the drug at a desired time for prolonged effect are
(a) Multicompressed tablets
(b) Multilayer tablet
(c) Enteric-coated tablets
(d) Sustained action tablets

28. The following is the filling principle in the capsule-filling machine except
(a) Auger filling (b) Vibratory principle
(c) Dosator principle (d) Hopper filling

29. The following are the capsule imprinting machine except:
(a) Hartnett (b) Macofar
(c) Markem (d) Ackley

30. In monolithic device of TDDS which of following is a rate-controlling step?
(a) Rate of drug diffusion from the device
(b) Rate of drug permeation through the stratum corneum
(c) Both of above
(d) Rate of drug dissolution in particular matrix system

31. The weight of one tablet was found to be 137.3 mg and weight of active ingredient was 75.2 mg. So according to I.P. which is the weight variation limit for this tablet?
(a) ± 10%
(b) ± 7.5%
(c) ± 5%
(d) No such limit specified in IP

32. Eudragit S is chemically
(a) Poly(methacrylic acid, methylmethacrylate) 1 : 1
(b) Methacrylic acid copolymer
(c) Poly(methacrylic acid, methylmethacrylate) 1 : 2
(d) Poly(ethyl acetate, methylmethacrylate) 2 : 1

33. Millard reaction in tablet formulation occurs due to which of the following reason:
(a) Lactose reacts with amino group of drug in absence of metal stearate
(b) Lactose reacts with amino group of drug in presence of metal stearate
(c) MCC reacts with basic group of drug protein
(d) Crosacarmelose reacts with acidic group of drug

34. The following are the types of encapsulation technique except:
(a) Air suspension
(b) Pan coating
(c) Spray drying-congealing
(d) Compression coating

35. The storage temperature for soft gelatin capsule shell is
(a) 21–24°C (b) 15–18°C
(c) 18–20°C (d) 25–27°C

36. Opalux is
(a) Opaquant colour concentrate for sugar coating
(b) Opaque colour concentrate for film coating
(c) Complete film coating concentrate
(d) None

37. The availability of drug for absorption decreases in the order:
(a) Capsules > Compressed tablet > Tablets > Enteric-coated tablets
(b) Enteric-coated tablets > Compressed tablet > Tablets > Capsules
(c) Capsules > Tablets > Compressed tablets > Enteric-coated tablets
(d) Tablet > Compressed tablet > Capsule > Enteric-coated tablet

38. NDA stands for
(a) New Drug Application
(b) New Drug Approval
(c) New Discovery Application
(d) New Drug Agency

39. Ratio of dry glycerin/dry gelatin for hard gelatin capsules
(a) 0.6 : 1 (b) 0.4 : 1
(c) 0.8 : 1 (d) 1 : 0.8

40. Which of the following process is not continuous for filling of soft gelatin capsules?
(a) Rotary die process
(b) Plate process
(c) Reciprocating die process
(d) Accogel/stern machine

41. Opadry is
(a) Opaquant colour concentrate for sugar coating
(b) Opaque colour concentrate for film coating
(c) Complete film-coating concentrate
(d) None

42. Which of the following causes sticking problem
(a) Stearic acid (b) PVP
(c) Lactose (d) Cellulose

43. ANDA stands for
(a) Application for New Drug Approval
(b) Abbreviated New Drug Application
(c) Application for New Drug Agency

44. Which one of the following test is not official in Indian Pharmacopoeia?
(a) Hardness (b) Friability
(c) Disintegration (d) Content uniformity test

45. Talc should not be used as lubricant in case of drugs
(a) Whose breakdown catalysed in presence of iron
(b) Which have high flow properties
(c) Which have magnesium stearate as a lubricant
(d) None of above

46. Which is not a type of a tablet?
(a) Troches and lozenges
(b) Effervescent tablets
(c) Pessaries
(d) Tablet triturates

47. The approximate particle size of microcapsule using solvent evaporation is
(a) 5–5000 μm (b) 100–10,000 μm
(c) 10–100 μm (d) 5–10 μm

48. Type A gelatin exhibits an isoelectric point at pH
(a) 2 (b) 4
(c) 9 (d) 11

49. In which step of sugar-coating process colorant is used
(a) Sealing (b) Syruping
(c) Subcoating (d) Polishing

50. Wurster's process is also better known as
(a) Rotary plate process
(b) Air suspension coating
(c) Coacervation process
(d) Pan coating

51. Which of the following is a water-insoluble polymer?
(a) Polyvinyl pyrolidone
(b) Methyl cellulose
(c) Ethyl cellulose
(d) Arabinogalactan

52. Capping is due to which of the following reasons?
(a) Air entrapment
(b) Too high compression force
(c) Too rapid expansion
(d) All of above

53. Which of the following capsules size accommodates the highest volume?
(a) 0 (b) 000
(c) 5 (d) 1

54. As per IP, the percentage of sucrose in simple syrup is
(a) 56% w/w (b) 66.7% w/v
(c) 66.7% w/w (d) 85% w/w

55. β-cyclodextrin consists of _____ gluopyranose units.
(a) 6 (b) 7
(c) 8 (d) 9

56. In the dispersion of sulphur in water, acacia is used as
(a) Complexing agent (b) Deflocculating agent
(c) Detergent (d) Wetting agent

57. Which of the following has highest solubility?
(a) Metastable form (b) Stable form
(c) Amorphous form (d) None

58. Influence of temperature on drug decomposition is expressed by
(a) Arrhenius equation
(b) Rutherford's equation
(c) Langmuir's isotherm
(d) BET equation

59. Guidelines on stability testing of drugs are given in
(a) ICH (b) USFDA
(c) Both (d) None

60. Loss of water is associated with
(a) Hygroscopic substances
(b) Polymorphic substances
(c) Efflorescent substances
(d) Deliquescent substances

61. Shelf life of a product is the time lapse during which allowed is the
(a) 50% drug degradation
(b) 90% of the degradation
(c) 90 % of the drug retained
(d) None

62. No drug, regardless of its shelf life, can be sold after a)
(a) 2 years (b) 3 years
(c) 5 years (d) 7 years

63. Permitted amount of degradation of drug during the shelf life is
(a) 5% (b) 10%
(c) 30% (d) 90%

64. Recommended amount of overages as per IPF (International Pharmaceutical Federation) is limited to a maximum of _____ of labelled potency

(a) 10%
(b) 30%
(c) 20%
(d) 50%

65. Following is not a method used for the characterization of polymorphs
(a) HPLC (b) XRPD
(c) TGA (d) Dissolution testing

66. Term hydrotrophy refers to a/an
(a) Increased solubility in water of various substances due to presence of large amount of complexing agent
(b) Increased solubility in water of various substances due to presence of large amount of additives
(c) Increased solubility in water of various substances due to presence of large amount of water
(d) Decreased solubility in water of various substances due to presence of large amount of complexing agent

67. What is the IP specification for solubility of sparingly soluble compounds?
(a) 1 part in 10–30 parts of solvent
(b) 1 part in 30–100 parts of solvent
(c) 1 part in 100–1000 parts of solvent
(d) 1 part in 1–10 parts of solvent

68. Temperature at which the drug polymorph changes to another polymorph is called)
(a) Phase inversion temperature
(b) Transition temperature
(c) Shift temperature
(d) Conversion temperature

69. Following is the true order of solubility:
(a) Amorphous > metastable > stable
(b) Metastable > amorphous > stable
(c) Stable > amorphous > metastable
(d) Stable > metastable > amorphous

70. Cold place as per IP indicates storage at
(a) 2–8 degree celsius
(b) 8–25 degree celsius
(c) 0 degree celsius
(d) 25 degree celsius

71. Zanasi instrument is used for
(a) To determine particle size
(b) To determine the rheology of semisolids
(c) For tablet coating
(d) Capsule machine

72. 3 size of capsule will have …….. ml capacity
(a) 1.3 (b) 0.95
(c) 0.68 (d) 0.30

73. Which test microorganism is used for moist heat sterilization technique?
(a) *Bacillus subtilis*
(b) *Bacillus pumilis*
(c) *Bacillus stereothermophilus*
(d) *Pseudomonas dimunita*

74. Dip coating means
(a) Repeated coating and drying
(b) Application of coating to substance which can conduct charge
(c) Air in coating pan is replaced by nitrogen
(d) Acid-insoluble coating

75. Magnesium stearate is used as
(a) Antioxidant (b) Antiadherent
(c) Tablet glidant (d) Film coating

76. In tablet defect "picking" means
(a) Colouring distribution is not proper
(b) Partial or complete removal of top or bottom of tablet
(c) Adhesion of tablet material to sides of the die
(d) Two distinct layer on tablet

77. Humectants means
(a) It reduces the particle size of the powder material
(b) It is used to increase the thickness of the ointment
(c) It is used to prevent the drying of the cream
(d) It is used to increase the spread of the coat over tablet

78. In film coating "peeling" is related to
(a) Large amount of film
(b) Uneven distribution of colour
(c) logo
(d) roughness of tablet surface

79. All of the following are antioxidant agents except
(a) Ascorbic acid (b) Propyl gallate
(c) Sodium chloride (d) Both (b) and (c)

80. Which sterilization method is used for vitamin B?
(a) Autoclaving (b) Heating
(c) Filtration (d) All of the above

81. Gelatin is used as a/an
(a) Encapsulating agent
(b) Antimicrobial agent
(c) Viscosity agent
(d) Tablet glidant

82. Due to the suspension concentration variable all of the following major defects in tablet coating occur except
(a) Bridging (b) Sticking
(c) Peeling (d) None of the above

83. Chilsonator is used as
(a) Tablet coating (b) Capsule filling machine
(c) Tablet granulator (d) None of the above

84. Moisture content of empty capsule shell should be between _____
(a) 12–15% (b) 5–8%
(c) 2–6% (d) 20–25%

85. _____ is specifically designed to fill pellets in capsule.
(a) Rotofill (b) Rotosort
(c) Accofil (d) All of above

86. Bloom is a measurement for _____ of gelatin molecules.
(a) Dissolution (b) Adhesiveness
(c) Elasticity (d) Cohesiveness

87. Which of the following is only applicable to solid core?
(a) Air suspension
(b) Spray drying
(c) Solvent evaporation
(d) Coacervation of phase separation

88. _____ is not a plastisizer.
(a) Polyethylene glycol
(b) Propylene glycol
(c) Polycarbonate
(d) Tween

89. Type B gelatin is having isoelectric point in the region _____
(a) 2–3 (b) 4–5
(c) 6–7 (d) 8–9

90. Empty capsules of gelatin should be handled at _____ %RH
(a) 1–5 (b) 15–30
(c) 30–45 (d) 45–60

91. _____ works on the principle of dielectric constant and removes the unfilled capsules.
(a) Rotoweigh (b) Vericap
(c) Accofil (d) Rotofil

92. _____ is responsible for reduced solubility of gelatin molecule by cross linking.
(a) –CHO (b) –COOH
(c) –C–O–C– (d) –C–X–C–

93. Gelatin used for soft gel manufacturing should not contain more than _____ ppm of iron.
(a) 5 (b) 15
(c) 25 (d) 35

94. More alkaline product in soft gel capsule can cause _____.
(a) Tanning (b) Leakage
(c) Roughness (d) All of above

95. Pick false statement for the steps of coacervation micro-encapsulation methodology.
(a) Formation of three immiscible phases
(b) Dissolution of coating
(c) Deposition of coating
(d) Rigidization of coating

96. _____ is an advantage of HP over CAP.
(a) More water solubility
(b) Sustained action
(c) Absence of labile group
(d) Low toxicity

97. _____ is widely used in chewable tablet.
(a) Starch (b) Mannitol
(c) Lactose (d) PVP

98. _____ is an enteric coating material.
(a) HPMC (b) Eudragit RS
(c) CMC (d) CAP

99. Temperature range for the dissolution test as per IP is
(a) 37±1°C (b) 37±0.1°C
(c) 37±2°C (d) 37±0.5°C

100. _____ is the main cause for capping.
(a) Rapid decompression
(b) Poor flow
(c) Binder
(d) Rapid compression

101. Seal coating is applied for_____.
(a) Taste masking
(b) Sustaining release instant release
(c) Prevention of moisture contact
(d) All

102. In tablet manufacturing, PVP is generally used as a_____.
(a) Glident (b) Disintegrant
(c) Binder (d) Diluent

103. Which of the following defect is due to highly viscous coating solution?

(a) Lamination (b) Orange peel
(c) Cracking (d) Blushing

104. _____ is also known as wurster coater?
(a) Pan coater (b) Perforated pan coater
(c) Fluid bed coater (d) None of above

105. For the bulk formation during sugar coating _____ is responsible.
(a) Seal coating (b) Sub-coating
(c) Syrup coating (d) Polishing

106. _____ does not show pH-dependent release.
(a) Eudragit-RL (b) Eudragit S
(c) Eudragit L (d) HP-55

107. Non uniformity in colour in tablet surface is called _____
(a) Orange peel effect (b) Blistering
(c) Mottling (d) Pitting

108. Dose dumping is a problem in the formulation of
(a) Compressed tablets
(b) Suppositories
(c) Soft gelatin capsule
(d) Controlled release drug products

109. One of the substances listed is used as mucoadhesive
(a) Acacia (b) SCMC
(c) Burnt sugar (d) Saccharin

110. Diclofenac tablet coated with cellulose acetate phthalate has been administered to a patient. Where do you expect the drug to be released?
(a) Stomach (b) Oral cavity
(c) Small intestine (d) Liver

111. The purpose of seal coating in sugar-coating process for tablet is
(a) To prevent moisture penetration into the tablet core
(b) To round the edge and build up the tablet weight
(c) To impart the desired colour to the tablet.
(d) To give lusture to the tablet

112. Durability of a tablet to combined effect of shock and abrasion is evaluated by using
(a) Hardness tester
(b) Disintegration test apparatus
(c) Friabilator
(d) Screw gauge

113. One of following is used as a pH-dependent controlled release excipient
(a) Carnauba wax. (b) HPMC phthalate
(c) Methyl cellulose. (d) Glyceryl monostearate

114. Which of the following dosage form is suitable for moisture sensitive?
(a) Tablet (b) Capsule
(c) Ointment (d) Both a and b

115. A superdisintegrants in tablet formulation is
(a) Sodium starch glycolate
(b) Starch
(c) PVP
(d) Mg-aluminium silicate

116. The sweetening agent commonly used in chewable tablet formula is
(a) Sucrose (b) Cyclamate sodium
(c) Saccharin Sodium (d) Mannitol

117. Subcoating is given to the tablets
(a) To increase the bulk and to round-up the edge
(b) To avoid the deterioration due to microbial attack
(c) To prevent the solubility in acidic medium
(d) To avoid stickiness

118. Lactose is the most widely used diluents in the tablet formulation. However it is not used in one of the following:
(a) Pyrazinamide (b) Ibuprofen
(c) Sulfacetamide (d) Isoniazide

119. Water for injection differ from sterile water for injection because it is free from
(a) CO_2 (b) Pyrogen
(c) Preservative (d) Antioxidant

120. A synthetic sweetening agent which is approximately 200 times sweeter than sucrose and has no after taste is
(a) Saccharine (b) Aspartame
(c) Cyclamate (d) Sorbitol

121. Which is the most recently used reagent for the validation of HEPA filter?
(a) Emory 3004 (b) LAL reagent
(c) Alcohol (d) None

122. The following tests are necessary for the quality testing of parenteral except
(a) Pyrogen test
(b) Total organic content
(c) Conductivity test
(d) All of the above

123. Disposable syringe are made of
(a) Polypropylene (b) Transparent polystyrene
(c) Glass (d) PTFE

124. LAL is an in vitro test and it is used in parental products to detect:
(a) Antigen (b) Micro-organism
(c) Antimicrobials (d) Pyrogen

125. The dose of intramuscular injection is
(a) 1–2 ml (b) 2–4 ml
(c) 6–8 ml (d) 8–9 ml

126. The following are the oily solvents used for parenteral except:
(a) Cotton seed oil (b) Sesame oil
(c) Ethyl oleate (d) Castor oil

127. The antimicrobial agent used in the ophthalmic solution is:
(a) Chlorhexidine
(b) Salicylic acid
(c) Sodium bicarbonate
(d) PEG 4000

128. The storage directions on a parenteralparental solution specify 'store "store in a cool place". This may be stored in:
(a) An air-conditioned area 26°C
(b) A refrigerator at 15°C
(c) A place whose temperature is set at 5°C
(d) Room temperature at 27°C

129. Which is correct for water for injection?
(a) Total solid 20 ppm, pyrogen free
(b) Total solid 10 ppm, pyrogen free.
(c) Total solid 10 ppm, sterile and pyrogen free
(d) Total solid 20 ppm, sterile

130. Ascorbic acid is a preservative used in paranteral formulation, which act through
(a) Chelating agent
(b) Reducing agent
(c) Preventing auto oxidation
(d) All of above

131. The vacuum applied for the leaker test for vials is
(a) – 27 mmHg (b) – 40 mmHg
(c) – 50 mmHg (d) –10 mmHg

132. Which of the following parenteral container material shows the highest Gas permeation?
(a) Polypropylene (b) Polystyrene
(c) Polyisoprene (d) Neoprene

133. Class 100 area utilized in aseptic filling of Parentral, which means
(a) More than 100 particles of ≥ 0.5 μm in one cubic metre
(b) Not more than 100 particles of ≥ 0.5 μm in one cubic foot
(c) More than 100 particles of > 0.5 μm in one cubic metre
(d) Not more than 100 particles of >0.5 μm in one cubic foot

134. DOP test is performed for measurement of efficiency of HEPA filter, anemometer is used with it for which reason?
(a) To measure particle size
(b) To measure velocity of air
(c) To measure pore size of HEPA filter
(d) None

135. As per GMP permitted limit of solute contents in water for injection is
(a) 100 ppm (b) 1 ppm
(c) 0.1 ppm (d) 10 ppm

136. In a batch of injectable solution consisting of 1000 ampoules each containing 5 ml of the product, the number of samples to be picked up randomly for sterility testing as per IP is
(a) **20%** (b) 10%
(c) 2% (d) 5%

137. Space required for manufacturing parenteral
(a) 50 m^2 (b) 60 m^2
(c) 80 m^2 (d) 100 m^2

138. LAL test stands for
(a) Linker allele lyase
(b) Limulus amoebocyte lysate
(c) Lecithin antigen linkage
(d) None

139. Non-parentral type of glass consists of which of the following type?
(a) I (b) II
(c) III (d) IV

140. Water attack test is performed on
(a) I (b) II
(c) III (d) IV

141. In injections, procaine undergoes the degradation reactions in the following sequence:
(a) Decarboxylation and hydrolysis
(b) Hydrolysis and decarboxylation
(c) Hydrolysis, decarboxylation and oxidation
(d) Oxidation, decarboxylation and hydrolysis

142. Multidose injections are packed in
(a) Vials (b) Ampoules
(c) Infusion bottles (d) Disposable sets

143. Which of the followings is commonly used as a preservative in eye drops
(a) Propyl paraben (b) Butylated hydroxyl toluene
(c) Phenol (d) Benzalkonium chloride

144. The dose of the intradermal injection is
(a) 0.1–0.2 ml (b) 2–4ml
(c) 1–2ml (d) 5–10ml

145. Which of the following is not a parenterals androgen?
(a) Testosterone
(b) Testosterone propionate
(c) Testosterone ethanthate
(d) Methyl testosterone

146. Sterilization is removal of
(a) All microorganisms
(b) All spores
(c) All living microorganism
(d) All bacteria

147. *Z* value in sterilization is
(a) Bioburden
(b) Resistance value
(c) Sterilization process eq. time
(d) Probability of nonsterility

148. Which of the below has minimum permissible solid content
(a) Distilled water (b) WFI
(c) SWFI (d) None of above

149. Surfactant not used parenterally
(a) PEG
(b) Tween
(c) Povidone
(d) Cetyl trimethyl ammonium bromide

150. WFI should not be held for more than …. at room temperature.
(a) 24 hours (b) 48 hours
(c) 72 hours (d) 36 hours

151. Which of following dye is used for the leak test
(a) Orange red (b) Methylene blue
(c) Methylene red (d) None of above

152. Test animal used for pyrogen testing is
(a) Rat (b) Mice
(c) Rabbit (d) Guinea pig

153. Integrity tests for a filter are performed
(a) To detect damaged membrane
(b) To detect ineffective sealing of filter
(c) To detect system leak
(d) All

154. Following is/are the integrity tests for filter
(a) Bubble point test (b) Forward flow test
(c) Both (d) None

155. Water attack test is used to identify the alkalinity in
(a) Type-I glass (b) Type-II glass
(c) Type-III glass (d) All the 3 types

156. Water for injection differ from sterile water for injection as it free from
(a) CO_2 (b) Pyrogen
(c) Preservative (d) Antioxidant

157. Which of the following dosages form is suitable for to get 100% bioavailability of drug?
(a) Tablet (b) Capsule
(c) IV injection (d) Transdermal patch

158. Options for sterilization include:_____ except
(a) Ethylene oxide
(b) Gamma irradiation
(c) 160°C dry heat for 30 minutes
(d) Low temperature steam of 73°C for 20 minutes

159. Ethylene oxide is commonly not used for the sterilization of
(a) Glassware
(b) Rubber tubings and catheters
(c) Prosthetic cardiac valves
(d) Respiratory ventilators

160. Which one is correct statement for *Z* value in sterilization?
(a) Bioburden
(b) Resistance value
(c) Sterilization process eq. time
(d) Probability of non-sterility

161. Which is not a correct statement?
(a) CIP means clean in place
(b) SIP means steam in place
(c) Media fill is used for aseptic process validation
(d) Negative pressure is normally present in aseptic area

162. Which of the below has minimum permissible solid content?
(a) Water for injection
(b) Distilled water
(c) Bacteriostatic WFI
(d) Sterile WFI

163. Which test animal is used for pyrogen testing?
(a) Rat (b) Mice
(c) Rabbit (d) Guinea pig

164. Class 100 area means
(a) Grade A area (b) Grade B area
(c) Grade C area (d) Grade D area

165. DOP or smoke test (dioctyl phthalate test) is usually used for
(a) HEPA filter integrity
(b) Filter validation
(c) Filter leak testing
(d) Filter compatibility testing

166. A 500 ml infusion bag of a formulation complies the particulate matter test if the average number of particles greater than or equals to 10 microns, present in the units does not exceeds
(a) 25 particles per ml
(b) 3 particles per ml
(c) 50 particles per ml
(d) 6000 particles per ml

167. A 100 mg/vial lyophilized formulation complies the particulate matter test if the average number of particles greater than or equals to 10 microns, present in the units does not exceeds
(a) 25 particles per container
(b) 3 particles per container
(c) 600 particles per container
(d) 6000 particles per container

168. Filter integrity testing can be carried out using
(a) Bubble point test
(b) Water intrusion test
(c) Diffusion flow test
(d) All

169. Aseptic area (sterile area) is
(a) Class 100 area
(b) Class 1000 area
(c) Class 10 area
(d) Class 10000 area

170. Meaning of Class 100 area is
(a) Particle count in air is not more than 100 per cubic foot of 0.5 micron size or larger size
(b) Particle count in air is not more than 100 per cubic foot of 5 micron size or larger size
(c) Particle count in air is not more than 100 per cubic cm of 0.5 micron size or larger size
(d) Particle count in air is not more than 100 per cubic metre of 0.5 micron size or larger size

ANSWER KEYS

1. (b)	**2.** (b)	**3.** (b)	**4.** (a)	**5.** (a)	**6.** (d)	**7.** (b)	**8.** (b)	**9.** (d)	**10.** (d)
11. (b)	**12.** (b)	**13.** (c)	**14.** (c)	**15.** (b)	**16.** (a)	**17.** (d)	**18.** (c)	**19.** (c)	**20.** (b)
21. (b)	**22.** (c)	**23.** (c)	**24.** (b)	**25.** (c)	**26.** (c)	**27.** (d)	**28.** (d)	**29.** (b)	**30.** (b)
31. (b)	**32.** (c)	**33.** (b)	**34.** (d)	**35.** (a)	**36.** (a)	**37.** (c)	**38.** (a)	**39.** (b)	**40.** (b)
41. (b)	**42.** (a)	**43.** (b)	**44.** (a)	**45.** (a)	**46.** (c)	**47.** (a)	**48.** (c)	**49.** (b)	**50.** (b)
51. (c)	**52.** (d)	**53.** (d)	**54.** (c)	**55.** (b)	**56.** (d)	**57.** (a)	**58.** (a)	**59.** (c)	**60.** (c)
61. (c)	**62.** (c)	**63.** (b)	**64.** (b)	**65.** (a)	**66.** (b)	**67.** (b)	**68.** (b)	**69.** (a)	**70.** (a)
71. (d)	**72.** (d)	**73.** (c)	**74.** (d)	**75.** (b)	**76.** (d)	**77.** (c)	**78.** (a)	**79.** (c)	**80.** (d)
81. (a)	**82.** (c)	**83.** (c)	**84.** (a)	**85.** (a)	**86.** (d)	**87.** (a)	**88.** (c)	**89.** (b)	**90.** (c)
91. (b)	**92.** (a)	**93.** (b)	**94.** (a)	**95.** (b)	**96.** (c)	**97.** (b)	**98.** (d)	**99.** (d)	**100.** (a)
101. (d)	**102.** (c)	**103.** (b)	**104.** (c)	**105.** (b)	**106.** (a)	**107.** (c)	**108.** (d)	**109.** (a)	**110.** (c)
111. (a)	**112.** (c)	**113.** (b)	**114.** (b)	**115.** (a)	**116.** (d)	**117.** (a)	**118.** (d)	**119.** (b)	**120.** (b)
121. (a)	**122.** (d)	**123.** (b)	**124.** (d)	**125.** (b)	**126.** (d)	**127.** (a)	**128.** (b)	**129.** (b)	**130.** (b)
131. (a)	**132.** (b)	**133.** (b)	**134.** (b)	**135.** (d)	**136.** (a)	**137.** (b)	**138.** (b)	**139.** (d)	**140.** (a)
141. (b)	**142.** (a)	**143.** (d)	**144.** (a)	**145.** (c)	**146.** (c)	**147.** (b)	**148.** (b)	**149.** (d)	**150.** (a)
151. (b)	**152.** (c)	**153.** (d)	**154.** (c)	**155.** (b)	**156.** (b)	**157.** (c)	**158.** (c)	**159.** (a)	**160.** (b)
161. (d)	**162.** (a)	**163.** (c)	**164.** (a)	**165.** (a)	**166.** (a)	**167.** (d)	**168.** (d)	**169.** (a)	**170.** (a)

CHAPTER 4

DISPENSING PHARMACY

PHARMACEUTICAL CALCULATION

Volume Measure

	Avoirdupois	Apothecaries
Fluid drachm	Fl. Dr.(Dram)	℥ (Drachm)
Fluid ounce	Fl.Oz	Z³
Pint	Pt	O
Gallon	gal	C

Avoirdupois Weight

1L b	7000 grains
1L b	16 Oz
1 Oz	437.5 gr
1 Oz	16 dram
1 dram	27.34 gr

Apothecaries Weight

1Lb (Pound)	5760 grains
1 Oz	8 drachm
12 Oz	1 L b
1 Oz	480 grains
1 drachm (℥)	60 grains
1 drachm (℥)	3 scruples (℈)
1 Scruples	20 grains

Fluid Volume–(In both system same)

Gallon = 160 fl.ounce = 8 pints
= 4 Quarts = 8 pints
Quart = 40 fl.ounce = 2 pints
fl.ounce = 480 minim = 8 fl.drachm

Relation

Imperial system	Metric system
1 grain	60 mg
15 grains	1 gm
1 drachm = 60 grains	4 gm
1 ounce = 480 grains	30 gm

15 minim	1 ml
1 fl.dram = 60 minim	4 ml
1 fl.Oz = 460 minim	30 ml
1 gallon	4.5 litre

Household Measures

House hold measure	Imperial Equivalent	Metric Equivalent
1 drop	1 minim	0.04 ml
1 teaspoonful	1 fl. dr	4 ml
1 desertspoonful	2 fl. dr	8 ml
1 tablespoonful	4 fl. dr	15 ml
1 wineglassful	2 fl.Oz	60 ml
1 teacupful	4 fl.Oz	120 ml
1 tumberlerful	8 fl.Oz	240 ml

Calculation Type A–Percentage Solution

Formula–for preparation of 1% solution

Solute	1 gr	4.35 gr	35 gr	1 Oz (Avoir)
Solvent upto	110 minim	1 fl.Oz	8 fl.Oz	100 fl.Oz

Question 1. Supply 2 fl.dr, ½% w/v atropine sulphate.

Ans. 2 fl. dr = 120 minims
gr in 110 minim gives 1% solution
gr in 220 minim will produce ½% solution

Hence 1 grain of atropine dissolved in 220 minim of solvent to supply ½% solution.

Question 2. Dispense 5 fl.Oz of 3% solution.

Ans. 4.35 grain in 1 fl.Oz gives -----1% solution
4.35 × 3 grain in 1 fl.Oz gives----3% solution
4.35 × 3 × 6 grain in 1× 6 fl.Oz gives---- 3% solution

78.30 grains in 6 fl.Oz gives--------- 3% solution w/v

Question 3. Dispense 12 fl.Oz of 1 part in 40 solutions.

Ans. 1 part in 40 means – (1/40) × 100 = 2.5%
35 grain in 8 fl.Oz gives ------1% solution
35 × 2.5 grain in 8 fl.Oz gives-----2.5% solution
87.5 grain in 8 fl.Oz gives-----2.5% solution
87.5 × 1.5 grains in 8 × 1.5 fl.Oz gives------ 3% solution w/v
87.5 × 1.5 grains in 12 fl.Oz gives--------- 3% solution w/v

131.25 grains in 12 fl.Oz gives--------- 3% solution w/v

Calculation Type B–Alcohol Strength Expression

1. Proof Spirit

It is defined as mixture of absolute alcohol and water.
57.1% v/v is 100% proof spirit.(IP/BP)
Hence 1% is equals to 1.753 proof spirit.
50% v/v is 100% proof spirit. (USP)

Proof Spirit = % v/v × 1.753 (IP/BP)

2. Proof Strength (Degree)

Proof Strength = Proof Spirit – 100

If (+) known as over proof (O.P.) If (–) known as under proof (U.P.)

3. Proof Gallon (taxable gallon)

It is used in USA.

Proof Gallon = gallon × % strength/50

% strength = proof spirit/2

Hence proof gallon = gallon × proof spirit/100

Question 1. An elixir contains 42% v/v alcohol, what is proof spirit?

Ans. Proof spirit (USA) = % strength × 2
= 42 × 2 = 84 proof spirit
Proof spirit (IP/BP) = % strength × 1.753
= 42 × 1.753
= 73.80 proof spirit

Question 2. Convert 90% v/v and 40% v/v alcohol into proof strength.

Ans. Proof Strength = Proof Spirit – 100
Proof Strength = (% v/v × 1.753) – 100
Proof Strength = (90 × 1.753) – 100
= 158.16 – 100 = 58.16
Number is positive hence 58.16 O.P.
b. Proof Strength = (40 × 1.753) – 100
= 70.3 – 100 = – 29.7
Number is Negative hence 29.7 U.P.

Question 3. What will be the percentage strengths corresponding to 50 O.P. and 30 U.P?

Ans. O.P. – Proof spirit = OP + 100
= 50 + 100
= 150

U.P. – Proof spirit = 100 – UP
= 100 – 30
= 70

Proof spirit = % × 1.753
% = Proof spirit/1.753
= 85.36% and 39.83%.

Calculation Type C–Stock Solution/ Concentration Solution

Formula–Proportion ratio

A : B : : C : D

Where A and D are extremes and B and C are means. Product of mean is equal to product of extremes.

A × D = B × C

Question 1. How many grams of solid is required to prepare 480 ml of a 1 in 750 solution?

Ans. Using ratio proportion:
1 in 750 means 1 gm dissolved in 750 ml.

1 g : 750 ml :: M g : 480 ml

M × 750 ml = 1 g × 480 ml

M = 480/750

= 0.64 g

Hence 0.64 g dissolved to produce 480 ml gives 1 in 750 solution.

Question 2. How many litres of 8% solution can be made from 500 g of a solid.

Ans. 8% means 8 g in 100 ml solution.

8 g : 100 ml :: 500 g : Y ml

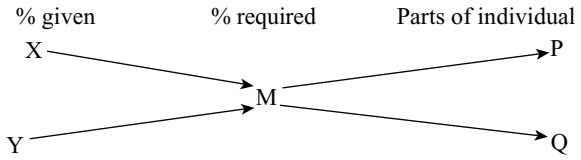
Y × 8 g = 100 ml × 500 gm

M = 50000/8 = 6250 ml or 6.25 lit.

Hence 500 g dissolved in 6.25 litre to produce 8% solution.

Calculation Type D–Alligation Rectangle or Alternate Method

Formula

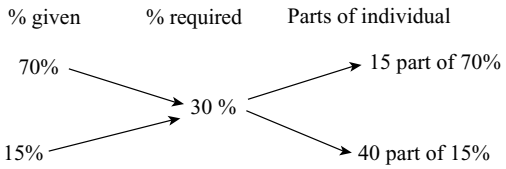


NOTE

- Substrate diagonally without considering sign.
- One component of the couple should be higher than required and other should be lower.

Question 1. A pharmacist has a 70% solution and 15% solution available with him. He is required to make 480 ml of 30% solution.

Ans.



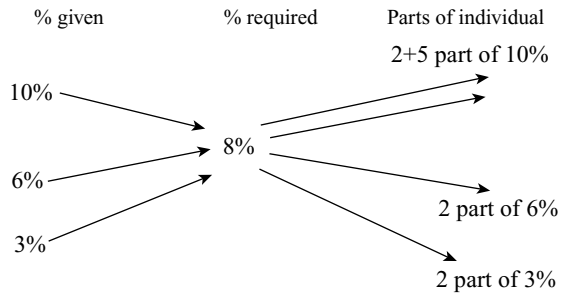
We require 480 ml of 30% solution.

By mixing 15 parts of 70% and 40 part of 15% we get 55 part of 30%.

(15/55) × 480 ml = 131 ml of 70%

(40/55) × 480 ml = 349 ml of 15%

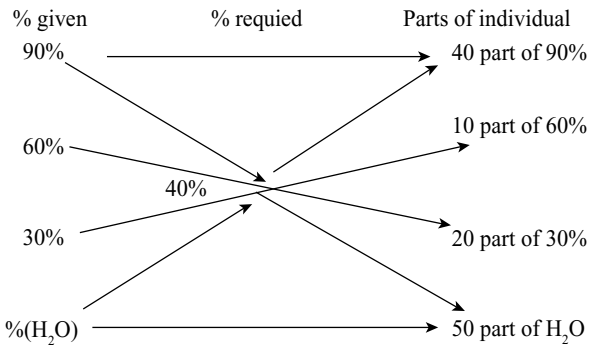
Question 2.



NOTE

Write strength in descending order.

Question 3.



Alligation Medical Formula

Quantity (Q)	Strength (S)	Product (Q × S)
A	X	A × X
B	Y	B × Y
C	Z	C × Z
M		W

Number of Resultant mix = W/M

Question 1. 30 gallon, 45 gallon and 23 gallon of 95%, 60% and 80% alcohols respectively are mixed. What is the % strength of the mixture?

Ans.

Quantity (Q)	Strength (S)	Product (Q × S)
30	95	30 × 95
45	60	45 × 60
23	80	23 × 80
98 gallon × % P		= 7390

% P = 7390/98 = 75.4%

Calculation Type E–Isotonicity Based

1. Blood serum freezes at –0.52 deg C and 0.9% w/v NaCl also freezes at this temperature.
   % of adjusting substance = (0.52 – a)/b
   Where a is freezing point depression (FPD) of drug and b is FPD od 1% adjusting substance.
2. G % of adjusting substance
   = (0.03 – % g mole of drug) × mol.wt of adj. Sub./No. of ions of adj.sub.
   % g mol of drug = (g of drug × no. of ions)/Mol.wt. of drug
3. $G_1 \times n_1/M_1 + g_2 \times n_2/M_2 + g_3 \times n_3/M_3$ ----- = 0.03
   Medicament Adjusting substances
   Where g is gram %, n is no. of ions, M is mol. Wt.

Question 1. Calculate the amount of sodium chloride required to make 200 ml of 1% solution of calcium disodium edentate isotonic with blood.

F.P. of 1% calcium disodium edentate is – 0.12 d e.g., C
F.P. of 1% sodium chloride is – 0.58 d e.g., C

Ans. % of adjusting substance = (0.52 – a)/b
% of adjusting substance = (0.52 – 0.12)/0.58
% of adjusting substance = 0.40/0.58 = 0.69%
Grams of NaCl required in 100 ml solution, for 200 ml quantity will be 0.69 × 2= 0.138 g

Question 2. Find the amount of sodium chloride required to render 100 ml of 3% w/v solution of sulphacetamide, isotonic with blood.

F.P. of 1% w/v solution of sulphacetamide sodium is– 0.132 d e.g.,C
F.P. of 1% w/v sodium chloride is –0.58 d e.g., C
F.P. of Blood is –0.52 d e.g., C

Ans. % of adjusting substance = (0.52 – a)/b
A = 0.132 × 3% = 0.396
% of adjusting substance = (0.52 – 0.396)/0.58
% of adjusting substance = 0.214/0.58 = 0.217 gm per 100 ml

Question 3. Calculate the amount of sodium chloride required to make 100 ml of 2% solution of Cocaine hydrochloride isotonic with blood.

Mol.wt of Cocaine hydrochloride = 339.5, yielding 2 ions
Mol.wt of sodium chloride = 58.5, yielding 2 ions

Ans. % g mol of drug = (g of drug × no.of ions)/Mol.wt. of drug
% gm mol of drug = (2×2)/339.5 = 0.0118 g mol per 100 ml
Now put in formula
G % of adjusting substance
= (0.03 – % g mole of drug) × mol.wt of adj. Sub./No. of ions of adj.sub.
= (0.03 – 0.0118) × 58.5/2
=0.53 g sodium chloride in 100 ml

Calculation Type F–Posology

- Young rule
  Child dose = (age in Year/age + 12) × Adult dose
- Clark rule
  Child dose = (Weight in pound/150) × Adult dose
- Dilling rule
  Child dose = (age in Year/20) × Adult dose
- Fried rule
  Child dose = (age in months/150) × Adult dose
- Body surface area
  Child dose = (body surface area of child in $metre^2$/1.73 $metre^2$) × Adult dose

MICROENCAPSULATION

Microencapsulation is the method of applying a thin film or coating to small particles of solids or droplets of liquids or and dispersion.

Uses

1. Sustain release effect
2. Taste masking purpose
3. Combination of incompatible ingredients
4. Diagnostic purpose
5. Cosmetic purpose

Methods

1. Air suspension method
2. Phase separation co-acervation method
3. Spray drying and spray-congealing
4. Polymerization technique

5. Solvent evaporation technique
6. Multi-orifice centrifugation method
7. Pan coating
8. Vacuum deposition and electrostatic deposition

Co-acervation Phase Separation Method

A. Formation of three immiscible chemical phases

- Liquid manufacturing vehicle phase
- Core material phase
- Coating material phase

B. Deposition of coating on the core material

- By change of temperature
- By addition of incompatible polymer
- By addition of Non-solvent
- By addition of salt
- By polymer–polymer interaction

C. Regidization of the coating

- By thermal treatment
- By cross-linking
- By desolvation technique

Microencapsulation process	Applicable core material	Approximate particle size (Micron)
Air suspension	Solids	35 to 5000
Coacervation-Phase separation	Solids and liquids	2 to 5000
Multiorifice centrifugation	Solids and liquids	1 to 5000
Pancoating	Solids	600 to 5000
Solvent evaporation	Solids and liquids	5 to 5000
Spray drying and Spray congealing	Solids and liquids	600

LIQUID AND SEMISOLID DOSAGE FORMS

Suspension

It is the biphasic liquid dosage form in which particles remain suspended in vehicle with the help of suspending agent.

Advantages

- Stability–Penicillin is unstable but Procaine–penicillin suspension is stable
- Masking the taste–Chloramphenicol's bitter taste is masked formulating in its palmitate salt suspension
- Sustain release–Protamine-zinc Insulin suspension
- Disadvantage–Cake formation

Flocculated Suspension	De-Flocculated Suspension
Solid particles are present as Flocs	Small particles are present as indivduals
Rate of sedimentation is high	Rate of sedimentation is low
Sediment is a loosely packed network, hard cake can not form so redisperse upon moderately shaking	Smaller particles fill the void between larger particles and form Hard cake which can not be redispersed.
Less bioavailability	Comparatively high BA

Settling in suspension–Stokes law

Sedimentation velocity of suspended particles $V = d^2 (\rho^1 - \rho^0) g/18 \eta$

Where, d = diameter of particle

ρ^1 = density of particle

ρ^0 = density of liquid

η = viscosity of liquid

- Used only for dilute suspension (less than 2% dispersed particles)
- Rate of sedimentation can be decreased by-
  1. Increasing the viscosity
  2. Decreaseing the particle size (r = ½) then V will ¼
  3. Decreaseing the density difference b/w particle and medium

Sedimentation volume

F = Ultimate volume of Sediment/total Volume of Suspension

- Value lies b/w 1 or less than 1. It can be above 1 due to formation of flocks.
- F = 1 means no sedimentation taken place
- F = 0 means complete instability

Degree of flocculation

β = Sedimentation volume of flocculated suspension/ sedimentation volume of suspension when deflocculated

Flocculation and deflocculation

Total force on suspended particle = Attraction force (V_A) + Repulsive force (V_R)

Surface free energy $\Delta G = \gamma$ (Interfacial tension) × ΔA (Change in surface area)

As the particle size increases–Surface free energy will also increases making the system unstable. To avoid this, wetting/suspending agents are added in the formulation which reduce the interfacial tension.

- Increase Zeta potential–Increase repulsive force compared to attraction forces so particle remains deflocculated.
- After addition of oppositive charged electrolyte–Attraction forces dominate over repulsive leading to formation of aggregates (Flocks).
- Larger amount of electrolyte–Deflocculation.

Suspension in structured vehicle

- Formulation of flocculated suspension in structured vehicle is most acceptable from pharmaceutical point of view. Because structured vehicle reduces the settling rate of particle during storage by entrapping the particles into its gel like matrix and upon shaking gain the sol like consistency. Thus thixotropic behaviour shown by structured vehicle is best for suspension preparation.
- Examples of structured vehicle: MC, CMC, Sod.CMC, Bentonite, Veegum

Suppositories

- Suppository is a medicated solid dosage form intended for administration into body cavity except oral cavity. These are used for either local or systemic effects. Their effect is either by melting at body temperature or by dissolving in an aqueous secretions of the mucous membrane and allowing release of the active medicament.

Types

1. Rectal suppositories
2. Vaginal (Pessaries)
3. Urethral (Bougies)
4. Nasal Bougies
5. Ear Cone

Types of suppositories base

A. Oleaginous/Fatty

1. Cocoa Butter (Theobroma oil)
2. Synthetic triglycerides mixture

B. Aqueous base

1. Gylcerinated gelatin
2. Soap glycerine
3. Macrogol/Carbowax (PEG)

C. Emulsifying base (Water-dispersible)

1. Massa esterinum
2. Witepsol
3. Massupol

Note

- Cocoa butter is a triglyceride containing oleo palmitostearin and oleo distearin. It melts between 30 to 35 degree C. It exhibits polymorphism (Form α, β, β prime, γ).

Methods of preparation

1. Hot Process–Fusion Method (Pour Moulding)
2. Cold process
   (a) Hand Rolling
   (b) Compression

Evaluation test

1. Appearance
2. Uniformity of Mixture
3. Uniformity of weight/Weight Variation–take 20 Suppositories and 5% variation is allowed.
4. Disintegration
5. Fragility (Breaking) Test
6. Melting Range Test
7. Softening or Liquefaction Time Test
8. Dissolution Test

Ointment

These are soft semisolid preparation intended for application to skin and mucous membrane. It serves mainly three functions:

1. Lubricants–Emollient
2. Treat disorder
3. Protective coverings

Ointment bases

1. Oleaginous and Hydrocarbons

(a) Natural–Olive oil, Almond oil, Seasame oil, Cotton seed oil (Plant origion) (Animal origion), Liquid paraffin, petrolatum, Microcrystalline wax, Plasti base (Minerals/Hydrocarbons)
(b) Synthetic–Silicones

2. Absorption Base They can take up large amount of water due to their high water number.

(a) Anhydrous–Hydrophilic petrolatum, Anhydrous lanolin (Wool fat)
(b) Hydrous Absorption base–Lanolin (Hydrous wool fat–70% wool fat 30% Purified water), Rose water ointment, Cold cream,Wool alcohol ointment

3. Emulsion Base

(a) W/O bases–Cold cream, Rose water ointment, Lanolin
(b) O/W bases–Emulsifying wax, Cetrimide emulsifying wax (Cationic), Hydrophilic ointment, and Cetomacrogol emulsifying ointment

4. Water soluble base (Greaseless ointment base)

High and low molecular weight poly ethylene glycols (PEG) known as Carbowax.

Method of preparations

1. By trituration
2. By fusion
3. Chemical reaction
4. Ointment mills

Creams

It is a viscous emulsion of semisolid consistency intended for the application to the skin or mucous membrane. It has opaque appearance while the ointment is translucent. These are washable, and do not form occlusive film.

Types of creams

1. Oily Cream (W/O): It contains water in oil emulgent which may be wool fat, wool alcohol, fatty acid ester of Sorbitan or Divalent soap.
   Examples–Sterol cream, Lime Cream
2. Aqueous Cream (O/W): It contains oil in water emulgent which may be emulsifying wax, Alkali soap (monovalent), Monostearin or poly ethylene glycols derivative of Sorbitan fatty acid ester.

Examples: Borax soap (Cold cream) prepared from monovalent soap emulgent. Initial O/W type but after being rubbed on skin, converts into W/O type due to evaporation of water.

Vanishing creams, non-ionic surfactant creams, cationic emulsifying wax cream.

Methods of preparation of creams

- Melt the fatty material on water bath
- Warm aqueous phase
- Both phases should be at 60 deg C
- Mix with trituration

Pastes

- Pastes are ointment like preparations for external application. They contain high (50%) insoluble solids. Normal insoluble solids are Zinc oxide, Starch, Calcium Carbonate, talc etc.
- They tend to absorb secretions. Pastes give protective barrier to noxious chemical ammonia.

Types of pastes

1. Fatty pastes: Zinc oxide paste with or without salicylic acid
2. Non-greasy pastes: containing glycerine with pectin, gelatin, tragacanth etc.

Bases for pastes

1. Hydrocarbon bases: Sot paraffin, lanolin, benzoinated lard
2. Water Miscible base: Emulsifying ointment/wax
3. Water soluble base: Macrogol base (mainly), Sodium CMC, Pectin and gelatine also can be used.

Jellies/Gels

- Gels are aqueous colloidal suspension of hydrated forms of insoluble medicaments. Jellies are transparent or translucent, non-greasy semi-solid preparation mainly used externally.
- They contain polymer less than 10%. Polymer can be:
  - Natural (Tragacanth, Pectin, Agar, Carrageen, Alginic acid)
  - Synthetic (MC, Hydroxy MC, Caropols, CMC)
  - Hygroscopic substances–To prevent dehydration of jellies

  Examples-Gylcerin, Propylene glycol, Sorbitol

Preservatives

Methyl hydroxy benzoate, Propyl hydroxy benzoate, benzalkonium chloride, chlorhexidine acetate, benzoic acid

Poultices (Cataplasm)

- It is a soft, viscous preparation for external use. They applied to skin when they are hot.
- They have been made from hot water and linseed meal or other cohesive materials which maintain intimate contact with skin and remaining hot and moist.
- They contain heavy Kaolin as an absorbent and glycerine as hygroscopic substance.

Syrup

A syrup is a thick, viscous liquid consisting primarily of a solution of sugar in water, containing a large amount of dissolved sugars but showing little tendency to deposit crystals. The viscosity arises from the multiple hydrogen bonds between the dissolved sugar, which has many hydroxyl (OH) groups, and the water.

The sugar is mainly used to:

- Preserve the finished product
- Aid in masking the unpleasant taste of the active ingredient(s)
- Enhance the flavour.

The concentration of sugar must approach but not quite reach the super-saturation point: the sugar concentration should be between 65 and 67% in weight. A lower percentage of sugar makes the syrup an excellent nutrient for yeast and other microorganisms.

Cap-locking

- A sugar saturated syrup leads to crystallization of a part of the sugar under conditions of changing temperature.
- To avoid Cap-locking problem, polyhydric alcohols are added to the formulation.

Syrups may also contain the following excipients:

- Sugar polyols like glycerol, maltitol and sorbitol
- Preservatives like parabens and benzoates and antioxidants like butylated hydroxytoluene (BHT) and sodium metabisulfite
- Acids like citric acid to prevent the recrystallisation of sugar
- Buffering agents
- Chelating agents like sodium ethylenediaminetetraacetic acid (EDTA)
- Flavouring agents and flavour enhancers
- Colouring agents
- Ethyl alcohol (3–4% in volume)

The syrup may also be sugar-free. The sugar is then replaced by sugar substitutes like the sugar polyols such as glycerol, isomaltol and sorbitol or artificial sweeteners like aspartame, neotame, sucralose and acesulfame potassium mixed to thickening agents like polyvinylpyrrolidone or polysaccharides like carrageenan, xanthan gum, and cellulose ethers. Sugar-free syrup will not contribute to dental caries.

- Syrup IP/BP–Sugar 66.67% w/w, No preservative required
- Syrup USP–Sugar 85% w/v (64.3% w/w), Preservative required

Liniment	Lotion
Alcoholic, oily or soap solution or emulsion	Aqueous or alcoholic solution or suspension in aqueous media
Applied with friction	Application without rubbing
Not applied on broken skin	Applied on broken skin
Applied with brush	Applied with absorbent material
E.g., Camphor liniment	E.g., Calamine lotion

Collodion

- These are fluid preparations for external use. They are applied with brush or rod.
- The film forming base is Pyroxillin (Nitro cellulose) in volatile solvent.
- Flexibility to film given by castor oil.

Linctuses

- These are viscous liquid oral preparations that are usually prescribed for relief of cough.
- Vehicle is always a syrup and sometimes containing glycerin.

Elixir

These are clear, pleasantly flavoured, sweetened Hydro alcoholic liquids.

Formulation

Main ingredients Ethanol (4–40%) and water

Other ingredients Glycerin, Sorbitol, Propylene glycone (PG), Flavouring agents, Syrups, Preservatives

Emulsion

- Biphasic system consisting two immiscible liquids, one of which is finely sub-divided (Dispersed phase) and uniformly distributed throughout the other dispersion medium or continuous phase.
- Globule Size range–0.1 to 100 μm
- Heterogeneous system (size of all globules are not same)
- Thermodynamically unstable

Advantages

- Mask the unpleasant taste (vit. A)
- Increased Bioavailability E.g., Griseofulvin in corn oil-water emulsion
- Sustain release via multiple emusion

Disadvantages

- Due to coalescence-emulsion shows short shelf life

Classification

- Based on the nature of dispersed phase–O/W(oil is internal phase, water is external phase) and W/O (water is internal phase, oil is external phase)
- Based on globules size–micro emulsion (transparent, size less than 0.1 micron) and fine emulsion(milky appearance, size between 0.25 to 25 micron)
- Multiple emulsion–O/W/O (Disperse O/W into oily phase) and W/O/W(Disperse W/O into aqueous phase)

Identification

1. Dye solubility test

Water soluble dyes–amaranth and methylene blue (form unifoem tine in O/W)

Oil soluble dyes–Sudan III and scarlet red (form uniform tine in W/O)

2. Dilution test

When a dispersion medium is added to an emulsion–no phase separation is possible

E.g., when water is added to O/W emulsion-no phase separation is seen

When oil is added to W/O emulsion–no phase separation is seen

3. Conductivity test

This test is based on the ability of water to conduct electicity. If water is the continuous phase–then the emulsion conducts electricity.

4. Creaming test

W/O–normally cream downwards as oil is usually less dense than water.

O/W – normally cream upwards

Theories of Emulsification

1. Reduction in interfacial tension by surfactant
2. Charge imparted on interfacial film by ionic surfactant
3. Monomolecular adsorption
4. Multimolecular adsorption
5. Solid particle adsorption such as colloidal clays and inorganic substances

Physical instability

1. Flocculation (Fluffy Agglomerates): Neighbouring globules comes closer to each other. It can be prevented by imparting charge on the globules surface.
2. Creaming: Due to density difference and due to concentration of globules at the top or bottom of the emulsion.

   W/O – downward creaming
   O/W – upward creaming
3. Coalescence (Compact Aggregates): Few globules tend to fuse with each other and form bigger globules and it is due to destroyed emulsifier film around the globules.
4. Breaking (Cracking): Indicates complete separation of oil and aqueous phase and it is due to completely destroy of protective coating around the globules.
5. Phase inversion: The change of emulsion type from O/W to W/O or vice versa. O/W emulsion made from monovalent soap E.g., Sodium stearate converted into W/O upon addition of divalent soap E.g., Calcium Chloride or Stearate.

Phase inversion can take place at

1. Change in Emulsifier
2. Alteration in Phase Volume Ratio
3. Heating which changes the solubility of Emulsifier.

Factors which improve physical instability

1. Particle size: When size of dispersed globules is less-decreased creaming
   According to Stokes law-diameter of globules is reduced to half-creaming rate is reduced to four fold.
   - Rate of Creaming = $d^2 (\rho^1 - \rho^0)\ g/18\ \eta$
     Where d = diameter of particle
     ρ^1 = density of particle
     ρ^0 = density of liquid
     η = viscosity of liquid
   - Used only for dilute suspension (less than 2% dispersed particles)
2. Particle size distribution: globules of same size (monosize) pack loosely.
   If the globules are not uniform–smaller size globules occupy the space between the larger globules → close packing → lead to coalescence.
3. Viscosity: When viscosity increases flocculation of globules decreases.
4. Phase volume ratio: Relative volume of water and oil is expressed as phase volume ratio. The upper limit is 74% (74% of internal phase).
5. Density of phases
6. Temperature Change: At high temperature, if water is the external phase, water evaporates and makes emulsion more concentrate and at low temperature it tends to freeze.

W/O emulsion	O/W emulsion
Mainly for external use	Internal as well external use
Moisturing Cream, Cleansing Cream, Cold Cream are examples of W/O emulsion.	Milk, Shaving Cream, Vanishing Cream are examples of O/W emulsion.

Bancroft Rule

It describes relationship between nature of emulsifying agent and type of emulsion formed.

- If surfactant is more soluble in water, then O/W emulsion will formed.
- If surfactant is more soluble in oil, then W/O emulsion will formed.

Emulgent

It reduces the interfacial tension between two liquids and stabilize.

- O/W – 8 to 16 HLB value examples–Tween (Polysorbate), Sodium lauryl sulphate, Acacia, Tragacanth
- W/O – 0 to 8 HLB value examples–Span (Polysorbate ester), Glyceryl monostearate

Preparation of Emulsion

1. Dry Gum method: oil + gum then triturate, add water, again triturate, result in primary emulsion.
2. Wet Gum method: (English method) – water + gum then triturate, add oil, again triturate, result in primary emulsion.
3. Bottle method: (Forbes method) – Used for volatile and non-viscous oils.

Proportion	Oil	Water	Gum
Fixed Oil	4	2	1
Volatile Oil	4	4	2

- Fixed oils–Caster oil, Cod liver oil, Shark liver oil, Olive oil, Almond oil
- Volatile oils–Turpentine oil, Sandal wood oil, Cinnamon oil, Peppermint oil
- Mineral oil–Paraffin oil

Preservatives

- Mostly used Para-hydroxy benzoate ester such as methyl and propyl paraben.
- Anti-Oxidants

  Alkyl Gallates such as ethyl and Propyl Gallate
  BHT (Butyl hydroxy Toluene) and BHA (Butyl hydroxy Anisole), Tocopherols.

Label–Shake well before use

Ostwald Ripening Phenomenon

It is the dissolution of small crystals or sol particles and the re-deposition of the dissolved species on the surfaces of larger crystals or sol particles. Ostwald ripening is generally found in water-in-oil emulsions, while flocculation is found in oil-in-water emulsions.

DRUG INCOMPATIBILITY

Drug Incompatibility refers to interactions between two or more substances which lead to changes in chemical, physical, therapeutic properties of the pharmaceutical dosage form.

Types of Drug Incompatibility

1. Therapeutic incompatibility
2. Physical incompatibility
3. Chemical incompatibility

1. Therapeutic incompatibility

It is the modification of the therapeutic effect of one drug by the prior concomitant administration of another. (It is also called drug interactions).

Mechanisms of therapeutic incompatibility

They are divided into two groups:

1. Pharmacokinetics: involve the effect of a drug on another from the point of view that includes absorption, distribution, metabolism and excretion.
2. Pharmacodynamic: are related to the pharmacological activity of the interacting drugs
   e.g synergism, antagonism, altered cellular transport, effect on the receptor site.

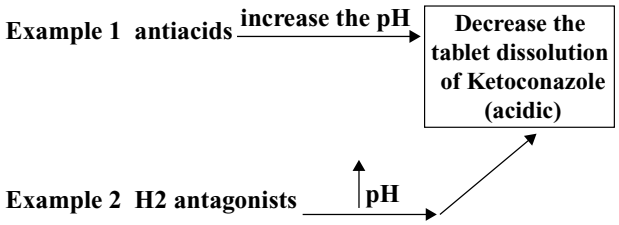
Pharmacokinetic interactions

1. Altered GIT absorption -

   a. Altered pH
   b. Altered bacterial flora
   c. Formation of drug chelates or complexes
   d. Drug induced mucosal damage and altered GIT motility

a. Altered pH:

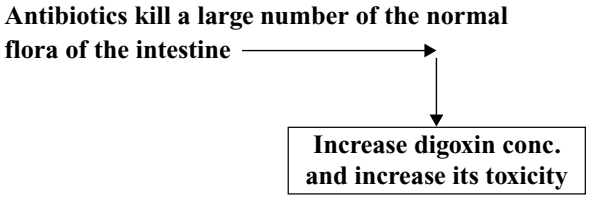
The non-ionized form of a drug is more lipid soluble and more readily absorbed from GIT than the ionized form does.



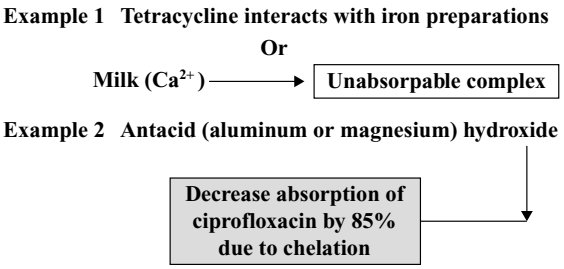
Therefore, these drugs must be separated by at least 2h in the time of administration of both.

b. Altered intestinal bacterial flora

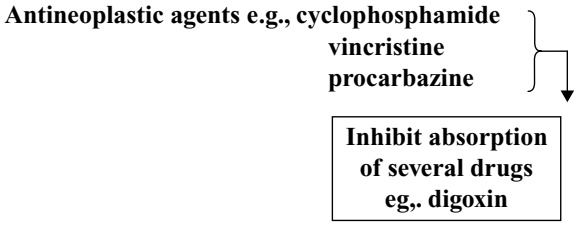
e.g. In 10% of patients receive digoxin → 40% or more of the administered dose is metabolized by the intestinal flora.



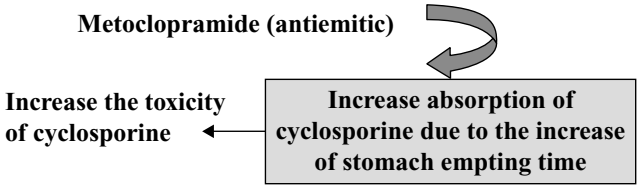
c. Complexation



d. Drug-induced mucosal damage:

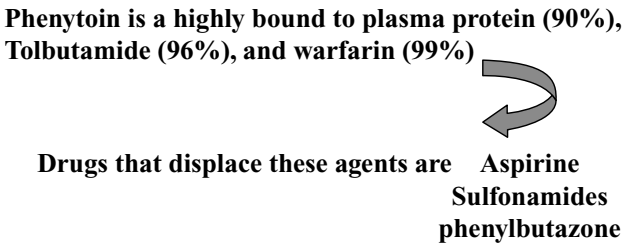


e. Altered motility



2. Displaced protein binding

It depends on the affinity of the drug to plasma protein. The most likely bound drugs is capable to displace others. The free drug is increased by displacement by another drug with higher affinity.



3. Altered metabolism

The effect of one drug on the metabolism of the other is well documented. The liver is the major site of drug metabolism but other organs can also do e.g., WBC, skin, lung, and GIT.

- CYP450 family is the major metabolizing enzyme in phase I (oxidation process).
- Therefore, the effect of drugs on the rate of metabolism of others can involve the following

Enzyme induction: A drug may induce the enzyme that is responsible for the metabolism of another drug or even itself

e.g. Carbamazepine (antiepileptic drug) increases its own metabolism Phenytoin increases hepatic metabolism of theophylline leading to decrease its level and Reduces its action and Vice versa.

NOTE

Enzyme induction involves protein synthesis, therefore, it needs time up to 3 weeks to reach a maximal effect.

Enzyme inhibition:

It is the decrease of the rate of metabolism of a drug by another one. This will lead to theincrease of the concentration of the target drug and leading to the increase of its toxicity.

Inhibition of the enzyme may be due to the competition on its binding sites, so the onset of action is short may be within 24h. e.g.

1. When an enzyme inducer (e.g.carbamazepine) is administered with an inhibitor (verapamil) → the effect of the inhibitor will be predominant

2. Erythromycin inhibit metabolism of astemazole and terfenadine → Increase the serum concentration of the antihistaminic agents leading to increasing the life threatening cardiotoxicity
3. Omeprazole Inhibits oxidative metabolism of diazepam

First-pass metabolism:

Oral administration increases the chance for liver and GIT metabolism of drugs leading to the loss of a part of the drug dose decreasing its action. This is more clear when such drug is an enzyme inducer or inhibitor.
e.g. rifampin lowers serum concentartion of verapamil level by increase its first pass.

Also, rifampin induces the hepatic metabolism of verapamil.

4. Altered renal execration:

a. Inhibition of renal tubular secretion:

It occurs in the proximal tubules (a portion of renal tubules). The drug combines with a specific protein to pass through the proximal tubules. When a drug has a competitive reactivity to the protein that is responsible for active transport of another drug .This will reduce such a drug excretion increasing its concentration and hence its toxicity.

e.g. Probenecid → Decreases tubular secretion of methotrexate.

Examples of drugs that Inhibit renal tubular secretion

Drugs causing inhibition	Drugs whose $t_{1/2}$, may be affected
Probenecid, Sulphinpyrazone, Phenylbutazone, Sulphonamides, Aspirin, Thiazide diuretics, Indomethacin	Penicillin, Azidothymidine, Indomethacin
Verapamil, Amiodarone, Quinidine	Diagoxin
Diuretics	Lithium
Indomethacin	Furosemide
Aspirin, NSAIDs	Methotrexate

b. Alteration of urine flow and pH:

Excretion and reabsorption (Passive tubular reabsorption) of drugs occur in the tubules by Passive diffusion which is regulated by concentration and lipid solubility.

Note

Ionized drugs are reabsorbed lower than non-ionized ones..

- Loop and thiazide diuretics indirectly increase proximal tubular reabsorption of Li+ (which is handled in a similar way as Na+) and this can cause Li+ toxicity in patients treated with lithium carbonate for mood disorders.
- The effect of urinary pH on the excretion of weak acids and bases is put to use in the treatment of poisoning, but is not a cause of accidental interactions.

Pharmacodynamic Interactions

It means alteration of the dug action without change in its serum concentration by pharmacokinetic factors.

a. Additive effect occurs when two or or more drugs having the same effect are combined and the result is the sum of the individual effects relative to the doses used. This additive effect may be beneficial or harmful to the client.
b. Synergistic effect occurs when two or more drugs, with or without the same overt effect, are used together to yield a combined effect that has an outcome greater than the sum of the single drugs active components alone.
c. Potentiation: describes a particular type of synergistic effect-a drug interaction in which only one of two drugs exerts the action that is made greater by the presence of the second drug.
d. Antagonistic: reactions have the opposite effect of synergism and result in a combined effect that is less than either active component alone.
eg. Protamine administered as an antidote toanticoagulant action of heparin

EX., Propranolol + verapamil → **Synergistic or additive effect**

Synergism means = 1 + 1 = 3

Additive means = 1 + 1 = 2

Potentiation means = 1 + 0 = 2

Antagonism means 1 + 1 = 0 or 0.5

On the other hand

Effect at the receptor site
- **Antiadrenegic**
- **anticholinergic**

Examples:

- β-adrenoceptor antagonists diminish the effectiveness of β-receptor agonists, such as salbutamol or terbutaline.
- Many diuretics lower plasma potassium concentration, and thereby enhance some actions of digoxin and predispose to glycoside toxicity.
- Monoamine oxidase inhibitors increase the amount of nor epinephrine stored in noradrenergic nerve terminals and thereby interact dangerously with drugs, such as ephedrine or tyramine that work by releasing stored nor epinephrine. This can also occur with tyramine-rich foods — particularly fermented cheeses such as Camembert.
- Warfarin competes with vitamin K, preventing hepatic synthesis of various coagulation factors. If vitamin K production in the intestine is inhibited (e.g. by antibiotics), the anticoagulant action of warfarin is increased. Drugs that cause bleeding by distinct mechanisms (e.g. aspirin, which inhibits platelet thromboxane A2 biosynthesis and can damage the stomach) increase the risk of bleeding caused by warfarin.
- Sulphonamides prevent the synthesis of folic acid by bacteria and other microorganisms; trimethoprim inhibits its reduction to tetrahydrofolate. Given together the drugs have a synergistic action of value in treating Pneumocystis carinii.
- Non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen or indomethacin, inhibit biosynthesis of prostaglandins, including renal vasodilator/natriuretic prostaglandins (PGE2, PGI2). If administered to patients receiving treatment for hypertension, they cause a variable but sometimes marked increase in blood pressure, and if given to patients being treated with diuretics for chronic heart failure can cause salt and water retention and hence cardiac decompensation.

Note

The interaction with diuretics may involve a pharmacokinetic interaction in addition to the pharmacodynamic effect described here, because NSAIDs can compete with weak acids, including diuretics, for renal tubular secretion...

- H1-receptor antagonists, such as mepyramine, commonly cause drowsiness as an unwanted effect. This is more troublesome if such drugs are taken with alcohol, and may lead to accidents at work or on the road.

2. Physical Incompatibility (pharmaceutical incompatibilities)

Interaction between two or more substances which lead to change in color, odor, taste, viscosity and morphology.

- Manifestations of physical incompatibility:

The following list outlines the various ways incompatibility between or among drug agents may be manifested.

1. Insolubility of prescribed agent in vehicle
2. Immiscibility of two or more liquids
3. Liquification of solids mixed in a dry state (called eutexia)

1. Insolubility:

The following factors affect the solubility of prescribed agent in vehicle and may render it less Soluble:

1. Change in pH
2. Milling
3. Surfactant
4. Chemical reaction
5. Complex formation
6. Co-solvent

Any change in previous factors may lead to precipitation of drugs and change in their properties.

Example 1:

Rx
Benzalkonium chloride
Sodium lauryl sulfate

They are not mixed together because benzalkonium chloride is positive charged while sodium lauryl sulfate has negative charge. By mixing together a precipitate is formed.

Example 2:

Rx
Ephedrine sulfate
Menthol
Liquid paraffin

This prescription is not prescribed because ephedrine sulfate is a salt which is soluble in water but insoluble in organic solvents, oil and paraffin.

2. Immiscibility of two or more liquids

- This manifestation appears clearly in emulsion, creams, lotions, some types of ointments.
- Separation in two phases is noticed in these pharmaceutical dosage forms.
- The following factors lead to immiscibility:
  1. Incomplete mixing
  2. Addition of surfactant with: Unsuitable concentration, false time of addition, Unsuitable for the type of emulsion.

3. Presence of microorganisms: Some bacteria grow on constituents of mixture i.e. gelatin Arabic gum, Others produce enzymes which oxidize the surfactant.
4. Temperature: Storage must be in room temperature to prevent separation

3. Liquification of solids mixed in a dry state (eutexia)

It means that when two solid substances are mixed together, conversion to a liquid state take place. It happens through the following methods:

1. Formation of liquid mixture: when the solid substance is soluble in another solid substance which lead to decrease of its melting point and conversion to a liquid in certain ratios.
2. Exit of crystalline water: By mixing hydrated crystals and dry crystals, crystalline water Diffuse to dry crystals.

3. Chemical Incompatibility

Reaction between two or more substances which lead to change in chemical properties of Pharmaceutical dosage form.

Types of chemical changes:

1. Oxidation
2. Hydrolysis
3. Polymerization
4. Isomerization
5. Decarboxylation
6. Absorption of CO_2
7. Combination
8. Formation of insoluble complexes

1. Oxidation: Oxidation is defined as loss of electrons or gain of oxygen.

Auto-oxidation: It is a reaction with oxygen of air which occur spontaneously without other factors.
Pre-oxidants: are substances catalyze oxidation process i.e. metals, some impurities.

Factors lead to oxidation:

1. Presence of oxygen
2. Light: it can cause photo-chemical reactions: chemical reaction occur in presence of light
3. Temperature: elevated temperature accelerate oxidation reaction
4. PH: each drug has its ideal pH for stability. Any change in pH affect drug stability and may accelerate oxidation reaction
5. Pharmaceutical dosage form: oxidation reaction occur in solutions faster than in solid dosage forms
6. Presence of pre-oxidants as metals and peroxides
7. Type of solvent used: oxidation reaction occurs faster in aqueous solution than others.
8. Presence of unsaturated bonds: as double and triple bonds (oils) which undergo easier than saturated bonds (margarine) for oxidation.

Protection of drugs from oxidation:

1. Addition of Antioxidants: Vitamin E, vitamin C and inorganic sulfur compounds: thiosulfate and polysulfide.
2. Addition of chemicals which form complexes with metals i.e. EDTA, Benzalkonium Chloride
3. Protection from light
4. Choice of suitable pharmaceutical dosage forms which reduce the possibility of oxidation process (solid dosage forms are better than solutions)
5. Maintenance of pH by using buffer solution
6. Choice of suitable solvent (rather than water)
7. Storage in low temperature
8. Protection from air by – a. using good closed containers b. Replacement of oxygen by nitrogen

Chemical groups which undergo oxidation:

1. Phenolic compounds: Phenylephrine
2. Catechol derivatives: Adrenaline and noradrenaline
3. Some antibiotics: Tetracyclines
4. Oils (fixed and volatile)
5. Vitamins (lipid and water soluble)

How to identify oxidation in pharmaceutical dosage form?

1. Change of colour, odour, viscosity of dosage form
2. For fixed and volatile oils: change of colour, taste, odour, and viscosity

2. Hydrolysis: A chemical reaction in which water is used to break down a compound; this is achieved by breaking a covalent bond in the compound by inserting a water molecule across the bond.

Types of hydrolysis:

1. Ionic hydrolysis:

- In which the compound is broken into ions by water.
- The covalent bond between ions of compound is broken down.
- It is reversible Example: Codeine phosphate ⟷ Codeine + Phosphate
- This type take place spontaneously
- Most affected are weak bases and salts.

2. Molecular hydrolysis:

- In which the molecule it self is broken down.
- It is slow process and irreversible.
- It must be avoided.
- Example: Acetylsalicylic acid ⟶ Salicylic acid + Acetic acid
- So there is no solutions as dosage forms for Aspirin

Chemical groups which undergo hydrolysis:

1. Esters – Benzocaine, Procaine
2. Amides – Chloramphenicol, Sulfonamide, Procainamide
3. Nitriles

Factors induce hydrolysis:

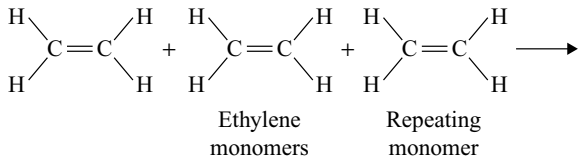
1. Presence of water
2. pH (Example Atropine: optimal pH=3.1–4.5)
3. High temperature (Problem by autoclave i.e. procaine)

Protection from hydrolysis:

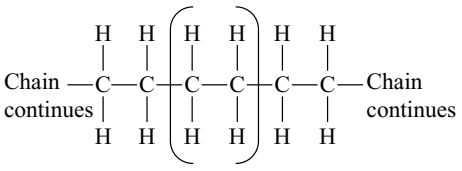
1. Protection from moisture by: Packaging with substances impermeable for moisture And Addition of substances that absorb water ($CaCO_3$)
2. using of solvent rather than water
3. Maintenance of pH by using buffer system
4. Formation of complexes: which protect the drug from the effect of water
5. using of surfactants (micelle formation)
6. Reducing of solubility of substance (i.e. Suspension instead of solution)

3. Polymerization:

- In polymerization, small repeating units called monomers are bonded to form a long chain Polymer.



Ethylene monomers — Repeating monomer



Polyethylene

- Formaldehyde → Paraformaldehyde (Polymer: white precipitate) To avoid this formaldehyde must be stored in suitable temperature and addition of methanol 15%.
- Ampicillin in high temperature forms polymers which cause allergy.

Factors induce Polymerization:

1. Temperature
2. Light
3. Solvent
4. pH
5. Impurities

4. Isomerization:

- It means conversion of drug to its isomer
- Isomers have: Identical molecular formulas and A different arrangement of atoms.

Types of isomerization:

a. Optical isomerization:

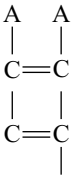
- Conversion of optical active drug into less active
- L-Adrenaline is converted to d-adrenaline by change of pH or temperature. L-adrenaline is more therapeutically active than d-adrenaline, although they have the same physical properties but different arrangement of atoms. This is not general for other drugs: d-tubocurarine is more active than l-type

Factors affect optical isomerization:

1. Temperature
2. pH
3. Solvent
4. Impurities

b. Geometric isomerization:

- One type of isomers
- Expressed by cis or trans



- Cis: means the groups A in the same direction:
- Trans: means the group A in opposite direction:
- Cis is more therapeutically active than trans (ex.: Vitamin A)

5. Decarboxylation:

Example: $NaHCO_3 \rightarrow Na + CO_2$

All drugs contain bicarbonate are not sterilized in high temperature

6. CO_2 – absorption:

- When some pharmaceutical dosage forms contain CO_2, precipitate is formed:
- Example: $Ca(OH)_2 + CO_2 \rightarrow CaCO_3$

7. Combination:

- Take place when the pharmaceutical dosage form contain substances with different charges
- Example: Surfactants with positive and negative charges

8. Formation of insoluble complexes:

- Example: Tetracycline + heavy metals

Multiple Choice Questions

1. Standard unit volume in metric system is
   (a) Microlitre (b) Milliliter
   (c) Centiliter (d) Liter
2. Colloidal mill is suitable for manufacturing of
   (a) Emulsion (b) Ointment
   (c) Tooth paste (d) Suspension
3. Indicate which of the following statements is true. Oil-soluble surfactants:
   (a) Have high HLB values
   (b) Are hydrophilic
   (c) Can be used as emulsifiers to produce water-in-oil emulsions
   (d) Are efficient solubilising agents
4. Which of the following properties are characteristic of microemulsions?
   (a) High surfactant content
   (b) Droplet size greater than 1 μm
   (c) Transparent systems
   (d) Thermodynamically stable
5. Which of the following properties are characteristic of deflocculatedsuspensions?
   (a) Close packing of the sediment to form a cake
   (b) Higher sedimentation rate
   (c) Formation of flocs
   (d) Rapid clearance of supernatant
6. In micro-emulsion pan coating process _____ size solid particles are used.
   (a) 35–5000 micron (b) 2–600 micron
   (c) 5–300 micron (d) 600–5000 micron
7. Bloom strength of gelatin ranges from
   (a) 50 to 150 g (b) 100 to 200 g
   (c) 150 to 250 g (d) 200 to 300 g
8. The viscosity of gelatin can range from
   (a) 25 to 45 millipoise (b) 30 to 50 millipoise
   (c) 30 to 50 poise (d) 25 to 45 poise
9. A polysorbate has a molecular weight of 1300, an ethylene oxide weightpercentage of 68 and a sorbitol weight percentage of 14. The HLB of thissurfactant is
   (a) 15.0 (b) 13.6
   (c) 16.4 (d) 2.8
10. 1 grain is equal to
    (a) 30 mg (b) 60 mg
    (c) 90 mg (d) 1 g
11. Following statement is true for lotion except;
    (a) Aqueous/alcoholic solution/suspension in aqueous media
    (b) Applied with fraction
    (c) Applied on broken skin
    (d) None of the above
12. An elixir contain 38% v/v alcohol, what is proof spirit according to USP,
    (a) 76% (b) 70%
    (c) 66.61% (d) 64.35%
13. Which of the following is used as suspending agent in parenterals?
    (a) Gelatin (b) Pectin
    (c) Both (a) and (b) (d) None of the above
14. 1 ml is equal to how much minim?
    (a) 30 (b) 15
    (c) 1 (d) 10
15. In Clerk's formula, weight is mentioned as
    (a) Pound (b) Gram
    (c) Kilogram (d) Grain
16. Cold cream is also known as _____.
    (a) Foundation cream
    (b) Soft cream
    (c) Skin moisturizer
    (d) Skin protective
17. Plasticizers are added in nail liquors to provide _____ to film.
    (a) Hardness (b) Flexibility
    (c) Toughness (d) Softness
18. Which of the following test is performed for lipsticks?
    (a) Breaking (b) Washability
    (c) Elasticity (d) None of the above
19. Which of the following is not moulding-related problem in lipstick?
    (a) Laddering (b) Cratering
    (c) Deformation (d) Sweating
20. Product size of 1–30 microns may be obtained using
    (a) Roller mill (b) Hammer mill
    (c) Fluid energy mill (d) Cutter mill

21. Particle size reduction will not enhance the absorption of
    (a) Hydrophobic compounds
    (b) Hydrophilic compounds
    (c) Weak acids
    (d) Weak bases
22. Following are the examples of O/W emulsion except
    (a) Milk (b) Shaving cream
    (c) Cold cream (d) Vanishing cream
23. Following ratio is used for the preparation of emulsion
    (a) Fixed oil:Water:Gum (4:2:1)
    (b) Volatile oil:Water:Gum (4:4:2)
    (c) Both of the above
    (d) None of the above
24. Young rule is
    (a) Child dose = (Age in year/age + 12) × Adult dose
    (b) Child dose = (Age in year/20 + 12) × Adult dose
    (c) Child dose = (Age in month/150 + 12) × Adult dose
    (d) Child dose = (Age in month/20 + 12) X Adult dose
25. 1 drop is equal to how much ml –
    (a) 0.6 (b) 0.006
    (c) 0.4 (d) 0.04

ANSWER KEYS

1. (d)	**2.** (d)	**3.** (c)	**4.** (a)	**5.** (a)	**6.** (d)	**7.** (c)	**8.** (a)	**9.** (c)	**10.** (b)
11. (b)	**12.** (c)	**13.** (c)	**14.** (b)	**15.** (a)	**16.** (c)	**17.** (b)	**18.** (a)	**19.** (d)	**20.** (c)
21. (b)	**22.** (c)	**23.** (c)	**24.** (a)	**25.** (d)					

CHAPTER 5

BIOPHARMACEUTICS

ABSORPTION OF DRUG

The process of movement of drug from its site of administration to the systemic circulation is called absorption.

Mechanisms of drug absorption

1. Passive diffusion
2. Pore transport
3. Facilitated diffusion
4. Active transport
5. Ionic/electrochemical
6. Ion-pair transport
7. Endocytosis

Passive Diffusion

- It is also called non-ionic diffusion. More than 90% drugs are absorbed through passive diffusion. The driving force for this process is concentration gradient or electrochemical gradient. In the transportation of drug, there is no energy required, therefore process is called passive diffusion.
- Passive diffusion is expressed by ***Fick's first law of diffusion.***

$$dq/dt = D.A.K._{M/W}\,(C_{GIT} - C)/h$$

- It is non-saturable, but depends on the square root of the molecular size of the drug.

Carrier-mediated transport

- Specialized transport mechanisms are important, without these, some essential water-soluble nutrients will be poorly absorbed. It involves carrier which is present in membrane.
- Carrier binds reversibly/non-covalently with solute and it traverses across the membrane to other side where it dissociates and discharged the solute.

  Carrier returns to its original site.
- Carrier may be an enzyme or some other membrane component.
- Characteristics:

  Specificity
  Saturable
  Occurs at specific sites:
- As more carriers are present in the intestinal tract-absorption window, so more absorption of drug takes place from that site.
- Drugs absorbed through absorption window are poor candidates for controlled release formulations.

There are two types of carrier-mediated transport systems:

(a) Facilitated diffusion

- It is down-hill transport as passive transport but at a much faster rate.
- As no energy is required, the process is not inhibited by metabolic poisons. Facilitated diffusion is of limited importance in the absorption of drugs.

Examples:

(i) Entry of glucose into RBC_s
(ii) Intestinal absorption of Vit-B_1 and B_2
(iii) GI absorption of Vit-B_{12}

(b) Active transport

- It is more important in the absorption of nutrients and drugs characters.
  - Transport against the concentration or uphill transport.
  - Energy is required inhibited by metabolic poisons e.g., fluorides, cyanide and dinitrophenol and lack of oxygen etc.

Examples:

Sodium, potassium, calcium, iron, glucose, amino acids, vitamins (Pyridoxine, ascorbic acid)

- Drugs having similar structure to endogenous substance are absorbed by active transport.

Endocytosits

- It is a minor transport mechanism.
- It involves engulfing extracellular materials within a segment of the cell membrane.

It is the cellular uptake of Macromolecular nutrients–e.g., fat3, starch, Oil Sol. Vitamin A, D, E and K, and drugs such as insulin.

Drug is absorbed into the lymphatic circulation so bypassing first-pass hepatic metabolism.

Endocytosis includes two types of processes:

A. Phagocytosis (Cell eating)
Absorptive uptake of solid particulates

B. Pinocytosis (Cell drinking)
Uptake of fluid solute e.g., orally administered Sabine polio vaccine, large protein molecules.

THEORIES OF DISSOLUTION

- Diffusion Layer Model (Film Theory)
- Danckwert's Model (Penetration or Surface Renewal Theory)
- Interfacial Barrier Model (Double Barrier Mechanism OR Limited Solvation Theory)

Diffusion Layer Model (Film Theory)

It is a simplest model where dissolution of crystal, immersed in liquid takes place without involving reactive or electrical forces.

It consists of two consecutive steps:

- Solution of the solid to form a thin film or layer at the solid/liquid interface called as **stagnant film** or diffusion layer which is saturated with the drug this step is usually rapid **(instantaneous).**
- **Diffusion** of the soluble solute is from the stagnant layer to the bulk of the solution. This step is slower and is therefore the **rate determining step** in the drug dissolution.

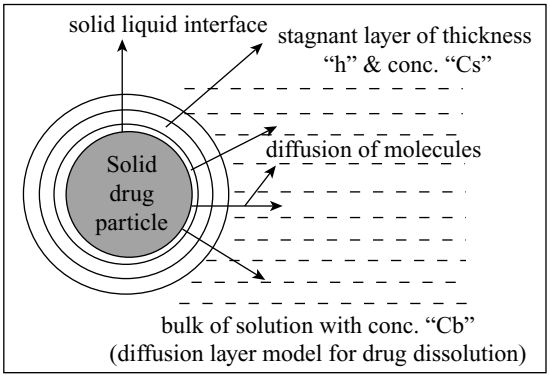


Figure 5.1 Diffusion layer model–Diagrammatic overview

Fick's law covers only diffusions under steady state conditions. Modifying it, Noyes and Whitney established another equation.

$$\frac{dc}{dt} = k\,(Cs - Cb) \_\_\_\_\_ A.$$

$\frac{dc}{dt}$ = dissolution rate of the drug

k = dissolution rate constant (first order)

Cs = conc. of drug in stagnant layer (saturation or max. drug solubility)

Cb = conc. of the drug in bulk of the solution at time t

Brunner and Tolloczko incorporated surface area 'A' in Noyes and Whitney equation.

$$dc/dt = k_1 A\,(Cs - Cb)$$

Afterwards, Brunner incorporated Fick's law of diffusion and expanded his given equation to include diffusion coefficient 'D', thickness of stagnant diffusion layer 'h' and volume of dissolution medium 'v'.

$$\frac{dc}{dt} = \frac{DAk_{w/o}\,(CS - cb)}{Vh} \_\_\_\_\_ B.$$

D = diffusion coefficient of the drug

A = surface are of dissolving solid

$k_{w/o}$ = water/oil partition coefficient of the drug considering the fact that dissolution body fluid are aqueous since the rapidity with which a drug dissolved depend on the $k_{w/o,}$ it is also called as the instrinsic dissolution rate constant

V = volume of dissolution medium

h = thickness of stangnant layer

(Cs – Cb) = conc. gradient for diffusion

This describes a first-order dissolution kinetics. It represents dissolution under non-sink conditions.

If volume is relatively large such that

Cs>>Cb so,

$$\frac{dc}{dt} = \frac{Ak_{w/o}}{Vh}\,Cs$$

Cs and D are constants for each specific chemical substance

$$\frac{dc}{dt} = k1\frac{Ak}{Vh}\ (\because k1 = k_{w/o}DCs)$$

V and A kept constant during dissolution test

$$\frac{dc}{dt} = k \_\_\_\_\_ C.$$

Dissolution rate **under sink condition follow zero order dissolution rate**.

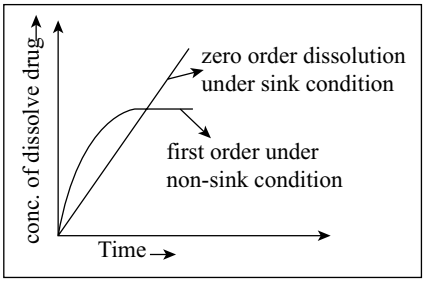


Figure 5.2 Dissolution under sink and non-sink condition–Graphical overview

Danckwert's Model (Penetration or Surface Renewal Theory)

- This theory assumes that solid–solution equilibrium is achieved at interface and mass transport is slow step in dissolution process.
- The model could be visualized as a very thin film having a conc. Ci which is less than saturation, as it is constantly being exposed to fresh surfaces of liquid having a conc. much less than Ci. According to the model, the agitated fluid consist of mass of eddies or packets that are continuously being exposed to new surfaces of solid and then carried back to bulk of liquid.
- Diffusion occurs into each of these packets during short time in which the packet is in contact with surface of solid.
- Since turbulence actually extends to surface, there is no laminar boundary layer and so no stagnant film exists. Instead, surface continually being replaced with fresh liquid.

$$V\frac{dc}{dt} = \frac{dm}{dt} = A(Cs \quad Cb\sqrt{rD})$$

where m = mass of solid dissolution
r = rate of surface renewal (or the interfacial tension)

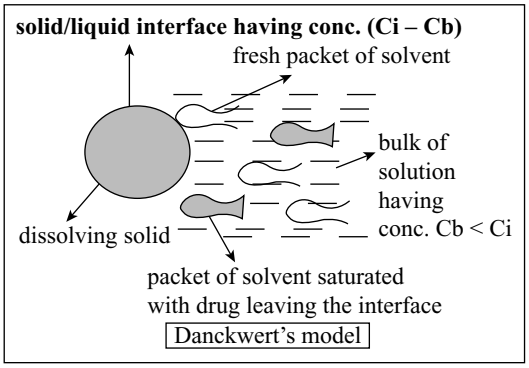


Figure 5.3 Surface renewal theory–Diagrammatic overview

Interfacial Barrier Model (Double Barrier or Limited Solvation Theory)

The Diffusion layer model and the Dankwert's model were based on two assumptions:

1. The rate determining step that controls dissolution is the mass transport.
2. Solid solution equilibrium is achieved at the solid/liquid interface.

According to interfacial barrier model, an intermediate conc. Cs can exist at the interface as a result of **solvation mechanism** and is a function of solubility rather than diffusion.

When considering the dissolution, the crystal will have a different interfacial barrier given by following equation,

$$G = Ki\,(Cs - Cb)$$

Where G = dissolution per unit area
Ki = effective interfacial transport constant

In this theory, the diffusivity D may not be independent of saturation conc. Cs.

The interfacial barrier model can be extended to both Diffusion layer model and the Dankwert's model.

Types of Models of Mechanism of Drug Release

	Special feature	Graph plotted
Zero-order	Drug release rate is independent of concentration of dissolved substance.	Cumulative % of drug release V/S time (h)
	$Q_t = Q_0 + K_0 t$	Straight line comes
First-order	Drug release rate is depends on concentration of dissolved substance.	Log cumulative % of drug remaining to be dissolved v/s time(h)
	$\log Q_t = \log Q_0 + Kt/2.303$	Straight line comes

	Special feature	Graph plotted
Higuchi model	Describe drug release by dissolution and with change in surface area and diameter of dissolved particles. $Q = K_H t^{1/2}$	Cumulative % of drug release v/s square root of time (h) Straight line comes
Hixon-crowel	It suggest drug release by diffusion mechanism $Q_0^{1/3} - Q_t^{1/3} = K_{HC} t$	Cube root of initial concentration minus cube root of % remaining V/S time (h) Straight line comes
Korsmeyer-Peppas	Equation – $(M_t/M) = K_m t^n$ n(release exponent) value – 1. n = 0.45----Fickian diffusion 2. 0.45 < n < 0.89----Anomalous or non-fickian diffusion means both diffusion and erosion controlled release 3. n = 0.89 or above----case-2 relaxation or supercase transport-2 Means erosion of polymeric chain	Log cumulative % of drug remaining to be dissolved v/v log time (hr) Straight line comes

Interpretation of Dissolution Profile Comparision

Among several methods investigated for dissolution profile comparison, f_2 is the simplest. Moore and Flanner proposed a model independent mathematical approach to compare the dissolution profile using two factors, f_1 and f_2.

$$f_1 = \{[\Sigma_{t=1}\, n \mid R_t - T_t \mid]/[\Sigma_{t=1}\, nR_t]\} \cdot 100$$

$$f_2 = 50 \cdot \log\{[1 + (1/n)\Sigma_{t=1}\, n(R_t - T_t)2] - 0.5 \cdot 100\}$$

Where R_t and T_t are the cumulative percentage dissolved at each of the selected n time points of the reference and test product respectively.

F_1 factor value = 0 to 50 (Differential factor)
F_2 factor value = 50 to 100 (Similarity factor)

- The factor f_1 is proportional to the average difference between the two profiles, where as factor f_2 is inversely proportional to the average squared difference between the two profiles, with emphasis on the larger difference among all the time-points.
- The factor f_2 measures the closeness between the two profiles. Because of the nature of measurement, f_1 was described as difference factor, and f_2 as similarity factor
- When the two profiles are identical, $f_2 = 100$.
- An average difference of 10% at all measured time point's results in f_2 value of 50.
- FDA has set a public standard of f_2 value between 50–100 to indicate similarity between two dissolution profiles.

Biowaivers

- Means to waive off doing bioavailability and bioequivalence studies.
- Conditions for justifying request of biowaiver:
  1. Drug must be highly soluble and permeable.
  2. Must be stable in GIT.
  3. Product is designed not to be absorbed in oral cavity.
  4. Must not have narrow therapeutic index.
  5. Excipients used in IR solid dosage forms must have no significant effect on rate and extent of oral drug absorption.

Official dissolution test

According to I.P. and E.P. for solid dosage forms (tablets and capsules) dissolution apparatus used are:

Apparatus I–Paddle Apparatus
Apparatus II–Basket Apparatus

According to B.P., apparatus used are:
Apparatus I–Basket Apparatus
Apparatus II–Paddle Apparatus
Apparatus III–Flow Through Cell Apparatus

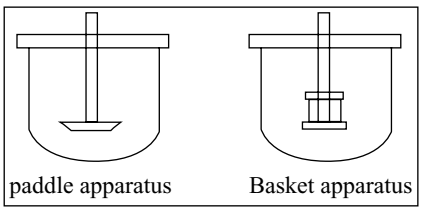


Figure 5.4 Official dissolution apparatus as per IP, BP and USP

According to USP, dissolution apparatus used are:

USP Apparatus types	Description	Dosage Form
I	Basket	IR,DR,ER
II	Paddle	IR,DR,ER
III	Reciprocating Cylinder	IR,ER
IV	Flow through Cell	ER, Poorly soluble API
V	Paddle over Disk	Transdermal
VI	Cylinder	Transdermal
VII	Reciprocating Holder	ER

ER-Extended release; IR-Immediate release; DR-Delayed Release

Conditions (For all in general)

- Temp. – 37±0.5°C
- PH – ±0.05 unit in specified monograph
- Capacity – 1000 ml
- Distance between inside bottom of vessel and paddle/basket is maintained at 25±2 mm.
- For enteric coated dosage form, it is first dissolved in 0.1 N HCl and then in buffer of pH 6.8 to measure drug release. (Limit – NMT 10% of drug should dissolve in the acid after 2h and about 75% of it should dissolve in the buffer after 45 min.)

Bio Pharmaceutical Classification

Class I–High solubility/high permeability

Example–Propranalol, Metoprolol

Class II–Low solubility/high permeability
Example–NSAIDs–ketoprofen Antiepileptic–Carbamazepine

Class III–High solubility/low permeability
Example–Ranitidine, Atenolol

Class IV–Low solubility/low permeability
Example–Hydrochlorothiazide, Furosemide

Class Boundaries of BCS

- A drug substance is considered highly soluble when the highest dose strength is soluble in ≤ 250 ml water over a pH range of 1 to 7.5.
- In the absence of evidence suggesting instability in the gastrointestinal tract, a drug substance is considered highly permeable when the extent of absorption in humans is determined to be ≥ 90% of an administered dose, based on mass-balance or in comparison to an intravenous reference dose.
- In this guidance, an IR drug product is considered rapidly dissolving when no less than 85% of the labeled amount of the drug substance dissolves within 30 minutes, using *U.S. Pharmacopeias* (USP) Apparatus I at 100 rpm (or Apparatus II at 50 rpm) in a volume of 900 ml or less in each of the following media:
  1. 0.1 N HCl or Simulated Gastric Fluid USP without enzymes;
  2. a pH 4.5 buffer;
  3. a pH 6.8 buffer or Simulated Intestinal Fluid USP without enzymes.

Pharmacokinetics

It is the study of "How Body acts to the administered dug". It includes four phases:

- Absorption
- Distribution
- Metabolism (Bio-transformation)
- Excretion

Biological Half-life

For a substance, the time required for the amount of that substance in a biological system to be reduced to one half of its value by biological processes, when the rate of removal is approximately exponential.

If C_0 is initial concentration and C is concentration at time 't', for **first order kinetics.**

$$\log C = \log C_0 - \frac{k_e t}{2.303}$$

$$\text{at 't'} = t_{1/2},\ C = C_0/2$$

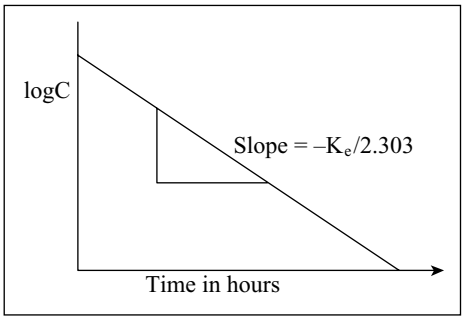


Figure 5.5 First order kinetics–Graphical overview

$$\therefore \log \frac{C_0}{2} = \log C_0 - \frac{k_e t}{2.303}$$

$$t_{1/2} = 2.303 \log 2/K_e$$

$$t_{1/2} = \frac{0.693}{K_e}$$

Where $\mathbf{K_e}$ = Elimination rate constant

Elimination is always first order and thus biological half-life is independent of drug concentration, exception is ethanol.

Value of K_e can be obtained by plotting graph of log C vs time.

Volume of Distribution

Volume of distribution (V)

It is the apparent space into which the drug distributes in the body. It is the measure of "extent" of distribution. "Where is the drug in the body"? The higher the value, the more extravascular distribution in the body.

$$\mathbf{A = V \cdot C}$$

A stands for amount of drug, C stands for plasma concentration.

Relationship Between $t_{1/2}$ and V

Consider a drug following one compartment kinetics

$$\text{Rate of elimination} = K_e{*}A = K_e{*}V{*}C = CL{*}C$$

$$CL = K_e{*}V$$

where K_e = elimination rate constant

$$K_e = CL/V$$

And $$t_{1/2} = 0.693/K_e$$

$$\mathbf{t_{1/2} = (0.693/CL) \times V}$$

Half-life of a drug depends not only on **clearance** (efficiency of removal from body) but also **volume of distribution** (distribution pattern of drug).

V rarely corresponds to a real volume

Approx physiological volumes for a 70 kg man:

- Plasma ~ 3 L
- ECF ~ 16 L
- TBW ~ 42 L

Some examples of drug V (approx for 70 kg man):

- Erythropoeitin ~ 3–5 L
- Digoxin ~ 500 L

It can exceed physiological volumes.

Why is apparent V sometimes greater than physiological volumes?

If drug has high affinity for tissues (Kp↑), Apparent tissue volume ($Kp{*}V_T$) is↑ Therefore V is ↑se.

Renal Clearance

It is the volume of blood from which the drug is totally removed in unit time through renal excretion. It is expressed as CL_R. It has units mL/min.

It is a major organ for excretion of drugs is the kidney.

- Functional units are:
  Nephron Bowman's Capsule Proximal Tubule
  Loop of Henle Distal Tubule Collecting Duct

Renal Clearance = Rate of Excretion/Plasma Concentration

- It can be used to quantitate renal excretion
- Used to study mechanism for renal excretion
  - GFR » 120 ml/min
  - Renal Blood Flow » 650 ml/min

Renal clearance = (Filtration rate + Excretion rate – Re absorption rate)/Plasma Concentration

Renal clearance can be calculated from k_e and V after Pharmacokinetic analysis. It can also be calculated from Excretion Rate and Cp

$$\mathbf{CL_R = f{*}K_eV}$$

Where ***f*** = Fraction of drug excreted through kidney.

K_e = Elimination rate Constant.

V = Volume of Distribution

- Renal function is determined by measuring GFR (Glomerular Filtration Rate).
- GFR is measured by exogenous or endogenous markers like Inulin or Creatinine.
- **Inulin clearance** is accurate measurement of GFR but tedious method while creatinine clearance (CL_{cr}) widely used clinically for assessment of renal function.

$$CL_{cr} = UV/P$$

where, U = Urinary creatinine concentration.

V = 24 hour urine volume.

P = Plasma or serum creatinine concentration.

- **Creatinine clearance**,
  F = 1.23 for Male, 1.04 for Female
  Value for normal males: 117 ± 20 ml/min
  Value for normal females: 108 ± 20 ml/min

Inulin Clearance

This is for inulin, and yields the glomerular filtration rate.

- Value for normal males:
  124.5 ± 9.7 ml/min

- Value for normal females:
  108.8 ± 13.5 ml/min

PHARMACOKINETIC MODELS

- Pharmacokinetics models provide concise means of expressing mathematically or quantitatively, the time course of drug(s) throughout the body and compute meaningful pharmacokinetics parameters.

Types of Pharmacokinetics Models

1. Compartmental models
2. Non-compartmental analysis
3. Physiologic modelling

Compartmental Models

- Mammillary model
- Caternary model

Non-Compartmental Model

Also called as the **model independent method**, as it does not require assumption of specific compartment model.

- Non–compartmental models describe the pharmacokinetics of drug disposition using time and concentration parameters.
- This method can however be applied to any compartment model provided the drugs or metabolites follow linear kinetics.
- The approach based on statistical moments theory, involves the collection of experimental data following a single dose of drug.
- If one considers the time course of drug concentration in plasma as a statistical distribution curve, then:

$$MRT = \frac{AUMC}{AUC}$$

Where MRT = Mean residence time

AUMC = area under the *first moment* curve

AUC = area under the *zero moment* curve.

AUMC is obtained from a plot of product of plasma concentration and time (C*t) versus time t from zero to infinity. Mathematically, it is expressed by equation:

$$AUMC = \int_0^\infty Ctdt$$

AUC is obtained from a plot of plasma drug concentration versus time from zero to infinity. Mathematically, it is expressed by equation:

$$AUC = \int_0^\infty Cdt$$

Practically, the AUMC and AUC can be calculated from the respective graphs by trapezoidal rule.

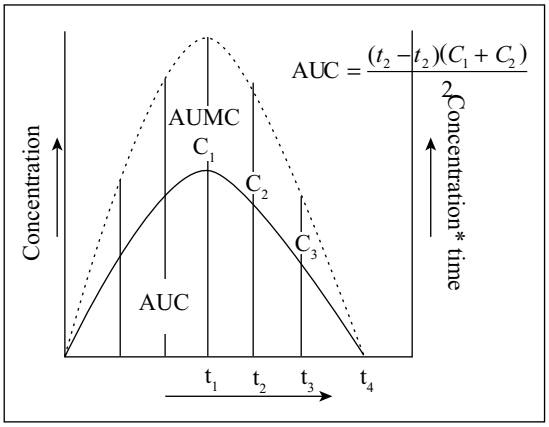


Figure 5.6 AUC and AUMC plots

- MRT is defined as the average amount of time spent by the drug in the body before being eliminated.
- Non-compartmental model is widely used to estimate the important pharmacokinetic parameters like bioavailability, clearance and apparent volume of distribution. The method is also useful in determining half life, rate of absorption and first order absorption rate constant of drug.

Advantages of non-compartmental model

- Ease of derivation of pharmacokinetic parameters by simple algebraic equations.
- The same mathematical treatment can be applied to almost any drug or metabolite provided they follow first order kinetics.
- A detailed description of drug disposition characteristics is not required.

Disadvantages of non-compartmental model

- It provides limited information regarding the plasma drug concentration–time profile; more often it deals with averages.

PHYSIOLOGIC MODEL

Also called as Blood flow rate –limited models and perfusion rate limited models.

One compartment open model (Instantaneous distribution model)

- This model thus applies only to those drugs that distribute rapidly throughout the body.

- The anatomical reference compartment is the plasma and concentration of drug in plasma is representative of drug concentration in all body tissues i.e., any change in plasma drug concentration reflects a proportional change in drug concentration throughout the body.
- The term **open** indicates that the input (availability) and output (elimination) are unidirectional and that the drug can be eliminated from the body.

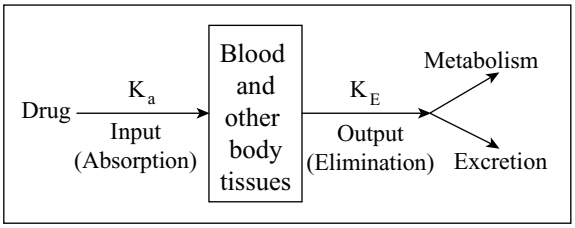


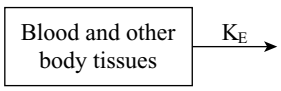
Figure 5.7 One compartment open model showing input and output processes.

One compartment open model is generally used to describe plasma levels following administration of a single dose of a drug. Depending upon the rate of input, several one compartment open models can be defined:

1. One compartment open model, intravenous bolus administration
2. One compartment open model, continuous intravenous infusion
3. One compartment open model, extravascular administration, zero order absorption and
4. One compartment open model, extravascular administration, first order absorption.

One compartment open model (Intravenous bolus administration)

- When a drug that distributes rapidly in the body is given in the form of a rapid intravenous injection (i.e., IV bolus or slug), it takes about one to three minutes for complete circulation and therefore the rate of absorption is neglected in calculations. The model can be depicted as follows:



$$\frac{dX}{dt} = \text{Rate in (availability)} - \text{Rate out (elimination)} \quad \textbf{---1}$$

Since the rate in or absorption is absent, the equation becomes

$$\frac{dX}{dt} = -\text{Rate out} \quad \text{------ 2}$$

If the rate out or elimination follows first order kinetics then:

$$\frac{dX}{dt} = -K_E X \quad \text{------ 3}$$

Where, K_E = First order elimination rate constant

X = amount of drug in body at any time t remaining to be eliminated.

Negative sign indicates that the drug is being lost form the body.

Elimination rate constant

- Elimination phase can be characterized by three parameters:
  - Elimination rate constant
  - Elimination half-life
  - Clearance

Integration of equation 3. yields

$$\ln X = \ln X_o - K_E t \quad \textbf{------ 4}$$

Where, X_o = amount of drug at time t = o i.e., the initial amount of drug injected.

Equation 4. can also be written in exponential form as:

$$X = X_o e^{-K_E t} \quad \textbf{----- 5}$$

It shows that disposition of drug that follows one compartment kinetics is monoexponential.

Transforming equation 4. into common logarithms (log base 10), we get:

$$\log X = \log X_o - \frac{K_E t}{2.303} \quad \textbf{------ 6}$$

- Since it is difficult to determine directly, the amount of drug in the body X, advantage is taken of the fact that a constant relationship exist between drug concentration in plasma C (easily measurable) and X;

Thus, $X = V_d C$ **------- 7**

Where, V_d = proportionality constant popularly known as apparent volume of distribution.

- It is a pharmacokinetic parameter that permits the use of plasma drug concentration in place of amount of drug in the body.

The equation 6. therefore becomes:

$$\log C = \log C_o - \frac{K_E t}{2.303} \quad \text{------ 8}$$

- Equation (8) is that of a straight line and indicates that a semi logarithmic plot of log C versus t will be linear with Y intercept log C_o.
- The elimination rate constant is directly obtained from slope of the line. It has unit of min^{-1}.
- Thus a linear plot is easier to handle mathematically than a curve which in this case will be obtained from a plot of C versus t on regular (Cartesian) graph paper.

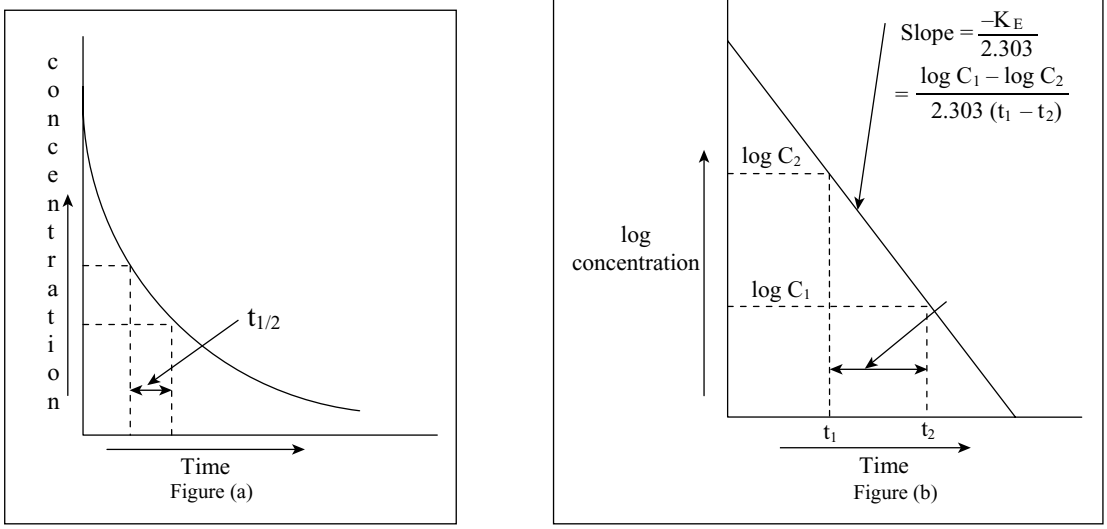


Figure 5.8 (a) Cartesian plot of a drug that follows one compartment kinetics and given by rapid IV injection and (b) Semi logarithmic plot for the rate of elimination in a one compartment model.

Elimination half-life

Half-life is related to elimination rate constant by the following equation:

$$t_{½} = \frac{0.693}{K_E} \quad \text{------ 11}$$

Most of the drugs are eliminated within 10 half-lives.

- Half-life is a secondary parameter that depends upon the primary parameters—clearance and apparent volume of distribution as follows:

$$t½ = \frac{.0693 V_d}{Cl_T} \quad \text{.....11(a)}$$

Apparent volume of distribution

- Apparent volume of distribution and clearance are two separate and independent pharmacokinetic characteristics of a drug. Since they are closely related with physiologic mechanisms in the body, they are called as primary parameters.

$$V_d = \frac{\text{Amount of drug in the body}}{\text{Plasma drug concentration}} = \frac{X}{C} \quad \text{------ 12}$$

- V_d is a measure of the extent of distribution of drug and is expressed in litres. The best and simplest way of estimating V_d of a drug is administering it by rapid IV injection and using following equation:

$$V_d = \frac{X_o}{C_o} = \frac{\text{i.v.bolusdose}}{C_o} \quad \text{------13}$$

- Equation (13) can only be used for the drugs that obey one compartment kinetics. This is because the V_d can only be estimated when distribution equilibrium is achieved between drug in plasma and that in tissues and such an equilibrium is instantaneously for a drug that follows one compartment kinetics.
- A more general, more useful non-compartmental method that can be applied to many compartment models for estimating the V_d is:

For drug given as IV bolus,

$$V_{d(area)} = \frac{X_o}{K_E.AUC} \qquad \text{-------(14.a)}$$

For drug given as extravascularly

$$V_{d(area)} = \frac{FX_o}{K_E.AUC} \qquad \text{-------(14.b)}$$

Where X_o = dose administered and F = fraction of drug absorbed into systemic circulation.

Clearance

- Clearance is the most important parameter in clinical drug applications and is useful in evaluating the mechanism by which a drug is eliminated by the whole organism or by a particular organ.
- Clearance is a parameter that relates plasma drug concentration with rate of drug elimination according to the following equation:

$$\text{Clearance} = \frac{\text{Rate of Elimination}}{\text{Plasma drug concentration}} \qquad \text{-------15}$$

Or

$$Cl = \frac{dX/dt}{C} \qquad \text{------16}$$

- Clearance is the theoretical volume of body fluid containing drug (i.e., that fraction of apparent volume of distribution) from which the drug is completely removed in a given period of time. It is expressed in ml/min or litres/hour.

One compartment open model (Intravenous Infusion)

- Rapid IV injection is unsuitable when the drug has potential to precipitate toxicity or when maintenance of a stable concentration or amount of drug in the body is desired.
- In such a situation, the drug is administered at a constant rate (zero order) by IV infusion.

Advantages of such a zero order infusion of drugs include

- Ease of control of rate of infusion to fit individual patient needs.
- Prevents fluctuating plasma level (maxima and minima), desired especially when the drug has a narrow therapeutic index.
- Other drugs, electrolytes and nutrients can be conveniently administered simultaneously by the same infusion line in critically ill patients.

The model can be presented as follows

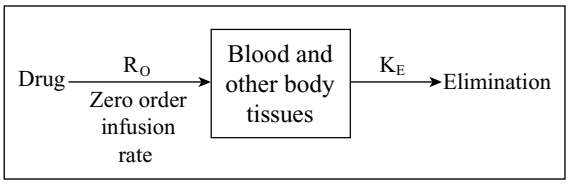


Figure 5.9 One compartment open intravenous infusion model.

- At any time during infusion, the rate of change in the amount of drug in the body, dX/dt is the difference between the zero order rate of drug infusion R_o and first order elimination, $-K_EX$:

$$dX/dt = R_o - K_EX \qquad \text{------ 33}$$

Integration and rearrangement of above equation yields

$$X = \frac{R_o}{K_E}(1 - e^{-K_E t}) \qquad \text{-------34}$$

Since $X = V_d C$, **equation (34)** can be transformed into concentration terms as follows:

$$C = \frac{R_o}{K_E V_d}(1 - e^{-K_E t}) = \frac{R_o}{Cl_T} - (1 - e^{-K_E t}) \qquad \text{------ 35}$$

- After infusion, as time passes, amount of drug rises gradually (elimination rate less than the rate of infusion) until a point after which the rate of elimination equals the rate of infusion i.e., the concentration of drug in plasma approaches a constant value called as steady state, plateau or infusion equilibrium.
- At steady-state, the rate of change of amount of drug in the body is zero hence the **equation (33)** becomes:

$$0 = R_o - K_E X_{SS}$$

Therefore, $K_E X_{SS} = R_o$ ------ 36

Transforming to concentration terms ($X_{SS} = V_d C_{SS}$) and rearranging the equation:

$$C_{ss} = \frac{R_o}{K_E V_d} = \frac{R_o}{Cl_T} \text{ i.e., } \frac{\text{Infusion rate}}{\text{Clearance}} \qquad \text{------ 37}$$

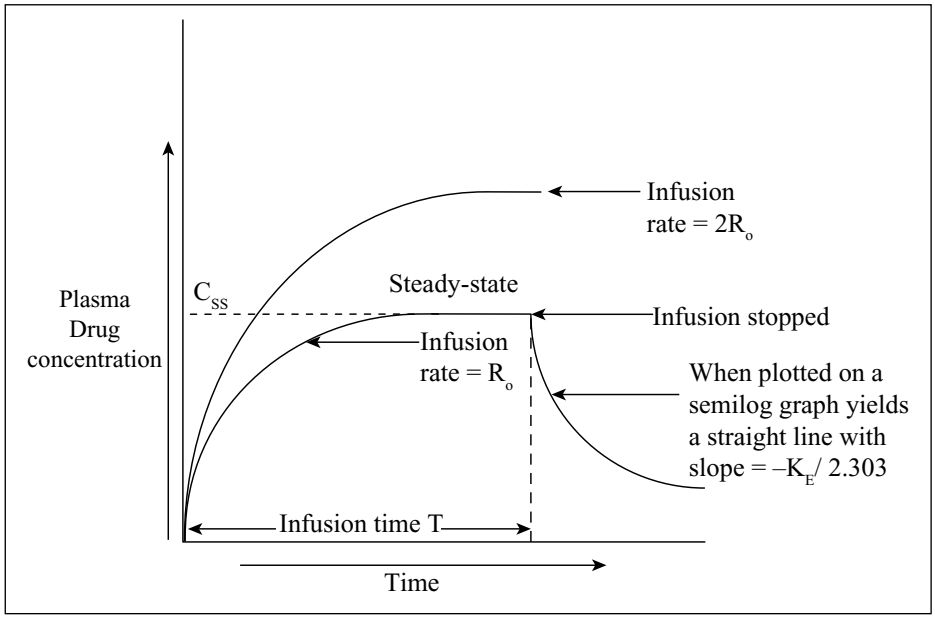


Figure 5.10 Plasma concentration time profile for a drug given by constant rate IV infusion (the two curves indicate different infusion rates R_o and $2R_o$ for the same drug).

Where X_{SS} and C_{SS} are amount of drug in the body and concentration of drug in plasma at steady state respectively.

- The value of K_E (and hence $t_{1/2}$) can be obtained from the slope of straight line obtained after a semilogarithmic plot (log C versus T) of plasma concentration-time data gathered from the time when infusion is stopped.
- Alternatively, K_E can be calculated from the data collected during infusion to steady state as follows:

Substituting $R_o/Cl_T = C_{SS}$ from equation (37) in equation 35 we get:

$$C = C_{SS}\,(1 - e^{-K_E t}) \qquad \text{------ 38}$$

- Rearrangement yields:

$$\left[\frac{Css - C}{Css}\right] = e^{-KEt} \qquad \text{------ 39}$$

- Transforming to log form, the equation becomes:

$$\log\left[\frac{Css - C}{Css}\right] = \frac{-K_E T}{2.303} \qquad \text{------ 40}$$

- Now, plot of $\log\left[\frac{Css - C}{Css}\right]$ versus **time** gives straight line with slope = $\frac{-K_E}{2.303}$

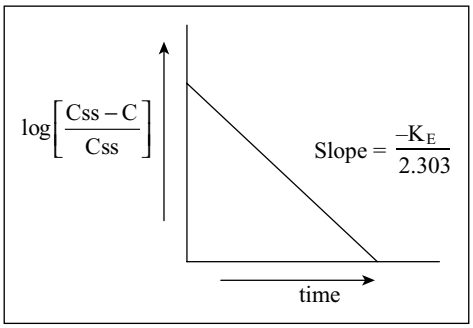


Figure 5.11 Plot of $\log\left[\frac{Css - C}{Css}\right]$ versus time

- The time to reach steady state concentration is dependent upon the elimination half life and not infusion rate. An increase in infusion rate will merely increase the plasma concentration attained at steady state (figure 7). If n is the number of half-lives passed since the start of infusion ($t/t_{1/2}$), equation (38) can be written as

$$C = C_{SS}\,[1 - (1/2)^n] \qquad \text{------ 41}$$

- The per cent of C_{SS} achieved at the end of each $t_{1/2}$ is the sum of C_{SS} at previous $t_{1/2}$ and the concentration of drug remaining after a given $t_{1/2}$ (Table 1).

Half life	% Remaining	% CSS achieved
1	50	50
2	25	50+25=75
3	12.5	75+12.5=87.5
4	6.25	87.5+6.25=93.75
5	3.125	93.75+3.125=96.875
6	1.562	96.875+1.562=98.437
7	0.781	98.437+0.781=99.218

- For therapeutic purpose, more than 90% of the steady state drug concentration in the blood is desired which is reached in 3.3 half lives. It takes 6.6 half lives for the concentration to reach 99% of the steady state. Thus, the shorter the half life (e.g., Penicillin G, 30 minutes), sooner is the steady state reached.

Infusion plus loading dose

- It takes a very long time for the drugs having longer half-lives before the plateau concentration is reached (e.g., Phenobarbital, 5 days).
- This can be overcome by administering an IV loading dose large enough to yield the desired steady state immediately upon injection prior to starting the infusion. It should then be followed immediately by IV infusion at a rate enough to maintain this concentration.

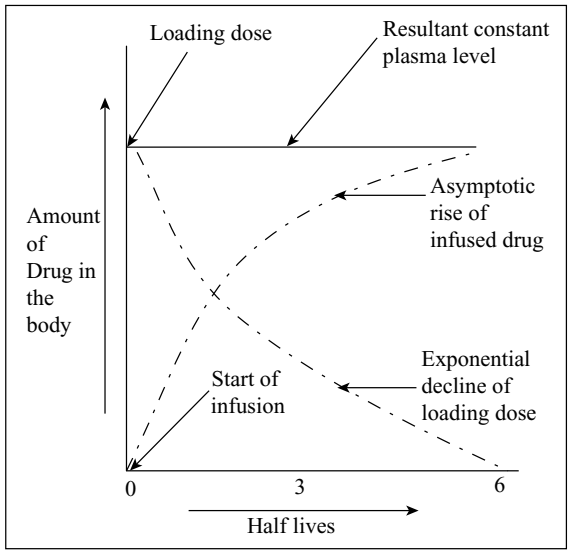


Figure 5.12 Intravenous infusion with loading dose. As the amount of bolus dose remaining in the body falls, there is a complementary rise resulting from the infusion.

- Recalling once again, the relationship $X = V_d C$, the equation for computing the loading dose $X_{O,L}$ can be given:

$$X_{O,L} = C_{SS} V_d \quad \text{------ 42}$$

- Substitution of $C_{SS} = R_o/K_E V_d$ from equation (37) in above equation yields another expression for loading dose in terms of infusion rate:

$$X_{O,L} = \frac{R_o}{K_E} \quad \text{------ 43}$$

- The equation describing the plasma concentration time profile following simultaneous IV loading dose (IV bolus) and constant rate IV infusion is the sum of following two equations (44 and 45) describing each process.
- If we recall **equation 5.** for IV bolus

$$X = X_o e^{-K_E t}$$

- And substituting $X = V_d C$ in above equation we get

$$C = \frac{X_o e^{-K} E^t}{V_d} \quad \text{------- 44}$$

- And from equation (35) for constant, rate IV infusion, we know that

$$C = \frac{R_o}{K_E V_d}(1 - e^{-K_E t}) \quad \text{------ 45}$$

$$C = \frac{X_{O,L}}{V_d} e^{-K_E t} + \frac{R_o}{K_E V_d}(1 - e^{-K_E t}) \quad \text{------ 46}$$

- It we substitute $\mathbf{C_{SS} V_d}$ **for** $\mathbf{X_{O,L}}$ (from equation 42) and $\mathbf{C_{SS} K_E V_d}$ **for** $\mathbf{R_o}$ (from equation 37) in above equation and simplify, it reduces to $\mathbf{C=C_{SS}}$ indicating that concentration of drug in plasma remains constant (steady) throughout the infusion time.

Zero Order Absorption Model

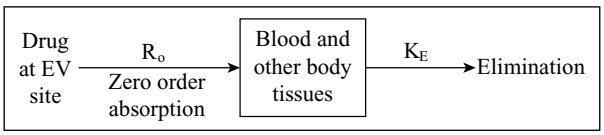


Figure 5.13 Zero order absorption model

- This model is similar to that of constant rate IV infusion.
- Example of zero order absorption, rate of drug absorption for controlled drug delivery systems.
- All equations that explain the plasma concentration-time profile for IV infusion are also applicable to this model.

- One of the better alternatives to curve fitting method in the estimation of K_a is Wagner-Nelson method. The method involves the determination of K_a from per cent unabsorbed time plots and does not require assumption of zero or first order absorption.
- A semilog plot of percent unabsorbed (i.e., per cent ARA) versus t yields a straight line whose slope is $-K_a/2.303$ (figure 15). If a regular plot of the same is a straight line, the absorption is zero order.

Note

- Optimum dosing frequency is Half-life ($T_{1/2}$).
- Plateau principle
  If the dosing interval is equal to plasma half life, then steady state plasma concentration is reached in approximately 5 half lives.
- **Loading Dose**–Initial dose given to achieve instant steady state condition.
- Priming dose/Loading dose = $(C_{ss} \times V_d)/F$
  F is bioavailable fraction
- Maintenance Dose (Dose Rate) = $(C_{ss} \times CL)/F$
- **Revised dose rate =** (Previous dose rate × C_{ss})/measured C_p
- Drugs with $T_{1/2}$ less than or equal to 4 hours are suitable candidates for controlled release formulations. For drugs with $T_{1/2}$ more than or equal to 12 hours, there is no need of development of controlled release formulations.
- Steady state plasma concentration C_{ss} after multiple dosing = $(F X_0)/CL_T \times$ dosing interval (T)

X_0 is amount of drug administerd.

Question1. Procainamide is to be administered to a 65 kg arrthymic patient as 500 mg tablet every 4 hours. The drug has half life of 3 hours, voume of distribution of 2 litre/kg and oral bioavailability of 0.85.Calculate C_{ss}.

Ans. Steady state plasma concentration $C_{ss} = (F X_0)/CL_T \times$ dosing interval

$$T_{1/2} = 0.693/K_E = 0.693\ V_d/CL$$

$$3 = 0.693 \times 2/CL$$

$$CL = 0.693 \times 2/3$$

$$\text{So } C_{ss} = (0.85 \times 500 \times 3)/0.693 \times 2 \times 4$$

$$= 3.53 \text{ mg/ml}$$

Non-Linear Kinetics

- Linear pharmacokinetics is **simple first order kinetics** where change in amount of drug in body or change in plasma drug concentration due to ADME is directly proportional to the doses and the pharmacokinetic parameters like F, CL_T, $t_{1/2}$ would not change when different doses of multiple doses of drug were given.
- Non-linear pharmacokinetics is observed in some drugs where increase in dosed or chronic medication can cause deviation from the linear pharmacokinetics profile so it is known as **Dose Dependent Kinetics.**
- Here rate processes of drug's **ADME** are dependent upon carrier or enzymes that are drug specific, having definite capacities and susceptible to saturation at higher doses, so it is also known as **Capacity Limited Kinetics.**
- At lower dose, drug shows first order kinetics but at higher dose, it shows zero order due to saturation, so it is also known as **Mixed Order Kinetics**.

Tests to detect non-linearity

- Determine C_{ss} (steady state plasma concentration) at different doses and if C_{ss} is directly proportional to the doses then it is linear pharmacokinetics else it is non-linear pharmacokinetics.
- Determine some of important pharmacokinetic parameters such as fraction bioavailable F, $t_{1/2,}$ total clearance at different doses. Any change in parameters which are usually constant, means non-linear pharmacokinetics.

Causes of non-linearity

1. **Drug Absorption:** There are three major causes of non-linearity in drug absorption:
   - **A.** When the absorption is solubility or dissolution rate limited for e.g., griseofulvin, at high dose a saturated solution of the drug is formed in the GIT or at any other extra vascular site and the rate of absorption attains a constant value. Decrease F, K_a, C_{max}, AUC
   - **B.** When absorption involve Carrier mediated transport: saturation at higher dose result in nonlinearity E.g., Riboflavin, Ascorbic acid. Decrease F, K_a, C_{max}, AUC

C. When pre systemic gut wall or hepatic metabolism attains saturation E.g., propranolol. Increase in F, K_a, C_{max}, AUC.
- Other causes are changes in gastric blood flow and gastric emptying.

2. **Drug Distribution:** There are two major causes:
   A. Saturation of plasma protein binding e.g., in case of Phenylbutazone
   B. Saturation of tissue binding sites e.g., in case of Imipramine
   - In both the cases, increase in free plasma drug concentration and increase in V_d. in the former case where as decrease in V_d in latter case.
   - Clearance of a drug with high ER is greatly increases due to saturation of binding site.
3. **Drug Metabolism:** There are two major causes for it:
   A. Capacity limited metabolism due to the enzyme or cofactor saturation. Example include Phenytoin, thoephylline, alcohol. Increase Css, decrease CL.
   B. Enzyme induction example in case of carbamazepine where decrease in plasma concentration is observed on repetitive administration over a period of time. Increase CL, decrease Css
   - Other cause of non-linearity are hepatotoxicity, change in hepatic blood flow and inhibitory effects of metabolites on enzymes.
4. **Drug Excretion:** Two active processes that are saturable.
   A. Active tubular secretion as in penicillin. Decreases renal clearance.
   B. Active tubular reabsorption as in water soluble vitamins and glucose. Increases renal clearance.
   - Other sources of non-linearity are forced dieresis, change in urine pH, nephrotoxicity.

MICHAELIS MENTEN EQUATION

- The kinetic of capacity limited or saturable process is best described by **Michaelis Menten Equation**. The elimination of drug by a saturable enzymatic process is described by Michaelis Menten equation.

$$\frac{-dC}{dt} = \frac{V\,max * C}{Km + C}$$

Where, C = plasma concentration

–dC/dt = elimination rate = V

Vmax = maximum elimination rate

Km = Michaelis-Menten constant

- When elimination rate is half of maximum elimination rate....

V = 0.5 Vmax, then Km = C

So Km is defined as concentration of the substrate at which rate of elimination is half of the maximum velocity, means 50% enzymes are bound when Km = C

Km is also known as brig's haldone's constant

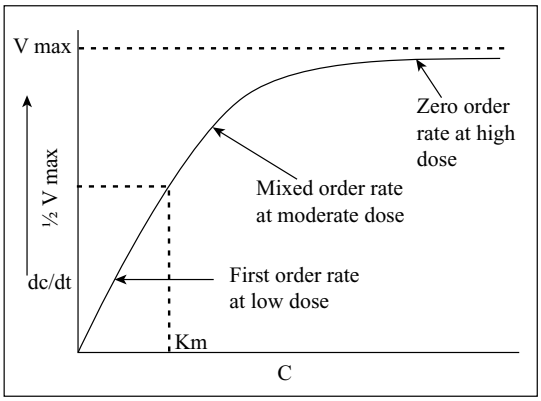


Figure 5.14 Graphical overview-Capacity limited or saturable kinetic process

Now, three situations can be considered depending upon the values of Km and C:

When C << Km	When C = Km	When C >> Km
So Km + C ≈ Km Now from eq. 1. –(dC/dt) = Vmax C/Km Vmax, Km are constant So – dC/dt α C Low dose → **first order**	So Km + C = 2C Now from eq. 1. –(dC/dt) = Vmax/2 So rate process is half of maximum elimination rate. Medium dose → **mixed order**	So Km + C ≈ C Now from eq. 1. –(dC/dt) = Vmax as Vmax is constant so dC/dt is constant High dose → **Zero order**

Bio-Availability

Bioavailability is defined as the rate and extent (amount) of absorption of unchanged drug from its dosage form.

- Bioavailability is an absolute term.
- Bioavailability from different route is in the following order:
  Parenteral (100% BA in case of IV route) > oral > Rectal > Topical
- Bioavailability from different dosage forms is in the following order:
  Solution > Emulsion > Suspension > Tablet/capsule

BA is enhanced by

- **Micronization**–E.g., Griseofulvin,Spironolactone

- **Use of surfactants**–Nonionic surfactant like Polysorbate eg Spironolactone
- **Salt formation –**E.g., Acidic drug–penicillin–penicillin sodium**,** basic drug–atropine or quinidine–Atropine sulphate or quinidine HCl
- **Alteration of pH**–Buffered Aspirin tablet
- **Use of Metastable form**-Beta form of Chloramphenicol palmitate is more soluble
- **Solid solution–**A binary system comprising of a solute molecularly dispersed in a solid solution. E.g., digitoxin-PEG 6000 solid solution
- **Eutectic mixture–**Prepared by fusion mixture**,** fused melt of solute–solvent show complete miscibility
- **Solid dispersion**
  Both solid and solid carrier solvent are dissolved in a common volatile liquid solvent (E.g., Alcohol) then freeze drying, results in amorphous precipitation of guest solute in crystalline carrier.
- **Molecular encapsulation with cyclodextrin**
- Alpha, beta and gamma CD consists of 6, 7 and 8 glucose molecules respectively. CD has hydrophilic surface on outer portion due to presence of COOH and OH groups while cavity is lipophilic in nature.

Solubility order

Solid solution > Eutectic mixture > Micronized drug > coarse drug

In case of oral route, the dose available to the patient is called Bio available dose which is often less than the administered dose.Therefore, the bio-available fraction F, refers to the fraction of administered dose that enters the systemic circulation.

$$F = \frac{\text{Bioavailable dose}}{\text{Ad min istered dose}}$$

Consideration in Bioavailability Study Design

Bioavailability–absolute versus relative

Absolute bioavailability When the systemic availability of a drug administered orally is determined in comparison to its intravenous administration, is called as absolute availability. (Denoted by F)

$$F = \frac{[AUC]_{oral}\,Div.}{[AUC]iv.D_{oral}}$$

AUC = Area under the Curve

D = Dose of administered drug

- Its determination is used to characterize a drug's inherent absorption properties from extra vascular site.
- Intravenous dose is selected as a standard due to its 100% bioavailability.
- If the drug is poorly water soluble, intramuscular dose can be taken as standard.

Relative bioavailability When the systemic availability of a drug after administration is compared with that of standard of the same drug it is referred to as relative bioavailability (Fr).

$$Fr = \frac{[AUC]_{test}\,D_{std}}{[AUC]_{std}\,D_{test}}$$

- In contrast to absolute bioavailability, it is used to characterize absorption of drug from its formulation.
- F and Fr are expressed in percentages.

Single dose versus multiple dose studies

- ***Single Dose Bioavailability studies*** are very common.
- They are easy, offer less exposure to drugs and are less tedious.
- However, it is difficult to predict the steady-state characteristic of a drug and intersubject variability with such studies.
- On the other hand, ***Multiple Dose study*** is difficult to control (poor subject compliance), exposes the subject to more drug and is highly tedious and time consuming. Nevertheless, such a study has a several advantages.
  1. More accurately reflects the manner in which the drug should be used.
  2. Easy to predict the peak and valley characteristic of the drug since the bioavailability is determined at steady state.
  3. Requires collection of fewer blood samples.
  4. The drug blood levels are higher due to cumulative effect which makes its determination possible even by the less sensitive analytic methods.
  5. Can be ethically performed in patients because of the therapeutic benefit to the patient.
  6. Better evaluation of the performance of a controlled release formulation is possible.
  7. Non-linearity in pharmacokinetics, if present, can be easily detected.

In Multiple Dose study, one must ensure that the steady state has been reached. For this, the drug should be administered for 5–6 elimination half-lives before collecting the blood samples.

Measurement of bioavailability

They can be broadly divided into two categories–pharmacokinetic method and Pharmacodynamic methods.

1. Pharmacokinetic methods

- These are indirect methods
- Assumption that–pharmacokinetic profile reflects the therapeutic effectiveness of a drug.
  - **A.** Plasma/blood level time profile
  - **B.** Urinary excretion studies
  - **C.** Other biological fluids

2. Pharmacodynamic methods

- Involves direct measurement.
- They involve determination of bioavailability from:
  - **A.** Acute pharmacological response
  - **B.** Therapeutic response

3. In-vitro dissolution studies

A. Closed compartment apparatus
B. Open compartment apparatus
C. Dialysis systems

A. Plasma level time profile

- This is the most reliable method and the method of choice in comparison to urine data.
- This method is based on the assumption that two dosage forms that exhibit superimposible plasma level time profiles in a group of subjects should result in identical therapeutic activity.
- The three parameters of plasma level time studies which are considered important in bioavailability studies are:
  1. **C_{max}:** The peak plasma concentration.
     Gives idea about the sufficient systemic absorption of drug to provide a therapeutic response.
  2. **t_{max}:** The peak time
     Gives indication of rate of absorption of drug.
  3. **AUC:** Area under the plasma level time curve.
     Gives a measure of extent of absorption of amount drug that reaches systemic circulation.

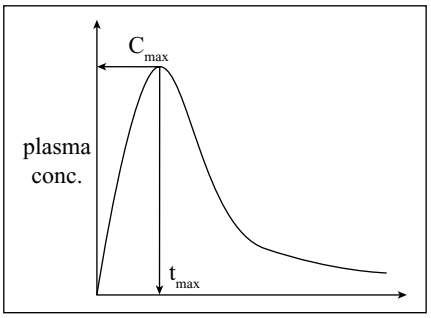


Figure 5.15 Drug plasmal level–time profile

B. Urinary excretion studies

- It is a non-invasive method and requires less sensitive analytical method.
- This method is based on the principle that the urinary excretion of unchanged drug is directly proportional to the plasma concentration of drug.
- The primary disadvantage is that they require the collection of samples for a longer period of time to ensure complete of absorbed drug.
- The three major parameters examined are:
  1. **$(dX_u/dt)_{max}$:** The maximum urinary excretion rate.
     Analogous to C_{max} → the rate of appearance of drug in the urine is proportional to concentration in systemic circulation.
  2. **$(t_u)_{max}$:** The time for maximum excretion rate.
     Analogous to t_{max} → the value decreases as the absorption rate increases.
  3. **X_u:** The cumulative amount of drug excreted in urine
     Related to the AUC of plasma level data → increase as the extent of absorption increases.

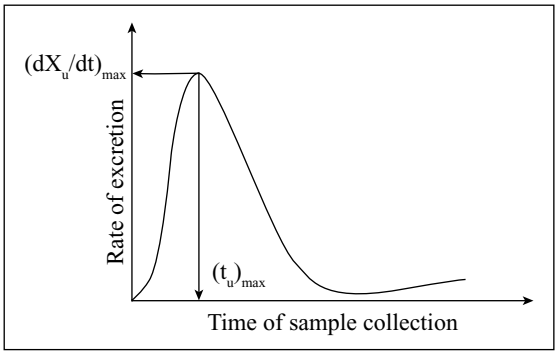


Figure 5.16 Drug Excretion– time profile

Bioequivalence Studies

Some relevant terms

A. Equivalence It is a relative term that compares drug products with respect to a specific characteristic or function or to a defined set of standards. There are several types of equivalences.

B. Chemical equivalence It indicates that 2 or more drug products contain the same labelled chemical substance as an active ingredient in the same amount.

C. Pharmaceutical Equivalence This term implies that two or more drug products are identical in strength, quality, purity, content uniformity, disintegration and dissolution characteristics; they may, however, differ in excipients.

D. Bioequivalence It is a relative term which denotes that the drug substance in two or more dosage forms, reaches the systemic circulation at the same relative rate and to the same relative extent i.e., their plasma concentration time profiles will be identical without significant statistical differences.

E. Therapeutic Equivalence When two or more drug products that contain the same therapeutically active ingredient, elicit identical pharmacologic response and can control the disease to the same extent.

F. Clinical Equivalence When the same drug from two or more dosage forms gives identical in vivo effects as measured by pharmacological response or by control over a symptom or a disease.

IN-VITRO IN-VIVO CORRELATION

- IVIVC has been defined by **FDA** as "**A predictive mathematical model describing relationship between in-vitro property of a dosage form and in-vivo response".**
- **In-vitro properties** are rate or extent of drug released under a given set of conditions and **in-vivo properties** are plasma drug concentration or amount of drug absorbed expressed in terms of Cmax, AUC, etc.
- To obtain IVIVC, **at least three batches** of same drug should be available, which differ in their in-vivo as well as in-vitro performance.

Levels of Correlation

There are four levels of IVIVC that have been described in the FDA guidance, which include levels A, B, C, and multiple C.

Level A correlation

- This correlation represents a predictive model for the point-to-point relationship between the entire *in vitro* release time course and entire *in vivo* response time course.
- In general, correlations are linear at this level. No formal guidance on the non-linear IVIVC has been established.
- **Level A correlation is the most informative and very useful from a regulatory perspective**.
- Level A correlation is usually estimated by a two-stage Deconvolution Method followed by comparison of the fraction of drug absorbed to the fraction of drug dissolved.

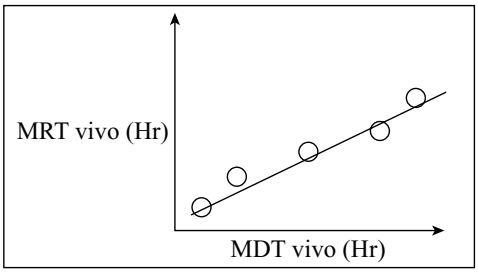


Figure 5.17 Graphical overview–Level B correlation

Level B correlation

- A predictive mathematical model for relationship between summary parameters that characterize the in-vitro and in-vivo time course.
- It compares

  [1] MDT vitro to MDT vivo, or
  [2] MDT vitro to MRT, or
  [3] In-vitro Dissolution Rate Constant (kd) to Absorption Rate Constant (ka).

- Comparison using **Statistical Moment Analytical Method.**
- This type of correlation uses all of the *in vitro* and *in vivo* data; but is not considered as a point-to-point correlation.
- This is of limited interest and least useful for regulatory purposes because more than one kind of plasma curve produces similar mean residence time.

Level C correlation

- A predictive mathematical model of relationship between the amount of drug dissolved in-vitro at a particular time (e.g., % drug dissolved in 1 hour) or time required for in-vitro dissolution of a fixed percent of dose (e.g., $T_{50\%}$, $T_{90\%}$) and a summary pharmacokinetic parameter that characterizes in-vivo time course. (e.g., C_{max}, T_{max}, $T_{1/2}$ or AUC).

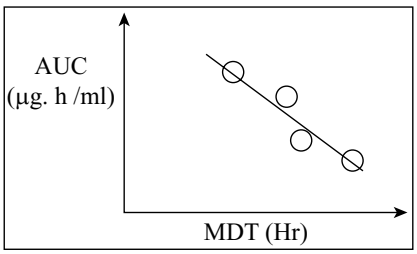


Figure 5.18 Graphical overview-Level C correlation

- It is considered as the lowest correlation level as it does not reflect a complete shape of the plasma concentration time curve.
- Level C correlations can be useful in the early stages of formulation development when pilot formulations are being selected.

Multiple level C correlation

- It relates one or more pharmacokinetic parameters to the percent drug dissolved at several time points of dissolution profile and thus may be more useful.
- If a Multiple Level C correlation is possible, then a Level A correlation is also likely and is preferred.

Various Parameters Used in IVIVC Depending on the Level

Level	In vitro	In vivo
A	Dissolution curve	Input (absorption) curves
B	Statistical Moments: MDT	Statistical Moments: MRT, MAT
C	Disintegration time, Time to have 10, 50, 90% Dissolved, Dissolution rate, Dissolution efficiency	C_{max}, T_{max}, K_a, Time to have 10, 50, 90% absorbed, AUC (total or cumulative)

Stability and ICH Guidelines

Stability

"The capacity of a drug product to remain within specifications established to ensure its identity, strength, quality and purity".

Purpose of stability study

- To provide evidence of how the quality of drug substances or products varies with time under the influence of environmental factors. (temperature, humidity and light)
- To establish a re-test period for the drug substances or the shelf-life for the drug products and recommended storage conditions.
- To ensure that drug products retain their full efficacy until the end of their expiration date.

Most important guidelines are

- Food and Drug Administration (FDA)
- International Conference on Harmonization (ICH)
- European Union Guidelines (EU)
- Japanese Guidelines (MHW)
- World Health Organization (WHO) Guidelines

ICH (April 1990)

The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) is a unique project that brings together the regulatory authorities of Europe, Japan and the United States and experts from the pharmaceutical industry in the three regions to discuss scientific and technical aspects of product registration.

Objectives of ICH

- More economical use of human, animal, and material resources.
- Elimination of unnecessary delay in the global development and availability of new medicines.
- Maintaining safeguards on quality, safety and efficacy, and regulatory obligations to protect public health.

Topics of ICH Four broad categories–**QSEM**

- Quality (Q): Topics related to Manufacturing QA.
- Safety (S): Topics related to non-clinical pharmacology and toxicology studies.
- Efficacy (E): Topics related to Clinical studies in humans.
- Multidisciplinary (M): Topics affecting more than one discipline.

Q1: Stability testing
Q2: Analytical methods validation
Q3: Impurity testing
Q4: Pharmacopoeias
Q5: Quality of Biotechnological products
Q6: Specifications for new drug substances and products
Q7: Good manufacturing Practice
Q8: Pharmaceutical Development
Q9: Quality risk Management
Q10: Pharmaceutical Quality System
Q11: Development and Manufacture of Drug substance

Type of Study	Storage Condition	Minimum Time Period Covered
LONG TERM	25°C ± 2°C/40% RH ± 5% RH or 30°C ± 2°C/65% RH ± 5% RH	12 months
INTERMEDIATE	30°C ± 2°C/65% RH ± 5% RH	6 months
ACCELERATED	40°C ± 2°C/75% RH± 5% RH	6 months

Definition and storage/test conditions for four climatic zones

Climatic zones	Definition	Storage/Test conditions	Examples
I	Temperate Climate	21°C ± 2°C and 45% RH ± 5% RH	Northern Europe, Canada
II	Mediterranean and Subtropical climate	25°C ± 2°C and 60% RH ± 5% RH	Southern Europe Japan, US
III	Hot, dry climate	30°C ± 2°C and 35% RH ± 5% RH	Egypt, Sudan
IV	Hot, humid climate	30°C ± 2°C and 75% RH ± 5% RH	Central Africa, South Pacific

India comes under IV climatic zone.

Multiple Choice Questions

1. On a product, the label states "protect from light". What type of decomposition does the product undergoes?
(a) Carboxylation (b) Decarboxylation
(c) Hydrolysis (d) Oxidation

2. Aspirin undergoes decomposition in a formulation. It can be prevented by
(a) Adding a chelating agent
(b) Adding an oxidant
(c) Protecting it from light
(d) Suppressing its solubility

3. Which one of the following is primarily not a chemical decomposition?
(a) Isomerization (b) Hydrolysis
(c) Oxidation (d) Volatilization

4. Which one of the following physicochemical properties is more important for passive diffusion of drugs from the gastrointestinal tract?
(a) Dissolution constant
(b) Lipid solubility
(c) Partition coefficient
(d) pH of the gastrointestinal fluids

5. Half life of drug may be useful to determine
(a) Dosage schedule of the drug
(b) Level of absorption
(c) Distribution in body system
(d) Time to get the steady state

6. Phase II reactions of a drug biotransformation
(a) Decreases its water solubility
(b) Includes activity of cytochrome P-450
(c) Distribution into different body system
(d) Lead to inactivation of drug

7. The rate of desorption is proportional to the
(a) Uncovered surface (b) Covered surface
(c) Internal area (d) All of the above

8. The release of maintenance dose in sustained release dosage form should follow
(a) Zero-order kinetics
(b) First-order kinetics
(c) Second-order kinetics
(d) Pseudo-order kinetics

9. The half-life for first-order photolysis of cefotaxime solution containing 150 mg drug is 50 min. If 1ml aliquot after 90 min of exposure to light was found to contain 0.43 mg of cefotaxime, what was the original volume the solution?
(a) 100 ml (b) 120 ml
(c) 80 ml (d) 140 ml

10. The normal creatinine clearance value in humans is _____ ml/min.
(a) 100–110 (b) 80–90
(c) 150–160 (d) 120–130

11. If the p*K*a of phenobarbitone is 7.4, what fraction of drug would be ionized at pH 8.4?
(a) 0.01 (b) 0.5
(c) 0.9 (d) 1

12. The applicability of Noyes-Whitney equation is to describe the
(a) First-order kinetics
(b) Zero-order kinetics
(c) Mixed-order kinetics
(d) Dissolution rate

13. Drug X has a constant bioavailability and first-order elimination its maintenance dose rate will be directly proportional to
(a) Plasma protein binding
(b) Volume of distribution
(c) Lipid solubility
(d) Total body clearance

14. Which category of drug is evaluated for dissolution?
(a) Highly diffusible
(b) Diffusion
(c) Poorly water soluble
(d) Water soluble

15. The biological half-life of procaine in a patient was 35 min and its V_d was estimated to be 60 litres.
The total clearance rate of procaine is
(a) 1.88 litres/min (b) 0.115 litres/min
(c) 11.5 litres/min (d) 5.57 litres/min

16. A tablet of aceclofenac is given to a patient. The dose of aceclofenac was 200 mg, after 2 h the concentration

was found to be 10 μg/ml. What is the volume of distribution of aceclofenac?

(a) 2 litres (b) 20 litres
(c) 200 litres (d) 2000 litres

17. Active tubular secretion is determined by

(a) Creatinine (b) Mannitol
(c) Iodopyracet (d) Sodium thiosulfate

18. Drug X has a molecular weight of 750 daltons. From which of the following route will it get excreted?

(a) Biliary excretion (b) Urinary excretion
(c) Both (d) Cannot say

19. Flip-flop phenomenon occurs when

(a) Ka/ke ≥ 3 (b) ke/ka ≥ 3
(c) ka = ke (d) None

20. Which of the following statement is correct?

(a) Alloxanthine is a long-acting competitive inhibitor
(b) Probencid ↓ t½ alloxanthine and allopurinol ↑ t½ of probencid
(c) NSAID ↑ the action of uricosuric drugs
(d) None of the above

21. Which of the following statement is correct?

(a) t½ ↑ or ↓ in the first-order kinetics due to ↑ or ↓ dose
(b) ↑ dose results ↓ CL, t½ ↑ zero-order kinetics
(c) In 4–5 half life nearly completely drug elimination occurs
(d) Both a and c

22. How much solvent is required to dissolve a sparingly soluble salt?

(a) 10 to 30 parts (b) 1 to 10 parts
(c) 100 to 150 parts (d) 100 to 1000 parts

23. Sigma–Minus method is used to determine the _____

(a) Rate of absorption (b) Rate of elimination
(c) Rate of exertion (d) Rate of metabolism

24. According to the pH partition theory, a weakly acidic drug will be absorbed more likely from the stomach, because the drug exists primarily in the:

(a) Form of weak acid and more soluble in acid medium
(b) Ionized, more water-soluble form
(c) Ionic form, which facilities diffusion
(d) Un-ionized, more lipid-soluble form

25. When the release of drug from a dosage form satisfies Higuchi's equation, the release of drug can be considered as

(a) Absorption rate controlled
(b) Diffusion rate controlled
(c) Dissolution rate controlled
(d) Dosing rate controlled

26. In biotransformation, Phase I reaction is also known as

(a) Conjugation
(b) Synthetic reaction
(c) Functionalization reaction
(d) None of above

27. According to the pH partition hypothesis the absorption of drug is maximum when

(a) Drug is ionized in biological fluid
(b) Drug is unionized in biological fluid
(c) Both
(d) Cannot say

28. What effect dose plasma protein binding have on bio transformation?

(a) Change the mechanism
(b) Increases the formation of metabolites
(c) Slows the process
(d) Has no effect

29. Apparent volume of distribution increases when

(a) More tissue binding of drug
(b) More protein binding of drug
(c) Both
(d) None

30. Zolmitryptan is given i.v to the patient in dose of 1.2 mg/kg (AUC = 450 μg.hour/I).Same drug was given as oral SR tablet in dose 8.0 mg/kg (AUC = 1040 μg.hour/I). What is the absolute bioavailability of SR tablet?

(a) 30% (b) 35%
(c) 38% (d) 42%

31. Which statement is correct?

(a) Mainly acidic drug binds to albumin
(b) Mainly basic drug binds to albumin
(c) Acidic drug binds only to α-acid glycoprotein
(d) None of the above

32. Calculate the dialysis clearance if the blood flow rate to the dialysis is 50 ml/min and concentration of drug entering and leaving the dialyzer dialyser is 100 and 20 μg/ml, respectively,

(a) 20 ml/min (b) 40 ml/min
(c) 35 ml/min (d) 50 ml/min

33. The reaction rate constant (k) is 2.0×10^{-3} min^{-1} for aspirin hydrolysis in 0.1 N hydrochloric acid at 1 mg/ml concentration. Under same conditions, if the product contains aspirin 4 mg/ml of the initial concentration, the k value in $minute^{-1}$ will be

(a) 0.5×10^{-3} (b) 2.0×10^{-3}
(c) 4.0×10^{-3} (d) 8.0×10^{-3}

34. The half life of a first-order reaction is 4 years. What is its shelf life (in years)?
(a) 0.02 (b) 0.03
(c) 0.17 (d) 0.61

35. Generally passage of drug molecules across a cell membrane from high concentration to a region of low concentration is known as:
(a) Carrier mediated (b) Dissolution
(c) Passive diffusion (d) Pinocytosis

36. The loading dose (D_L) of a drug is usually based on the
(a) Total body clearance (CL) of the drug
(b) Percentage of drug bound to plasma protein
(c) Apparent volume of distribution (V_D) and desired drug concentration in plasma
(d) Area under the plasma drug concentration versus time curve (AUC)

37. Following is not true for p*K*a of a drug
(a) pH at which half of the molecules of solute in solution are ionized
(b) It is determined using Handerson-Hasselbatch equation
(c) It affects the solubility of a drug at a given pH
(d) At pH above this the solute exists in ionized forms

38. Following is true for *K*w/o in Brunner's equation:
(a) Partition coefficient of drug is between the lipoidal membrane and the aqueous GI fluids
(b) Higher the value of *K*w/o, faster the dissolution
(c) It is an intrinsic dissolution rate constant
(d) Both (b) and (c)

39. Capacity limited process is best described by
(a) Michaelis–Menten Equation
(b) Lineweaver–Burk Equation
(c) Hanes–Woolf plot
(d) All

40. In Michaelis–Menten equation when *K*m = C
(a) The rate of process is equal to half of maximum rate
(b) Equation becomes identical to first order elimination of drug
(c) Indicates zero-order process
(d) The rate process occurs at a constant rate

41. The initial distribution of a drug into tissue is determined chiefly by
(a) Rate of blood flow to the tissue
(b) Plasma protein binding of the drug
(c) Affinity for the tissue
(d) Stomach emptying tissue

42. When absorption is solubility or dissolution, the rate-limited order of reaction will be
(a) First order
(b) Zero order
(c) Mixed order
(d) Rate limited process does not affect the order of reaction

43. Compartment modelling is explained by assuming
(a) Rate of drug presentation is first order
(b) Drug disposition is first order
(c) Rate of drug absorption is constant
(d) Both (a) and (b)

44. Surfactant increases the bioavailability of a drug by
(a) Promoting the wetting and penetration of dissolution fluid into the solid drug particles
(b) Forming adsorptive layer on drug molecule and inhibiting Ostwald ripening
(c) Enhancement of dissolution rate
(d) All of the above

45. Drugs which bind selectively to extravascular tissue have apparent Vd
(a) < 42 litres (b) = 42 litres
(c) 42 litres (d) = 3 litres

46. Absorption of contraceptives from vaginal route follows
(a) Passive diffusion
(b) Endosytosis
(c) Carrier-mediated transport
(d) Pore transport

47. Glucoronidation process results in
(a) Increased billiary excretion of drug
(b) Increased renal excretion of drug
(c) Decreased billiary excretion of drug
(d) Both (a) and (b)

48. An agent used to determine the hepatic function is
(a) Inulin
(b) Mannitol
(c) Sulphobromophthalein
(d) Raffinose

49. When Statistical Moment theory is used for IVIVC
(a) Mean dissolution time is correlated with mean residence time
(b) LD50 is correlated with rate constant of dissolution

(c) Drug excreted unchanged in urine is correlated with percent drug dissolved
(d) 63.2% of drug dissolved is correlated with 63.2% of initial concentration reduction

50. One compartment open model, i.v. bolus, can be explained mathematically by
(a) Multi-exponential equation
(b) Mono-exponential equation
(c) Calculating loading dose and Css
(d) Calculating % ARA

51. Absolute bioavailability is denoted by
(a) [AUC]oral/[AUC]i.v.
(b) [AUC]test/[AUC]std
(c) [AUC]oral.Div/ [AUC]iv. Doral
(d) AUC]test.Dstd/ [AUC]std. Dtest

52. The order of dissolution of different dosage forms of drugs is _____.
(a) Metastable > stable > amorphous
(b) Stable > amorphous > metastable
(c) Amorphous > metastable > stable
(d) Amorphous > stable > metastable

53. Which of following are not characteristics of facilitated diffusion?
(a) Carrier-mediated transport
(b) Concentration gradient is required
(c) Structural specificity
(d) Nonsaturable

54. The main mechanism of most drug absorption in GI tract is:
(a) Active transport (carrier-mediated diffusion)
(b) Filtration
(c) Endocytosis and exocytosis
(d) Passive diffusion (lipid diffusion)

55. During the primary drying stage in lyophilization the temperature of the product must remain below its critical temperature. This temperature is termed
(a) Collapse temperature
(b) Breakdown temperature
(c) Lyophilization temperature
(d) Subcritical temperature

56. Most commonly used bulking agent in lyophilized product is
(a) Methyl cellulose (b) Mannitol
(c) Sodium chloride (d) All

57. Nucleation process is involved in
(a) Distillation (b) Crystallization
(c) Filtration (d) None

58. Secondary drying stage of freeze drying is to
(a) Remove solvent (ice) from the product by evacuation of chamber
(b) Remove bound water from solute to a level that assures long-term stability of product
(c) Both of above
(d) None of above

59. Ideal solid content of a freeze dried product should be
(a) 5–30% (b) 40–50%
(c) 40–60% (d) 70%

60. Which of the following mechanisms of drug absorption is saturable type?
(a) Passive diffusion (b) Pore diffusion
(c) Carrier mediated (d) None of above

61. Micronization of hydrophobic drug decrease solubility of drug This is because
(a) Drug adsorbs air on to their surface
(b) Particles reaggregate to form larger particle
(c) Surface charges may prevent wetting
(d) All of above

62. Which of the following polymorphic form of drug has the highest solubility of drug
(a) Amorphous (b) Metastable
(c) Stable (d) Hydrated

63. Very weak bases (p*K*a = 5.0) nature drug absorbed in which of the following part in our body?
(a) Stomach (b) Intestine
(c) Colon (d) Entire length of GIT

64. Higher absorption of drug through small intestine is due to
(a) Kekckring (b) Villi
(c) Microvilli (d) None of above

65. Drug disposition include
(a) Drug absorption and distribution
(b) Drug absorption and metabolism
(c) Drug distribution, metabolism and excretion
(d) Drug metabolism and excretion

66. Which of the following process is responsible for loss of drug irreversible
(a) Elimination (b) Distribution
(c) Both a and b (d) None of above

67. Which of the following types of drugs has tissue permeability as a rate-limiting step for drug distribution?

(a) Lipophilic (b) Hydrophilic
(c) Polar, hydrophilic (d) Both a and b

68. Which of the following part of brain where BBB does not exist
(a) Trigger area (b) Hypothalamic
(c) Both a and b (d) None of the above

69. Which of the following approaches have been used to promote crossing the BBB by drug?
(a) Use of permeation enhancers such as DMSO
(b) Osmotic disruption of BBB by mannitol
(c) Use of dihydropyridine redox system
(d) All of above

70. Which of the following junctions is responsible for low distribution of drug to cerebrospinal from blood
(a) Choroidal cell junction
(b) Glial cell junction
(c) Basement cell junction
(d) Both a and b

71. Which of the following barrier is responsible for transfer of nutrients from mother to foetus?
(a) Simple cell membrane barrier
(b) Blood–brain barrier
(c) Plasma barrier
(d) Blood–cerebrospinal fluid barrier

72. Which one of the following marker is used to measure total body water
(a) Antipyrine (b) Evans blue
(c) Na^+ (d) Mannitol

73. Innulin is used as a marker for measurement of
(a) Plasma (b) ECF
(c) ICF (d) Total body water

74. Unit of apparent volume of distribution is
(a) Litre (b) Litre/Kg
(c) Both a and b (d) kg/litre

75. Which of the following binding site is not available in HSA?
(a) Azapropazane (b) Diazepam
(c) Digitoxin (d) Phenytoin

76. Which one of the following plasma protein has high affinity for binding with drug?
(a) HSA (b) α-acid glycoprotein
(c) Lipoprotein (d) Globulins

77. Larger dose of digoxin requirement to infants as compared to young age patient is due to
(a) Greater protein binding of drug
(b) Large renal clearance of drug
(c) Both a and b
(d) None of above

78. Which one of the following process is responsible for higher half-life of drug?
(a) Drug absorption (b) Excretion
(c) Metabolism (d) Protein binding

79. The term bioavailability refers to the
(a) Relationship between the physical and the chemical properties of a drug and the systemic absorption of drug.
(b) Measurement of the rate and extent of therapeutically active drug that reaches the systemic circulation
(c) Movement of drug into the body tissues over time.
(d) Dissolution of a drug in the GIT.

80. If a drug has very small volume of distribution (V_d) it is likely that this drug
(a) Has a short biological life.
(b) Does not accumulate in various and organs
(c) Is not bioavailable
(d) Will not be effective

ANSWER KEYS

1. (d)	**2.** (d)	**3.** (d)	**4.** (c)	**5.** (d)	**6.** (d)	**7.** (b)	**8.** (a)	**9.** (a)	**10.** (d)
11. (c)	**12.** (d)	**13.** (d)	**14.** (c)	**15.** (a)	**16.** (b)	**17.** (c)	**18.** (a)	**19.** (b)	**20.** (b)
21. (c)	**22.** (d)	**23.** (b)	**24.** (c)	**25.** (b)	**26.** (c)	**27.** (b)	**28.** (c)	**29.** (a)	**30.** (b)
31. (a)	**32.** (b)	**33.** (d)	**34.** (d)	**35.** (c)	**36.** (c)	**37.** (d)	**38.** (d)	**39.** (d)	**40.** (a)
41. (a)	**42.** (c)	**43.** (b)	**44.** (d)	**45.** (c)	**46.** (a)	**47.** (a)	**48.** (c)	**49.** (a)	**50.** (b)
51. (c)	**52.** (c)	**53.** (d)	**54.** (d)	**55.** (a)	**56.** (b)	**57.** (b)	**58.** (b)	**59.** (a)	**60.** (c)
61. (d)	**62.** (a)	**63.** (d)	**64.** (c)	**65.** (c)	**66.** (a)	**67.** (d)	**68.** (c)	**69.** (d)	**70.** (a)
71. (c)	**72.** (a)	**73.** (b)	**74.** (c)	**75.** (d)	**76.** (a)	**77.** (c)	**78.** (d)	**79.** (b)	**80.** (c)

CHAPTER 6

JURISPRUDENCE

Sr No.	Act	Year
1	Drug and cosmetic Act	1940
2	Pharmacy act	1948
3	Patent act	1970
4	Poisonous Act	1919
5	Drug price control order	1995

Sr No.	Act	Year
6	Narcotic and psycotroic substance act	1985
7	The All India Council for Technical education Act	1994
8	Drug and magic remedies act	1954
9	The medical termination of pregnancy act	1971
10	The factories act	1949

Drugs Technical Advisory Board (DTAB)
Total members = 18

Ex-officio members Total = 08	Nominated Members Total = 05	Elected Members Total = 05
Director General of Health Services (Chairman)	• **Two persons** nominated by the central government from amongst person who are incharge of drugs control in states. • **One person** from the pharmaceutical industry, nominated by the central government. • **Two** government analysts, nominated by the central government	• A teacher in pharmacy or pharmaceutical chemistry or pharmacognosy on the staff of an Indian University or an affiliated college, elected by the executive committee of the pharmacy council of India. • A teacher in medicine or therapeutics on the staff of an Indian University or an affiliated college, elected by the executive committee of the medical research. • One Pharmacologists elected by the governing body of the Indian Council of Medical Research (ICMR). • One person elected by the council of the central medical association. • One person to be elected by the council of the Indian Pharmaceutical Association (IPA).
Drugs Controller of India		
Director, Central Drug Laboratory, Calcutta		
Director, Central Research Institute, Kasauli		
Director, Indian Veternary research Insittute, Izatnagar		
Precident, Pharmacy Council of India		
Precident, Medical Council of India		
Director, Central Drug Research Institute, Lucknow		

Misbranded Drugs	Adulterated Drugs	Spurious Drugs
• If it is so **coloured, coated, powdered or polished** that damage is concealed or if it is made to appear of better or greater therapeutic value than it really is; or • If it is **not labelled** in prescribed manner; or • If its label or container or any thing accompanying the drugs bears any statement, design or device which is false or misleading in any particular.	• If it consists, in whole or in part of any filthy, putrid or decomposed substance. **Or** • If it has been prepared, packed or stored under insanitary condition where by it may have been rendered injurious to health	• If it is manufactured under the name of other drug. **Or** • If it has been substituted wholly or in part by another drug or substances

Schedule to the Act

First Schedule Names of book under Ayurvedic, Sidha and Unani Tibb system.

Second Schedule Standard to be complied with by imported by drugs manufactured for sale, sold, stocked or exhibited for sale or distributed.

Prescribed Appendices:

Appendix I-Data required to be submitted with application for the permission to market a new drug.

Appendix II-Format for submission of clinical trial reports.

Appendix III-Animal toxicity requirement for clinical trials and marketing of a new drug.

Appendix IV-Number of animals for long term toxicity studies.

Appendix V-Patients consent form for participating in a Phase I clinical trial.

Appendix VI-Four groups of fixed dose combination and their data requirement.

Schedule	Guideline/Rules
A	Proforma for the application for the licences, issue and renewal of licenecs, for sending memo-randa under the act
B	Fees for analysis of drugs or cosmetics that have to be paid to the central drug laboratories or other government laboratories.
C	List of biological and immunological products, antibiotics, ophthalmic, lotions, ointments and all products for parenteral use
C	List of drugs from biological origin, namely alkaloids, hormones, vitamins and antibiotics for oral use.
D	Exemptions that have been granted to drugs and importers of drugs from complying with the requirements of import of the drugs and also the condition for such exemptions.
E	List of poisons for which labelling and other requirements were to be complied with.
E(I)	List of poisonous substance under Ayurvedic, Sidha and Unani system of medicine
F	Manufacturing, testing and labelling of biological products for human use like sera and vaccines
F(I)	Manufacturing, testing and labelling of veterinary biological
F(II)	Standard for surgical dressing
F(III)	Standard for umbilical tapes
FF	Standard for ophthalmic preparations
G	List of substances that are required to be used under only medical supervision and which are to be labelled accordingly.
H	List of prescribed drugs.
J	Disease or ailments which a drug may not purport to prevent or cure
K	Drugs exempted from certain provisions relating to the manufacture of the drugs.
M	Good manufacturing practice (GMP) requirements of factory premises, plants and equipments
M(I)	Requirements of factory premises for manufacturing of homeopathic preparation.
M(II)	Requirements of factory premises for manufacturing of cosmetics.
M(III)	Requirements of factory premises for manufacturing of medical devices.
N	List of minimum equipments for efficient running of a pharmacy.
O	Standard for disinfectant fluids
P	Life period of the drugs
P(I)	Pack size of the drugs
Q	Part-I-List of dyes, colours and pigments permitted in cosmetics and soaps. Part-II-List of colours permitted in soaps
R	Standards for condoms which are made up of rubber latex intended for single use and other mechanical contraceptives.
R(I)	Standards for medical devices
S	Standards for cosmetics
T	Requirement of factory premises and hygienic condition for Ayurvedic (including Sidha) and Unani drugs.
U	Particulars to be shown in manufacturing, raw material and analytical record of the drugs

Schedule	Guideline/Rules
U(I)	Particulars to be shown in manufacturing, raw material and analytical record of the cosmetics
V	Standard for patent or proprietary medicines
W	Drugs marketed under generic names only

Schedule	Guideline/Rules
X	Names of narcotic and psychotropic drugs for which special control measure have been laid down.
Y	Requirements and guidelines on clinical trials for import and manufacture of the new drugs.

Sr No.	Types of Licence	Form No.
1.	Import Licence	Form 8 to 12 B
2.	Sales Licence	Forms-19, 19 A, 19 AA, 19 C
		Forms-20, 20 A, 20 B,20 BB, 20 F, 20 G
		Forms-21, 21 A, 21 B, 21 BB, 21 C, 21 CC
3.	Licence to manufacture dugs	Forms-24, 24 A, 24 B, 24 F,
		Forms-25, 25 A, 25 B, 25 F
		Forms-26, 26 A, 26 B, 26 F, 26 G, 26 H
		Forms-27 A, 27B, 27C, 27D
		Forms-28A, 28B, 28C, 28D and 30
4.	Licence for homeopathic medicines	Forms 19B, 20C, 20D, 20E, 24C, 25C and 26C
5.	Licence for Ayurvedic, Sidha and Unani drugs	Forms 24D, 24E, 25D, 25E, 26D and 26E
6.	Licence for cosmetics	Forms 31, 31A, 32, 32A, 33 and 33A

Sr. No	Form No.	Guidelines given
1.	19	It is an application which has to be made for grant or renewal of the sale licence by retail or whole-sale to the state licencing authority.
2.	20	It is a licence granted to sell by retail drugs,drugs other than schedule C and C(I) drugs.
3.	20 B	It is a licence granted to sell by wholesale drugs, drugs other than schedule C and C(I) drugs.
4.	21	It is a licence granted to sell by retail drugs, specified in schedule C and C(I) drugs.
5.	21 B	It is a licence granted to sell by wholesale to distribute drugs, specified in schedule C and C(I) drugs.
6.	24	It is an application which has to be made for grant or renewal of a licence to manufacturing of the drugs other than schedule C and C(I) and X drugs.
7.	27	It is an application which has to be made for grant or renewal of a licence to manufacturing of the drugs specified in schedule C and C(I) and X drugs.
8.	24 A	It is an application which has to be made for grant or renewal of a Loan licence to manufacturing of the drugs other than schedule C and C(I) drugs.

Sr. No	Form No.	Guidelines given
9.	27A	It is an application which has to be made for grant or renewal of a loan licence to manufacturing of the drugs specified in schedule C and C(I) drugs excluding schedule X.
10.	25	It is a licence granted to manufacture drugs other then schedule C and C(I) and X drugs.
11.	28	It is a licence granted to manufacture drugs specified in schedule C and C(I) excluding schedule X.
12.	25A	It is a loan licence granted to manufacture drugs other than schedule C and C(I) and X drugs.
13.	28 C	It is a licence granted to operate blood bank, for processing whole blood for components.
14.	28 D	It is a licence granted to manufacture large volume parenterals/sera and vaccines.
15.	29	Test Licence

Sr No	Storage condition	Drugs
1	Store in a cool place	Ampicillin, Adramycin, Amoxycillin, Bacitracin, Cephalexin, Chloramphenicol, Chlortetracycline, Cloxacillin, D-cycloserine, Doxycycline, Erythromycin, Gentamycin, Griseofulvin, Kanamycin, Neomycin, Mitomycin, Penicillin, Polymixin B, Rifampicin, Streptomycin, Tetracycline, Heparin injection
2	Store in a cold place	Liquid plasma, liquid normal human serum albumin, all vaccine, sera and toxoids, Other vaccine like BCG, Cholera, DHL, Measles, Hague, Rabies, Typhoid, Typhus vaccine, yellow fever vaccine, All antitoxin, Adrenalin, Corticotrophin, Liquid extract of ergot, Pitutary injection
3	At temperature not exceeding 5°C	Carbencillin, Mystatin
4	Store in a well closed container, protect from light, in a cool place	Thiamine, Riboflavin,Vitamin B_6, Cynocobalamine, Hydroxycobalamin, Calcium panothenate, Vitamin C, Vitamin D_2/D_3, Vitamin E, Folic acid, Vitamin K, Niacinamide

Sr No.	Definition	Under Section of D and C Act
1.	Drug	Section 3(b)
2.	Registered Pharmacists	Rule 15
3.	Government Analyst	Section 3 (c)
4.	Misbranded drugs	Section 17
5.	Spurious drugs	Section 17-B
6.	Adulterated drugs	Section 17-A
7.	Drug Inspector	Section 3 (e)
8.	Drug store	Rule 65[15 (e)]
9.	Pharmacy	Rule 65[15 (c)]
10.	Chemists and druggist	Rule 65[15 (b)]

Points	Pharmacy Council of India	State Pharmacy Council	Joint State Pharmacy Council
Members **(Elected)**	**Six members,** among whom there shall be one teacher from each subject: 1. Pharmaceutical Chemistry 2. Pharmacy, 3. Pharmacology	**Six members** elected amongst themselves by registered pharmacist of state.	Between **3 to 5 members** elected amongst the registered pharmacists.
Members **(Nominated)**	**Six members** nominated by central government of whom: → Four (minimum) shall be possessing degree or diploma in subject: 1. Pharmacy and practicing pharmacy or 2. Pharmaceutical chemistry	Five members nominated by state government of whom at least three person possessing: 1. Prescribe Degree or diploma in pharmacy or 2. Pharmaceutical Chemistry or 3. Registered Pharmacist	**1. NLT 2 and NMT 4** members nominated by each participating state government of whom more than half should possess 2. Degree or diploma in pharmacy or 3. Pharmaceutical Chemistry or 4. Registered Pharmacist
Medical council of India	One member elected from medical council of India	One member elected by medical council of India	One member elected by the members of each medical council.
UGC and AICTE	One members from each body	--------	---------
State Government Nominee	One member nominated from each state shall be registered pharmacists	--------	---------
Ex-Officio Members	Director general of health services.	Chief administrative medical officer of the state.	Chief administrative medical officer of each participating state.
	Drug controller of India	The officer incharge of drugs controllers organization of the state.	The officer in charge of drugs controllers organization of each participating state (appointed under D and C Act, 1940)
	Director of central drug laboratory	Government analyst. Appointed (Under D and C Act, 1940)	Government analyst. Appointed by each participating (Under D and C Act, 1940)
		If there are more than such analysts, one may be nominated by government.	-------

Multiple Choice Questions

1. Standard for disinfectant fluids comes under
(a) Schedule O (b) Schedule R
(c) Schedule S (d) Schedule E

2. One of the following forms is needed for the cosmetic manufacture.
(a) Form 36 (b) Form 32
(c) Form 20 (d) Form 24

3. How many members are elected among themselves by registered pharmacist of state?
(a) Three (b) Four
(c) Five (d) Six

4. Nominated or elected members in "State Pharmacy Council" hold office for a term of
(a) Three years (b) Four years
(c) Five years (d) Six years

5. Pharmacy Act is established in
(a) 1948 (b) 1940
(c) 1995 (d) 1919

6. Which pharmaceutical product is not included in Schedule C?
(a) Toxins (b) Sera
(c) Antigen (d) Capsule

7. Names of drugs which shall be marketed under generic names only come under
(a) Schedule W (b) Schedule X
(c) Schedule Y (d) Schedule U

8. Pharmacy Council of India is doing all of below functions except
(a) To regulate minimum educational standard in pharmacy institute
(b) To prescribe the minimum standard of education required for registered as a pharmacist
(c) To compile and maintain central register for pharmacist
(d) To prescribe drug

9. Blood Bank comes under the schedule
(a) Schedule B (b) Schedule D
(c) Schedule F (d) Schedule G

10. Crocin is sale under
(a) Schedule H (b) Schedule G
(c) Schedule W (d) Schedule Y

11. "Ampicillin capsule should be used within 24 months." This statement comes under
(a) Schedule C (b) Schedule R
(c) Schedule M (d) Schedule P

12. If the drug contains in filthy, putrid or decomposed substance then is known as
(a) Misbranded drug (b) Adulterated drug
(c) Spurious drug (d) Drug

13. Schedule M_2 states that
(a) Requirements of factory premises for the manufacture of medical devices
(b) Requirements of factory premises for the manufacture of homeopathy
(c) Requirements of factory premises for the manufacture of cosmetics
(d) Requirements of factory premises for the manufacture of allopathy

14. Pharmacy Council of India has_____ state government nominated member(s)
(a) 1 (b) 2
(c) 3 (d) 4

15. In AICTE the chairman is appointed by
(a) State Government of Delhi
(b) Central Government
(c) Election of Registered Pharmacists
(d) President

16. In the "Joint State Pharmacy Council" elected member(s) among the Registered Pharmacists is/are
(a) 1 (b) 3
(c) 2 (d) 5

17. Manufacturing and analytical records of cosmetics are included in which schedule?
(a) Y (b) U
(c) U1 (d) V

18. Insulin injection according to Schedule P is should be stored
(a) At temperature 2˚C to 8 ˚C and it must not allow to freeze
(b) At temperature which not exceed 5°C
(c) At temperature which not exceed 20°C
(d) In cold place

19. Appendix II is about
(a) Number of animals for long-term toxicity studies
(b) Patient consent for participation in a Phase I clinical trial
(c) Format for submission of clinical trial reports
(d) Four groups of fixed dose combination and their data requirements

20. "Schedule F3" is related with
(a) Standard for surgical dressing
(b) Standard for sterilized umbilical tapes
(c) Standard for ophthalmic preparation
(d) Standard for production of sera

21. Spurious drug comes under
(a) Section 17 (b) Section 17A
(c) Section 17B (d) Section 3B

22. Insulin comes under
(a) Schedule H (b) Schedule J
(c) Schedule G (d) Schedule O

23. Form 20 states that
(a) Licenses to sell stock or exhibit or offer for sell or distribute by retail other than specified C, C_1 and X.
(b) Licenses to sell stock or exhibit or offer for sell or distribute by wholesale other than specified C, C_1 and X.
(c) Licenses to sell stock or exhibit or offer for sell or distribute by retail other than specified C, C_1.
(d) Licenses to sell stock or offer for sell or redistribute by retail other than specified C, C_1 and X

24. Application for grant of a licence to manufacture Ayurvedic, Sidhha or Unani drugs requires
(a) Form 24D (b) Form 25E
(c) Form 20 (d) Form 21

25. Private testing laboratory for carrying out tests on drugs requires
(a) Form 32 (b) Form 31
(c) Form 30 (d) Form 36

26. List of coal tar colours permitted to be used in cosmetics is covered under
(a) Schedule O (b) Schedule P
(c) Schedule Q (d) Schedule R

27. Schedule J is related to
(a) GMP
(b) Curable disease
(c) List of diseases and ailments which drug cannot claim.
(d) Pack sizes of drug.

28. Injection syringe and needle are covered under
(a) Schedule A (b) Schedule B
(c) Schedule C (d) Schedule D

29. "Dettol" comes under
(a) Schedule N (b) Schedule O
(c) Schedule P (d) Schedule Q

30. If blood group is "AB" then colour label used is
(a) Red (b) White
(c) Yellow (d) Blue

31. Schedule N states
(a) List of minimum equipment for efficient running of pharmacy
(b) List of minimum equipment required for manufacturing of drug
(c) Requirement of factory premises and hygienic condition to be complied
(d) Standard for cosmetics

32. Schedule C is related to
(a) List of Biological and Immunological product
(b) List of Homeopathy product
(c) List of Ayurvedic product
(d) List of Allopathic product

33. "Kala jadu or Kavach" comes under
(a) Schedule J (b) Schedule K
(c) Schedule L (d) Schedule P

34. Pharmacy Council of India contain comprises _____ member(s) from AICTE and UGC.
(a) 1 (b) 2
(c) 3 (d) 4

35. Proforma for sending memorandum is included in which schedule?
(a) D (b) A
(c) FF (d) Q

36. The schedule in Drug and Cosmetics Act that deals with requirement and guidelines of clinical trial, import and manufacture of new drug is
(a) Schedule O (b) Schedule M
(c) Schedule F (d) Schedule Y

37. State Pharmacy Council should have the following number of elected members:
(a) Six (b) Five
(c) Nine (d) Seven

38. Schedule D as per D & C Act is concerned with
(a) List of drug exempted from the provision of import of drugs
(b) Disease or ailments which a drug may not purport to prevent or cure
(c) Requirement of factory premises
(d) List of prescription drugs

39. One of the following is/all are ex officio member(s) of State Pharmacy Council
(a) Chief pharmacist of government hospital
(b) Chief administrative medical officer of the state
(c) Assistant drug controller
(d) All

40. The Education Regulation is published in official gazette by
(a) Ministry of Education
(b) Central Government
(c) Drug Controller
(d) President, Pharmacy Council of India

41. List of drugs whole import, manufacture and sale, labelling and packaging are governed by special provisions are included in schedule
(a) X (b) K
(c) H (d) G

42. Biological and Biotechnological products are included in Schedule
(a) A (b) B
(c) C and C_1 (d) X

43. Drug and Magic Remedies Act is enacted in
(a) 1954 (b) 1948
(c) 1985 (d) 1919

44. Diabetes comes under
(a) Schedule G (b) Schedule H
(c) Schedule D (d) Schedule J

45. Grant of licence to manufacture a drug requires
(a) Form 24 (b) Form 25
(c) Form 26 (d) Form 27

46. List of drugs which should be used by patient under medical supervision is covered under _____ as per D & C Act
(a) Schedule G (b) Schedule H
(c) Schedule I (d) Schedule J

47. As per D and C Act Schedule T states about
(a) Requirements of factory premises for the manufacture of medical devices
(b) Requirements of factory premises for the manufacture of Homeopathy drugs
(c) Requirements of factory premises for the manufacture of Ayurveda, Sidhha and Unani drugs
(d) Requirements of factory premises for the manufacture of Allopathy drugs

48. TGA is regulatory agency of _____.
(a) Denmark (b) Austria
(c) Australia (d) Zimbabwe

49. MHRA is regulatory agency of _____
(a) UK (b) Denmark
(c) Brazil (d) South Africa

50. Schedule _____ of Drugs and Cosmetics Act includes requirements and guidelines on clinical trials for import and manufacture of new drugs.
(a) W (b) X
(c) Y (d) V

51. For parenteral preparation in glass containers minimum area required is
(a) 250 square metres (b) 400 square metres
(c) 500 square metres (d) 150 square metres

52. MCC is regulatory agency of _____
(a) UK (b) Denmark
(c) Brazil (d) South Africa

53. In State Pharmacy Council all following are ex officio members except
(a) President of India
(b) Chief Administrator Medical Officer of State
(c) The Officer In Charge of Drug Control Organization
(d) Government Analyst

54. Schedule X of Drugs and Cosmetics Act comprises
(a) List of incurable diseases
(b) Guidelines for clinical trials
(c) List of generic drugs
(d) None of the above

55. As per D and C Act "Schedule N" is related with
(a) List of maximum equipments for efficiently running pharmacy
(b) Area for opening retail pharmacy
(c) List of minimum equipment for efficiently running pharmacy
(d) Area required to open wholesale drug store

56. As per D & C Act "Schedule FF" is related with
(a) Parenteral preparation
(b) Ointment formulation

(c) Skin cosmetic preparation
(d) Ophthalmic preparation

57. Which of the following is prohibited to be imported?
(a) Toilet preparations
(b) Ayurvedic drugs
(c) Schedule 'C' and 'G' drugs
(d) Misbranded drugs

58. Hatch Waxman Act is related to
(a) Banned dugs (b) Over-the-counter drugs
(c) Dangerous drugs (d) Generic drugs

59. Coca, opium and hemp come under:
(a) Insecticide Act
(b) Poisons Act
(c) Dangerous Drugs Act
(d) Spurious Drug Act

60. The first edition of Indian Pharmacopoeia was published in the year:
(a) 1940 (b) 1950
(c) 1955 (d) 1985

61. Pharmacy Council of India is reconstituted:
(a) Every 2 Years (b) Every 3 Years
(c) Every 5 Years (d) Every 6 Years

62. In Phase-II trial following number of patient should be studied
(a) 10–12 patients (b) 1–10 patients
(c) 100 patients (d) 500 patients

63. Purpose of Phase-III trial is
(a) To determine maximum tolerated dose in humans, Pharmacodynamic effects, Adverse effects
(b) Determine Possible therapeutic uses, Effective doses range
(c) Efficacy and Ssafety of drug in larger number of patients (500 patients)
(d) Long time adverse effects after marketing drug

64. Standard for mechanical contraceptive comes under Schedule _____ as per D and C Act
(a) R (b) R_1
(c) S (d) O

65. If drug is so coloured, coated or polished that damage its therapeutic value or it is made to appear of better or greater therapeutic value than it really is known as
(a) Adulterated Drug (b) Spurious Drug
(c) Misbranded Drug (d) True Drug

66. Patent Act is established in
(a) 1948 (b) 1940
(c) 1970 (d) 1919

67. Pack size of drug is covered under
(a) Schedule P (b) Schedule R
(c) Schedule P_1 (d) Schedule O

68. For licence granted to sell by retail drugs, specified in schedule C and C(I) drugs form no. require is
(a) 20 (b) 20B
(c) 21 (d) 21B

69. As per Schedule P Carbenicillin Sodium Powder should be stored in/at
(a) A cool place
(b) A cold place
(c) Temperature not exceeding 5°C
(d) Well closed container, Protect from light, in cool place, protect from light

70. DTAB has _____ ex officio members.
(a) Five (b) Six
(c) Four (d) Eight

71. For Schedule X drug use of Human beings Special Labelling requirement require is
(a) Symbol X given in red
(b) Symbol N in red displayed on left top corner of the label
(c) Symbol N displayed on left top corner of the label
(d) Symbol H displayed on right top corner of the label

72. Aspirin sodium comes under
(a) Schedule G (b) Schedule H
(c) Schedule J (d) Schedule W

73. Example of Schedule G drug is
(a) Metformin (b) Enalapril
(c) Cefuroxime (d) Barbital

74. In 1954 one of the following act is passed
(a) Narcotic and Psychotropic Substance Act
(b) Drug and Magic Remedies Act
(c) The Medical Termination of Pregnancy Act
(d) Poisonous Act

75. Post marketing Surveillance comes under clinical trail
(a) Phase I (b) Phase II
(c) Phase III (d) Phase V

ANSWER KEYS

1. (a)	**2.** (b)	**3.** (d)	**4.** (c)	**5.** (a)	**6.** (d)	**7.** (a)	**8.** (d)	**9.** (c)	**10.** (c)
11. (d)	**12.** (b)	**13.** (c)	**14.** (a)	**15.** (b)	**16.** (b)	**17.** (c)	**18.** (a)	**19.** (c)	**20.** (b)
21. (c)	**22.** (c)	**23.** (a)	**24.** (a)	**25.** (d)	**26.** (c)	**27.** (c)	**28.** (c)	**29.** (b)	**30.** (b)
31. (a)	**32.** (a)	**33.** (a)	**34.** (a)	**35.** (b)	**36.** (d)	**37.** (a)	**38.** (a)	**39.** (d)	**40.** (b)
41. (a)	**42.** (c)	**43.** (a)	**44.** (d)	**45.** (b)	**46.** (a)	**47.** (c)	**48.** (c)	**49.** (a)	**50.** (c)
51. (a)	**52.** (d)	**53.** (a)	**54.** (d)	**55.** (c)	**56.** (d)	**57.** (d)	**58.** (d)	**59.** (c)	**60.** (c)
61. (c)	**62.** (a)	**63.** (c)	**64.** (b)	**65.** (c)	**66.** (c)	**67.** (c)	**68.** (c)	**69.** (c)	**70.** (d)
71. (b)	**72.** (d)	**73.** (a)	**74.** (b)	**75.** (d)					

CHAPTER 7

COSMETICS PREPARATION

COSMETICS

It is any external application intended to beautify and improve the complexion, skin or hair.

Dentifrices

These are preparations intended for use with a toothbrush for the purpose of cleaning the accessible surfaces of the teeth. They also reduce the incidence of tooth decay, help maintain healthy gingival and reduce the intensity of mouth odours.

Functions

1. Clean the accessible surface of teeth i.e., removal of food debris, plaque, foreign matter
2. Decrease the tooth decay
3. Mouth deodorant (Mouth refresher)
4. Improve gingival health

Formulation

A. Abrasives (polishing agent)

- It has two functions:
  1. Removal of dental plaque and stain
  2. To polish the enamel
- Abrasives contribute about half (50%) the total weight of dentifrices.
  Examples: Calcium carbonate, Dicalcium phosphate, Tri calcium phosphate Calcium pyrophosphate, Insoluble sodium metaphosphate, Hydrated Alumina, Silica and Silicates

B. Detergent and foaming agents

- It imparts more effective cleansing due to the lower surface tension.
  Examples: Soap, SLS (2%), Sodium salt of sulphated mono glyceride, Sodium-N-lauroyl Sarcosinate

C. Humectants

- It is used only in toothpaste.
- An essential function of humectants is to retain moisture when paste is exposed to air, and preventing the paste from hardening.
  Examples: Glycerin, Sorbitol, Propylene glycol

D. Binders

- It is used only in toothpaste.
- Admixture of the solid and liquid phases gets separated during storageWWWW. To avoid this binder is added.
  Examples: Gum Acacia, Agar, Alginates, Bentonite, Sodium CMC, Veegum, Glycerin of Starch, Carbopol –934

E. Flavours

Examples: Spearmint, Peppermint, Cinnamon-mint, Wintergreen

F. Sweetner

Example: Saccharin

G. Other ingredients

- Preservatives–Formalin, Parabens, Benzoates, Dichlorophene
- Stain removers–PVP, Dextrans, Organo-polysiloxanes
- Bleaches (Oxidizing Agents)–Sodium perborate, Potassium chlorate, Hydrogen peroxide-Urea

H. Therapeutic agent

1. Ammonium Compound–Urea and Dibasic Ammonium Phosphate
   - Ammonia loosened the bacterial plaques, easily removable by tooth brushing.
   - Urea counteracts the influence of carbohydrates in lowering the pH of the dental plaques. Urea solution reduces acid formation.
   - Dibasic Ammonium phosphate reduces bacterial counts.
2. Chlorophyll derivatives
3. Penicillins
4. Enzymes–Pancreatic, Fungal Enzyme-Dextranase
5. Flurides

Types of dentifrices

a. Tooth powder
b. Tooth paste
c. Liquids (Mouth washes)
d. Solid Blocks

Liquid dentifrices (mouth washes)

- They consist of Aqueous-alcoholic solution of essential oils designed to have a delicate odour and impart a refreshing and pleasant flavour.
- Glycerine is used as solvent and for its demulcent or conditioning effect. A small quantity of Saccharin to counter act bitterness of flavour and antiseptic materials.

Nail Polish

Formulation

Nail polish basically consists of pigments suspended in a volatile solvent to which film formers have been added. The ingredients are as follows:

- Primary film former (nitrocellulose, methacrylate polymers, vinyl polymers)
- Secondary film-forming resin (formaldehyde, *p*-toluene sulfonamide, polyamide, acrylate, alkyd, vinyl resins)
- Plasticizers (dibutyl phthalate, dioctyl phthalate, tricresyl phosphate, camphor)
- Solvents and diluents (acetates, ketones, toluene, xylene, alcohols)
- Colourants (organic DandC pigments, inorganic pigments)
- Specialty fillers (guanine, fish scale, titanium dioxide–coated mica flakes, or bismuth oxychloride for iridescence)
- Suspending agents
  - Nitrocellulose is the most commonly used primary film-forming agent in nail lacquer. It produces a shiny, tough, nontoxic film that adheres well to the nail plate. The film is somewhat oxygen permeable, allowing gas exchange between the atmosphere and the nail plate; this gas exchange is important for ensuring nail plate health. Resins and plasticizers are then added to increase the flexibility of the film, minimizing chipping and peeling.
  - The most popular resin used to enhance the nitrocellulose film is toluene-sulfonamide-formaldehyde; however, it is the source of allergic contact dermatitis in some nail enamels. Hypoallergenic nail enamels use polyester resin or cellulose acetate butyrate, but sensitivity is still possible.
  - Guanine, fish scale, bismuth oxychloride, or titanium dioxide-coated mica flakes can be added to enhance light reflection and to give a frosted appearance.

Anti-perspirant

- These are astringents used to reduce the amount of sweat secretions.they are considered to have a coagulating effect on skin protein and block the opening of sweat ducts.
- Examples: Aluminium suphate (effective), Aluminium chloride, Aluminium phenolsulphonate, Zinc phenolsulphonate

Depilatory Preparation

- A **depilatory** is a cosmetic preparation used to remove the hair from the skin on the human body.
- Currently, a common active ingredient is calcium thioglycolate, which breaks down the disulfide bonds in keratin and weakens the hair so that it is easily scraped off where it emerges from the hair follicle.
- This breakdown reaction is affected by the calcium hydroxide (an alkali). The resulting combination of calcium hydroxide and thioglycolic acid is calcium thioglycolate (CaTG). The calcium hydroxide is present in excess to enable the thioglycolic acid to react with the cystine present in hair protein.

$2SH\text{-}CH_2\text{-}COOH$ (thioglycolic acid) + R-S-S-R (cystine) -----> 2R-SH + $COOH\ CH_2\ SS\ CH_2\ COOH$ (dithiodiglycolic acid).

Active ingredients–which will cause the hair fibres to swell and produce a cleavage of cysteine bond	Sulphides–barium sulphide, Strontium sulphide, Sodium sulphide Stannites–Sodium stannite Substituted mercaptans–Calcium Thioglycolate Enzymes–keratinase
Humectant	Glycerol, Sorbitol
Thickening agent	Methyl cellulose

Talcum Powder

Formulation

1. Talc is used to make baby powder (and talcum powder) Talc is a hydrous silicate mineral composed of magnesium (Mg), silicon and oxygen (SiO_2, silica), and water. Its chemical formula is $Mg_3Si_4O_{10}(OH)_2$.
2. ZnO is sometimes added up to 5% as a mild astringent.
3. Light magnesium carbonate added in order to mix perfume.
4. Iron oxide may present to impart colour.

Baby Powder

It is similar to talcum powder but contains additional antiseptic material. Boric acid is used in this.

Face Powder Loose

Covering power agents (10 to 25%)	Light Kaolin, Zinc oxide, Titanium Oxide
Adhesives (up to 3%)	Zinc stearate, magnesium stearate, Calcium/Magnesium salt of Myristic acid
Absorbents (Up to 30%)	Colloidal Kaolin, Starch, Precipitated chalk, Avicel
Slip(70% or more)	Talc, Zinc stearate, Starch
bloom	Rice starch, chalk

Compact Face Powder

Binding agent is extra additive compared to loose face powder. Binders used are:

- Dry binder–Metallic stearates
- Oil binder–Mineral oil, Isopropyl myristate, Lanolin derivative
- Water soluble binder–solution of gum (Acacia, Tragacanth), PVP, MC, CMC

Cleansing Cream

Cold cream

- An emulsion of water and certain fats, usually including beeswax and various scent agents, designed to smooth skin and remove makeup. The name derives from the cooling feeling that the cream leaves on the skin. Cooling effect is due to slow evapouration of water content.
- Cold cream now replaces the olive oil with mineral oil or other oils, which are slower to spoil, as well as alcohol, glycerine, and lanolin.
- Jojoba oil became a common ingredient. Another common ingredient in modern cold cream is borax, which is also responsible for the whiteness of cold cream.

Borax-bees wax Cream

Initially, o/w type emulsion but when cream is rubbed on skin, converts into w/o emulsion due to evaporation of water.

Vanishing Cream

An oil-in-water emulsion containing potassium, ammonium, or sodium stearate with water and holding in emulsified form more or less free stearic acid; it also contains a hygroscopic ingredient such as glycerol, and a small amount of a fatty ingredient; it leaves a protective, invisible film of stearic acid on the skin.

Hair Products

Shampoo

A shampoo is a product (preparation of surfactant) for cleaning dirt, sebum and sweat off hair and scalp.

Formulation ingredients:

Principal surfactant – It serves as to foam and clean the hair. Non-ionic, Cationic, Anionic surfactant are used.	Fatty acid soaps Alkyl sulphates Alkyl ether sulphates Paraffin sulphonates Alkyl benzene sulphonates
Secondary surfactant- They modify detergent and surfactant properties of principal surfactant. Anionic and Ampholytic detergent are used.	Secondary Alkyl sulphates Monoglyceride sulphates Alkyl sulpho succinates Acyl Amino acids Acyl sarcosines
Additives	
1. Germicides– Anti-dandruff	Parachlorometaxylenol Parachlorometacresol Hexachlorophene Bithionol Quaternary Ammonium Compounds Chlorhexidine Resorcinol Salicylates Selenium Compound Sulphur Zinc undecylenate
2. Conditioning Agents	Secondary detergents Fatty materials (Lanolin, mineral oil) Natural products (herbal, Amino acids, Polypeptides, Egg) Polymeric materials (PVP)
3. Pearlscent Agent	Guanine Dodecyl ammonium Montmorillonite
4. Sequestrants	EDTA
5. Preservatives	P-hydroxy benzoic acid ester Formaldehyde Phenyl mercuric salts
6. Perfumes	
7. Colours	

Evaluation tests

1. Foam and foam stability
2. Detergency and Cleaning action
3. Wetting action
4. Conditioning action
5. Irritation to eyes
6. pH
7. Fragrance
8. Soap or detergent content
9. Effect in Hard water
10. Viscosity

Multiple Choice Questions

1. Macrogol 1000 is the base used for the semi-solid dosage form, it is also called
(a) PEG 500 (b) PEG 20
(c) PEG 200 (d) PEG 1000

2. Which is an example of cationic surfactant?
(a) Benzalkonium chloride
(b) Polysorbate 80
(c) Sodium lauryl sulphate
(d) Sorbitol mono oleate

3. The temperature at which the solubility of the surfactant is equal to CMC is
(a) Kraft point (b) Boiling point
(c) Melting point (d) a and b

4. Creep testing is applied to analyse the viscoelastic property of
(a) Emulsions (b) Lotion
(c) Ointments (d) Suspensions

5. The numerical designation of propellant butane is
(a) A-108 (b) 11
(c) A-17 (d) A-109

6. Which of following technique(s) is/are used to determine particle size of aerosol?
(a) Microscopy
(b) Cascade impactor
(c) Light scatter decay
(d) Both (b) and (c)

7. Vanishing cream is an ointment that may be classified as
(a) Water-soluble base
(b) Oleaginous base
(c) Absorption base
(d) Emulsion base

8. 30 psig = __ psia
(a) 14.7 (b) 15.3
(c) 30 (d) 4.7

9. Paste is a semi-solid preparation which is a
(a) Magma
(b) Concentrated emulsion
(c) Gel
(d) Concentrated suspension

10. Span 40 is dissolved in paraffin oil. At slightly above the critical micelle concentration, the arrangement of span molecule is;
(a) Heads face the centre of the micelle
(b) Laminar arrangement
(c) Tails face the air at the interface
(d) Tails face the centre of the micelle

11. Addition of _____ to nail polish preparation improves flexibility and lasting power
(a) Acetylated monoglycerides
(b) Di-butyl stearate
(c) Di-octyl phthalate
(d) Resins

12. Which of the following is oleaginous base for suppository?
(a) Cocoa butter
(b) Synthetic fat
(c) Hydrogenated palm kernel oil
(d) All of above

13. Which of the following is the lowest melting point polymorphic form of cocoa butter?
(a) β (b) γ
(c) α (d) β^1

14. An early sign of instability in emulsion is detected by
(a) Appearance of bigger size globules
(b) Separation of layer
(c) Appearance of caking
(d) Breaking

15. Different suspension can be compared by using _____ as a quality control parameter.
(a) Settling
(b) Rheological evaluation
(c) Physical evaluation
(d) Both b and c

16. Structured vehicle is included in the formulation of a suspension in order to
(a) Prevent the cake formation
(b) Decrease the interfacial tension
(c) Prevent the sedimentation of particles
(d) None of the above

17. Auxiliary emulsifying agents stabilize the emulsion by
(a) Adjusting the viscosity of continuous phase
(b) Changing the HLB value
(c) Strengthening the polar head of emulsifier
(d) Strengthening the non polar head emulsifier

18. Gegenions means
(a) Amphiphiles
(b) Ions having a charge opposite to the potential determining ions
(c) Ions having same charge as that of potential determining ions
(d) Potential determining ions

19. Which of the following is hydrophilic base for suppository?
(a) Massupol
(b) Maccrogol
(c) Soap glycerine
(d) Both (b) and (c)

20. The numerical designation Propellent 11 refers to
(a) Dichloro difloromethane
(b) Dichloro difloroethane
(c) Trichloro monoflouoromethane
(d) Butane

21. Actuators are normally used in the aerosols
(a) To deliver aerosol in proper and desired form
(b) To provide housing to gasket
(c) To create minute particles of foam -based aerosols
(d) Nne of the above

22. Aerosol is the reverse of:
(a) Emulsion (b) Liquid foam
(c) Smoke (d) Solid foam

23. A blend between Tween 20 and Span 20 form _____ type of emulsion.
(a) O/W (b) W/O
(c) Milky (d) Multiple emulsions

24. When the suspended particles are hydrophobic in nature, the formulation of a suspension includes a:
(a) Wetting agent (b) Emulsifying agent
(c) Suspending agent (d) All of the above

25. Antoniff's rule is applicable to:
(a) Highly polar liquids against water
(b) Nonpolar liquids against water
(c) Polar liquid against other immiscible liquids
(d) Slightly polar liquids against water

26. An example for colloidal system is
(a) Clay and gels
(b) Ointments and pastes
(c) Solutions of soaps and proteins
(d) Suspensions and emulsions

27. The costitutionconstitution of Bbetadine is?
(a) 10% Iodine in complex form
(b) 2% Iodine in complex form
(c) 5% Iodine in complex form
(d) 15% Iodine in complex form

28. Flammability and combustibility of aerosol is determined by
(a) Flash point
(b) Flame projection
(c) Light scatter decay
(d) Both (a) and (b)

29. The main film-forming agent in the nail polish is
(a) Nitrocellulose
(b) Sulphonamide-formaldehyde
(c) Ethyl lactate
(d) *n*-butyl acetate

30. The concentration of plasticizer is nail polish is
(a) 1% (b) 5%
(c) 15% (d) 25%

31. Creams are basically:
(a) Semi-solids
(b) Emulsions
(c) Ointment-like preparation
(d) None

32. The different forms of polymorphic cocoa butter is all except:
(a) α (b) β
(c) β^1 (d) α^1

33. The amount of fatty substances in shaving creams is
(a) 20% (b) 30%
(c) 45% (d) 15%

34. Depilatories are substances which:
(a) Removes hair without removing skin
(b) Moisturizes the skin
(c) Imparts colour to the hair
(d) Are used to held the hair in the position

35. The following combination of dye-colour are true except:
(a) Amaranth-Red
(b) Indigo Carmine-Blue
(c) Tartrazine-Yellow
(d) Erythrosine-Blue

36. Sequestrants are included in the shampoo to
(a) Bind with metal ions in the hair
(b) Form complex with metal ions in shampoo and prevent formation of insoluble salts
(c) Quench oxygen from shampoo
(d) None

37. Which of the following wax is not used in the lipstick preparation?
(a) White bees wax
(b) Candelilla wax
(c) Ozokerite wax
(d) Cetrimide emulsifying wax

38. Pastes are a form of:
(a) Creams (b) Ointment
(c) Suppositories (d) Solidified emulsion

39. Theobroma oil is a type of _____suppositories base.
(a) Oleagenious (b) Hydrophilic
(c) Emulsifying (d) None

40. Witepsol is a type of
(a) Aqueous base (b) Emulsifying base
(c) Oleogenous base (d) None

41. Yield value is indicative of
(a) Force of flocculation
(b) Degree of flocculation
(c) De-flocculation
(d) None of the above

42. Which of the following is not an ideal requirement for suppository?
(a) It should melt at body temperature
(b) Compatible with large variety of drug
(c) It should have metastable form
(d) Melting point and solidification point should be close

43. XEROGEL is a type of:
(a) Suppositories (b) Jellies
(c) Cream (d) None

44. Which of the following is used as a Humectant in dental preparation?
(a) Agar (b) Sorbitol
(c) Methyl cellulose (d) Carbopol-93

45. Shrinkage of gel by extrusion of liquid is called:
(a) Syneresis (b) Dilatancy
(c) Plasticity (d) Ebullition

46. Vanishing creams are called so because
(a) They disappear during formulation mix
(b) They vanish during removal from skin surface
(c) They disappear after rubbing application
(d) None of the above

47. The main application of foundation cream is:
(a) To form a base for application of powders/make-up
(b) To form a foundation for the formulation of facial creams
(c) To mix it with fatty acids for preparing soluble lotions
(d) None of the above

48. The most frequently used surfactants in shampoos are:
(a) Anionic (b) Cationic
(c) Non-ionic (d) All

49. The major constituent in the after-shave lotion is
(a) Emollient (b) Anti septics
(c) Alcohol (d) Perfumes

50. CARBOWAX is a type of
(a) Absorption base
(b) Modern ointment
(c) Water-soluble bases
(d) Oleaginous and hydrocarbon

51. Which of following technique is used to determine the particle size of aerosol?
(a) Microscopy (b) Cascade impactor
(c) Light scatter decay (d) Both (b) and (c)

52. The maximum pressure to be filled in plastic aerosol containers is
(a) 25 psi (b) 50 psi
(c) 10 psi (d) 15 psi

53. The dip tube in the aerosol is generally made up of
(a) Polypropylene (b) Polystyrene
(c) Polyethylene (d) Nylon

54. The numerical designation of propellant butane is:
(a) A-108 (b) 11
(c) A-17 (d) A-108

55. During storage, crystal growth is observed in a suspension due to
(a) Absorption of water
(b) Fluctuations in the ambient temperatures
(c) Presence of suspending agent
(d) Volatilization

56. In the formulation development of emulsions and suspensions, what type of diameter is important?
(a) Length number (b) Projected diameter
(c) Sieve (d) Stokes diameter

57. While using sedimentation method for size analysis, addition of a deflocculating agent to a suspension is necessary in order to:
(a) Accelerate the process of sedimentation
(b) Make the particles spherical
(c) Prevent the aggregation
(d) Satisfy Reyonlds number

58. Resins are used in the nail-polish preparation
(a) As film former
(b) To give film more gloss and adhesion
(c) To give colour to nail polish
(d) As a diluents

59. Which of the following is not used as an anti-dandruff agent in shampoos?
(a) Zinc undecylenate (b) Zinc pyruvate
(c) Cadmium sulphide (d) Selenium sulphide

60. Which of the following is not a hair remover?
(a) Zinc sulphide
(b) Calcium sulphide
(c) Arsenic trisulphide
(d) Copper sulphate

61. In aerosol for determination of density _____ equipment is used.
(a) Gas chromatogram (b) Cascade impactor
(c) Pycnometer (d) Both b and c

62. For aerosol formulation cascade impactor is used for
(a) Identification of propellent
(b) Determineing particle size
(c) Flash point
(d) Determineing moisture content

63. Following is/are not absorption base(s):
(a) Non-emulsifiable bases
(b) W/O emulsion bases
(c) Both
(d) None

64. Creams are
(a) Translucent (b) Transparent
(c) Opaque (d) None

65. Following is true for pastes:
(a) Pastes are ointments
(b) Pastes contain high percentage of insoluble solids
(c) Pastes are used for protective function
(d) All

66. Which of the following is a semisolid preparation?
(a) Creams (b) Ointments
(c) Gels (d) All

67. Emulsions are
(a) Homogeneous system
(b) Thermodynamically instable system
(c) Liquid-liquid dispersions
(d) Biphasic systems

68. Following is not true for jellies
(a) Nongreasy preparation
(b) Semisolid in nature
(c) Generally applied internally for systemic use
(d) Used for medication and lubrication

69. Displacement values are related to manufacture of
(a) Pastes (b) Gels
(c) Pessaries (d) Ointments

70. Suppositories can be prepared by
(a) Compression
(b) Triturition
(c) Solvent evaporation method
(d) Hot melt extrusion method

71. Suppositories used for ear infection are called
(a) Rockets
(b) Cones
(c) Bougies
(d) Pessaries

72. Following is considered during the preparation of nasal drops to have little effect on cilial action except
(a) It should be iso-osmotic with nasal mucosal secretion
(b) It should have pH on the acid side of neutral
(c) It should have viscosity similar to nasal mucosa
(d) It should have low amount of emulsifiers

73. Carbopols are
(a) Polyoxythylene ethers with carboxy groups
(b) Synthetic vinyl polymers with ionizable carbolyl group
(c) Mineral waxes with hydrocarbon content ranging from C35 to C55
(d) Polyoxyethylene derivatives of plyoxypropylene

74. Addition of enough $CaCl_2$ in emulsion stabilized by a soap solution causes
(a) Cracking of emulsion
(b) Phase inversion from o/w to w/o
(c) Phase inversion from w/o to o/w
(d) Precipitation of emulsifier

75. Eliminate wrong sentence
(a) Liniments are stimulating preparations
(b) Lotions are soothing preparations
(c) Liniments are applied generally to broken and wounded skins
(d) Liniments are solutions

76. Spans and Tweens are
(a) Highly polymerized mannuronic acid anhydrides
(b) Phospholipids
(c) Polyoxyalkalene derivatives
(d) Glycosides

77. Following can be used as viscosity builders in ophthalmic solutions except
(a) Veegum (b) Methyl cellulose
(c) PEG (d) PVP

78. Veegum is a/an
(a) Polyol (b) Organic gum
(c) Synthetic gum (d) Clay

79. All of the following are true sentences except
(a) Lozenges are intended for systemic use
(b) Lozenges are prepared by compression at very high pressure
(c) Lozenges don't contain disintegrant
(d) Lozenges contain high percentage of binder

80. Following is a clear liquid preparation containing a low solubility drug solubilized by means of proper solvents usually alcohol
(a) Elixirs (b) Mixtures
(c) Linctuses (d) Emulsion

81. Cold creams are
(a) O/W-type borax cream
(b) W/O-type borax cream
(c) O/W-type cationic emulsifier wax cream
(d) W/O-type trietahnolamine cream

82. Ca soaps tend to produce
(a) W/O emulsion (b) O/W emulsion
(c) Both (d) Microemulsion

83. Auxiliary emulsifier acts by _____
(a) Forming electrical double layer
(b) Decreasing the viscosity
(c) Increasing the viscosity
(d) Decreasing the difference in the densities of both phases

84. _____ is also known as irreversible aggregation of globules?
(a) Creaming (b) Flocculation
(c) Coalescence (d) Both (a) and (c)

85. _____ is also known as micellar solution.
(a) Microemulsion
(b) Multiple emulsion
(c) Nanosuspension
(d) O/W emulsion

86. Housing in aerosol container is made up of
(a) Nylon (b) Delrin
(c) Both (d) None

87. _____ allows escape of vaporized propellant along with liquid product.
(a) Mounting cup (b) Stem
(c) Vapor tap (d) Gasket

88. Ferrule in aerosol valve is for _____
(a) Proper attachment of valve to container
(b) Metered dose delivery
(c) Both
(d) None

89. Stem in aerosol container is made up of
(a) Tin-plated steel (b) Copper
(c) Nylon (d) Neoprene

90. Dip tube in aerosol container is made up of
(a) Polyethylene/polypropylene
(b) Propylene glycol
(c) PEG
(d) All

91. _____ type of propellant is having the highest amount of propellant.
(a) Foam (b) Spray
(c) Solid stream (d) All

92. Tube spacer in MDI is used for
(a) Metering the dose
(b) Proper delivery to oropharynx
(c) Decrease systemic absorption of active ingredients
(d) All of above

93. Stable form of cocoa butter is having a melting point of ___°C
(a) 25 (b) 35
(c) 45 (d) 55

94. Bougies are used for _____ applications.
(a) Rectal (b) Urethral
(c) Vaginal (d) All are true

95. Solid fat index (SFI) can be used to recognize _____ of the total base.
(a) Melting range
(b) Hardness
(c) Amount of crystalline fat
(d) All are true

96. _____ can be used to determine type of the glyceride of the total fat.
(a) Hydroxyl value (b) Saponification value
(c) Acid value (d) Iodine value

97. _____ can be used to determine unesterified sites on glyceride molecules.
(a) Hydroxyl value (b) Saponification value
(c) Acid value (d) Iodine value

98. _____ increases with increase in the iodine value.
(a) Melting point (b) Density
(c) Hydrolysis (d) Rancidity

99. Solid Fat Index (SFI) can be determined/characterized using following/followings:
(a) Viscometer (b) Dilatometer
(c) Densitometer (d) All

100. _____ indicates presence of free acid only in the fat/oil.
(a) Hydroxyl value (b) Saponification value
(c) Acid value (d) Iodine value

101. _____ does not require lubricant in the mould when used to formulate suppositories.
(a) *Theobroma* oil (b) Glycero-gelatin
(c) Glecerol (d) PEG-1000 + PEG-4000

102. _____ is a hydrocarbon base.
(a) Soft paraffin (b) Macrogol
(c) Bees wax (d) Wool fat

103. _____ contains the highest amount of solid content.
(a) Ointment (b) Gel
(c) Jellies (d) Paste

104. _____ is not a gelling agent.
(a) Pectin (b) Na CMC
(c) Carbomer (d) Wool fat

105. _____ is not a natural emulsifier.
(a) Acacia (b) Na alginate
(c) Agar (d) Tween

106. Solid Fat Index (SFI) can be determined/characterized using following/followings:
(a) Viscometer (b) Dilatometer
(c) Densitometer (d) All

107. _____ indicates presence of free acid only in the fat/oil.
(a) Hydroxyl value (b) Saponification value
(c) Acid value (d) Iodine value

108. Solvent used with water to solubilize digitalis glycoside is
(a) Acetone (b) Ethanol
(c) Methanol (d) Chloroform

109. For faster absorption of a water-insoluble drug, the critical factor is
(a) Deaggregation (b) Dissolution
(c) Disintegration (d) Denaturation

110. Sink condition is related to
(a) In vitro evaluation
(b) In vivo evaluation
(c) Sink condition
(d) All

111. The more flocculated the suspension, _____ will be the yield value.
(a) Higher (b) Lesser
(c) Same (d) None of above

112. Liquification is anexample of ……. incompatibility.
(a) Immediate (b) Delayed
(c) Both a and b (d) None of above

113. Creaming in emulsions is governed by ____.
(a) Gay–Lussacs law
(b) Newton's law law
(c) Stoke's law
(d) Charles' law

114. Crystallization is an example of _____ incompatibility
(a) Immediate
(b) Delayed
(c) Both a and b
(d) None of above

115. Doubling the diameter of the oil globules increases the creaming rate by a factor of ……
(a) 2 (b) 4
(c) 6 (d) 8

116. Sediments are formed slowly and leading to a hard cake in _____.
(a) Flocculated suspension
(b) Deflocculated suspension
(c) Both of above
(d) None of above

117. In oil in water type emulsion, creaming occurs in _____ direction.
(a) Upward (b) Downward
(c) Both directions (d) Does not occur

118. In flocculation occurring in suspension, the particles in floccules are held by _____.
(a) Repulsive forces (b) Gravitational force
(c) Van der Waals forces (d) None of above

119. The dip tube in aerosol container is made from one of the following. Choose the correct one
(a) Polypropylene (b) Glass
(c) Stainless steel (d) Aluminum

120. A plasticizer and a high boiling point solvent used in the preparation of nail lacquers are
(a) Butyl stearate (b) Ethyl lactate
(c) Ethanol (d) (a) and (b)

ANSWER KEYS

1. (b)	**2.** (a)	**3.** (a)	**4.** (c)	**5.** (c)	**6.** (d)	**7.** (a)	**8.** (b)	**9.** (d)	**10.** (a)
11. (a)	**12.** (d)	**13.** (b)	**14.** (a)	**15.** (b)	**16.** (c)	**17.** (a)	**18.** (b)	**19.** (d)	**20.** (c)
21. (a)	**22.** (b)	**23.** (a)	**24.** (a)	**25.** (d)	**26.** (c)	**27.** (a)	**28.** (d)	**29.** (a)	**30.** (b)
31. (b)	**32.** (d)	**33.** (b)	**34.** (a)	**35.** (d)	**36.** (b)	**37.** (d)	**38.** (b)	**39.** (a)	**40.** (b)
41. (a)	**42.** (c)	**43.** (b)	**44.** (b)	**45.** (a)	**46.** (c)	**47.** (a)	**48.** (a)	**49.** (c)	**50.** (c)
51. (d)	**52.** (a)	**53.** (a)	**54.** (c)	**55.** (b)	**56.** (d)	**57.** (c)	**58.** (b)	**59.** (b)	**60.** (d)
61. (c)	**62.** (b)	**63.** (c)	**64.** (c)	**65.** (d)	**66.** (d)	**67.** (a)	**68.** (c)	**69.** (c)	**70.** (a)
71. (b)	**72.** (d)	**73.** (b)	**74.** (b)	**75.** (c)	**76.** (c)	**77.** (a)	**78.** (d)	**79.** (a)	**80.** (a)
81. (b)	**82.** (a)	**83.** (c)	**84.** (c)	**85.** (a)	**86.** (b)	**87.** (c)	**88.** (a)	**89.** (c)	**90.** (a)
91. (b)	**92.** (c)	**93.** (b)	**94.** (b)	**95.** (d)	**96.** (b)	**97.** (a)	**98.** (d)	**99.** (b)	**100.** (c)
101. (d)	**102.** (a)	**103.** (d)	**104.** (d)	**105.** (d)	**106.** (b)	**107.** (c)	**108.** (b)	**109.** (b)	**110.** (a)
111. (a)	**112.** (a)	**113.** (c)	**114.** (b)	**115.** (b)	**116.** (b)	**117.** (a)	**118.** (c)	**119.** (a)	**120.** (d)

CHAPTER 8

MICROBIOLOGY

DEFINITIONS

A. Immunogen

A substance that induces a specific immune response.

B. Antigen (Ag)

A substance that reacts with the products of a specific immune response.

C. Hapten

A substance that is non-immunogenic but which can react with the products of a specific immune response. Haptens are small molecules which could never induce an immune response when administered by themselves but which can when coupled to a carrier molecule. Free haptens, however, can react with products of the immune response after such products have been elicited. Haptens have the property of antigenicity but not immunogenicity.

D. Epitope or Antigenic Determinant

A portion of an antigen that combines with the products of a specific immune response.

E. Antibody (Ab)

A specific protein which is produced in response to an immunogen and which reacts with an antigen.

F. Adjuvants

Substances that can enhance the immune response to an immunogen are called adjuvants. The use of adjuvants, however, is often hampered by undesirable side effects such as fever and inflammation.

G. Pathogens Microorganism which has the ability to cause a disease.

H. Virulence Capacity of M.O. to invade the body.

I. Attenuation Reduction in normal virulence of a pathogen.

J. Exaltation Any increase in virulence.

CHEMICAL NATURE OF IMMUNOGENS

A. Proteins

The vast majority of immunogens are proteins. These may be pure proteins or they may be glycoproteins or lipoproteins. In general, proteins are usually very good immunogens.

B. Polysaccharides

Pure polysaccharides and lipopolysaccharides are good immunogens.

C. Nucleic acids

Nucleic acids are usually poorly immunogenic. However, they may become immunogenic when single stranded or when complexed with proteins.

Lipids

In general, lipids are non-immunogenic, although they may be haptens.

Exotoxin	Endotoxin
They are metabolic products	They are structural elements
Produced mainly by Gram positive bacteria but also from gram negative E.g., Shigella, cholera, E.colli	Produced by gram negative bacteria
They are water soluble	They liberated only when cell die or disintegrate
Chemically, they are high molecular weight proteins and enzymes.	Chemically, they are complexes of phospholipids, polysaccharide and proteins
They are thermolabile and lose activity at about 60°C	They are thermostable
Highly potent and antigenic	Much less toxic

Types of Antigens

A. T-independent antigens

T-independent antigens are antigens which can directly stimulate the B cells to produce antibody without the requirement for T cell help. In general, polysaccharides are T-independent antigens.

B. T-dependent antigens

T-dependent antigens are those that do not directly stimulate the production of antibody without the help of T cells. Proteins are T-dependent antigens.

Hapten-Carrier Conjugates

Hapten-carrier conjugates are immunogenic molecules to which haptens have been covalently attached. The immunogenic molecule is called the carrier. Hapten-carrier conjugates have native antigenic determinants of the carrier as well as new determinants of the hapten.

Superantigens

When the immune system encounters a conventional T-dependent antigen, only a small fraction (1 in $10^4 - 10^5$) of the T cell population is able to recognize the antigen and become activated (monoclonal/oligoclonal response). However, there are some antigens which polyclonally activate a large fraction of the T cells (up to 25%). These antigens are called **superantigens**.

Examples of superantigens include: Staphylococcal enterotoxins (food poisoning), Staphylococcal toxic shock toxin (toxic shock syndrome), Staphylococcal exfoliating toxins (scalded skin syndrome) and Streptococcal pyrogenic exotoxins (shock).

IMMUNOGLOBULINS–STRUCTURE AND FUNCTION

Immunoglobulin (Ig)

Immunoglobulins are glycoprotein molecules that are produced by plasma cells in response to an immunogen and which function as antibodies.

Basic structure of immunoglobulins

A. Heavy and light chains

All immunoglobulin's have a four chain structure as their basic unit. They are composed of two identical light chains (23kD) and two identical heavy chains (50–70kD)

B. Disulfide bonds

1. **Inter-chain disulfide(-S-S-) bonds**–The heavy and light chains and the two heavy chains are held together by inter-chain disulfide bonds and by non-covalent interactions. The number of inter-chain disulfide bonds varies among different immunoglobulin molecules.
2. **Intra-chain disulfide(-S-S-)bonds**–Within each of the polypeptide chains, there are also intra-chain disulfide bonds.

C. Variable (V) and constant (C) regions

When the amino acid sequences of many different heavy chains and light chains were compared, it became clear that both the heavy and light chain could be divided into two regions based on variability in the amino acid sequences.

These are the:

1. **Light Chain**–VL (110 amino acids) and CL (110 amino acids)
2. **Heavy Chain**–VH (110 amino acids) and CH (330–440 amino acids)

D. Hinge region

This is the region at which the arm of the antibody molecule forms a Y. It is called the hinge region because there is some flexibility in the molecule at this point.

E. Domains

Three dimensional images of the immunoglobulin molecule show that it is not straight as depicted in figure 2A. Rather, it is folded into globular regions each of which contains an intra-chain disulfide bond. These regions are called domains.

1. **Light Chain Domains**–VL and CL
2. **Heavy Chain Domains**–VH, $CH_1 - CH_3$ (or CH_4)

F. Oligosaccharides

Carbohydrates are attached to the CH_2 domain in most immunoglobulins. However, in some cases, carbohydrates may also be attached at other locations.

Immunoglobulin Fragments: Structure/Function Relationships

Immunoglobulin fragments produced by proteolytic digestion have proven very useful in elucidating structure/function relationships in immunoglobulins.

A. Fab

Digestion with papain breaks the immunoglobulin molecule in the hinge region before the H-H inter-chain disulfide bond.

This results in the formation of two identical fragments that contain the light chain and the VH and CH_1 domains of the heavychain.

Antigen binding–These fragments were called the Fab fragments because they contain the antigen binding sites of the antibody. Each Fab fragment is monovalent whereas the original molecule was divalent.

B. Fc

Digestion with papain also produces a fragment that contains the remainder of the two heavy chains each containing a CH_2 and CH_3 domain. This fragment was called Fc because it was easily crystallized.

C. F(ab')2

Treatment of immunoglobulins with pepsin results in cleavage of the heavy chain after the H-H inter-chain disulfide bonds resulting in a fragment that contains both antigen binding sites. This fragment was called F(ab′)2 because it is divalent. The Fc region of the molecule is digested into small peptides by pepsin. The F(ab′)2 binds antigen but it does not mediate the effector functions of antibodies.

Human Immunoglobulin Classes and Types

Immunoglobulin classes

The immunoglobulins can be divided into five different classes, based on differences in the amino acid sequences in the constant region of the heavy chains.

1. IgG – Gamma heavy chains
2. IgM – Mu heavy chains
3. IgA – Alpha heavy chains
4. IgD – Delta heavy chains
5. IgE – Epsilon heavy chains

Immunoglobulin types

Immunoglobulins can also be classified by the type of light chain that they have. Light chain types are based on differences in the amino acid sequence in the constant region of the light chain.

1. Kappa light chains
2. Lambda light chains

Antibodies, also called **immunoglobulins** or Igs [with molecular weights of 150–900 Md], constitute the *gamma globulin* part of the blood proteins. They are soluble proteins secreted by the plasma offspring (clones) of primed B cells.

- IgE-Responsible for autoimmune responses, such as allergies and diseases like arthritis, multiple sclerosis, and systemic lupus erythematosus).
- IgG is the only antibody that can cross the placental barrier to the fetus and it is responsible for the 3 to 6 month immune protection of newborns that is conferred by the mother.
- IgM is the dominant antibody produced in primary immune responses.
- IgG dominates in secondary immune responses.
- IgM is physically much larger than the other immunoglobulins.

Types of allergic reaction	Characteristics	Signs appear within	Examples
Type I Anaphylaxis	IgE binds to mast cell or basophills causes degranulation of mast cell and release histamine	< 30 min	Anaphylactic shock from drug, venoms, common allergic condition as hay fever, asthama
Type II Cytotoxic	Antigen causes formation of IgM and IgG that bind to target cell, when combined with action of complement destroy target cells.	5–12 hrs	Transfusion
Type III Immune complex	Ag and Ab form complex that causes inflammation.	3–8 hrs	Arthus reaction, Serum sickness
Type IV Cell mediated or delayed type	Ag causes formation of Tc that kills target cell	----	Rejection of transplanted tissue, poison ivy, such chronic diseases like tuberculosis, leprosy

Structure and Some Properties of Ig Classes

IgG	IgM
Structure All IgG's are **monomers** (7S immunoglobulin). **Half life** 23 days **% total serum Antibody** 75–80% (most abundant in serum) **Properties** IgG is the most versatile immunoglobulin because it is capable of carrying out all of the functions of immunoglobulin molecules. a) IgG is the major Ig in serum – 75% of serum Ig is IgG b) IgG is the major Ig in extra vascular spaces and in blood and lymph. c) Placental transfer–Transfer is mediated by a receptor on placental cells for the Fc region of IgG. d) Fixes complement–Not all subclasses fix equally well; IgG4 does not fix complement	**Structure** IgM normally exists as a **pentamer** (19S immunoglobulin) but it can also exist as a monomer. **Half life** 05 days **% total serum Antibody** 5–10% **Properties** a) IgM is the third most common serum Ig. b) IgM is the first Ig to be made by the fetus and the first Ig to be made by a virgin B cells when it is stimulated by antigen. c) As a consequence of its pentameric structure, IgM is a good complement fixing Ig. Thus, IgM antibodies are very efficient in leading to the lysis of microorganisms. d) As a consequence of its structure, IgM is also a good agglutinating Ig . Thus, IgM antibodies are very good in clumping microorganisms for eventual elimination from the body.
IgA	**IgD**
Structure Serum IgA is a **monomer** but IgA found in secretions is a **dimer**. **Half life:** 06 days **% total serum Antibody**: 10–15% **Properties** a) IgA is the 2nd most common serum Ig. b) IgA is the major class of Ig in secretions–tears, saliva, colostrums, mucus. IgA is important in local (mucosal) immunity. c) Normally, IgA does not fix complement, unless aggregated.	**Structure** IgD exists only as a **monomer.** **Half life:** 03 days **% total serum Antibody**: 0.2% **Properties** a) IgD is found in low levels in serum; **its role in serum is uncertain.** b) IgD is primarily found on B cell surfaces where it functions as a receptor for antigen. c) IgD does not bind complement.
IgE	
Structure IgE exists as a **monomer** and has an extra domain in the constant region. **Half life:** 02 days **Per cent total serum Antibody**: 0.002% **Properties** a) IgE is the least common serum Ig. b) Involved in allergic reactions. c) IgE also plays a role in parasitic helminth diseases. Since serum IgE levels rise in parasitic diseases, measuring IgE levels is helpful in diagnosing parasitic infections. d) IgE does not fix complement.	

IMMUNITY

Immunity can be natural or **artificial**, **innate** or **acquired** = **adaptive**, and either **active** or **passive**.

- Active natural (contact with infection): develops slowly, is long term, and antigen specific.
- Active artificial (immunization): develops slowly, lasts for several years, and is specific to the antigen for which the immunization (Vaccine) was given.
- Passive natural (transplacental = mother to child): develops immediately, is temporary, and affects all antigens to which the mother has immunity.

- Passive artificial (injection of gamma globulin): develops immediately, is temporary, and affects all antigens to which the donor has immunity.

Innate Immunity

The innate immunity system is what we are born with and it is non-specific; all antigens are attacked pretty much equally. It is genetically based and we pass it on to our offsprings.

Adaptive or Acquired Immunity

Lymphocytes come in two major types: B cells and T cells.

- **B cells** are produced in the **stem cells** of the bone marrow; they produce antibody and oversee humoral immunity.
- **T cells** are non-antibody-producing lymphocytes which are also produced in the bone marrow but sensitized in the **thymus** and constitute the basis of cell-mediated immunity.

There are two fundamental adaptive mechanisms: cell-mediated immunity and humoral immunity.

Cell-mediated Immunity

Macrophages engulf antigens, process them internally, then display parts of them on their surface together with some of their own proteins. This sensitizes the T cells to recognize these antigens.

T cells are primed in the thymus, where they undergo two selection processes. The first *positive* selection process weeds out only those T cells with the correct set of receptors that can recognize the MHC molecules responsible for self-recognition. Then a *negative* selection process begins whereby T cells that can recognize MHC molecules complexed with foreign peptides are allowed to pass out of the thymus.

Cytotoxic or **killer T cells** (CD8+) do their work by releasing **lymphotoxins**, which cause cell lysis.

Helper T cells (CD4+) serve as managers, directing the immune response. They secrete chemicals called **lymphokines** that stimulate cytotoxic T cells and B cells to grow and divide, attract neutrophils, and enhance the ability of macrophages to engulf and destroy microbes.

Suppressor T cells inhibit the production of cytotoxic T cells once they are unneeded, lest they cause more damage than necessary.

Memory T cells are programmed to recognize and respond to a pathogen once it has invaded and been repelled.

Humoral Immunity

An immunocompetent but as yet immature B-lymphocyte is stimulated to maturity when an antigen binds to its surface receptors and there is a T helper cell nearby (to release a cytokine). This **sensitizes** or **primes** the B cell and it undergoes **clonal selection**, which means it reproduces asexually by mitosis. Most of the family of clones become plasma cells. These cells, after an initial lag, produce highly specific antibodies at a rate of as many as 2000 molecules per second for four to five days. The other B cells become long-lived **memory cells**.

Antigen–Antibody Interaction

(a) **Complement fixation** (proteins attach to antigen surface and cause holes to form, i.e., cell lysis),
(b) **Neutralization** (binding to specific sites to prevent attachment—this is the same as taking their parking space),
(c) **Agglutination** (clumping),
(d) **Precipitation** (forcing insolubility and settling out of solution), and other more arcane methods.

Active Immunity (vaccine)	Passve Immunity (Immunoglobulins/ Anti sera)
Slowly develops but long lasting effect	Quickly develops and immediate effect or temporary
Antigen containing preparation	Antibody containing preparation
Immunological memory present	No memory
Used mainly for Prophylaxis	Used for treatment
Both cell mediated and Humoral Immunity take part	Exclusively humoral immunity involved
Effective after a lag period	Immediate effect

Vaccine types

1. Inactivated or attenuated microorganism

2. Subunit

Protein subunit–rather than introducing an inactivated or attenuated microorganism to an immune system (which would constitute a "whole-agent" vaccine), a fragment of it can create an immune response. Examples include the subunit vaccine against Hepatitis B virus that is composed of only the surface proteins of the virus (previously extracted from the blood serum of chronically infected patients, but now produced by recombination of the viral genes into yeast), the virus-like particle (VLP) vaccine against human papillomavirus (HPV) that is composed of the viral major capsid protein, and the hemagglutinin and neuraminidase subunits of the influenza virus.

3. Conjugate

Certain bacteria have polysaccharide outer coats that are poorly immunogenic. By linking these outer coats to proteins (e.g., toxins), the immune system can be led to recognize the polysaccharide as if it were a protein antigen. This approach is used in the *Haemophilus influenzae* type B vaccine.

Valence

- *Monovalent* (also called *univalent*) vaccine is designed to immunize against a single antigen or single microorganism.
- *Multivalent* (also called *polyvalent*)–It is designed to immunize against two or more strains of the same microorganism, or against two or more microorganisms.

Type	Live attenuated Vaccine	Killed vaccine
Bacterial	Tuberculosis (BCG)	Cholera Typhoid Whooping cough
Viral	Small Pox Rubella Measles Yellow fever Mumps	Poliomyelitis Influenza Rabies
Rickettsial		Typhus
Toxoids	Diphtheria Tetanus	

Types of Vaccines	Source	Storage and Route of Administration
Cholera Vaccine	Vibrio cholera (2 strains–Inaba and Ogawa)	2–8°C and By Sub cutaneous route (S.C.)
BCG Vaccine (Freeze-Dried)	Bacillus of Calmette and Guerin strain of Mycobacterium tuberculosis var. Bovis.	2–8°C and by Intra cutaneous route
Small Pox (Freeze-Dried)	Vaccinia/Variola virus	2–8°C Puncture into skin
Yellow fever vaccine	17 D strain of yellow fever virus	2–8°C and By Sub cutaneous route (S.C.)
Rabies vaccine (Freeze-Dried)	Rabies virus	2–8°C and By S.C. or I.M route
Typhus Vaccine	Rickettsia prowazeki	2–8°C and by S.C.
Polio Vaccine	Salk or inactivated/ dead polio vaccine prepared by three strains 1. Mahoney 2. MEF-1 3. Saukett. Inactivated by formalin. Sabine (live-Attenuated vaccine)	(Salk-parenteral) (Sabine-Oral)

Excipients

Beside the active vaccine itself, the following excipients are commonly present in vaccine preparations:

- ***Aluminum salts (Aluminium Sulphate)*** or gels are added as adjuvants. Adjuvants are added to promote an earlier, more potent response, and more persistent immune response to the vaccine; they allow for a lower vaccine dosage.
- ***Antibiotics*** are added to some vaccines to prevent the growth of bacteria during production and storage of the vaccine.
- ***Egg protein*** is present in influenza and yellow fever vaccines as they are prepared using chicken eggs. Other proteins may be present.
- ***Formaldehyde*** is used to inactivate bacterial products for toxoid vaccines. Formaldehyde is also used to kill unwanted viruses and bacteria that might contaminate the vaccine during production.
- ***Monosodium glutamate*** (MSG) and 2-phenoxyethanol are used as stabilizers in a few vaccines to help the vaccine remain unchanged when the vaccine is exposed to heat, light, acidity, or humidity.
- ***Thimerosal*** is a mercury-containing preservative that is added to vials of vaccine that contain more than one dose to prevent contamination and growth of potentially harmful bacteria.

Immuno Sera

- They immediately provide antibody for both prevention and treatment of established disease.
- Horses are chief source for production but cattle, goats and sheep can be used.
- Plasma is separated, diluted with water, digested with pepsin and fractionated with ammonium sulphate.

- Example–Botulinum anti-toxin, Diphtheria anti toxin, Gas gangrene (From Perfringens, Novyi, Septicum), Rabies antiserum, Tetanus anti-toxin

Toxoids

- Prepared from Exo toxins which diffuse out from the cell during normal metabolic processes. Exo toxin produced from Corynebacterium diphtheria and Clostridium tetani.
- They provide active immunity.
- They are detoxified exo-toxins. Detoxification is done using Formaldehyde or Alum. Detoxification process removes toxicity but retains antigenicity.

CLASSIFICATION AND IDENTIFICATION OF BACTERIA

Cocci

1. **Gram Positive**
   Staphylococcus, Streptococcus, Pneumococcus, Micrococcus, Sarcincoccus
2. **Gram Negative**
   Neisseria gonococcus, Neisseria meningococcus

Types of Bacilli

1. **Gram Positive**

a. Spore not formed–
   Ziehl Neelsen stain (Positive)–Mycobacterium, Nocardia
   Ziehl Neelsen stain (Negative)–Lactobacillus, Corynebacterium, Actinomyces

b. Spore formed–
   Aerobic–Bacillus anthracis, Bacillus subtilis
   Anaerobic–Clostridium tetani, Clostridium botulinum, Clostridium perfrigens

2. **Gram Negative**
   Pseudomonadaceae, Enterbacteriaceae, brucellaceae

Bacilli

Gram Negative

1. Motile–Vibrio, Salmonela, E.coli, Proteus, Citrobacter
2. Non-Motile–Shigella, klebsiella, Brucella, Pasturella, Haemophilus

Gram Positive

1. Motile–Clostridium, B.anthracoid
2. Non-Motile–Corynebacterium, Mycobacterium, Lactobacillus, Actinomyces, Clostridium perfrigens

Types of Bacteria

Gram-positive bacterium	Gram-negative bacteria
Cytoplasmic lipid membrane	Cytoplasmic membrane. There is a space between the layers of peptidoglycan and the secondary cell membrane called the periplasmic space
Thick peptidoglycan layer • Teichoic acids and lipoids are present, forming lipoteichoic acids which serve to act as chelating agents, and also for certain types of adherence.	Thin peptidoglycan layer (which is much thinner than in Gram-positive bacteria)
Capsule polysaccharides (only in some species)	Outer membrane containing lipopolysaccharide (LPS, which consists of lipid A, core polysaccharide, and O antigen) outside the peptidoglycan layer
Flagellum (only in some species) • If present, it contains two rings for support as opposed to four in Gram-negative bacteria because Gram-positive bacteria have only one membrane layer.	If present, flagella have four supporting rings instead of two.
In Gram-positive bacteria, the S-layer is attached to the peptidoglycan layer.	The S-layer is directly attached to the outer membrane.
Unique to Gram-positive bacteria is the presence of teichoic acids in the cell wall.	No teichoic acids or lipoteichoic acids are present. Lipoproteins are attached to the polysaccharide backbone.

Gram Positive	Gram Negative
Bacillus species	**Citrobacter species**
Clostridium perfringens	**Enterobacter species**
Staphylococcus aureus	**Escherichia coli**

Gram Positive	Gram Negative
S. pyrogens	**Haemophilis influenza**
S. pneumoniae	**Neisseria gonorrhoeae**
	Pseudomonas species
	Salmonella species

Disease	Causative Organism
Meningitis	Neisseria meningitidis
Lobar Pneumonia	Diplococcus pneumoniae
Boils, carbuncles	Staphylococcus species
Scarlet fever	Staphylococcus Scarlatinae
Food poisioning	Clostridium botulinum
Tetanus	Clostridium tetani
Diphtheria	Corynebacterium diphtheria
Tuberculosis	Mycobacterium tuberculosis
Plague	Pasturella pestis/Yersinia pestis
Typhoid	Salmonella typhi
Cholera	Vibrio cholera
Syphilis	Treponema palladium

Disease	Test suggested for confirmation
Tuberculosis	1. Niacin test 2. Neutral red test 3. Amidase test 4. Nitrate reduction test 5. Aryl sulphate test 6. Catalase peroxide test 7. Tuberculin 8. Mantoux Test
AIDS	1. ELISA 2. Western blot test for HIV antibody 3. Polymerase chain reaction 4. Reverse immunoblot asssay 5. Fujirebio agglutination 6. Karpas's test
Typhoid	Widal test
Leprosy	Lapromin test
Syphilis	VDRL, Kahn's test, Wasserman test

Disease	Test suggested for confirmation
Diphtheria	Shick test, Elek test
Scarlet fever	Dick test
Haemophilis	Ducrey test
Brucellosis	Coombs test
Rheumatoid Arthritis	Rose water test

Special Note

- Most ***pathogenic*** bacteria in humans are Gram-positive organisms.
- Gram-positive-and negative bacteria are chiefly differentiated by their ***cell wall structure.***
- The pathogenic capability of Gram-negative bacteria is often associated with certain components of Gram-negative cell walls, in particular, the lipopolysaccharide (also known as LPS or endotoxin) layer.

STAINING METHODS IN MICROBIOLOGY

1. Simple stains

The surface of a bacterial cell has an overall acidic characteristic because of large amount of carboxyl groups located on the cell surface due to acidic amino acids.

A positively charged dye like (methylene blue) attaches to the negatively surface and gives it a coloured appearance.

2. Negative stains

Acidic dyes like eosin and nigrosin are employed for this method. The colouring power of acidic dye e.g., eosin in sodium eosinate is having negative charge, therefore, it does not combine with the negatively charged bacterial cell surface. On the other hand, it forms a deposit around the cell, resulting into appearance of bacterial cell colourless against dark background. The method is used to view viruses, bacteria, bacterial flagella, biological membrane structures and proteins or protein aggregates, which all have a low electron-scattering power.

3.Differential stains

(A) Gram stain

This technique divides bacteria into two groups (i) Gram positive those which retain primary dye like crystal violet and appear deep violet in colour and (ii) Gram negative, which lose the primary dye on application of decolourizer and take the colour of counterstain like safranin or basic fuchsin.

Gram-positive bacteria have a thick mesh-like cell wall made of peptidoglycan (50–90% of cell wall), which stains purple while gram-negative bacteria have a thinner layer (10% of cell wall), which stains pink. Gram-negative bacteria also have an additional outer membrane which contains lipids.

There are four basic steps of the Gram stain, which include:

- Applying a primary stain (crystal violet) to a heat-fixed smear of a bacterial culture
- Followed by the addition of a trapping agent (Gram's iodine)
- Rapid decolourization with alcohol or acetone
- And *counterstaining* with safranin. Basic fuchsin is sometimes substituted for safranin counterstain.

Gram staining is used to determine gram status to classify bacteria broadly. It is based on the composition of their cell wall. Gram staining uses crystal violet to stain cell walls, iodine as a mordant, and a fuchsin or safranin counterstain to mark all bacteria.

Gram-positive bacteria stain dark blue or violet. Their cell wall is typically rich with peptidoglycan and lacks the secondary membrane and lipopolysaccharide layer found in Gram-negative bacteria.

Gram-negative organisms will appear red or pink because they are counterstained. Due to the presence of higher lipid content, after alcohol-treatment, the porosity of the cell wall increases, hence the CVI complex (Crystal violet-Iodine) can pass through. Thus, the primary stain is not retained. Also, in contrast to most Gram-positive bacteria, Gram-negative bacteria have only a few layers of peptidoglycan and a secondary cell membrane made primarily of lipopolysaccharide.

(B) Acid-fast-stains

Acid fast staining is another widely used differential staining procedure in bacteriology. This stain was developed by Paul Ehrlich in 1882. Some bacteria resist decolourization by both acid and alcohol and hence they are referred as acid-fast organisms. Acid alcohol is very intensive decolourizer. This staining technique divides bacteria into two groups:

(i) Acid-fast
(ii) Non acid-fast

This procedure is extensively used in the diagnosis of tuberculosis and leprosy.

Acid-fastness property in certain *Mycobacteria* and some species of *Nocardia* is correlated with their high lipid content. Due to high lipid content of cell wall, in some cases 60% (w/w), acid-fast cells have relatively low permeability to dye and hence it is difficult to stain them. For the staining of these bacteria, penetration of primary dye is facilitated with the use of 5% aqueous phenol which acts as a chemical intensifier. In addition, heat is also applied which acts as a physical intensifier. Once these cells are stained, it is difficult to decolourize.

4. Ziehl-Neelsen-method

The procedure for staining is as follows:

- Prepare a smear and fix it by gentle heat.
- Flood the smear with carbol fuchsin (S19) and heat the slide from below till the steam rises for 5 minutes. Do not boil and ensure that stain does not dry out. Allow the slide to cool for 5 minutes to prevent the breakage of slide in the subsequent prevent step. Wash well with water.
- Decolourize the smear till red colour no longer comes out in 20% sulphuric acid.
- Wash with water. Counterstain with 1% aqueous solution of malachite green or Loeffler's methylene blue (S18) for 15–20 seconds.
- Wash, blot dry and examine under oil-immersion objective.

5. Endospore staining

Bacterial **endospores** are metabolically inactive, highly resistant structures produced by some bacteria as a defensive strategy against unfavorable environmental conditions. The bacteria can remain in this suspended state until conditions become favourable and they can germinate and return to their **vegetative** state.

- The **primary stain** applied is **malachite green**, which stains both vegetative cells and endospores.
- **Heat** is applied to help the primary stain penetrate the endospore.
- The cells are then **decolourized** with **water**, which removes the malachite green from the vegetative cell but not the endospore.
- **Safranin** is then applied to **counterstain** any cells which have been decolourized. At the end of the staining process, vegetative cells will be pink, and endospores will be dark green**.**

FEW IMPORTANT ASSAY

Radioimmunoassay (RIA)

It is an ***in vitro*** technique used to measure concentrations of antigens (for example, hormone levels in the blood) without the need to use a bioassay.

The ***RAST test (radioallergosorbent test)*** is an example of radioimmunoassay. It is used to detect the causative allergen for an allergy.

Procedure

- A known quantity of an antigen is made radioactive, frequently by labelling it with gamma-radioactive isotopes of iodine attached to tyrosine.
- This radio labelled antigen is then mixed with a known amount of antibody for that antigen, and as a result, the two chemically bind to one another.
- Then, a sample of serum from a patient containing an unknown quantity of that same antigen is added. This causes the unlabelled (or "cold") antigen from the serum to compete with the radiolabeled antigen ("hot") for antibody binding sites. As the concentration of "cold" antigen is increased, more of it binds to the antibody, displacing the radiolabelled variant, and reducing the ratio of antibodybound radiolabelled antigen to free radiolabeled antigen.
- The bound antigens are then separated from the unbound ones, and the radioactivity of the free antigen remaining in the supernatant is measured using a gamma counter. Using known standards, a binding curve can then be generated which allows the amount of antigen in the patient's serum to be derived.

Elisa

The *enzyme-linked immunosorbent assay* (ELISA), or *enzyme immunoassay* (EIA), was the first screening test commonly employed for HIV. It has a high sensitivity.

Procedure

- A person's serum is diluted 400-fold and applied to a plate to which HIV antigens have been attached. If antibodies to HIV are present in the serum, they may bind to these HIV antigens.
- The plate is then washed to remove all other components of the serum. A specially prepared "secondary antibody" —an antibody that binds to human antibodies—is then applied to the plate, followed by another wash. This secondary antibody is chemically linked in advance to an enzyme.
- Thus the plate will contain enzyme in proportion to the amount of secondary antibody bound to the plate. A substrate for the enzyme is applied, and catalysis by the enzyme leads to a change in colour or fluorescence.

Western blot

Like the ELISA procedure, the ***western blot is an antibody detection test***. However, unlike the ELISA method, the viral proteins are separated first and immobilized. In subsequent steps, the binding of serum antibodies to specific HIV proteins is visualized.

Specifically, cells that may be HIV-infected are opened and the proteins within are placed into a slab of gel, to which an electrical current is applied. Different proteins will move with different velocities in this field, depending on their size, while their electrical charge is levelled by a surfactant called sodium lauryl sulfate. Some commercially prepared Western blot test kits contain the HIV proteins already on a cellulose acetate strip.

GENETIC RECOMBINATION IN BACTERIA

Bacteria have no sexual reproduction in the sense that eukaryotes do. They have

- No alternation of diploid and haploid generations
- No gametes
- No meiosis

But the essence of sex is genetic recombination, and bacteria do have three mechanisms to accomplish that:

- Transformation
- Conjugation
- Transduction

Transformation

Many bacteria can acquire new genes by taking up DNA molecules (e.g., a plasmid) from their surroundings. The ability to deliberately transform the bacterium **E. coli** has made possible the cloning of many genes—including human genes—and the development of the biotechnology industry.

The first demonstration of bacterial transformation was done with Streptococcus pneumoniae and led to the discovery that DNA is the substance of the genes. (Griffith)

The cells of **S. pneumoniae** (also known as the pneumococcus) are usually surrounded by a gummy capsule made of a polysaccharide. When grown on the surface of a solid culture medium, the capsule causes the colonies to have a glistening, smooth appearance. These cells are called **"S"** cells.

Conjugation

Some bacteria, **E. coli** is an example, can transfer a portion of their chromosome to a recipient with which they are in

direct contact. As the donor replicates its chromosome, the copy is injected into the recipient. At any time when the donor and recipient become separated, the transfer of genes stops. Those genes that successfully made the trip replace their equivalents in the recipient's chromosome.

Transduction

Bacteriophages are viruses that infect bacteria. In the process of assembling new virus particles, some host DNA may be incorporated in them.

The virion head can hold only so much DNA so these viruses

- While still able to infect new host cells
- May be unable to lyze them.

Instead, the hitchhiker bacterial gene (or genes) may be inserted into the DNA of the new host, replacing those already there and giving the host an altered phenotype. This phenomenon is called **transduction**.

ANTIBIOTICS—MICROBIAL ASSAYS

The activity (potency) of antibiotics may be demonstrated under suitable conditions by their inhibitory effect on microorganisms.

Two general methods are employed, the **cylinder-plate or "plate" assay** and the **turbidimetric or "tube" assay.** The first depends upon diffusion of the antibiotic from a vertical cylinder through a solidified agar layer in a Petri-dish or plate to an extent such that growth of the added microorganism is prevented entirely in a circular area or **"zone"** around the cylinder containing a solution of the antibiotic. The turbidimetric method depends upon the inhibition of growth of a microbial culture in a uniform solution of the antibiotic in a fluid medium that is favorable to its rapid growth in the absence of the antibiotic.

Units and reference standards

The potency of antibiotics is designated in either **"Units" or "µg"** of activity.

Methods of Antibiotics Assay

Cylinder-plate assay methods (CP)	Turbidimetric assay methods (T)
Amphotericin B (CP)	Amikacin (T)
Bacitracin Zinc (CP)	Candicidin (T)
Bleomycin (CP)	Capreomycin (T)
Carbenicillin (CP)	Chloramphenicol (T)
Cephalothin (CP)	Chlortetracycline (T)
Cephapirin (CP)	Cycloserine (T)
Cloxacillin (CP)	Demeclocycline (T)
Colistimethate Sodium (CP)	Dihydrostreptomycin (T)
Colistin (CP)	Doxycycline (T)
Dihydrostreptomycin (CP)	Gramicidin (T)
Erythromycin (CP)	Kanamycin (T)
Gentamicin (CP)	Methacycline (T)
Nafcillin (CP)	Neomycin (T)
Natamycin (CP)	Oxytetracycline (T)
Neomycin (CP)	Rolitetracycline (T)
Netilmicin (CP)	Streptomycin (T)
Novobiocin (CP)	Tetracycline (T)
Nystatin (CP)	Thiostrepton (T)
Paromomycin (CP)	Tobramycin (T)
Penicillin G (CP)	Troleandomycin (T)
Polymyxin B (CP), Vancomycin (CP)	Tylosin (T)
Sisomicin (CP), Ticarcillin (CP)	

Test Organisms for Antibiotics Assayed

Test Organism	Antibiotics
Staphylococcus aureus	Amikacin, Doxycycline, Demeclocycline, Cycloserine, Cloxacillin, Chlortetracycline, Cephapirin, Cephalothin, Kanamycin, Methacycline, Nafcillin, Oxytetracycline, Penicillin G, Rolitetracycline, Tetracycline Tobramycin, Rolitetracycline

Test Organism	Antibiotics
Saccharomyces cerevisiae	Amphotericin B, Nystatin
Micrococcus luteus	Bacitracin, Erythromycin
Mycobacterium smegmatis	Bleomycin
Saccharomyces cerevisiae	Candicidin
Klebsiella pneumoniae	Capreomycin, Dihydrostreptomycin, Neomycin, Streptomycin, Troleandomycin

Test Organism	Antibiotics
Pseudomonas aeruginosa	Carbenicillin
Escherichia coli	Chloramphenicol, Spectinomycin
Bordetella bronchiseptica	Colistimethate Sodium, Colistin, Polymyxin B
Bacillus subtilis	Dihydrostreptomycin, Vancomycin
Staphylococcus epidermidis	Gentamicin, Paromomycin, Netilmicin, Novobiocin, Neomycin, sisomycin
Enterococcus hirae	Gramicidin, Thiostrepton, Polymyxin B

Multiple Choice Questions

1. Talcum powder is commonly sterilized by
(a) Dry heat
(b) Moist heat
(c) Gaseous sterilization
(d) None of the above

2. Which test is performed for the diagnosis of Typhoid?
(a) Dick test (b) Widal test
(c) Tine test (d) Schik Test

3. Which of the following strain of cholera is used in Vaccine?
(a) Oka strain (b) Inaba and Ogawa
(c) Wistar RA37/3 (d) Both a and c

4. In dry heat sterilization object is heated at
(a) 160°, 3h (b) 180°, 2h
(c) 180°, 1 h (d) 160°, 2 h

5. Anaphylaxis reaction is due to which antibody?
(a) IgA (b) IgE
(c) IgM (d) IgG

6. Varicella zoster is the causative organism for
(a) Small pox
(b) Dermatophytosis
(c) Herpes
(d) Infectious monocucleosis

7. Contact dermatitis and photosensitization are which type of allergic reaction?
(a) I (b) II
(c) III (d) IV

8. Antiglobulin or Coomb's test is for
(a) Detection of non agglutinating antibodies (Brucellosis)
(b) Detection of agglutinating antibodies
(c) Detection of all type of antibodies
(d) Detection of mycoplasmal pneumonia

9. Transtuzumab belongs to which type of monoclonal antibody?
(a) Murine
(b) Chimeric
(c) Humanized
(d) Human monoclonal antibody

10. Biological indicator used for moist heat sterilization is
(a) *Bacillus subtilis*
(b) *Bacillus pumilis*
(c) *Clostridium sporogenes*
(d) *Aquaticus thermophilus*

11. India Ink method is used for
(a) Flagella staining (b) Capsule staining
(c) Gram staining (d) Spore staining

12. Anaphylaxis reaction is due to which antibody?
(a) IgA (b) IgE
(c) IgM (d) IgG

13. As per IP surgical dressings should be stored at a temperature not exceeding:-
(a) 50°C (b) 60°C
(c) 40°C (d) 25°C

14. Which test is performed for the diagnosis of scarlet fever?
(a) Widal test
(b) Frie's test
(c) Schultz Charton test
(d) Tine test

15. During autoclaving of dextrose solution, a straw colour is observed. It is due to the presence of substance called
(a) Furfural
(b) 5-hydroxymethylfurfural
(c) 5-hydroxyfurfural
(d) 5-methylfurfural

16. Dose of gamma radiation used for sterilization is
(a) 20 kGy (b) 25 kGy
(c) 30 kGy (d) 50 kGy

17. Which of the following is an example of roundworm?
(a) *Taenia saginata*
(b) *Ascaris lumbricoids*
(c) *Trichiuris trichiura*
(d) None of these

18. *Staphylococcus epidermidis* is used for the assay of
(a) Gentamycin (b) Neomycin
(c) Clarithromycin (d) Both (a) and (b)

19. Anaphylaxis reaction happens due to which antibody?
(a) IgA (b) IgE
(c) IgM (d) IgG

20. Which antibody is responsible for the host to protect from bacteria and virus and provide passive immunity to foetus?
(a) lgM (b) lgA
(c) lgG (d) lgD

21. *Staphylococcus epidermidis* is used for the assay of
(a) Gentamycin (b) Neomycin
(c) Clarithromycin (d) Both (a) and(b) both

22. α-amylase is obtained from which micro organism?
(a) *Aspergillus oryzae*
(b) *Aspargillus niger*
(c) *Bacillus subtilis*
(d) All of above

23. Fragile heat-sensitive equipments are sterilized by which method?
(a) Gama radiation
(b) Ethylene oxide
(c) Chemical sterilization
(d) None

24. All metal syringes are sterilized by which method?
(a) Moist heat (b) Gamma radiation
(c) Dry heat (d) Ethylene oxide

25. *Mycobacterium smegmat* is used for the assay of which of the following?
(a) Tetracyclin (b) Amikacin
(c) Bleomycin (d) Novobiocin

26. Sabine polio vaccine is absorbed from GIT by which mechanism?
(a) Passive diffusion (b) Pinocytosis
(c) Active transport (d) Phagocytosis

27. Which test is performed to test the susceptibility to diphtheria?
(a) Schik test (b) Mantoux test
(c) Lepromin test (d) Dick test

28. Temperature used for sterilization of vaccines is _____.
(a) 71–72°C (b) 61–62°C
(c) 55–60°C (d) 98–100°C

29. Which test is performed for the diagnosis of typhoid?
(a) Dick test (b) Widal test
(c) Tine test (d) Schik test

30. Riedel walker coefficient of grade 2 disinfectant is
(a) 5 (b) 10
(c) 15 (d) 20

31. Kanamycin B is assayed using one of the following micro organisms:
(a) *Bacillus cereus* (b) *Bacillus subtilius*
(c) *Bacillus pumilus* (d) *Micrococcus luteus*

32. Plastic containers are normally sterilized with
(a) Ethylene oxide (b) Dry heat
(c) Millipore (d) Autoclaving

33. Which of the following antibody is pentamer?
(a) Ig G (b) Ig M
(c) lg A (d) Ig D

34. Teichoic acids are the main surface antigen of which organism?
(a) Gram negative (b) Gram positive
(c) Virus (d) None

35. Which of the following is not an acid fast organism?
(a) Mycobacteria
(b) Ascospore of certain yeast
(c) Spirochetes
(d) Exoskeleton of insects

36. Fontana's method is for the staining of which of the following?
(a) Spore of bacteria (b) Spirochetes staining
(c) Flagella (d) Capsule staining

37. Lovastatin is obtained from
(a) *Aspergillus* (b) *Bacillus*
(c) *Staphylococcus* (d) *Streptococcus*

38. Syphilis is the STD caused by
(a) *Clostridium tetani*
(b) *Clostridium botulinum*
(c) *Treponema palladium*
(d) None

39. As per the WHO suggestion, microbial load for Salmonella in case of "Ready for internal use" is
(a) NIL (b) 10^3
(c) 10^4 (d) 10^7

40. Rifamycin is obtained from which micro organism
(a) *Streptomyces spectabilis*
(b) *Streptomyces fluorescens*
(c) *Streptomyces mediterranei*
(d) *Streptomyces griseus*

41. The causative organism of hepatitis B is
(a) Single-strand DNA
(b) Double-strand DNA
(c) Single-strand RNA
(d) All of above

42. A highly sensitive semi-quantitative method of detecting microbial antigens in biological fluid is
(a) Counter-immune electrophoresis
(b) Nitroblue tetrazolium dye assay
(c) Coomb's test
(d) Radio-immune electrophoresis

43. Which of the following is murine-type antibody?
(a) Adalimumab (b) Transtuzumab
(c) Rituxumab (d) Tositumomub

44. Which of following source is used for DNA polymerase in PCR?
(a) *E.coli*
(b) *Staphylococcus species*
(c) *Thermus aquaticus*
(d) *Plasmodium species*

45. Which of the following is used as live-attenuated vaccine?
(a) BCG (b) Sabin vaccine
(c) Both (a) and (b) (d) Salk vaccine

46. Methicillin-resistant *Staphylococcus aureus* (MRSA)
(a) Is usually sensitive to vancomycin
(b) Is more likely to cause deep-seated infection
(c) Is often resistant to many antistaphylococcal antibiotics
(d) May cause asymptomatic colonization

47. Aminoglycoside antibiotics, such as gentamicin
(a) Act on the bacterial cell wall
(b) Are active against staphylococci
(c) Are effective in the treatment of anaerobic myositis
(d) Are contraindicated in patients with renal impairment

48. The following are causes of gas gangrene in man except
(a) *Clostridium histolyticum*
(b) *Clostridium septicum*
(c) *Clostridium novyi*
(d) *Clostridium sporogenes*

49. Triple vaccine for the prevention of virus infections protects against
(a) Mumps virus (b) Coxsackie virus
(c) Measles virus (d) Rubella virus

50. HIV can be detected and confirmed by
(a) Polymerase chain reaction
(b) Reverse transcriptase-PCR
(c) Real-time PCR
(d) All

51. Virus mediated transfer of host DNA from one cell to another is known as?
(a) Transduction (b) Transformation
(c) Transcription (d) Integration

52. The serum concentration of which of the following human IgG subclass is maximum?
(a) IgG1 (b) IgG2
(c) IgG3 (d) IgG4

53. The following Gram negative bacteria are known to cause corneal ulcer except
(a) *Pseudomonas aeruginosa*
(b) *Moraxella lacunata*
(c) *Bacillus brevis*
(d) *Klebsiella pneumoniae*

54. Causative organism for whooping cough is _____
(a) *Clostridium titanium*
(b) *Bacillus pertussis*
(c) *Treponema palladium*
(d) *Vibrio cholera*

55. Coomb's test is for
(a) Typhoids (b) Syphilis
(c) Yellow fever (d) Antiglobulin

56. Bacteria spores:
(a) Allow the bacteria to multiple in adverse condition
(b) Are usually formed by Gram-negative bacteria
(c) Can be identified with Gram stains.
(d) Are killed by temperature of 120° for 20 minutes.

57. The following are used to detect antibodies: except
(a) Complement fixation
(b) Haemaglutination inhibition
(c) Coagulase test
(d) Indirect immunofluorescence

58. Stains useful for identifying fungus include the following, except
(a) Gram stain
(b) Haematoxylin and eosin
(c) Gomori methanamine silver
(d) PAS (Periodic acid-Schiff)

59. The following contain live-attenuated live vaccines, except
(a) Polio (b) Hepatitis A
(c) Yellow fever (d) Measles

60. Hepatitis B virus, except
(a) Is a DNA virus
(b) The presence of antigen indicates increased infectivity
(c) Antibody to surface antigen usually appears within 2 weeks of infection
(d) Is a recognized cause of liver cancer

61. The following drug acts by inhibiting cell wall synthesis of the micro-organisms:
(a) Gentamicin (b) Cefuroxime
(c) Amphotericin b (d) Erythromycin.

62. All options are true for Mantoux test, except
(a) It involves injecting PPD (purified protein derivative) intradermally
(b) Is more sensitive than the tine test
(c) It becomes positive within 3 weeks of acquiring tuberculosis
(d) It involves CD4 cells

63. The following are true about *Pseudomonas aeruginosa*, except
(a) It is a Gram-negative bacteria
(b) It can cause osteomyelitis
(c) It is sensitive to chloramphenicol
(d) It is sensitive to ciprofloxacin

64. All are true with *Staphylococcus aureus*, except
(a) Is sensitive to fusidic acid
(b) Is resistant to phagocytosis by neutrophils
(c) It produces exotoxins
(d) Is the most common cause of carbuncle

65. Causative organism for syphilis is _____
(a) *Clostridium titanium*
(b) *Bacillus pertussis*
(c) *Treponema palladium*
(d) *Vibrio cholera*

66. With regard to antibiotics which sentence is not correct:
(a) Vancomycin and penicillin inhibit bacterial cell wall synthesis through the same mechanisms.
(b) Vancomycin is poorly absorbed from the gut
(c) Metronidazole crosses the blood–brain barrier readily
(d) Sulphonamides crosses the blood–brain barrier readily

67. The following are true about disinfectants that can be used effectively for skin:
(a) Glutaraldehyde
(b) Chlorhexidine
(c) Ethyl alcohol with povidone-iodine
(d) Both (b) and (c)

68. Viral with oncogenic properties in humans include the following: Eexcept
(a) Measles virus (b) Hepatitis B virus
(c) Papovavirus (d) Epstein–Barr virus

69. Antibiotics that inhibit cell wall synthesis include: Except
(a) Cefuroxime (b) Erythromycin
(c) Vancomycin (d) Benzylpenicillin

70. Aminoglycosides
(a) Act on the bacterial cell wall
(b) Are useful against anaerobes
(c) Should not be used in patients with renal failure
(d) Damage the cochlear nerve

71. With regard to interferons all are true, except
(a) They are produced by B lymphocytes
(b) IFN alpha is produced by cells infected with virus
(c) IFN alpha increases MCH class I and II expression in antigen presenting cell
(d) They have anti-tumour activity

72. False option in case of *Clostridium tetani* is that it
(a) Causes gas gangrene
(b) Produces an exotoxin
(c) Has a terminal spore
(d) Is an obligatory anaerobe

73. *Staphylococcus aureus* is sensitive to:
(a) Vancomycin (b) Cefuroxime
(c) Clindamycin (d) All of above

74. Widal test is for _____
(a) VDRL (b) Kahn's test
(c) AIDS (d) Typhoids

75. Diphtheria is caused by _____
(a) Bacteria (b) Viral
(c) Both A and B (d) None of above

76. Polio is caused by _____
(a) Bacteria (b) Virus
(c) Both a and b (d) None of above

77. BCG is _____ type of vaccine.
(a) Live (b) Subunit
(c) Killed (d) All

78. Sabin is _____ type of vaccine.
(a) Live (b) Subunit
(c) Killed (d) All

79. Toxoids are used for _____
(a) Tuberculosis (b) Typhoid
(c) Enteric fever (d) Diphtheria

80. *Bacillus subtilis* is used in assay of _____ antibiotics.
(a) Kanamycin B (b) Rifampicin
(c) Streptomycin (d) All

81. *Bacillus cereus* is used in assay of _____ antibiotics.
(a) Kanamycin B (b) Rifampicin
(c) Streptomycin (d) Tetracycline

82. *Staphylococeus aureus* is used in assay of _____ antibiotics.
(a) Kanamycin sulphate
(b) Doxycycline
(c) Cephalexin
(d) All

83. *E coli* is used in assay of _____
(a) Carbencillin (b) Chloramphenicol
(c) Gentamycin (d) Nystatin

84. Autotrophs isare bacteria that _____
(a) Derive energy from sunlight
(b) Derive energy by chemical reaction
(c) Synthesis all their organic components
(d) Do not synthesize their organic components

85. Presence of tuberculosis in human is detected by _____ test.
(a) Amidase test
(b) Niacin test
(c) Catalase peroxidase test
(d) All

86. Presence of leprosy in human is detected by _____ test.
(a) Lapromin test
(b) Niacin test
(c) Catalase peroxidase test
(d) All

87. Small pox vaccine contain
(a) Inactivated or killed virus
(b) Living virus of vaccine
(c) Sterile preparation of killed or fixed virus of rabies in only dried form
(d) Sterile suspension of killed typhoid bacilli

88. Polio virus is storage at
(a) 2–8ºC (b) 5°C
(c) Below 0°C (d) –10°C

89. Chocolate agar is made from
(a) Mineral salt solution, glycerol, whole egg
(b) Nutrient broth and agar (2–3%)
(c) Nutrient agar and 5–10% sheep blood horse blood
(d) Peptone water + agar bile salt 0.5% lactose + 1% neutral red

90. *Bacillus subtillis* suspension is storage at less than 4°C for
(a) 1 week (b) 2 weeks
(c) 3 months (d) 6 months

ANSWER KEYS

1. (a)	**2.** (b)	**3.** (b)	**4.** (d)	**5.** (b)	**6.** (c)	**7.** (d)	**8.** (b)	**9.** (c)	**10.** (c)
11. (b)	**12.** (b)	**13.** (d)	**14.** (c)	**15.** (b)	**16.** (b)	**17.** (b)	**18.** (d)	**19.** (b)	**20.** (c)
21. (d)	**22.** (d)	**23.** (b)	**24.** (c)	**25.** (c)	**26.** (b)	**27.** (a)	**28.** (c)	**29.** (b)	**30.** (b)
31. (b)	**32.** (a)	**33.** (b)	**34.** (b)	**35.** (c)	**36.** (b)	**37.** (a)	**38.** (c)	**39.** (a)	**40.** (d)
41. (a)	**42.** (a)	**43.** (d)	**44.** (c)	**45.** (c)	**46.** (b)	**47.** (b)	**48.** (d)	**49.** (b)	**50.** (b)
51. (a)	**52.** (a)	**53.** (c)	**54.** (b)	**55.** (d)	**56.** (d)	**57.** (c)	**58.** (a)	**59.** (b)	**60.** (c)
61. (b)	**62.** (c)	**63.** (c)	**64.** (b)	**65.** (c)	**66.** (a)	**67.** (d)	**68.** (a)	**69.** (b)	**70.** (d)
71. (a)	**72.** (a)	**73.** (d)	**74.** (d)	**75.** (a)	**76.** (b)	**77.** (a)	**78.** (a)	**79.** (d)	**80.** (d)
81. (d)	**82.** (d)	**83.** (b)	**84.** (c)	**85.** (d)	**86.** (a)	**87.** (b)	**88.** (d)	**89.** (c)	**90.** (d)

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Unit 2

PHARMACOLOGY

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CHAPTER 1

BASIC PHARMACOLOGY

PHARMACOLOGY AND ROUTES OF ADMINISTRATION

Drug

Drug is any substance or product that is used or intended to be used to modify or explore physiological system or pathological states for the beneficial of the recipient.

Orphan Drugs

These are drugs or biological products that are used for diagnosis/treatment/prevention of a rare disease.

Routes of administration Drugs usually enter the body at sites remote from the target tissue or organ and thus require transport by the circulation to the intended site of action. Common routes of administration and some of their features include the following:

Factors governing choice of routes

- Physical properties of drug: pH, solubility, irritancy.
- Site of desired action: local or systemic.
- Effect of digestive juices and first pass metabolism on the drug.
- Condition of patient: conscious or unconscious.

Local routes Action on particular local area and systemic absorption of drug is minimal.

1. Topical: The topical route includes application to the skin or to the mucous membrane of the eye, nose, throat, airway, or vagina for local effect.
2. Deeper tissue: Injection in the deep capsulated areas of body and systemic absorption is slow. Example Intra–articular injection (hydrocortisone), intrathecal injection (amphotericin B for meningitis), retrobulbar injection (hydrocortisone acetate).
3. Arterial supply: Intra arterial injection of contrast media in the angiography.

Systemic routes Drug is absorbed into the blood circulation and distributed all over including site of action.

Routes	Features
Oral	• The oral route offers maximum convenience, and slower absorption compared to parentral. • But associated with some limitation: gastric irritancy, nausea, vomiting. • Some drugs are affected or degraded by Gastric juice. Example, Penicillin G and In liver E.g. Nitroglycerine, Lignocaine, Testosterone
Buccal and sublingual	• Between the pouch of gums and cheek and permits ***direct absorption*** into the systemic venous circulation, ***bypassing the hepatic portal circuit and firstpass*** metabolism. E.g., Nitroglycerine, Clonidine
Rectal (suppository)	• The rectal route offers partial avoidance from the firstpass effect. Larger amounts of drug and drugs with unpleasant taste are better administered rectally. But this method is inconvenient and embrassing. E.g., Enema, aminophylline, paraldehyde, diazepam.
Transdermal	• The transdermal route involves application to the skin for systemic effect. Absorption usually occurs very slowly, but the first-pass effect is avoided. E.g., Patches of Nitroglycerine, Fentanyl, Nicotine etc.
Inhalation	• Volatile liquid and gases are given by inhalation for systemic action E.g., General anaesthetics, bronchodilator spray used in asthma. This route provides rapid absorption because of the large alveolar surface area available.

Routes	Features
Parenteral	Beyonds the intestine: prevent from gastric irritancy and vomiting but it requires sterilized preparation for administration. • ***Subcutaneos (s.c.):*** Irritant substance cannot be injected but absorption is slower. *Self injection is possible. **Dermojet:** In this method, needle is not used. • ***Intramuscular (i.m.):*** Drugs are injected in the skeletal muscle–deltoid, triceps, and gluteus maximus rectus femoris etc, (depot preparation injected through S.C. & i.m.). • ***Intravenous (i.v.):*** The intravenous route offers instantaneous and complete absorption (by definition, bioavailability is 100%). This route is more dangerous, because of the high blood levels that are produced if administration is too rapid. • ***Intradermal:*** Drug injected in the skin E.g., BCG vaccine

PHARMACOKINETICS

Pharmacokinetics The actions of the body on the drug, including absorption, distribution, metabolism, and excretion. Elimination of a drug may be achieved by metabolism or by excretion. Biodisposition is a term used to describe the processes of metabolism and excretion.

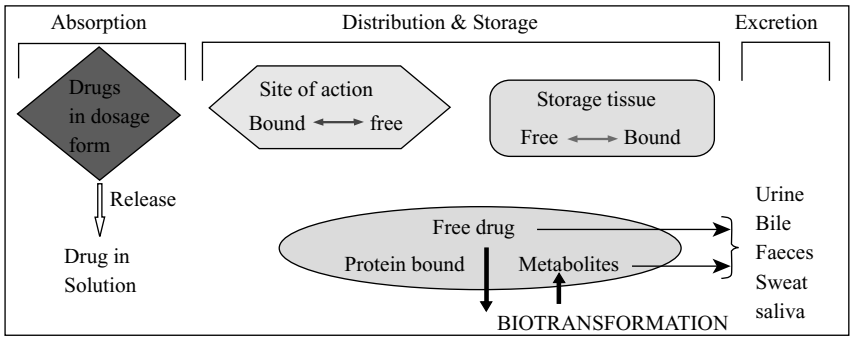


Figure 1.1 Pharmacokinetics process

All pharmacokinetic processes involve transport of drug across biological membrans. Drugs are transported across the membranes by:

A. Passive diffusion and filtration Drug diffuses the direction of its Concentration Gradient. Lipid soluble drug diffusion α (Lipid/water) partition coefficient

$$pH = pKa + Log [A]/[HA]$$

- *Weakly acidic drugs* form salts with cations of strong base, E.g., Sod. Phenobarbitone, sod. Sulfadiazine, pot. Penicillin-V etc., ionize more at basic pH.
- *Weakly basic drugs* form salt with anion with strong acids, E.g., Atropine sulphate, morphine sulphate etc., ionize more at acidic pH.

Acidic drug unionized at acidic pH in the stomach absorb (diffused) from the gastric mucosa and ionized at basic and not diffuse through the membrane. Converse effect shows with basic drugs.

Acidic drug attain higher concentration in the alkaline urine and do not back diffuse in the tubules and excreted faster. (This phenomenon used in facilitate the excretion of acidic drugs in the poisoning cases and conversely with basic drugs).

Specialized Transport

Carrier transport Drugs (polar molecule) combined with carrier (ionophores) and transport across the membrane.

Active transport Transport against the concentration gradient that needs energy.

Facilitated diffusion Facilitation of substance diffusion along the concentration gradient.

Pinocytosis Cell transport the molecules by the drinking/vesicle formation.

Absorption Movement of drug from its site of administration into the circulation.

Factors Affecting Absorption

Aqueous solubility of preparation,
Concerntration/amount,
area of absorbing surface
& tissue vascularity
} Absorption

Routes of Administration

Oral route

Non-ionize and lipid solubility → increase absorption from stomach as well as intestine.

- Acidic drugs E.g., Salicylates, barbiturates etc., are unionized at acidic pH → absorb from stomach mucous membrane but this has small surface area so affect the absorption.
- Basic drugs, morphine, atropine, quinine etc. are unionize at alkaline pH and absorb in the intestine.
- Drugs can degrade by the gastric juice, E.g., Penicillin G, Levodopa and insulin so these drugs ineffective orally.

Presence of food

- Decrease the salicylate absorption. Ca^{+2} ion of food forms complex with tetracycline decrease in absorption.
- Concurrently administered drugs form insoluble complexes, e.g., Tetracyclines with iron preparation and antacids, Phenytoin with sucralfate etc. → Decrease in absorption.

Subcutaneous and intramuscular

- Vasoconstrictor action reduces the absorption E.g., Adrenaline (vasoconstrictor) with anaesthetic agents.
- Hyluronidase increases tissue permeability → increase absorption.

Bioavailability

- Fraction of administered drug which reached to the systemic circulation/available for action. (I.V. administration provides 100% bioavailability).
- Reduce the particle size → increase absorption
  E.g., Microfine tablets of aspirin
- Microfine the spironolactone and griseofulvin
  } ↑ bioavailability

Distribution

- Drugs get in the tissues from circulation. It is affected by pH, lipid solubility, plasma and tissue protein binding.
- *Lipid insoluble* and *highly protein binding* drugs largely restricted to the vascular compartment and have very low volume of distribution. E.g., Streptomycin, Gentamycin, phenylbutazone, warfarin.
- Drugs which are sequesterted in other tissue shows volume of distribution(Vd) more than total body water E.g., Digoxin.
- Lipid soluble drugs can penetrate across the blood brain barrier, testicular barrier etc.
- Inflammation of meninges increases the permeability of brain barrier.
- Acidic drug binds with the albumin protein E.g., Barbiturates, Benzodiazapines, NSAIDs, Penicillin, Phenytoin, Sulfonamides, Warfarin, Tolbutamide etc.
- Basic drug binds with α_1–glycoprotein E.g., β–blockers, lignocaine, Disopyrmide, Imipramine, Methadone, Prazosin, Quinidine, Verapamil etc.

High degree of protein binding → prolongs action of drugs because bound fraction is not available for metabolism and excretion.

One drug can bind many sites on the plasma protein and conversely more than one drug can bind with same site. This can give rise to displacement intractions among drugs bind to the *same site.*

Examples

- Phenylbutazone and salicylate displace tolbutamide.
- Indomethacin, Phenylbutazone displaces warfarin.
- Sulfonamides and vitamin K displaces bilirubin from protein binding site → kernicterus in neonates.

Displaced drug sometimes require dose adjustment because increased plasma concentration of free drug may give toxic effect.

- Highly lipid soluble and protein bind drug may accumulate in the specific tissue.
  E.g., Retina: chloroquine, neuroleptics
- Bone and teeth: tetracyclines.

Biotransformation (Metabolism)

"Chemical alteration of the drug in the biological system". In this process, in metabolic sites like liver, kidney lungs, plasma etc. various chemical alteration of drug molecule i.e., inactivation, active metabolite form an active drug, activation of inactive drug (prodrug) and finally non-polar compound converts into polar compounds → which are excreted in urine.

Active Metabolite from Active Drug

E.g., Digitoxin → Digoxin, Spironolactone → Canrenone, Codeine → Morphine, Phenacetin → Paracetamol

Activation of Inactive Drug

E.g., Levadopa → Dopamine, Dipivefrine → Adrenaline, Cyclophosphamide → Aldophosphamide, Phosphoramide mustard, Nabumentone-6-MNA (6-methoxy-2-naphthylacetic acid

Non-synthetic reactions Oxidation, reduction, hydrolysis, cyclization and decyclization etc.

Synthetic Reactions

Glucuronide conjugation Hydroxyl or carboxylic acid group are easily conjugated with glucuronic acid. E.g., Chloramphenicol, Aspirin, Morphine, Metronidazole, Steroids, and throxine hormone.

Acetylation Compounds which have amino or hydrazine group are conjugated with acetyl coenzyme-A. E.g., Sulfonamides, Isoniazid, PAS etc.

Sulfate conjugation E.g., phenolic group compounds E.g., Steroids, Chloramphenicol, Catecholamines etc.

Glutathione conjugation Forming a mercaptopurate E.g., Paracetamol.

Hofmann elimination Inactivation of drugs in body fluid by spontaneous rearrangement without any arrangement. E.g., Atracurium

Inhibition of enzymes Drugs may competitively inhibit the enzymes used in other drug metabolism → decreases metabolism of that drug.

Example of enzyme inhibitor drugs; Ketoconazole, Cimetidine, Isoniazid, Phenylbutazone, Chloramphenicol, Disulfiram etc.

Microsomal enzyme induction Drugs may induce the microsomal enzymes and induce the metabolism of other drugs.

E.g., Phenytoin, Barbiturates, Rifampin, Glucocorticoids etc.

Excretion

Excretion means "passage out of systemic absorbed drug".

Renal excretion

1. **Glomerular filteration:** Non-protein bound drug filtered in the filterate.
2. **Tubular reabsorption:** Lipid soluble unionized drug reabsorbed from Proximal Convoluted Tubule but non lipid soluble drug (ionized) excretes in unchanged form as parallel to Glomerular Filtration Rate (GFR) E.g. Aminoglycosides.
   *weak bases ionize more and less reabsorb in acidic urine.
   *weak acidic drug ionize more and less reabsorb in alkaline urine.
3. **Tubular secretion:** Drugs utilize same active transport, and compete with each other.
   E.g., Salicylates block the uricosuric action of probenecid and sulfinpyrazone and decrease tubular secretion of methotrexate.

Probenecid decreases the concentration of Nitrofurantoin in urine, increase the duration of action of penicillin and impairs secretion of methotrexate.

Quinidine decreases renal and biliary clearance of Digoxin → doubling the concentration.

Rate of elimination = CL × C

Zero order (linear) kinetics rate of elimination remains constant and not dependent on concentration.

First order (exponential) kinetics rate of elimination α drug concentration.

***Therapeutic drug monitoring (TDM)** required for drugs which have narrow safety margin: Digitoxin, Anticonvulsants, and Theophylline. Gentamycin, Lithium, Tri-Cyclic Antidepressants etc.

***'Hit and run drugs'**–whose effect lasts much longer than the drug itself. E.g., Reserpine, Guanethidine, MAO inhibitors, Omeprazole. (These drugs do not require TDM)

* Drugs with $t_{1/2} \leq 4h$ are suitable for controlled release formulations, while there is no need of such formulations for drugs with $t_{1/2} \geq 12$ h.

PHARMACODYNAMICS

The actions of a drug on the body, including receptor interactions, dose-response phenomena, and mechanisms of therapeutic and toxic action.

- **Drug receptors:** The molecular components of the body with which a drug interacts to bring about its effects.
- **Effector:** Component of the biologic system that accomplishes the biologic effect after being activated by the receptor; often a channel or enzyme.
- **Affinity:** Ability of the drug to combine the receptor.
- **Intrinsic activity (AI or efficacy):** Ability of a drug to activate the receptor after occupation with drug or maximum effect a drug can bring about, regardless of dose.
- **Agonist** drugs bind to and activate the receptor in some fashion, which directly or indirectly brings about the effect (IA = 1).
- **Partial agonist:** A drug that binds to its receptor but produces a smaller effect at full dosage than a full agonist (IA = 0 to 1).

- **Antagonist**: Block the agonist action (have affinity but IA=0)
- **Inverse antagonist:** Gives inverse action of the agonist by binding with the same receptor (have efficacy but IA in –ve 0 to 1).
- **Physiologic antagonist:** A drug that counters the effects of another by binding to a different receptor and causing opposing effects.
- **Potency:** The dose or concentration required to bring about 50% of a drug's maximal effect.

Drug Action

- **Non-receptor action:** Physical action and chemical action
- **Through enzymes**
- **Through receptors**

Physical action Physical property responsible for its action.

E.g., Osmotic activity of Magnesium sulphate and Mannitol, adsorptive action of charcoal, kaolin, radioopacity of barium sulphate.

Chemical action E.g., Neutralization of gastric HCl by antacids, chelating agent complex formation in the metal ion poisoning.

Through Enzymes

Stimulation of enzymes: Many drugs stimulate microsomal enzymes, E.g., Phenytoin

Inhibition of Enzymes

a) Competitive inhibition (equilibrium type)

Drug competes with normal substrate or coenzyme and K_m increases and V_{max} remain unchanged.

E.g.,

- Allopurinol competes with hypoxanthine for xanthine oxidase.
- Sulfonamides compete with PABA for bacterial folate synthatase.
- Carbidopa and Methyldopa competes with levadopa for dopa decarboxylase.

Non-equilibrium type Drugs compete for same catalytic site.

E.g., Methotrexate competes with normal substrate (Dihydro folic acid) for dihydrofolate reductase enzyme.

b) Non-competetive inhibitors react with adjacent site

E.g., Acetazolamide → inhibits to carbonic anhydrase, Digoxin → Na^+ K^+ ATPase, Propylthiouracil → peroxidase in thyroid, Disulfiram → aldehyde dehydrogenase.

Receptors

- **Therapeutic window:** Range of plasma concentration of drug which produce optimal therapeutic effects.
- **Safety margin or Therapeutic index:** Concentration range of drug for the response exerts between the therapeutic effects to adverse effect.
- **Therapeutic range:** Dose concentration range which expressed minimal therapeutic effect to maximal acceptable adverse effect.
- **Synergism: "**Action of one drug facilitates or increase by other drug". (by additive or potetiation effect).
- ***Additive effect:***

  [1+1 = 2] *Therpaeutic index* = $\frac{median\ lethal\ dose}{median\ effective\ dose}$

  or $\frac{LD_{50}}{ED_{50}}$ effect of drugs P+Q = effect of P + effect of Q
- E.g., Aspirin + Paractamol = analgesic/antipyretic effect
- ***Potentiation (Supraadditive):*** Effect of combination is greater than the individual or additive effect drugs (2 >1+1). E.g., Levodopa + carbidopa**,** Sulfamethoxazole + Trimethoprim = Cotrimoxazole
- **Antagonism:** When one drug decrease or inhibit the effect of another drug → antagonistic action.

Physical Antagonism

E.g., Charcoal adsorbs alkaloids and prevents their absorption.

Sucralfate adsorb Digitoxin and prevent its absorption.

Chemical antagonism Two drugs react chemically and form inactive product;

E.g.,– $KMnO_4$ oxidized to alkaloids → inactive complex formed

- BAL-British anti-Lewisite,Ca & Di-Sodium EDTA Complex with metal ion (As, and Pb) → formation of unabsorbable complex.

Factors Modifying Drug Action

- **Body size:** increases body size and weight upto adult stage → increases dose
- **Age:** With ↑ sing age also increased dose of drug but the children and elderly patients require less dose.
- **Sex:** Govern the selection of drug such as in females in special condition like pregnancy, lactation etc.
- **Species, races and genetics**
- **Route of administration:** Affect the action of drug; E.g., when $MgSO_4$ applied topically gives Antiseptic action, orally–gives purgative action and i.e.,–gives hypotensive action.
- **Pathological states:** disease state affects the amount of administered dose.

E.g., In the renal failure the required dose adjustment (reduction) of following drugs: Aminoglycosides, Cephalexin Vancomycin, Acyclovir, Flucytocine etc.

- **Cross tolerance:** One drug exerts tolerance of another drug; E.g., alcohol produce cross tolerance of barbiturates.
- **Tacyphylaxis:** rapid development of tolerance.
- **Adverse effect** is any undesirable or unintended consequence of drug administration.
- **Side effects:** These are unwanted but often unavoidable phrmacodynamic effects that occur at therapeutic doses.
- **Toxic effects:** These are the result of excessive pharmacological action of the due to overdose or prolonged use.
- **Idiosyncrasy:** It is generally determined abnormal reactivity to chemical.
- **Drug Allergy:** Immunological mediated reaction.

Types of drug allergy

A. Humoral

1. **Type-I (anphylactic) reactions:** Drug directly act as antigen and reagenic antibody (IgE) are produced and fix to the mast cells (immediate hypersensitivity).
2. **Type-II (Cytolytic) reactios:** Drug+specific component of a specific tissue cell act as antigen and antibodies generate IgG and IgM → cytolysis; E.g., Theombocytopenia, agranulocytosis etc.
3. **Type-III (retarded, Arthus) reactions:** mediated by circulating antibodies (IgG); take usually 1–2 weeks. E.g., Stevens–Johnson reaction

B. Cell mediated

4. **Type-IV (delayed hypersensitivity) reactions:** These are mediated through production of sensitized T–lymphocytes carrying receptors for the antibody. Reaction takes > 12 hours.

- **Teratogenicity:** Capacity of a drug to cause foetal abnormalities when administered to the pregnant women. Examples are:
- Thalidomide → Phocomelia (small limbs), multiple defects
  - Androgen → virilization, cardiac defects
  - Warfarin → nose, eye and hand defects, growth retardation
  - Carbamazepine neural tube defect
  - Aspirin → premature closure of ductus arterious
  - Stlibesterol → vaginal carcinoma
  - Phenytoin → hypoplastic phalanges, cleft lip
- **Iatrogenic (drug induced/physician induced) :** Disease arise due to drug. Examples are: Peptic ulcer by salicylates and corticosteroids and Parkinsonism by phenothiazine, hepatitis by isoniazid.

Multiple Choice Questions

1. Following statements are true:

[P] An epidermic means simple application of medicament on the skin

[Q] An epidermic means application of medicament by rubbing

[R] Iontophoresis means application of medicament to and pushing it through skin to reach the blood vessels by electric transmission

[S] Inunction means simple application of medicament on the skin

(a) P and Q (b) Q and R
(c) Q and S (d) P and R

2. Following statements are true for intradermal route:

[P] The drug is injected under skin

[Q] This route is used for testing sensitivity to drug like penicillin

[R] The drug is given within the skin layer

[S] Special process of infusing large amount of drugs like glucose

(a) P and R (b) Q and R
(c) Q and S (d) P and S

3. $MgSO_4$ exerts their various effects through following route are true:

[P] It produces purgative effect if given orally

[Q] It produces depressant effect if given parenterally

[R] It does not produce any effect if given parenterally

[S] It increases intracranial tension if given enema

(a) P and Q (b) R and S
(c) Q and S (d) P and S

4. Following statements are true for passive diffusion:

[P] It is saturable

[Q] It is nonselective
[R] It is energy dependent
[S] It is energy independent

(a) P and R (b) Q and R
(c) Q and S (d) P and S

5. Following statement are true for facilitated diffusion:

[P] It is unsaturable
[Q] It is Non selective
[R] It is energy dependent
[S] It is energy independent

(a) P and R (b) Q and R
(c) Q and S (d) P and S

6. Transport diffusion is proportional to concentration gradient in

[P] Active transport
[Q] Facilitated diffusion
[R] Passive diffusion
[S] Ion pair transport

(a) P and R (b) Q and R
(c) Q and S (d) R and S

7. Following drug have more than 99% protein-binding capacity

[P] Digoxin [Q] Aspirin
[R] Thyroxine [S] Warfarin

(a) P and Q (b) P and R
(c) Q and S (d) R and S

8. Following drug have less than 50% protein-binding capacity

[P] Insulin
[Q] Aminoglycoside antibiotic
[R] Diazepam
[S] Aspirin

(a) P and Q (b) Q and R
(c) Q and S (d) P and S

9. Spironolactone is a prodrug and its active metabolite is

(a) Desmethyl spironolactone
(b) Canrencne
(c) Acetylspironolactone
(d) None of the above

10. Most of the drug is absorbed through

(a) Active transport (b) Facilitated diffusion
(c) Passive diffusion (d) Ion pair transport

11. Morphine's affects the eye by:

(a) Producing miosis through an action on the oculomotor nerve
(b) Producing mydriasis through an action on the sympathetic system
(c) Decreasing pupillary responses to light
(d) Directly acting on the smooth muscles of the iris

12. pD_2 value means

(a) Negative log of molar concentration of an antagonist which produces half of the maximum response
(b) Negative log of molar concentration of an antagonist which produces of the maximum response
(c) Negative log of molar concentration of an agonist which produces of the maximum response
(d) Negative log of molar concentration of an agonist which produces half of the maximum response

13. Drug having high affinity but low intrinsic activity is called

(a) Partial agonist
(b) Antagonist
(c) Non-competitive antagonism
(d) Competitive antagonism

14. Phentolamine is competitive antagonism of

(a) Acetylcholine (b) Isoprenaline
(c) Noradrenaline (d) Atropine

15. pA_2 can be defined as

(a) Negative log of molar concentration of an antagonist which produces half of the maximum response
(b) Negative log of molar concentration of an agonist which produces half of the maximum response
(c) Negative log of molar concentration of an antagonist in the presence of which double dose of agonist required to produce same effect as produced in absence of antagonist
(d) Negative log of molar concentration of an antagonist in the presence of which half dose of agonist required to produce same effect as produced in absence of antagonist

16. Following are the chloride channel blocker

[P] Amiloride [Q] Cadmium
[R] Picrotoxin [S] Ketamine

(a) R and S (b) Q and R
(c) Q and S (d) P and S

17. Following statements are true

[P] Synergism means if two or more drugs are taken simultaneously they increase the potency and/or duration of other drug

[Q] Addition means in which total effect of two drugs is just equal to the sum of their individual effects

[R] Potentiation means one drug produces own effect and increases the effect of other drug

[S] Synergism means one drug does not produce any effect but increases the effect of other drug

(a) P and Q (b) Q and R
(c) Q and S (d) P and S

18. Acetylcholine and physostigmine are examples of _____ type drug interaction.

(a) Synergism (b) Addition
(c) Potentiation (d) Antagonism

19. In the bioassay the convulsion activity in mice is observed during _____ use.

(a) Insulin (b) Histamine
(c) Prolactin (d) Oxytocin

20. Following drugs have volume of distribution more than 200:

[P] Warfarin [Q] Amitryptyline
[R] Digoxin [S] Alcohol

(a) P and Q (b) Q and R
(c) Q and S (d) P and S

21. Isolated rabbit jejunum is used

(a) To check adrenergic activity and mechanism
(b) To check the activity of skeletal muscle
(c) To check the activity straight muscle
(d) None of the above

22. Bioassays are carried out to:

(a) Measure the pharmacological activity of a drug
(b) Avoid clinical trials for new drugs
(c) Detect the impurity in a given drug
(d) Screen from pharmacogenetic influences of new drugs

23. Which of the following is CYP450 enzyme inhibitor?

(a) Grape juice (b) Rifampicin
(c) Barbiturates (d) Carbamazepine

24. Which of the following receptor shows the slowest response?

(a) GPCR (b) Ion channel
(c) Enzyme linked (d) Steroid receptor

25. Most common Phase-II reaction is

(a) Sulfate conjugation:
(b) Glucuronide conjugation
(c) α amino acid conjugation
(d) Methylation

ANSWER KEYS

1. (d)	**2.** (b)	**3.** (a)	**4.** (c)	**5.** (c)	**6.** (b)	**7.** (d)	**8.** (a)	**9.** (b)	**10.** (c)
11. (c)	**12.** (d)	**13.** (a)	**14.** (c)	**15.** (c)	**16.** (a)	**17.** (a)	**18.** (c)	**19.** (a)	**20.** (b)
21. (a)	**22.** (a)	**23.** (a)	**24.** (d)	**25.** (b)					

CHAPTER 2

AUTONOMIC NERVOUS SYSTEM

The autonomic or involuntary part of the nervous system controls the functions (effector organs are: smooth muscle, cardiac muscle and glands) of the body carried out 'automatically', i.e., initiated in the brain below the level of the cerebrum. The efferent (motor) nerves of the autonomic nervous system arise from nerve cells in the brain and emerge at various levels between the midbrain and the sacral region of the spinal cord.

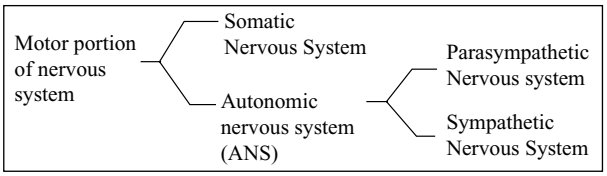


Figure 2.1 Efferent = Motor neurons, Afferent = Sensory neurons

A-Parasympathomimetics = Cholinomimetics

	Sympathetic	Parasympathetic
Origin	Thoraco-lumber T_1 to L_2 or L_3	Cranio-sacral (III, VII, IX, X; S_2–S_4)
Distribution	Wide	Wide
Ganglia	Away from the organs	Close to the organs
Neurotransmitter	Noradrenaline (major), Adrenaline (minor), ACH (Presynaptic)	Acetylcholine
Main function	In stress and emergency	Assimilation of food, conservation of energy

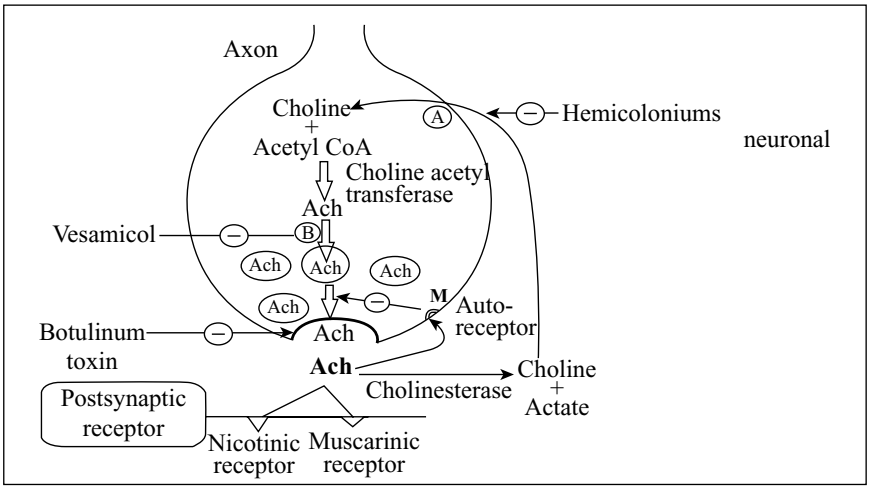


Figure 2.2 Parasympathomimetic Receptors

Characteristics of Muscarinic Receptors

	M_1	M_2	M_3
Location and function	*CNS neurons, sympathetic postganglionic Neurons:* stimulation. Some presynaptic sites	Myocardium, smooth muscle, SA and AV node: decrease heart rate and slow down the conduction. Some presynaptic sites: decreases Ach release.	Exocrine glands: increase secretions. Vessel (smooth muscle and endothelium): release NO → vasodilation. *Visceral smooth muscle:* contraction
Nature	G–protein coupled, 7TM	G-protein coupled, 7TM	G-protein coupled, 7TM
Transducer mechanism	IP_3/DAG pathway → increase intracellular level of Ca^{2+}	K^+ channel opening and decreases cAMP	IP_3/DAG pathway→ increase intracellular level of Ca^{2+}
Agonist	Oxotremorine	Methacholine	Bethanchol
Antagonist	Pirenzepine, Telenzepine	Methoctramine	Darifenacin

Characteristics of Nicotinic Receptors

	N_N	N_M
Location and function	*Autonomic ganglia:* depolarization–Postganglionic neurons, *some presynaptic cholinergic terminals:* site specific excitation and inhibtion	*Skeletal muscle neuromuscular end plates:* contraction of muscle.
Nature	Pentameric (α2, β £ or ¥ or d)	Has intrinsic ion channel, pentamer of only αβ subunit and 4-TM
Transducer mechanism	Opening of cation (Na^+, K^+, Ca^{2+}) channels	Opening of cation (Na^+, K^+) channels
Agonist	Dimethyl phenyl piperazinium (DMPP), Nicotine	Phenyl trimethyl ammonium (PTMA), Nicotine
Antagonist	Tubocurarine, α-Bungarotoxin	Hexamethonium

Classification

1. **Cholinergic agonist direct-acting cholinomimetic agents or Cholinergic Agonist or Direct Acting Cholinoceptor Stimulants:**
   This directly binds to and activates muscarinic or nicotinic receptors → stimulates parasympathetic actions.
   Choline esters: Acetylcholine, Methacholine, carbachol, bethanchol
   Alkaloids: Muscarine, Pilocarpine, Arecoline
2. **Indirect-Acting Agents or Anti Cholinesterase:**
   Inhibits acetylcholinesterase → slow down the hydrolysis of acetylcholine into choline and acetic acid → increase the endogenous acetylcholine concentration → stimulates parasympathetic actions.
   [Anticholinesterase: Reversible inhibitors bind with both *aromatic anionic* and *estaric site* and irreversible inhibitors (organophosphate) bind only with estaric site of cholinesterase → Inhibits acetylcholinesterase].
   Revesible:
   Carbamates: Neostigmine, Physostigmine, Pyridostigmine, Donepezil, Galantamine
   Acridine: Tacrine
   Irreversible:
   Orgnophosphates: Ecothiophate, Parathion, Diazinon
   Carbamates: Carbaryl, Propoxur.

Agonist Action on Cholinergic Receptors

Organ System and Receptors		Pharmacological Action
EYE	Sphincter papillae (M_3) Ciliary muscle	Contraction → Miosis Contraction → accommodation for near vision
HEART	SA Node and AV (M_2)	Negative inotropy and decreases Heart rate
BLOOD VESSELS (M_3)		Vasodilation due to releasing of *endothelium relaxing factor*–NO (EDRF)
LUNGS	Bronchioles (M_3) Glands (M_3)	Contraction → bronchospasm increase mucous secretion
GI tract	Stomach (M_3) Intestine (M_3) Glands (M_3)	increase gastric acid secretion increase intestinal peristalsis → abdominal cramps, involuntary defecation and diarrohea. increase mucous secretion
Ureter and Urinary bladder (M_3)		Contraction (detrusor), relaxation (trigone and sphincter), voiding, urinary incontinence
GLANDS		increase secretion → sweat (thermoregulatory), salivation, and lacrimation
Autonomic ganglia (N_N)		site specific and dominance basis excitation and inhibtion
Nerumuscular end plate junction		Contraction of skeletal muscle. High dose: muscle fassiculation.

Adverse effects miosis, lacrymation, sweating, abdominal muscle cramps, diarrohea, involuntary defecation and micturition and bronchospasm, and bradycardia.

Pilocarpine

- Obtained from pilocarpus macrophyllus and used in open and close angle glaucoma treatment as miotic which increase the trabecular outflow of aqueous humour → decreases intraocular tension.
- Neostigmine is used in Myasthenia gravis disease which is autoimmune disease.
- Bethanchol is used in postoperative/postpartum non-obstructive urinary retention.
- Neostigmine+Atropine is used in cobra bite.
- Physostigmine is used in Atropine (Belladona) poisoning.
- Donepezil, Galantamine and Rivastigmine are used in the Alzhiemer's disease.
- Atropine, Pralidoxime and Diacetyl monoxine are used in the anticholiesterase poisoning.

Myasthemia Gravis

- It is an auto immune disorder in which antibodies develop and occupy N_M receptor at the muscles and result in decrease in number of Ach receptors, finally leading to weakness and fatigueability.

Treatment

Neostigmine, Corticosteroids, Immunosuppressant (Azathioprine, CyclosporineA), Thymectomy

Diagnosis test for myasthemia gravis

- Amelorative test-Edrophonium IV
- Provocative test-d-Tubocuranine IV

Alzheimer's Disease

It is a neurodegenerative disorder which primarily affects cholinergic neurons in brain leading to dementia (Amentia).

- Treatment-Cerebroselective Anti Cholinesterase agents Tacrine, Rivastigmine, Donezepil, Galantamine

Glaucoma

1. Acute congestive glaucoma (narrow angle)

Narrow irido-corneal angle → reduced aqueous humor out flow → Increase intra-ocular tension (IOT) → Optic nerve Damage → Loss of sight

Treatment

1. Miotics–Pilocarpine
2. Carbonic anhydrase inhibitors–Acetazolamide
3. Hypertonic mannitol (20%) and Glycerol(10%)
4. Topical β blockers–Timolol
5. α-2 agonist–Apraclonidine, Brimonidine

2. Chronic (wide angle Glaucoma)

1. Miotics-Pilocarpine, Physostigmine
2. β Adrenergic Blockers Timolol (β_1 and β_2), Betaxolol (β_1), Levobunolol, Metipranolol
3. α adrenergic agonist-Adrenaline, Phenylepinephrine
4. Carbonic-anhydrase-inhibitors-Acetazolamide (Orally), Dorzolamide (Topical), Brinzolamide (Topical)
5. Prostaglandins-Latanoprost (Iris pigmentation is common side effect) and Isopropyl unoprostone ($PGF_{2\alpha}$)

Drugs in Glaucoma	Mode of Action
Pilocarpine	Increase trabecular outflow
Phenylepinephrine	Decrease aqueous humor production
Apraclonidine	Decrease aqueous humor secretion
Prostaglandins	Increase uvescleral outflow
Carbonic anhydrase inhibitors	Decrease aqueous humor production

B-Anticholinergic drugs and ganglionic blockers

Anti-cholinergic drugs = Parasymatholytics = Muscarinic receptor antagonist.

Ganglionic blocker = Neuromuscular blocker = Nicotinic antagonist

Drugs

Natural alkaloids Atropine, Hyoscine

Semisynthetic derivatives Homatropine, Atropine methonitrate, Ipratropium bromide, Tiotropium bromide

Synthetic compounds

(a) *Mydriatics:* Cyclopentolate, Tropicamide
(b) *Antisecretory antispasmodics:*
Quaternary compounds: Propantheline, Oxyphenonium, Clidinium, Isopropamide, Glycopyrrolate
Tertiary amines: Dicyclomine, Oxybutynin, Pirenzepine, Telezepine
(c) Antiparkinsonian: Trihexyphenidyl (Benzhexol), Procyclidine, Biperiden, Benztropine, Cycrimine

Atropine is the racemic mixture while Scopolamine is the levo-hyoscine.

Pharmacological actions (atropine as prototype)

CNS

M_1 receptor blockade by Atropine → Stimulates respiratory, vagal, vasomotor centres → depress vestibular excitation → anti-motion sickness → block the cholinergic activity in basal ganglia (anti-parkinsonian effect.)

CVS

- M_2 receptors block in the heart → increase rate of impulse generation through SA node → increase heart rate → tachycardia.
- On i.m. injection of atropine: Vagal stimulation and blocking of autoreceptors on vagal nerve endings → bradycardia.
- Tachycardia and vasomotor center stimulation → increase BP

EYE

Topical instillation of atropine → M_3 receptor blockade → mydriasis and cycloplegia (loss of accomdation of ciliary muscle) and blurring of vision and photophobia.

Smooth muscles Atropinic action due to M_3 receptors blockade

GIT

Decrease the peristalsis of GIT → constipation

Bronchial muscles

Relaxation and bronchodilation → reduces the airway resistance

Urinary system

Relaxation of bladder and ureter and contraction of sphincter → urinary retention in the prostatic hypertrophy.

Glands

M_3 receptor blockade → decreases glandular secretion (salivation, lacrymation, sweat, tracheobronchial secretion, gastric acid). Increase body temperature due to decrease in the sweating as well as stimulation of temperature regulating center.

Quaternary compounds Common features:

- Incomplete oral absorption.
- Do not penetrate brain and eye, central and ocular side effects are not seen after parentral/oral administration.
- Prolonged action than atropine.
- Primarily have nicotinic blocking propertiy.

Dicyclomine M_3 receptor blockade → smooth muscle relaxant action → exerts *antispasmodic* action.

***Drotaverine* It is non anticholinergic smooth muscle antispasmodic → selectively inhibits the phosphodiesterase (PDE-4) in smooth muscle → increase cAMP level → smooth muscle relaxation and spsmolytic action.

Adverse effect Headache, constipation, flushing.

- Side-effects and toxicity of anticholinergics
- Dry mouth (Xerostomia), difficulty in swallowing and talking, flushed and hot skin, fever, urinary retention.
- Mydriasis, photophobia, blurring of near vision.
- Excitement, hallucination, delirium, ataxia.

Treatment Poisoning with atropine: gastric lavage with ***tannic acid***. Patient should be kept in a dark quiet room. Cold sponging or ice bags are applied for reducing body temp. Administered Physostigmine 1–3 mg S.C. or i. e.,

Uses

- Preanaesthetic medication, Peptic ulcer, Antispasmodic
- Bronchial asthma, asthmatic bronchitis, COPD: reduce the tracheobroncheal secretion and airway resistance
- *As mydriatic and cycloplegic: for testing error of refraction, both mydriasis and cycloplegia are needed (use atropine, homatropine, cyclopentolate).
- *Fundoscopy needed only mydriasis so phenylephrine (adrenergic) is preferred.
- Atropine used as vagolytic in partial heart block.
- As antiparkinsonian: (centrally acting anticholinergics)
- Motion sickness: (Hyoscine, dicyclomine)
- *Hyoscine earned has reputation as ***lie detector***.

Drugs Affecting Ganglia

Ganglionic stimulants		Ganglionic blocking agents
Selective nicotinic agonist: Nicotine (small dose), Lobeline, Dimethyl phenyl piperazinium iodide (DMPP)	*Non selective nicotinic agonist:* Acetylcholine, Carbachol, Pilocarpine, MCN 343-A	*Competitive blockers:* Hexamethonium, Pentolinium, Mecamylamine, Pempidine, Trimethaphan camforsulfonate

Effects of Ganglionic Blockers on Organ Function

Organ system	Effects
Heart and blood vessels	Tachycardia, vasodilation, decreases BP
Eye	Mydriasis, Cycloplegia
Intestine	decreases peristalsis and constipation
Bladder	Urinary retention
Male sexual function	Inhibition of erection (para-symp.) and ejaculation (symp.) → impotance
Salivary and sweat gland	inhibit salivation (dry mouth) and inhibit sweating

Adrenergic Drugs

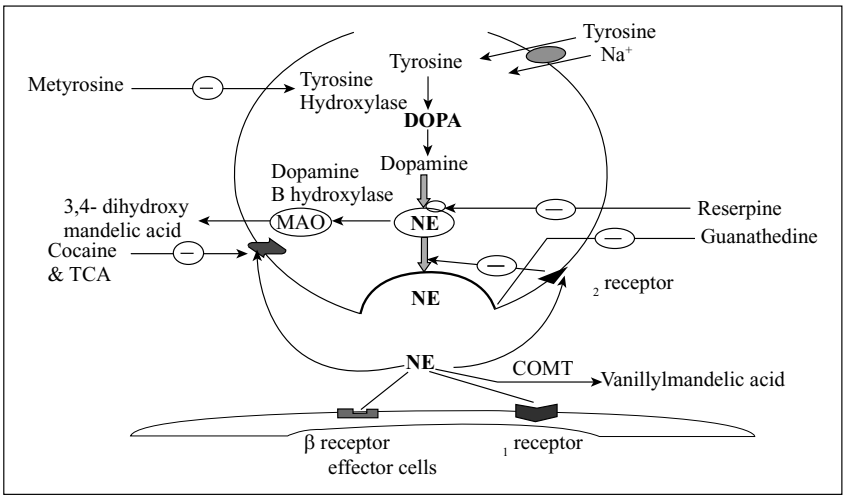


Figure 2.3 Adrenergic Neurotransmission

Nordrenaline = Norepinephrine = NA = NE;
COMT = catechol-O-methyl transferase;
MAO = mono amineoxidase

- ***Tyrosine hydroxylase*** can be inhibited by methyl–p–tyrosine and is subject to feedback inhibition by high levels of NE in the mobile pool.
- *Prejunctional* α *Receptors* Activators of prejunctional α receptors (e.g., clonidine, alpha methyldopa) cause inhibition of NA release from synaptic vesicles.
- *Axonal uptake* of NA and Adr inhabited by → Cocaine, Desipramine, and congeners, Guanethidine and H_1 antihistaminics.
- *Granular uptake* of NA or Adr inhibited by *Reserpine*.
- *NA release inhibition* and displacement of granular NA by guanethidine

Adrenergic Receptors

Receptor	Location	Agonist	Antagonist	Effector pathway
α_1	Postsynaptic effector cells	Phenylephrine, Methoxamine	Clonidine	IP_3/DAG↑, Ca^{2+}↑
α_2	Presynaptic endings, postsynaptic also in brain, pancreatic β cells Platelets, smooth muscles,	Clonidine	Yohimbine	cAMP↓, K^+↑
β_1	Heart, JG cells of kidney	Dobutamine	Atenolol, Metoprolol	cAMP ↑, Ca^{2+}↑
β_2	Bronchi, blood vessels, uterus, urinary tract, eye	Salbutamol, Terbutaline	Butoxamine	cAMP↓, K^+↑
β_3	Adipocytes	BRL 37344	ICI 118551	cAMP ↑, Ca^{2+}↑
D_1 and D_5	Brain, smooth muscle of renal cells			cAMP ↑, Ca^{2+}↑
D_2, D_3 and D_4	Brain, smooth muscle, presynaptic nerve terminals			cAMP↓, K^+↑

Aderenergic drugs (sympathomimetics)

Direct sympathomimetics Adrenaline, Noradrenaline, Isoprenaline, Dopamine, Phenylephrine, Xylometazoline, salbutamol, Terbutaline etc.

Indirect sympathomimetics increase NA release by acting on neurons E.g., Tyramine

Mixed action sympathomimetics Ephedrine, Amphetamine, Mephentermine

Agonist Action of Adrenergic Receptors

Organ System and Receptors		Pharmacological Action
EYE	Dialator papillae (Radial muscle α_1) Ciliary muscle (α_1 and α_2)	Contraction → Mydriasis without cycloplegia Reduced aqueous formation & secretory activity of ciliary muscle
HEART	SA Node and AV (β_1) Stimulation of vasomotor centre	↑ force of contraction → +ve inotropy & increase Heart rate (chronotopy) increase BP
BLOOD VESSELS (β_2) α_1 and α_2		Vasodilation due to increase cAMP Vasoconstriction due to ($\alpha 1 \rightarrow \uparrow Ca_{2+}$) ($\alpha_2 \rightarrow \downarrow$cAMP) ↑ BP
LUNGS	Bronchioles (β_2)	bronchodialation
Metabolism	Carbohydrate (β_2) Fat (β_3)	Gycogenolysis in liver and muscles increase lipolysis

Organ System and Receptors	Pharmacological Action
Bladder trigone and sphincter (α_1) **JG cells of Kidney** (β_1)	Contraction → urinary retention increase release of renin
Uterus (β_2)	Relaxation of uterine muscles → tocolytic action
Male sex organs (α_1)	Vas deferens contraction → ejaculation
Glandular secretion: **Pancreas** (α_2 & β_2) Posterior pituitary (β_2)	 decreases insulin secretion → hyperglycemic effect increase ADH secretion
Platelets	Aggregation
Prejunctional nerve terminal as autoreceptor (α_2)	decreases Transmitter release and NE synthesis
Splenic capsule (α)	Contraction → more RBCs poured in Blood
Skeletal muscle	Slow the contraction (decreases the release of Ach) by α receptor

Therapeutic classification of adrenergic drugs

- ***Pressor agents (used in hypotension):*** Noradrenaline (α_1+α_1+β_1), Dopamine, Phenylephrine, Ephedrine, Methoxamine
- ***Cardiac stimulants (used in CHF):*** Adrenaline, Dobutamine, Isoprenaline
- ***Bronchodilators (used in asthma):*** Adrenaline, Isoprenaline, Terbutaline, Salmeterol, Salbutamol, Formeterol
- ***Nasal decongestants:*** Phenylephrine, Naphazoline, Xylometazoline, Pseudoephedrine, Phenylpropanoamine
- ***CNS stimulants:*** Amphetamine, Dexamphetamine, Methamphetamine
- ***Anorectics:*** Fenfluramine, Sibutramine, Dexfenfluramine
- ***Uterine relaxant and vasodilators*** (*used in premature labour and peripheral vascular disease):* Ritodrine, Isoxsuprine, Terbutaline, Salbutamol
  - **Amphetamine:** increase alertness, increased concentration, and attention span, euphoria, talkativeness, and increased work capacity. It is the single adrenergic drug which is included in the **Dope test** for athletes. This stimulates reticular activating system and suppress hunger (anorectic) center in hypothalamus. It has weak anti motion sickness, analgesic, anticonvulsant activity.
  - **Sibutramine (**has noradrenergic and serotonergic property**)** is the anorectic drug which is recently banned in India due to alteration of lipid metabolism profile and CVS side effect.
  - Adrenergic drugs used in Parkinsonism, narcolepsy–Amphetamine.

ANTIADRENERGIC DRUGS

Antiadrenergic drugs = adrenergic antagonists: block the agonist action of adrenergic drugs.

Blockade action of α receptors

- α_1 receptor blockade → blockade of vasoconstrictor action → ↓peripheral resistance → decreases venous return and cardiac output → ↓ BP hypotension and syncope.
- α_2 receptor blockade → centrally increase the sympathetic outflow → increase one of vasomotor centre → counteract the low BP and reflex tachycardia.
- α blockade action → nasal stiffness, miosis, and increase intestinal motility (Diarrhoea may occur) and reduce the tone of bladder trigone sphincter and prostate and inhibit ejaculation (impotency).

Side effects of α blockade action

Postural hypotension, Palpitation, Loose Motion, Inhibition of ejaculation and Impotance.

- β_1 blockade action: decreases force of contraction of myocardium muscles, decreases cardiac output, heart rate and oxygen demand and renin release from kidney.
- β_2 blockade action → increase peripheral resistance → ↑BP
- β_2 receptor blockade: decreases aqueous formation in eye → reduce intra ocular tension in glucoma, bronchoconstriction, increase uterine contraction and premature labour.
- Metabolism: ↓ glycogenolysis.

Alpha adrenergic blocking agents

1. Non-equilibrium type: Phenoxybenzamine
2. Equilibrium type (competitive)

A. Non selective:
   (i) Ergotamine, Ergotoxine, Dihydroergotamine
   (ii) Imidazolines: Tolazoline, Phentolamine
   (iii) Miscellaneous: Chlorpromazine, Ketanserine
B. α_1 selective: Parazosin, Terazosin, Doxazosin, Timazosin, Alfuzosin
   α_2 selective: Yohimbine

Uses of α blockers Use in the pheochromocytoma, peripheral vascular disease, Hypertension (α_1), Benign hypertrophy of prostate (BHP) secondary shock and impotance due to failure of erection.

Phenoxybenzamine

Cyclize spontaneously in the plasma and gives active form ethyleniminium intermediate which exerts α blockade action. i.m. and s.c. injection is very painful → should not be given. It is used in Pheochromocytoma tumor of adrenal gland.

Adverse effect: postural hypotension

Prazosin

Prototype of all selective blocker. Less reflex tachycardia (because NA feedback mechanism is intact), but postural hypotension occurs (first-dose syncope). Clinical uses include mild-to-moderate hypertension and benign prostatic hyperplasia (BPH).

Phentolamine test

I.V. administration of 5 mg Phentolamine → fall in BP >35 mm Hg systolic and or > 25 mm Hg in diastolic BP indicates pheochromocytoma.

Papaverine/Phentolamine injection in the corpus cavernoum → induced penile erection and tumescence. But priapism is and penile fibrosis is the limitation for repeated use.

Sildenafil

It is Phosphodiesterase (PDE-5) inhibitor which increase cAMP level by slowing the degradation of cAMP into AMP → relaxation of corpus cavernosum smooth muscles → blood filled in cavernosum blood sinus → penile erection. Used in the erectile dysfunction and pulmonary hypertension.

It has no effect on penile tumescence in the absence of sexual activity.

Side effect *fall in BP,* flushing, headache, loose motion, impairment of colour discrimination.

Beta Blockers

Drugs	Adverse effects	Uses
Non selective (β_1 + β_2) With intrinsic activity: Propanolol, Timolol, Sotalol *Without intrinsic activity:* Pindolol *α + β blocking property:* Lebetalol, Carvedilol *β_1 selective blockers:* Atenolol, Metoprolol, Acebutolol, Esmolol, Celiprolol *β_2 selective blockers:* Butoaxamine	Myocardial insufficiency, fall in BP, precipitate asthmatic attacks, partial heart block, alteration of plasma lipid profile–increase HDL, lack of drive, nightmares, hallucination	Hypertension Anginapectoris Cardiac arrhythmia, Myocardial arrhythmia, Congestive heart failure (CHF), Migraine, Tyrotoxicosis, Anxiety, Glucoma, Hypertrophic cardiomyopathy

MULTIPLE CHOICE QUESTIONS

1. Cholinergic M_2- and M_3- receptors produce following effects:

[P] Decreased heart rate
[Q] Dilatation effect on salivary gland
[R] Increased heart rate
[S] Effect on erectile tissue

(a) P and Q (b) Q and R
(c) Q and S (d) P and S

2. Following statements are true:

[P] Substance P is located at sympathetic ganglia
[Q] Neuropeptide Y is located at postganglionic sympathetic neurons
[R] Nitric oxide located at enteric neurons
[S] Gonadotrophin-releasing hormone is not located at sympathetic ganglia

(a) P and Q (b) P and R
(c) Q and R (d) R and S

3. Following statements are true:

[P] GABA transmitter is responsible for peristaltic reflex
[Q] Neuropeptide Y facilitates constrictor action of adrenaline and inhibits adrenaline release
[R] Substance P is co-transmitter with acetylcholine
[S] Dopamine transmitter is responsible for vasoconstrictor

(a) P and Q (b) Q and R
(c) P and R (d) R and S

4. Following are the agonist of nicotinic receptor $(\alpha 3)_2$:

[P] Carbachol [Q] Trimetaphan
[R] Hexamethonium [S] Acetylcholine

(a) P and S (b) Q and R
(c) P and R (d) R and S

5. Following are the agonist of muscarinic receptor M_2:

[P] Dicycloverine [Q] Ipratropium
[R] Carbachol [S] Talsaclidine

(a) Q and S (b) Q and R
(c) P and Q (d) R and S

6. Following are the antagonist of nicotinic receptor $(\alpha 1)_2$:

[P] Cytosine [Q] Epibatidine
[R] Atracurium [S] Vecuronium

(a) Q and S (b) Q and R
(c) P and Q (d) R and S

7. Following are the antagonist of muscarinic receptor:

[P] Oxotremorine [Q] Oxybutynin
[R] Tolterodine [S] Carbachol

(a) Q and S (b) Q and R
(c) P and Q (d) R and S

8. M2 receptor is responsible for following effects:

[P] Cardiac inhibition [Q] Neural inhibition
[R] Gastric secretion [S] Vasodilatation

(a) P and Q (b) P and R
(c) Q and S (d) Q and R

9. Following drugs lower the interocular pressure

[P] Pilocarpine [Q] Lananoprost
[R] Atropine [S] Tiotropium

(a) P and Q (b) P and R
(c) Q and S (d) Q and R

10. In urinary incontinence following drug is widely used:

(a) Pirenzepine (b) Cyclopentolate
(c) Darifenacin (d) Hyoscine

11. The main side effect of tubocurarine is

[P] Bradycardia [Q] Bronchoconstriction
[R] Hypotension [S] Cardiac arrhythmia

(a) R and S (b) P and R
(c) Q and S (d) Q and R

12. Following statements are true:

[P] Hemicholinium inhibits the acetylcholine synthesis
[Q] Parathion is a short duration anticholineterase
[R] Botulinum toxin inhibits acetylcholine release
[S] Physostigmine is used in treatment of myasthenia gravis

(a) Q and R (b) P and R
(c) R and S (d) P and Q

13. In the treatment of myasthenia gravis, the best agent for distinguishing between myashenic crisis and cholinergic crisis, given intravenously, is

(a) Pyridostigmine (b) Edrophonium
(c) Physostigmine (d) Neostigmine

14. Which of the following drug may cause cycloplegia when used topically in the eye?
(a) Bethanechol (b) Physostigmine
(c) Atropine (d) Pilocarpine

15. Epinephrine is added to local anaesthetics
(a) To cause haemeostasis
(b) To prolong the action of local anaesthetics
(c) To stimulate wound healing
(d) All of the above

16. Neostigmine may cause all of the followings except
(a) Block accommodation reflex
(b) Reversible inhibition of acetyl cholinesterase
(c) Constipation
(d) Bronchoconstriction

17. Following statements are true for β_2 receptor
[P] It produces glycogenolysis effect
[Q] It produces lipolysis effect
[R] It relaxes uterus
[S] It produces constriction effect on bronchi
(a) Q and S (b) Q and R
(c) P and R (d) P and Q

18. Following statements are true for ritodrine
[P] It is β_2 agonist
[Q] It produces arrhythmia as side effect
[R] It is β_1 agonist
[S] It is used for nasal decongestion
(a) P and Q (b) Q and R
(c) P and R (d) Q and S

19. Following statement is true for labetalol
[P] It is α and β antagonist
[Q] It produces tachycardia as side effect
[R] It is non-selective β antagonist
[S] It is used in hypertension in pregnancy
(a) Q and R (b) P and Q
(c) P and S (d) R and S

20. Atropine over dosage may causes all of the following except
(a) Miosis
(b) Increased heart rate
(c) Relaxation of GIT smooth muscle
(d) Mental aberration

21. Orally effective sympathomimetics agent is
[P] Epinephrine [Q] Isoproterenol
[R] Ephedrine [S] Amphetamine
(a) P and Q (b) Q and R
(c) Q and S (d) R and S

22. Pilocarpineis classified as
(a) Cholinesterase inhibitor
(b) Sympathomimetic
(c) Cholinomimetic
(d) Cholinolytics

23. Propranolol is contraindicated in patients with
(a) Angina pectoris
(b) Supraventricular arrhythmias
(c) Glaucoma
(d) Hypertension

24. Mechanism of action of organic phosphate parathion is
(a) Phosphorylation of the cationic site of cholinesterases
(b) Phosphorylation of the esteratic site of cholinesterases
(c) Acetylation of the esteratic site of cholinesterases
(d) Acetylation of the cationic site of cholinesterases

25. Muscarinic receptor M3 are mainly located at
[P] Exocrine gland [Q] Cerebral cortex
[R] Heart [S] CNS
(a) P and S (b) Q and R
(c) P and R (d) R and S

26. Neostigmine effectively antagonizes skeletal muscle relaxation produced by
(a) Tubocurarine (b) Gallamine
(c) Pancuronium (d) All of the above

27. All of the following statements related to neostigmine are correct except
(a) Neostigmine is a quaternary ammonium compound
(b) Neostigmine is medium duration of action
(c) Neostigmine has direct effect on neuromuscular junctions
(d) All of the above

28. Muscarinic receptor M4 are mainly located at
(a) Exocrine gland (b) Cerebral cortex
(c) Heart (d) CNS

29. Antidote of atropine is
(a) Neostigmine (b) Pralidoxime
(c) Physostigmine (d) None of above

30. Atropine blocks the muscarinic actions of acetylcholine by
(a) Inhibiting synthesis of ACH
(b) Inhibiting release from storage sites
(c) Competing at receptor sites
(d) All of the above

31. Sweating is inhibited by
(a) Atropine (b) Phenothiazines
(c) Scopolamines (d) All of the above

32. Beta agonist used in bronchial asthma exert action by
(a) Blocking B1 receptor
(b) Blocking B2 receptor
(c) Stimulating B1 receptor
(d) Stimulating B2 receptor

33. Which of the following agent irreversibly bound with acetyl cholinesterase
(a) Dispropyl flurophosphate
(b) Ecothiopate
(c) Both a and b
(d) None of the above

34. Alcuronium is a semisynthetic derivative with similar properties of
(a) Gallamine (b) Pancuronium
(c) Succinylcholine (d) D-tubocurarine

35. Which of the following a is directly acting sympathomimetic agent?
(a) Ephedrine (b) Amphetamine
(c) Dopamine (d) All of the above

36. Antidote of organo phosphorous poisoning is
(a) Physostigmine (b) Pralidoxime
(c) Neostigmine (d) Tubocurarine

37. Action of D-tubocurarine is
(a) Competitive blockade of musscarinic receptors
(b) Competitive blockade of nicotinic receptors
(c) Irreversible blockade of muscarinic receptor
(d) None of above

38. Gingival hyperplasia is an oral condition possible in using
(a) Phenobarbital (b) Phenytoin
(c) Pentobarbital (d) Valproic acid

39. Which of the following agent is a cholinesterase re-activator?
(a) Pilocarpine (b) Pralidoxime
(c) Neostigmine (d) Physostigmine

40. Which of the following drug inhibits the acetylcholine synthesis?
(a) Neomycin (b) Vasamicol
(c) Botulinum toxin (d) Atropine

41. Tachyphylaxis is an unwanted effect of
(a) Methohexamine (b) Methylphenidate
(c) Ephedrine (d) Methamphetamine

42. Activation of alpha-2 receptors in the pancreatic islets causes
(a) Suppression of insulin secretion
(b) Stimulation of insulin release
(c) Suppression of glucagon secretion
(d) None of above

43. Darifenacin is a
(a) M1 antagonist (b) M2 antagonist
(c) M3 agonist (d) M3 antagonist

44. Which of the following drugs. do(es) not cross the blood–brain barrier?
(a) Physostigmine (b) Neostigmine
(c) Atropine (d) All of the above

45. Drug of choice in the treatment of cardiogenic shock is/are
(a) Isoproterenol (b) Epinephrine
(c) Dopamine (d) All of the above

46. Which of the following muscle relaxant has peripheral action?
(a) Diazepam (b) Mephenesin
(c) D-Tubocurarine (d) Orphenadrine

47. Pilocarpine is best used in
(a) Congential glaucoma
(b) Open angle glaucoma
(c) Secondary glaucoma
(d) All of the above

48. Timolol reduces the intraocular pressure by which mechanism of action?
(a) Muscarinic agonist
(b) Anticholinestarase
(c) Carbonic anhydrase inhibitor
(d) Beta-adrenoceptor antagonist

49. For glycogenolysis in liver one of the following adrenoreceptor is responsible:
(a) Alpha-1 receptor
(b) Alpha-2 receptor
(c) Beta-1 receptor
(d) Beta-2 receptor

50. Cardiac effects of epinephrine includes all except
(a) Act on B – receptor of myocardium
(b) Induced cardiac arrhythmias are blocked by propranolol
(c) Prolong refractory period of AV nodes
(d) Decrease the Amplitude of the T-waves of ECG

51. Serious unwanted effect of epinephrine is
(a) Respiratory difficulty
(b) Palpitation
(c) Cerebral heamorrhage
(d) Tremor

52. Drug of choice in motion sickness is
(a) Atropine (b) Scopolamine
(c) Carbamazepine (d) Metoclopromide

53. In belladonna poisoning convulsions can be controlled by
(a) Paraldehyde (b) Phenytoin
(c) Diazepam (d) Carbamazepine

54. Atropine are is used prior the administration of a general Aanaesthetics agent due tobecause it
(a) Inhibits salivation and secretions of respiratory tract
(b) Inhibits GIT motility
(c) Prevents miosis
(d) Causes skeletal muscle relaxation

55. Major adverse effect of clonidine is
(a) Bradycardia (b) Tachycardia
(c) Sexual dysfunction (d) Dry mouth

56. Ganglionic blocking agents may cause all of the following except
(a) Mydriasis
(b) Loss of accommodation
(c) Reduced sweating is reduce
(d) Inhibit erection and ejaculation

ANSWER KEYS

1. (a)	**2.** (a)	**3.** (c)	**4.** (c)	**5.** (d)	**6.** (d)	**7.** (a)	**8.** (a)	**9.** (a)	**10.** (c)
11. (d)	**12.** (b)	**13.** (b)	**14.** (c)	**15.** (b)	**16.** (c)	**17.** (c)	**18.** (a)	**19.** (c)	**20.** (a)
21. (d)	**22.** (c)	**23.** (c)	**24.** (b)	**25.** (a)	**26.** (d)	**27.** (d)	**28.** (d)	**29.** (c)	**30.** (d)
31. (d)	**32.** (d)	**33.** (c)	**34.** (d)	**35.** (c)	**36.** (b)	**37.** (b)	**38.** (b)	**39.** (b)	**40.** (b)
41. (c)	**42.** (a)	**43.** (d)	**44.** (b)	**45.** (c)	**46.** (c)	**47.** (b)	**48.** (d)	**49.** (a)	**50.** (c)
51. (c)	**52.** (b)	**53.** (c)	**54.** (a)	**55.** (d)	**56.** (d)				

CHAPTER 3

ENDOCRINE PHARMACOLOGY

"Hormone is a substance of intense biological activity that is produced by specific cells in the body and is transported through circulation to act on its target cells.

Site and Action of Hormone Receptors

Sites	Mechanism	Example
At cell membrane receptors	(a) Through alteration of intracellular cAMP concentratione alteration of protein kinase A → regulation of cell function by change in level of Ca^{2+} which acting as third messenger in some situations.	Adrenaline, Glucagon, TSH, FSH, LH, PTH, Calcitonin, ACTH, some hypothalamic releasing hormones: GHRH, Vasopressin (V_2)
	(b) Through IP_3/DAG generation: release of intracellular Ca^{2+} and protein kinase C activation.	Vasopressin (V_1), Oxytocin
	(c) Direct transmembrane activation of tyrosine protein kinase → phosphorylation cascade → regulation of various enzymes.	Insulin, Growth hormone, Prolactin
At cytoplasmic receptors	Penetrating cell membrane, hormone combines with a cytoplasmic receptors →Express its DNA binding → domain migrates to nucleus and binds to specific genes → DNA mediated mRNA synthesis → synthesis of functional proteins → new proteins alter cell's activity.	Steroidal hormones, Glucocorticoids, Mineralocorticoids, Androgens, Estrogens, Progestins, Calcitriol
At nuclear receptors	The hormone penetrates the nucleus → combine with its receptor → alter DNA–RNA mediated protein synthesis	Thyroid hormones: Triiodothyronin, Thyroxine

ANTERIOR PITUITARY HORMONES

Pituitary gland = Master gland = Adenohypophysis + Neurohypophysis: It occurs in the sella tersica of besi–sphenoid and attached with stalks infundibulum.

Anterior lobe (Adenohypohysis) It secretes peptide hormones i.e.,

- From *acidophils cells:* Growth hormone (GH) and Prolactin
- From *basophils cells:*
- Thyroid stimulating hormone (TSH)
- Gonadotropins: [Follicle stimulating hormone (FSH) and Lutenizing hormone (LH)]
- Adrenocorticotropic hormone (ACTH)
- Melanocyte stimulating hormone (MSH) [from pars intermedia of pituitary gland]

These hormone secretions are controlled by the hypothalamus through releasing stimulatory and inhibitory hormones.

Hormone of hypothalamus All are peptide hormones except P[R]IH. (Prolactin release inhibiting hormone)

- Thyrotropin releasing hormone (TRH)
- Corticotropin releasing hormone (CRH)

- Gonadotropin releasing hormone (GnRH)
- Prolactin release Inhibitory hormone (PRIH): Dopamine
- Prolactin releasing hormone (PRH)
- Growth hormone releasing hormone (GHRH)
- Somatostatin (Growth hormone release inhibtory hormone; GHRIH): Peptide (14 AAs)

Growth hormone (Somatotropine) Peptide in nature and consists of 191 amino acid.

- It induced the (increase cell division) growth of all body organs: acts on epiphysial plate in the bones and increase the length of bones.
- Stimulate the metabolism of carbohydrate via glucogenolysis in liver → increase blood glucose level.
- Positive nitrogen balance (increase uptake of amino acids) and induce lipolysis.
- Secretion of GH, regulated by the hypothalamus via releasing (GHRH) and releasing inhibitory (GHRIH) hormones.
- GHRIH (somatostatin) produced by hypothalamus and d cells of pancreas.
- Stimuli for secretion of GH: Hypoglycemia, stress, fasting, exercise etc.

Excess in GH Secretion

Child increase GH secretion → *Gigantism*

Adult increase GH secretion → Acromegaly (extra enlargement of face and head).

Hyposecretion of GH

Child hyposecretion of GH → inhibit the growth (shortness of height–pituitary dawarfism or joker of circus).

In the adult Simmonds Disease.

Somatostatin (Growth hormone release inhibtory hormone; GHRIH) Peptide (14 AAs)

Octerotide octapeptide and sarrogate of somatostatin and suppress the GH secretion.

Use For acromegaly and secretory diarrhoea associated with carcinoids, AIDS, cancer chemotherapy and diabetes.

Adverse effect Abdominal pain, nausea, steaorrhoea, and gall stone.

Prolactin = **milk synthesizing hormone** → induce the synthesis of milk and after parturition induces milk secretion. Prolactin receptor is analogues to GH receptor and similar action.

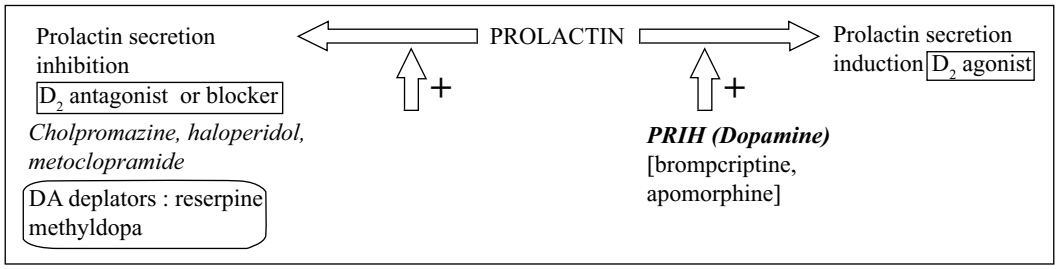


Figure 3.1 Prolactin process

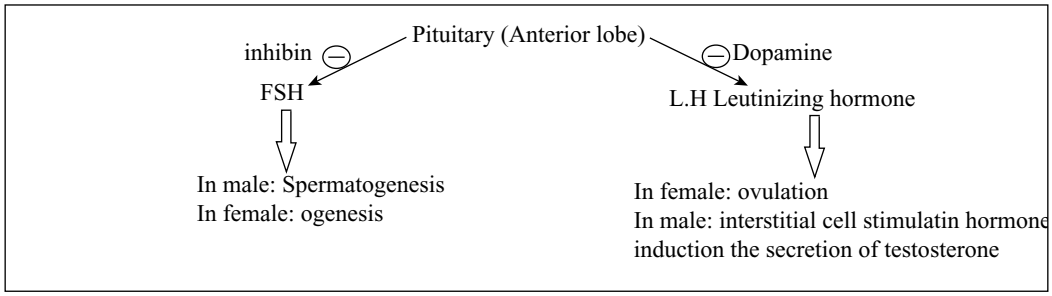


Figure 3.2 Pituitary process

Increased Prolactin level galactorrhoea and amenorrhoea → infertility syndrome. In males: Gynaecomastia, loss of libido and depressed fertility and hypercholesteromia.

Gonadotropins FSH and LH

Indadequate secretion Amenorrhoea and infertility in females; oligozoospermia, impotance and infertility in males. Excess secretion in females: polycystic ovaries.

Menotropins (FSH+LH) is a preparation obtained from urine of menopausal womens.

Urofollitropin or Menotropin (pure FSH) Used for ovula-

tion in women with polycystic ovarian disease.

Uses Amenorrhea and infertility, Hypogonadotrophic hypogonadism in males, cryptoorchism (hidden testes) and to add in-vitro fertilization.

Adverse effects Polycystic ovary, precocious puberty and malignancies of prostate and breast.

Gonadotropin releasing hormone (GnRH); Gonedorelin Synthetic GnRH and pulsatile (sustained release) administration use in above mention conditions.

Other superactive GnRH agonists Buserelin, Goserelin, Leuprolide, Nafarelin and Histerlin.

Nafarelin used as mention above and adverse effects are hot flashes, loss of libido, vaginal dryness, and osteoporosis.

ACTH Promotes steroidogenesis in adrenal cortex by increase cAMP

Cosyntropin is synthetic ACTH and use as same purpose of corticosteroids.

OXYTOCIN AND DRUG ACTING ON UTERUS

These drugs act on uterus and primarily affect endometrium and myometrium by the stimulant and relaxant action.

Uterine Stimulants (Oxytocics, Ecobolics, Abortificiants)

These drugs increase uterine motility at term.

1. Posterior pituitary hormone: Oxytocin.
2. Ergot alkaloids: Ergometrine, Methylergometrine
3. Prostaglandins: PGE2, PGF2α, 15-methyl PGF2α, Misoprostol
4. Miscellaneous: Ethacridine and Quinine.

Oxytocin = milk ejecting hormone= birth hormone

Posterior lobe secrets both oxytocin (Pitocin) and ADH which are synthesized in the nerve cell bodies in supraoptic and paraventricular nuclei and of hypothalamus; are transported down the axon and stored in the neurohypophysis.

Actions

- Increase uterine contraction (through IP_3/DAG, $\uparrow Ca^{2+}$) in the third trimester, due to increase the responsiveness of oxytocin by estrogen.
- Milk ejection. ADH like action on kidney.

Use

- Induction of labour in the postmaturity or prematurely in toxemia of pregnancy.
- Uterine inertia and breast engorgement.

Adverse effect: dilated birth cannal, maternal and foetal tissue damage and water intoxication due to ADH like action.

Ergot alkaloids: stimulate phasic contraction in the uterus at term through the partial agonist action on 5-HT_2 and α adrenergic receptors.

Uterine relaxants (Tocolytics)

These drugs decrease the uterine motility and delay the labour and arrest threatenedabortion.

- **Adrenergic agonist:** Ritodrine–through β_2 receptors → increase cAMP → uterine relaxant action. But associated with CVS adverse effects.
- **Calcium channel blockers:** Block influx of Ca^{2+} ion → uterine relaxation.
- **Magnesium sulphate:** When administered i.e., the suppress uterine contraction → delay the labour. Adverse effects are arrhythmia, muscular paralysis, and respiratory depression.
- **Oxytocin and Vasopressin Antagonist:** Atosiban.

THYROID AND PARATHYROID HORMONES

- Thyroid gland is the largest endocrine gland which is bilobed gland and homlogus with endostyle of protochordaes.
- Thyroid gland secrets: Thyroid hormone (Triiodothyroxine T_3 and Tetraiodothyroxine T_4) and Calcitonin hormone.
- Paratyroid gland: Two pair of this gland occur in the human and secretes parathyroid = Phillip–colip hormone.

Function of Parathyroid Hormones (Pth)

- Increase the osteoclast cells activity → resorption of bone Ca^{2+} → increase blood Ca^{2+} level → hypercalcemia.
- Increase the intestinal absorption of Ca^{2+} → increase blood Ca^{2+} level
- Increase Po_4^{-3} excretion.

Function of calcitonin: Opposite to Parathyroid hormone.

Hypoparthyroidism Low plasma level of Ca_{2+} and tetany, laryngospasm.

Hyperparathyroidism Hypercalcemia, decalcification of bones (osteoporosis) ostitis fibrosa cystic and renal stone.

PTH is not used therapeutically because plasma Ca^{2+} level can be elevated and kept in the normal range by vitamin D therapy.

Use of Calcitonin In the hypercalcaemic stage, postmenopoausal osteoporosis and *Paget's disease* (decreases Ca^{2+} level due to abnormal function of osteoclast).

Vitamin D

D_2 Calciferol (ergocalciferol): Obtained from plant sources–food.

D_3 Cholecalciferol: Synthesized in the skin under the influence of UV radiation.

$D_3 \rightarrow$ Calcitriol (active form of D_3 –1, 25 dihydroxy cholecalciferol) which is responsible for physiological function and which is similar to parathyroid hormone.

Alfacalcidol: It is 1 hydroxy cholecalciferol which is of vitamin D. This does not require hydroxylation at position 1 which is the limiting step in the generation of active form of vitamin D.

Dihydrotachysterol: Synthetic analogue of vitamin D_2.

Uses of vitamin D: In rickets, senile or postmenopausal osteoporosis, hypoparathyroidism, and Fanconi syndrome.

*Cholestyramine and chronic use of liquid paraffin can reduce vitamine D absorption.

Bisphosphates: E.g. Etidornate, Pamidornate and Alendornate.

Tiludronate, Risedronate, Zolendronate and Ibendronate.

Bisphosphates prevents resorption of bone by accelerating the apoptosis of osteoclasts and disrupting the cytoskeleton of osteoclast cells.

Uses: Osteoporosis, Paget's disease, osteolytic bone hypercalcaemia.

Etidornate produces adverse effects like gastric irritation, bone pain, headache, *metallic taste*, pyrexia.

Alendronate: adverse effect as esophagitis.

Thyroid hormone

Active form of thyroid hormone is T_3 and T_3 is 3 to 5 times more active than T_4 ($T_3 > T_4$) so in the liver and kidney T_4 converts into T_3.

Physiological action

Growth and development: Metamorphosis of tadpole of frog. Growth and development of nervous tissue, reproductive organs etc.

Metabolism

Glucogenolysis and gluconeogenesis →increase blood glucose level. ↑ lipolysis.

Increase BMR, induction of haemopooesis and increase peristalsis of GIT.

- **Hypothyroidism:** Deficiency of thyroid hormones revealed the following effects:
  - **In the Children:** *Cretinism* (mentally retarded, dwarf).
  - **In the adult:** Myxoedema: myxomatous tissues get deposited on the face and lead to weight gain, decrease BMR, heart rate, body temperature.and in the females, additionally cause amenorrhoea.
  - **Endemic goiter:** Increase the size of thyroid gland.
  - **Hashimotodisease:** It is autoimmune disease and in this disease antibodies formed against thyroid gland which destroy thyroid follicles (succide of thyroide glands).
  - **Hyperthyroidism:** Excess of thyroid hormone level.
  - **Graves disease:** This is autoimmune disease and in this disease, antibodies are (IgG) formed which stimulate the thyroid follicle for secretion of hormones. Due to excess stimulation there is increase in the size of thyroid gland. In this disease, myxomatous tissue deposited into eye orbot → *exopthalamic goiter.*

Increased BMR, heart rate, sweating in the female menorrhagia.

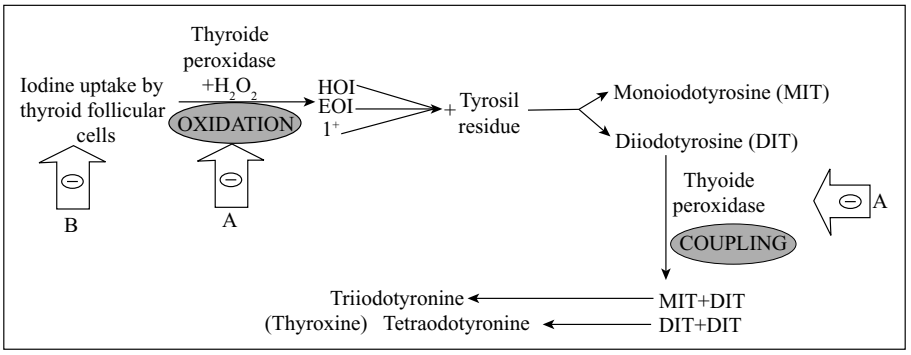


Figure 3.3 Thyoid Hormone Secretion.

A. Inhibit hormone synthesis: Propyluracil, Methimazole, Carbimazole

B. Inhibit iodide trapping (ionic inhibitors): Thiocynates (–SCN), Perchlorate (CLO_4–), Nitrates (NO_3–)

C. Inhibit hormone release: Iodine, Iodide of Na and K, organic iodides

D. Destroyed thyroid tissue: Radioactive iodine (^{131}I, ^{125}I, ^{123}I).
Groups A + B compounds = goitrogens

Other drugs produce hypothyroidism as an adverse effect.

Lithium: Inhibits the release of thyroid hormone.

Amiodarone and β–blockers: Inhibits the peripheral conversion of T_4 into T_3.

Sulfonamides and PAS Inhibt the iodination and coupling reation.

Inhibit hormone synthesis: Inhibit iodination of tyrosine residue in thyroglobulin and inhibit coupling of iodotyrosine residues to form T_3 and T_4.

Adverse effects: *Hypothyroidism,* intolerance, joint pain, rashes, loss or graying of hair and *agranulocytosis.*

Insulin, Hypoglycaemic Drugs and Glucagon

Diabetes: It is a metabolic disorder characterized by hypergycaemia, glycosuria, hyperlipemia, negative nitrogen balance and ketonemia.

Diabetes

1. Diabetes mellitus
   (a) Type I (IDDM)
   (b) Type II (NIDDM)
2. Diabetes insipedus
   (a) Neurogenic
   (b) Nephrogenic

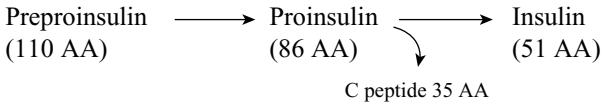
Type I Diabetes	Type II Diabetes
Insulin dependent diabetes melitus	Non-insulin dependent diabetes melitus
Onset before the age of 30 years, most often in childhood or adolescence	Generally onset after the age of 35 years
Destruction of β–cells in pancreatic: Due to idiopathic, altered immune response (autoimmune disease) and environmental trigger.	Decrease in beta cell responsiveness for the insulin or reduced beta–cell mass, dysfunction of beta cells and inefficient glucose utilisation by the peripheral tissues
Minor genetic susceptibility	Major genetic susceptibility
Symtomps: Increased thirst and appetite, excessive urination and weight loss	Postprandil hyperglycaemia, appetite, excessive urination, and weight loss
Diabetic ketoacidosis	Ketosis is nelegible

- Carbohydrate metabolism regulated by the insulin which is sereted by the pancreas iselet.
- Pancreas hormone: Pancreas have many type cells which secrete different type of hormones.

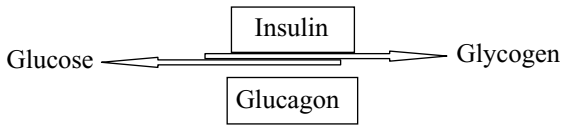
  (i) α-cells: Glucagon,
  (ii) β-cells: Insulin,
  (iii) δ-cells: Somatostatin

Insulin

Synthesized in pancreatic β cells as



Insulin has two chain polypeptide (21AA in A chain + 30 AA in B chain) which are attached by disulfide bond (7-s-s-7 and 20-s-s-20) and molecular weight is 6000.



Physiological function of insulin

- Insulin increase the uptake/absorption of glucose and glycogenesis in the liver, skeletal muscle etc.
- Insulin inhibits the gluconeogenesis and protein break down means facilitate positive Nitrogen balance.
- Insulin inhibits lipolysis and favours triglyceride synthesis.

Regulation of insulin secretion

- β–cell has glucoreceptor which is activated by the glucose → glucose enters in the cells through glucose transporter and indirectly inhibits to the ATP sensitive K^+ channel and intracellular Ca^{2+} → secretion of insulin.
- Somatostatin (GHIH) inhibits insulin as well as glucagon.
- Insulin inhibits the glucagon secretion.
- Glucagon increases/stimulates the release of insulin as well as somatostatin.
  - Adrenergic α_2 receptor activation → decreases cAMP and K^+ channel ↑ → decreases insulin secretion.
  - Adrenergic β_2 receptor activation → increase cAMP and K^+ channel ↓ → increase insulin secretion.
  - Cholinergic–Muscarinic activation → ↑ IP_3/DAG and K^+ channel ↓ → increase insulin secretion.

Mechanism of action of Insulin: Insulin acts through membrane kinase receptor which has enzymatic activity.

Insulin receptor (heteromeric receptor) consisting of 2 extra cellular α and 2 transmembrane β subunit linked together by disulfide bonds. Insulin binds with α subunit then activation of tyrosine kinase which is attached with β subunit → activated tyrosine kinase phosphorylated → metabolic reaction of insulin.

Coventional preparation of insulin (CPI)

- CPI derived from beef or pork insuin (impurity of other proteins 1% or 10,000 ppm). Pure insulin is inactive/degrade when administered orally and has short half life $t_{1/2}$ = 5–9 min. For the long-term action, modify the CPI and adding Zinc or protamine → get prolong active insulin formulations.
- All preparations of insulin are given subcutaneous route only.
- Higly purified insulin preparation (HPIP):
- Single peak insulin: purified by gel filteration and repeated crystallization, they contain 50–200 ppm proinsulin.
- Monopeak insulins: after gel filteration, it is further purified by ion exchange chromatography and proinsulin is < 20 ppm.

Human insulin

- Human insulin which is produced by recombinant DNA technology in Escherichia coli.
- Advantage of Human insulin/HPIP:
- Indicated in following cases: insulin resistance, allergy to CPI, During pregnancy.

Pharmacological action of insulin

- Hypoglycaemia
- Injection site lipodystrophy, edema;
- Allergy: due to contaminating proteins in insulin.

Interactions

- Thiazides, Furosemide, Corticosteroides, oral contraceptives, Salbutamol, Nifedipine, tend to rise blood sugar → reduce the therapeutic effect of insulin.
- Ingestion of alcohol can precipitate the hypoglycaemia.
- Salicylates, lithium enhance the secretion of insulin → accentuate the hypoglycaemic effect of insulin.

Use: Used in diabetes mellitus in the following cases:

- Not controlled by diet and exercise.
- Faliure of oral hypoglycaemic.
- Under weight patients.
- Any complications of diabetes; E.g., ketoacidosis, gangrene of extremities.

ORAL HYPOGLYCAEMICS

1. **Sulfonyl ureas:**
   First generation: Tolbutamide, Chlorpropamide
   Second generation: Glibenclimide, Glypizide, Gliclazide, Glimepiride
2. **Biguanides:** Phenformin, Metformin
3. **Meglitinide analogues**: Repaglinide, Nateglinide
4. **Thiazolidinediones:** Rosiglitazone, Pioglitazone
5. **α Glucosidase inhibitors:** Acarbose, Miglitol

Sulfonyl Ureas

Mechanism of action These bind with sulfonyl urea receptor on β cell membrane → inhibition of ATP sensitive K^+ channel → increase the intracellular level of Ca^{2+} which triggers the release of insulin.

Interactions

- Salicylates, Phenylbutazone, clofibrate, sulfonamide, PAS etc., displace the sulfonyl ureas from its plasma protein binding sites → enhances the hypoglycaemic effect.
- Ezyme inhibitors; phenylbutazone, cimetidine, sulfonamides, warfarin, chloramphenicol etc., inhibits the metabolism of sulfonyl urea and synergises the hypoglycaemic effect.
- They should be cautiously used in patients with liver or kidney dysfunction.
- Chlorpropamide in addition causes cholestatic jaundice.

Biguanides

Mechanism of action These drugs suppress the gluconeogenesis and glycogenolysis (glucose output from

liver) and increase the peripheral utilization of glucose by enhancing anaerobic glycolysis.

Adverse effect Abdominal pain, anorexia, metallic taste, loose motion; hypoglycaemia in overdose.

Lactic acidosis is common with Phenformin and vitamin B_{12} deficiency with Metformin.

Meglitinide analogues They do not cause insulin release but presence of some insulin is essential for their action.

MOA Similar like sulfonyl ureas and they should be administerd, before each major meal to control postprandil hyperglycaemia.

They should be avoided in liver diease.

Thiazolidinediones

MOA Agonist action on peroxisome proliferator–activated receptor γ (PPARγ) → enhance the transcription of insulin responsive genes → reverse the insulin resistance and increase glucose absorption in the muscles and fat.

Adverse effect Edema, weight gain, headache, myalgia; liver dysfunction and cardiovascular side effects.

Thiaglitazone has been withdrawn globally due to serious liver toxicity.

Rosiglitazone has been banned in India in 2010 due to alteration in lipid profile and cardiovascular events.

MULTIPLE CHOICE QUESTIONS

α Glucosidase Inhibitors

Dietary starch and oligosaccharides (e.g., sucrose)

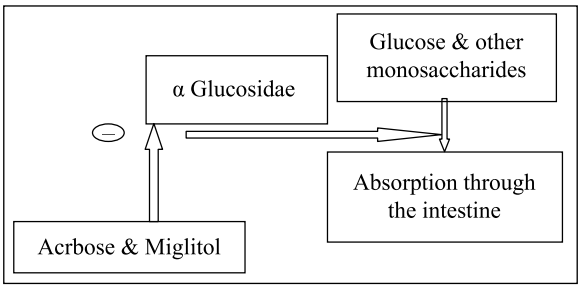


Figure 3.4 α Glucosidase Inhibitors

Acarbose and miglitol both reduce the intestinal absorption of glucose and reduce post prandil hyperglycaemia.

Adverse effects: Flatulence and abdominal bloating.

All oral hypoglycaemics used in the type II diabetes mellitus.

1. Correct statement regarding testosterone include all except
   (a) It is converted by 5α-reductase to active dihydrotestosterone
   (b) It is inactivated in liver
   (c) It causes gynecomastia and cholestatic hepatitis
   (d) It increases the excretion of water and sodium

2. Which of the following steroid is not a mineralocorticoid?
   (a) Hydrocortisone
   (b) Desoxycorticosterone
   (c) Spironlactone
   (d) Fludrocortisone

3. Which of the thyroid preparation is preferred for the maintenance of replacement therapy?
   (a) Thyrotropin
   (b) Thyroglobulin
   (c) Liothyronine sodium
   (d) Iodine

4. Which of the following insulin preparation has the longest duration of action?
   (a) Semilente (b) Isophane
   (c) Lente (d) Protamine zinc

5. All of the following drugs bind to specific receptors in the cytoplasm of sensitive cells except
   (a) Cortisol (b) Dexamethasone
   (c) ACTH (d) Triamcinolone

6. The use of oral contraceptives by premenopausal women was associated with
   (a) Vaginal adenosis
   (b) Precocious puberty
   (c) Endometrial carcinoma
   (d) Hirsutism

7. Principle source of oestrogen in postmenopausal women is
   (a) Placenta (b) Ovary
   (c) Adipose tissue (d) Adrenal gland

8. Glucocorticoids can _____
   (a) Elevate the plasma concentration of glucagons
   (b) Produce deposition of glycogen in the liver
   (c) Produce peculiar alteration in fat distribution
   (d) All of the above

9. Which of the following agent can be used diagnostically to distinguish between pseudo hypoparathyroidism and hypoparathyroidism?
(a) Calcitriol (b) Calcitonin
(c) P TH (d) NaF

10. Correct statement(s) regarding thyroid- stimulating hormone include(s)
(a) Stimulates the thyroid adenylcyclase
(b) Enhances the production of diacylglycerol
(c) Induces a rise in cytosolic calcium
(d) All of the above

11. All of the following organs concentrate iodide except
(a) Mammary gland (b) Placenta
(c) Uterus (d) Skin

12. A subunit of gonadotropins commonly contains
(a) Serine-linked carbohydrate moiety
(b) Glycogen-linked polysaccharide chain
(c) Asparagine-linked oilgosaccharide chain
(d) None of the above

13. All of the following may enhance the action of sulfonylureas except
(a) Clofibrate (b) Salicylates
(c) Ethanol (d) Prednisolone

14. Cyanosis and potential cyanide poisoning are possible with
(a) Nitroglycerin (b) Nitroprusside
(c) Nitrofurantoin (d) Nitrous oxide

15. In insulin-dependent diabetic patient to control severe ketoacidosis, which of the following antidiabetic agent is used?
(a) Tolbutamide (b) Protamine zine insulin
(c) Isophane (d) Crystalline zinc insulin

16. Bromocriptine is used to treat amenorrhoea because
(a) It stimulates the ovary
(b) It stimulates the GRH release
(c) It suppresses the prolactin release
(d) It stimulates FSH release

17. Most serious adverse effect of antithyroid drug, propylthiouracil is
(a) Drug fever (b) Agranulocytosis
(c) Alopecia (d) Nephritis

18. The mechanism of action of sulfonyl urea is that they
(a) Decrease degradation of glucose
(b) Lower the blood glucose concentration by producing insulin-like effect
(c) Stimulate the release of insulin from B cells of pancreas
(d) Increase glucose utilization in the periphery

19. Minipill containing only progesterone was introduced because
(a) It is more effective than combinel pill
(b) Progesterone alone causes more regular menstrual cycle
(c) Progesterone alone less likely causes cerebral and coronary thrombosis
(d) All of the above

20. The action of chlorpropamide is that it
(a) Increases glycogenolysis
(b) Increases peripheral utilization of glucose
(c) Increases insulin secretion
(d) All of the above

21. Hormones that increase cyclic AMP in the larger organ include all except
(a) Prolactin (b) F S H
(c) LH (d) Vasopressin

22. The use of oestrogen antagonist clomiphene can lead to
(a) Ovarian hyperstimulation
(b) Multiple pregnancy
(c) Both
(d) None

23. Undesirable effects of oral contraceptives include all except
(a) Hypertension
(b) Cerebral thrombosis
(c) Dysmenorrhoea
(d) Breast carcinoma

24. Tolbutamide is contraindicated in
(a) IDDM (b) Pregnancy
(c) Renal insufficiency (d) All of the above

25. Which of the following may be induced by long-term use of glucocorticoids?
(a) Psychosis (b) Subcapsular cataracts
(c) Osteoporosis (d) All of the above

26. Clomiphene is used to treat infertility because it
(a) Stimulates LH secretion
(b) Stimulates folicular development
(c) Stimulates ovulation
(d) None of the above

27. Dantrolene sodium (Dantrium) is used to treat

(a) Hypertension
(b) Malignant hyperthermia
(c) Malignant hypertension
(d) Cancer

28. Which of the following oral hypoglycemic agent causes lactic acidosis?
(a) Tolbutamide (b) Acetohexamide
(c) Tolazemide (d) Phenformin

29. Tolbutamide increases
(a) Insulin synthesis
(b) Sensitivity of receptors
(c) Number of insulin receptor
(d) All of the above

30. Which of the following sulfonylurea least bound to plasma protein?
(a) Tolbutamide (b) Glipizide
(c) Acetohexamide (d) Chlorpropamide

31. Oxytocin is a
(a) Pentapeptide (b) Heptapeptide
(c) Octapeptide (d) Decapeptide

32. First-generation sulfonylureas include all the following except
(a) Acetohexamide (b) Glipizide
(c) Tolazamide (d) Tolbutamide

33. Which of the following preparation has both progestinic and oestrogenic effects?
(a) Metroxyprogesterone acetate
(b) Hydroxy progesterone caproate
(c) Norgestrel
(d) Megestrol acetate

34. Antithyroid drugs except _____ clinical utility.
(a) Propylthiouracil (b) Pottasium thiocyanate
(c) Methimazole (d) Carbimazole

35. Mechanism of action of oestrogen is through
(a) Intracytoplasmic receptors
(b) Nuclear receptor
(c) Mitochondrial receptor
(d) Cellmembrane receptor

36. Insulin causes decrease in the circulating concentration of all amino acids except
(a) Phenylalanine (b) Histidine
(c) Alanine (d) Arginine

37. The syndrome of acute salicylate overdose in children is characterized by
(a) Peripheral edema
(b) Marked hypothermia secondary to an antipyretic effect
(c) Fever
(d) Disturbance in acid–base and electrolyte balance

38. Which is the treatment of choice for myxoedemacoma (emergency treatment)?
(a) Thyroxine (b) Glucocorticoids
(c) Methimazole (d) Liothyroxine

39. Which of the pair(s) is/are correct?
(a) Bronchodilator–omalizumab
(b) Mast cell stablizers–ketotifen
(c) Leukotriene antagonist–montelukast
(d) Both b and c

40. Which hormone is released at all postganglionic sympathetic fiber?
(a) Adrenaline (b) Noradrenaline
(c) Dopamine (d) Acetylcholine

41. Following statements are true except
(a) Prolactin is a milk-synthesizing hormone
(b) Oxytocin is a milk-ejecting hormone
(c) ACTH inhibits steroidgenesis in adrenal cortex
(d) Growth hormone secretion decreases –and gigantism occurs

42. Drug that lacks the sulfonylurea moiety but stimulates insulin secretion by blocking the sulfonylurea receptor on KATP channels in pancreatic β cells is
(a) Repaglinide (b) Rosiglitazone
(c) Glipizide (d) Metformine

43. There are only rare reports of hepatotixicity with currently marketed thiazolidinedione, _____.
(a) Ciglitazone (b) Pioglitazone
(c) Troglitazone (d) None of above

44. Which drug may decrease iodide uptake by thyroid?
(a) Repaglinide (b) Rosiglitazone
(c) Glipizide (d) Tolbutamide

45. Radioiodine emits which particles in treatment of hyperthyroidism?
(a) α particle (b) β particle
(c) γ particle (d) None of above

46. The inactive derivative of progesterone is
(a) 17-α-hydroxyl progesterone
(b) Hydroxy progesterone caproate

(c) Medroxy progesterone
(d) Chlormedione acetate

47. The steroid metabolite that acts as main regulator of gonadotrophin secretion is _____.
(a) Testosterone (b) Androstenolone
(c) Androstanediol (d) Androstenediol

48. The steroid having role in promoting maturation of the lung in foetus is
(a) Androgen (b) Estrogen
(c) Progestine (d) Glucocorticoids

49. Which of the followings are naturally occurring female hormones?
(a) Estradiol (b) Estriol
(c) Mestranol (d) Estrone

50. Receptors for steroid hormones can be found in the
(a) Plasma membrane
(b) Cytosol
(c) Mitochondria
(d) Ribosomes

51. The binding of insulin to the insulin receptor triggers
(a) The interaction of the receptor with protein G
(b) The activation of adenylcyclase
(c) The activation of phospholipase C
(d) Tyrosine kinase activity

52. Gout is characterized by elevated uric acid concentrations in blood and urine due to a variety of metabolic abnormalities that lead to the overproduction of purine nucleotides. Allopurinol is used in the treatment of gout because this drug, and its metabolic product, alloxanthine, act as inhibitors of
(a) Xanthine oxidase
(b) PRPP synthatase
(c) Adenyl succinate synthase
(d) Hypoxanthine guanine phosphorybosil transferase

53. The accumulation of _____ in the lens produces cataracts in diabetic patients:
(a) Glucose (b) Galactose
(c) Galactitol (d) Sorbitol

54. Which of the following increases the tissue sensitivity to insulin?
(a) Acarbose (b) Gliclazide
(c) Rosiglitazone (d) Metformine

55. Which of the following drug increases the sensitivity of β-cells to glucose?
(a) Rosiglitazone (b) Tolbutamaide
(c) Acarbose (d) None of the above

56. Which of the following is IL-1 antagonist?
(a) Auranofin (b) Etanercept
(c) Anakinra (d) Prednisolone

57. Drug for therapy of acromegaly (a condition in which there is oversecretion of growth hormone in an adult) and of bleeding oesophageal varices is _____.
(a) Vasopresine (b) Cabergoline
(c) Quinagolide (d) Octreotide

58. Which drugs increase ADH effect?
(a) Lithium (b) Colchicine
(c) Vinca alkaloid (d) All of above

59. Warfarin interacts with this antiasthmatic drug and increases prothrombin time
(a) Budesonide (b) Zafirlukast
(c) Salmeterol (d) Bambuterol

60. Desmopressin
(a) Increases factor X
(b) Increases factor V
(c) Increases factor VIII activity
(d) Can be used to improve haemostasis in haemophilia

61. Which of the following is true for the plasma half-life of heparin?
(a) Clearance affected by warfarin
(b) Depends on site of injection
(c) Less for low MW heparins
(d) Depends on dose given

62. Oxytocin
(a) Is a ringed octapeptide
(b) Has ADH-like effect
(c) Effects on uterus antagonized by beta agonists
(d) None of above

63. The gonadal hormones like estrogens, androgens and progestin bind with:
(a) Receptors located in the cytoplasm
(b) Receptors located in the nucleus of the cell
(c) Receptors located in the contractile vacuoles
(d) None of the above

64. Mechanism of action of antithrombic agent is,
(a) Conversion of plasminogen to plasmin
(b) Activation of clotting factors
(c) Inhibition platelet function

(d) Agonist of vitamin K

65. Which hormone is released at all postganglionic sympathetic fiber?

(a) Adrenaline (b) Dopamine
(c) Noradrenaline (d) Isoprenaline

66. Which of the following statement is incorrect?

(a) Histamine injected means triple response
(b) Betahistine H_1 selective histamine analogue
(c) Cetrizine is metabolite of hydroxyzine
(d) Terfenadineopen is the K+ rectifier channel

67. Deficiency of which of the following causes respiratory distress syndrome?

(a) Phosphetidylserine
(b) Sphingomyelin
(c) Plasmogens
(d) Dipalmitoyllecithin

68. Which of the following act as mucolytic?

(a) Guaiphenesin (b) Noscapine
(c) Ephedrine (d) Bromhexine

69. _____ is a 5-lipoxygenase inhibitor.

(a) Zarfirlucast (b) Zileuton
(c) lmontelukast (d) None of above

70. Which of the following is LOX inhibitor?

(a) Zileuton (b) Zafirlukast
(c) Montelukast (d) c & b both

ANSWER KEYS

1. (d)	**2.** (c)	**3.** (c)	**4.** (d)	**5.** (c)	**6.** (c)	**7.** (c)	**8.** (d)	**9.** (c)	**10.** (d)
11. (c)	**12.** (c)	**13.** (d)	**14.** (b)	**15.** (d)	**16.** (c)	**17.** (b)	**18.** (c)	**19.** (c)	**20.** (c)
21. (a)	**22.** (c)	**23.** (c)	**24.** (d)	**25.** (c)	**26.** (c)	**27.** (b)	**28.** (d)	**29.** (b)	**30.** (d)
31. (c)	**32.** (b)	**33.** (c)	**34.** (b)	**35.** (b)	**36.** (c)	**37.** (a)	**38.** (d)	**39.** (d)	**40.** (a)
41. (d)	**42.** (a)	**43.** (b)	**44.** (d)	**45.** (b)	**46.** (b)	**47.** (d)	**48.** (a)	**49.** (d)	**50.** (b)
51. (d)	**52.** (a)	**53.** (d)	**54.** (c)	**55.** (b)	**56.** (c)	**57.** (d)	**58.** (d)	**59.** (b)	**60.** (c)
61. (d)	**62.** (a)	**63.** (b)	**64.** (a)	**65.** (a)	**66.** (d)	**67.** (d)	**68.** (d)	**69.** (b)	**70.** (a)

CHAPTER 4

CENTRAL NERVOUS SYSTEM

SEDATIVE HYPNOTICS

CNS Transmitters and Receptors

- **Glutamic acid:** Excitatory via increase influx of cations (direct coupling and G–protein linked); the NMDA receptor is a potential target for ketamine and PCP (Phencyclidine).
- **GABA:** Inhibitory via increase Cl^- influx or ↑ K+ efflux (direct coupling); activities ↑ by anticonvulsants, sedatives, hypnotics, and some muscle relaxants.
- Ach, Dopamine, Norepinephrine, Serotonin, Opioid peptides
  - **Sedatives:** Drugs which decreases activity, moderate excitement, and calms.
  - **Hypnotics:** Drugs which produce drowsiness and facilitate the onset and maintenance of a state of sleep resembling natural sleep and from which the recipient can be aroused easily.

Hypnotics used in high dose can produce general anaesthesia.

Sleep: Sleep cycle duration is 80 − 100 min (Non-rapid eye movement + Rapid eye movement)

Non-rapid eye movement (NREM) Stage 0 + Stage 1 + Stage 3 (deep sleep) + Stage 4 (cerebral sleep–night terror may occur).

REM sleep (paradoxical sleep)

Sedative and hypnotics drugs

1. Barbiturates
   a. Long acting: Phenobarbitone, Mephobarbitone
   b. Short acting: Butabarbitone, Pentobarbitone, Secobarbital
   c. Ultrashort acting: Thiopentone, Hexabarbitone
2. Benzodiazpines (BZDs)
   a. Hypnotic: Diazepam, Flurazepam, Nitrazepam, Temazepam, Midazolam
   b. Antianxiety: Diazepam, Chlordiazepoxie, Oxazepam, Lorazepam
   c. Anticonvulsant: Diazepam, Clonazepam, Clobazam
   d. Centrally acting skeletal muscle relaxant: Diazepam, Clonazepam
3. Newer non-BZDs hypnotics

Zolpidem, Zopiclone

Mechanism of Action

Benzodiazepines (BZDs) potentiate the $GABA_A$ by increasing the *frequency* of Cl^- ion channel opening (facilitatory action) → hyperpolarization. This action is blocked by flumazenil, a BZDs receptor antagonist.

Barbiturates increase the *duration* of Cl^- ion channel opening (mimic action). (At high doses, they also open Cl^- ion channels and inhibit Na^+ channels and inhibit Ca^+ dependent release of neurotransmitter.) Flumazenil does not block the effects of barbiturates.

Action of barbiturates and Benzodiazepines

Organ system	Barbiturates	Benzodiazapine
CNS	Dose dependent sedation Sedation → sleep → anaesthesia → coma Stage 3 and 4 and REM is decreasesd Physiological and physical dependence +ve Nightmares and withdrawl symptoms *Hangover At smaller dose drowsiness and ↓ anxiety Amnesia and impire judgement and euphoria Anti-convulsant action	High therapeutic index Stage 2 increase Dependence less marked Anti-anxiety and Amnesia Anti-convulsant action

Organ system	Barbiturates	Benzodiazapine
Respiration	Respiration centre depressed	Not affected
CVS	Fall in BP, ganglionic blockade	Not affected
Skeletal muscles	Slight reduce contraction	Centrally mediated relaxtion
Smooth muscles	Motility of bowel decreases	Do not affect majorly
Kidney	↓ BP and ↑ ADH release → ↓ urine out flow	
Liver	Microsomal enzyme induction → enhance the metabolism of other drugs	Do not alter

Adverse effects of BZDs: Dizziness, vertigo, ataxia, amnesia, impairment of psychomotor skills (should not drive). Dry mouth, blurring of vision.

Adverse effects of Barbiturates: *Hangover*

- Idiosyncrasy and skin hypersensitivity reactions
- Barbiturates are contraindicated in the Porphyria due to increase the synthesis of heam.
- Barbiturates induce the metabolism of many drugs and reduce their effect Example, Warfarin, steroids and oral contraceptives, tolbutamide, griseofulvin etc.

Zopiclone Cycopyrrolone derivative hypnotic and agonist at $GABA_A$ receptor potentiate an by binding to the site other than BZDs. This does not decrese REM and increase 3 and 4 stages.

Adverse effect Metallic taste, impaired judgement, dry mouth.

Used in the treatment of insomnia.

Zolpidem Imidazopyridine derivative and bind with BZDs receptor.

Drugs	Special Features
Muscimol	Agonist at $GABA_A$ site
Picrotoxin	Block Cl^- ion on picrotoxin sensitive site
Barbiturates	Agonist at picrotoxin site
β–carboline (DMCM)	Inverse agonist of GABA
Flumazenil	Competitive antagonist of BZD
Melatonin	Used in treatment of jet–jag, shift workers.

ANTIEPILEPTIC DRUGS

Epilepsy refers to a disorder of brain function characterized by the periodic and unpredictable occurrence of seizures. Seizures develop when the balance between excitatory and inhibitory mechanisms is disturbed at the cellular or the synaptic level. A sustained depolarization of the membrane with a burst of action potentials arise in the epilepsy which are Na^+ dependent at their onset and Ca^{+2} dependent at the end.

During seizures of almost all types, the extracellular concentration of Ca^{+2} drops significantly. Extracellular K^+ rises after a brief delay in comparison with the drop in Ca^{+2}. The extracellular Na^+ falls moderately with a smaller rise in extracellular Cl .

Neurotransmitter imbalance At the synaptic level, there is an imbalance between the excitatory transmitters like glutamate and inhibitory ones like gamma amino butyric acid (GABA) and glycine. This may explain the heterogeneity of seizures.

Solitary lesions of neurocysticercosis are an important cause of epilepsy in India.

Epileptic seizures have been classified into partial seizures, which begin *focally in a cortical site*, and generalized seizures, which involve both *hemispheres* widely from the outset.

Seizure Type	Features	Conventional Antiseizure Drugs
Partial seizures		
Simple partial	Consciousness is not lost, jerking of one hand or twitching of one half of the face, spikes pattern in ECG	Carbamazepine, phenytoin, valproate, Gabapentin, lamotrigine, tiagabine, topiramate

Seizure Type	Features	Conventional Antiseizure Drugs
Complex partial seizure (CPS)	Motionless stare with altered consciousness With automatisms	
Partial seizures evolving into secondarily generalised seizures	tonic–clonic seizure with loss of consciousness and sustained contractions (tonic) of muscles throughout, the body followed by periods of muscle contraction alternating with periods of relaxation (clonic), typically lasting 1 to 2 minutes.	
Generalized seizures		
Absence seizures	Sudden and momentary lapses of awareness with staring and rhythmic blinking, occurs in children (lasting <30 seconds)	*Valproate*
Myoclonic seizures	A brief (perhaps a second), shock-like contraction of muscles which may be restricted to part of one extremity or may be generalized.	*Valproate*, Lamotrigine, topiramate
Tonic–clonic seizures	Abrupt loss of consciousness with tonic extension of all four limbs and the trunk, followed by synchronous clonic muscle jerking (less than 90 seconds)	Carbamazepine, phenytoin, Phenobarbitone, Valproate
Atonic seizures	Sudden loss of muscle tone in the whole body, usually resulting in a fall and severe injury	*Valproate*, Clonazepam, Clobazepam

- Increase inhibitory tone by facilitation of GABA-mediated hyperpolarization; E.g., barbiturates, benzodiazepines
- Decrease axonal conduction by preventing Na' influx through fast Na channels; eg carbamazepine, phenytoin; also, at high doses, barbiturates and valproic acid
- Presynaptic Ca^{2+} influx through type-T channels in thalamic neurons-ethosuximide and valproic acid
- Excitatory effects of glutamic acid lamotrigine, topiramate (blocks AMPA receptors);felbamate (blocks NMDA receptors)

ANTIEPILEPTIC DRUGS

Drugs	Mechanism of Action	Adverse Effect
Barbiturates: Phenobarbitone, Pirimidone	Mimic action on GABA Primidone is prodrug and in the liver convert into Phenobarbitone and phenyl ethyl malonamide (PEMA).	Like sedative hypnotics
BZDs: Diazepam, Clonazepam, Clobazam	Facilitation of GABA (γ-amino butyric acid)	
Hydantoin: *Phenytoin*, Fosphenytoin	↓ axonal conduction by preventing Na^+ influx through voltage sensitive Na channels	
Iminostilbene: *Carbamazepine*, Oxcarbamazepine	Resembles with phenytoin	Neurotoxicity–vertigo, diplopia and ataxia. Teratogenic effect (neural defect)

Succinimide: Etosuccimide	↓ presynaptic Ca^{2+} influx through type–T channels in thalamic neurons	Gastrointestinal intolerance
Carboxylic acid: Valproic acid, Divalproex	a) Na channel inactivation. b) ↓ presynaptic Ca^{2+} influx through type–T channels in thalamic neurons	Anorexia, vomiting (common) Alopecia and thrombocytopenia, *Fluminant hepatitis* (*serious*). Spinal bifida and neural tube defect in foetus.
Pheyltriazine: Lamotrigine	↓ axonal conduction by preventing Na^+ influx through voltage sensitive Na channels (prolong inactivation of Na channel)	Diplopia
GABA analogue: Gabapentine	Facilitation of $GABA_A$ mediated channel opening. * first line drug in the CPS and pain due to diabetic neuropathy	Sedation, dizziness
Newer drugs:		
Tiagabine	Blocks GABA transporter	Mild sedation, nervousness
Topiramate	Blocks glutamate (AMPA) receptors; ↑ GABA effects	
Vigabetrine	Inhibits GABA transaminase → preven degradation of GABA	
Zonisamide	Prolongs inactivation of Na channel	

Phenytoin It is a hydantoin derivative and action is given by blocking the axonal Na channel that gives membrane stabilizing action.

Adverse effects Gum hypertyrophy, hirsutism, megaloblastic anaemia; osteomalacia;

Teratogenic effect as hydantoin syndrome–synaptic cleft, hare lip, microcephaly (due to toxic metabolite areneoxide).

Fall in BP and arrhythmia in only on i.e., administration.

Interactions

Phenytoin act as enzyme inducer and induces metabolism/degradation of many drugs; E.g., Steroids (failure of oral contraceptives), digitoxin, doxycycline, theophylline

Valproate displaces protein bound phenytoin → phenytoin toxicity

ANTI PARKINSON'S DRUGS

Parkinsonism

It is an extrapyramidal disorder related to dysfunction of the basal ganglia. It results in disturbance of movement and posture without significant paralysis.

Movement disorders can be divided into:

(a) Akinetic rigid syndromes (**parkinsonism**) in which there is paucity of movement (akinesia or bradykinesia) often accompanied by an increase in muscle tone (rigidity) and
(b) Hyperkinesias or dyskinesias which are associated with excessive abnormal involuntary movements.

Normally, equilibrium exists between acetylcholine and dopamine. With dopamine deficiency, there is acetylcholine hyperactivity; this may be a mechanism for parkinsonian symptoms.

Dopamine receptors

D_1 and D_5 (excitatory) Occurs in the brain cortex, limbic system, striatum and cardiovascular system and acting through ↑ cAMP and ↑ Phospholipase C

D_2, D_3 and D_4 (inhibitory) Occurs in the brain cortex, limbic system, striatum, pituitary and cardiovascular system and acting through ↓ cAMP, K^+ channel ↑ and Ca^{2+} channel ↓

Note

***D_1 receptor enhances release of inhibitory transmitter GABA through the direct pathway while D_2 receptor negatively modulates the GABAnergic relay and an excitatory glutameric transmission. So stimulation of D_1 excitatory as well as D_2 inhibtory receptors in the striatum, net effect exerts as reduced muscle rigidity and tone.

Anti parkinsonian drugs

1. **Drugs affect brain dopaminergic system:**
   a. Dopamine precursor: Levodopa
   b. Dopamine decarboxylase inhibitors: Carbidopa, Beneserazide
   c. Dopaminergic agonist: Bromcriptin, Ropinirole, Pramipixole
   d. MAO B inhibitors: Selegiline
   e. COMT inhibitors: Talcapone
   f. Dopamine facilitators: Amantadine
2. Central acting anticholinergics: Trihexphenidyl, procyclidine, Biperiden
3. Antihisaminics: Orphenadrine, Promethazine

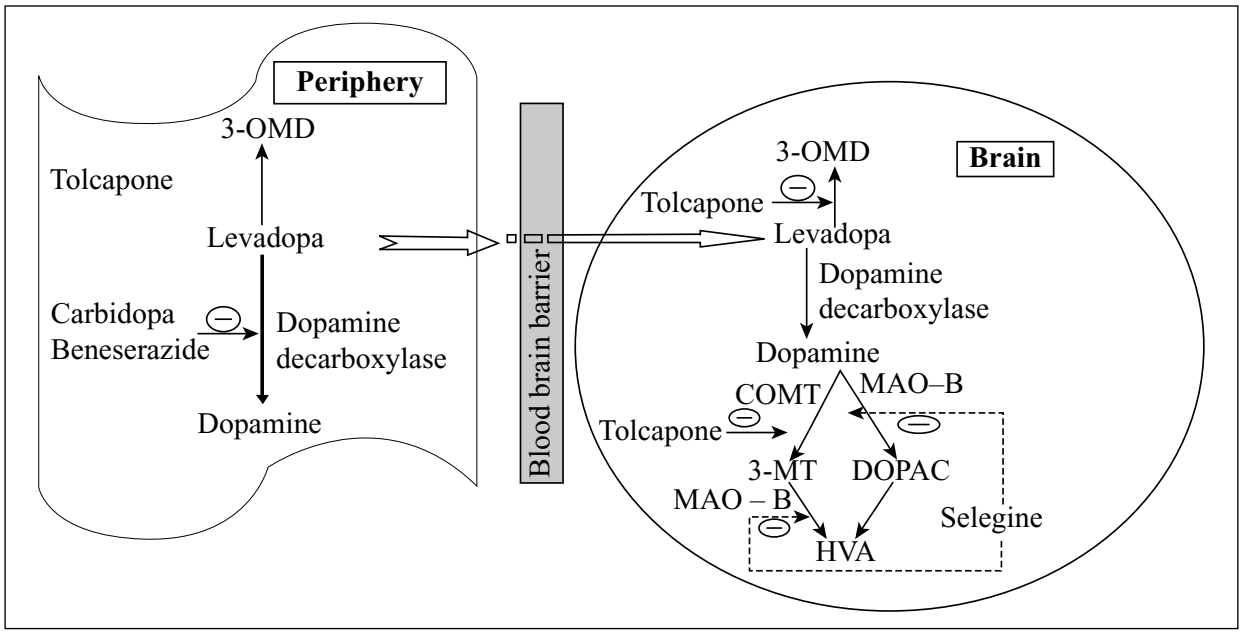


Figure 4.1 Schematic presentation of anti parkinsonian drugs

Levodopa It is the precursor and prodrug of dopamine and after the decarboxylation converts into dopamine in the peripheral tissue as well as brain Neuron. Peripheral generated dopamine responsible many side effects.

Mono amino oxidase (MAO): After the penetration, levodopa converts into dopamine which acts on D_1 and D_2 receptor → resolve bradykinesia, rigdity and tremor → smoothening the muscular movements.

Actions

1. CNS: reduce bradykinesia, rigidity, and tremor but give alerting response (excitement–fran psychosis) may occur.
   increased sexual activity and ↓ Prolactin release.
2. Dopamine stimulates to CTZ → nausea and vomiting
3. CVS: through D_1 receptors stimulation of heart → tachycardia.

Adverse effect: *Postural hypotension*, nausea and vomiting; arrhythmia etc.

Prolonged therapy effect: Facial tics, choreoathetoid movement, nighmares, mania, hallucination and "end of dose and "on–off" effect.

Interactions

- Pyridoxine increase the peripheral decarboxylation of levodopa → drastically reduce the therapeutic effect of levodopa.

***Carbidopa and Beneserazide

These drugs inhibits, dopa decarboxylase in the peripheral tissue and these do not penetrate in brain so do not inhibit conversion of levodopa in brain → only prevents the peripheral degradation of levodopa and potentiation of anti parkinson action.

They increase the $t_{1/2}$ of levodopa and reduce the dose to approximately 1/4. On–off effect is minimized.

Drug	Mechanism of Action (MOA)	Adverse effect
Bromocriptine	D_1 and D_2 agonist action	Vomiting, hallucination, hypotension
Ropinirole, Pramipixole	D_2 agonist action	Nausea, hallucination, hypotension
Selegiline	MAO–B inhibition → prevent dopamine dgradation	Postural hypotension, nausea, confusion
Amantadine	Enhance the presynaptic synthesis and release of dopamine	Insomnia, nightmares

MULTIPLE CHOICE QUESTIONS

1. Patients who have received MAO inhibitors may experience severe hypertensive crisis if they ingest
(a) Cheese (b) Beer
(c) Fish (d) All of the above

2. Following are the $GABA_A$ receptor agonists:
[P] Muscimol [Q] Gaboxadol
[R] Gabazine [S] Flumazenil
(a) P and Q (b) Q and R
(c) P and R (d) Q and S

3. Spiperone is mainly an antagonist on
[P] D_1 receptor [Q] D_2 receptor
[R] D_3 receptor [S] D_5 receptor
(a) P and R (b) Q and R
(c) P and S (d) R and S

4. Following are the partial agonist of dopamine receptor
[P] Sulpride [Q] Haloperidol
[R] Ariprazole [S] Apomorphine
(a) Q and R (b) P and Q
(c) P and S (d) R and S

5. Following statement are true for dopamine receptors:
[P] D2 receptor is implicated in schizophrenia
[Q] D4 receptor shows marked polymorphism in human
[R] Behavioural effects are because of dopamine antagonist agent
[S] Dopamine does not act on CTZ
(a) P and R (b) Q and R
(c) P and Q (d) R and S

6. Sumatriptan is used to treat
(a) Anxiety (b) Depression
(c) Migraine (d) Vomiting

7. All anesthetic agents depress respiration system except
(a) Nitrous oxide (b) Halothane
(c) Sevoflurene (d) Desflurene

8. Paracetamol drugs are substrate for
(a) CYP1A2 isoenzyme P450
(b) CYP2E1 isoenzyme P450
(c) CYP1B6 isoenzyme P450
(d) CYP1C9 isoenzyme P450

9. Correct statement regarding amitriptyline is
(a) It stimulates adrenergic receptors
(b) It has no significant CV effect
(c) Therapeutic effects become manifest after 2–3 weeks of administration
(d) It has mood-elevating effect

10. All of the following benzodiazepines are biotransformed to active products except
(a) Diazepam (b) Alprazolam
(c) Lorazepam (d) Prazepam

11. All commonly used inhalation anaesthetics cause
(a) Renal toxicity
(b) Decreased blood flow
(c) Increased cardiac out put
(d) Respiratory depression

12. Carbidopa is useful in the treatment of Parkinson's disease because it
(a) Is a precursor of L-dopa
(b) Prevents the breakdown of dopamine
(c) Promotes the increased concentration of L-dopa in the nigrostriatum
(d) Can readily penetrate the CNS

13. Correct statements concerning methadone include all except
(a) Effective analgesic
(b) Well absorbed from GIT
(c) Useful in treatment of opioid abstinence syndrome
(d) Phenytoin decrease the metabolism of methadone

14. The preferred treatment of status epilepticus is IV administration of
(a) Ethosuximide (b) Sodium valproate
(c) Diazepam (d) Chlorpromazine

15. Which of the following agent selectively inhibits serotonin uptake?
(a) Desipramine (b) Maprotoline
(c) Fluoxetine (d) Imipramine

16. Which of the following gas anesthetic has low potency with a high MAC value?
(a) Halothane (b) Nitrous oxide
(c) Enflurane (d) None of the above

17. Correct statements concerning mechanism of drugs used in the treatment of Parkinsonism include
(a) Levodopa enhances the synthesis of dopamine
(b) Bromocriptine is an agonist at dopaminergic receptors
(c) Amantadine acts by stimulating the release of dopamine from storage sites
(d) All of the above

18. Postoperative hallucinations or delusions are characteristics features of
(a) Nitrous oxide (b) Fentanyl
(c) Halothane (d) Ketamine

19. Principal action of Mono amine oxidase inhibitors is
(a) Inhibition of Noradrenaline
(b) Increase stores of GABA
(c) Increase stores of Noradrenaline and 5HT
(d) Block 5HT

20. Adrenaline is used with the administration of a local anaesthetics agent to
(a) Inhibit salivation and secretions of respiratory tract
(b) Prolong the duration action
(c) Prevent miosis
(d) Cause skeletal muscle relaxation

21. All of the following are pharmacological effects of narcotic analgesic agonist drug except
(a) Suppression of cough reflex
(b) Decreased intestinal peristalsis
(c) Activation of chemoreceptor trigger zone
(d) Decreased arterial pCO_2

22. The primary mechanism of action of local anesthetics is
(a) Blockade of potassium channel
(b) Blockade of calcium channel
(c) Blockade of sodium channel
(d) Blockade of neurotransmitter action

23. Toxic effect of L-dopa can be reversed by administration of
(a) Folic acid (b) Vitamin B_{12}
(c) Pyridoxine (d) Thiamine

24. Which of the following drug is useful in treating trigeminal neuralgia?
(a) Phenytoin (b) Carbamazepine
(c) Sodium valproate (d) Ethosuximide

25. Which of the following drug is contraindicated in the treatment of Parkinsonism?
(a) Pyridoxine (b) Alpha-methyl dopa
(c) Carbidopa (d) None of above

26. Antidote for warfarin overdose is
(a) Protamine zinc insulin
(b) Protamine sulfate
(c) Vitamin K
(d) None of the above

27. Local anaesthetic with vasoconstrictor effect is
(a) Procaine (b) Lidocaine
(c) Bupivacaine (d) Cocaine

28. Which one of the following prevents the development of an abstinence syndrome in a heroin user?

(a) Nalbuphine (b) Naloxone
(c) Methadone (d) Dextropropoxyphene

29. Correct statements concerning carbamazepine include all except
(a) Used in trigeminal neuralgia
(b) Useful in the treatment of generalized tonic–clonic seizures
(c) Initial dose should be high
(d) Untoward effects are drowsiness, vertigo and blurred vision

30. Correct statement concerning phenelzine include
(a) It is an MAO Inhibitor
(b) It produces orthostatic hypotension
(c) It produces hypertensive crisis when food containing tyramine is ingested
(d) All of the above

31. Which of the following reduces peripheral decarboxylation of L-dopa to enhance its therapeutic effects in Parkinson's disease?
(a) Carbidopa (b) Amantadine
(c) Pyridoxine (d) None of the above

32. Correct statement regarding phenytoin include all except
(a) Used in grandmal epilepsy
(b) Phenylbutazone reduce metabolism of phenytion
(c) Phenytoin binds to plasma proteins
(d) Used in petitmal epilepsy

33. Amphetamine gives sympathomimetic activity by
(a) Inhibiting MAO release
(b) Noradreanaline release
(c) CNS stimulant
(d) All of the above

34. Ester local anaesthetic with short half-life and low surface activity is
(a) Bupivacaine (b) Cocaine
(c) Procaine (d) Lidocaine

35. Side effects of phenothiazines include all except
(a) Blood dyscrasias
(b) Obstructive jaundice
(c) Orthostatic hypotension
(d) Increased GIT motility

36. Treatment of insomnia due to anxiety is with
(a) Paraldehyde (b) Meprobamate
(c) Ether (d) Morphine

37. Which of the following should not be given along with levodopa?
(a) Carbidopa (b) Benserazide
(c) COMT inhibitors (d) Procyclidine

38. 5-Hydroxytr yptamine is biosynthesized from _____ aminoacid.
(a) Tryptophan (b) Tryrosine
(c) Phenylalanine (d) Alanine

39. Which of the following facilitates the action of GABA?
(a) Chlorpromazine (b) Ethanol
(c) Diazepam (d) Imipramine

40. Which of the following local anaesthetics is/are only useful for topical administration
(a) Procaine (b) Bupivacaine
(c) Benzocaine (d) All of the above

41. Diffusion hypoxia is produced by following inhalation anaesthetic.
(a) Halothane
(b) Methoxyflurane
(c) Isoflurane
(d) N_2O

42. Heroin differs from morphine in all respects except
(a) Synthetic congener of morphine
(b) More constipation
(c) Slowly metabolized to morphine
(d) None of above

43. All of the following are monoamine oxidase inhibitors except:
(a) Phenelzine (b) Isocarboxazid
(c) Tranylcypromine (d) Maprotiline

44. Which of the following is the only IV anesthetic to produces cardiovascular stimulation?
(a) Etomidate (b) Ketamine
(c) Fentanyl (d) Thiopental

45. The antiepileptic which inhibits the seizures induced by the administration of picrotoxin is _____
(a) Phenytoin (b) Carbamazepine
(c) Ethosuximide (d) Sodium valproate

46. Barbiturate excretion in urine may be increased by
(a) Dialysis (b) Acidification
(c) Alkalization (d) None of above

47. Phenytoin metabolism is inhibited by
(a) Disulfiram
(b) Chloramphenicol, INH, cimetidine
(c) Dicumarol, warfarin
(d) All of the above

48. Correct statementS. concerning cocaine is/are
(a) Effectively blocks nerve conduction
(b) Blocks reuptake of norepinephrine
(c) Produces tachycardia and vasoconstriction
(d) All of the above

49. Amantadine in Parkinsonism acts by
(a) Stimulating the release of dopamine from storage sites
(b) Decreasing the decarboxylation of dopamine
(c) Increasing norepinephrine from adrenals
(d) None of the above

50. Drug of choice in uteric colic is
(a) Pethidine (b) Nitrates
(c) Adrenaline (d) All of the above

51. Mechanism of actionS. of cyproheptadine if given prophylaxis in migraine includeS.
(a) 5-HT2 receptor antagonist
(b) Blocks calcium channel
(c) Blocks histamine receptor
(d) All of the above

52. Correct statements concerning imipramine include
(a) It is tricyclic antidepressant
(b) Increases anxiety in normal subjects
(c) It is biotransferred to an active product, desipramine
(d) All of the above

53. Halogenated anaesthetic agents obtained considerable favour because
(a) Cheap
(b) Non-explosive
(c) Not respiratory depressant
(d) Not CVS depressant

54. Which of the following benzodiazepine is used as antidepressant?
(a) Diazepam (b) Mianserin
(c) Flumazenil (d) Lorazepam

55. Stage II anaesthesia is a stage of
(a) Analgesia
(b) Respiratory depression
(c) Excitement or delirium
(d) Surgical anaesthesia

56. Nitrous oxide is contraindicated in patients with
(a) Myasthenia gravis
(b) Polycythemia vera
(c) Cerebral degeneration
(d) All of the above

57. All of the following prostanoid produce bronchoconstriction except
(a) PGI_2 (b) PGD_2
(c) $PGF_{2\alpha}$ (d) TXA_2

58. Effect of curare is potentiated by following anestheticS.
(a) Enflurane (b) Diethyl ether
(c) Halothane (d) All of the above

59. Which of the following anesthetic should not be used with adrenaline?
(a) Thiopental (b) Nitrous oxide
(c) Cyclopropane (d) Ether

60. Short half-life of thiopental is primarily due to
(a) Excretion of drug
(b) Metabolism of drug
(c) Redistribution of drug
(d) All of the above

61. Drug contraindicated in head injury is
(a) Phenothiazines (b) Carbamazepines
(c) Phenytoin (d) Morphine

62. If heparin is contraindicated then for inhibiting platelet aggregation one of the following prostanoids is used
(a) Carboprost (b)Gemeprost
(c) Misoprostol (d) Epoprostenol

63. Most frequent side effect of long-term carbamazepine therapy is
(a) Respiratory depression
(b) Drowsiness
(c) Peripheral neuritis
(d) All of the above

64. Out of the following the only drug having 100 % bioavailability
(a) Gabapentin (b) Levetiracetam
(c) Topiramate (d) Valproate

65. The principal action of noscapin is
(a) Analgesic (b) Antiemetic
(c) Antitussive (d) Antihistaminic

66. All of the following is a partial/mixed agonists of opiod receptor except
(a) Nalorphine (b) Naltrexone
(c) Nalbupine (d) Pentazocine

67. Neuroleptic analgesia can be converted to neuroleptic anaesthesia by the administration of

(a) Thiopental in oxygen
(b) Cyclopropane in oxygen
(c) N_2O in oxygen
(d) All of the above

68. One of the following is not a example of Inhalation anaesthesia
(a) Halothane
(b) Thiopental sodium
(c) Isoflurane
(d) Trichloroethylene

69. Therapeutic doses of phenytion become toxic when isoniazide administered concomitantly due to
(a) Acceleration of membrane stabilizing action of phenytoin
(b) Decreased metabolism of phenytoin
(c) Increased concentration of phenytoin
(d) Inhibition of hepatic microsomal enzyme systems

70. All of the following are NSAID prodrug except
(a) Nabumetone (b) Parecoxib
(c) Sulindac (d) Piroxicam

71. Correct statement regarding morphine includes all except
(a) Overdose of morphine producecoma and respiratory depression
(b) Acts as emetics by stimulating CTZ
(c) Pinpoints pupil
(d) It decreases pain threshold

72. Which of the following statement is true concerning lidocaine?
(a) Slow onset of action
(b) Used as antiarrhythmic agent
(c) Poor tissue penetration
(d) All of the above

73. Drug of choice in acute attack of migraine is
(a) Methylsergide
(b) Serotonin
(c) Ergotamine tartrate
(d) Caffeine

74. Drug of choice in epilepsy with pregnancy
(a) Carbamazepine (b) Ethosuximide
(c) Phenobarbiton (d) Phenytoin

75. Which of the barbiturates can cause choleresis?
(a) Thiopental (b) Pentobarbital
(c) Phenobarbital (d) Methohexital

76. Metabolism of carbamazepine is inhibited by
(a) Tetracycline (b) Phenobarbital
(c) Erythromycin (d) Phenytoin

77. Oxygen therapy is most useful in
(a) CO_2 poisoning
(b) Methaemoglobinaemia
(c) Left ventricular failure
(d) All of the above

78. Barbiturate poisoning include all except
(a) Pupil constriction
(b) Babinski sign is positive
(c) Hypothermia can occur
(d) Hypotension can occur

79. Chlorpromazine is effective as an antiemetic by
(a) Depressing vomittingcentre
(b) Decrease the nervous input from the vestibular apparatus to the vomiting centre
(c) Blocking the CTZ
(d) All of the above

80. Which of the following is highly selective COX-1 antagonist?
(a) Ketorolac (b) Salicylate
(c) Rofecoxib (d) Diclofenac

81. When used with ethanol, the following compound produces a "Mickey Finn"?
(a) Glutathemide (b) Paraldehyde
(c) Chloral hydrate (d) Meprobamate

82. Which of the phenothiazines have least extrapyramidal effect?
(a) Chlorpromazine (b) Fluphenazien
(c) Thioridazine (d) Prochlorperazine

83. Spina bifida is associated with the material use of
(a) Phenytoin
(b) Carbamazepine
(c) Sodium valproate
(d) All of the above

84. Which one of the following H1-receptor antagonist is sedative?
(a) Levocetrizine (b) Loratidine
(c) Fexofenadine (d) Doxylamine

85. Photodermatitis is seen with
(a) Phenothiazines (b) Alcohol
(c) Nicotine (d) All of the above

86. Hypnotic used in geriatric patients is
(a) Methyl prylone (b) Meprobamate
(c) Paraldehyde (d) Etomidate

87. Mechanism of action of colchicine which is clinically used for gout is
(a) Inhibiting uric acid synthesis
(b) Increasing uric acid excretion
(c) Increasing uric acid synthesis
(d) Reduceing leucocyte migration in to joints

88. An anticholinergic drug used in Parkinsonism is
(a) Naloxone (b) Benztropine
(c) Levodopa (d) Physostigmine

89. Infliximab is used as
(a) Anticytokines agent
(b) Crohn's disease
(c) Psoriatic arthropathy
(d) All of the above

90. Which of the following drug is used in hypertensive patients for the diagnosis of pheochromocytoma?
(a) Reserpine (b) Guanethidine
(c) Clonidine (d) Methyldopa

91. The most specific agent for treatment of petit mal epilepsy is
(a) Primidone (b) Phenytoin
(c) Gabapentin (d) Ethosuximide

92. Recognized side effect of treatment with lithium carbonate is
(a) Proximal tubular degeneration
(b) Hypomagnesaemia
(c) Polyuria and polydipsia
(d) Hypochloremia

93. The appropriate antidote in the treatment of pentazocine over dosage is
(a) Nalorphine (b) Levallorphan
(c) Naloxone (d) Any of the above

94. Pharmacologic agentwho has the potential to cause increased biliary tree pressure is
(a) Morphine (b) Warfarin
(c) Phenytoin (d) Acetazolamide

95. Drug which is known to include "hirsutism" as a side-effect is:
(a) Thallium (b) Phenytoin
(c) Cephalosporin (d) Heparin

96. All of the following are used for the treatment of Alzeimer's disease except
(a) Donezepil (b) Rivastigmine
(c) Galanamine (d) Selegiline

97. Halothane is used as
(a) Intravenous anesthesia
(b) Inhalation anesthesia
(c) Local anesthesia
(d) None of the above

98. Zolpidem is used in the treatment of
(a) Dementia (b) Parkinson's disease
(c) Hypnotic (d) CNS stimulant

99. Risperidone is agonist of following receptor except
(a) D2-receptor (b) D1-receptor
(c) H1-receptor (d) 5-HT2

100. Following statements of tricyclic antidepressant agent are true except
(a) Imipramine is nonselective against nor-adrenaline and 5–HT receptor
(b) Venafaxine is weak nonselective against nor-adrenaline and 5-HT receptor
(c) Phenelzine is selective against nor-adrenaline
(d) Duloxetine is potent selective against nor-adrenaline and 5-HT receptor

ANSWER KEYS

1. (d)	**2.** (a)	**3.** (b)	**4.** (d)	**5.** (c)	**6.** (c)	**7.** (a)	**8.** (b)	**9.** (c)	**10.** (c)
11. (d)	**12.** (c)	**13.** (d)	**14.** (c)	**15.** (c)	**16.** (b)	**17.** (d)	**18.** (d)	**19.** (c)	**20.** (b)
21. (d)	**22.** (c)	**23.** (c)	**24.** (b)	**25.** (b)	**26.** (c)	**27.** (d)	**28.** (c)	**29.** (c)	**30.** (a)
31. (a)	**32.** (d)	**33.** (d)	**34.** (c)	**35.** (d)	**36.** (b)	**37.** (c)	**38.** (a)	**39.** (c)	**40.** (c)
41. (d)	**42.** (b)	**43.** (b)	**44.** (b)	**45.** (d)	**46.** (c)	**47.** (d)	**48.** (d)	**49.** (a)	**50.** (a)
51. (d)	**52.** (d)	**53.** (b)	**54.** (b)	**55.** (c)	**56.** (c)	**57.** (a)	**58.** (c)	**59.** (c)	**60.** (c)
61. (d)	**62.** (d)	**63.** (b)	**64.** (b)	**65.** (c)	**66.** (b)	**67.** (c)	**68.** (b)	**69.** (b)	**70.** (d)
71. (d)	**72.** (b)	**73.** (c)	**74.** (a)	**75.** (c)	**76.** (c)	**77.** (b)	**78.** (b)	**79.** (c)	**80.** (a)
81. (c)	**82.** (c)	**83.** (c)	**84.** (d)	**85.** (a)	**86.** (b)	**87.** (d)	**88.** (b)	**89.** (d)	**90.** (c)
91. (a)	**92.** (a)	**93.** (d)	**94.** (d)	**95.** (b)	**96.** (d)	**97.** (b)	**98.** (c)	**99.** (b)	**100.** (d)

CHAPTER 5

CHEMOTHERAPY AND CHEMOTHERAPY OF CANCER

BETA LACTAM ANTIBIOTICS

Penicillin

- All penicillins are derivatives of 6-aminopenicillanic acid (thiazolidine ring is attached to a β–lactam ring that carries a secondary amino group (RNH–)) and contain a beta–lactam ring structure that is essential for antibacterial activity.
- Beta–lactam antibiotics are narrow spectrum and bactericidal drugs. Peinicilins are obtained from P. cryssogenum.
- Penicillins degrade by the acidic pH and amide linkage destruction through β–lactamase enzyme which is produced by gram negative bacteria. β–lactams acts only multiplying cells.

Mechanism of action β–lactams bind with specific receptors (penicillin-binding proteins; PBPs) and inhibit the transpeptidase and carboxypeptidase enzymes that act to cross-link linear peptidoglycan chains which form part of the cell wall → cross linking does not take place → cell becomes incapable of withstanding the osmotic gradient → cell death.

Pharmacokinetic Penicillins degrade by the acidic pH and amide linkage destruction through β–lactamase enzyme which is produced by gram negative bacteria. β–lactams acts only multiplying cells.

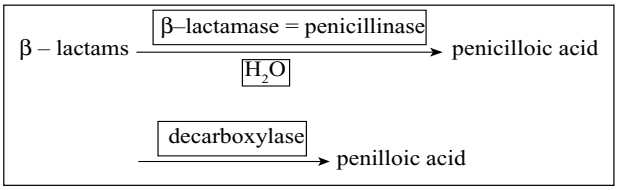


Figure 5.1 Beta Lactam - Penicillin

*penicllins are organic acids excreted by tubular secretion which is inhibited by **probenecid** → prolonged the action of penicillin.

Salts of penicillin with organic base such as Benzathine, Procaine have limited water solubility and useful in depot forms → prolonged action.

Adverse effect

- *Thrombophlebitis*: Pain and inflammation at the site of injection.
- Hypersensitivity reaction: Due to degrade ptoduct of penicillin (penicilloic acid).
- Anaphylactic shock (IgE) and
- *Diarrhea*: Due to disruption of normal balance of intestinal micro flora.
- *Jarisch–Herxheimer reaction* in syphilitic patient.

Penicillin G (Benzyl penicillin) Acid liable and penicillinase susceptible β–lactam antibiotic.

Drugs	Features	Uses	Adverse Effect
Penicillin V (Phenoxymethylpenicillin)	Acid liable and penicillinase susceptible		
Methicillin, Oxacillin, Cloxacillin	Penicillinase resistant		Interstitial nephritis Neutropenia Hepatitis
Extended spectrum penicillin:			
Ampicillin	Acid resistant and penicillinase susceptible food ↓ its absorption	Meningitis, gonorrhea, SABE,	Diarrhoea

Drugs	Features	Uses	Adverse Effect
Amoxicillin	Similar to ampicllin but absorption not affected by food.	Respirtory tract infection	
Carbenicilin	Acid liable and penicillinase susceptible	Antipseudomonal	
Piperacillin		Most potent antipseudomonal, used in netropenic patient	

Interactions

- Hydrocortisone inactivates to ampicillin if mixed in the i.v. solution.
- Ampicillin inhibts the colonic micro flora and interferes with the decogulation and enterohepatic cycling of oral contraceptives → failure of contraception.
- Probenecid inhibits the tubular secretion of ampicillin → increase the duration of action.

β–lactamase Inhibitors

Clavulanic acid Obtained from Streptomyces clavuligerus and inhibits to β–reclaimant or penicillinase → prevents the degradation of β–lactam antibiotics. It is a suicidal inhibitor.

Coamoxiclav = Amoxicillin + Clavulanic acid

Sulbactam semisythetic β–lactamase inhibitor related with clavulanic acid.

Sultamicillin tosylate = Ampicillin + Sulbactam

Tazobactam β–lactamase inhibitor like sulbactam.

Piperacillin in combination with tazobactam is used in antibacterial therapy.

Cephalosporins

- Cephalosporins comprise a large group of semisynthetic drugs, most of which are derived from cephalosporin C, a substance obtained from a species of Cephalosporium. Chephalosporins have β–lactam ring and a dihydrothiazine ring (7–aminocephalosporanic acid). Addition of any side chain in β–lactam ring at 7 position modify the spectrum of activity and in the dihydrothiazine ring at 3 position modify the pharmacokinetic properties. All cephalosporins are bactericidal and have the same mechanism of action as penicillin → cell wall synthesis inhibition.
- Cephalosporins have greater acid and β–lactamase resistance property and wide range of antibacterial activity.
- Most cephalosporins excreted primarily by renal tubular secretions → probencid inhibits tubular secretion like penicillins.

Cephalsporin Drugs

Oral Compounds	Parentral Compounds
First generation: Cefalexin, Cefradine, Cefadroxil	First generation: Cefalotin, Cefazolin
Second generation: Cefaclor, Cefuroxime axetil	Second generation: Cefuroxime, Cefoxitin
Third generation: Cefixime, Cefpodoxime proxetil, Cefdinir	Third generation: Ceftriaxone, Cefoperazone, Cefotaxime
Fourth generation: Cefepime, Cepriome	

Adverse reaction

- Pain at the site of (i.m.) injection.
- Diarrhoea and hypersensitivity reaction like penicillins.
- Nephrotoxicity is highest with cephaloridine.
- Platelet dysfunction and bleeding.
- Disulfiram like reaction.

Uses

- In the penicillin producing staphylococcal infections E.g., cephalothin.
- In the gonorrhea caused by penicillinase producing organism; E.g., cefuroxime and cefotaxime.
- Septicemias caused by gram negative organism.

Other β–Lactam Antibiotics

Monobactams

Aztreonam

- It is a monocyclic novel β–lactam antibiotic which has resistance to β–lactamase. It is active against gram neg-

ative bacilli, H. influenza and Pseudomonas but does not affect gram positive cocci.
- It is used in the patient allergic to penicillin or cephalosporins.
- Adverse effect: hypersensitivity reactions and thrombophlebitis.

Carbapenems

Imipenem, Meropenem and Ertapenem

- Penicillin like, but sulphur atom of thiazolidine ring is replaced with a carbon atom. These are potent and very broad spectrum, β–lactam antibiotic. It is resistant to β–lactamase.
- Unlike Meropenem and Ertapenem, Imipenem is rapidly inactivated by dehydroxypeptidase. For this reason, imipenem combined with dehydroxypeptidase inhibitor called cilastatin, which has similar pharmacokinetics with imipenem ($t_{1/2}$ of both = 1h).
- Probencid inhibits tubular secretion of imipenem like penicillins.
- Carbapenem exerts cross sensitivity with penicillins. Cephalosporins and other beta lactams and should not be administered to patients who are allergic to these drugs.
- Contraindicated in epileptic patients, higher dosage can produce convulsions.

CHLORAMPHENICOL

Chloramphenicol is broad spectrum antibiotics with bacteriostatic activity and wide spectrum of activity but currently a backup drug for infections due to *Salmonella typhi, B. fragilis,* Rickettsia, and possibly in bacterial meningitis.

It was initially obtained from *Streptomyces vanezualae.*

Chloramphenicol palmitate Prodrug designed for masking the bitter taste.

Chloramphenicol succinate Prodrug designed for increase water solubility.

Mechanism of Action

Chlormphenicol binds with 50S ribosome → blocks the transfer of aminoacyl t–RNA to the acceptor site for amino acid incorporation → inhibits protein synthesis.

Adverse Effects

Dose-dependent ***bone marrow suppression*** is common; aplastic anemia is rare (1 in 35, 000).

Gray baby syndrome in neonates (decreases glucuronysyl transferase) and optic neuritis in children.

Superinfection Results

Inhibits metabolism of phenytoin, sulfonylureas, and warfarin.

Hepatic failure requires dose adjustment of chloramphenicol.

TETRACYCLINE

Tetracyclines are bacteriostatic and broad spectrum antibiotics obtained from soil actinomycetes and having a nucleus of four cyclic rings. These are water unstable and concentrated in liver and spleen and bind to the connective tissued of bones and teeth.

Mechanism of Action

Binds to the 30S ribosome and inhibit aminoacyl tRNA attachment to the acceptor site → inhibits protein synthesis.

Drugs	Adverse effects
Tetracycline, Chlortetracycline	GI distress (Nausea, Vomiting, Diarrhoea), superinfections leading to candidiasis or colitis.
Oxytetracycline	Tooth discolouration and possible bone growth in children (avoid).
Demeclocycline	Renal dysfunction, kidney damage (Fanconi syndrome) with outdated drugs (due to formation of epitetracyciles, anhydrotetracyclines, and epianhydrotetracyclines).
Methacycline	Phototoxicity (*demeclocycline, *doxycycline).
Lymecycline	Have caused liver dysfunction during pregnancy at very high doses (contraindicated)
Doxycycline	Vestibular dysfunction (*minocycline, *doxycycline)
Minocycline	Diabetes insipidus due to decreases ADH secretion

Used in Granuloma inguinale due to Calymm granuloma, Atypiacl pneumonia, cholera, Brucellosis, Plague and rickettsial infection and prolonged therapy in the acne.

AMINOGLYCOSIDE ANTIBIOTICS

- Aminoglycosides are natural products or semisynthetic derivatives of compounds produced by a variety of soil actinomycetes. These are a group of natural and semisynthetic antibiotics having polybasic amino groups linked glcosidically to two or more amino sugars [streptidine (found in streptomycin), 2–deoxy streptamine (found in all other available aminoglycosides), garosamine) residues.
- They are water-soluble, stable in solution, and more active at alkaline than at acid pH.
- Aminoglcosides are active against aerobic gram negative bacilli and gives bactericidal action irreversible inhibition of protein synthesis.

Mechanism of action

Antibiotics penetrate the cell wall → bind with 30S –50S subunit (Streptomycin with 30S and other amino glycosides 50S ribosomes) of ribosome → interfere with the initiation of peptide formation, interfere with polysome formation and misreading of mRNA → irreversibly protein synthesis inhibition → death of cell.

Mechanism of resistance Microorganisms produce a transferase enzyme or that inactivate the aminoglycoside by adenylation, acetylation, or phosphorylation. Impaired the entry of aminoglycosides into the cell. Mutation in the 30S ribosomal subunit receptor protein.

Drug	Source	Uses
Streptomycin	*Streptomyces griseus*	Tuberculosis, Tularemia, Subacute bacterial endocarditis (SABE), plague
Gentamicin	*Micromonospora purpurea*	SABE, Meningitis
Kanamycin	*S. kanamyceticus*	
Tobramycin	*S. tenebrarius*	
Amikacin	*Semisynthetic derivative of kanamycin*	
Sisomycin	*Micromonospora inyoensis*	
Netilmicin	*Semisynthetic derivative of sisomycin*	
Neomycin	*S. fradiae*	Neomycin is too toxic for parentral use. Used topically only.
Framycetin	*S. lavendulae*	Similar to neomycin, used topically.

Adverse Effects

Nephrotoxicity Tubular damage in kidney. Neomycin, Tobramycin and Gentamycin are most nephrotoxic drugs.

Ototoxicity (loss of hearing)

(a) *Cochlear damage:* Neomycin, Kanamycin and Amikacin are most ototoxic drugs.
(b) *Disturbance of vetibular function:* Vertigo and loss of balance (Streptomycin and Gentamycin most vetibulotoxic).

Neuromuscular blockade curare like effect.

Interactions

- Concurrent use with loop diuretics (E.g., Ethacrynic acid, furosemide) and other nephrotoxic drugs (E.g., Amphotericin B, vancomycin and cisplatin) → potentiate nephrotoxicity.
- Concurrently used with muscle relaxant and neuromuscular blockers → muscular weakness.
- Avoid during pregnancy: risk of foetal ototoxicity.

MACROLIDES AND OTHERS ANTIBIOTICS

The macrolides are a group of closely related compounds characterized by a macrocyclic lactone ring (usually containing 14 or 16 atoms) to which deoxy sugars are attached. These are acid unstable so are administered in enteric coated formulation.

Mechanism of Action

Binds with 50s ribosomal RNA → inhibits the amino acyl translocation and formation of initiation compex → inhibits, protein synthesis.

Erythromycin

- Obtained from *Streptomyces erythreus* and has 14 membered macrocyclic rings with deoxy sugars.
- Erythromycin is used for infections caused by *gram-positive cocci* (not MRSA), atypical organisms (Chlamydia, Mycoplasma, and Ureaplasma species), Legionella pneumophila, *Campylobacter jejuni* and *Bordetella pertussis*. First choice drug for whooping cough and Chancroid.
- Erythromycin (estolate is best absorbed in oral form)-wide distribution into tissue and is eliminated mainly via biliary excretion.

Adverse reaction and Interaction *gastrointestinal irritation* (common), skin rashes, and eosinophilia. Hypersensitivity based–acute cholestatic hepatitis may occur with erythromycin estolate.

Erythromycin inhibits several forms of hepatic cytochrome P450 → increase the plasma levels of anticoagulants, carbamazepine, cisapride, digoxin and theophylline. Cardiac arrhythmias occurred when erythromycin was administered to patients taking astemizole or terfenadine (the two antihistaminic drugs have been discontinued in the USA).

Clarithromycin Clarithromycin causes less GI distress than erythromycin, but it also inhibits P450 and causes reversible deafness at high doses. Animal studies have shown teratogenic effects

Azithromycin It is semisynthetic derivative (azalide congener) of erythromycin and safe in pregnancy and does not inhibit drug metabolism.

Roxithromycin It is semisynthetic, acid stable and long active macrolide and activity spectrum resembles with erythromycin.

Ketoides These are semisynthetic 14-membered-ring macrolides, differing from erythromycin by substitution of a 3–keto group for the neutral sugar L–cladinose. E.g., Telithromycin

Telithromycin Used for the treatment of respiratory tract infections, including community-acquired bacterial pneumonia, acute exacerbations of chronic bronchitis, sinusitis, and streptococcal pharyngitis.

OTHER ANTIBIOTICS

Clindamycin It is a chlorine–substituted derivative of lincomycin, an antibiotic that is elaborated by *Streptomyces lincolnensis*. Clinical activity and mechanism of action resembles with erythromycin (not effective against MRSA and aerobic gram negative baceria).

Adverse effects Rashes, urticaria, abdominal pain and *diarrhoea.*

Superinfection as Pseudomembranous enterocolitis due to *Clostridium difficile.*

Quinupristin-dalfopristin This is a combination of two streptogramins—quinupristin, a streptogramin B and dalfopristin, a streptogramin A—in a 30:70 ratio. It is rapidly bactericidal and has a prolonged post antibiotic effect.

It is active against most gram positive cocci including MRSA and VRSA.

Fusidic Acid This is a narrow spectrum steroidal antibiotic which blocks bacterial protein synrhesis. And active against penicillinase producing gram positive bacteria. It is used topically only.

Linezolid It is a new class of synthetic (Oxazolidinones derivative) antimicrobials. It is active against gram-positive organisms including staphylococci, streptococci, enterococci, gram-positive anaerobic cocci and gram-positive rods. It is primarily a bacteriostatic agent except for streptococci for which it is bactericidal.

Linezolid inhibits protein synthesis by binding with 23S ribosomal RNA of the 50S subunit → preventing formation of the ribosome complex that initiates protein synthesis.

Vancomycin

Vancomycin is a glycopeptide antibiotic produced by Streptococcus orientalis. With the single exception of flavobacterium, it is active only against gram negative bacteria, particularly staphylococci and MRSA.

Mechanism of Action

Binding with the D-Ala-D-Ala terminus of nascent peptidoglycan pentapeptide → This inhibits the transglycosylase, → preventing further elongation of peptidoglycan and cross-linking (inhibits cell wall synthesis) → lysis of cell wall and death.

Adverse reaction Throbophlebitis (pain and inflammation at site of injection) and "***Red man***" or "red neck" syndrome. Dose dependence cause kidney damage and gives additively enhanced nephrotoxic and ototoxic effect with aminoglycosides, loop diuretics etc.

Teicoplanin It is a glycopeptide antibiotic and resembles with Vancomycin in mechanism of action and antibacterial spectrum but shows less toxicity.

Fosfomycin An analog of phosphoenolpyruvate and inhibits the bacterial cell wall synthesis in very early stage.

Mechanism of action It inhibits the cytoplasmic enzyme enolpyruvate transferase → blocking the addition

of phosphoenolpyruvate to UDP–N–acetylglucosamine → Preventing the formation of UDP–N–acetylmuramic acid → inhibit cell wall synthesis.

Use Treatment of uncomplicated lower urinary tract infections in women.

Bacitracin It is a cyclic peptide and obtained from the *Bacillus subtilis*. It is active against gram-positive microorganisms (both cocci and bacilli).

Mechanism of action Bacitracin interfers with dephosphorylation in cycling of the lipid carrier that transfers peptidoglycan subunits to the growing cell wall → inhibits cell wall formation.

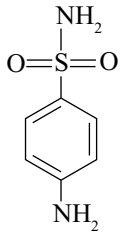
Adverse effect Nephrotoxic (when administered systemically so use topically), protein urea, haematuria, hypersensitivity.

Cycloserine Produced by *Streptomyces orchidaceus* and it is water-soluble and very unstable at acid pH. Cycloserine inhibits many gram-positive and gram-negative organisms, but it is used almost exclusively to treat tuberculosis caused by strains of *M tuberculosis* resistant to first line drug.

Adverse effect Dose-related central nervous system toxicity with headaches, tremors, acute psychosis and convulsions.

SULFONAMIDES

The sulfonamide drugs were the first effective chemotherapeutic agents to be employed systemically for the prevention and cure of bacterial (pyogenic bacterial) infections in humans. Sulfonamide can be considered as derivatives of para-aminobenzenesulfonamide (sulfanilamide).



- The—SO_2NH_2 group (N1) is not essential and govern: Solubility, Potency, Pharmacokinetic property.
- The para–NH_2 group (the N of which has been designated as N4) is essential for anti-bacterial activity.

Most of them are relatively insoluble in water, but their sodium salts are readily soluble.

Mechanism of Action

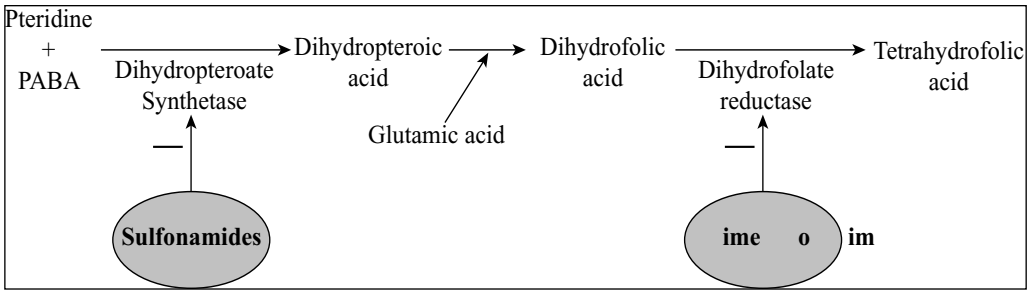


Figure 5.2 Mechanism of Action

Sulfonamide Drugs

Drugs	Adverse effect
Short acting: Sulfadiazine Intermediate acting: Sulfamethoxazole Long acting: sulfadoxine Special purpose sulfonamides: Sulfasalazine, Mefenide, Silver sulfadiazine	Nausea, vomiting, crystalurea, photosensitization, **Stevention–Johnson syndrome* and exfoliative dermatitis. Hepatitis, haemolysis. **Kernicterus* in new born

Silver Sulfadiazine

- Used for preventing infections of burnt surfaces (antibacterial action due to Ag^+ ions).
- Triple sulfa → mixture of equal quantities of Sulfadiazine, Sulfamerazine and sulfamethizine. This combination gives additive antibacterial action and minimizes the crystalluria.

Sulfasalazine

- Compound of 5–Amino salicylic acis (5–ASA) with sulfapyridine linked through an azo bond.
- Sulfapyridine mostly serve as carrier for 5–ASA and anti–inflammatory action shows due to 5–ASA.

Olalazine Two molecule of 5–ASA coupled together by azo bond.

Mesalazine (Mesalamine)

- It is a 5–ASA formulation as delayed release preparation by coating with acrylic polymer → formulation delivers 5–ASA in the small bowel and colon.
- All 5–ASA prodrugs used in ulcerative colitis.

Cotrimoxazole = Sulfamethoxazole **(5)** + Trimethoprim **(1) [**Combination based on similar $t_{1/2}$= 10hours.**]**

Bacteriocidal ⟸ Bacteriostatic + Bacteriostatic (action of this combination)

Adverse effects Megaloblastic anaemia due to folic acid deficiency and other sulfonamide's adverse effects.

Interactions Diuretics with Cotrimoxazole produce higher incidence of thrombocytopenia.

Uses Used in urinary tract infection and prostatitis, respiratory tract infections, typhoid, Chancroid-bacterial diarrhea and dystentry and Pneumonia due to *Pneumocystis carinii*.

Cotrimazine

Trimethoprim (90 mg) + Sulfadiazine (410 mg) ⟹ utility similar to that of Cotrimoxazole.

Sulfadiazine + Pyrimehamine ⟹ This combination is used in leishmaniasis and toxoplasmosis.

Sulfadoxine and Sulfamethopyrazine are ultra long acting compounds and those show >1 week action.

ANTITUBERCULAR DRUGS

- Tuberculosis is caused by *Mycobacterium tuberculosis*, which can produce either a silent, latent infection or a progressive, active disease.
- M. tuberculosis preferentially infects humans.
- M. bovis causes a similar disease in cattle and other livestock.
- *M. tuberculosis* is transmitted from person-to-person by coughing or sneezing. Today, airborne *M. tuberculosis* is the main threat to humans.

TB = Consumption (pronounced weight loss) = wasting disease = white plague.

Note

The "black plague," or bubonic plague, is a separate disease caused by *Yersinia pestis.*

Signs and Symptoms

- Patients typically present with weight loss, fatigue, a productive cough, fever and night sweats.
- Frank hemoptysis.

Diagnosis

Mantoux test (TB skin test) It uses tuberculin purified protein derivative (PPD), and Mantoux test is quantitative.

Standard 5-tuberculinunit PPD intracutaneously on the volar aspect of the forearm. This injection should produce a small, raised, blanched wheal appears in 48 to 72 hours. The area of induration (the "bump") is the important end point, not the area of redness.

Specimens of sputum from patients with suspected pulmonary TB, examined microscopically using either a fluorescent stain (auramine) or the more traditional Ziehl-Neelsen staining → smear positive → detection of bacilli.

Treatment of TB

First line drugs Drugs have high antitubercular efficacy as well as low toxicity.

Second line drugs Drugs have either low antitubercular efficacy or high toxicity or both.

First line treatment regines for tuberculosis in adults

Drugs	Mechanism of action	Adverse effects
Isoniazid (H)	Inhibits mycolic acid synthesis.	Peripheral neuropathy (due to Pyridoxine defeciency); hepatitis
Rifampicin (R)	Inhibits DNA-dependent RNA polymerase. Resistance via change in enzyme.	Hepatitis; gastrointestinal upsets, respiratory syndrome, flu syndrome. *Faliure of contraceptives due to microsomal enzyme induction

Pyrazinamide (Z)	Unknown, but metabolically activated by bacteria strains lacking the bioactivating Enzyme are resistant.	Gastrointestinal upsets; hyperuricemia, gout
Ethambutol (E)	Inhibits synthesis of arabinogalactan (cell wall component)	Retrobulbar neuritis
Streptomycin (S)	Binds with 30 S ribosome and protein synthesis inhibition	Ototoxicity, nephrotoxicity

Second-line drugs for the treatment of tuberculosis

Drug	Characters	Adverse effects
Thiacetazone (Tzn)	** Not to be used in HIV positive cases*	Gastrointestinal intolerance, **Stevens-Johnson syndrome**, bone marrow depression, ototoxicity, hepatitis.
Ethionamide (Etm) (Protionamide)		Gastrointestinal intolerance, anorexia, hepatitis, hypersensitivity, convulsions, depression, alopecia, optic neuritis and red green colour discrimination
Cycloserine (Cys)	Analogue of D-alanine and inhibits bacterial cell wall synthesis by inactivating the racemase enzyme	Seizures, psychoses, various central nervous system effects
Amikacin (Am)	Semisynthetic derivative of Kanamycin	Nephrotoxicity, ototoxicity, rash, neuromuscular blockade, eosinophilia
Capreomycin (Cpr)		Nephrotoxicity, ototoxicity, hypersensitivity
Kanamycin	Obtained from *S. kanamyceticus*	Nephrotoxicity, ototoxicity, hypersensitivity
Ciprofloxacin		Gastrointestinal intolerance, crystaluria, tremor, convulsions, rash, hepatitis, renal failure
Para aminosalicylic acid (PAS)		Gastrointestinal intolerance, hypersensitivity, hypothyroidism, crystaluria
Rifabutin (Ansamycin)	Structure and mechanism relared to Rifampin. **Active against M. avium complex (MAC) in AIDS*	Gastrointestinal intolerance, granulocytopenia, uveitis

ANTILEPROTIC DRUGS

- Leprosy = Hansen disease: It is chronic infectious disease of the skin and peripheral nerves caued by *Mycobacterium leprae.*
- *M. leprae is* obligate intracellular parasite which grows on 32 to 34 °C temperature of skin.
- Diagnosis: Lepromin test (skin smear test).

Drugs

1. Sulfones: Dapsone
2. Phenazine derivatives: Clofazimine,
3. Antitubecular drug: Rifampin, Ethionamide

4. Other drugs: Ofloxacin, Minocycline, Clarithromycin

Dapsone

- It is chemically diaminodiphenylsulfone and derivative of Sulfonamide. Mechanism of action resembles like sulfonamide i.e., inhibition of PABA incorporation into folic acid.
- Pharmacokinetics: Dapsone metabolite through acetylation as wellas glucuronide conjugation. Acetylated metabolite has half life > 24 hours and accumulate in the tissues.

Adverse Effects

Haemolytic anaemia (more common with patients have G–6–PD deficiency).

- Gastric intoleranace: nausea and anorexia
- Phototoxicity, rashes, exfoliative, and dermatitis.

Lepra reaction Jarish Herxheimer (arthus) type reaction) and it is erythema nodosum leprosum.

Lepra reaction treatment Discontinue Dapsone and start daily administration of Clofazimine 200 mg daily.

Chloroquine and Thalidomide also inhibits the lepra reaction but thalidomide shows teratogenic effects–phocomalia, multiple defects.

Contraindication Dapsone should not be used in patients with severe anaemia.

Clofaziminie It is a red coloured phenazine dye with leprostatic and anti-inflammatory activity. It acts by interferencing in DNA synthesis.

Pharmacokinetics Accumulates in fatty tissues in crystalline form and $t_{1/2}$= is **70 days.**

Adverse effects *Redish–black discolouration* of skin and discolouration of hair, sweat, tears etc.

GI intolerances: nausea, anorexia, loose stool, and abdominal pain.

Contraindication Avoid during early pregnancy and liver and renal disease.

ANTIFUNGAL DRUGS

Fungi are universally present in nature but only a few are pathogenic to man. They belong to the Eumycetes group. Fungi need organic compounds as nutrients and they function as scavengers, breaking down complex carbohydrates and proteins of the dead bodies of other organisms. Fungal infection is termed as mycoses.

Types of Anti-fungal Drugs

Polyenes

Amphotericin B (AMB)

It is obtained from *Streptomyces nodosus*. Amphotericin B is an amphoteric polyene macrolide (polyene = containing many double bonds; macrolide = containing a large lactone ring of 12 or more atoms) and gives fungicidal action. It is nearly insoluble in water (orally for topical infections), and is therefore prepared as a colloidal suspension of amphotericin B and sodium desoxycholate for intravenous injection (for systemic infections).

Mechanism of action

Amphotericin B binds with ergosterol (component of fungal cell membrane) → AMB–ergosterol complex alter the membrane permeability → creates pore in the membrane → pores allows the leakage of intracellular ions, amino acids, and micromolecules → cell death.

Clinical uses

AMB topically applied for oral, vaginal and cutaneous candidasis and paretrally used for systemic infections.

AMB is the most effective drug for resistant case of kala–azar.

Adverse effects

Infusion-Related Fever, chills, muscle rigor, hypotension (histamine release) occur during i.v. infusion (a test dose is advisable) and can be alleviated partly by pretreatment with NSAIDs, antihistamines, meperidine, and adrenal steroids.

Dose-Dependent Nephrotoxicity which decreases GFR, tubular acidosis, decreases K^+ and $Mg2^+$, and anemia through decreases erythropoietin is protected by Na^+ loading, use of liposomal AMP B permitting decreases in AMB dose.

Interaction 5–Flucytocine gives supra–additive action with AMB (AMBincrease the penetration of 5–FC into the fungus).

Nystatin Obtained from *S. nousei*, it is similar to AMB in anti-fungal action and other properties.

Hamycin It was isolated from S. Pimprina and developed by Hindustan Antibiotics at pimpri.

Heterocyclic benzofuran

Griseofulvin

- It is isolated from *Penicillium griseofulvum* and cures infections due to dermatophytes (ringworm) when administered orally.
- It is ineffective against *Candida albicans.*

Mechanism of action

Griseofulvin interacts with microtubules of mitotic spindle

and with cytoplasmic microtubules → disorientation of mitotic microtubules and interferes in the mitosis → inhibits the growth of fungal hyphae.

- Griseofulvin is very low water soluble drug → low absorption → absorption improved by taking with fatty meals and microfines the drug particles. Now use ultrafine microparticles → increase Griseofulvin absorption and reduce to ½ dose compare to microfine particle formulations.

Adverse effects Headache, GIT disturbances, peripheral neuritis, rashes, lukopenia.

Interactions Griseofulvin induces warfarin metabolism and reduces efficacy of oral contraceptives.

Antimetabolite

Flucytosine (5–FC)

- It is pyrimidine analogue related to the chemotherapeutic agent 5–FU (5–fluorouracil).

Mechanism of action

This permeates the fungal cell wall and converts into 5–fluorouracil → phosphorylation of 5–FU and formation of UDP and UTP → which inhibits to thymidylate synthesis → inhibits the DNA and RNA synthesis → inhibits the fungal cell growth.

Adverse effect Bone marrow depression, Leucopenia, rash, diarrhoea, hepatitis.

Azoles

(A) Imidazoles (Topical): Clortimazole, Econazole, Miconazole, (Systemic): Ketoconazole

(B) Triazoles (Systemic): Fluconzole, Itraconzole

Mechanism of azoles

Inhibits the fungal cytocrome enzyme lanosterol 14–demethylase → impair ergosterol synthesis.

Ketoconazole

Orally used in mucocutaneous candidiasis or dermatophytoses.

Adverse effect

- Nausea and vomiting (reduced by giving with meals).
- decreases androgen production and displaces testosterone from protein binding sites → Gynaecomastia, loss of libido, and hair, and oligozoospermia.
- Menstrual irregularities in the females.

Interactions Ketoconazole inhibit cyto P450 and increase plasma level of Terfenadine, Astemazole, and cisapride → polymorphic ventricular tachycardia and fatal ventricular fibrillation.

Allylamine

Terbinafine

- Active only against dermatophytes by inhibiting squalene epoxidase → inhibit ergosterol synthesis.
- Possibly superior to griseofulvin in onychomycoses.

Adverse effects: GI distress, rash, headache, ↑ liver function tests (LFTs) → possible hepatotoxicity.

Other topical agents: Tolnaftate, Undecylnic acid, benzoic acid Ciclopirox olamine, sod. Thiosulfate.

ANTIHELMINTICS

Drugs	Mechanism of action	Adverse effects
Mebendazole (benzimidazole)	Act by blocking of glucose uptake in the parasite and depletion of its glycogen stores → Results in loss of intracellular microtubules.	Diarrhoea, nausea, and abdominal pain. Allergic reaction, loss of hair (alopecia) and granuloctopenia at higher dose.
Albendazole (benzimidazole)		Diarrhoea, nausea, and abdominal pain, alopecia, neutropenia.
Piperazine	Piperazine compounds contraindicated: during pregnancy, Impaired renal or hepatic function, epilepsy or chronic neurologic disease.	Nausea, vomiting, diarrhoea, abdominal pain and nephrotoxicity
Diethylcarbamazine (piperazine derivative)	Diethylcarbamazine immobilizes microfilariae	Headache, anorexia, weakness, nausea, vomiting

Ivermectin (Antibiotic): Semisynthetic macrocyclic lactone, is a mixture of avermectin B_{1a} and B_{1b}	Intensifying GABA-mediated transmission → hyperpolarization paralyze nematodes. *Ivermectin should not be used in pregnancy*	Fatigue, nausea, vomiting, Abdominal pain and rashes. In *onchocerciasis* treatment, the adverse effects is *Mazotti reaction*: fever, headache, rash, increased pruritus, diarrhea, joint and muscle pains, hypotension, Tachycardia and peripheral edema.
Pyrantel pamoate (tetrahydropyrimidine derivative)		Nausea, vomiting, diarrhoea, abdominal cramps, headaches, insomnia and rash
Praziquantel (isoquinoline–pyrazine derivative)	increase the permeability of trematode and cestode cell membranes → leakage of Ca^{2+} → paralysis, dislodgement, and death.	Nausea and abdominal pain.
Levamisole (l–Tetramisole)	Stimulates ganglia in worm → tonic paralysis → expulsion of live worm.	Nausea, abdominal pain and fatigue.
Niclosamide (salicylamide–derivative)	inhibition of oxidative Phosphorylation or stimulation of ATP ase activity in mitochondria and anaerobic generation of ATP by the worm.	

Drugs for the Treatment of Helminthic Infections

Infectious worm	First choice of drug	Alternatives
Roundworm *Ascaris lumbricoides*	Albendazole or Pyrantel or Mebendazole	Piperazine
Whipworm *Trichuris trichiura* *Trichinella spiralis*	Mebendazole or albendazole	Oxantel/pyrantel
Hookworm *Necator americanus* *Ancylostoma duodenale*	Pyrantel pamoate or mebendazole or albendazole	
Pinworm Enterobius vermicularis	Mebendazole or pyrantel Pamoate	Albenbazole
Threadworm *Strongyloides stercoralis*	Ivermectin	Thiabendazole, albendazole1
Tapeworms *Taenia saginata* (beef tapeworm) *Diphyllobothrium latum* (fish tapeworm) *Taenia solium* (pork tapeworm) *Cysticercosis* (pork tapeworm larval stage) *Hymenolepis nana* (dwarf tapeworm)	 Praziquantel or niclosamide Praziquantel or niclosamide Praziquantel or niclosamide Albendazole Praziquantel	 Albendazole Praziquantel Niclosamide
Filaria *Wuchereria bancrofti* (filariasis)	Diethylcarbamazine	Ivermectin

Infectious worm	First choice of drug	Alternatives
Guinea worm *Dracunculus medinensis*	Metronidazole	Thiabendazole or mebendazole
Hydatid disease Echinococcus granulosus Echinococcus multilocularis	Albendazole	

** Thiabenabzole and Praziquantel are contraindicated at machinery operation and driving.

ANTI MALARIAL DRUGS

Plasmodium species that infects humans (*Plasmodium falciparum, P. malariae, P. ovale, P. vivax*) are spread by the female Anopheles mosquito and after inoculation into the human host, undergo a primary developmental stage in the liver (primary tissue phase). They then enter the blood and parasitize erythrocytes (erythrocytic phase). Plasmodium falciparum and P malariae have only one cycle of liver cell invasion; there after, multiplication is confined to erythrocytes.

- **Tissue schizonticides:** Drugs that eliminate developing or dormant liver forms of hypozoites; E.g., Primaquine, Pyrimethamine, and proguanil.
- **Blood schizonticides:** Those that act on erythrocytic parasites; E.g., Quinine, Chloroquine, Amodiaquine, Mefloquine, Artemisinin, Proguanil, and tetracycline
- **Gametocides:** Those that kill sexual stages and prevent transmission to mosquitoes. Quinine, Chloroquine and Artesunate (these not for *P. falciparum*) *Primaquine effective for all species.

Radical cure Eliminate both hepatic and erythrocytic stages and prevent from relaps. For P. vivax-Proguanil and Primaquine.

Causal prophylactic drugs Capable of preventing erythrocytic infection. Proguanil, Primaquine.

Drugs	Mechanism of action and Uses	Adverse effect
4-aminoquinoline: Chloroquine	Prevents polymerization of the hemoglobin and prevent breakdowns of heme into hemozoin thus interfere/disrupts heme sequestration. Intracellular accumulation of heme is toxic to the parasite. Use: Non-falciparum and sensitive falciparum malaria Amoebic liver disease Rheumatoid arthritis.	Nausea, vomiting, anorexia, difficulty in accomodation and headache. Photoallergy, rashes
4-quinoline: Mefloquine	MOA similar to Chloroquine.	Nausea, vomiting, anorexia, diarrhoea, difficulty in accomodation and headache. Photoallergy, rashes. *concurrent use with Alofantrine/quinine/chloroquine → cardiac arrest.
Acridine: Mepacrine		
Cinchona alkaloid: Quinine		Cinchonism: Nausea, vomiting, headache, vertigo, diarrhoea, difficulty in hearing and vision. Photoallergy, rashes.
Biguanides: Proguanil	Inhibit DHFRs (Dihydro folate reductase)	

Drugs	Mechanism of action and Uses	Adverse effect
8–aminoquinolines: Primaquine	Act as cellular oxidants	Dose related Haemolysis (G–6–PD deficient more sensitive), methamoglobinemia, tachypnoea, and cyanosis. *avoid durig pregnancy (foetus is G–6–PD deficient)
Diaminopyrimidines: Pyrimethamine **Sulfonamides:** Sulfadoxine, Sulamethopyrzine, Dapsone Tetracyclines, Doxycyclines	Folate antagonist inhibits DHFRs and sulfonamides action as inhibition of PABA incorporation and folate synthase.	Like Sulfonamides
Sesquiterpine lactones: Artesunate, Artemether, Arteether Artemisinin obatained from *Artemisia annua* (Quinghaosu in china)	Structural epoxide bridge interact with heme in the parasite → iron mediated cleavage of bridge → generation of free radicals → lipid peroxidation and decreasesd protein synthesis and lysis of cell (death). **active agains P. falciparum resistant to all other antimalarial drug*	Nausea, vomiting, itching, abnormal bleeding. First degree AV blocks, QTc prolongation. **concurrent administration of Terfenadine, Astemazole, antiarrhythmics, TCAs → risk of cardiac conduction defect.
Phenanthrene methanol: Halophantrine	Used in multiresistant falciparum Malaria	Nausea, vomiting, abdominal pain, diarrhoea, Prolongation of QTc and ventricular arrhythmia *(CVS toxicity).* *Cross tolerance with Mefloquine*
Napthaquinone: Atovaquone	It collapses the plasmodial mitochondrial membrane and interferes with ATP production and acts as erythrocytic schizontocide for P. falciparum and other species	Diarrhoea, vomiting, headache

ANTI AMOEBIC AND OTHER ANTIPROTOZOAL DRUGS

Drug for Amoebiasis

Amoebiasis is an infection caused by *Entamoeba histolytica.* This agent can cause asymptomatic intestinal infection, mild to moderate colitis, severe intestinal infection (dysentery), ameboma, liver abscess and other extra intestinal infections.

1. Tissue amoebocides

(a) For both intestinal and extraintestinal amoebiasis:
Nitroimidazoles: Metronidazole, Tinidazole, Secnidazole, Ornidazole, Satranidazole
Alkaloids: Emetine, Dehydroemetine

(b) For extraintestinal amoebiasis only; Chloroquine

2. Luminal amoebiasis

(a) Amide: Diloxanide furoate
(b) 8-Hydroxy quinolines: Quinodochlor, Diiodohydroxyquin (Iodoquinol)
(c) Antibiotics: Tetracyclines

Metroniadzole

It exerts action through generation of Nitro radical which destabilized the DNA helix and breakage of strands → DNA damage.

Adverse effects Nausea, vomiting, *metallic taste* and abdominal pain.

Headache, dryness of mouth, rashes and neutropenia and thrombophlebitis.

Prolonged administration causes *peripheral neuropathy*.

Use Use in Amoebiasis, Giardiasis, Tricomomnas vaginitis, Ulcerative gingivitis, and Helicobactor pylori gastritis.

Diloxanide furoate

It is converted in the gut to the diloxanide freebase form, which is the active amoebicide. And used in asymptomatic amoebiasis.

Adverse effect Flatulence and nausea.

8–hydroxyquinolines

These are active against Entamoeba, Giardia, Tricomonas and some fungi and bacteria.

Adverse effect Nausea *loose and green stool,* pruritis and after prolonged use it causes goiter.

Iodism–inflammation of mucous membrane due to chronic iodine overload.

Prolonged use causes neuropathic syndrome [subacute myelo–optic neuropathy (SMON)].

DRUG FOR LEISHMANIASIS

Visceral leishmaniasis (Kala–azar) caused by *Leishmania donovani* and it is transmitted by female sand fly phlebotomus.

Antimonials Sodium stibogluconate, Meglumine antimonite

Diamidine Pentamidine

Others Amphotericin B, Ketoconazole, Miltefosine, allopurinol

Sodium Stibogluconate

It acts by inhibiting of–SH (Thiol Group) dependent enzymes and interfere with the bioenergetics of parasite.

Adverse effect Nausea, vomiting, *metallic taste*, abdominal pain, cough.

Pentamidine

It is active against *L. donovani, Trypanosomes, Pneumocystis carinii* and some bacteria and fungi.

Toxicity More toxic than Sod. Stibogluconate.

Releases histamine and produces acute reactions: sharp fall in BP, cardiovascular collapse, dyspnoea, palpitation, kidney and liver damage, and cytolysis of pancreatic β cells → Hyperglycemia and IDDM.

*This drug can be supplied only through government agencies.

ANTIVIRAL AGENTS

1. Anti–retroviral

A. **Nucleoside reverse transcriptase inhibitors (NRTIs):** Abacavir, Didanosine (ddI), Lamivudine (3TC), Stavudine (d4T), Tenofovir, Zalcitabine (ddC), Zidovudine (AZT), Emtricitabine

B. **Non–nucleoside reverse transcriptase inhibitors (NNRTIs):** Delavirdine, Efavirenz, Nevirapine

C. **Protease inhibitors:** Nelfinavir, Amprenavir, Saquinavir, Ritonavir, Indinavir, Lopinavir, Atazanavir, Fosamprenavir, Tiranavir

D. **Fusion inhibitors:** Enfuvirtide

2. Anti–Herpes Virus [Herpes Simplex Virus(HSV) and Cytomegalovirus(CMV)]

Iodoxuridine, Acyclovir, Penciclovir, Famciclovir, Ganciclovir, Fomivirsen, Cidofovir, Valaciclovir, Foscarnet

3. Anti–Influenza Virus

Amantadine, Rimantadine, Oseltamivir, Zanamivir

4. Anti–Hepatitis B

Adefovir, dipivoxil, Entecavir

5. Drugs for other viral infections

Interferon α, Peginterferon α–2b, Ribavirin

Anti-retro-viral Agent

NRTIs

NRTIs in the presence of host cell thymidine kinase converts into active triphosphate metabolite (nucleotides) → competes with corresponding nucleotide for incorporation into viral DNA → inhibits reverse transcriptase enzyme and termination of viral DNA synthesis.

Zidovudine (AZT) It is thymidine analogue and also known as azidothymidine. It is converted into active triphosphate metabolite and incorporates in the viral DNA that inhibit revesrse transcriptase enzyme and terminate the DNA chain synthesis.

*Zidovudine treatment significantly reduces the incidence of in utero transmission of HIV from infected mother to foetus.

*Zidovudine and Stavudine are not used together because they appear to be antagonistic action.

Adverse effects

- All NRTIs shows lactic acidosis, hepatic steatosis and lipodystrophy (all higher with stavudine).
- Zidovudine: *Bonemarrow suppression*–anaemia, neutropenia; gastrointestinal intolerance, headache.
- Didanosin: *pancreatitis, peripheral neurpathy*, gastrointestinal intolerance.
- Stavudine: *pancreatitis, peripheral neurpathy*
- Tenofovir (diphosphonate diester of nucleoside): Headache, gastrointestinal intolerance, renal impairment.

NNRTIs

NNRTIs Drugs bind directly to reverse transcriptase and disrupte catalytic site. Hence NNRTIs do not require phosphorylation for activity.

*These drugs have cross resistance in different NNRTIs.

*Efavirenz is most potent NNRTIs for these reasons, it is preferred to give NNRTI for initial treatment of adult patients with HIV infection.

Adverse effects

- All NNRTI: rash (most common). Rash can progress to Stevens–Johnson syndrome.
- Nevirapine: Haepatotoxicity, rash including Stevens–Johnson syndrome, induces the metabolism of protease inhibitors and oral contraceptives.
- Efavirenz: *Neuropsychiatric reactions* and teratogenic

Protease inhibitors

Protease inhibitors bind to the active site of protease enzyme → prevents the cleavage of gag–pol polyprotein → inhibit the maturation of virus → resulting production of immature, non-infectious viral particles.

*The administration of Ritonavir with another PI is known as *boosted therapy.*

All PI metabolized in the liver and excreted in the fecal.

Adverse effects

- All protease inhibitors: *lipdystrophy* (fat accumulation Fat redistribution- Buffalo Hump), hyperlipidemia, insulin resistance and diabetes, elevated liver function tests, inhibits metabolism of other protease inhibitors.
- Amprenavir, Fosamprenavir: Gastrointestinal intolerance, rash
- Atazanavir: Hyperbilirubilirubinemia, PR interval prolongation
- Lopinavir: gastrointestinal intolerance
- Ritonavir: gastrointestinal intolerance, hepatits, inhibits metabolism of other drugs, including antiarrhythmic drugs, opioids, TCAs.

Fusion inhibitors GL120 & GP41

Enfuvirtide is a synthetic polypeptide and bind with viral surface glycoprotein 120 and 41 → inhibit the fusion of HIV with host cells ($CD4^+$ T helper cell) before the virus enters the cell and begins its replication process.

Adverse reaction Injection site reaction, hypersensitivity reactions

Treatment Considerations for HIV Therapy

When CD4+ cell count < 200 cells/µl or if viral load is more than 100,000 copies/ml (HIV RNA copies per mililiter) should be considered for treatment.

Treatment initial regimens for treatment are:

2–NRTIs + 1–PI

2–NRTIs + 1–NNRTIs

3–NRTIs

These above treatment is also referred as HAART – Highly active Anti-Retro-viral Treatment

ANTI-HERPES AGENT

Mechanism of action

- *Nucleoside analogues* drugs in the presence of viral thymidine kinase converted into mono phosphate neucleoside which converts into active triphosphate nucleotide → active nucleotide inhibit the DNA polymerase and inhibit DNA synthesis.
- *Foscarnet* directly blocks DNA polymerase and reverses transcriptase enzyme and inhibits the DNA synthesis.

Anti-Influenza Agent

- Amantadine and Rimantadine prevents the uncoating of the influenza A virus and entry in the host cells.
- Oseltamivir and Zanamivir inhibits the neuraminidase (sialidase) in Influenza A and B → prevent the release of virions from host cells (spreading of virus).

Use	Drug	Adverse effects
Hepatitis B	Adefovir, dipivoxil, Entecavir	

Influenza A	Amantadine, Rimentadine, Oseltamivir, Zanamivir	
Influenza A + B	Oseltamivir, Zanamivir	
Herpes simplex; Varicella–zoster (HSV)	Acyclovir, Valaciclovir, Famciclovir	Acyclovir: renal toxicity–↓ in G.F.R.
Cytomegalovirus (CMV)	Fomivirsen, Foscarnet, Cidofovir, Ganciclovir	Foscarnet: renal impairment and acute renal failure, haematologic deficiencies, arrhythmia and heart fliure, seizures
Chronic hepatitis	Lamivudine, Ribavirin, Pegyated interferon α–2b	
Anogenital warts (HPV)	Interferons: Pegyated interferon α–2b	

CHEMOTHERAPY OF CANCER

Cancer is a group of diseases characterized by uncontrolled growth and spread of abnormal cells. All cancers involve the malfunction of genes that control cell growth and division.

Tumors may arise from any of the four basic tissue types.

Epithelial tissue, Connective tissue (i.e., muscle, bone, and cartilage), lymphoid tissue and Nerve tissue.

- **Carcinomas:** Malignant growths arising from epithelial cells.
- **Sarcomas:** Malignant growths of muscle or connective tissue.
- **Adenocarcinoma:** Malignant tumor arising from glandular tissue

Cytotoxic actions of anticancer drugs follow first–order kinetics: they kill a fixed percentage of tumor cells, not a fixed number.

Cell Cycle Specificity

- Cell cycle specific (CCS): Drugs that act on cells that are actively proliferating → schedule dependent. In most cases, CCS drugs are also phase specific.
- Cell cycle non-specific: Drugs acting on non–proliferating cells → dose-dependent.
- Cell cycle non-specific: Chlorambucil, cyclophosphamide, L–asparginase, cisplatin, procarbazine

Cell cycle specific (CCS)

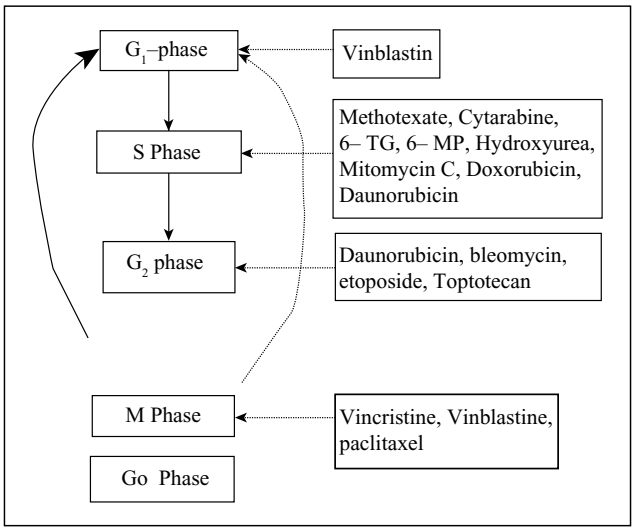


Figure 5.3

Anticancer Drugs

Drug	Mechanism of Action	Uses	Adverse effects
Methotrexate	Antimetabolite-inhibits DHF reductase (S phase)	Leukemias, lymphomas, breast Cancer; Rheumatoid arthritis, psoriasis	BMS, mucositis, crystalluria; leucovorin (folic acid) rescue decrease the incidence of adverse effect of Methotrexate
Cyclophosphamide	Alkylating agent–attacks guanine N7–dysfunctions of DNA	Non-Hodgkin's, ovarian, breast CA, neuroblastoma	BMS, mucositis, *hemorrhagic cystitis* (MESNA-traps acrolein and it is used to reduce acrolein toxicity), hepatotoxicity (high dose)
Nitrosourea; Carmustine (BCNU) Lomustine (CCNU) Dacrabazine	Highly lipid soluble alkylating agent and penetrate into CNS blood barrier. Dacrbazine primary affect the RNA synthesis while all other alkylting agent primarily affect to DNA	Meningeal leukemia and brain tumor	Nausea, vomiting
Cisplatin	Alkylating agent cross Nephrotoxicity (hydrate and use links DNA strands	Testicular, ovarian, bladder, lung Cancer	Nephrotoxicity (hydrate and use mannitol), neurotoxicity (deafness)
Procarbazine	Alkylating agent	Hodgkin's (MOPP)	BMS, pulmonary toxicity, hemolysis, neurotoxicity, leukemogenic
Doxorubicin	Intercalator, forms free radicals, inhibits topoisomerase II	Hodgkin's (ABVD), breast, endometrial, lung, ovarian CA	BMS-delayed CHF (dexrazoxane, free radical trapper protects), alopecia, vesicant, radiation "recall"
Bleomycin	Complexes with Fe and O_2 → DNA strand scission (G2 phase)	Hodgkin's, testicular, head, neck, skin CA	Pneumonitis, *pulmonary fibrosis*, mucocutaneous reactions (blisters), alopecia, hypersensitivity
6–Mercaptopurine	Purine antimetabolite (S phase) bioactivated by HGPR transferase	Acute lymphocytic leukemia immunosuppression (azathioprine forms 6–MP)	BMS, hepatotoxicity (jaundice, necrosis), GI distress
	Pyrimidine antimetabolite bioactivated (5–FdUMP)to inhibit thymidylate synthetase	Breast, ovarian, head, and neck Cancer-topical for basal cell Cancer and keratoses	BMS, GI irritation, alopecia
Vincristine and Vinblastine	↓ Microtubular polyrnerization-spindle poisons (M phase)	Vinblastine–Hodgkin's (ABVD), testicular CA, Kaposis's sarcoma vincristine–Hodgkin's (MOPP), leukemias, Wilms'	BMS, GI, alopecia Neurotoxicity (neuropathy)
Taxens: Paclitaxel	Promotes microtubule assembly and arrests cell cycle and G2 & M-phases	Metastatic ovarian and breast carcinoma	Myelosuppression and 'stocking and glove neuropathy'

Drug	Mechanism of Action	Uses	Adverse effects
Etoposide and Teniposide	Increases degradation of DNA by interaction with topoisomerase II.	Lung (smallcell), prostate, and testicular carcinoma.	Gastrointestinal irritations, alopecia and bone marrow suppression.
Camptothecinanalogues: Topotecan *Irinotecan*	Interact with topoisomerase I and allow single strand break in the DNA It is a *prodrug* and in the liver, converts into active metabolite via decarboxylation.	Carcinoma of ovary, small cell lung cancer Colorectal carcinoma, cancer lung/cervix/ ovary etc.	Neutropenia Diarrhoea, neutropenia, thrombocytopenia
Mitomycin (Antibiotics)		Adenocarcinomas of the cervix, stomach, pancreas, and lung.	Toxic for liver, lung, and kidney.

Hormonally Active Agents

Category	Special feature	Uses	Adverse Effects
Antiandrogen: Flutamide	Its active metabolite 2–hydroxyflutamide blocks androgenic action.	Prostate carcinoma	Hot flushes, transient elevations in liver function tests, gynaecomastia, loss of libido.
5–α reductase inhibitors Finasteride	Inhibits the conversion of testosterone to dihydrotestosterone.	Prostate carcinoma	Decrease volume of ejaculate, skin rashes
Progestins: Megestrol acetate		Metastatic carcinoma of breast	
Antiestrogen: Tamoxifen		carcinoma of breast	
Imatinib		Chronic myelogenous leukemia	Nausea and vomiting, fluid retention with ankle and periorbital edema, diarrhoea, myalgias

BMS= bone marrow suppression.

Drug	Toxicity
*Cisplatin, methotrexate, cyclophosphamide	Renal
6–MP, busulfan, cylophosphamide	Hepatic
*Bleomycin, Busulfan, Procarbazine	Pulmonary
Doxorubicin, Daunorubicin	Cardiac
*Vincristine, Cisplatin, Paclitaxel	Neurologic
Methotrexate, Cyclophosphamide, Cytarabin, dactinomycin	Immunosuppressive
Cyclophosphamide (haemorrhagic cyctitis), Asparaginase (pancreatitis), Procarbazine (lukemia)	

Toxicity of Anticancer Drugs

Rapidly proliferating cells such as the bone marrow, GI tract mucosa, hair follicles, and gonads are most sensitive to cytotoxic drugs.

- Cyclophosphamide act, as prodrug and after the metabolism convert into aldophosphamide, phosphoramide mustard and acroline.

- Cystitis is caused by (metabolite product–acroline) cyclophosphamide and Ifosphamide which blocks administration of *mesna* and bladder irrigating with N-acetylcysteine.
- Bone marrow suppression toxicity caused by Methotrexate can countract by the administration of folinic acid.
- All purines antimetabolites metabolized by xanthine oxidase their metabolism is inhibited by allopurinol and reduce the dose ¼ to ½ times and reduce the hyperuricaemia.
- Cytotoxic drug induced vomiting can controlled by 5HT3 antagonis E.g., *Ondasetron*

Immunosuppressants and Immunomodulating Agents

Immunosuppressants are the drugs that inhibit or prevent activity of the immune system. They are used in immunosuppressive therapy to:

- Prevent the rejection of transplanted organs and tissues (e.g., bone marrow, heart, kidney, liver)
- Treat autoimmune diseases or diseases that are most likely of autoimmune origin (e.g., rheumatoid arthritis, multiple sclerosis, myasthenia gravis, systemic lupus erythematosus, Crohn's disease, pemphigus, and ulcerative colitis).
- Treat some other non-autoimmune inflammatory diseases (e.g., long term allergic asthma control).

Drugs

1. T–cell inhibitors (calcineurin inhibitor): Cyclosporin, Tacrolimus, Sirolimus
2. Cytotoxic drugs: Methotrexate, Cyclophoshamide, Azothioprine, Mycophentolate mofetil,
3. Glucocorticoids: Prednisolone and others
4. Antibodies: Daclixumab, Basiliximab Muromonab, Trastuzumab, Etanercept

Cyclosporine

It is cyclic polypeptide with 11 amino acids, obtained from a fungus.

MAO Binds to cyclophilin → inhibits calcineurin (cytoplasmic phosphatase) → ↓ activation of T-cell transcription factors → decreases IL–2, IL–3, and interferon, TNFα etc.

Toxicity Nephrotoxicity, hypertension, hyperglycemia, liver dysfunction, rise in BP, anorexia, precipitation of diabetes and hirsutism.

Use Renal, Liver, Heart, Bone marrow and other transplantations.

Also used in rheumatoid arthritis, uveitis, inflammatory bowel disease etc.

Interactions: all nephrotoxic drugs like aminoglycosides, vancomycin, Amphotericin B etc., when administerd concurrently with cyclosporine → enhance the renal toxicity.

Tacrolimus is an immunosuppressant macrolide antibiotic produced *by Streptomyces tsukubaensis*. It is not chemically related to cyclosporine, but their mechanisms of action are similar. Cyclosporine binds to cyclophilin, while tacrolimus binds to the immunophilin FK–binding protein (FKBP). Both complexes inhibit calcineurin.

Sirolimus is a macrolide lactone, produced by the Actinomycetes *Streptomyces hygroscopicus*. It is used to prevent rejection reactions. Although it is a structural analogue of tacrolimus, it acts somewhat differently and has different side-effects. It is also known as Rapamycin and used as "Rapamycin coated stents" to prevent smooth muscle proliferation.

Adverse effect: Thrombocytopenia, hepatotoxicity, diarrhoea, hypertriglyceridemia, and headache.

Mycophenolate Mofetil

Mycophenolate mofetil is a semisynthetic derivative of mycophenolic acid, isolated from the mold *Penicillium glaucum.*

MAO Mycophenolate mofetil is hydrolyzed into mycophenolic acid which inhibits inosinemonophosphate dehydrogenase → leads to inhibtion of De novo (guanosine nucletotides) purine synthesis

Adverse effect Gastrointestinal disturbances (nausea and vomiting, diarrhoea, abdominal pain) and myelosuppression (primarily neutropenia).

Azathioprine

Azathioprine is a derivative of mercaptopurine and, like the parent drug, functions as a structural analog or antimetabolite. Azothioprine converts into mercaptopurine which inhibits De novo purine synthesis and damages DNA.

Used in the prevention of renal graft rejection.

Adverse effect Bone marrow suppression and leucopenia.

Leflunomide Leflunomide is a prodrug of an inhibitor of pyrimidine synthesis and used in rheumatoid arthritis.

Toxicity Elevation of liver enzymes with some risk of liver damage, renal impairment, and teratogenic effects.

Monoclonal Antibodies (MABs)

Monoclonal antibody	Use/action
Abciximab	Antiplatelet → antagonist of IIb/IIIIa receptors
Daclixumab and Basilix-imab	Kidney transplants → blocks IL–2 receptors
Infliximab	Rheumatoid Arthritis and Crohn's → binds TNFα
Muromonab (OKT3) CD_3	Allograft rejection block in renal transplants → against CD3
Palivizumab	Respiratory syncytial virus → blocks Respiratory syncytial virus protein
Rituximab	Non–Hodgkin lymphoma → binds to surface protein
Trastuzumab	Breast Cancer → antagonist to HER2lneu receptor
Imatinib	Chronic myelogenous lukemia
Etanercept	rheumatoid arthritis, polyarticular Course juvenile rheumatoid arthritis and psoriatic arthritis. → binds TNFα and TNFβ
Adalimumab	rheumatoid arthritis → TNFα
Alefacept	plaque psoriasis → inhibits activation of T cells by CD2
Alemtuzum-ab	chronic lymphocytic leukemia → binds to CD5

Triple drug therapy Cyclosporine+Azathioprine+Prednisolone used for immunosuppression.

Anti–D Immunoglobulin

Human IgG antibodies to red cell Rh (D) antigens.

Use

Administer to Rh(D) negative mother within 72 h of Rh positive delivery to prevent hemolytic disease of newborn in subsequent pregnancy. Should also be used in miscarriage for the same reason.

Immunomodulating Agents

These agents modulate the immune response rather than suppress and major potential uses are in immunodeficiency disorders, chronic infectious diseases, and cancer; E.g., BCG vaccine and levamisole.

Cytokines

Cytokines	Action
IFN–α	Treatment of several neoplasms, including hairy cell leukemia, chronic myelogenous leukemia, malignant melanoma, and Kaposi's sarcoma, and hepatitis B andC.
IFN–β	Relapsing-type multiple sclerosis
IFN–γ	Chronic granulomatous disease
IL–2	Metastatic renal cell carcinoma and malignant melanoma

BCG is a viable strain of *Mycobacterium bovis* that has been used for immunization against tuberculosis.

Levamisole increases the magnitude of delayed hypersensitivity or T cell-mediated immunity in humans. In immune deficiency associated with Hodgkin's disease, levamisole has been noted to increase the number of T cells in vitro and to enhance skin test reactivity.

Multiple Choice Questions

1. Antimicrobial action of penicillin is inhibition of
(a) Protein synthesis
(b) Cell wall synthesis
(c) Cell membrane synthesis
(d) DNA synthesis

2. Peripheral neuritis of INH therapy in tuberculosis can be prevented by giving
(a) Vitamin B1 with INH
(b) Vitamin B2 with INH
(c) Vitamin B6 with INH
(d) Vitamin B12 with INH

3. Which anthelmintic drug acts by depolarizing the helminth neuromuscular junction causing spasm and paralysis?

(a) Ivermectin (b) Diethylcarbamazine
(c) Piperazine (d) Mebendazole

4. First drug of choice in gonorrhoea is
(a) Cephalosporin (b) Sulphonamides
(c) Penicillin (d) Sulfone

5. The betalactam antibiotics are
(a) Penicillin (b) Cephalosporin
(c) Imipenem (d) All of the above

6. One of the following anti microbial agent that damages cytoplasmic membrane is
(a) Sufonamide (b) Cycloserine
(c) Bacitracin (d) Nystatin

7. Drug of choice in bacteroides infection is
(a) Penicillin G (b) Niridazole
(c) Metronidazole (d) Tetracyclin

8. Emetine HCl is used in
(a) Pinworm infection
(b) Roundworm infection
(c) Extraintestinal amoebiasis
(d) Bacillary dysentery

9. Antiviral activity of zidovudine is due to
(a) Inhibition of viral protein synthesis
(b) Inhibition of the viral RNA-dependent DNA polymerase
(c) Inhibition of the viral RNA polymerase
(d) None of the above

10. Antimalarial drug active against chloroquine-resistant *P. falciparum* is
(a) Pyrimethamine (b) Primaquine
(c) Mefloquine (d) Quinine

11. Which of the following drug is synergistic with sulfadoxin against malarial parasite?
(a) Chloroquine (b) Primaquine
(c) Pyrimethamine (d) Pentamidine

12. In patient with hepatic coma, the choice of antibiotics is
(a) Chloramphenicol (b) Penicillin G
(c) Neomycin (d) Erythromycin

13. Streptomycin inhibits bacterial protein synthesis by binding to
(a) DNA
(b) mRNA
(c) 50s ribosomal subunit of cell ribosomes
(d) 30s ribosomal subunit of cell ribosomes

14. The following drugs interfere with the synthesis of cell wall except
(a) Bacitracin (b) Vancomycin
(c) Colistin (d) Cycloserine

15. The antimicrobial activity of penicillin is due to
(a) Thiazolidine ring (b) Betalactam ring
(c) 6-APA (d) None

16. One of the following drugs is useful in the treatment of pulmonary tuberculosis:
(a) Carbenicillin (b) Cephalosporin
(c) Rifampicin (d) Pyrazinamide

17. Correct statements about methimazole include all except
(a) It is an antithyroid drug
(b) It can cross placenta
(c) It interferes with iodination of tyrosine
(d) It inhibits the peripheral conversion of thyroxin of triiodo thyronine

18. Metronidazole is the drug of choice in the treatment of
(a) Giardiasis
(b) Trichomoniasis in female
(c) Infection with *Bacteroides fragilis*
(d) All of the above

19. Thiabendazole, an anthelmintic drug, is used to treat infections caused by
(a) Ascariasis (b) Cutaneous larve migrans
(c) Stronglyloids (d) All of the above

20. Antiviral action of zidovudin is
(a) Inhibition of free extracellular virus
(b) Inhibition of reverse transcriptase
(c) DNA polymerase inhibition
(d) Post-translation event Inhibiter

21. Zidovudine-resistant strains of HIV can be treated with
(a) Acyclovir (b) Ribavarin
(c) Dideoxycytidine (d) All of the above

22. Which of the following drug is effective against malarial parasite in the liver but not within erythrocyte?
(a) Proguanil (b) Chloroquine
(c) Pyrimethamine (d) Primaquine

23. Primaquine sensitivity is due to deficiency of
(a) Glucose-6-phosphatase
(b) Glucose-6-phosphate dehydrogenase
(c) Pseudocholinesterases
(d) None of the above

24. Antimicrobial agent primarily administered topically include
(a) Bacitracin (b) Polymyxin
(c) Neomycin (d) All of the above

25. Bactericidal inhibitor of protein synthesis is
(a) Erythromycin (b) Gentamycin
(c) Tetracyclin (d) Penicillin-G

26. Drug of choice for streptococcal infection is
(a) Tetracyclin (b) Erythromycin
(c) Penicillin (d) Sulphadiazine

27. Sulphones are recommended in the treatment of
(a) Tuberculosis (b) Dysentery
(c) Leprosy (d) All of the above

28. Which of the following antitubercular drugs is an inhibitor of DNA-dependent RNA polymerase?
(a) Rifampicin (b) Streptomycin
(c) Ethambutol (d) Thioacetazone

29. Which of the following antitubercular drugs is an inhibitor of protein synthesis with potential for neuphrotoxicity effects?
(a) Ethambutol (b) Dapsone
(c) Streptomycin (d) INH

30. Methotrexate is an antagonist of
(a) Cobalamine (b) Folic acid
(c) Riboflavin (d) All of the above

31. The cytotoxic drug with maximum emetic activity is
(a) Chlorambucil (b) Methotrexate
(c) Busulfan (d) Cisplatin

32. All are the side effects of chloroquine except
(a) Blurring of vision (b) Psychotic episodes
(c) Skin rash (d) Hemolytic anaemia

33. Treatment of choice in cerebral malaria is
(a) Chloroquine (b) Amodiaquine
(c) Quinine (d) Primaquine

34. Chloroquine is treatment of choice for
(a) *P. ovale* (b) *P. vivax*
(c) P. Malariae (d) All of the above

35. Candidiasis of the vagina, GIT and oral cavity is treated primarily with
(a) Griseofulvin (b) Miconazole
(c) Rifampicin (d) Nystatin

36. All of the following statements concerning sulfonamides are correct except
(a) They are bacteriostatic
(b) Inhibit dihydrofolate reductase
(c) Crystaluria may occur
(d) They are antimetabolites of PABA

37. Pharmacologic effects of thioridazine include all of the following except
(a) Control of psychotic behaviour
(b) Orthostatic hypotension
(c) Antiemesis
(d) Hypoprolactinemia

38. The action of penicillin requires the presence of cell wall that contains
(a) Proteoglycans
(b) Peptidoglycans
(c) N-acetyl glucosamine
(d) N-acetyl muramic acid

39. Which of the following adverse effect is characteristic of ampicillin?
(a) Maculopapular rash
(b) Vomiting
(c) Nephritis
(d) Hemolytic anaemia

40. Optic neuritis is a chief adverse effect of
(a) INH (b) Pyrazinamide
(c) Rifampicin (d) Ethambutol

41. Skin discoloration from red brown to black is caused by
(a) Dapsone (b) Clofazimine
(c) Ethambutol (d) All of above

42. Diloxanide furoate is not useful in
(a) Intestinal amoebiasis
(b) Cyst passers
(c) Extraintestinal amoebiasis
(d) None of above

43. Disruption of the purine and pyrimidine bases of DNA pairing occurs with
(a) 5-flurouracil (b) Methotrexate
(c) Cyclophosphamide (d) All of the above

44. The mechanism of antibacterial action of tetracyclines

involves
(a) Stimulation of ribosomal peptidyl transferase
(b) Inhibition of DNA-dependent RNA polymerase
(c) Interference with the binding of aminoacyl t-RNA to bacterial ribosomes
(d) Inhibition of transpetidase enzymes

45. Mechanism of action of cephalosporins involves
(a) Inhibition of beta-lactamases
(b) Inhibition of peptide synthesis
(c) Inhibition of transpeptidase enzymes
(d) Interference with the synthesis of cytoplasmic membrane

46. All of the statements about aminoglycosides are correct except
(a) Inhibition the bacterial protein synthesis
(b) Resistance is usually plasmid-mediated
(c) Used for Gram-negative infection
(d) Antibacterial action occurs through inhibition of dihydro folate reductase

47. The antineoplastic agent that is classified as an alkylating agent is
(a) Vincristine (b) Tamoxifen
(c) Bleomycin (d) Busulfan

48. Treatment of *Mycoplasma pneumoniae* is
(a) Becitracin (b) Gentamycin
(c) Tetracycline (d) Penicillin-G

49. *S. typhi* is sensitive to
(a) Cephazolin (b) Cephalothin
(c) Cephaloridine (d) None

50. The organisms usually sensitive to streptomycin are
(a) *M.tuberculosis*
(b) *E. coli*
(c) *Pseudomonas aeruginosa*
(d) All of the above

51. RBCs are hemolysed by _____ in G6PD deficiency.
(a) Clofazimine (b) Dapsone
(c) Streptomycin (d) All of the above

52. Chloroquine should not be given along with phenylbutazone because it
(a) Produces blindness
(b) Produces hypotension
(c) Produces dermatitis
(d) All of the above

53. Treatment of systemic fungal infection is
(a) Meconazole (b) Clotrimazole
(c) Ketaconazole (d) Amphotericin-B

54. Which of the following is not an antifungal agent?
(a) Amphotericin-B (b) Clotrimazole
(c) Hamycin (d) Neomycin

55. Streptomycin is more effective at
(a) Acidic pH (b) Alkaline pH
(c) Neutral pH (d) None

56. The activity of dihydrofolate reductase is inhibited by
(a) Sulfasaxazole (b) Trimethoprim
(c) Sulpha dimidine (d) Sulfasalazine

57. The most common drug causing anaphylaxis is
(a) Streptomycin (b) Indomethacin
(c) Penicillin (d) Paracetamol

58. Diethyl carbamazine is used in the treatment of
(a) Hook worm infestation
(b) Round worm infestation
(c) Filariasis
(d) Tapeworm infestation

59. Repeated total leucocytes count is essential in therapy with
(a) Ampicillin (b) Gentamycin
(c) Carbenicillin (d) Chloramphenicol

60. Which of the sulfonamide is used in the treatment of malaria?
(a) Sulfadoxine (b) Sulfadimidine
(c) Sulfafurazole (d) Sulfasalazine

61. Clavulanic acid is
(a) Potent inhibitor of cell wall transpeptidase
(b) Inactivates bacterial 13-lactamases
(c) Specific for Gram-negative organisms
(d) None

62. Peripheral neuritis caused by isoniazide can be prevented by pretreatment with
(a) Riboflavine (b) Pyridoxine
(c) Thiamine (d) All of the above

63. Pyrantel pamoate is used in the treatment of
(a) Protozoal infection
(b) Amoebiasis
(c) Pinworm infection
(d) Schistogomiasis

64. Antimalarial activity of chloroquine is due to
(a) Inhibition of protein synthesis in plasmodia
(b) Inhibition of phosphate incorporation into the RNA and DNA of plasmodia
(c) Paralyses the plasmodia
(d) None of the above

65. Prolonged dilantin use may lead to
(a) Vitamin A deficiency
(b) Hypoglycemia
(c) Folic acid, iron and vitamin C deficiency
(d) Abnormality in folic acid metabolism

66. The metabolism of griseofulvin is accelerated by
(a) Carbamazepine (b) Aspirin
(c) Phenobarbitone (d) All of the above

67. Which of the following antimalarial drugs is safe during pregnancy?
(a) Chloroquine (b) Primaquine
(c) Proguanil (d) Amodiaquine

68. Antimalarial drug used to eradicate tissue form of plasmodia is
(a) Chloroquine (b) Primaquine
(c) Quinine (d) None of above

69. Which of the following drug is used in the treatment of multidrug resistant strain of *P. falciparum*?
(a) Artemisinin (b) Proguanil
(c) Pyrimethamine (d) Mefloquine

70. Tetracycline should be avoided during pregnancy and child hood because of
(a) Susceptibility to superinfection
(b) Intolerance
(c) Bone marrow toxicity
(d) Selectively taken up by growing bones

71. Choice in ring worm infection is
(a) Clotrimazole (b) Primaquin
(c) Nystatin (d) Griseofulvin

72. Auditory nerve damage is caused by
(a) Gentamycin
(b) Neomycin
(c) Dihydrostreptomycin
(d) All of the above

73. Hepatic microsomal enzymes are induced by
(a) Oestrogen (b) Progesterone
(c) Aldosterone (d) Streptomycin

74. Which of the following drug does not cross blood–brain barrier?
(a) Sulfonamide (b) Thiopentone
(c) Penicillin (d) None

75. The failure of oral contraceptives is seen with
(a) Ethambutol (b) INH
(c) Rifampicin (d) Pyrazinamide

76. The side effect of pyrazinamide is
(a) Peripheral neuritis (b) Aplastic anaemia
(c) Liver dysfunction (d) All of the above

77. Which of the following statement is incorrect?
(a) Ketoconazole has androgenic adverse effect
(b) Clotrimazole is effective in ring worm infection
(c) Terbinafine is a competitive inhibitor of squalene epoxiadase
(d) Voriconazole-QTc prolongation

78. Which of the following statement is correct?
(a) Pyrimethamine has 2000 times more affinity for mammalian enzyme
(b) Progunail changed into cycloguanil is an inactive metabolite
(c) Minocycline is used as an antimalarial drug
(d) First-line drug for cerebral malaria- is Aartemisnin

79. Following is cell cycle non-specific:
(a) Actinomycin D (b) 6-Mercapto purine
(c) Vincristine (d) Docetaxel

80. Which of the following is incorrect?
(a) Mesna is given in acrolein toxicity
(b) Folic acid is used to treat Mtx toxicity
(c) Cyclophosphamide also used immunosuppressant
(d) None of the above

81. To treat oestrogen-sensitive breast cancer _____ is used.
(a) Tamoxifen (b) Raloxifen
(c) Teripatide (d) Clomiphene

82. Which of the antifungal drug affects DNA?
(a) AMB (b) Terbinafin
(c) Griseofulvin (d) Ketoconazol

83. Which of the following statement is incorrect?
(a) Cefepirome: Zwitterion character increases better penetrability to Gram-negative bacteria
(b) First-generation drug shows mainly adverse effect related to blood

(c) Nephrotoxicity is highest with cephalodrine
(d) Bleeding due to some cephalosporin has methyltetrazole

84. Which of the following matching shows antagonism?
(a) Imipenam + cilastatin
(b) Nitofurantoin + nalidixic acid
(c) Aspirin + warfarin
(d) Ceftazimide + gentamicin

85. _____ can be given in renal toxicity.
(a) Demeclocycline (b) Minocycline
(c) Doxycycline (d) Tetracycline

86. The mechanism of antiparasitic action of mebendazole and thiabendazole involves
(a) Stimulation of acetylcholine receptor at neuromuscular junctions
(b) Inhibition of dihydrofolate reductase
(c) Interference with microtubule synthesis and assembly
(d) Block thiamine transport

87. Isoniazid is a primary antitubercular agent that,
(a) Requires niacin supplementation
(b) Causes ocular complications that are reversible if the drug is discontinued
(c) Is ototoxic and nephrotoxic
(d) Should never be used due to hepatotoxic potential

88. Ganciclovir is the drug of choice for which of the following?
(a) Influenza virus (b) Cytomegalo virus
(c) Pox virus (d) Adeno virus

89. Which of the following is vitamin D analogue used in psoriasis?
(a) Calcitriol (b) Feracrylum
(c) Tazarotene (d) Resorcinol

90. Which of the following statement is incorrect?
(a) Methotrexate DHFR inhbitor acts as immunosuppressant and anti-inflammatory
(b) Azathioprine inhibits enzyme thiopurine methyl transferase
(c) Leflunomide inhibits dihydroorotate dehydrogenase and pyrimidine synthesis
(d) Infliximab is a TNF-α stimulator

91. Which of the cephalosporin generation shows weaker activity against Gram-negative bacteria?
(a) I (b) III
(c) IV (d) II

92. Which of the following statement is incorrect?
(a) All aminoglycoside are active at alkaline pH
(b) Kanamycin has highest nephrotoxicity
(c) Gentamicin is used in meningitis caused by gram-negative bacteria
(d) Aminoglycoside acts intracellularly

93. Which of the following statement is incorrect?
(a) Mantoux is used in the diagnosis of tuberculosis
(b) Corticosteroid are contraindicated in intestinal tuberculosis
(c) Pyrazinamide is more lethal to intracellular bacilli
(d) Thiactazone is preferred in HIV-positive cases having tuberculosis

94. Which of the following drug inhibits the entry of virus in the cell?
(a) Zioduvadine
(b) Lopinavir
(c) Ritonavir
(d) Enfuvirtide

95. Traveler's diarrhea is treated with
(a) Sulphadiazine
(b) Cotrimoxazole
(c) Dapsone
(d) Pyrimethamine

96. Sulphonamide blocks the synthesis of which of the following?
(a) PABA (b) DFA
(c) DHFA (d) TFA

97. Which sulfonamide is used topically?
(a) Sulphadoxine
(b) Sulphamethoxazole
(c) Silver sulfamide
(d) Dapsone

98. Which of the following is true for dapsone?
(a) Not much used due to toxicity
(b) Inhibits folate synthesis in bacteria
(c) Is reduced by intestinal bacteria to a salicylate
(d) Is reduced by intestinal bacteria to a sulphonamide

99. Which of following is non-steroidal anti-androgens and useful as anticancer agent?
(a) Tamoxifen (b) Flutamide
(c) Etoposide (d) Aminoglutethimide

100. Which of the following a free radical alkylating drug?
(a) Carmustine (b) Thiotepa
(c) Procarbazine (d) Altretamine

ANSWER KEYS

1. (b)	**2.** (c)	**3.** (c)	**4.** (c)	**5.** (d)	**6.** (d)	**7.** (c)	**8.** (c)	**9.** (b)	**10.** (d)
11. (c)	**12.** (c)	**13.** (d)	**14.** (c)	**15.** (c)	**16.** (d)	**17.** (d)	**18.** (d)	**19.** (d)	**20.** (b)
21. (c)	**22.** (d)	**23.** (b)	**24.** (d)	**25.** (b)	**26.** (c)	**27.** (c)	**28.** (a)	**29.** (c)	**30.** (b)
31. (d)	**32.** (d)	**33.** (c)	**34.** (d)	**35.** (d)	**36.** (b)	**37.** (b)	**38.** (b)	**39.** (a)	**40.** (d)
41. (b)	**42.** (c)	**43.** (c)	**44.** (c)	**45.** (c)	**46.** (d)	**47.** (d)	**48.** (c)	**49.** (c)	**50.** (d)
51. (b)	**52.** (c)	**53.** (d)	**54.** (d)	**55.** (b)	**56.** (b)	**57.** (c)	**58.** (c)	**59.** (d)	**60.** (a)
61. (b)	**62.** (b)	**63.** (c)	**64.** (b)	**65.** (a)	**66.** (c)	**67.** (c)	**68.** (b)	**69.** (d)	**70.** (d)
71. (d)	**72.** (c)	**73.** (d)	**74.** (c)	**75.** (c)	**76.** (c)	**77.** (c)	**78.** (d)	**79.** (a)	**80.** (d)
81. (a)	**82.** (c)	**83.** (b)	**84.** (b)	**85.** (c)	**86.** (c)	**87.** (d)	**88.** (b)	**89.** (a)	**90.** (d)
91. (a)	**92.** (d)	**93.** (d)	**94.** (d)	**95.** (b)	**96.** (c)	**97.** (c)	**98.** (c)	**99.** (d)	**100.** (b)

CHAPTER 6

THERAPEUTIC ASPECT OF INFLAMMATORY DISORDERS

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS AND ANTIPYRETIC–ANALGESICS

NSAIDs = Non-narcotic = Non-opioids

A. Non Selective COX inhibitors

1. Salicylates: Aspirin
2. Pyrazolones: Phenylbutazone, Oxyphenbutazone
3. Indole derivatives; indomethacines, sulindac
4. Propionic acid derivetives: Ibuprofen, Naproxen, Ketoprofen, flubiprofen
5. Anthranilic acid derivatives; mefanemic acid
6. Aryl–acetic acid derivatives: Diclofenac, Aceclofenac
7. Oxicam derivatives; Piroxicam, Tenoxicam
8. Pyrrolo–pyrrole derivatives: Ketorolac.

B. Preferential COX–inhibitors

Nimesulide, Meloxicam, Nabumetone

C. Selective COX–2 inhibitors

Celecoxib, Rofecoxib, Valdecoxib (banned in India due to cardiac vascular toxicity).

Etoricoxib, Lumaricoxin

D. Analgesic–antipyretic with poor anti-inflammtory activity

1. Paraaminophenol derivative: Paracetamol
2. Pyrazole derivatives: metamizole (Dipyrone)
3. Benzoxazocine derivatives: Nefopam

NSAIDs inhibit the Prostaglandins synthesis through the inbition of cyclooxygenase (COX) enzyme. All NSAIDs inhibit the COX in reversible manner except Aspirin (irrverssibley).

Actions of NSAIDs

Effects	MOA/Reason (COX inhibition)
Analgesic	Block the preripheral pain sensation mechanism which is induced by mediators like bradykinin, interlukins etc.
Anti-inflammatory	Inhibit the release of inflammatory mediators as PGs
Antipyretic	Inhibit synthesis of PGs → reduce body temp by blocking the response of pyrogen
Antiplateletic effect	Inhibit the synthesis of platelete aggregatory factor TXA_2 and pro aggregatory factor PGG_2 and PGH_2
Gastric mucosal damage	decreases PGs synthesis and mucous secretion
Renal/salt retention	decreases synthesis of PGE_2 and PGI_2
Delay in labour	decreases PGs synthesis
Dutus arteriosus closer	decreases PGs synthesis
Spirin sensitive asthma precipitation	

Adverse effects of NSAIDs Gastric irritation, nausea, peptic ulceration, headache, bleeding, thrombocytopenia, asthma, Na and water retention → edema etc.

Aspirin Effects as mentioned in the above table.

Contrindication (C.I.) Aspirin contraindicates in the Diabetus, asthmatics and in liver disease.

It should be avoided in the G-6PD deficient patients.

Interactions

1. Aspirin displaces Warfarin, sulfonylureas, and methotrexate from its plasma protein binding site → toxicity may occur.
2. It inhibits the tubular secretion of uric acid and interferes with the uricosuric action of probenecid.
3. It interferes with the tubular secretion of (active metabolite of spironolactone) canrenone and blocks the diuretic action.

Uses Analgesic, antipyretic, anti-inflammatory, Acute rheumatic fever, Rheumatoid arthritis, in low dose (75–100 mg) for postmyocardial infection and post-stroke patients.

Drug	MOA/Specific Features	Adverse Effect
Indomethacin		Common side effect: frontal headache, gastric intolerance and CNs effects. C I. in machine operaters, drivers, psychiatric patients
Sulindac	It is prodrug and by the metabolism converts into active sulfide metabolite.	
Naproxen	Potentially inhibits the migration of leukocyte	
Mefanemic acid	Mefanemic acid produces peripheral as well as central analgesic action.	Common side effect: diarrhoea
Piroxicam		Heart burn, nausea, vomiting
Ketorolac	Use in postoperative and acute musculoskeletal pain	
Nimesulide	Action through COX inhibition and reduced he generation of superoxide by neutrophil.	Heart burn, nausea, loose motion, rashes. *Hepatic failure*
Nabumetone	It is a prodrug and converts into active metabolite 6-MNA	
Paracetamol		Toxic metabolite of paracetamol-N-acety-p-benzoquinoeimine (NABQI) which necrocised to liver and kidney tubule cells.

DRUGS FOR COUGH

Cough is a protective reflex, for the expulsion of respiratory secretions or foreign particle from air passage.

Drugs

Pharyngeal

Pheryngeal demulcent These drugs demulcents and shoots the inflamed tissue of respiratory air-way's mucosa and gives symptomatic relief from dry cough.

Lozenges, Linctuces, glycerine, Liquorice

Expectorants (Mucokinetics) These drugs increase the bronchial secretion or decrease its viscosity → improve facilitation of its removal by coughing.

(a) Bronchial secretion enhancer: Sod. or Pot.citrate, Pot. Iodate, Guaiphensin, balsam of tolu, vasaka, Ammo. Chloride.
(b) Mucolytics: Bromhexine, Ambroxol, acetyl cysteine, Carbocysteine

Anti-tussives (Cough center suppressant)

These drugs raise the threshold of cough centre.

(a) Opiods: Codeine, Pholocodeine
(b) Nonopioids: Noscarpine, dextromethorphan, Chlophedianol.
(c) Antihistamines: Chlorpheniramine, Diphenhydramine, Promethazine

Adjuvant antitussives Salbutamol, Terbutaline

Bromhexine It is a derivative of vasicine obtained from *Adhatoda vasica.* It depolymerizes the mucopolysaccharides and decreases viscosity and improve mucociliary action→ removal of respiratory secretions.

Side effects: rhinorrhoea, lacrimation, gastric irritation.

Dextromethorphan: l-isomer→analgesic; d-isomer → antitussive action

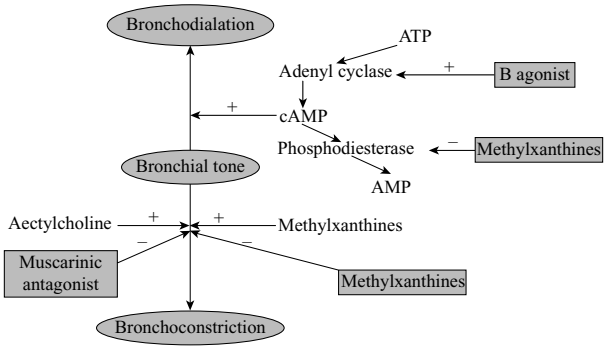
ASTHMA

Asthma is an inflammatory disease of the airways in which the mucous membrane and muscle layers of the bronchi become thickened and the mucous glands enlarge, reducing airflow in the lower respiratory tract.

Signs Severe episodic dyspnoea, shortness of breath, chest tightness, or burning with wheezing.

Drugs Used in Asthma

Drugs	Mechanism of Action	Adverse Effects
Bronchodialators *Sympathomimetics* Adrenaline, Ephedrine, Isoprenaline, Salbutamol, Terbutaline, Bambuterol, Salmeterol, Formoterol	Agonist action on β_2 receptors → activation of adenyl cyclase → increase intracellular level of cAMP → Bronchodialation	Cardiac stimulation: tachycardia, increase BP,
Methylxanthines Theophylline, Aminophylline, Theophylline ethanolate of piperazine	Bronchodilates via inhibition of phosphodiesterase (PDE) → increase cAMP and also by antagonism of adenosine (a bronchoconstrictor)	Gastrointestinal distress, abdominal pain, nervousness, anxiety, insomnia, high dose produces arrhythmia
Anticholinergics Atropine methonitrate, Ipratropium bromide, Tiotropium bromide	Blockade of M_3 receptors in bronchial muscles → inhibit IP_3/DAG Pathway → decreases intracellular level of Ca^{2+} → Bronchodialation.	Dry mouth, bad taste, nervousness
Leukotriene antagonists		



Drugs	Mechanism of Action	Adverse Effects
Montelukast, Zafirlukast, Zileuton	Antgonistic action on LT_1 receptors → prevent from leukotriene mediated bronchoconstriction and recruitment of eosinophils. Zileuton: 5- LOX inbitors → blocks LTC_4/D_4 as well as LTB_4	Allergic granulomatous angiitis (Churg Strauss syndrome)
Mast cell stabilizers Sodium cromoglycate, Nedocromil, Ketotifen (H_1 antagonist)	Inhibits degranulation of mast cells → inhibits release of inflammatory mediators PGs, LTs, PAF, interlukins etc.	Bronchospsm, throat irritation and cough
Corticosteroids Hydrocortisone, Prednisolone, Beclomethasone dipropionate, Budesonide, Flunisolide	After the penetration of cell membrane, binds with cytoplasmic receptors → receptor complex migrate into the nucleus and bind with chromatin → transcription of specific m RNA → immunosuppression (Cell mediated immunity suppression)	Hoarseness of voice, dyspnea, sore throat, asymptomatic or symptomatic oropharyngeal candidasis.

Adrenaline and Ephedrine: $\alpha+\beta_1+\beta_2$ receptor agonist

- Isoprenaline: only $\beta_1+\beta_2$ receptor agonist
- Albuterol, Levalbuterol, Pirbuterol and Terbutaline are rapid acting β_2 receptor agonist and used in prevent or treat acute bronchospasm.
- Levalbuterol is R-enantiomer of Albuterol, is claimed to less cardiac side effect.
- Salmeterol and Formeterol are slower and longer acting β_2 receptor agonist useful in preventing nocturnal asthmatic attack.
- Bambuterol is the prodrug of (Biscarbamatmate ester) Terbutaline.

EICOSANOIDS

These are 20 carbon unsaturated fatty acids derivatives including Prostaglandins, Leukotrienes and Thromoxanes. These all are inflammatory mediators.

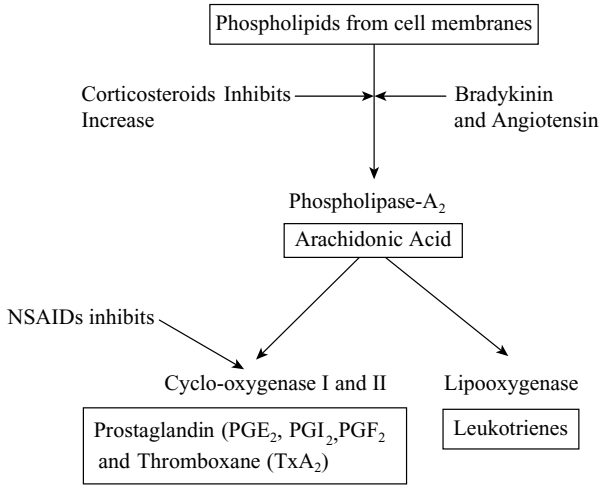


Figure 6.1 Phospholipids from cell membranes

Prostaglandins

Prostaglandins ligate is a sub-family of cell surface seven-transmembrane receptors, G-protein-coupled receptors.

Type of PG	Receptor	Function
PGI_2	IP	Vasodilation, Inhibits platelet aggregation, bronchodilatation
	EP_1	Bronchoconstriction, GI tract smooth muscle contraction
	EP_2	Bronchodilatation, GI tract smooth muscle relaxation, vasodilatation
PGE_2	EP_2	Bronchodilatation, GI tract smooth muscle relaxation, vasodilatation
	EP_3	↓ Gastric acid secretion ↑ gastric mucus secretion uterus contraction (when pregnant) GI tract smooth muscle contraction lipolysis inhibition ↑ autonomic neurotransmitters ↑ platelet response to their agonists and ↑ atherothrombosis in vivo
$PGF_{2\alpha}$	FP	Uterus contraction bronchoconstriction
	Unspecified	Hyperalgesia pyrogenic

Prostaglandin Antagonists

- NSAIDs (inhibit cyclooxygenase I and II)
- Corticosteroids (inhibit phospholipase A2 production)
- COX-2 selective inhibitors or coxibs.
- Cyclopentenone prostaglandins may play a role in inhibiting inflammation.

Clinical Uses of Prostaglandins

Therapeutic Abortion	PGE_1 Misoprostol with mifepristone (a progesterone antagonist)
Gastric cytoprotection (Gastric ulcer)	PGE_1 Misoprostol
Impotence	PGE_1 Alprostadil
Maintenance of patent Ductus arteriosus	PGE_1 Alprostadil
Pulmonary Hypertension	PGI_2 epoprostenol (Flolan)

Agents	Number of Peptide
Angiotensin I and Kallidin	Deca peptide
Angiotensin II	Octapeptide
Oxytocin, Vasopressin (Antidiuretic harmone ADH), Bradykinin	Nonapeptide

Leukotrienes

- **Leukotrienes** are fatty molecules of the immune system that contribute to inflammation in asthma and allergic rhinitis. Leukotriene antagonists are used to treat these diseases.
- Leukotrienes are naturally produced eicosanoid lipid mediators.
- Leukotrienes are produced in the body from arachidonic acid by the enzyme 5-lipoxygenase.

Examples of leukotrienes are LTA_4, LTB_4, LTC_4, LTD_4, LTE_4, and LTF_4, LTC4, LTD4 and LTE4 are often called **cysteinyl leukotrienes** due to the presence of the amino acid cysteine in their structure.

Functions

- Leukotrienes act principally on a subfamily of G protein-coupled receptors. They may also act upon peroxisome proliferator-activated receptors. Leukotrienes are involved in asthmatic and allergic reactions and act to sustain inflammatory reactions.
- Leukotrienes are very important agents in the inflammatory response. Some leukotrienes such as LTB4 have

a chemotactic effect on migrating neutrophils, and as such help to bring the necessary cells to the tissue. Leukotrienes also have a powerful effect in bronchoconstriction and increase vascular permeability.

Leukotrienes in Asthma

Leukotrienes contribute to the pathophysiology of asthma, causing or potentiating the following symptoms:

- airflow obstruction
- increased secretion of mucus
- mucosal accumulation
- bronchoconstriction
- infiltration of inflammatory cells in the airway wall
- A **leukotriene antagonist** (sometimes referred to as a leukast) is a drug that inhibits leukotrienes, which are fatty compounds produced by the immune system that cause inflammation in asthma and bronchitis, and constrict airways.
- Leukotriene inhibitors (or modifiers), such as montelukast, zafirlukast and zileuton, are used to treat those diseases. They are less effective than corticosteroids and thus less preferred in the treatment of asthma.

There are two main approaches to block the actions of leukotrienes:

Inhibition of the 5-lipoxygenase pathway

Drugs such as zileuton block 5-lipoxygenase, inhibiting the synthetic pathway of leukotriene metabolism.

Antagonism of cysteinyl-leukotriene type 1 receptors

Montelukast and zafirlukast block the actions of cysteinyl leukotrienes at the CysLT1 receptor on target cells such as bronchial smooth muscle.

Platelet Activating Factor (PAF)

- Platelet-activating factor is a potent phospholipid activator and mediator of many leukocyte functions, including platelet aggregation, inflammation, and anaphylaxis.
- It is produced in response to specific stimuli by a variety of cell types, including, neutrophils, basophils, platelets, and endothelial cells.
- Like eicosanoids, it is not stored in cells but synthesized after stimulation.

Chemistry

- Its alkyl group is connected by an ether linkage at the C1 carbon to a sixteen carbon chain.
- The acyl group at the C2 carbon is an acetate unit (as opposed to a fatty acid) whose short length increases the solubility of PAF, allowing it to function as a soluble signal messenger.
- The C3 has a phosphocholine head group, just like standard phosphatidylcholine.

Function

- It is an important mediator of bronchoconstriction.
- It causes platelets to aggregate and blood vessels to dilate. Thus it is important to the process of hemostasis.
- PAF antagonist-Ginkolide-B

E-Drug Actions on 5-Hydroxytryptamine (Serotonin) 5HT Receptors

- All serotonin receptors are G protein couple receptors, except to $5HT_3$

  $\uparrow$ cAMP $\rightarrow$ 5 HT_4, 5 HT_6, and 5 HT_7

  $\downarrow$ cAMP$\rightarrow$ 5 HT_1

  IP_3/DAG $\rightarrow$ **5 HT_2**

  Lignad gated ion channels: $5HT_3$
- **$5HTI_{(A-G)}$**

  Found in the CNS (usually inhibitory) and smooth muscle (excitatory or inhibitory).

Buspirone

Partial agonist at 5HTIA receptors $\rightarrow$ anxiolytic (generalized anxiety disorder [GAD]).

- **$5HT_{1D}$**

  Sumatriptan: Agonist at $5H_{1D}$, receptors in cerebral vessels-used in migraine pain.

  Adverse effects of "triptansn-possible asthenia", chest or throat pressure or pain
- **$5HT_2$**

  Found in CNS (excitatory). In periphery, activation $\rightarrow$ vasodilation, contraction of GI, Bronchial, and uterine smooth muscle, and platelet aggregation.

Olanzapine

Antagonist at $5HT_{2A}$ receptors in CNS $\rightarrow\downarrow$ symptoms of psychosis and newer antipsychotics.

Cyproheptadine

$5HT_2$ antagonists used in carcinoid, other GI tumors, and post gastrectomy. Also used for anorexia nervosa. Has marked H_1-blocking action.

- $5HT_3$

  Found in area postrema, peripheral sensory and enteric nerves. Activation opens ion channels (no second messengers).

Ondansetron and "setrons"

Antagonists $\rightarrow\downarrow$ emesis in chemotherapy and radiation and postoperatively.

- $5HT_4$

  Found in GI smooth muscle and myenteric nerves.

Note

Key points about density

- **Cisapride-**Receptor activator → prokinetic in GERD, but a cardiac K^+ channel blocker → arrhythmias (contraindicated in use)
- Allopurinol is ahypoxanthine analogue drug which when used in the Gout inhibts the xanthin oxidase enzyme and reduces the uric acid synthesis
- Lithium carbonate and valproate and carbamazepine are drugs used as anti manic drug.
- Buspirone is a drug used as anxiolytic agent.

Multiple Choice Questions

1. Zafirlukast is a
(a) Selective COX-2 inhibitor
(b) Leukotriene antagonist
(c) PGI_2 antagonist
(d) Selective LOX inhibitor

2. All of the following is prodrug,
(a) Piroxicam (b) Sulindac
(c) Naproxen (d) Ketorolac

3. All of the following is mast cell stabilizer except
(a) Sodium cromoglycate
(b) Nedocromil
(c) Ketotifen
(d) Zileuton

4. Following statements are true except
(a) Pharyngeal demulcent shoots the inflamed tissue of respiratory airway's mucosa and gives symptomatic relief from dry cough
(b) Expectorant increases bronchial secretion or decrease viscosity to facilitate removing of cough
(c) Antitussives agent suppresses cough centre
(d) None of the above

5. Bromhexine
(a) Suppresses cough center
(b) Is pharyngeal demulcent
(c) Is mucolytics
(d) Both (b) and (c)

6. Following statements are true except
(a) Analgesic agents block the peripheral pain sensation which is induced by bradykinin, interlukins, etc.
(b) Antipyretic agents inhibit synthesis of prostaglandins and reduce body temperature
(c) Both (a) and (b)
(d) None of the above

7. Bronchitis means
(a) Inflammations of the lung parenchyma
(b) Inflammations of the bronchi
(c) Inflammations of the small bronchi and bronchioles
(d) Both (b) and (c)

8. In *H.influenzae* infection following antibiotic is preferred
(a) Amoxicillin (b) Cefuroxime
(c) Cefixime (d) Tetracycline

9. Acute pyelonephritis,
(a) Is a syndrome of dysuria and urgency which usually suggests infection restricted to the lower urinary tract
(b) Manifests the presence of at least 100000 bacteria per ml of urine
(c) Indicates acute infections of one or both kidney
(d) Is a particular type pathology of the kidney, which may or may not be due to the infections

10. In lower urinary tract infection which oral antibiotic is not used?
(a) Amoxicillin (b) Cefalexin
(c) Nitofurantoin (d) Tetracycline

11. All of the following antibiotics are contraindicated in pregnant women who suffer from pyelonephritis except
(a) Gentamicin (b) Ciprofloxacin
(c) Both (a) and (b) (d) None of the above

12. All of the following statements are false, except
(a) Gastric mucosal damage drugs increase prostaglandin synthesis and mucous secretion
(b) Anti-inflammatory agents stimulate inflammatory mediators like prostaglandin
(c) Both (a) and (b)
(d) None of the above

13. Chief mode of spread of *Vibrio* cholera is
(a) Food (b) Water
(c) Sea foods (d) Faecal–oral

14. All of following bacteria spread through food or water except,
(a) *Camphylobacter* (b) *Salmonella species*
(c) *Shigella* (d) *Vibrio cholera*

15. Which antibiotic is preferred in diarrhea?
(a) Ciprofloxacin (b) Metronidazole
(c) Erythromycin (d) All of the above

16. Which bacterial infection causes meningitis?
(a) *E.coli*
(b) Streptococci
(c) *Listeria monocytogenes*
(d) All of the above

17. In meningitis following symptoms is appear except,
(a) Sudden onset headache
(b) Neck stiffness
(c) Diarrhea
(d) Vomiting

18. A pregnant lady who is suffering from TB, the following drug is contraindicated.
(a) Streptomycin (b) Ethionamide
(c) Clofazimine (d) Kanamycin

19. Hepatitis has adverse effect on the following antitubercuous drugs except
(a) Isoniazide (b) Rifampicin
(c) Pyrazinamide (d) Ethambutol

20. BCG vaccine contains
(a) A live-attenuated strain derived from *M. bovis*
(b) A live-attenuated strain derived from *M. Africanum*
(c) A live-attenuated strain derived from *M. tuberculosis*
(d) A dead-attenuated strain derived from *M. Africanum*

21. BCG vaccines are given for the prevention of _____ disease
(a) Typhoid
(b) Malaria
(c) Tuberculosis infection
(d) Cholera

22. Endoscopy is generally used for the investigation of
(a) Urinary tract infection
(b) Peptic ulcer
(c) Cardiovascular block
(d) Meningitis infection

23. Crohn's disease affects _____ part.
(a) Gastrointestinal tract
(b) Kidney
(c) Lung
(d) Heart

24. Following drug(s) is/are the choice for treatment of inflammatory bowel disease,
(a) Sulfasalazine (b) Mesalazine
(c) Prednisolone (d) All of the above

25. Ursodeoxycholic acid is used in the treatment of
(a) Jaundice
(b) Urinary tract infection
(c) Malaria
(d) Gastrointestinal tract infection

ANSWER KEYS

1. (a)	**2.** (b)	**3.** (d)	**4.** (d)	**5.** (c)	**6.** (d)	**7.** (b)	**8.** (a)	**9.** (c)	**10.** (d)
11. (d)	**12.** (c)	**13.** (b)	**14.** (c)	**15.** (d)	**16.** (d)	**17.** (c)	**18.** (b)	**19.** (d)	**20.** (a)
21. (c)	**22.** (b)	**23.** (a)	**24.** (d)	**25.** (a)					

CHAPTER 7

DRUGS ACTING ON CARDIO-VASCULAR SYSTEM

ANTI HYPERTENSIVE DRUGS

Diuretics	Loop diuretics: bumetanide, ethacrynic acid, furosemide, torsemide Thiazide diuretics: Epitizide, Hydrochlorothiazide and chlorothiazide, bendroflumethiazide Thiazide-like diuretics: indapamide, chlorthalidone, metolazone Potassium-sparing diuretics: amiloride, triamterene, spironolactone
Adrenergic receptor antagonist	Beta-blockers: Atenolol, metoprolol, nadololoxprenolol, pindolol, propranolol, timolol Alpha-blockers: Doxazosin, phentolamine, phenoxybenzamine, prazosin(Fainting and Postural hypotension side effect, always taken at bed time), terazosin, tolazoline Mixed Alpha + Beta blockers: Bucindolol, carvedilol, labetalol
ACE inhibitors	Captopril, Enalpril, Fosinopril, Lisinopril, Quinapril, Ramipril, Benazepril (Drug persistent cough is common side effect of ACE inhbtors)
Angiotensin II receptor antagonist	Losartan, Candesartan, Irbesartan, olmesartan, valsartan, telmisartan
Calcium channel blockers	Dihydropyridines: the prototype agent in this group is nifedipine, a first generation dihydropyridine Second generation agents include isradipine, nicardipine, and felodipine. Amlodipine is considered a third generation dihydropyridine. Non-dihydropyridines: Diltiazem(Benzothiazipinederivatives), verapamil(Phenylalkylamine derivatives)
Centrally acting adrenergic drugs (Alpha-2 agonist)	Clonidine(Marked rise in BP side effect), , Alpha-methyldopa(Positive coombs test as hypersensitivity reaction), Guanfacine,
Vasodialators	Diazoxide(K channel opener), Hydralazine(through No generation)(Parenthesias, Lupus erythematous side effect), Sodium nitropruside(through No generation), Minoxidil (K channel opener)(in Male Balness or in alopecia Mainly used)
Aldosterone receptor antagonist	Spironolactone, eplerenone

Adrenergic neuron blockers	Guanethidine(Displace NA from storage granules and release NA is degraded by MAO) (Weakness is side effect), Reserpine(Inhibit granular uptake of Nor-adrenaline so NA is progressively degraded by Mono amino oxidase enzyme)(Suicidal tendency side effect)

DRUGS USED TO TREAT CHF

CHF is a condition in which the heart is unable to pump sufficient blood to meet the demand of body during rest or exercise. It is caused by:

- Weakness of myocardial muscles
- Bio-chemical defect (In-effective conversion of ATP and Creatnine phosphate) and Atheriosclerotic heart disease.

Drugs Used to Treat CHF

Vasodialator	ACE inhibitors-Captopril, Enalpril, Fosinopril, Lisinopril, Quinapril Hydralazine, Isosorbide, Minoxidil, Sodium nitroprusside
Diuretics	Bumetanide, Furosemide, Hydrochlorthiazide, Metolazone
Ionotropic agents	Cardiac Glycosides-Digitoxin, Digoxin (Hypokalemia as side effect) β-adrenergic agonist-Dobutamine Phosphodiesterase III inhibitors-Amrinone, Milrinone

Inotropic Agents

An **inotrope** is an agent that alters the force or energy of muscular contractions.

- Positive inotropic agents increase myocardial contractility, and are used to support cardiac function in conditions such as decompensated congestive heart failure, cardiogenic shock, septic shock, myocardial infarction, cardiomyopathy, etc.

Cardiac glycosides	Digoxin, Digitoxin
Catecholamines	Dopamine, Dobutamine, Epinephrine (adrenaline), Isoprenaline (isoproterenol) Norepinephrine (noradrenaline)
Phosphodiesterase inhibitors	Milrinone and Amrinone, Theophylline

- Negative inotropic agents decrease myocardial contractility, and are used to decrease cardiac workload in conditions such as angina. While negative inotropism may precipitate or exacerbate heart failure, certain beta blockers (e.g. carvedilol, bisoprolol and metoprolol) have been shown to reduce morbidity and mortality in congestive heart failure.

Beta blockers	
Calcium channel blockers	Diltiazem, Verapamil
Class IA antiarrhythmics	Quinidine, Procainamide, disopyramide
Class IB Phenytoin	Mexiletine
Class IC antiarrhythmics	Flecainide

Mechanism of cardiac glycosides

- Normally, sodium-potassium pumps in the membrane of cells (cardiac myocytes) causes potassium ions influx and sodium ions efflux. Cardiac glycosides inhibit this, so that sodium cannot be extruded: intracellular sodium concentration therefore increases.
- A second membrane ion exchanger is responsible for 'pumping' calcium ions out of the cell and sodium ions in (3Na/Ca); raised intracellular sodium levels inhibit this pump, so calcium ions are not extruded and will also begin to build up inside the cell.
- Increased cytoplasmic calcium concentrations cause increased calcium uptake into the sarcoplasmic reticulum. Raised calcium stores in the SR allow for greater calcium release on stimulation, so the myocyte can achieve faster and more powerful contraction by cross-bridge cycling.
- Binding of Cardiac Glycoside to Na-K ATPase is slow, and also, after binding, intracellular Calcium increases gradually. Thus, delayed action of Digitalis (even on i.v. injection).
- Raised extracellular potassium decreases binding of cardiac glycosideto Na-K ATPase. So, increased toxicity of these drugs in the presence of Hypokalemia.
- FAB antibodies used to reverse the toxicity of digitalis.

Type of agent	**Effect on Preload** (Cardiac-filling pressure) **and After load** (Pressure overcome by the heart to pump blood into circulation)
Calcium Channel Blocker, Directvasodialator (eg Hydralazine), Prazocin (Alpha 1 blocker)	Mainly decrease After load
Nitrate and Diuretics	Mainly decrease Pre load
Sodium nitroprusside, ACE inhibitors and Vasodilators	Decrease Pre and After load

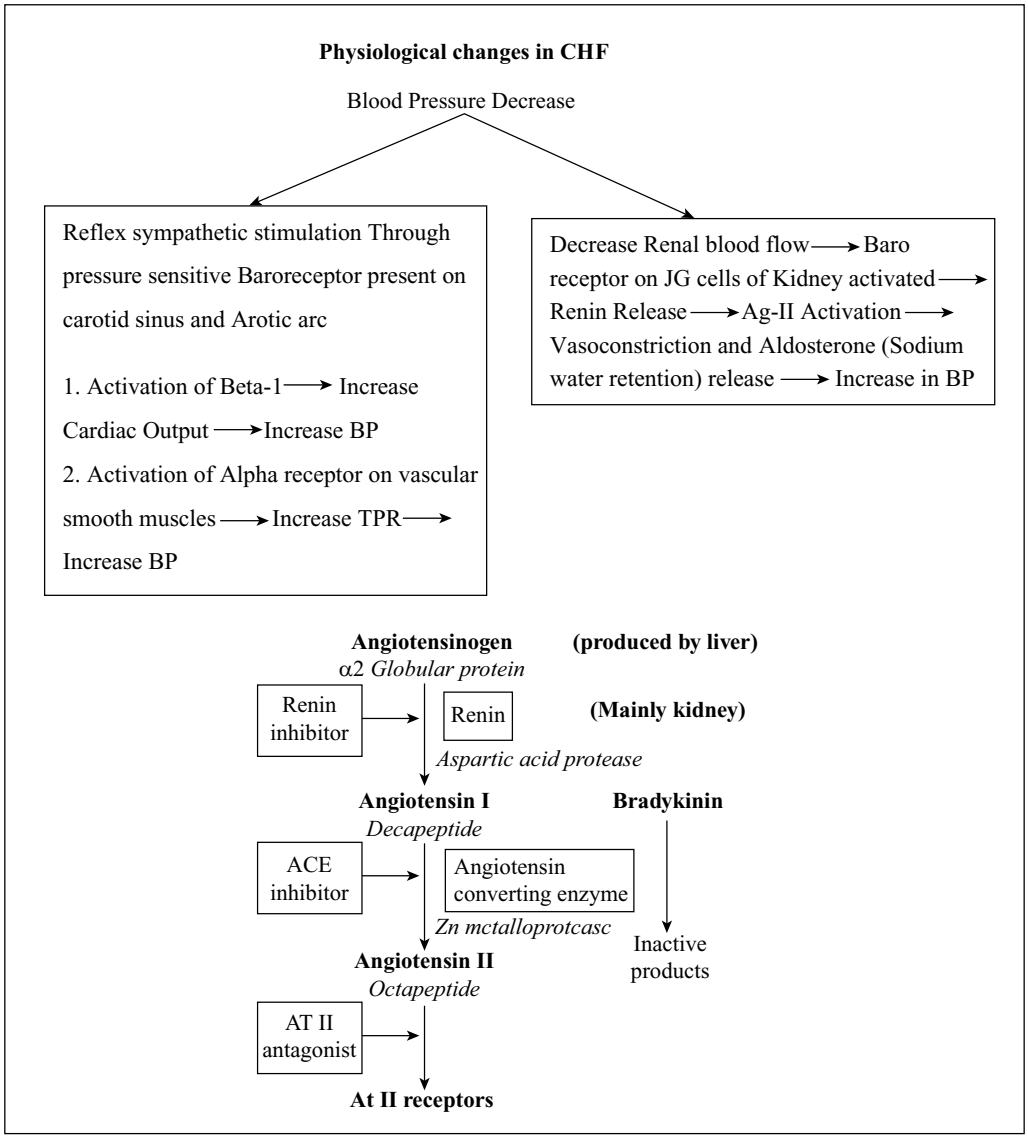


Figure 7.1 Physiological changes in CHF

Calcium-channel Blockers

Cardiac effects

Decrease contractility (negative inotropy), Decrease heartrate (negative chronotropy), Decrease conduction velocity (negative dromotropy)

Vascular effects

Smooth muscle relaxation (vasodilation)

Mechanism of action

Inhibit passage of calcium through the voltage gated L-type (for Large/Long-lasting current) calcium channel on vascular smooth muscle cells and cardiac myocytes, reducing calcium availability for muscle contraction. Note that an inhibitor of the T-type (Transient current) cardiac calcium channel, MIBEFRADIL, has recently been terminated due to unacceptable drug interactions. Ion channel blockade explains the observed:

- Peripheral vasodilatation
- Negative inotropic and negative chronotropic effects

Adverse effects

- Flushing
- Headache
- Palpitations-reflecting the reflex tachycardia in response to vasodilatation.
- May worsen heart failure due to their negative inotropic effect

Therapeutic Indications

Hypertension

- By causing vascular smooth muscle relaxation, CCBs decrease systemic vascular resistance, which lowers arterial blood pressure. These drugs primarily affect arterial resistance vessels, with only minimal effects on venous capacitance vessels.

Angina

- The anti-anginal effects of CCBs are derived from their vasodilator and cardiodepressant actions. Systemic vasodilation reduces arterial pressure, which reduces ventricular afterload (wall stress) thereby decreasing oxygen demand. The more cardioselective CCBs (verapamil and diltiazem) decrease heart rate and contractility, which leads to a reduction in myocardial oxygen demand, which makes them excellent antianginal drugs. CCBs can also dilate coronary arteries and prevent or reverse coronary vasospasm (as occurs in Printzmetal's variant angina), thereby increasing oxygen supply to the myocardium.

Arrhythmias

- The antiarrhythmic properties (Class IV antiarrhythmics) of CCBs are related to their ability to decrease the firing rate of aberrant pacemaker sites within the heart, but more importantly are related to their ability to decrease conduction velocity and prolong repolarization, especially at the atrioventricular node. This latter action at the atrioventricular node helps to block reentry mechanisms, which can cause supraventricular tachycardia.

Different Classes of Calcium-channel Blockers

- There are three classes of CCBs. They differ not only in their basic chemical structure, but also in their relative selectivity towards cardiac versus vascular L-type calcium channels.
- The most smooth muscle selective class of CCBs are the **dihydropyridines**. Because of their high vascular selectivity, these drugs are primarily used to reduce systemic vascular resistance and arterial pressure, and therefore are primarily used to treat hypertension. They are not, however, generally used to treat angina because their powerful systemic vasodilator and pressure lowering effects can lead to reflex cardiac stimulation (tachycardia and increased inotropy), which can dramatically increase myocardial oxygen demand.

Non-dihydropyridines

- **Verapamil** (phenylalkylamine class), is relatively selective for the myocardium, and is less effective as a systemic vasodilator drug. This drug has a very important role in treating angina (by reducing myocardial oxygen demand and reversing coronary vasospasm) and arrhythmias.
- **Diltiazem** (benzothiazepine class) is intermediate between verapamil and dihydropyridines in its selectivity for vascular calcium channels. By having both cardiac depressant and vasodilator actions, diltiazem is able to reduce arterial pressure without producing the same degree of reflex cardiac stimulation caused by dihydropyridines.

ANTI-ANGINAL DRUGS

- An anti-anginal is any drug used in the treatment of *angina pectoris*, a symptom of ischaemic heart disease.

- Angina results from a reduction in the oxygen supply/demand ratio.

Rationale for Treating Angina

- Increase Oxygen Delivery: 1.Coronary vasodilators 2.Anti-thrombotic drugs
- Decrease Oxygen Demand: 1.Vasodilators *(reduce afterload and preload)* 2.Cardiac depressants *(reduce heart rate and contractility)*

Drugs that block coronary vasospasm (coronary vasodilators) or inhibit clot formation are used to treat variant and unstable angina, respectively. These drugs act by increasing coronary blood flow and oxygen supply, or by preventing vasospasm and clot formation, and associated decreases in blood flow.

Drugs that reduce myocardial oxygen demand are commonly used to prevent and treat episodes of ischemic pain associated with fixed stenotic lesions (i.e., , chronic stable angina). Some of these drugs reduce oxygen demand by decreasing heart rate (decreased chronotropy) and contractility (decreased inotropy), while other drugs reduce afterload and or preload on the heart. Afterload and preload reducing drugs act by dilating peripheral arteries and veins.

Nitrates

- Nitrates cause vasodilation of the venous capacitance vessels by simulating the endothelium-derived relaxing factor (EDRF).
- Used to relieve both exertional and vasospastic angina by allowing venous pooling, reducing the pressure in the ventricles and so reducing wall tension and oxygen requirements in the heart.
- Agents include nitroglycerin (glyceryl trinitrate) or pentaerythritol tetranitrate.

Beta Blockers

- Beta blockers are used in the prophylaxis of exertional angina by reducing the work. The heart is allowed to perform below the level that would provoke an angina attack.
- They cannot be used in vasospastic angina and can precipitate heart failure.
- Agents include either cardioselectives such as acebutolol or metoprolol, or non-cardioselectives such as oxprenolol or sotalol.

Calcium Channel Blockers

Calcium ion (Ca++) antagonists (Calcium channel blockers) are used in the treatment of both exertional and vasospastic angina.

- Class I agents have the most potent negative inotropic effect and may cause heart failure.
- Class II agents do not depress conduction or contractility.
- Class III agent has negligible inotropic effect and causes almost no reflex tachycardia.

Examples include Class I agents (*e.g.*, verapamil), Class II agents (*e.g.*, amlodipine, nifedipine), or the Class III agent diltiazem.

	Peripheral and coronary vasodilation	Depression of cardiac contractility	Depression of SA node	Depression of AV node
Nifedipine	+++++	+	+	0
Diltiazem	+++	++	+++++	++++
Verapamil	++++	++++	+++++	+++++

Dihydropiridines have minimal effect on cardiac conduction or heart rate, while they have potent actions as arteriolar vasodilators. This class of drugs can cause reflex tachycardia when peripheral vasodilation is marked.

On the other hand, **verapamil and diltiazem** slow AV conduction and decrease SA node automaticity, they also decrease heart rate. Diltiazem is used in the treatment of variant angina because of its coronary antispasmodic properties.

ANTI-ARRHYTHMIC AGENT

Antiarrhythmic agents are used to suppress abnormal rhythms of the heart (cardiac arrhythmias), such as atrial fibrillation, atrial flutter, ventricular tachycardia, and ventricular fibrillation.

Phase of Cardiac Action Potential

Phase-O Influx of sodium occurs at threshold potential and depolarization occur.

Phase-1 Initiation of influx calcium occurs.

Phase-2–Calcium influx occurs and contraction takes place.

Phase-3-Potassuim efflux occurs and repolarization occurs and resting potential take place.

Phase-4–slowly depolarization occurs and reaches thresold potential.

There are five main classes in the Singh Vaughan Williams classification of antiarrhythmic agents:

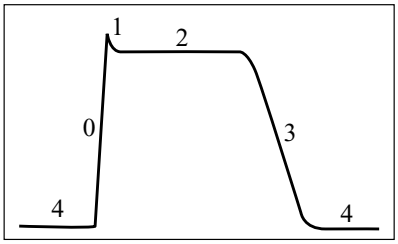


Figure 7.2 Phase of Cardiac Action Potential

Anti-arrhythmic Drugs

Class	Known as	Examples	Mechanism	Clinical uses
Ia	fast-channel blockers	• Quinidine • Procainamide • Disopyramide	(Na^+) channel block (intermediate association/ dissociation)	Ventricular arrhythmias Prevention of paroxysmal recurrent atrial fibrillation (triggered by vagal overactivity), *procainamide in Wolff-Parkinson-White syndrome
Ib		• Lidocaine • Phenytoin • Mexiletine	(Na^+) channel block (fast association/dissociation)	Treatment and prevention during and immediately after myocardial infarction
Ic		• Flecainide • Propafenone • Moricizine	(Na^+) channel block (slow association/dissociation)	Prevents paroxysmal atrial fibrillation Treats recurrent tachyarrhythmias of abnormal conduction system.
II	Beta-blockers	• Propranolol • Esmolol • Timolol • Metoprolol • Atenolol • Bisoprolol	beta blocking Propranolol also shows some class I action	Decreases myocardial infarction mortality Prevents recurrence of tachyarrhythmias
III		• Amiodarone • Sotalol • Ibutilide • Dofetilide	K^+ channel blocker Sotalol is also a beta blocker	In Wolff-Parkinson-White syndrome Sotalol-ventricular tachycardias and atrial fibrillation Ibutilide-atrial flutter and atrial fibrillation
IV	slow-channel blockers	• Verapamil • Diltiazem	Ca^{2+} channel blocker	Prevents recurrence of paroxysmal supraventricular tachycardia, Reduce ventricular rate in patients with atrial fibrillation
V		• Adenosine • Digoxin	Work by other or unknown mechanisms (Direct nodal inhibition)	Used in supraventricular arrhythmias, especially in Heart Failure with AtrialFibrillation, Contraindicated in ventricular arrhythmias.

Class I Agents

- The class I antiarrhythmic agents interfere with the sodium channel.
- Class I agents are called Membrane Stabilizing agents. They decrease the excitogenicity of the plasma membrane.
- Class I agents are divided into three groups (1a, 1b and 1c) based upon their effect on the length of the action potential.
- 1a lengthens the action potential (right shift)
- 1b shortens the action potential (left shift)
- 1c does not significantly affect the action potential (no shift)

Class II Agents

- These agents are conventional beta blockers. They act by blocking the effects of catecholamines at the β_1-adrenergic receptors, thereby decreasing sympathetic activity on the heart.
- These agents are particularly useful in the treatment of supraventricular tachycardias. They decrease conduction through the AV node.

Class III Agents

Class III agents predominantly block the potassium channels, thereby prolonging repolarization.Since these agents do not affect the sodium channel, conduction velocity is not decreased.

Class IV Agents

Class IV agents are slow calcium channel blockers. They decrease conduction through the AV node, and shorten phase two (the plateau) of the cardiac action potential. They thus reduce the contractility of the heart, so may be inappropriate in heart failure. However, in contrast to beta blockers, they allow the body to retain adrenergic control of heart rate and contractility.

Other Agents ("Class V")

Agents include

- Digoxin, which decreases conduction of electrical impulses through the AV node and increases vagal activity via its central action on the central nervous system.
- Adenosine
- Magnesium sulfate, which has been used for torsades de pointes.

Type of Arrhythmias	Drug of Choice
PSVT(Paroxysmal supra ventricular tachycardia)	Adenosine
Atrial flutter	Cardioversion
Atrial Fibrillation	Cardioversion
Atrial extra systole	Quinidine
Ventricular extrasystole	Due to MI------- Lignocaine Due to Digitalis--- Lignocaine
Ventricular tachycardia	Ligocaine
Wolff-Parkinson-White syndrome	Cardioversion

Digitalis Toxicity	Drug of Choice for treatment
Tachy arrhythmia	KCl Intravenous Injection
ventricular Tachy arrhythmia	Lignocaine Intravenous Injection.
Supra ventricular Tachy arrhythmia	Propranolol Intravenous Injection
AV block	Atropine Intravenous Injection

Digitoxin	Digoxin
Lipid soluble	Relatively Polar
Slow onset of action	Rapid onset of action
More plasma protein binding (PPB)	Less plasma protein binding (PPB)
Half life is more	Comparatively less Plasma Half-life
Metabolism-mainly in liver and converts into digoxin. Partly undergoes in entero-hepatic circulation.	Excreted unchanged in urine

DRUGS AFFECTING COAGULATION, BLEEDING TIME AND THROMBOSIS

Blood is a liquid connective tissue which provides one of the means of communication between the cells of different parts of the body and the external environment, E.g., it carries: oxygen, carbon dioxide, hormones, clotting factors and protective substances, e.g. antibodies

Blood Clotting Factors and Clotting Events

I. Fibrinogen
II. Prothrombin
III. Tissue factor (thromboplastin)
IV. Calcium (Ca^{2+})
V. Labile factor, proaccelerin, Ac–globulin
VII. Stable factor, proconvertin
VIII. Antihaemophilic globulin (AHG), antihaemophilic factor A
IX. Christmas factor, plasma thromboplastin component (PTA), antihaemophilic factor B
X. Stuart Prower factor
XI. Plasma thromboplastin antecedent (PTA), antihaemophilic factor C
XII. Hageman factor
XIII. Fibrin stabilising factor

**There is no Factor VI*

*Vitamin K is essential for synthesis of Factors II, VII, IX and X

Function of vitamin K Synthesis of clotting factor II, VII, IX and X and make the —carboxylation of these which is essential for the ability $Ca^{2+}$and to get bound to phospholipid surface → further cascade of coagulation.

Deficiency of vitamin K Due to liver disease, obstructive jaundice, malabsorption, long term antimicrobial therapy E.g., Tetracyclines, —lactams etc.

Local haemostatics (Synaptics)

- Substances used to stop bleeding from a local approachable site; E.g., tooth pocket, open wounds etc.
- Thrombin
- Fibrin
- Russels viper venom
- Vasoconstriction: 1% adrenaline
- Astringent: tannic acid

Anticoagulating agents Prevents blood clotting in vitro or in vivo or both

1. Used in vitro:
   a. Organic acid: Heparin
   b. Organic acid salt: EDTA, Sod. citrate, sod. oxalate
2. Used in vivo:

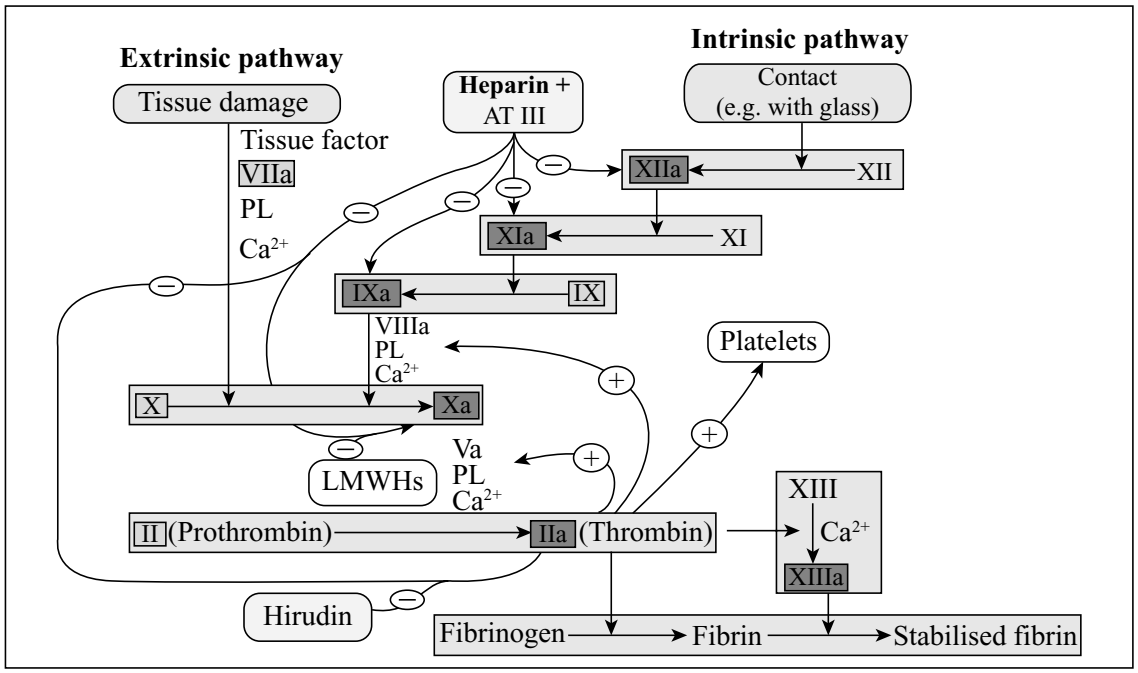


Figure 7.3 Blood Clotting Factors and Clotting Events

Heparin

Heparinoids Heparan sulfate, Danaproid, Lepirudin, Ancord

Oral anti–coagulants:

Coumarins Warfarin, Acenocumarol

Indendione phenindione.

Features	Heparin	Warfarin
Chemical nature	Sulfated polysaccharide of D–glucosamine–D–glucuronic acid, electronegative	Coumarine derivative
Kinetics	Given parenterally (IV, SC), hepatic and reticuloendothelial elimination, half-life = 2 h, no placental access and cross BBB	Given orally, 98% protein bound, liver metabolism, half-life = 30+ h, placental access
Mechanism	↑ Activity of antithrombin III→ Resulting in the inactivation of factors IIa and Xa. Actions in vivo and in vitro.	↓ The plasma level of K–dependent factors II, VII, IX, X active form → coumarins prevent generation of active hydroquinone form of vit. K and γ-carboxylation→ incapable binding with Ca^{2+} and block further cascade of clotting; In vivo effects only.
Antagonist	Protamine sulfate	Vit. K
Use	Rapid anticoagulation (intensive) for thromboses, emboli, unstable angina, disseminated intravascular coagulation (DIC), open-heart surgery, etc. Drug of choice during pregnancy	Longer–term anticoagulation (controlled) for thromboses, emboli, post-MI, heart valve damage, atrial arrhythmias, etc.
Adverse effect	***Bleeding**, osteoporosis, heparin–induced thrombocytopenia (HIT), ***hypersensitivty**	Warfarin: alopecia, dermatitis, diarrhea **teratogenic (bone dysmorphogenesis)* Acenocumarol: oral ulceration, GIT disturbances, dermatitis, alopecia

- Aspirin (salicylates) displace the warfarin from its protein binding site and also gives antiplatelet action → may include toxicity of warfarin or causes hazardous bleeding.
- Oral contraceptives reduce the effect of warfarin by enhancing the blood level of clotting factor.

Danaparoid (Heparan sulfate) A heparin of different structure, it may be safer in hypersensitivity to heparin.

Phenindione Used as oral anticoagulant. It produce serious toxic effecs; E.g., rashes, fever, hepatitis, nephropathy, *agranulocytosis* orange urine.

Low-molecular–weight (LMW) Heparins (e.g., enoxaparin) have potential advantage of longer half-life, less thrombocytopenia, and possibly enhanced activity against factor Xa.

Direct thrombin inhibitors

Hirudin and bivalirudin These are bivalent DTIs that bind at both the catalytic or active site of thrombin as well as at a substrate recognition site → prevents formation of fibrin and cotting of blood.

Argatroban is a small molecule thrombin inhibitor that is FDA approved for use in patients with heparin–induced thrombocytopenia (HIT) with or without thrombosis and coronary angioplasty in patients with HIT.

Fibrinolytic or Thrombolytics

These agents lyse thrombin by catalysing the formation of the endogenous fibrinolytic plasmin (a serine protease) from its precursor, plasminogen.

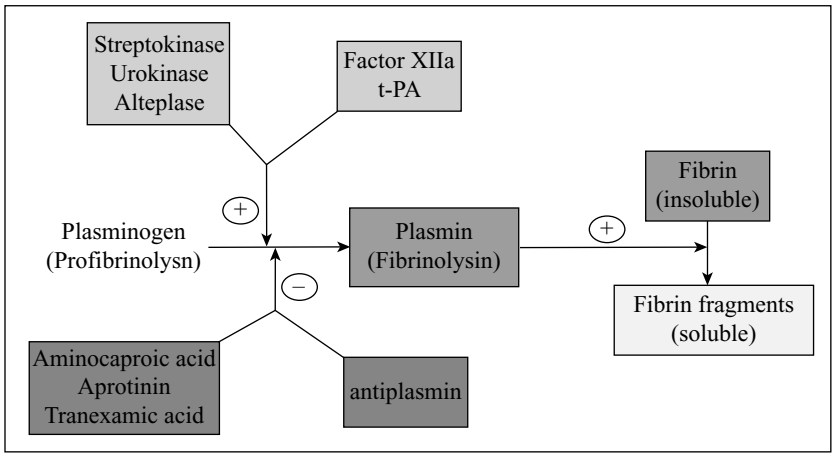


Figure 7.4 Heparin process

Thrombolytics

Features	Streptokinase	Urokinae	Alteplase
Source	β–haemolytic *Streptococci group C.*	Enzyme isolated from human urine	By DNA recombinant technology from human tissue culture
Action	Activator complex formed with circulatory plasminogen	Activates plasminogen directly	Activates plasminogen in the gel phase
Adverse effect	Hypersensitivity, anaphylactic reaction	Fever and hypotension	Nausea and hypotension
Uses	Acute myocardial infection, deep vein thrombosis, pulmonary embolism		
	Throbolytic therapy contraindicated in renal trauma, surgery, biopsies, aneurysm, beeding disorder etc.		

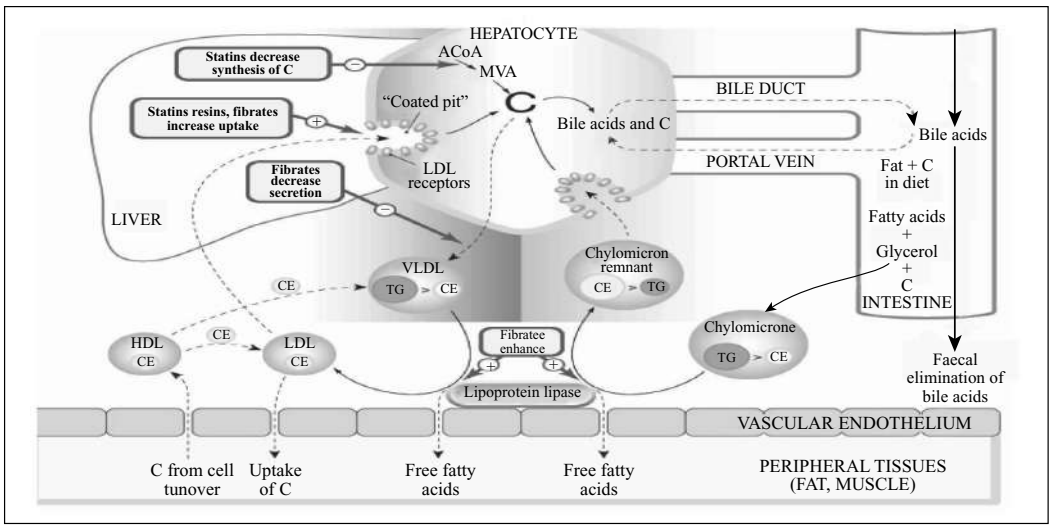


Figure 7.5 Blood Clotting Factors and Clotting Events

Anti-fibrinolytic agents

Clot formation:

- Platelet adhesion to site of vascular injury
- Activation of platelets by factors that include TXA, ADP, collagen, 5HT, and thrombin
- ↑ expression of glycoprotein II_b/III_a receptors

Aggregation of platelets by a cross-linking reaction due to fibrinogen binding to glycoprotein IIb/IIIIa receptors.

Drugs	MOA	Adverse effects	Uses
Aspirin	COX inhibition → ↓ TXA_2 → ↓ platelete aggregation at low dose		Angina pectoris, cerbro-vascular disease, coronary bypass
Dipyridam-ole	Inhibt the PDE → ↑ cAMP → potentiate to PGI_2 → ↓ platelete aggregation		implants, venous throboembolism
Abciximab	It is a monoclonal antibody and acts against glycoprotein II_b/III_a receptors.	**haemorrhage thrombocy-topenia*	

AGENTS USED IN HYPERLIPIDEMIA

- A number of metabolic disorders that involve elevations in levels of any of the lipoprotein species are thus termed hyperlipoproteinemias or hyperlipidemias.
- Lipids and cholesterol are transported through the bloodstream as macromolecular complexes of lipid and protein known as lipoproteins. These consist of a central core of hydrophobic lipid (including triglycerides and cholesteryl esters) encased in a hydrophilic coat of polar phospholipid, free cholesterol and apolipoprotein
- Atherosclerosis is the deposition of plaque of low desity (LDL), intermedidate density (IDL), very low density (VLDL) lipoproteins with foam cells on the artery wall → blockage/narrowing the lumen of atery → reduce oxygen and blood supply to the tissues.

High-density lipoproteins (HDL) exert several antiatherogenic effects. They participate in pathways that retrieve cholesterol from the artery wall and inhibit the oxidation of atherogenic lipoproteins.

C =cholesterol; CE= cholesteryl ester; HMG–CoA reductase, 3–hydroxy–3–methylglutaryl–coenzyme A reductase; MVA, mevalonate; TG= triglyceride.

Rationale Use of Hypolipidemic Drugs

Decrease the LDL, IDL, VLDL and ↑ the HDL blood plasma level → cardiovascular complication with due to Atherosclerosis.

Hypolipdemic Drugs

1. Statins: Lovastatin, Simvastatin, Pravastatin, atorvastatin, Fluvastatin, Rosuvastatin
2. Resins: Cholestyramine, Colestipol
3. Fibrates: Clofibrate, Gemfibrozil, Benzafibrate, denofibrate
4. Nicotinic acid–Niacin
5. Others: Probucol, Gugulipid, Ezetimibe

Statins

MOA These drugs inhibt the HMG–CoA reductase enzyme and block the synthesis of cholesterol.

- Effect– ↓ LDL and HDL ↑
- Atorvastatin is the most potent statin.
- Statins should be administered at bed time.

Adverse effects

****Myopathy* *myalgia;* headache, nausea, sleep disturbances; livertoxicity due to elevation of aminotransferase level.

Resins

MOA The bile-acid sequestrants are highly positively charged and bind negatively charged bile acids → preventing their reabsorption from the GI tract and increase its fecal excretion → indirectly enhance the liver cholesterol metabolism/utilization and ↑ LDL receptor expression.

Adverse effect Bloating, constipation, steatorrhoea, deficiency of fat soluble vitamin E; hyperchloremic acidosis.

Interaction ↓ absorption of digoxin, thiazides, tetracyclines, warfarin, and vitamin K.

*They increase triglyceride levels; severe hypertriglyceridemia is a contraindication to the use of cholestyramine

and colestipol.

Drugs	MOA	Adverse effects
Gemfirozil	Stimulates the PPARα receptor → increase the synthesis of lipoprotein lipase and oxidation of fatty acid	*Loose motion* (common); rashes, body ache, eosinophilia, impotance, blurred vision. Myalgia. *Gemfibrozil+ statins → severe myopathy
Niacin	Reduces the VLDL in liver by inhibiting triglyceride synthesis, ↓ liolysis in adepocytes and increase activity of lipoprotein lipase → plasma clearance of TGs	Dyspepsia; Hyperuricaemia–gout; Hyperglycaemia (should not be used in diabetics).
Probucol	Inhibit the oxidation of LDL	
Ezetimibe	Inhibits dietary cholesterol absorption by enterocytes in the small intestine.	*allergic reactions,* myopathy

Plama Expander Higher molecular weight substances which exert colloidal osmotic pressure, and when infused i.e., retains fluid in the vascular compartment.

1. Human albumin: obtained from pools of human plasma
2. Dextran: polysaccharide obtained from sugar beat. dextran70 (MW 70000) is more commonly used preparation; dextran–40.
3. *Polygeline: MW 30000 and exert oncotic pressure (Colloid osmotic pressure) similar to albumin and its not antigenic.
4. Hydroxy ethyl starch
5. Polyvinylpyrrolidone (PVP): MW 40000 and used up to 3.5% solution.

DIURETICS

Drugs inducing a state of increased urine flow are called diuretics. These agents are inhibitors of renal ion transporters that decrease the reabsorption of Na^+ at different sites in the nephron.

Glomerular filteration

Net filteration = [capillary hydrostatic pressure–(blood colloidal osmotic pressure + capsular hydrostatic pressure)

Net filteration = 55 – (30+15)

Reabsorption of substances from filterate:

1. Complete 100 % reabsorbed substances: Glucose, AA etc.
2. Semi–adsorbed/threshold substances: Water and salts as Na^+, Ca^{2+}, K^+, Cl–etc.
3. Non-absorbable substances: creatinine

Tubular reabsorption of Na^+

- Proximal convoluted tubule (PCT >60%).
- Thick ascending limb of the loop of Henle (TAL <25%).
- Distal convoluted tubule (DCT < 10%).
- The collecting tubules and ducts (CT <4%).

Diuretic drugs

1. **Loop diuretics/high ceiling diuretics:** Ethacrynic acid, furosemide
2. **Benzohiazides and thiazide like/medium efficacy:** Chlorthiazide, Benzothiazide, Xipamide, Chlorthalidone
3. Weak or adjunctive diuretics:
   a. Carbonic anhydrase inhibitors: acetazolamide
   b. Potassium sparing diuretics: Spironolactone (aldosterone antagonist), Amiloride, Triamterene
   c. Osmotic diuretics: Mannitol
   d. Xanthines: Theophylline

Loop diuretics

MOA These drugs inhibit the Na^+–K^+–$2Cl^-$ cotransport (symporter) in the thick ascending loop of henle.

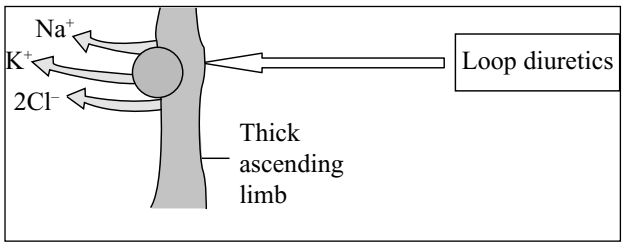


Figure 7.6 Loop diuretics

Uses Edema; Acute pulmonary edema; cerebral edema; hypertension; hypercalcaemia and in kidney stone; forced dieresis in the poisoning.

Thiazide and related diuretics

MOA These agents inhibt the Na^+–Cl^- symport in the cortical segment of loop of henle and early portion of DCT.

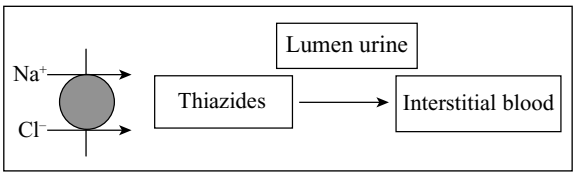


Figure 7.7 Thiazide and related diuretics

Uses Edema; hypertension; in diabetes insipidus E.g., Chlorthiazide; hypercalciurea.

Complicationor adverse effect with loop/heigh ceiling and thiazide type diuretics:

- **Hypokalemia:** ↓ K^+ level or excess loos of K^+ (**more significant with thiazides*) → arrhythmia.
  Prevented by:
  - concurrent use of potassium sparing diuretics
  - high dietary intake and supplement of K^+
- **Hypergycaemia** due hypokalemia.
- ***Ototoxicity** with loop diuretics (more with ethacrynic acid)
  - GIT and CNS disturbances: nausea, vomiting and diarrhea (most common with ethacrynic acid)
  - Allergic reactions: mostly with furosemide.
  - Hyperuricaemia:for this, thiazide has higher incidence than furosemide

Ca^{2+} level ↓ Ca^{2+} level (hypocalcaemia) with loop diuretics; ~~–~~↑ Ca^{2+} level (hypercalcaemia) with thiazides.

Magnesium level: decreases Mg^{2+} with thiazide as well as loop diuretics → arrhythmia.

Interactions

Due to Hypokalemia

- Enhance the digitalis toxicity by ↑sing the binding capacity of digitoxin with Na^+–K^+–ATPase pump.
- Increase the incidence of Ventricular arrhythmia (torsade de point)due to quinidine and other and toxicy of quinidine.
- High ceiling diuretics (ethacrynic acid) gives additive effect with aminoglycosides → may permanent loss of hearing (ototoxicity).
- High ceiling diuretic may enhance the nephrotoxicity of aminoglycosides.
- Probenecid inhibits the diuretic action of furosemide and thiazides due to inhibition of its tubular secretion.

Carbonic anhydrase inhibitors

MOA These agents inhibit to carbonic anhydrase enzyme which is responsible for the reabsorption of Na^+ ion in the exchange of H^+ ion in the Proximal Convoluted Tubule. Inhibition of this enzyme prevents the reabsorption of Na+ ion from PCT.

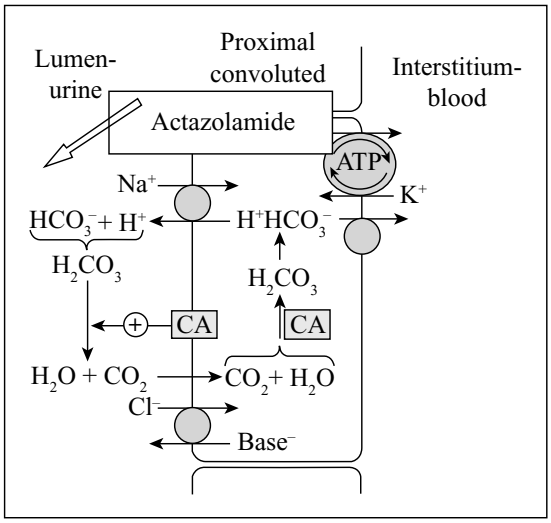


Figure 7.8 Carbonic anhydrase inhibitors

Adverse effect Acidosis, hypokalemia, ftigue;
Hypersensitivity reactios; **Bonemarrow depression*.
It is contraindicated in the iver disease.

*Potassium sparing diuretics

Spironolactone, amiloride, and triamterene act at the level of the collecting tubules and DCT.

*Sipronolactone It is chemically mineralocorticoid related steroid.

MOA In the liver, Spironolactone converts into active metabolite canrenone → reach at the site of action through tubular secretion → inhibits the formation of Aldosterone induced protein formation → ↓ Na^+ reabsorption or ↑ Na^+ excretion and ↓ K^+ secretion → gives potassium sparing action.

Uses

- Concurrent administered, with thiazides and loop diuretic for countraction of K^+ loss.
- Edema; hypertension.

Note

Key point to remember

Aspirin blocks the action of spironolactone action by inhibiting its tubular secretion.

Adverse effect Confusion, Gyanecomastia, hirsutism, irregularties in menstrual cycle.

Amiloride and Triamterene blocks the Na^+ in DCT and CD cells $\rightarrow \downarrow Na^+$ absorption.

Antidiuretics

Diabetes insipidus: excessive amounts of dilute urine due hyposecretion of ADH (vasopressin) due to damage to the hypothalamus by, e.g., trauma, tumour, encephalitis or by decreases the sensitivity of CD cells ADH receptors.

Nephrogenic diabetes Decrease the sensitivity of CD cells ADH receptors for aldosterone $\rightarrow\uparrow$urine volume.

Neurogenic diabetes Damage the pituitary ADH secretoy cells or non responsive for the secretion of ADH.

ADH receptor:

$V_1 \rightarrow \uparrow IP_3/DAG$ and $Ca^{2+}\uparrow$ present on smooth muscle and blood vessels

$V_2 \rightarrow \uparrow cAMP$ and $Ca^{2+}\uparrow$ present on CD cells and blood vessels; function ADH secretion.

Anti-diuretic agent

Drug	MOA	Use
Antidiuretic hormone (ADH, vasopressin), Desmopressin, lypressin	Agonist action at V_2 receptor $\rightarrow$ $\uparrow$ ADH secretion and action	Diabetic insipidus in nepgrogenic as well as neurogenic; Bed wetting in children and nocturia; Renal concentration test; haemophilia $\rightarrow \uparrow$ VIII clotting factor synthesis.
Clorpropamide	Sensitize the kidney cells for ADH	Nephrogenic
Carbamazepine	Sensitize the kidney cells for ADH	Nephrogenic
Amiloride		In the lithium induced Nephrogenic

Heavy Metal Intoxication and Chelators

Heavy metals exert their toxic effects by combining and inactivating functional groups of enzymes or other critical biomolecules.

Chelating agents are compounds which form stable, non-toxic complex with toxic metallic ions and make it easily excreted substances. They should have higher affinity than body ligands for the toxic metal ions.

Drugs	Adverse effects	Uses
Dimercaprol (British Anti Lewisite; BAL): Oily, colourless liquid with a strong mercaptan like odour.	increase BP, Tachycardia, vomiting, inflammation of mucous membranes, sweating, headache and anxiety.	It is used in As, Hg, Au, Bi, Ni and Sb metal poisoning. It is used as an adjuvant to Ca Na_2 EDTA in lead poisoning and with penicillamine in Cu poisoning and in Wilson's disease. ***Fe** and **Pb** metal complex with BAL is **toxic** so it is contraindicated in this case.
Dimercaptosuccinc acid	Nausea, anorexia and loose motion	Pb poisoning

Drugs	Adverse effects	Uses
Disodium edentate (Na2 EDTA)	i.v. injection leads tetany, nephrotoxicity, including renal tubular necrosis.	Hypercalcaemia
Calcium disodium edentate (Ca Na_2 EDTA)	Nephrotoxicity, including renal tubular necrosis.	Pb, Zn, Cd, Mn and Cu
Penicillamine	Nephrotoxicity with proteinuria, pancytopenia, and autoimmune dysfunction, including lupus erythematosus and hemolytic anemia, and collagen tissue toxicity	Copper (copper poisoning and of Wilson's disease), lead, arsenic, gold
Deferoxamine	Erythema, urticaria, hepatic and renal dysfunction and coagulopathies.	Iron intoxication
Deferiprone	Anorexia, vomiting, altered taste, joint pain	Iron intoxication

Multiple Choice Questions

1. Drugs that activate potassium channel are

[P] Cromakalim [Q] Sumatripatan
[R] Hydralazine [S] Minoxidil

(a) P and Q (b) Q and R
(c) Q and S (d) P and S

2. Phosphodiesterase inhibitor is

[P] Sodium nitropruside
[Q] Milrinone
[R] Methylxanthines
[S] Propofol

(a) P and R (b) Q and R
(c) Q and S (d) R and S

3. Phosphodiesterase inhibitor is used as

(a) Vasocontrictor (b) Vasodilator
(c) Hypotension (d) Antidiuretic agent

4. The common side effects of alpha-1 adrenoceptor antagonist, antihypertensive agent, are _____.

[P] Gout
[Q] Ankle oedema
[R] Postural hypotension
[S] Hypotension

(a) P and Q (b) P and R
(c) Q and S (d) R and S

5. The common side effects thiazide diuretic are_____

[P] Impotence [Q] Gout
[R] Fetal toxicity [S] Renal dysfunction

(a) P and Q (b) Q and R
(c) P and S (d) R and S

6. Most widely used pulmonary hypertension drug of choice is

[P] Ramipril [Q] Bosentan
[R] Treprostinil [S] Metoprolol

(a) P and R (b) Q and R
(c) Q and S (d) R and S

7. Statin and fibrate which are use as antihyperlipidemic agents have _____ as common side effect.

(a) Palpitation (b) Diarrhoea
(c) Myositis (d) Flushing

8. Ezetimibe

(a) Acts by bile acid sequester
(b) Releases nicotinic acid
(c) Reduces VLDL and triglyceride
(d) Acts as cholesterol absorption inhibition

9. Following drugs increase the rate of degradation of warfarin:

[P] Rifampicin [Q] Metronidazole
[R] Cimetidine [S] Griseofulvin

(a) P and R (b) Q and R
(c) P and S (d) Q and S

10. Following drugs potentiate the activity of warfarin:
[P] Barbiturates [Q] Carmazepine
[R] Ciprofloxacin [S] Chloramphenicol

(a) P and R (b) Q and R
(c) P and S (d) R and S

11. One of the following is procoagulant drug:
(a) Warfarin (b) Vitamin K
(c) Heparin (d) Aspirin

12. Clopidogrel has the following characteristics:
[P] It is a prodrug
[Q] It is phosphodiesterase inhibitor
[R] It inhibits platelet responses to ADP and its actions are additive with aspirin.
[S] Its action is slow and takinges 3–7 days to reach maximal effect

(a) P and R (b) Q and R
(c) R and S (d) Q and S

13. Tenecteplase is used in acute myocardial infarction which
(a) Is thromboxen receptor antagonist
(b) Inhibits fibrinolysis
(c) Is tissue plasminogen activator
(d) Directs thrombin inhibitor

14. Following statements are true:
[P] Zafirlukast is cysteinyl leukotriene receptor antagonist
[Q] Tiotropium is muscarinic receptor antagonist
[R] Salmeterol is $ß_2$-receptor antagonist
[S] Angiotensin converting enzyme does not produce cough

(a) P and Q (b) Q and R
(c) P and R (d) R and S

15. Acetazolamide has following characteristics:
[P] Acting on proximal tubule
[Q] Inhibits carbonic anhydrase
[R] Competitively antagonizes aldosterone
[S] Inhibits sodium secretion in the distal tubule

(a) P and R (b) Q and R
(c) P and Q (d) Q and S

16. All of the following drugs act on distal tubule except
(a) Hydrochlorothiazide
(b) Chlorthalidone
(c) Indapamide
(d) None of the above

17. Thiazide diuretic is usesd in
[P] Primary hyperaldosteronism
[Q] Nephrogenic diabetes insipidus
[R] Idiopathic hypercalciuria
[S] Hypercalcaemia

(a) P and R (b) Q and R
(c) Q and S (d) R and S

18. Side effect of loop diuretics is
[P] Hypovolaemia [Q] Hypokalaemia
[R] Hypercalcaemia [S] Hypouricaemia

(a) P and S (b) Q and R
(c) P and Q (d) Q and S

19. Dysrhythmias arise because of
[P] Intrinsic myocardial contractility
[Q] Vasodilator metabolites
[R] Delayed after depolarization, which triggers ectopic beats
[S] Reentry resulting from partial conduction block

(a) P and Q (b) Q and R
(c) P and S (d) R and S

20. Sotalol used as antidysrhymic agent acts by
(a) Sodium channel blockade
(b) Calcium channel blockade
(c) Potassium channel blockade
(d) Beta-adrenoceptor antagonism

21. Teytrodotoxin acts by
(a) Blocking the voltage-gated sodium channel
(b) Blocking the voltage-gated calcium channel
(c) Blocking the renal tubule sodium channel
(d) Blocking the potassium channel

22. Which of the following is not a function of beta blocker?
(a) Block in the release of renin from juxtaglomerular apparatus
(b) Decrease in cardiac output
(c) Decrease in heart rate
(d) All of the above

23. Beta-blockers are contraindicated in patient with
(a) Supraventricular tachycardia
(b) Hyperthyroidism
(c) Coronary artery disease
(d) All of the above

24. Ligand-gated ion channels is also known as
(a) Metabotropic receptor
(b) Ionotropic receptor
(c) Kinase linked receptor
(d) Neclear receptor

25. Angiotensin II
(a) Is increased in the presence of enalapril
(b) Causes drops in aldosterone levels
(c) Can result in water retention
(d) Increases sodium excretion

26. The antihypertensive agent also used for hair regrowth is
(a) Nitroglycerin (b) Nitroprusside
(c) Minoxidil (d) Verapamil

27. Selective B_2 broncho-dilator available for parenteral use for the treatment of status asthmatic is
(a) Albuterol (b) Isoetharine
(c) Terbutaline (d) Pirabuterol

28. Butoxamine is
(a) Selective β1 agonist
(b) Selective β2 agonist
(c) Selective β1 antagonist
(d) Selective β2 antagonist

29. Tamsulosin is most clinically used for
(a) Pheochromacytoma
(b) Bening prostatic hypertrophy
(c) Cardiac arrest
(d) Anaphylaxis

30. Carvedilol is a
(a) Selective β1 agonist
(b) Selective β2 agonist
(c) Both α-β agonist
(d) Both α -β antagonist

31. Antihypertensive effect of methyl dopa is by
(a) Blocking alpha-adrenergic receptor
(b) Dilating the arteriolar smooth muscle
(c) Stimulating the alpha-2 adrenergic receptors in the brain stem
(d) Inhibiting the angiotensin-converting enzyme

32. Frequent cause of intoxication of digitalis is by administration of
(a) Phenytoin (b) Hydrochlor thiazide
(c) Neomycin (d) All of the above

33. Verapamil exerts itseffects by following mechanism:
(a) Inhibiting the opening of fast sodium channels
(b) Increasing the potassium influx
(c) Inhibiting the entry of calcium through slow channels
(d) All of the above

34. Which of the following antihypertensive drug produces its effects by blocking alpha-1 adrenergic receptor?
(a) Minoxidil (b) Methyl dopa
(c) Terazosin (d) Labetolol

35. Which of the following antiarrhythmic drug increases the plasma concentration of digoxin?
(a) Lidocaine (b) Quinidine
(c) Phenytoin (d) Procainamide

36. Digitalis overdose can be reversed by administration of
(a) Phenytion
(b) Potassium
(c) Fab fragments of digoxin specific antibody
(d) Calcium

37. Effect of digitalis on electrical functions of the heart include
(a) Slowed SA nodal rate
(b) Prolonged AV refractory period
(c) Decreased ventricular rate in atrial fibrillation
(d) All of the above

38. Correct statements concerning nitroglycerin include all except
(a) Used in treatment of CCF
(b) Causes headache and tachycardia
(c) It decreases the coronary blood flow
(d) It can activate guanylate cyclase and increases the synthesis of cyclic GMP

39. Nitroglycerin results in all of the following except
(a) Decreases the requirement of myocardium for Oxygen
(b) Decreases ventricular and diastolic pressure
(c) Decreases both preload and after load
(d) Decreases cardiac force

40. Reserpine is contraindicated in patients with a history of
(a) Epilepsy (b) Anxiety
(c) Mental depression (d) Schizophrenia

41. The treatment of CCF with diuretics include all except
(a) Causes reduction in preload
(b) Decreases the cardiac size

(c) Decreases total body stores of K
(d) Causes reduction in after load

42. Correct statements regarding quinidine include all except
(a) Increases the sinus rate by cholinergic blockade
(b) Prolongs the ERP
(c) Increasess· the cardiac contractility
(d) Causes thrombo cytopaenia

43. Drug of first choice in supraventricular arrhythmias is
(a) Quinidine (b) Procainamide
(c) Verapamil (d) Amiodarone

44. Which drug often cause[S] tachycardia when given in low doses?
(a) Propranolol (b) Verapamil
(c) Nitroglycerin (d) All of the above

45. Which of the following antihypertensive drugs tend to elevate plasma triglycerides?
(a) Calcium channel blockers
(b) Alpha-adrenergic receptor blocker
(c) Thiazide diuretics
(d) ACE inhibitors

46. When digitalis is administered to patient with CCF its beneficial effects are primarily due to
(a) Decreased heart size
(b) Slow conduction thro' AV node
(c) Positive inotropic effect
(d) None of the above

47. Propranolol controls the ventricular rate in patients with atrial fibrillation by
(a) Increasing the duration of action potential
(b) Increasing the conduction velocity
(c) Blocking the B-adrenergic influences on the AV node
(d) Decreasing the AV conduction time

48. Calcium channel blocker with predominant peripheral action is
(a) Nicardepine (b) Verapamil
(c) Nifedepine (d) Diltiazem

49. Captopril exerts action by
(a) Inhibiting the rennin release
(b) Inhibiting conversion of angiotensin I to II
(c) Inhibiting conversion of angiotensin II to I
(d) Inhibiting conversion of angiotensiogen to angiotensin I

50. Long-term administration of nitrates can cause
(a) Cardiac arrhythmias
(b) Anemia
(c) Tolerance
(d) Loss of accommodation

51. Amylnitrate is given
(a) Sublingually (b) Orally
(c) By inhalation (d) IM

52. Angiotensin II blocker is
(a) Enalapril (b) Saralasin
(c) Losartan (d) Trimethaphan

53. All of the following can cause bradycardia except
(a) Methyldopa (b) Clonidine
(c) Reserpine (d) Hydralazine

54. Which of the following drug inhibits the release of norepinephrine from the sympathetic nerve terminal?
(a) Minoxidil (b) Guanethidine
(c) None of the above
(d) Hydralazine

55. Correct statements concerning reserpine include all except
(a) Acts by depleting catecholamine stores
(b) Less expensive
(c) Causes tachycardia
(d) Contraindicated in patients with history of mental depression

56. Which antihypertensive drug has to be avoided in a diabetic patient who is taking insulin?
(a) Guanethidine (b) α-methyl dopa
(c) Propranolol/ (d) Hydralazine

57. Aspirin should not be used in _____
(a) Gout (b) Myocardial infarction
(c) Both a and b (d) None of the above

58. Potassium antagonizes the toxic effects of cardiac glycosides by
(a) Inhibiting the Na-K-ATPase pump
(b) Increasing the binding of sodium to the sarcolem
(c) Decreasing binding of digitalis to the heart
(d) All of the above

59. Propranolol is given with nifedipine in the treatment of exertion angina because
(a) Propranolol prevents reflex tachycardia caused by nifedipine

(b) Propranolol prevents myocardial ischemia caused by nifedipine
(c) Both
(d) None of above

60. Which of the following factor increases the secretion of renin?
(a) Fall in sodium concentration in the distal tubule
(b) Reduction in renal perfusion pressure
(c) PGI_2
(d) All of the above

61. Which of following mechanism is responsible for vascular smooth muscle contraction?
(a) Increasing intracellular cAMP
(b) Release of intracellular calcium via inositol triphosphate
(c) Inhibiting calcium entry through voltage-gated calcium channel
(d) All of the above

62. Correct statement concerning sodium nitropruside include all except
(a) Causes bradycardia
(b) Dilates both aerterioles and ventricles
(c) Causes thiocyanate poisoning with excessive dose
(d) Used in acute aortic dissection

63. Nitrates are used as an antianginal agent by
(a) Increasing the synthesis of cyclic AMP
(b) Increasing the synthesis of cyclic GMP
(c) Phosphorylation of myosin light chains
(d) All of the above

64. In the treatment of angina which of the following can be applied to the skin for absorption
(a) Amylnitrate
(b) Glyceryl trinitrate
(c) Isosorbide dinitrate
(d) Pentaerythritol tetranitrate

65. Immunosuppressant effect of tacrolimus is produced by
(a) Inhibiting IL-2 production
(b) Inhibiting cytokine gene expression
(c) Inhibiting purine or pyrimidine synthesis
(d) Blocking the T-cell surface molecules involved in signalling

66. Which of the following antiarrhythmic drug does not have antimuscarinic action?
(a) Qunidine (b) Procainamide
(c) Lidocaine (d) All of the above

67. Correct statement regarding qunidine is
(a) Reduces refractory period of ventricle
(b) Mainly blocks calcium channel
(c) Displaces digitalis from the plasma proteins
(d) All of the above

68. Which of the following antihyperlipidemic drug inhibits the synthesis of cholesterol by blocking HMG Co-A reductase ?
(a) Clofibrate (b) Pravastatin
(c) Probucol (d) Nicotinic acid

69. Calcium channel blockers are used in cardiac infraction because it
(a) Increase cardiac out put
(b) Increase blood pressure
(c) Reduce the size of infract
(d) Increase conduction along the muscle

70. Which of the following drug is used to treat hypertension during pregnancy?
(a) Hydralazine (b) Diazoxide
(c) Clonidine (d) Minoxidil

71. Antidysrhythmic drug flecainide exerts their effect by
(a) Fast sodium channel dissociation block
(b) Medium sodium channel dissociation block
(c) Slow sodium channel dissociation block
(d) Potassium channel dissociation block

72. Precautions advisable before lovastatin therapy include
(a) Serum transaminase measurement
(b) Slit-lamp examination of eye
(c) Creatine kinase levels
(d) All of the above

73. All of the following are antiplatelet agents except
(a) Acetylsalicylic acid
(b) Acetaminophen
(c) Ticlopidine
(d) Dipyridamole

74. Chylomicrones and VLDL lipoprotein are elevated then atherosclerosis risk is
(a) High (b) Medium
(c) Low (d) Not elevated

75. Which antihyperlipidemic drug is a benzophoneone derivative?
(a) Ezetimide (b) Probucol
(c) Fenofibrate (d) Dalvastatin

76. What is the mechanism of nitrates?
(a) Inhibiting phosphoesterase
(b) Stimulating guanylate cyclase
(c) β-blockers
(d) Calcium-channel blocker

77. Which of the following is the drug of choice for the long-acting organonitrate?
(a) Isosorbide dinitrate
(b) Amylnitrate
(c) Glyceryl nitrate
(d) Erythrityl tetra nitrate

78. Which statin lowers serum cholesterol in patients with homozygous familial hypercholesterolaemia?
(a) Simvastatin (b) Lovostatin
(c) Pravastatin (d) Atorvastatin

79. Which bile acid binding resin is used in hyperlipidemia?
(a) Colestipol (b) Cilostazol
(c) Probucol (d) Ezetimibe

80. Which drug inhibits cholesterol absorption?
(a) Colestipol (b) Cilostazol
(c) Probucol (d) Ezetimibe

81. Indicate which one of the following drugs may interfere with the uptake of ^{123}I in the thyroid gland
(a) Beta-blockers
(b) Alpha blockers
(c) Calcium channel blockers
(d) Amiodarone

82. Which positive inotrope with additional vasodilator properties attributed to sensitization of cardiac muscle to $[Ca^{+2}]_i$ and activation of K_{ATP} in vascular smooth muscle?
(a) Levosimendone (b) Minoxidil
(c) Hydralazine (d) Nicorandil

83. Which of the following statement is true?
(a) Streptokinase is prepared from the human kidney cell
(b) Urokinase acts on plasminogen directly
(c) Heparin has slower action than warfarin
(d) Menadione -natural form of VITK

84. One of them is not a prodrug. Identify.
(a) Benzepril (b) Captopril
(c) Quinapril (d) Ramipril

85. The risk of digitalis toxicity is significantly increased by concomitant administration of
(a) Triamterene (b) Lidocaine
(c) Captopril (d) Hydrochlorthiazide

86. Which drug inhibits Na^+ reabsorption by blocking luminal sodium channel and decreasing K^+ excretion
(a) Furosemide (b) Spirenolactone
(c) Epleronone (d) Triamterine

87. Sodium channel blocks with fast dissociation of
(a) Ivabradin (b) Amiodaron
(c) Flecainide (d) Lidocaine

88. An anion exchange resin, which lowers plasma phosphate used in renal failure is
(a) Sevelamer (b) Spirenolactone
(c) Eplerenone (d) Triamterene

89. Choose the drug that often causes tachycardia when given in regular doses.
(a) Verapamil (b) Guanethidine
(c) Propranolol (d) Isosorbide dinitrate

90. Minoxidil
(a) Multiple sites including α-2 agonist
(b) Catecholamine release
(c) Sympathetic neuronal block
(d) Non-selective vasodilation

91. An agent used in prinzmetal angina has spasmolytic action which increases coronary blood supply is
(a) Nitroglycerine (b) Nifedipine
(c) Timolol (d) Isosorbide monbnitrate

92. HMG-Co A reductase, a key enzyme in the pathway, catalyses
(a) Side chain cleavage in the conversion of cholesterol to steroid hormones
(b) The reduction of the thio-ester group to an alcohol in mevalonate biosyntheis.
(c) The reduction of the hydroxyl group of mevalonate to vitamin D.
(d) Steroid condensation reaction in the biosynthesis of bile acids

93. Which calcium antagonist has the most marked negative inotropic action, and therefore being contraindicated in heart failure?
(a) Diltiazem (b) Amlodipine
(c) Verapamil (d) Nifedipine

94. Which drug inhibits endotheline converting enzyme?
(a) Evabradine (b) Cromacalim
(c) Losartan (d) Phosphoramidon

95. Drug combination warfarin/vitamin K results in a specific interaction. Identify.

(a) Antagonistic
(b) Increased sedation
(c) No known interaction
(d) Harmful only in the presence of oxidizing agent

96. The mechanism of action of digitalis is
(a) Decreases intracellular sodium concentration
(b) Inhibits sodium potassium ATPase
(c) Activatesadenylcyclase which produces cAMP
(d) Decreases release of calcium from sarcoplasmic reticulum

97. Which of the following is the early marker of the myocardial infarction?
(a) Cardiac troponoine T
(b) Lactate dehydrogenase
(c) Cardiac troponine I
(d) None of the above

98. To avoid lithium toxicity, a patient using lithium carbonate for mood disorders should not be prescribed
(a) Acetazolamide (b) Hydrochlorthiazide
(c) Mannitol (d) Propranolol

99. A patient receiving digoxin for CCF is found to have an elevated serum cholesterol. Which hypolipidemic agent should not be prescribed?
(a) Clofibrate (b) Cholestyramine
(c) Lovastatin (d) Niacin

100. Following is the example of Class I(b) antidysrhythmic agent
(a) Lidocaine (b) Flecainide
(c) Amiodarone (d) Procainamide

ANSWER KEYS

1. (d)	**2.** (b)	**3.** (b)	**4.** (d)	**5.** (a)	**6.** (b)	**7.** (c)	**8.** (d)	**9.** (c)	**10.** (d)
11. (b)	**12.** (a)	**13.** (c)	**14.** (a)	**15.** (c)	**16.** (d)	**17.** (b)	**18.** (c)	**19.** (d)	**20.** (c)
21. (a)	**22.** (d)	**23.** (c)	**24.** (b)	**25.** (c)	**26.** (c)	**27.** (a)	**28.** (d)	**29.** (b)	**30.** (d)
31. (c)	**32.** (b)	**33.** (c)	**34.** (c)	**35.** (b)	**36.** (b)	**37.** (d)	**38.** (c)	**39.** (c)	**40.** (c)
41. (d)	**42.** (c)	**43.** (c)	**44.** (c)	**45.** (c)	**46.** (c)	**47.** (c)	**48.** (c)	**49.** (b)	**50.** (c)
51. (c)	**52.** (b)	**53.** (d)	**54.** (b)	**55.** (c)	**56.** (c)	**57.** (a)	**58.** (c)	**59.** (a)	**60.** (d)
61. (b)	**62.** (a)	**63.** (b)	**64.** (b)	**65.** (a)	**66.** (c)	**67.** (c)	**68.** (b)	**69.** (c)	**70.** (a)
71. (c)	**72.** (b)	**73.** (b)	**74.** (d)	**75.** (a)	**76.** (b)	**77.** (b)	**78.** (d)	**79.** (a)	**80.** (d)
81. (d)	**82.** (a)	**83.** (b)	**84.** (b)	**85.** (d)	**86.** (d)	**87.** (d)	**88.** (a)	**89.** (d)	**90.** (d)
91. (d)	**92.** (b)	**93.** (c)	**94.** (d)	**95.** (a)	**96.** (b)	**97.** (c)	**98.** (b)	**99.** (c)	**100.** (a)

CHAPTER 8

DRUGS FOR GASTROINTESTINAL TRACT DISORDER

DRUGS FOR PEPTIC ULCER

A. Reduction of gastic acid secretion:
   1. H_2 antihistamines: Cimetidine, Rantidine, Famotidine, Roxatidine, Loxatidine
   2. Proton pump inhibitors: Omeprazole, Lansoprazole, Pantoprazole, Rabeprazole, Esmoprazole
   3. **Muscarinic receptor antagonist:** Pirenzepine, Propanthaline, Oxyphenonium
   4. **Prostaglandin analogues**: Misoprostol, Enprostil
B. Gastric acid neutralizing agents:
   Sod. Bicarbonate, Sod. Citrate, Magnesium hydroxide, Aluminium hydroxide, Calcium carbonate
C. Cytoprotective drugs: Sucralfate, Colloidal bismuth subcitrate
D. Ulcer healing agent: Carbenexolone sodium
E. Anti. Helicobacter pylori drugs: Amoxicllin, clarithromycin, Metronidazole, Tetracycline

H_2 Blockers

MOA These agents competitively block the H_2 receptor on parietal cells → suppress secretory responses to food stimulation and nocturnal secretion of gastric acid via their ability to decrease (indirectly) the activity of the proton pump. H_2 blockers also partially antagonize HCl secretion caused by vagal stimulation or by gastrin.

Uses

Acid peptic disease (overall less effective than proton pump inhibitors), gastroesophageal reflux dystrophy (GERD), Zollinger-Ellison syndrome.

Adverse Effects

GI distress, dizziness, somnolence; slurred speech and delirium possible in elderly.

Cimetidine has antiandrogenic activity → Results in Gynaecomastia, loss of libido, impotance and reversible oligozoospermia.

Cimetidine is a major inhibitor of P450 isoforms → drug interaction via inhibits the metabolism o drugs → ↑ effects of quinidine, phenytoin, tricyclic antidepressants, and warfarin.

Proton Pump Inhibitors

MOA Active metabolites of proton pump inhibitors bind with H+, K+–ATPase antiport which is located on the parietal cells → directly inhibit the H+ ion secretion.

Omeprazole is inactivated at neutral pH and activated in pH<5.

Esomeprazole is the S–enantiomer of omeperazole.

Uses

They are more effective than H_2 blockers in peptic ulcer disease (PUD) and are also effective in GERD and Zollinger-Ellison syndrome.

Prostaglandin Analogues

MOA These agents like PGE2 and PGI2 sereve cytoprotective action via increase mucus and bicarbonate secretion and through the ↓ cAMP → ↓ acid secretion also.

Antacids

MOA Gstric antacids chemically neutralize the stomach acid → increase the gastric acid pH.

Antacids	Adverse Effects
Sod. bicarbonate	Absorbed systemically (except to this others are non systemic) Alkalosis in renal insufficiency, acid rebound, belching, gas; Risk in hypertension
Magnesium hydroxide	Hypermagnesemia + loss of deeptendon reflexes, respiratory paralysis
Aluminium hydroxide	Constipation, hypophosphatemia, osteomalacia

Antacids	Adverse Effects
Calcium carbonate	Hypercalcaemia, hypercalciurea, alkalosis and kidney stone; acid rebound

Sucralfate It is a complex of aluminum hydroxide and sulfated sucrose. Sucralfate polymerizes at pH < 4 by cross linking → forms complex gel of sucralfate which faciliates its binding with normal and necrotic mucosa cells and make a physical barrier that impairs diffusion of HCl and prevents degradation of mucus by pepsin and acid.

Interactions

- Sucralfate adsorb many drugs and retard their absorption; E.g., tetracyclines, fluoroquinolines, cimetidine, digitoxin.
- Concurrently administered antacids reduce the efficacy of sucralfate.

Colloidal Bismuth Subcitrate

At the pH < 5 colloidal bismuth precipitate on gastric epithelium → make physical barrier that impairs diffusion of HCl and prevents degradation of mucus by pepsin and acid. Also increase the bicarbonate and mucous secretion and detach the H. pylori from gastric mucosa.

***Adverse effect** Diarrhoea, headache and dizziness;

*Osteodystophy and encephalopathy due to Bismuth toxicity in proloned use;

*Blackening of tounge, dentures and stools.

EMETICS AND ANTIEMETICS

Nausea and vomiting are protective reflexes that serve to rid the stomach and intestine of toxic substances and prevent their further ingestion. The process coordinated by a central emesis center in the lateral reticular formation of the mid–brainstem adjacent to both the chemoreceptor trigger zone (CTZ) in the area postrema (AP) (at the bottom of the fourth ventricle) is outside the blood–brain barrier and the solitary tract nucleus (STN) of the vagus nerve.

The CTZ has high concentrations of receptors for serotonin (5–HT_3), dopamine (D_2), and opioids, while the STN is rich in receptors for enkephalin, histamine, and ACh, and also contains 5–HT_3 receptors.

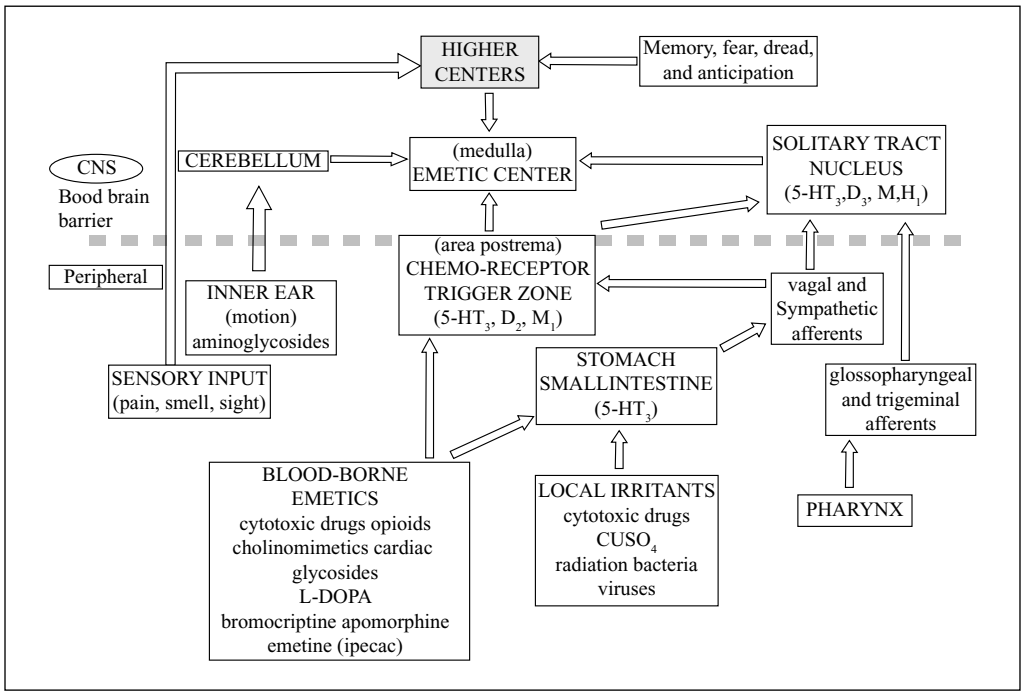


Figure 8.1 Pathway involved in the emesis

Anti-emetics

Drugs	MAO	Adverse Effect	Use
Hyoscine	Centrally as well as muscarinic recetor antagonists	Anticholinergic effect.	Motion sickness
Metoclo-pramide (prokinetic drug)	Centrally acting dopamine (D_2) receptor antagonists; 5–HT_3 receptor antagonism; 5–HT_4 receptor angonism $\rightarrow \uparrow$ GI motility and transit of material in the GI tract	Diaphoresis, Extrapyramidal effects; Should be avoid in lactating mother	Cytotoxic drug–induced emesis. **Should not be used in levodopa induced vomiting*
Domperidone	Peripheral acting dopamine (D_2) receptor antagonists	Dry mouth, loose stool, Galactorrhoea.	**Used in levodopa induced vomiting*
Cisapride	Prokinetic drug with 5–HT_3 receptor antagonistic activity		Torsades de points/Severe ventricular arrythmia
Chlorproma-zine	Dopamine (D_2) receptor antagonists	Extrapyramidal effects, muscle dystonia	Drug induced and postanaesthetic nausea and vomiting; Diseaseinduced vomiting; **Not effective in morning sickness but used in hyperemesis gravidarum*
Droperidol			
Promethazine	Histamine H_1 receptor antagonists, Centrally M_1 receptor blocker		Cytotoxic drug–induced emesis
Cyclizine	Histamine H_1 receptor antagonists		Vestibular (motion sickness)
Cinnarizine			Antivertigo
Meclizine			Sea sickness
Ondansetron, Dolasetron, Granisetron, Palonosetron, Ramosetron	5–HT_3 receptor antagonists	*headache*	Cytotoxic drug–induced emesis
Betametha-sone			Adjuvant in Cytotoxic drug–induced emesis
Dronabinol	Cannabinoid receptor agonists	hallucination	In Cytotoxic drug–induced emesis

Prokinetic agents enhance coordinated GI motility and transit of material in the GI tract.

Common Genital Tract Infections and Their Treatment

Disease	Causative Agent	Antimicrobial Agent
Urethral discharges		
Gonorrhoea	*Neisseria gonorrhoeae*	Cefixime, ceftriaxone
Non–specific urethritis	*Chlamydia, Ureaplasma or Mycoplasma spp.*	Tetracyclines (azithromycin)

Disease	Causative Agent	Antimicrobial Agent
Vaginal discharges		
Thrush	*Candida albicans*	Nystatin (clotrimazole)
Trichomoniasis	*Trichomonas vaginalis*	Metronidazole
Non-specific vaginosis	*Gardnerella vaginalis and Mobiluncus spp.*	Metronidazole
Genital sores		
Syphilis	Treponema pallidum	Penicillin (doxycycline)
Chancroid	Haemophilus ducreyi	Cotrimoxazole,
Lymphogranuloma venereum	Chlamydia	Erythromycin (tetracyclines) Tetracyclines (erythromycin),
Herpes	Herpes simplex virus	Aciclovir

Multiple Choice Questions

1. An organism which has been implicated as a possible cause of chronic gastritis and peptic ulcer is
(a) *Campylobacter jejuni*
(b) *Escherichia coli*
(c) *Helicobacter pylori*
(d) *Giardia lamblia*

2. Famotidine acts as
(a) H_1-histamine antagonist
(b) H_2-histamine antagonist
(c) Proton pump inhibitor
(d) H_1 agonist

3. Alcoholic patient should not be given
(a) Metronidazole (b) Emetine
(c) Niridazole (d) All of the above

4. In *Helicobacter pylori* infection following drug combination is preferred:
(a) Only proton pump inhibitor
(b) Proton pump inhibitor and sucralfate
(c) Proton pump inhibitor, amoxicillin and metronidazole
(d) Proton pump inhibitor, clarithomycin

5. Following are the cytoprotective agent
(a) Bismuth chelate (b) Sucralfate
(c) Lansoprazole (d) Both (a) and (b)

6. Mechanism of action of prostaglandins E_2 which used in peptic ulcer is
(a) Inhibit proton pump
(b) H2 receptor antagonist
(c) Antacid
(d) Inhibition of acid secretion and stimulation of mucus and bicarbonate secretion

7. Peptic ulcer occurs because of
(a) Gastric mucosa with *Helicobacter pylori* infection
(b) Imbalance between the mucosal-damaging and mucosal-protecting agents
(c) Both (a) and (b)
(d) None of the above

8. Following agents are stimuli the parietal cells except
(a) Gastrin (b) Acetylcholine
(c) Histamine (d) Prostaglandin E_2

9. Mechanism of action of lansoprazole which is used for peptic ulcer is
(a) Histamine H2 receptor antagonist
(b) Proton pump inhibitor
(c) Antacid
(d) Inhibit gastrin secretion

10. Simethicone is used
(a) As antacid
(b) To increase the viscosity and adherence to mucous to the oseophageal mucosa
(c) Both (a) and (b)
(d) None of the above

11. Alginate is used
(a) As antacid
(b) To increase the viscosity and adherence to mucous to the oseophageal mucosa
(c) To relieve bloating and flatulence
(d) Both (b) and (c)

12. Cyclizine used as an antiemetic agent acts through
(a) Histamine H1 receptor antagonist
(b) Histamine H2 receptor antagonist
(c) Muscarinic receptor antagonist
(d) Dopamine D2 receptor antagonist

13. One of the following acts as an antiemetic agent to antagonize the D2 receptor
(a) Metoclopramide (b) Ondansetron
(c) Nabilone (d) Cyclizine

14. Mechanism of action of ondasetron is
(a) Muscarinic receptor antagonist
(b) Histamine H_2 receptor antagonist
(c) Histamine H_1 receptor antagonist
(d) $5HT_3$ receptor antagonist

15. One of the following is not H_1 receptor antagonist which is used as an anti emetic agent
(a) Meclizine (b) Promethazine
(c) Prochlorperazine (d) Cinnarazine

16. Apretant is used as
(a) Antiemetic agent (b) Vomiting stimuli
(c) Gastric antacid (d) Proton pump inhibitor

17. Lactulose is a
(a) Purgative agent
(b) Antidiarrhoeal agent
(c) Antispasmodic agent
(d) Antacid

18. One of the following is faecal softener:
(a) Bisacodyl (b) Docusate sodium
(c) Ispaghula husk (d) Cisapride

19. Following are the agents that decrease motility of stomach except
(a) Loperamide (b) Diphenoxylate
(c) Atropine (d) Cisapride

20. Example of stimulant purgative is
(a) Ispaghula husk (b) Cisapride
(c) Senna (d) Lactulose

21. Lactulose is a
(a) Osmotic laxative
(b) Bulk laxative
(c) Faecal softener
(d) Stimulant purgative

22. Following is an approach to the treatment of acute diarrhoea except
(a) Treatment with antidiarrhoeal agent
(b) Treatment with antiinfective agent
(c) Maintenance of fluid and electrolyte balance
(d) Giving purgative agent

23. Magnesium aluminium silicate is used as
(a) Oral rehydration salt
(b) Absorbent
(c) Antimotility agent
(d) Anti emetic agent

24. Mechanism of action of sucralfate, which is used as antacid, is
(a) To protect the mucosa by releasing aluminium in presence of acid
(b) To neutralize acid
(c) To decrease acid secretion
(d) As proton pump inhibitor

25. Following statements are true except,
(a) Purgative agents accelerate the passage of the food through intestine
(b) Antispasmodic agents decrease smooth muscle tone
(c) Laxative drugs increase gastric motility
(d) Domperidone is a dopamine receptor antagonist

ANSWER KEYS

1. (c)	**2.** (b)	**3.** (a)	**4.** (c)	**5.** (d)	**6.** (d)	**7.** (c)	**8.** (d)	**9.** (b)	**10.** (b)
11. (d)	**12.** (a)	**13.** (a)	**14.** (d)	**15.** (c)	**16.** (a)	**17.** (a)	**18.** (b)	**19.** (d)	**20.** (c)
21. (a)	**22.** (d)	**23.** (b)	**24.** (a)	**25.** (c)					

CHAPTER 9

PHARMACOLOGICAL DRUGS CLASSIFICATION

DRUGS ACTING AT AUTONOMIC NERVOUS SYSTEM

1. Cholinergic Drugs

- Direct-acting drugs:
- Muscarinic agonists: Acetylcholine, Muscarine, Carbachol, Bethanechol, Pilocarpine
- Nicotinic agonists: Acetylcholine, Nicotine, Carbachaol, Succinylcholine,
- Indirect-acting drugs/Anti-cholinesterase/choline esterase Inhibitors,
- Alcohol: Edrophonium (Reversible)
- Carbamates: Neostigmine, Pyridostigmine, Physostigmine, Carbaryl (Reversible)
- Organophosphates: Echothiophate, Malathion, (Irreverssible)

2. Anti-cholinergic Drugs

- Muscarinic blockers:
- Non-selective: Atropine, Scopolamine, Glycopyrrolate, Ipratropium, Cyclopentolate Beztropine, Homatropine, Methscopolamine, Tropicamide
- M_1-selective: Pirenzepine, Telenzepine
- Nicotinic blockers:
- Ganglion blockers: Hexamethonium, Trimethaphan
- Neuromuscular blockers: Tubocurarine, Pancuronium, Atracurium, Chandocurium
- Cholinesterase regenerator-Pralidoxime (PAM), Obidoxime

3. Sympathomimetics

- General agonists:
- Direct: Ephedrine
- Indirect, releasers: Tyramine, Amphetamine
- Indirect, uptake inhibitors: Cocaine, Tricyclic antidepressants
- Selective agonists:
- Alpha-1: Norepinephrine, Phenylephrine, Methoxamine, Metaraminol
- Alpha-2: Clonidine, Methyl norepinephrine,
- Beta-1: Isoproterenol, Dobutamine
- Beta-2: Terbutaline, Albuterol, Metaproterenol, Ritodrine
- Dopamine: Dopamine, Bromocriptine, Apomorphine

4. Adreno-receptor Blockers

- Alpha-blocker:
- Non-selective: Phenoxybenzamine, Phentolamine
- Alpha 1-selective: Prazocin, Terazosin, Doxazocin
- Alpha 2-selective: Yohimbine
- Beta-blockers:
- Non-selective: Propranolol Timolol Nadolol
- Beta 1-selective: Metoprolol Atenolol Esmolol
- Beta 2-selective: Butoxamine

CARDIO-VASCULAR DRUGS

1. Drugs Used in Hypertension

- Diuretics:
- Thiazides: Hydrochlorothiazide, Chlorothalidone Loop diuretics: Furosemide, Bumetanide
- K+sparing diuretics: Triamterene, Amiloride
- Sympathoplegics: Carotid sinus sensitizers: Veratrum alkaloids
- Centrally acting agents: Clonidine, Methyldopa, Guanabenz, Guanfacine
- Ganglion blockers: Trimethaphan, Hexamethonium
- Ganglionic neuron blockers: Reserpine, Guanethidine
- Alpha-adrenoceptor blockers: Prazocin, Phenoxybenzamine, Phentolamine
- Beta-adrenoceptor blockers: Propranolol, Metoprolol
- Vasodilators-
- Arterial: Hydralazine Minoxidil Diazoxide
- Arterial and venous: Sodium nitroprusside
- Calcium channel blockers: Nifedepine Verapamil Diltiazem, Nicardipine, Nimodipine, Nitrendepine Amlodipine

- Angiotensin Converting Enzyme (ACE) inhibitors: Captopril Enalapril Lisinopril
- Angiotensin receptor (AT-1) antagonists: Losartan

2. Drugs Used in Angina Pectoris

- Nitrates: Nitroglycerin, Isosorbide dinitrate, Amyl nitrite Erythrityl tetranitrate Pentaerythritol
- Calcium channel blockers: Nifedipine, Verapamil, Diltiazem, Nimodipine, Bepridil
- Beta-blockers: Propranolol

3. Cardiac Glycoside and CHF

- Cardiac glycosides-Digoxin, Digitoxin, Oubain
- Positive inotropic digitalis substitutes: Dobutamine
- Phosphodiesterase (PDE) inhibitors: Amrinone, Milrinone, Theophylline
- ACE Inhibitors: Captopril, Enalapril, Lisinopril
- Diuretics: Furosemide, Hydrochlorothiazide
- Vasodilators: Nitroprusside, Nitroglycerin, Hydralazine, Isosorbide Theophylline

4. Anti-arrhythmic Drugs

I. Sodium channel blockers**:**
   - Moderate phase-O depression-Quinidine, Procainamide Disopyramide, Moricizine
   - Minimal phase-O depression-Lidocaine, Mexiletine, Phenytoin, Tocainide
   - Marked phase-O depression-Encainide, Flecainide, Propafenone, Indecainide

II. Beta-adrenoceptor blockers: Propranolol, Acebutalol, Esmolol

III. Potassium channel blockers: Kromakalin, Bemakalin

IV. Calcium channel blockers: Verapamil, Diltiazem

DIURETICS

- Carbonic anhydrase inhibitors: Acetazolamide
- Loop diuretics: Furosemide, Ethacrynic acid
- Thiazides and thiazide-like drugs: Hydrochlorothiazide, Indapamide, Metolazone
- Potassium-sparing diuretics: Spiranolactone, Amiloride, Triamterene
- Osmotic diuretics: Mannitol
- Antidiuretic agonists: Vasopressin, Desmopressin
- Antidiuretic antagonists: Demeclocycline, Lithium
- AcidifYing agents: Ammonium chloride

HISTAMINE, SEROTONIN AND ERGOT ALKALOIDS

- Histamine agonists: Histamine Methyl-histamine
- H_1-blockers: Diphenhydramine, Terfenadine, Chlorpheniramine Cyproheptadine, Promethazine, Astemizole
- H_2-blockers: Cimetidine, Ranitidine, Famotidine, Nizatidine
- 5-HT agonists: Serotonin, Sumatriptan
- 5-HT antagonists: Ketanserin, Ondensetron, Cyproheptadine
- Ergot alkaloids: Bromocriptine, Ergonovine, Ergotamine, LSD Methysergide

VASOACTIVE PEPTIDE

- Angiotensin-II, Atrial natriuretic peptide, Bradykinin,
- Calcitonin generelated peptide, Endothelin, Neuropeptide,
- Myotrophin, Substance P, Vasoactive intestinal peptide

PROSTAGLANDINS AND EICOSANOIDS

- Prostaglandins: PGE-2, PGF-2
- Prostacyclin: PGI-2
- Thromboxane: TXA-2
- Leukqtrienes: L TC-4, L TB-4, L TD-4
- Phospholipase inhibitors: Prednisone, Hydrocortisone
- Cycloxygenase-1 and 2 inhibitors: Aspirin, buprofen, Diclofenac sodium Indomethacin
- Cycloxygenase-2 inhibitors: Nimuselide

ANTI-ASTHMATIC DRUGS

- Beta-adrenoceptor agonists: Terbutaline, Salmeterol, Metaproterenol, Albuterol, Formoterol
- Methylxanthines: Theophylline, Aminophylline, Caffeine, Theobromine
- Muscarinic antagonist: Ipratropium, Tiotropium
- Release inhibitors: Cromolyn sodium, Nedocromil
- Glucocorticoids-Beclomethasone, Prednisolone
- Leukotriene antagonists-Zafirlukast, Zileuton, Montelukast

DRUGS ACTING AT CNS

- Non-peptide neurotransmitters of CNS-Acetylcholine, Dopamine, Nor-epinephrine Serotonin, GABA, Glutamate, Aspartate, Glycine
- Benzodiazepines: Chlordiazepoxide, Diazepam, Temazepam, Alprazolam, Flurazepam Lorazepam, Nitrazepam, Oxazepam, Triazolam

- Barbiturates: Phenobarbital, Pentobarbital, Thiopental sodium, Secobarbital Methohexital
- Carbamates: Meprobamate
- Alcohols: Ethanol, Chloral hydrate
- Nonbenzodiazepines: Buspirone, Zolpidem, Zaleplon, Rozerem

1. Anti-epileptic Drugs

- Barbiturates: Phenobarbital, Primidone, Mepharbital
- Benzodiazipine-Diazepam, Lorazepam, Clorazepate, Clonazepam, Nitrazepam
- Carboxylic acids: Valproic acid, Sodium valproate
- Hydantoins: Phenytoin, Fosphenytoin
- Succinimides: Ethosuximide, Methsuximide
- Tricyclics: Carbamazepine, Oxcarbazepine
- Newer agents: Felbamate, Gabapentin, Lamotrigine, Vigabatrin, Levetiracetam Tiagabine, Topiramate, Zonisamide, Rufinamide

2. General Anaesthetics

- Inhaled anesthetics:
- Volatile liquids: Halothane, Enflurane, Desflurane, Isoflurane, Methoxyflurane
- Gases: Nitrous oxide
- Intravenous anesthetics:
- Barbiturates: Thiopental sodium, Thiamylal, Methohexital
- Opiods: Morphine Fentanyl
- Propafols: Propafol
- Benzodiazepines: Midazolam
- Dissociative anesthetics: Ketamine
- Steroidal anaesthetics: Alfaxolone, Alfadolone

3. Local Anaesthetics

- Esters: Procaine Cocaine, Tetracaine Benzocaine
- Amides: Lidocaine Bupivacaine Etidocaine Prilocaine

4. Skeletal Muscle Relaxants

- Renal elimination, long duration: Tubocurarine, Pancuronium
- Hepatic elimation, intermediate duration: Vecuronium, Rocuronium, Chandocuronium
- Spontaneous or plasma cholinesterase, intermediate-short duration: Atracurium, Mivacurium
- Depolarizing blockers: Succinylcholine
- Spasmolytic drugs: Diazepam, Baclofen, Dantrolene, Cyclobenzaprine

5. Drugs Used in Parkinsonism and Other Movement Disorders

- Dopamine pro-drug: Levodopa
- COMT Inhibitors – Tolcapone, Entacapone
- DOPA decarboxylase inhibitor: Carbidopa
- Dopamine Agonist: Amantidine, Bromcriptine, Pergolide, Ropinirole
- MAO inhibitors: Selegiline Antimucarinic Benztropine Biperiden Orphenadrine Trihexyphenidyl
- Drugs used in Tremor: Propranolol
- Drugs used in Huntington's disease, Tourette "syndrome: Haloperidol Phenothiazines
- Drugs used in Wilsons's disease:" Penicillamine

6. Anti-psychotic Drugs

- Phenothiazines:
- Aliphatic: Chlorpromazine
- Piperidine: Thioridazine, Mesoridazine
- Piperazine: Trifluoperazine, Perphenazine, Fluphenazine
- Thioxanthenes: Thiothixene
- Butyrophenones-Haloperidol, Droperidol
- Heterocyclics: Clozapine, Molindone, Pimozide, Loxapine, Risperidone
- Antimanic drugs: Lithium, Carbamazepine, Clonazepam

7. Antidepressants

- Tricyclic drugs-
- First-generation drugs: Imipramine, Amitriptyline, Desipramine, Nortriptyline Doxepin, Protriptyline
- Second-generation drugs: AmoxCipine, Bupropion, Maprotiline, Trazodone
- Third-generation drugs: Mirtazapine, Nefazodone, Vanlafaxine
- Selective serotonin reuptake inhibitors: Fluoxetine, Paroxetine, Sertraline, Citalopram Fluvoxamine
- MAO inhibitors: Phenelzine, Moclobemide, Tranylcypromine, Isocarboxazid

Opioid analgesic and antagonists

- Strong agonists: Morphine, Heroin, Meperidine, Methadone, Fentanyl
- Moderate agonists: Codeine, Oxycodone, Hydrocodone
- Weak agonists: Propoxyphene
- Mixed agonist-antagonists: Pentazocine, Nalbuphine, Buprenorphine Butorphanol
- Antagonists: Naloxone, Naltrexone

- Antitussives: Dextromethorphan, Codeine
- Antidiarrheal: Diphenoxylate

Drugs of abuse

- Sedative-hypnotics: Ethanol, Phenobarbital, Chlordiazepoxide, Secobarbital Diazepam, Methaqualone, Meprobamate
- Opioids: Heroin, Meperidine, Morphine
- Stimulants: Amphetamine, Methamphetamine, Cocaine, Caffeine, Nicotine
- Hallucinogens: LSD, Phencyclidine, Mescaline, Scopolamine

DRUGS ACTING ON BLOOD, INFLAMMATION AND GOUT

1. Drugs Used in Anemias

- Oral iron supplements: Ferrous sulfate Ferrous gluconate Ferrous fumarate
- Parenteral iron: Iron dextran
- Vitamin B_{12}: Cyanocobalamin Hydroxycobalamin
- Folic acid: Pteroylglutamic acid
- Erythropoietin: Erythropoietin
- Granulocyte-macrophase Colony-stimulating factor: Sargramostim
- Granulocyte colony-stimulating factor:Filgrastim

2. Drugs Used in Coagulation Disorders

- Anticoagulants:
- Parenteral: Heparin, Enoxaprin
- Oral: Warfarin, Dicoumaral
- **Antiplatelet drugs:**
- Inhibitors of ADP-induced platelet aggregation: Dipyridamole Ticlopidine, Clopidogrel
- Fibrinogen receptor (glycoprotein IIblllla) antagonists: Abciximab, Tirofiban Lamifiban, Xemilofiban
- Thromboxane synthaselreceptor inhibitors: Aspirin, Isbogrel
- Thrombolytic drugs:
- Tissue plasminogen activator (t-PA) Streptokinase, Alteplase, Anistreplase, Urokinase
- Clotting factors: Factor VII Factor IX
- Vitamin K: Phytomenadione, Menadione
- Antifibrinolysin drugs: Aminocaproic acid, Tranexamic acid

3. Anti Hyperlipidemic Drugs

- Bile acid-binding resins: Choleslyramine, Colestipol
- Cholesterol synthesis inhibitors: Lovastatin, Pravastatin, Simvastatin, Fluvastatin
- VLDL secretion inhibitors: Niacin
- Lipoprotein lipase stimulants: Gemfibrozil, Febofibrate, Clofibrate
- Antioxidant agents: Probucol

Non-steroidal anti-inflammatory and anti-gout drugs

- Anti-inflammatory drugs:
- Salicylates: Aspirin, Sodium salicylate
- Newer non-steroidals: buprofen, Indomethacin, Naproxen, Piroxicam
- Slow-acting antirheumatic drugs: Methotrexate, Hydrochloroquine Penicillamine, Gold
- Acetaminophen class: Paracetamol Phenacetin
- Drugs used in Gout:
- Anti-inflammatory drugs: Colchicine, Indomethacin, Ibuprofen
- Uricosurics: Probencid, Sulfinpyrazone
- Xanthine-oxidase inhibitors: Allopurinol

ENDOCRINE DRUGS

- Growth hormone analogue: Somatrem
- Somatostatin analogue: Octreotide
- ACTH analogue: Cosyntropin
- Gonadotropin-Releasing hormone analogues: Leuprolide, Gaserelin, Nafarelin
- Follicle-Stimulating hormone activity: Urofollitin
- Leutinising hormone activity:Human chorianic gonadotrophin
- FSH and LH activity: Menotropins
- Inhibitors of prolactin release: Bromocriptine
- Antidiuretic hormone analogue: Desmopressin

1. Thyroid and Anti-thyroid Drugs

- Thyroid hormones: Thyroxine, Triiodothyronine
- Antithyroid drugs: Propylthiouracil, Iodide salts, Radioactive iodine, Ipodate, Methimazole
- Miscellaneous: Propranolol

2. Adrenocorticosteroids and Antagonists

- Corticosteroid agonists:
- Glucocorticoids: Cortisol, Dexamethasone, Triamcinolone, Beclomethasone, Triamcinolone acetonide
- Mineralocorticoids: Aldosterone, Fludrocortisone
- Corticosteroid antagonists:
- Receptor antagonists: Spironolactone, Mifepristone
- Synthesis inhibitors: Aminoglutethimide, Metyrapone, Ketokonazole

3. Gonadal Hormone and Inhibitors

- Estrogens:
- Natural: Estradiol, Estrone, Estriol
- Synthetic: Ethinyl estradiol, Mestranol, Diethylstilbestrol
- Estrogen partial agoriists:Tamoxifen, Clomiphene
- Progestins:
- Natural: Progesterone
- Synthetic: Norgestrel, Medroxyprogesterone, Norethindrone
- Partial agonists: Danazol
- Antiprogestins: Mifepristone
- Androgens:
- Natural: Testosterone
- Synthetic: Methyltestosterone, Fluoxymesterone
- Anabolic steroids: Oxandrolone Stanozolol
- Antiandrogens:
- Synthesis inhibitors: Finasteride
- Receptor antagonists: Flutamide Cyproterone

4. Insulin and Oral Anti-diabetic Agents

- Insulin preparations:
- Rapid-acting: Insulin (Regular, crystalline zinc insulin) Insulin zinc suspension (semilente)
- Intermediate-acting: Isophane insulin suspension (NPH insulin), Insulin zinc suspension (Iente)
- Long-acting: Protamine zinc insulin suspension (PZI), Insulin zinc suspension extended (ultralente)
- Oral anti-diabetic agents:
- Sulfonylureas: Tolbutamide, Chlorpropamide, Glyburide, Glipizide
- Biguanides: Phenformin, Metformin, Buformin
- Thiozolidinediones: Englitazone, Pioglitazone
- Glycosidase inhibitor: Acarbose

5. Hormones Affecting Calcium Homeostasis

- Major hormones:
- Parathyroid hormone
- Calcitonin
- Vitamin D analogues: Cholecalciferol (Vitamin D_3) Ergocalciferol (Vitamin D_2) Calciferol (25-Hydroxy Vitamin D_3) Calcitriol (1, 25-Dihydroxy Vitamin D_3) Secalcifediol (24, 25-dihydroxy Vitamin D_3) Dihydrotachysterol
- Drugs Affecting Bone Mineral Homeostasis
- Endogenous agents: PTH, Vitamin D, ‘Calcitonin, Estrogen, Glucocorticoids
- Exogenous agents: Bisphosphonates: Alendronate, Residronate Fluoride

CHEMOTHERAPY

1. Antibiotics

- Penicillins:
- Limited spectrum: Penicillin G, Penicillin V
- Beta-Iactamase-resistant: Methicillin, Nafcillin, Oxacillin, Cloxacillin
- Wider spectrum: Ampicillin, Carbencillin, Amoxicillin, Ticarcillin
- Cephalosporins:
- First-generation: Cephalothin Cefazolin Cephradine Cephapirin
- Second-generation: Cefamandole Cefaclor Cefotetan Cefoxitin
- Third-generation: Cefoperazone Cefotaxime Ceftazidime Ceftriaxone
- Carbapenam: Imipenam
- Monobactam: Aztreonam
- Beta-Iactamase inhibitors: Clavulanic acid, Sulbactam, Tazobactam
- Chloramphenicol: Chloramphenicol
- Tetracyclines: Demeclocycline, Doxycycline, Minocycline
- Aminoglycosides:
- Systemic: Gentamycin Tobramycin Amikacin Netilmycin Streptomycin
- Local: Neomycin Gentamycin Kanamycin
- Aminocyclitols: Spectinomycin
- Polymyxins: Polymyxin B, Colistin (Polymyxin E)

2. Anti-mycobacterial Drugs

Anti-tubercular drugs

- Pyridines: Isoniazid, Ethionamide, Pyrazinamide
- Rifamycins: Rifampacin
- Diamines: Ethambutol
- Aminoglycosides: Streptomycin
- Salicylates: p-Aminosalicyclic acid (PAS)
- Antibiotics: Capreomycin, Cycloserine, Viomycin

Anti-leprotic drugs

- Sulfones: Dapsone Acedapsone
- Phenazines: Clofazimine
- Thiosemicarbazones: Amithiozone

3. Sulphonamides

Sulfonamides

- Oral agents: Sulfisoxazole, Triple sulfas, Sulfamethoxazole, Sulfadiazine
- Local agents: Sulfacetamide, Sulfasalazine, Mafenide, Sulfadiazine
- Combination agents:
  Co-trimoxazole: Trimethoprim-sulfamethoxazole Pyrimethamine-sulfadoxine
- Folate reductase inhibitors: Trimethoprirn, Pyrimethamine

4. Anti-fungal Drugs

- Drugs for systemic mycoses: Amphotericin B, Flucytosine, Fluconazole Itraconazole, Ketoconazole, Voriconazole
- Drugs for Suferficial infections:
- Oral: Griseofulvin, Ketoconazole
- Topical: Nystatin, Miconazole, Clotrimazole, Tolnaftate

5. Anti-viral Drugs

- Drugs for Herpes-Acyclovir, Ganciclovir, Foscarnet
- Drugs for Influenza-Amantadine, Ramantidine, Zanamivir, Oseltamivir
- Drugs for HBV and HCV-Interferon-alpha, Lamivudine, Ribavirin
- Drugs for HIV
- Fusion inhibitors: Indinavir, Alnpenavir, Lopinavir, Nelfinavir, Ritonavir Saquinavir
- Protease inhibitors: Enfuvirtide
- Reverse transcripatase inhibitors:
- Nucleoside type: Zidovudine, Abacavir, Didanosine, Lamivudine, Stavudine Zalcitabine
- Non-nucleoside type: Delavirdine, Efavirenz, Nevirapine, Tenofovir

6. Fluoroquinolones, Macrolides and Urinary Antiseptics

- Fluoroquinolones: Norfloxacin, Ciprofloxacin, Ofloxacin, Pefloxcin, Temafloxacin
- Macrolides: Erythromycin, Azithromycin, Roxithromycin, Clarithromycin
- Lincosamides: Lincomycin, Clindamycin
- Glycopeptides: Vancomycin
- Nitroimidazoles: Metronidazole
- Urinary tract antiseptic-
- Nitrofurans: Nitrofurantoin
- Quinolones: Nalidixic acid Cinoxacin
- Methenamines: Methenamine mandelate Methynamine hippurate Cycloserine

7. Disinfectants and Antiseptics

- Alcohols, aldehydes and acids: Ethanol, Formaldehyde, Acetic acid, Isopropanal, Glutaraldehyde, Salycylic acid
- Halogens: Iodine, Chlorine, Povidone-iodide, Halazone
- Heavy metals: Silver nitrate, Mercury bichloride, Silver sulfadiazine, Nitromersol Thimerosol
- Chlorinate phenols: Hexachlorophene, Trilocarban, Chlorhexidine
- Cationic surfactants: Benzalkonium chloride, Cetylpyridinium chloride

8. Drugs for Malaria

- Tissue schizontocides used for causal prophylaxis: Pyrimethamine, Primaquine
- Tissue schizontocides used to prevent relapse: Primaquine, Pyrimethamine
- Schizontocides (Blood schizontocides) used for clinical or suppressive cure: Chloroquine, Quinine, Mefloquine, Halofantrine
- Gametocidocytes: Chloroquine, Quinine
- Sporontocides: Primaquine, Chloroguanide

9. Drugs for Amoebiasis

- Asymptomatic intestinal: Diloxanide furoate, Iodoquinol, Paramomycin
- Mild-to-severe intestinal: Metronidazole plus diloxanide, Chloroquine, Paramomycin
- Hepatic abscess: Metronidazole plus diloxanide, Emetine followed by chloroquine plus diloxanide

10. Drugs for Trypanosomiasis

Pentamidine, Melarsopral, Nifurtiniox, Suramin

11. Drugs for Leishmaniasis

Sodium stibogluconate, Pentamidine, Metronidazole, Amphotericin B

12. Anti-helminthic Drugs

- Drugs that act against Nematodes: Mebendazole, Thiabendazole, Diethylcarbamazine, Ivermectin, Pyrental Pamoate, Levamisole, Albendazole
- Drugs that act against Trematodes: Praziquantel, Bithionol, Metrifonate Oxamniquine
- Drugs that act against Cestodes: Niclosamide

ANTI CANCER DRUGS

Alkylating Agents

- Nitrogen mustards: Cyclophosphomide, Mecloretha-mine, Chlorambucil
- Nitrosoureas: Carmustine, Lomustine, Semustine
- Alkyl sulfonates: Busulfan
- Platinum complex: Cisplatin, Carboplatin
- Triazines:. Dacarbazine
- Hydrazines: Procarbazine

Anti-metabolites

- Folate analogues: Methotrexate
- Purine analogues: Mercaptopurine, Thioguanine
- Pyrimidine analogues: Fluorouracil, Cytarabine
- Plant alkaloids:
- Vinca alkaloids: Vinblastine Vincristine
- Podophyllotoxins: Etoposide Teniposide
- Taxols: Paclitaxel Taxotere

Antibiotics

- Anthracyclines: Doxorubicin, Daunorubicin
- Bleomycins: Bleomycin
- Actinomycins: Dactinomycin
- Mitomycins: Mytomycin

Hormones

- Adrenocorticoids: Prednisolone Hydrocortisone
- Androgens: Testosterone Fluoxymesterone
- Estrogens: Diethylstilbestrol Ethinyl estradiol
- Progestins: Hydroxyprogesterone Medroxy estradiol
- Antiestrogens: Tamoxifen
- Antiandrogens: Flutamide
- Gonadotropin-releasing hormone agonists: Leuprolide Goserelin

IMMUNOSUPPRESANTS

- Steroids: Prednisolone
- Antibiotics: Cyclosporine, Tacrolimus, Dactinomycin, Rapamycin
- Antimetabolites: Azathioprine, Mercaptopurine, Cyta-rabine, Methotrexate
- Alkylating agents: Cyclophosphamide, Chlorambucil
- Antibodies: Lymphocyte immune globulin Mura-monab-CD3, Rho-(D) globulin

IMMUNOSTIMULATORS

- Figrastim, Interferon-gamma, Levamisole, Sargramostim

DRUGS USED IN GASTROINTESTINAL DISORDERS

1. Laxative and Purgatives

- Irritant: Castor Oil, Cascara, Senna, Phenolphalein
- Bulk-forming: Bran, Isabgol, Methylcellulose
- Saline cathertics: Sodium phosphate, Magnesium sulfate, Milk of magnesia
- Stool-softening: Dioctyl sodium sulfosuccinate (docusate)
- Lubricating: Mineral oil, Glycerin

2. Anti-ulcer Drugs

- Histamine H_2-receptor antagonists: Cimetidine, Raniti-dine, Famotidine, Nizatidine
- Inhibitors of H/K-ATPase (Proton pump): Omeprazole, Lanceprazole
- Specific muscarinic antagonists: Pirenzepine, Telenz-epine
- Prostaglandins: Misoprostol
- Mucoprotective agents: Sucralfate, Bismuth salts, Liquorice
- Antacids:
- Aluminium-containing antacids: Aluminium hydroxide gel, Basic aluminium carbonate gel, Dihydroxyaluminum sodium carbonate, Aluminum phosphate gel
- Calcium-containing antacids: Calcium carbonate
- Magnesium-containing antacids: Magaldrate, Magne-sium hydroxide gel
- Sodium-containing antacids: Sodium citrate

3. Anti-emetic Drugs

- Phenothiazines: Chlorpromazine, Perphenazine, Prochlorperazine, Promethazine Thiethylperazine, Triflupromazine
- Butyrophenones: Droperidol
- Benzamides: Metoclopramide, Trimethobenzamide
- Cannabinoids: Dronabinol, Nabilone

Prokinetic agents

- Domperidone, Cisapride

Poisoning or Overdose	Specific Antidotes
Acetaminophen	Acetyl cysteine
Chlolinesterase inhibitors (Physostigmine)	Atropine, Oximes (Pralidoxime)
Iron salts	Desferoxamine
Digoxin	Digoxin specific FAB antibodies
Caffeine, Theophylline	Esmolol
Benzodiazepine	Flumazenil
Lead	EDTA sodium
Gold, Arsenic or Heavy metals	Dimercaprol (BAL)
Copper	Penicillamine
Opioid Analgelsic	Naloxone, Nalorphine
Ethanol	Disulfiram
LSD	Phenothizine
Leptazole	Dimercaprol
Organophosphorous	Pralidoxime

Disease	Causative Organism
Anthrax	Bacillus anthrosis
Malaria	Plasmodium vivax P. falciparam, P. Ovale, P. Malariae
Cholera	Vibrio cholera
Diphtheria	Cornybacterium diphtheria
Plague	Yersinia pestis
Gonorrhea	Niesseria gonorrhea
Gas gangrene	Clostridium perfrengens
Amoebiasis	Entameoba histolytica
Syphilis	Tropnema pellidum
Whooping cough	Boardetella pertusis
Urinary tract infections	E. Coli and Pseudomonas species
Kala-azar	Leishmenia donavani
Tetanus	Clostridium tetani
Typhoid	Salmonella typhi
Gastroenteritis	Shigella dysenterica
Tuberculosis	Mycobacterium tuberculosis
Leprosy	M.leprae
Endocarditis	Streptococci

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UNIT 3

PHARMACEUTICAL CHEMISTRY

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CHAPTER 1

PHYSICAL CHEMISTRY

THERMODYNAMIC AND ENERGETICS

- **Thermodynamics:** The study of interconversion of heat and other forms of energy is called thermodynamics.
- **System:** A specific portion of the universe which is under thermodynamic study is called a system.
- **Surroundings:** The portion of the universe other than that selected for the purpose of thermodynamic study is called the surroundings.

Types of Thermodynamic Systems

Open system

A system that can exchange matter as well as energy with its surroundings is called an open system.

Closed system

A system that can exchange only energy but not matter with its surroundings is called a closed system.

Isolated system

A system that can exchange neither energy nor matter with its surroundings is called an isolated system.

Properties of Thermodynamics System

Intensive properties

The properties which do not depend on the total quantity of matter present in the system, are called intensive properties. Example: Temperature, pressure, density.

Extensive properties

The properties which depend on the total quantity of matter present in the system, are called extensive properties. Example: amount of heat, volume, weight.

Thermodynamic equilibrium

A system is said to be in thermodynamic equilibrium, if its macroscopic (measurable) properties such as temperature, pressure and composition do not undergo any change with time.

Process

The path by which the system changes from one state to another is called process.

Difference between isothermal process and adiabatic process

	Isothermal Process	Adiabatic Process
1.	In an isothermal process, temperature of the system remains constant.	In an adiabatic process, temperature of the system changes.
2.	In this process, the system exchanges heat with the surroundings.	In this process, the system does not exchange heat with the surroundings.
3.	Total internal energy of the system remains constant ($\Delta E = 0$).	Total internal energy ΔE of the system changes.
4.	Total heat content of the system changes ($\Delta H \neq 0$).	Total heat content of the system remains constant ($\Delta H = 0$).
5.	In this process, the system is not thermally isolated.	In this process, the system is thermally isolated.
6.	This process can be made reversible.	This process cannot be made reversible.
7.	In this process, $Q = W$ as $\Delta E = 0$.	In this process, $W = \Delta E$ as $\Delta Q = 0$

Isobaric process

The process which takes place at a constant pressure is called an isobaric process.

Isochoric process

The process which takes place at a constant volume is called an isochoric process.

Cyclic process

The process involving a series of operations which finally bring the system back to its original state is called a cyclic process.

Difference between reversible process and irreversible process

	Reversible Process	Irreversible Process
1.	The process whose direction can be reversed at any stage by an infinitesimal increase in the opposing force is called a reversible process.	The process whose direction cannot be reversed by an infinitesimal increase in the opposing force is called an irreversible process.
2.	Such a process is not spontaneous, takes place infinitesimally slowly and takes infinite time for completion.	Such a process is spontaneous and takes finite time for completion.
3.	In this process, the thermodynamic equilibrium is always maintained between the system and the surroundings.	The thermodynamic equilibrium is attained only when the process is completed.
4.	The opposing force is infinitesimally less than the driving force.	The opposing force is significantly smaller than the driving force.
5.	It is an ideal or hypothetical process.	It is a practical or real force.
6.	Maximum work can be derived from such a process.	Work derived from such a process is always less than maximum work.

Expression for the work obtained in an isothermal and irreversible process (against constant pressure)

$$W = P(V_2 - V_1) = P\Delta V$$

where

W = Work done

P = Pressure

V_1 = Initial volume

V_2 = Final volume

ΔV = Change in volume

Work done in vacuum

As $P = 0$, $W = 0$ i.e., when a gas expands in vacuum, no work is done.

Work done in a cyclic process

As $\Delta V = 0$, $W = 0$ i.e., work done in a cyclic process is always zero.

- Expression for maximum work obtained in an isothermal reversible expansion of an ideal gas

$$W_m = 2.303\ nRT \log 10 \frac{V_2}{V_1}$$

$$W_m = 2.303\ nRT \log \frac{P_2}{P_1}$$

where

W_{max} = Maximum work done

n = Number of moles

R = Gas constant

T = Temperature in kelvin

V_1 = Initial volume

V_2 = Final volume

P_1 = Initial pressure

P_2 = Final pressure

Laws of Thermodynamics

First law of thermodynamics (law of conservation of energy)

This law suggests that energy can be transferred from one system to another in many forms. Also, it cannot be *created* or *destroyed*. Thus, the total amount of energy available in the Universe is constant.

Einstein's famous equation (written below) describes the relationship between energy and matter:

$$E = mc^2$$

In the equation above, **energy (E)** is equal to **matter (m)** times the square of a constant **(c)**.

Einstein suggested that energy and matter are interchangeable.

Second law of thermodynamics

Heat cannot be transfered from a colder to a hotter body. As a result of this fact of thermodynamics, natural processes that involve energy transfer must have one direction, and all natural processes are irreversible.

This law also predicts that the entropy of an isolated system always increases with time. Entropy is the measure of the disorder or randomness of energy and matter in a system. Because of the second law of thermodynamics, both energy and matter in the Universe are becoming less useful with the passage of time.

Third law of thermodynamics

The third law of thermodynamics states that if all the thermal motion of molecules (kinetic energy) could be removed, a state called absolute zero would occur. Absolute zero results in a temperature of 0 Kelvin or –273.15° Celsius.

$$\text{Absolute Zero} = 0 \text{ Kelvin} = -273.15^\circ \text{ Celsius}$$

The Universe will attain absolute zero when all energy and matter is randomly distributed across space. The current temperature of empty space in the Universe is about 2.7 Kelvin.

First law of thermodynamics

It can be stated in any one of the following forms:

a. Energy can neither be created nor destroyed; however, it may be converted from one form into another.
b. Whenever energy in one form disappears, an equivalent amount of energy in another form appears.
c. It is not possible for any machine to produce work without consuming energy. Such a machine is called a perpetual motion machine.
d. The total energy of the universe remains constant.

Expression for first law of thermodynamics

$$Q = \Delta E + W \text{ or } Q = \Delta E + P\Delta V$$

where
Q = Amount of heat absorbed
ΔE = Change in the internal energy
W = Work done

a. For isothermal process, temperature (T) remains constant.

$$\Delta E = 0$$
$$\Delta Q = P\Delta V$$

b. For isochoric process, volume (V) remains constant.

$$\Delta V = 0$$
$$\Delta Q = \Delta E$$

c. For isobaric process, pressure (P) remains constant.

$$\Delta Q = \Delta E + P\Delta V$$

d. For adiabatic process, heat is neither absorbed not lost.

$$\Delta Q = 0$$
$$\Delta E = P\Delta V$$

Note

If heat flows into a system or the surroundings to do work on it, the internal energy increases and the sign of *q* or *w* is positive.

Conversely, heat flowing out of the system or work done by the system will be at the expense of the internal energy, and will therefore be negative

Internal energy or intrinsic energy (E)

The sum of all forms of energy associated with the matter present in a system is called internal energy or intrinsic energy of the system. The absolute or actual value of the internal energy cannot be determined but the change in the internal energy (ΔE) can be measured.

$$\Delta E = E_2 - E_1$$

The change in the internal energy of in a process is independent of the path taken and depends only on the initial and final states of the system. Hence, it is a state function.

Enthalpy of a system (H)

The total heat content a system is called enthalpy of the system.

$$H = E + PV$$

Expression for change in enthalpy (ΔH):

$$\Delta H = \Delta E + P\Delta V$$

For an isochoric process, volume remains constant.

$$\Delta V = 0$$
$$\Delta H_v = \Delta E$$

For an isobaric process, pressure remains constant.

$$\Delta H_p = \Delta E + P\Delta V$$

Thermochemistry

The branch of chemistry which deals with the quantitative study of the heat changes associated with chemical reactions is called thermochemistry.

Heat of reaction (ΔH)

The quantity of heat absorbed or evolved (enthalpy change) during the complete transformation of the reactants into the products as shown in the corresponding thermo chemical equation, at constant temperature and pressure, is called the heat of reaction.

$$\Delta H = \Delta H_{(products)} - \Delta H_{(reactants)}$$

Example: $C_{(s)} + O_{2\,(g)} \longrightarrow CO_{2\,(g)}$; $\Delta H = 393.6$ kJ

Relationship between heats of reaction at constant pressure (ΔH) and at constant volume (ΔE)

$$\Delta H = \Delta E = P\Delta V \text{ or}$$
$$\Delta H = \Delta E + \Delta nRT \text{ or}$$
$$Q_p = Q_v + \Delta nRT$$

Heat of formation (ΔH_f)

The quantity of heat absorbed or evolved when one mole of a compound is formed from its constituent elements, with every substance being in its standard physical state is called heat of formation.

Heat of neutralization (ΔH_n)

The quantity of heat liberated when one gram equivalent of an acid is completely neutralized by one gram equivalent of a base in a very dilute solution is called the heat of neutralization.

Heat of combustion (ΔH_c)

The quantity of heat evolved when one mole of a compound is completely oxidised to its stable oxidation products, with every substance being in its standard physical state, is called heat of combustion.

Heat of solution (ΔH_s)

The quantity of heat absorbed or evolved when one mole of a compound dissolves completely in a large excess of a solvent so that further dilution of the solution produces no heat change, under standard conditions, is called the heat of solution of the compound in that solvent.

Example – $KCl_{(s)}$ + Water (Excess) → $KCl_{(aq)}$ + 18.4KJ

Molar Heat Capacity

The quantity of heat required to raise the temperature of one mole of a substance through one degree kelvin is called molar heat capacity of the substance.

Molar heat capacity at constant pressure (C_p)

The quantity of heat required to raise the temperature of one mole of a substance through one degree kelvin at constant pressure is called molar heat capacity at constant pressure.

$$C_p = \left(\frac{dq}{dt}\right)_p = \left(\frac{\Delta H}{\Delta T}\right)_p$$

Molar heat capacity at constant volume (C_v)

The quantity of heat required to raise the temperature of one mole of a gas by one degree kelvin at constant volume is called molar heat capacity at constant volume.

$$C_p = \left(\frac{dq}{dt}\right)_v = \frac{\Delta E}{\Delta T}$$

Relationship between C_p and C_v (Mayer's Relationship)

$$C_p - C_v = R$$

i.e., $C_p > C_v$

Kirchhoff's equation

Expression showing the effect of temperature on the heat of reaction at constant pressure:

$$\frac{\Delta H_2 - \Delta H_1}{T_2 - T_1} = \Delta C_p$$

Where

$\Delta C_p = (C_p \text{ of products}) - (C_p \text{ of reactants})$

ΔH_1 = Heat of reaction at temperature T_1

ΔH_2 = Heat of reaction at temperature T_2

Hess's law of constant heat summation

The total enthalpy change accompanying a chemical reaction is always constant (at constant pressure or constant volume) and is independent of the number of steps and the path taken to complete the reaction.

i.e., $\Delta H = \Delta H_1 + \Delta H_2 + \Delta H_3 + \ldots\ldots$

KINETICS OF A REACTION

Molecularity

Molecularity is the number of molecules involved in forming the product. For example, $N_2O_5 \rightarrow 2NO_2 + ½\ O_2$ is a slow unimolecular reaction and $½\ O_2 + ½\ O_2 \rightarrow O_2$ is a fast bimolecular reaction.

Order of Reaction

Consider the reaction:

$$A + B \longrightarrow C + D$$

The rate of the reaction is proportional to the concentration of A to the power of x, $[A]^x$ and also the rate

may be proportional to the concentration of B to the power of y, $[B]^y$.

The overall equation is, Rate = $k [A]^X [B]^Y$

The overall order of reaction is **x + y**

Rate Constant

A rate constant is a proportionality constant that appears in a rate law. For example, *k* is the rate constant in the rate law d[A]/dt = k[A].

Rate constants are independent of concentration but depend on other factors, most notably temperature.

Zero Order Reaction

- When the reaction rate is independent of concentration of the reacting substance, it depends on the zero power of the reactant and therefore is zero order reaction.
- In this type of reaction, the limiting factor is something other than concentration, for example, solubility or absorption of light in certain photochemical reactions.

Rate of concentration decrease

$$= \frac{-dCx}{dt} = K \quad \text{.....(1)}$$

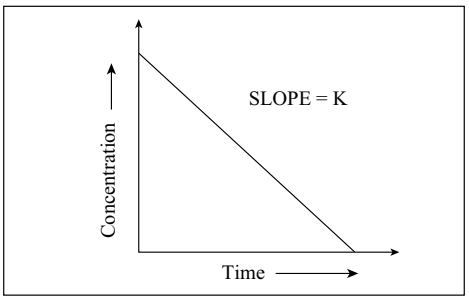


Figure 1.1 Rate of Concentration Decrease

Integrating the equation yields X = Kt + constant ..…… (2)

A plot of X vs time results in straight line with slope equal to K. The value of K indicates the amount of drug that is degraded per unit time, and intercept of line at time zero is equal to constant in equation (2).

The unit of K is conc $time^{-1}$, with typical units of mole $L^{-1} s^{-1}$.

Half-life is given by equation $t_{1/2} = Co/2k$.

Examples: Vitamin A acetates to anhydrous vitamin A.
Photolysis of cefotaxime.
Loss in colour of multi sulpha product.
Intravenous infusion.
Drug released from transdermal drug delivery systems.

First Order Reaction

When the reaction rate depends on the first power of concentration of a single reactant, it is considered to be **first order**.

Examples are

- Absorption, distribution, elimination rates.
- Microbial death kinetics.

Thus the rate of reaction is directly proportional to the concentration of reacting substance and can be expressed as follows:

Rate of concentration decrease

$$= \frac{-dCx}{dt} = KCx \quad \text{.....(3)}$$

If concentration of reactant X is 'a' at the beginning of reaction when t = 0, and if amount that has reacted after time t is denoted by x, then amount of X remaining at time t will be (a–x).

Therefore equation (3) can be rewritten as:

$$\frac{dCx}{dt} = K(a - x)$$

$$= \frac{dCx}{(a - x)} = -Kdt \quad \text{.....(4)}$$

Integrating equation (4) between time limit 0 to t

$$\int_z^{a-x} \frac{dCX}{dt} = -K\int_0^t dt$$

$$\ln (a - x) - \ln a = -Kt$$

$$\log (a - x) - \log a = -kt/2.303$$

$$\log (a - x) = \log a - Kt/2.303 \quad \text{.....(5)}$$

Equation (5) is like y = mx + c (linear relationship)

If first order law is obeyed, then a graph of log (a – x) v/s time t will give straight line with slope of –K/2.303 and an intercept of log a at t = 0.

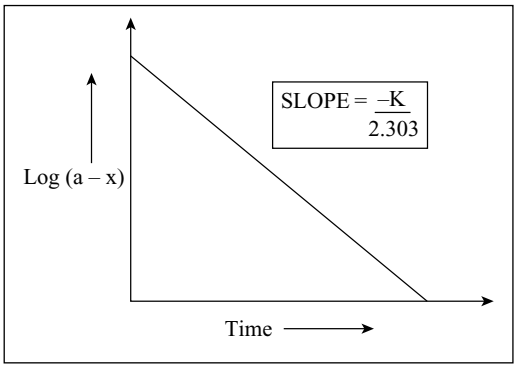


Figure 1.2 First Order Reaction

Rearranging equation (5) we have

$$K = \frac{2.303}{t} \log (a/a-x) \text{.....(6)}$$

Unit of K for first order is **time^{-1}** i.e., SI unit is (sec)$^{-1}$ because K is inversely proportional to t.

The half-life, $t_{1/2,}$ of a drug is the time required for 50% of drug to degrade and can be calculated as follows:

$$t_{\frac{1}{2}} = \frac{2.303}{k} \log \frac{C_0}{C} = \frac{2.303}{k} \log \frac{100}{50}$$

$$= \frac{2.303}{k} \log 2 = \frac{0.693}{k}$$

Therefore, $t_{\frac{1}{2}} = \frac{0.693}{k}$ .....(7)

Shelf life

It is the time required to reduce the concentration of the reactant to 90% of its initial concentration. The $t_{10\%}$ value can be calculated as

$$t_{10\%} = \frac{2.303}{k} \log \frac{100}{90} = \frac{0.104}{k}$$

$$t_{10\%} = \frac{0.104}{k} \text{.....(8)}$$

or $t_{10\%} = 0.152\, t_{\frac{1}{2}}$

Number of half life elapsed	Initial concentration remaining	Completeness of process
0	100	0 %
1	50	50 %
2	25	75 %
3	12.5	87.5 %
4	6.25	93.75 %
5	3.13	96.87 %
6	1.56	98.44 %
7	0.78	99.22 %

Question 1 Penicillin solution containing 500 units per ml has a half life of 10 days. What will the concentration be 7 days?

Ans. $K = 0.693/t_{1/2}$

$K = 0.693/10 = 0.0693$ Days^{-1}

$\ln C_o/C = kt$

$\ln$ 500 units per ml/C = kt

$\ln$ 500 units per ml/C = 0.0693 × 7 = 0.483

500/C = Anti ln (0.483) = 1.62

C = 308 units per ml

Question 2 A penicillin solution has a half life of 21 days. How long it will take for the potency to drop to 90% of the initial potency?

Ans. $K = 0.693/t_{1/2}$

$K = 0.693/21 = 0.033$ Days^{-1}

$\ln C_o/C = kt$

$\ln$ 100 %/90% = 0.033 × t

t = 3.2 days

Question 3 A penicillin solution has an initial potency of 125 mg/5 ml. After one month in refrigerator, the potency is found to be 100 mg/5 ml. What is the half life of penicillin under these conditions?

Ans. $\ln C_o/C = kt$

$\ln$ 125 mg per 5 ml/100 mg per 5 ml = k × 30 days

k = 0.0074 days^{-1}

$t_{1/2} = 0.693/k$

$t_{1/2} = 0.693/0.0074 = 94$ Days

Pseudo–Zero Order Reaction

In solid state, many drugs decompose by pseudo zero order i.e., reaction between drug and moisture in solid dosage form. The system behaves like suspensions and because of the presence of excess solid drug; the first order rate actually becomes pseudo zero order. Equation for it is similar to zero order except K is replaced by K'.

Example: Suspension degradation follows pseudo zero order reaction.

Pseudo-First Order Reaction

Here, a second order or bimolecular reaction is made to behave like first order. This is found in the case in which one reacting material is present in great excess or is maintained at constant concentration as compared with other substance. Here reaction rate is determined by one reactant even though two are present.

Examples:

- Decomposition of ascorbic acid tablet.
- Aspirin hydrolysis.

Summary of Parameters

Order of reaction	Integrate rate equation	$t_{1/2}$	Linear Graph			
			Ordinate	Abscissa	Slope	Intercept
0	X = Kt	= a/2K	X	t	K	0
1	log (a/a–x) = Kt/2.303	= 0.693/K	log (a–x)	t	–K/2.303	log a
2 (a = b)	X/a (a–x) = Kt	= 1/aK	1/a–x	t	K	1/a

Unit of order of reaction

Order of reaction	Unit of K
Zero	$M\ L^{-1}Sec^{-1}$
First	Sec^{-1}
Second	$M^{-1}Sec^{-1}$

Half-life determination method

- The relationship in general between half-life of a reaction in which the concentrations of all reactants are identical, is

$$t_{1/2} \propto 1/a^{n-1}$$

Where ***n*** is the order of reaction.

Determination of $t_{10\%}$ by Arrhenius equation

- Temperature influences rate and order of reaction. So the shelf life of product can be obtained under exaggerated condition.
- It is said that for every 10°C rise, rate of reaction increases by 2–3 times.
- For this, **Arrhenius equation** is used i.e., $\mathbf{K = Ae^{-\varepsilon a/RT}}$

where A = frequency factor,
R = gas constant,
K = rate constant,
εa = energy of activation

Therefore, $$\log K = \log A - \frac{\varepsilon a}{2.303RT}$$

- Graph of log K v/s 1/T gives straight line with slope $\frac{\varepsilon a}{2.303R}$ and intercepts at t = 0.
- εa represents energy required by a molecule to react and undergo reaction. The higher is the value of εa, higher is the dependency on temperature.
- Rate constant at different temperature can be obtained by

$$\log(K2/K1) = \frac{\varepsilon a(T2 - T1)}{R(T2 * T1)}$$

- With help of K at different temperature we can predict $T_{10}\%$

$t_{10\%} = 0.105/k$ *(for first order only)*

$t_{10\%} = C_0/10*k$ *(for zero order only)*

KINETIC THEORY OF GASES AND SOLUTION CHEMISTRY

Kinetic Theory Assumptions About Ideal Gases

There is no such thing as an ideal gas, of course, but many gases behave approximately as if they were ideal at ordinary working temperatures and pressures.

The assumptions are:

- Gases are made up of molecules which are in constant random motion in straight lines.
- The molecules behave as rigid spheres.
- Pressure is due to collisions between the molecules and the walls of the container.
- All collisions, both between the molecules themselves, and between the molecules and the walls of the container, are perfectly elastic. (That means that there is no loss of kinetic energy during the collision.)
- The temperature of the gas is proportional to the average kinetic energy of the molecules.

Now, two key assumptions, because these are the two most important ways in which real gases differ from ideal gases:

- There are no (or entirely negligible) intermolecular forces between the gas molecules.
- The volume occupied by the molecules themselves is entirely negligible relative to the volume of the container.

The ideal gas equation is:

$$\mathbf{pV = nRT}$$

Pressure, p: Pressure is measured in Pascal, Pa, sometimes expressed as Newton per square metre, $N\ m^{-2}$.

Volume, V–SI unit of volume is the cubic metre, m^3
Number of moles, n

$$pV = \frac{\text{mass(g)}}{\text{mass of 1 mole(g)}} \times RT$$

The gas constant, R–The SI value for R is 8.311 J K^{-1} mol^{-1}.

The temperature, T–The temperature has to be in Kelvin.

Molar volume at STP

1 mole of any gas occupies 22.4 dm^3 at STP (standard temperature and pressure, taken as 0°C and 1 atmosphere pressure).

The molar volume of an ideal gas is therefore 22.4 dm^3 at STP.

The van der Waals Equation for Real Gases

$$\left(p + \frac{an^2}{V^2}\right)(V - nb) = nRT$$

- The measured pressure is less than the ideal pressure for a real gas. van der Waal has added a term to compensate for that.
- In the volume term, van der Waal has subtracted the value nb to allow for the space taken up by the molecules themselves.
- a and b are constants for any particular gas, but they vary from gas to gas to allow for the different intermolecular forces, and molecular sizes.

Boyle's Law

For a fixed mass of gas at constant temperature, the volume is inversely proportional to the pressure i.e., **pV = constant**

That means that, for example, if you double the pressure, you will halve the volume. If you increase the pressure 10 times, the volume will decrease 10 times.

Charles' Law

For a fixed mass of gas at constant pressure, the volume is directly proportional to the kelvin temperature i.e., **V = constant × T**

That means, for example, that if you double the kelvin temperature from, say to 300 K to 600 K, at constant pressure, the volume of a fixed mass of the gas will double as well.

Colligative Properties

Colligative properties are a subset of the intensive properties of a system and can only be applied to solutions. It depends only on the ratio of the number of particles of solute and solvent in the solution, not the identity of the solute.

1. Vapour Pressure Depression
2. Boiling Point Elevation
3. Freezing Point Depression
4. Osmotic Pressure

Ideal Solutions

An ideal solution is the one in which the molecules attract one another with equal forces irrespective of their nature. Thus, a solution composed of two components A and B will be an ideal one if the forces between A and A, B and B should be the same. An ideal solution possesses the following characteristics:

(i) Volume change of mixing should be zero.

$$\Delta V_{mix} = 0;\ V_{solvent} + V_{solute} = V_{solution}$$

(ii) Heat change on mixing should be zero.

$$\Delta H_{mix} = 0 \text{ (Heat is neither absorbed nor evolved).}$$

(iii) There should be no chemical reaction between the solvent and the solute.

(iv) Solute molecules should be not dissociate or associate in the ideal solution.

(v) Ideal solutions must obey Raoult's law at all concentrations.

Comparison between ideal and non-ideal solutions

Ideal solutions	Non-ideal solutions	
	Positive deviation from Raoult's law	Negative deviation from Raoult's law
1. Obey Raoult's law at every range of concentration.	1. Do not obey Raoult's law.	1. Do not obey Raoult's law.
2. $\Delta H_{mix} = 0$; It is neither evolved nor absorbed during dissolution.	2. $\Delta H_{mix} > 0$. Endothermic dissolution; heat is absorbed.	2. $\Delta H_{mix} < 0$. Exothermic dissolution; heat is evolved.
3. $\Delta V_{mix} = 0$; total volume of solution is equal to sum of volumes of the components.	3. $\Delta V_{mix} > 0$. Volume is increased after dissolution.	3. $\Delta V_{mix} < 0$. Volume is decreased during dissolution.

Ideal solutions	Non-ideal solutions	
	Positive deviation from Raoult's law	Negative deviation from Raoult's law
4. $P = pA + pB = p_A^0X_A + p_B^0X_B$ i.e., $p_A =$	4. $p_A > p_A^0X_A$; $p_B > p_B^0X_B$ $\therefore p_A + p_B > p_A^0X_A + p_B^0X_B$	4. $p_A < p_A^0X_A$; $p_B < p_B^0X_B$ $\therefore p_A + p_B < p_A^0X_A + p_B^0X_B$
5. A—A, A—B, B—B interactions should be same, i.e., 'A' and 'B' are identical in shape, size and character.	5. A—B attractive force should be weaker than A—A and B—B attractive forces. 'A' and 'B' have different shape, size and character.	5. A—B attractive force should be greater than A—A and B—B attractive forces. 'A' and 'B' have different shape, size and character.
6. Escaping tendency of 'A' and 'B' should be same in pure liquids and in the solution.	6. 'A' and 'B' escape easily showing higher vapour pressure than the expected value.	6. Escaping tendency of both components 'A' and 'B' is lowered showing lower vapour pressure than expected ideally.
Examples: dilute solutions; benzene + toluene: n-hexane + n-heptane; chlorobenzene + bromobenzene; n-butyl chloride + n-butyl bromide.	**Examples:** acetone + ethanol acetone + CS_2; water + methanol; water + ethanol; CCl_4 + toluene; CCl_4 + $CHCl_3$; acetone + benzene; CCl_4 + CH_3OH; Cyclohexane + ethanol	**Examples:** acetone + aniline; acetone + chloroform; CH_3OH + CH_3COOH; H_2O + HNO_3; Choloroform + diethyl ether, water + HCl; acetic acid + pyridine; Chloroform + benzene.

Raoult's Law

According to this law, the partial pressure of any volatile constituent of a solution at a constant temperature is equal to the vapour pressure of pure constituent multiplied by the mole fraction of that constituent in the solution.

Let a mixture (solution) be prepared by mixing n_A moles of liquid A and n_B moles of liquid B. Let p_A and p_B be the partial pressures of two constituents A and B in solution and p_A^0 and p_B^0 the vapour pressures in pure state respectively.

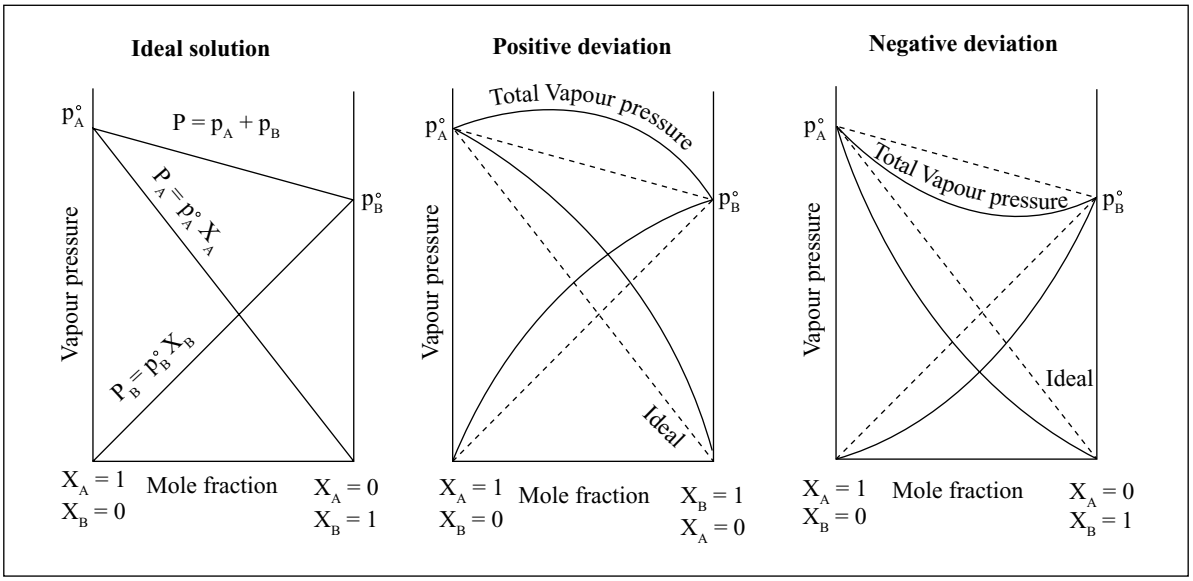


Figure 1.3 Raoult's Law

Thus, according to Raoult's law,

$$p_A = n_A/n_A+n_B\ p_A^0 = \text{mole fraction of } A \times p_A^0 = X_A p_A^0$$

$$p_B = n_B/n_A+n_B\ p_A^0 = \text{mole fraction of } B \times p_B^0 = X_B p_B^0$$

If the total pressure be P, then

$$P = p_A + p_B = n_A/n_A+n_B\ p_A^0 + n_B/n_A+n_B\ p_A^0 = X_A P_A^0 + X_B P_B^0$$

Ideal solutions obey Raoult's law at every range of concentration. Non-ideal solutions do not obey Raoult's law. They show either positive or negative deviation from Raoult's law.

Relation between Dalton's law and Raoult's law

The composition of the vapour in equilibrium with the solution can be calculated by applying Dalton's law of partial pressures. Let the mole fractions of vapours A and B be Y_A and Y_B respectively. Let P_A and P_B be the partial pressures of vapours A and B respectively and total pressure P.

$$p_A = Y_A P \quad .. (i)$$

$$p_B = Y_B P \quad .. (ii)$$

$$p_A = X_A P_A^0 \quad .. (iii)$$

$$p_B = X_B P_B^0 \quad .. (iv)$$

Equating (i) and (iii)

$$Y_A P = X_A P_A^0$$

or $$Y_A = X_A P_A^0/P = p_A/P$$

Similarly, equation (iii) and (iv)

$$Y_B = X_B P_B^0/P = p_B/P$$

Thus, in case of ideal solution the vapour phase is richer with more volatile components i.e., the one having relatively greater vapour pressure.

Reverse Osmosis

When a solution is separated from pure water by a semipermeable membrane, water moves towards solution on account of osmosis. This process continues till osmotic pressure becomes equal to hydrostatic pressure or osmosis can be stopped by applying external pressure equal to osmotic pressure on solution. If external pressure greater than osmotic pressure is applied, the flow of solvent molecules can be made to proceed from solution towards pure solvent, i.e., in reverse direction of the ordinary osmosis. This type of osmosis is termed reverse osmosis. Reverse osmosis is used for the desalination of sea water for getting fresh drinking water.

Van't Hoff Theory of Dilute Solutions

Van't Hoff realized that an analogy exists between gases and solutions, provided, osmotic pressure of solutions is used in place of ordinary gas pressure. He showed that for dilute solutions of **non-electrolysis**, the following laws hold good.

Boyle-Van't Hoff law

The osmotic pressure (P or α) of a solution is directly proportional to its concentration (C) when the temperature is kept constant. The concentration of the solution containing one gram mole in V litres is equal to 1/V (C = 1/V)

Thus $P \propto C$ (when temperature is constant)

or $P \propto 1/V$

or $PV = \text{constant}$

or $\varpi V = \text{constant}$

Van't Hoff presumed that the osmotic pressure is due to the bombardment of solute molecules against the semipermeable membrane as the gas pressure is due to hits recorded by gas molecules against the walls of its container.

Pressure-temperature law (Gay-Lussac-Van't Hoff Law)

Concentration remaining same; the osmotic pressure of a dilute solution is directly proportional to its absolute temperature (T), i.e.,

$$P \propto T$$

or $P/T = \text{constant}$ or μ/T constant

Combining the two laws, i.e., when concentration and temperature both are changing, the osmotic pressure will be given by:

$$P \propto CT$$

or $P = kCT$

or $P = k.1/V.T$ (since C = 1/V)

or $PV = ST$ or $\varpi V = ST$

S is called molar solution constant.

Here V is the volume of solution containing one gram mole of the solute. The value of 5 comes out to 0.082 lit atm K^{-1} mol^{-1} which is in agreement with the value of R, the molar gas constant. In case the solution contains n gram moles in V litres, the general equation would become

$$PV = nST \quad \text{or} \quad \varpi V = ST$$

Third law

Equimolecular solutions of different solutes exert equal osmotic pressure under identical conditions of temperature. Such solutions which have the same osmotic pressure are termed isotonic or iso-osmotic. When two isotonic solutions are separated by a semipermeable membrane, no flow of solvent molecules is observed on either side.

The law is similar to Avogadro's hypothesis. It can be stated as, "Equal volumes of dilute solutions of different solutes, having the same temperature and osmotic pressure, contain equal number of molecules."

$$\text{For solution I, } PV = n_1ST$$

$$\text{For solution II, } PV = n_2ST$$

Thus, n_1 must be equal to n_2 when P, V and T are same.

This led van't Hoff to suggest that a solute in dissolved state (i.e., in solution) behaves as a gas and the osmotic pressure of the solution is equal to the pressure which the solute would exert if it were a gas at the same temperature and occupying the same volume as that of the solution. This statement is known as van't Hoff.

Henry's Law

The solubility of a gas in a liquid depends on temperature, the partial pressure of the gas over the liquid, the nature of the solvent and the nature of the gas. The most common solvent is water.

Gas solubility is always limited by the equilibrium between the gas and a saturated solution of the gas. The dissolved gas will always follow Henry's law.

The concentration of dissolved gas depends on the partial pressure of the gas. The partial pressure controls the number of gas molecule collisions with the surface of the solution. If the partial pressure is doubled, the number of collisions with the surface will double. The increased number of collisions produce more dissolved gas.

$$P_{gas} = kC \text{ at constant T.}$$

The Henry's law constant "k" is different for every gas, temperature and solvent. The units on "k" depend on the units used for concentration and pressure.

The value for k is the same for the same temperature, gas and solvent. This means the concentration to pressure ratio is the same when pressures change. The following equation can be used to relate pressure and concentration changes.

$$\frac{C_1}{P_1} = \frac{C_2}{P_2}$$

Osmolarity

- It is a **colligative property.**
  Colligative property means when a non-volatile solute is dissolved in a solvent, the resulting property of solution is independent of the nature of solute but is determined by the concentration of solute particle.
- **Osmoles:** Number of osmotically active particles in solution.
- **Osmolarity:** Osmoles or milliosmoles **per liter of solution**.
- **Osmolality: Osmoles** or milliosmoles **per kg of solvent**.
- **Iso-osmotic:** When two different solutions separated by semipermiable membrane have same osmotic pressure, they are called as isoosmotic.
- **Isotonic:** When two different solutions separated by biological membrane have same osmotic pressure, they are called as isotonic.

METHODS OF EXPRESSING THE CONCENTRATION OF A SOLUTION

(i) **Mass percentage or % by mass**

It is defined as the amount of solute in grams present in 100 grams of the solution.

Mass percentage = Mass of solute/Mass of solution × 100

= Mass of solute/Mass of solute +Mass of solvent × 100

= Mass of solute/Volume of solution × Density of solution × 100

The ratio Mass of solute/Mass of solvent is termed as mass fraction.

Thus, Mass percentage of solute = Mass fraction × 100

10% solution of sugar means that 10 grams of sugar is present in 100 grams of the solution, i.e., 10 grams of sugar has been dissolved in 90 grams of water.

(ii) **Per cent by volume**

It is defined as the volume of solute in mL present in 100 mL solution.

Per cent of solute by volume = Volume of solute/Volume of solution × 100

(iii) **Per cent mass by volume**

It is defined as the mass of solute present in 100 mL of solution.

Per cent of solute mass by volume = Mass of solute/Volume of solution × 100

(iv) **Strength or concentration (Grams per litre)**

It is defined as the amount of the solute in grams present in one litre of the solution.

Concentration of solution = Mass of solute in grams/Volume of the solution litres

= Mass of solute in grams/Volume of the solution in mL × 100

Concentration in grams per litre is also termed as strength of the solution. Let wg of the present in V litre of solution, then

Strength or concentration of the solution = w/V gL^{-1}

Note

V is not the volume of the solvent. V is actually the final volume after dissolving a definite quantity of solute in the solvent.

(v) **Parts per million (ppm)**

When the solute is present in trace quantities, it is convenient to express the concentration in parts per million (ppm). It is defined as the quantity of the solute in grams present in 10^6 grams of the solution.

ppm = Mass of solute/Mass of solute × 10^6

Atmospheric pollution in cities is also expressed in ppm by volume. It refers to the volume of the pollutant in 10^6 untis of volume. 10 ppm of SO_2 in air means 10 mL of SO_2 is present in 10^6 mL of air.

(vi) **Mole fraction**

Components	A	B	C
Mass (in grams)	W_1	w_2	w_3
Molecular mass	m_1	m_2	m_3
No. of g moles	w_1	w_2	w_3
	m_1	m_2	m_3

Total number of g moles = $w_1/m_1 + w_2/m_2 + w_3/m_3$

Thus, Mole fraction of A – $w_1/m_1/w_1/m_1 + w_2/m_2 + w_3/m_3 = f_A$

Mole fraction of B = $w_2/m_2/w_1/m_1 + w_2/m_2 + w_3/m_3 = f_B$

Mole fraction of C = $w_3/m_3/w_1/m_1 + w_2/m_2 + w_3/m_3 = f_C$

The sum of mole fractions of a solution is equal to 1,

i.e., $f_A + f_B + f_C = 1$.

In a binary solution,

Mole fraction of solute + Mole fraction of solvent = 1

Let n moles of solute (A) and N moles of solvent (B) be present in a solution.

Mole fraction of solute = n/N + n = X_A

Mole fraction of solvent = N/N + n = X_B

Thus, $X_A + X_B = 1$

Mole fraction is independent of temperature of the solution.

(vii) **Molality**

It is defined as the number of the moles of the solute present in 1 kg of the solvent. It is denoted by m.

Molality (m) = Number of moles of solute/Number of kilo/grams of the solvent

Let w_A grams of the solute of molecular mass m_A be present in w_B grams of the solvent, then

Molality (m) = $w_A/m_A \times w_B \times 1000$

Relation between mole fraction and molality

$X_A = n/N + n$ and $X_B = N/N + n$

$X_A/X_B = n/N$ = Moles of solute/Moles of solvent = $w_A/m_B/w_B \times m_A$

$X_A \times 1000/X_B \times m_B = w_A \times 1000/w_B \times m_A = m$

or $X_A \times 1000/(1 - X_A) = m$

NOTE

(i) **Molality** is the most convenient method to express the concentration because it involves the mass of liquids rather than their volumes. It is also independent of the variation in temperature.

(ii) **Molality and solubity** are related by the following relation:
Molality = Solubility×10/Molecular mass of the solute
[Solubility = Mass of solute in grams/Mass of solvent in grams × 100]

(viii) **Molarity (Molar concentration)**

It is defined as the number of moles of the solute per litre or per dm^3 of the solution, i.e.,

Molarity (M) = Number of moles of solutes/Number of litres of solution

or Molarity × number of litres of sol. = Number of moles of sol.

Let w_A g of the solute of molecular mass m_A be dissolved in V litre of solution.

Molarity of the solution = $w_A/m_A \times V$

or Molarity × $m_A = w_A/V$ Strength of the solution

If V is taken in mL (cm^3), then

Molarity of the solution = $w_A/m_A \times V \times 1000$

$M = x \times d \times 10/m_A$

The unit of molarity is mol $litre^{-1}$ or mol dm^{-3}. d = density of solution in g/mL

m_A = molecular mass of solute.

Molarity of dilution

Before dilution After dilution

$M_1V_1 = M_2V_2$

Molarity of mixing Let there be three samples of solution (containing same solvent and solute) with their molarity M_1, M_2, M_3 and volumes V_1, V_2, V_3 respectively. These solutions are mixed; molarity of mixed solution may be given as:

$M_1V_1 + M_2V_2 + M_3V_3 = M_R(V_1 + V_2 + V_3)$

where M_R = resultant molarity

$V_1 + V_2 + V_3$ = resultant molarity

NOTE

Molarity is dependent on volume; therefore, it depends on temperature.

1 M	Molar solution, i.e., molarity is 1
0.5 M or M/2	Semimolar
0.1 M or M/10	Decimolar
0.01 M or M/100	Centimolar
0.001 M or M/1000	Millimolar

Normality It is defined as the number of gram equivalents of solute present per litre of solution. It is denoted by 'N'.

Normality (N) = Number of gram equivalents of solute/Number of litres of the solution

or Normality × Number of llitres of the solution

= Number of gram equivalents of the solute

Let w_A gram of the solute of equivalent mass E_A be present in V litres of the solution, then,

Normality = $w_A/E_A/V = w_A/E_A \times V$

Normality × Equivalent mass – w_A/V

= Strength of the solution g/L.

Relationship between normality and molarity

Normality = n × Molarity

Formality

It is the number of formula mass in grams present per litre of solution. In case formula mass is equal to molecular mass, formality is equal to molarity. Like molarity and normality, the formality is also dependent on temperature. It is used for ionic compounds in which there is no existence of molecule. Mole of ionic compounds is called formole and molarity as formality.

ELECTROCHEMISTRY

The study of the inter-relation between chemical reactions and electrical energy is called electrochemistry. There are two types of cells that can be used for a chemical reaction to take place:

Electrochemical Cell

The device which is used to convert chemical energy into electrical energy at the expense of spontaneous oxidation reduction reaction is called an electrochemical cell. Example: Daniel cell.

Electrolytic Cell

The device which is used to bring about a non-spontaneous chemical reaction using electrical energy is called an electrolytic cell. Example: Electrolysis of fused sodium chloride.

Basic Terminology

Specific conductivity (K) It is the conductivity of 1 cubic-centimeter of a solution.

Equivalent conductivity It is the conductivity of a solution containing 1 equivalent of the solute between two parallel electrodes separated by 1 cm.

$$\lambda_{eq} = \frac{1000K}{N} \text{ S cm}^2 \text{ equivalent}^{-1}$$

Molar conductivity It is the conductivity of a solution containing 1 mole of a solute between two parallel electrodes separated by 1 cm.

$$\lambda_m = \frac{1000K}{N} \text{ S cm}^2 \text{ mol}^{-1}$$

Kohlrausch's law It states that the molar conductivity at infinite dilution of an electrolyte is equal to the sum of the molar conductivities at infinite dilution of the ions produced by the electrolyte.

$$\lambda_m^\infty = v + \lambda_+^\infty + V - \lambda^\infty$$

Ohm's law It states that the strength of an electric current is directly proportional to the potential difference and inversely proportional to the resistance of the circuit.

$$V = IR$$

V is potential difference in volts

I is current in ampere

R is resistance in ohms

Degree of Ionization It is the extent of dissociation of an electrolyte.

Strong electrolyte An electrolyte that ionizes completely in a solution is called a strong electrolyte.

Weak electrolyte An electrolyte that ionizes partially in solution is called a weak electrolyte.

Cell constant It is the ratio l/A for a conductivity cell where l is the distance between the electrodes and A is the area of the electrode.

$$\text{Cell constant} = \frac{1}{A} = K \times R$$
$$= \text{Specific conductivity} \times \text{Resistance}$$

Battery It is a combination of two or more galvanic cells electrically connected to work together to produce electric energy.

Electrolysis

The process of decomposition of an electrolyte by the passage of an electric current through its aqueous solution or fused mass is called electrolysis. Example: Electrolysis of sodium chloride.

Electrolysis of fused sodium chloride

The electrolytic cell consists of 2 electrodes of platinum or graphite. Fused sodium chloride dissociates to form sodium cations and chloride anions. The sodium ions are discharged at the cathode as sodium atoms (metallic sodium). The chloride ions are discharged at the anode as molecular chlorine.

Reaction at cathode:

$$2Na^+ + 2e^- \rightarrow 2Na \text{ (Reduction)}$$

Reaction at anode:

$$2Cl^- \rightarrow 2Cl + 2e^- \text{ (Oxidation)}$$

$$2Cl \rightarrow Cl_2 \text{ (g)}$$

Faraday's laws of electrolysis

Faraday's first law of electrolysis

The amount (weight) of any substance deposited or liberated or dissolved at an electrode is directly proportional to the quantity of electricity passed through the electrolyte.

$$W = Z\Delta Q.$$

$$\text{Hence, } W = Z\,it$$

$$W = Zit$$

where, i = current (ampere)

t = time in seconds

Z = electrochemical equivalent

Faraday's Second Law of Electrolysis

The amounts (weights) of different substances deposited or dissolved by passing the same quantity of electricity through different electrolytes, connected in series are directly proportional to their equivalent weights.

$$\frac{W_A}{W_B} = \frac{E_A}{E_B}$$

where WB = wt. of substance A
WA = wt. of substance B
EA = equivalent of A
EB = equivalent of B

Faraday

Quantity of electricity passed in order to deposit or dissolve or liberate one gram equivalent (one equivalent) of a substance during electrolysis is called one Faraday (F).

1 Faraday = 96, 500 coulombs
E = 96, 500 × Z or
E = F × Z where,
E = chemical equivalent
Z = electrochemical equivalent
F = 96, 500 coulombs

Electrochemical equivalent (Z)

The weight (amount) of the element deposited or liberated at the electrode when one coulomb of electricity is passed through the electrolyte is called the electrochemical equivalent.

W = ZQ
Z = W/Q kg/coulomb

Electrochemical cell Electrochemical cells are cells in which **chemical energy is converted into electrical energy.** Electrical energy is made available at the expense of spontaneous oxidation reduction reaction taking place within the cell.

Example Daniel cell with a salt bridge.

The cell consists of two beakers–one containing copper sulphate solution and a copper rod that acts as a positive electrode and the other beaker contains zinc sulphate solution with a zinc rod that acts as a negative electrode. A metallic wire is used to connect the two electrodes. The two solutions are connected with a salt bridge.

Cell representation: $^{\ominus}Zn \mid Zn^{++}_{(aq)} \parallel Cu^{++}_{(aq)} \mid Cu^{\oplus}$

Cell reaction:

At anode (oxidation electrode)

$Zn_{(s)} \rightarrow Zn^{2+}_{(aq)} + 2e^{-}$ (oxidation half cell reaction)

At cathode (reduction electrode):

$Cu^{2+}_{(aq)} + 2^{e-} \rightarrow Cu_{(s)}$

(reduction half cell reaction)

Total reaction

$Zn_{(s)} + CU^{2+}_{(aq)} \rightarrow Zn^{2+}_{(aq)} + Cu_{(s)}$ (Redox reaction)

The e.m.f. of the Daniel cell is about 1.1 volt.

Salt bridge

It is an inverted U-shaped glass tube filled with a saturated solution of KCl or KNO_3 or NH_4NO_3< in agar-agar gel. The ends of the glass tube are plugged with glass wool. The two ends of the salt bridge are immersed in the solution of the two half cells.

Functions of the salt bridge

- It connects the two half cells.
- It prevents mixing of two electrolytes.
- It minimizes the liquid junction potential between the two electrolytes.
- It maintains electrical contact between the two electrolytes.
- It maintains electrical neutrality in the cells.

Conventions used for representing the voltaic cells

- Negative electrode (zinc electrode in the voltaic cell) is written on the left hand side.
- Positive electrode (copper electrode in the voltaic cell) is written on the right hand side.
- The vertical single line is drawn between the electrode and the electrolyte.
- A vertical double line is between two electrolytes that indicate indirect contact of the two electrolytic solutions.
- Concentration of the activities of the two solutes are written in brackets like (C_1), (C_2), or (a_1), (a_2).

In case of a gas electrode, the gas is shown along with an inert electrode, used on the left hand side.

Standard Calomel Electrode (SCE)

The electrode consists of a broad glass tube with a side tube. The broad glass tube consists of pure Hg at the bottom, covered with a saturated paste of Hg_2Cl_2 and Hg. The tube is then covered with saturated KCl. Electrical contact with Hg is made by a platinum wire sealed in the glass tube. The side tube is immersed in the desired solution.

Electrode potential depends upon concentration of KCl solution.

$$Pt, Hg (l) \mid Hg_2Cl_2 (s) \mid KCl (aq) (a = x)$$

At 298K, oxidation potentials are:

(a) Sat. KCl: – 0.242V
(b) 1N KCl or 1M KCl: – 0.280V
(c) 0.1 N KCl or 1M KCl: – 0.334V

$$\text{Oxidation: } 2Hg (l) + 2Cl^- (aq) \rightleftharpoons Hg_2Cl_2 (s) + 2e^-$$

$$\text{Reduction: } Hg_2Cl_2 (s) + 2e^- \rightleftharpoons 2Hg (l) + 2Cl^- (aq)$$

Advantages of standard calomel electrode

- It is very handy, compact and easy to transport.
- Its potential can remain constant and it can easily be reproduced.

It is easy to construct and maintain.

Measurement of electrode potential

The electrode potential of a single electrode can be measured by combining it with a reference electrode to form a cell. The e.m.f. of the cell is measured with a potentiometer.

Concept of electrode potential

When an electrode is dipped in its solution containing its ions, there are two opposing processes taking place– electronation and de-electronation. This is known as Nernst theory of electronation and de-electronation.

Nernst equation for single electrode potential

$$E = E^\circ - \frac{2.303RT}{nF} \log 10\left[M^{n+}_{(aq)}\right]$$

Single electrode potential

The difference in potentials between the electrode and the surrounding solution at equilibrium in a half cell is called single electrode potential or half cell potential.

Standard oxidation potential (E_{oxd})

The electric potential developed between an electrode and the surrounding electrolyte due to the oxidation process when a metal is dipped into an electrolyte containing the same metal ions at 1 M concentration at 298 K is called standard oxidation potential.

Standard reduction potential (E_{red})

The electric potential developed between an electrode and the surrounding electrolyte due to the reduction process when a metal is dipped into an electrolyte containing the same metal ions at 1M concentration at 298 K is called the standard reduction potential.

EMF of the Cell

The potential difference, which is responsible for the flow of current from an electrode of higher potential to the electrode of lower potential is called the electromotive force (e.m.f.) or the effective voltage of the cell and expressed in volts.

$$E_{cell} = E_{oxd} (anode) – E_{oxd} (cathode)$$
$$E_{cell} = E_{oxd} (anode) + E_{red} (cathode)$$

EMF Series

It may be defined as the series of elements in which elements are arranged in the decreasing order of their standard oxidation potential as compared to the standard hydrogen electrode. Also, called as electromotive series or electro-chemical series.

$Li \rightarrow K \rightarrow Ba \rightarrow Ca \rightarrow Na \rightarrow Mg \rightarrow Al \rightarrow Mn \rightarrow Zn \rightarrow Cr \rightarrow Fe \rightarrow Cd \rightarrow Ni \rightarrow Sn \rightarrow Pb \rightarrow H_2$ (SRP = 0)

SRP is Negative

$\rightarrow Cu \rightarrow I_2 \rightarrow Hg \rightarrow Ag \rightarrow Br_2 \rightarrow Cl_2 \rightarrow Pt \rightarrow Au \rightarrow F_2$

SRP is Positive

NOTE

- Metals having positive SRP will make cathode and positive SRP will make anode during electrolysis.
- Negative SRP (Standard reduction potential) metals will preferentially reduced first.

ACID-BASE AND IONIC EQUILIBRIUM

Introduction

Acids are substances which are sour in taste and turn blue litmus to red.

Bases are bitter in taste, soapy to touch and turn red litmus to blue.

Arrhenius Theory of Acids and Bases

Acid is a substance that releases H^+ ions (proton) in aqueous solution.

e.g., $$HCl_{(aq)} \rightleftharpoons H^+_{(aq)} + Cl^-_{(aq)}$$

$$H_2SO_{4\,(aq)} \rightleftharpoons H^+_{(aq)} + HSO_4^-{}_{(aq)}$$

Base furnishes hydroxide ions (OH^-) when dissolved in water.

e.g., $NaOH_{(aq)} \rightleftharpoons Na^+_{(aq)} + OH^-_{(aq)}$

$Ca(OH)_{2\,(aq)} \rightleftharpoons Ca^{+2}_{(aq)} + 2OH^-_{(aq)}$

Limitations of Arrhenius theory

- The theory defines acids and bases in terms of their aqueous solutions rather than on the basis of the substances themselves.
- It considers substances like HCl as acid only in water and not in non-aqueous solvents.
- The theory does not explain basic nature of substances like pyridine, NH_3, etc., which do not have OH^- ions in their structure.
- The theory does not explain amphoteric behaviour of compounds like $Zn(OH)_2$.

It does not explain acidic nature of salts like $FeCl_3$ and basic nature of ammonia.

Lowry-Bronsted Theory

Acid substances which donate hydrogen ions (H^+).

Example HCl, H_2SO_4, CH_3COOH.

Base substances which accept protons (H^+) are called bases.

Example NH_3, H_2O, OH^-.

Conjugate acid-base pair

Pair of acid and base which differ only by a proton. Acid donates proton to form a base, while base accepts the proton. Thus, an acid loses a proton to form a conjugate base and a base accepts to form a conjugate acid.

Examples

1. Cl^- is a conjugate base of HCl.
2. H_3O^+ is a conjugate acid of a base H_2O.

Water is amphoteric according to Lowry and Bronsted theory. It functions as acid as well as base depending upon the nature of substance dissolved in it.

Lewis Acid-based Theory

Acid is a substance which can accept a lone pair of electrons.

Example H^+, $AlCl_3$, BF_3.

Base substance which can donate a lone pair of electrons.

Example Cl^-, H_2O, OH^-.

Ionization

Ionization: Formation of ions from substances which are not in the ionic state.

Dissociation: Formation of free ions capable of carrying electric current.

Degree of dissociation (α)

The fraction of total number of molecules of an electrolyte, which undergoes dissociation at equilibrium, is called degree of dissociation.

Dissociation constant for a weak acid and weak base

Weak acid K_a is the ratio of concentration of cation (H^+) and anion (A^-) at equilibrium with concentration of undissociated acid at equilibrium.

$$HA \rightleftharpoons H^+ + A^-$$

$$K_a = \frac{[H^+][A^-]}{HA}$$

Weak base K_b is the ratio of product of concentration of cation and the anion (OH^-) formed at equilibrium and concentration of undissociated base at equilibrium.

$$BOH \rightleftharpoons B^+ + OH^-$$

$$K_b = \frac{[B^+][OH^-]}{[BOH]}$$

Ostwald's Dilution Law

The degree of dissociation of a given weak electrolyte is inversely proportional to the square root of concentration of solution or directly proportional to the square root of dilution.

$$\alpha = \sqrt{KV} = \sqrt{\frac{K}{C}}$$

where C = concentration or moles of an electrolyte

V = dilution

For a weak base $k_b = \alpha^2 C$

$$\alpha = \sqrt{\frac{K_b}{C}}$$

or

$$\alpha = \sqrt{\frac{1}{C}}$$

Ionic product of water

The product of the ionic concentration of hydrogen ions and hydroxide ions in pure water or in any aqueous solution is called ionic product of water. It is constant at any given temperature. At 298K it is 1.0×10^{-14}.

Ionic product of water is

$$K_w = [H^+]\,[OH^-]$$

Hydrogen ion concentration pH scale

pH The negative logarithm, to the base 10, of the hydrogen ion concentration is known as the pH of a solution.

$$-\log[H^+] = \log_{10}\frac{1}{H^+} = \text{pH}$$

pOH = The negative logarithm, to the base 10, of the hydroxyl ion concentration is known as pOH of a solution.

$$-\log[OH^-] = \log_{10}\left[\frac{1}{OH}\right] = \text{pOH}$$

Relation Between pH and pOH

$$[H^+]\,[OH^-] = K_w = 10^{-14} \text{ at } 298 \text{ K}$$

$$\text{pH} + \text{pOH} = pK_w = 14 \text{ at } 298 \text{ K}$$

Common ion effect

The suppression of the degree of dissociation of a weak electrolyte by the addition of a strong electrolyte having an ion in common with the weak electrolyte is called the common ion effect.

Applications

a. Purification of NaCl:

- Addition of HCl, Cl^- is a common ion.
- Concentration of Cl^- ions increases.
- Suppresses solubility of NaCl and it precipitates.
- $NaCl \rightleftharpoons Na^+ + Cl^-$
- $HCl \rightleftharpoons H^+ + Cl^-$
- Precipitation takes place when ionic product > solubility product.

b. Salting out of soap:

- Saturated solution of NaCl is added to soap solution.
- Concentration of Na ions increases.
- Due to common ion Na^+, solubility of soap decreases.
- Results in precipitation of soap.
- $RCOONa \rightleftharpoons RCOO^- + Na^+$
- $NaCl \rightleftharpoons Na^+ + Cl^-$

c. Gravimetric analysis:

- Precipitate obtained is washed with solution of strong electrolyte having common ion with precipitated solid.
- Solubility of precipitate decreases.
- Minor losses due to dissolution are avoided.
- Example, $BaSO_4$ washed with dilute H_2SO_4
- $BaSO_4 \rightleftharpoons Ba^{+2} + SO_4^{2-}$
- $H_2SO_4 >> 2H^+ + SO_4^{2-}$

Solubility product

The product of the ionic concentration of the ions of a sparingly soluble electrolyte present in its saturated solution at a given temperature is called a solubility product of the electrolyte.

For a salt,

$$AB \rightleftharpoons A^+ + B^- \qquad K_{sp} = [A^+]\,[B^-]$$

$$AB_2 \rightleftharpoons A^{2+} + 2B^- \qquad K_{sp} = [A^{2+}]\,[B^-]^2$$

$$A_2B \rightleftharpoons 2A^+ + B^{2-} \qquad K_{sp} = [A^+]^2\,[B^{2-}].$$

Applications

In qualitative analysis:

- Group II metal cations (Hg^{+2}, Cu^{+2}, Bi^{+3}, Ph^{+2}, etc.) are precipitated as sulphides by passing H_2S in presence of HCl.
- Group III B metal cations (Co^{+2}, Mn^{+2}, etc.) are precipitated by passing H_2S in presence of NH_4OH.
- Group III A cations (Al^{+3}, Cr^{+3}, Fe^{+2}, Fe^{+3}) are precipitated in the form of their hydroxides using NH_4OH.

Prediction of precipitation

For a salt, when ionic product exceeds solubility product, precipitation occurs.

Buffer solutions

A buffer solution is the one whose pH does not change on dilution or on adding a small quantity of acid or base on storage.

Acidic buffer solutions It is a solution containing weak acid and its salt with a strong base. It is used to obtain pH lower than 7.

Basic buffer solutions It is a solution having weak base and its salt with a strong acid.

Preparation of acidic buffer solution It is prepared by adding a weak acid to a solution of its salt with a strong base.

Preparation of basic buffer solution It is prepared by adding a weak base to a solution of its salt with a strong acid.

Properties

- pH does not change on dilution.
- pH does not alter on storage.
- Addition of small quantity of acid or alkali does not change pH.

Buffer action

a. Acidic Buffer: The salt in the acidic buffer dissociates completely and gives common ions. The weak acid dissociates feebly.

Example: ($CH_3COOH + CH_3COONa$)

$CH_3COOH \rightleftharpoons CH_3COO^- + H^+$ (incomplete)

$CH_3COONa \rightleftharpoons CH_3COO^- + Na^+$ (complete)

- Addition of acid, hydrogen ions from acid and acetate ions combine to form weak acetic acid. Hence, pH does not change.

$H^+ + CH_3COO^- >> CH_3COOH$

- Addition of base, OH ions react with acid producing anions and water. Hence concentration of H^+ and OH^- does not change and pH is not altered.

$CH_3COOH + OH^- >> CH_3COO^- + H_2O$

b. Basic Buffer: The weak base of the buffer dissociates feebly but the salt dissociates completely.

Example: ($NH_4OH + NH_4Cl$)

$NH_4OH \rightleftharpoons NH_4^+ + OH^-$ (incomplete)

$NH_4Cl >> NH_4^+ + Cl^-$ (Complete)

- When small quantity of acid is added, hydrogen ions from acid combine with base producing corresponding cations and water; addition of acid does not change the pH of the buffer.

$H^+ + NH_4OH >> NH_4^+ + H_2O$

- When small quantity of base is added, OH^- ions combine with NH_4^+ ions to form NH_4OH.Hence, H^+ or OH^- concentration does not change, pH does not change.

$OH^- + NH_4^+ >> NH_4OH.$

Applications of buffer solution

- pH of human blood is maintained constant at 7.35 – 7.45.
- pH is maintained at certain level for enzymatic reaction.
- Helps in preparation of antibiotics, alcohols by fermentation.
- Number of food and pharmaceutical samples preserved.
- Used in qualitative and quantitative analysis.
- pH of soil is maintained using phosphate buffer.

Hydrolysis of salt

The reaction in which the anions or the cations or both of a salt react with water to produce acidity or basicity is called hydrolysis.

Degree of hydrolysis (h)

The fraction of total number of moles of the salt which have undergone hydrolysis at equilibrium is called the degree of hydrolysis of the electrolyte.

Hydrolysis constant (k_h)

The equilibrium constant of the hydrolysis equilibrium of a salt is called hydrolysis constant of the salt.

Salts of strong acid and strong base do not undergo hydrolysis.

Degree of hydrolysis of strong acid and weak Base

$K_h = h^2C$ or $h = \sqrt{\frac{k_h}{C}}$ h = Degree of hydrolysis

C = Concentration, mol dm^3

K_h = Hydrolysis constant

Weak acid–strong base

$K_h = h^2C$ or $h = \sqrt{\frac{k_h}{C}}$ h = Degree of hydrolysis

C = Concentration, mol dm^3

K_h = Hydrolysis constant

Weak acid–weak base

$$K_h = h^2$$

$$h = \sqrt{K_h}$$

Relation between hydrolysis constant, dissociation constant of acid and ionic product of water

For weak acid–strong base: $K_h = \frac{K_w}{K_a}$

For strong acid–weak base: $K_h = \frac{K_w}{K_b}$

For weak acid–weak base: $K_h = \frac{K_w}{K_a \times K_b}$

where K_w = ionic product of water

K_h = hydrolysis constant

K_a and K_b = dissociation constant for an acid and base respectively.

RADIOACTIVITY

The phenomenon of spontaneous disintegration of unstable nuclei of certain heavy elements with the emission of some radioactive radiation is called radioactivity.

It is not affected by external factors like temperature, pressure, catalyst and the state of existence, i.e., whether it is an element or in a combined state.

Characteristics of α, β and γ rays

	α-rays	β-rays	γ-rays
Charge and mass	(+2) charge and 4 a.m.u. mass	(–1) charge and Mass slightly greater than electron	Chargeless and zero mass
Origin	$^4_2$He nucleus	Electron	Electromagnetic radiation
Velocity	1/10th to 1/100th the velocity of light	99% of the velocity of light	Same as the velocity of light
Penetrating power	Poor; can hardly pass through 0.02 cm thick Al sheet.	Greater than α rays; can pass through 0.2 cm thick Al sheet.	Very high; can pass through 100 cm thick Al sheet.
Ionizing power	High	Lower than α-rays	Very low
Deflection in an electric field	Towards the negative plate	Towards the positive plate	No deflection

Types of Nuclear Reactions

i. Natural radioactivity
ii. Artificial transmutation
iii. Artificial radioactivity
iv. Nuclear fission
v. Nuclear fusion

Natural radioactivity

The spontaneous emission of radiation from the nuclei of heavy elements is called natural radioactivity.

Artificial radioactivity

The phenomenon of conversion of a stable nucleus (non-radioactive) into an unstable radioactive nucleus by artificial disintegration is called artificial radioactivity.

$$\underset{\text{boron}}{^{10}_5\text{B}} + \underset{\alpha\text{–particle}}{^4_2\text{He}} \rightarrow \underset{\text{nitrogen}}{^{13}_7\text{N}^*} + \underset{\text{neutron}}{^1_0\text{n}} \quad \text{(Bombardment)}$$

$$^{13}_7\text{N}^* \rightarrow \underset{\text{carbon}}{^{13}_6\text{C}} + \underset{\text{position}}{^0_{+1}\text{e}} \quad \text{(Radioactivity)}$$

Artificial transmutation

The process of conversion of a stable isotope of one element into a stable isotope of another element by bombarding it with suitable high energy (nuclear) particles is called artificial transmutation.

$$\underset{\text{(target)}}{^{14}_7\text{N}} + \underset{\text{(projectile)}}{^4_2\text{He}} \rightarrow \underset{\text{(product / recoil nucleus)}}{^{17}_8\text{O}} + \underset{\text{(emission)}}{^1_1\text{H}}$$

Nuclear forces (exchange force)

i. The strong attractive forces which exist between the protons and neutrons present in the nucleus of an atom are called nuclear forces. They are (p – n), (p – p) and (n – n) forces.
ii. They are short range forces operating in the range of 10^{-15}. They are also called exchanged forces.
iii. The origin of nuclear forces was explained by Japnese scientist Yukawa in 1935.
iv. It is 10^{40} times stronger than gravitational force and 10^2 times stronger than the electromagnetic force.

The nuclear force is due to the constant exchange of mesons (Pions Π^+ or Π^- or $\Pi 0$) between protons and neutrons. Pions are most unstable particles (Very short life span).

Mass defect (Δ m)

The difference between the total mass of the nucleons (protons and neutrons) present in the nucleus of an atom and the actual mass of the nucleus is called the mass defect of the nucleus.

$$\Delta m = [Zm_H + (A - Z)m_n] - M_{nucleus}$$

Where m_H = mass of an atom of hydrogen isotope ^1_1H

M = mass of nucleus

Binding energy (BE)

The amount of energy required to break the nucleus of an atom into its constituent nucleons is called binding energy of the nucleus.

$$B.E. = \Delta m \times 931 \text{ MeV}$$

$$\text{B.E. per nucleon} = \frac{\text{Total B.E}}{\text{Mass number(A)}} = \frac{\Delta m \times 931 \text{ Mev}}{A}$$

Binding energy affects the stability of the nucleus.

Soddy's group displacement law

i. When an element emits α-particle,

$$^A_ZX \rightarrow {}^{A-4}_{Z-2}Y + {}^0_{-1}e$$

ii. When an element emits β-particle,

$$^A_ZX \rightarrow {}_{Z+1}{}^AY + {}^0_{-1}e$$

iii. During γ-emission, A and Z remain the same.

Disintegration law

The number of atoms disintegrated per unit time is a constant fraction of the total number of the atoms present at that instant.

Decay or disintegration constant (λ)

The fraction of the total number of atoms (nuclei) undergoing radioactive disintegration per unit time is called decay or disintegration constant of the element.

$$\lambda = \frac{-d\,N/N}{dt}$$

Or $$\lambda = \frac{2.303}{t} \text{Log}\left(\frac{N_0}{N_t}\right),$$

where N_0 = total number of radioactive atoms initially present (t = 0).

N_t = total number of radioactive atoms present at time t.

Half-life period ($t_{1/2}$)

The time required for the disintegration of a radioactive element to reduce to half of the original amount is called half-life period.

$$t_{1/2} = 0.693/\lambda$$

Radioisotopes

The naturally unstable elements which spontaneously emit some radiations like beta-particles, protons, neutrons, gamma-rays, etc., are called as radioisotopes.

Radio isotope dating was developed by W. F. Libby.

Uses of radioisotopes

C^{14} (Beta emmiter)	Age of archaeological material, to study photosynthesis in plant
Na^{24}	To study blood circulation
I^{131}	To diagnose and treat thyroid disorder
P^{32}	To treat leukemia, to study plant metabolism and usefulness of phosphorous fertilizers
Co^{60}	To treat certain type of cancers
Ca^{40}	To find out uptake of calcium by plant from soil
Ni^{60}	To stop growth of cancer cell

Multiple Choice Questions

1. When there are no external forces, the shape of a liquid drop is determined by
(a) Surface tension of the liquid
(b) Density of liquid
(c) Viscosity of liquid
(d) Temperature of air only

2. Choose the wrong statement from the following.
(a) Small droplets of a liquid are spherical due to surface tension
(b) Oil rises through the wick due to capillarity
(c) In drinking the cold drinks through a straw, we use the phenomenon of capillarity
(d) Gum is used to stick two surfaces. In this process we use the property of adhesion

3. When the angle of contact between a solid and a liquid is 90°, then
(a) Cohesive force > Adhesive force
(b) Cohesive force < Adhesive force
(c) Cohesive force = Adhesive force
(d) Cohesive force >> Adhesive force

4. Rain drops are spherical in shape because of
(a) Surface tension
(b) Capillary
(c) Downward motion
(d) Acceleration due to gravity

5. Ammonia has a net dipole moment while boron trifluoride has zero dipole moment because
(a) Fluorides is more electronegative
(b) Fluorides is more electronegative
(c) Boron trifluoride is pyramidal in shape while NH_3 is planar
(d) NH_3 is pyramidal in shape while BF_3 is planar

6. The SO_4 consists of a central sulphur atom with four equivalent oxygen atoms. What should be the internal O-S-O bond angle be
(a) 6° (b) 9°
(c) 109.5° (d) 117

7. Which of the following statements is incorrect?
(a) Hydrogen can give an electropositive ion by losing its electrons
(b) Hydrogen can form an electronegative ion by gaining another electron
(c) Hydrogen can combine with some other elements by means of covalency
(d) Hydrogen can enter into a coordinate linkage with other atoms

8. The Phase rule is applicable to _____
(a) Homogenous system
(b) Reversible system
(c) Irreversible system
(d) Heterogeneous system whether physical or chemical

9. A dilatometer is an apparatus used to measure
(a) Transition temperature
(b) Triple point
(c) Eutectic point
(d) All of these

10. The nature of bonding between Al and chlorine in $AlCl_3$ is
(a) Electrovalent
(b) Covalent
(c) Covalent with polar character
(d) Coordinate covalent

11. Pick out the molecule which has zero dipole moment
(a) NH_3 (b) H_2O
(c) BCl_3 (d) SO_2

12. "Equal volume of all gases at the same temperature and pressure contains equal number of molecules" is a statement of _____
(a) Combined Gas Law
(b) Charle's Law
(c) Boyle's Law
(d) Avogadro's Law

13. The entropy is measured in _____
(a) Cal K^{-1} mol^{-1} (b) JK^{-1} mol^{-1}
(c) Entropy unit (d) All of above

14. Mixing of two or more gases is a _____
(a) Spontaneous Process
(b) Non-spontaneous Process
(c) Reversible Process
(d) None of these

15. The free energy function (G) is defined as
(a) G = H + TS
(b) G = TS – H
(c) G = H – TS
(d) None of these

16. The Second Law of Thermodynamics stated that
(a) It is impossible to take heat from a hotter reservoir and convert it completely into work by a cyclic process without transferring a part of heat to a cooler reservoir.
(b) It is impossible to transfer heat from a body at a lower temperature to one at higher temperature
(c) The efficiency of heat engine in always less than 1
(d) All of above

17. The unit in which surface tension is measured is:
(a) Dyne.cm (b) $Dyne.cm^{-1}$
(c) $Dyne^{1}.cm$ (d) $Dyne^{1}.cm^{1}$

18. The reciprocal of viscosity is called _____
(a) Surface tension
(b) Frictional resistance
(c) Fluidity
(d) None of these

19. A crystalline solid does not have one of the following properties:
(a) Anisotropy
(b) Sharp melting point
(c) Isotropy
(d) Definite and regular geometry

20. 36 g of glucose (molecular mass – 180) is present in 500 g of water,the molality of the solution is
(a) 0.2 (b) 0.4
(c) 0.8 (d) 1.0

21. The molarities of 0.1N HCl and 0.1 N H_2SO_4 is respectively:
(a) 0.1M HCl and 0.05 M H_2SO_4
(b) 0.05 M HCl and 0.1 M H_2SO_4
(c) 1 M HCl and 0.2 M H_2SO_4
(d) 0.05 M HCl and 0.1 M H_2SO_4

22. Which of the following includes all the aims of kinetics?
(i) To measure the rate of reaction
(ii) To be able to predict the rate of a reaction
(iii) To be able to establish the mechanism by which reaction occurs
(iv) To be able to control a reaction
(a) i , ii and iii (b) i and ii
(c) i and iii (d) i, ii, iii and iv

23. For first order reaction the rate constant *K*, has the unit(s)
(a) $1\ mol^{-1}$ (b) $Time^{-1}$
(c) $(Mol/L)^{-1}$ (d) $Time.mol\ L^{-1}$

24. Thermodynamics is applicable for _____
(a) Microscopic system
(b) Macroscopic system
(c) Heterogenous system
(d) Homogenous system

25. A system in which no thermal energy pass into or out of the system is called _____
(a) Adiabatic System (b) Open System
(c) Closed System (d) Reversible System

26. An alfa particle is _____
(a) An electron
(b) One neutron and one proton
(c) Two protons and two neutrons
(d) An X-ray emission

27. In a Geiger Muller counter, one count is directly due to _____
(a) A secondary electron
(b) A primary electron
(c) Many electron and ions
(d) A beta particle

28. Following is an example of extensive properties _____
(p) Mass
(q) Pressure
(r) Temprature
(s) Volume
(a) (p) and (q) (b) (p) and (r)
(c) (q) and (r) (d) (p) and (s)

29. Following all are the examples of endothermic process, except one
(a) Melting of solid salts
(b) Evaporation of water
(c) Producing sugar by photosynthesis
(d) Mixing of water with calcium chloride

30. At a triple point _____
(a) Both the temperature and pressure are fixed
(b) Only temperature is fixed
(c) Only pressure is fixed
(d) Sometimes temperature and sometime pressure are fixed

ANSWER KEYS

1. (a)	**2.** (c)	**3.** (c)	**4.** (a)	**5.** (d)	**6.** (c)	**7.** (d)	**8.** (d)	**9.** (a)	**10.** (c)
11. (c)	**12.** (d)	**13.** (d)	**14.** (a)	**15.** (c)	**16.** (d)	**17.** (b)	**18.** (c)	**19.** (c)	**20.** (b)
21. (a)	**22.** (d)	**23.** (b)	**24.** (b)	**25.** (a)	**26.** (c)	**27.** (c)	**28.** (d)	**29.** (d)	**30.** (a)

CHAPTER 2

ORGANIC CHEMISTRY

ATOMIC STRUCTURE

Structure of an Atom

- An atom consists of negatively charged electrons, positively charged protons, and neutral neutrons.
- Atomic number: numbers of protons in its nucleus (E.g., ${}_{6}C$, ${}_{7}N$, ${}_{8}O$)
- Mass number: the sum of number of protons and neutrons in a atom (E.g., ${}^{12}_{6}C$, ${}^{14}_{7}N$)

Characteristics of protons, neutrons and electrons

	Protons	Electrons	Neutrons
Charge	Unit positive	Unit negative	Charge less
Mass	Nearly the same as the mass of H_2 atom	1/1837th the mass of proton or H_2 atom.	Very close to the mass of H_2 atom
Symbol	${}^{1}_{+1}P$ ${}^{1}_{+1}H$	${}^{1}_{-1}e$	${}^{1}_{0}n$

- **Isotopes** have the same atomic number but different mass numbers (E.g., ${}^{12}_{6}C$, ${}^{13}_{6}C$, ${}^{14}_{6}C$)
- **Isobars** Isobars are atoms of different elements having the same atomic mass but different atomic number.

Isotopes are chemically same and physically different. But the converse is true in isobars. That is, isobars are elements which are chemically different but physically same. Since their number of electrons is different, their chemical properties are different. Examples of isobars are Fe^{58} and Ni^{58}.

- **Isotones**
  Isotones are elements having the same number of neutrons. Examples of isotones are Chlorine-37 and Potassium-39. Both have 20 neutrons in their nuclei.
- The atomic weight: The average weighted mass of its atoms
- Molecular weight: The sum of the atomic weights of all the atoms in the molecule.

Distribution of electrons in an atom

- The atomic orbital closer to the nucleus has the lowest energy.
- Degenerate orbital's have the same energy.

Distribution of electrons in first four shells				
	First shell	Second shell	Third shell	Fourth shell
Atomic orbitals	s	s, p	s, p, d	s, p, d, f
No. of atomic orbitals	1	1, 3	1, 3, 5	1, 3, 5, 7
Maximum no of electrons	2	8	18	32

Electronic configuration of some smallest elements

Atoms	Atomic no.	1S	2S	2Px	2Py	2Pz	3S
H	1	↑					
He	2	↑↓					
Li	3	↑↓	↑				
Be	4	↑↓	↑↓				
B	5	↑↓	↑↓	↑			
C	6	↑↓	↑↓	↑	↑		
N	7	↑↓	↑↓	↑	↑	↑	
O	8	↑↓	↑↓	↑↓	↑	↑	

Atoms	Atomic no.	1S	2S	2Px	2Py	2Pz	3S
F	9	↑↓	↑↓	↑↓	↑↓	↑	
Ne	10	↑↓	↑↓	↑↓	↑↓	↑↓	
Na	11	↑↓	↑↓	↑↓	↑↓	↑↓	↑

Rules for determining electronic configuration

The Aufbau principle Electrons occupy the orbital with the lowest energy orbital first.

E.g., $^{10}_{5}$B-1S and 2S orbital first filled than one electrons go with 2Px orbitals

The Pauli exclusion principle Only two electrons can occupy one atomic orbital and the two electrons have opposite spin.

Hund's rule Electrons will occupy empty degenerated orbitals before pairing up in the same orbital.

Bonding and Hybridization

Bond

In a molecule, the atoms are held together by a strong force of attraction to form a bond. The force of attraction may be due to oppositely charged ions or due to orbital overlap.

Types of bonds

Three different types of bonds are formed depending on the electropositive or electronegative character of atoms involved.

a. Electropositive element + electronegative element = **Ionic Bond**
b. Electropositive element + Electropositive element = **Metallic bond**
c. Electronegative element + electronegative element = **Covalent bond**

Ionic compounds are formed when an electropositive element transfers electron (s) to an electronegative element or transfer of valance shell electron.

E.g., Na^+ and Cl^-, In which Na^+ having one electron in its outer orital while Cl^- having 7 electon in its outer shell so, Na^+ donate its valance shell electron to Cl^- to complete the Octet.

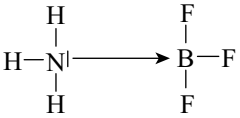
Covalent Compound:

Mutual sharing of electrons: non-polar covalent bond (e.g., H_2)

Co-ordinate covalent Bond:

It is a bond formed due to transfer of electron pair from one atom to other.

E.g.,



Electronegativity of an atom

- It depends upon ***Atomic number*** and ***atomic radius*** of an atom.
- Any atom having more atomic number and lower atomic radius is more electronegative than other atom.

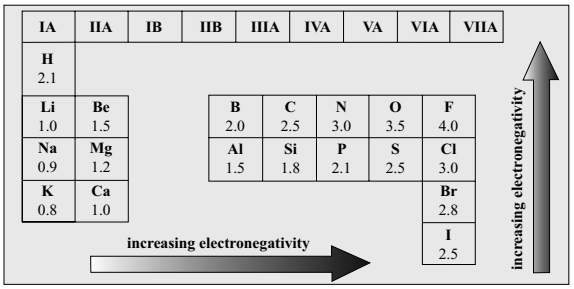


Figure 2.1 Electronegativity of an atom

Polar bond

A polar bond has a negative end and a positive end (E.g., $C^{+\delta}$—$Cl^{-\delta}$).

Non-polar bond A bond which is made up by same charged atom is known as non-polar bond. (H-H, C-C)

Dipole moment It depends upon:

1. Molecule having more than one dipole
2. If centre of negatively charged does not concide with centre of positively charged.

$$\textbf{Dipole moment (D)} = \mu = e \times d$$

Where, *e is* magnitude of the charge on the atom measured in e.s.u (electron spin unit), *d is* distance between the two charges (in cm), μ is dipole moment of molecule (Debye unit)

Formal charge = number of valence electrons–(number of lone pair electrons +1/2 number of bonding electrons

Molecular Orbital (MO)

- Bonding MO–In-phase overlap forms a bonding MO
- Anti-bonding MO–Out-of-phase overlap forms an anti-bonding MO.
- Sigma bond (s) is formed by end-on overlap of two *p* orbitals
- Pi (ϖ) bond is formed due to side by side overlapping of two p orbital.

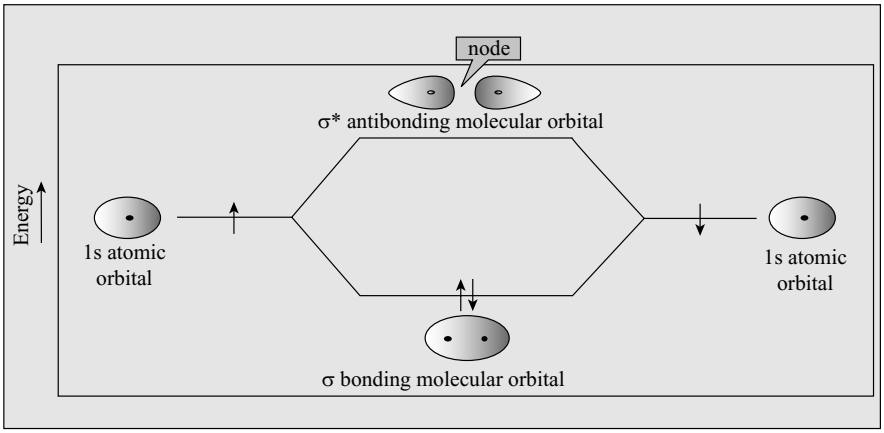


Figure 2.2 Molecular Orbital

Octet rule

During bond formation, the atoms gain, lose or share electrons so that the outermost or valence shell of an atom has **eight electrons** as in inert gases.

Electronic Theory

Put forth by Kossel and Lewis in 1916. The main postulates are

- Valence shell electrons take part in bond formation.
- Inert gases have stable outermost configuration.
- Elements tend to acquire inert gas configuration by gaining or losing electrons. On this basis, **Ionic** and **Covalent bonds** are explained.

a. **Ionic Bond:** Bonds formed by gaining or losing electrons in which the ions formed are held together by electrostatic force of attraction.

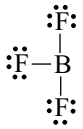
Limitations of octet rule

- It fails to explain formation of compounds with incomplete and expanded octets.
- It fails to explain about nature of forces responsible for the combination of atoms.
- It does not explain energy, stability and reactivity of molecule.
- It does not explain geometry and shape of different molecules.

Exceptions to the octet rule

Elements in groups IA, IIA and IIIA do not follow the octet rule.

Electron-dot formula for BF_3, the boron will not have eight electrons.



Some elements having low-energy d-orbitals also form exceptions to the "octet rule", in that, more than eight electrons are accommodated around the central atom. The central atom in most of these compounds will be bonded to highly electronegative elements such as fluorine, oxygen and chlorine.

A surprising element in this group is the inert gas, xenon. If xenon is exposed to fluorine gas in the presence of light for several weeks, it can form XeF_2, a colourless crystalline solid.

Hybridization of Atomic Orbitals and the Shape of Molecules

The valence shell electron-pair repulsion model (VESPR) was devised to account for these molecular shapes. In this model, atoms and pairs of electrons will be arranged to minimize the repulsion of these atoms and pairs of electrons.

Postulates of the valence bond theory

1. Covalent bond is formed by overlapping of atomic orbitals and hence energy of the system decreases.
2. Atomic orbitals of two atoms having unpaired electrons overlap to form a covalent bond.
3. Electrons in overlapping orbitals should have opposite spins and in the process, spins are neutralized.
4. Overlapping of orbitals causes increase in electron density in the region where overlapping occurs.

5. Overlapping orbitals should have comparable energies.
6. The bond formed has directional character and the strength of the bond is directly proportional to the extent of overlap.
7. Number of unpaired electrons which an atom possesses determines number of bonds formed, and hence its valency.

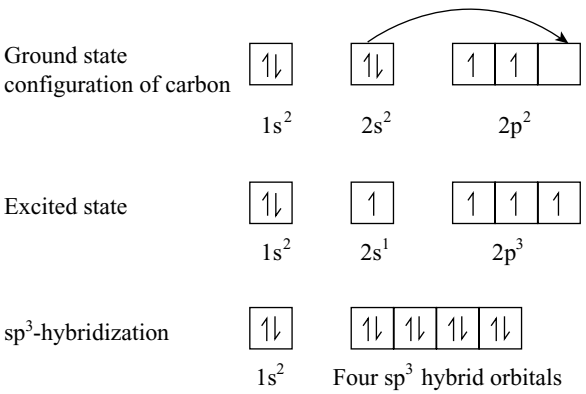
The number of these new hybrid orbitals must be equal to the numbers of atoms and non-bonded electron pairs surrounding the central atom.

Hybridization

Definition The process of mixing and recasting to form same number of equivalent orbitals with maximum symmetry and definite orientation in space is called hybridization.

Hybridization involves the following steps

1. **Formation of Excited State:** Paired electrons jump to higher energy levels to create, if necessary, more number of half-filled orbitals.
   Examples:



2. **Mixing and Recasting of Atomic Orbitals:** Orbitals of valence shell mix to form new set of atomic orbitals having same energy. The new orbitals then formed are called hybrid orbitals.
3. **Orientation of Hybrid Orbitals in Space:** Hybrid orbitals are then arranged symmetrically in available space.

Need for the concept of hybridization

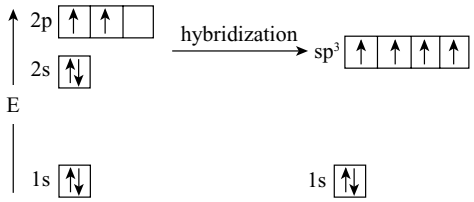
- To explain valencies of element.
- To explain equivalence of bonds.
- To explain geometry of molecule.

Types of Hybridization

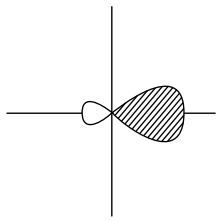
- **Sp^3-Hybridization:** Mixing and recasting of's' orbitals with three 'p' orbital of same atom forming four identical orbitals tetrahedrally arranged in space.
- **Sp^2-Hybridization:** One's' and two 'p' orbitals of the same atom mix and form three identical orbitals trigonally arranged in space.
- **Sp-Hybridization:** One's' and one 'p' orbital of the same atom mix and form two identical orbitals diagonally arranged in space.

Examples:

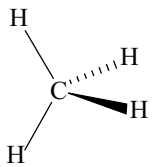
In the case of methane, the three 2p orbitals of the carbon atom are combined with its 2s orbital to form four new orbitals called "sp^3" hybrid orbitals. The name is simply a tally of all the orbitals that were blended together to form these new hybrid orbitals. Four hybrid orbitals were required since there are four atoms attached to the central carbon atom. These new orbitals will have energy slightly above the 2s orbital and below the 2p orbitals as shown in the following illustration. Notice that no change occurs with the 1s orbital.



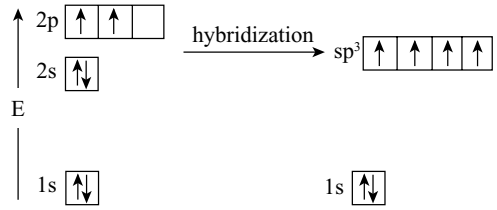
These hybrid orbitals have 75 per cent p-character and 25 per cent s-character which gives them a shape that is shorter and fatter than a p-orbital. The new shape looks a little like



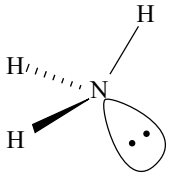
A stick and wedge drawing of methane shows the tetrahedral angles... (The wedge is coming out of the paper and the dashed line is going behind the paper. The solid lines are in the plane of the paper.)



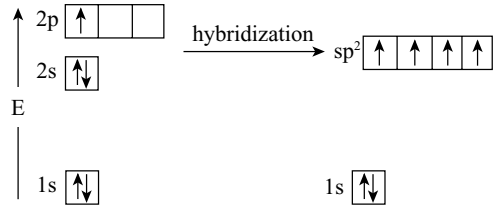
In the case of ammonia, the three 2p orbitals of the nitrogen atom are combined with the 2s orbital to form four sp^3 hybrid orbitals. The non-bonded electron pair will occupy a hybrid orbital.



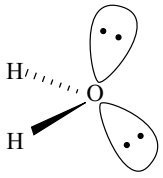
A stick and wedge drawing of ammonia showing the non-bonding electrons in a probability area for the hybrid orbital.



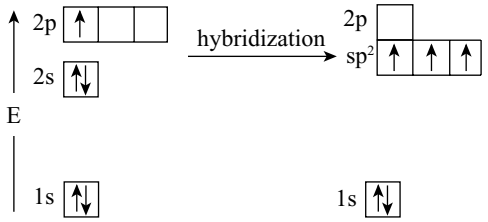
In the case of water, the three 2p orbitals of the oxygen atom are combined with the 2s orbital to form four sp^3 hybrid orbitals. The two non-bonded electron pairs will occupy hybrid orbitals.



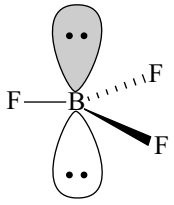
A stick and wedge drawing of water showing the non-bonding electron pairs in probability areas for the hybrid orbital.



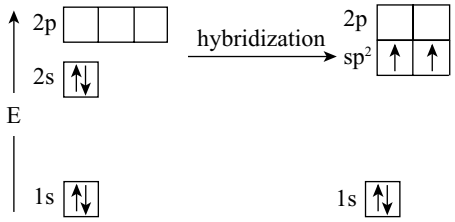
In the boron tri-fluoride molecule, only three groups are arranged around the central boron atom. In this case, the 2s orbital is combined with only two of the 2p orbitals (since we only need three hybrid orbitals for the three groups—thinking of groups as atoms and non-bonding pairs) forming three hybrid orbitals called sp^2 hybrid orbitals. The other p-orbital remains un-hybridized and is at right angles to the trigonal planar arrangement of the hybrid orbitals. The trigonal planar arrangement has bond angles of 120°.



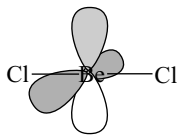
In the following stick model, the empty p orbital is shown as the probability area—one end shaded blue and the other is white—there are no electrons in this orbital.



In the beryllium dichloride Molecule since only two groups are attached to beryllium, we only will have two hybrid orbitals. In this case, the 2s orbital is combined with only one of the 2p orbitals to yield two sp hybrid orbitals. The two hybrid orbitals will be arranged as far apart as possible from each other with the result being a linear arrangement. The two un-hybridized p-orbitals stay in their respective positions (at right angles to each other) and perpendicular to the linear molecule.



In the following stick model, the empty p orbitals are shown as the probability areas—one green and one blue.

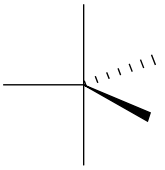


Hybridization involving d-orbitals

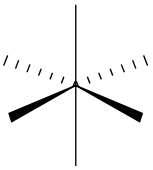
Some 3rd row and larger elements can accommodate more than eight electrons around the central atom. These atoms will also be hybridized and have very specific arrangements of the attached groups in space. The two types of hybridization involved with d orbitals are sp^3d and sp^3d^2.

The groups will be arranged in a trigonal bipyramidal arrangement with sp^3d hybridization...bond angles will be

120° in the plane with two groups arranged vertically above and below this plane.

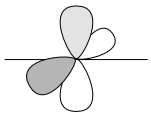
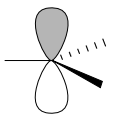
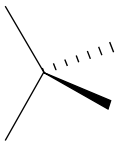
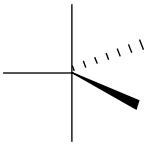
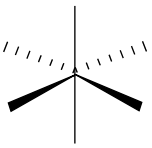


There will be an octahedral arrangement with sp^3d^2 hybridization...all bond angles are at 90°.

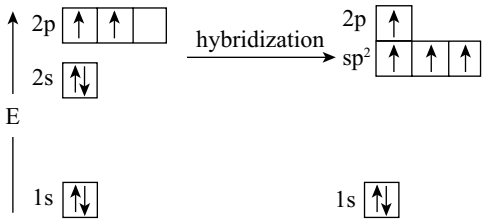


Non-bonded electron pairs are always placed where they will have the most space...in the trigonal plane for sp^3d hybridization.

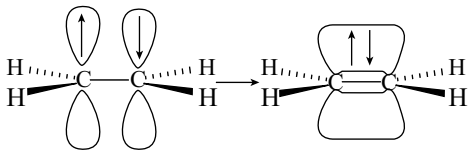
If there are six groups (Remember to count non-bonding electron pairs as groups.) it will have sp^3d^2 hybridization. If it has five groups, it will have sp^3d hybridization. Examples are SF_6, PF_5, SF_4, ClF_3, XeF_2.

Number of Groups Attached to a Central Atom	Description and 3-Dimensional Shape
Two Groups...sp	2 groups = sp hybridization 180 degree bond angle linear electron-pair geometry 
Three Groups... sp^2	3 groups = sp^2 hybridization 120 degree bond angles trigonal planar electron-pair geometry 
Four Groups...sp^3	4 groups = sp^3 hybridization 109.5 degree bond angles tetrahedral electron-pair geometry 
Five Groups...sp^3d	5 groups = sp^3d hybridization 120 and 90 degree bond angles trigonal bipyramidal electron-pair geometry 
Six Groups...sp^3d^2	6 groups = sp^3d hybridization 90 degree bond angles octahe dral electron-pair geometry 

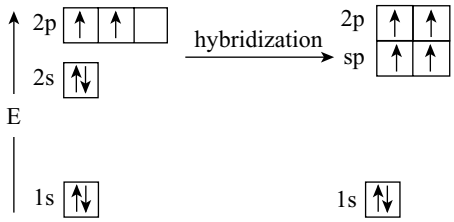
In the molecule C_2H_4, ethene, both carbon atoms will be sp^2 hybridized and have one unpaired electron in a non-hybridized p orbital.



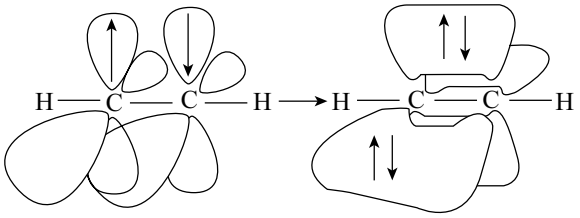
These p-orbitals will undergo parallel overlap and form one pi bond with bean-shaped probability areas above and below the plane of the six atoms. This pair of bean-shaped probability areas constitutes one pi-bond and the pair of electrons in this bond can be found in either bean-shaped area.



In H_2C_2 (acetylene), both carbon atoms will be sp hybridized and have one electron in each of two unhybridized p orbitals.



These p orbitals will undergo parallel overlap to form two pi-bonds at right angles to each other.



Type of Hybrid	sp^3	sp^2	sp
Atomic orbitals used	s, p, p, p	s, p, p	s, p
Number of hybrid orbitals formed	4	3	2
Number of atoms bonded to the C	4	3	2
Number of sigma bonds	4	3	2
Number of left over p orbitals	0	1	2
Number of pi bonds	0	1	2
Bonding pattern	| – C – |	\ C = /	= C = or C-Triple bond

Sigma Bonds

This particular kind of covalent bond in which electrons are shared between atoms is called a sigma bond.

The sigma-bond is defined as the linear overlap of atomic orbitals (hybrids except for hydrogen) in which two electrons are directly between the two bonded nuclei.

The distinguishing feature of a sigma bond (or sigma bonding orbital) is that the **overlap region lies directly between the two nuclei**.

Pi Bonds

Pi bonds involve the electrons in the leftover p orbital (unhybridized) for each carbon atom. Those p orbitals are the electron clouds or orbitals that are shown going up above and below each carbon atom.

Pi-bonds are defined as the parallel overlap of p-orbitals. A double bond has one sigma-bond and one pi-bond. A triple bond thus consists of a sigma-bond and two pi-bonds with the pi-bonds in different planes.

Notice that the **overlapping occurs in two places**, above and below the sigma bond. The pi bond does not overlap in the region directly between the two carbon atoms where the sigma bond is formed.

Sigma Bond	Pi (π) bond
Linear overlap along inter-nuclear axis	Lateral overlap perpendicular to inter-nuclear axis.
Maximum overlap occurs.	Extent of overlap is less.
Bond is rotationally symmetrical along inter-nuclear axis.	Not rotationally symmetrical.
Stronger than Pi-bond.	Weaker than a sigma bond.

Hybridization Summary

SP Hybridization	SP^2 Hybridization	SP^3 Hybridization
Occurs in triple bond compounds (E.g., Acetylene)	Occurs in double bond compounds (E.g., Ethylene)	Occurs in single bond compounds (E.g., Methane)
S-character-50%	S-character-33%	S-character-25%
Linear shape	Trigonal Shape	Tetrahedral shape
Bond angle:180°	Bond angle:120°	Bond angle: Methane:109.5° Water: 105° Ammonia: 107°

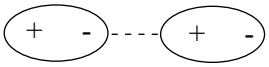
Bond dissociation energy The amount energy is consumed or liberated when a bond is formed or broken is called bond dissociation energy.

Intramolecular forces A force applicable within the molecules is known as intramolecular force.

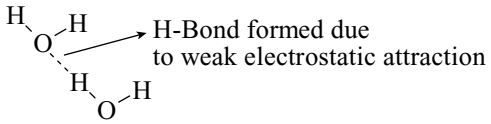
- **Repulsive forces** Applicable on same charged molecule.
- **Attractive Forces** Applicable on opposite charged molecule.

Intramolecular forces A force applicable between two molecules is known as inter molecular force.

1. **Dipole–Dipole interaction:** Attraction of positive end of one dipole with negative end of other dipole is known as dipole–dipole interaction.



2. **Hydrogen Bonding:** H atom serves as a bridge between two most electro negative atom is known as H-bonding.
   Intermolecular H-bonding: It is a bond formed between two molecules.
   E.g., Water molecule



   Intermolecular H-bonding It is a bond formed within a molecule.
   E.g., Salicylic acid
3. ***Van der Waals force*** It is a force applicable to non-polar molecule.

Hofmann Rule

When 4° ammonium hydroxide is strongly heated (≤125°C) it decomposes to yield a 3° amine, water and alkene is known as Hofmann elimination or β-elimination.

$$Me_3\overset{+}{N}—CH_2—CH_2—CH_3 \longrightarrow Me_3N + CH_2 = CH = CH_3 + H_2O$$

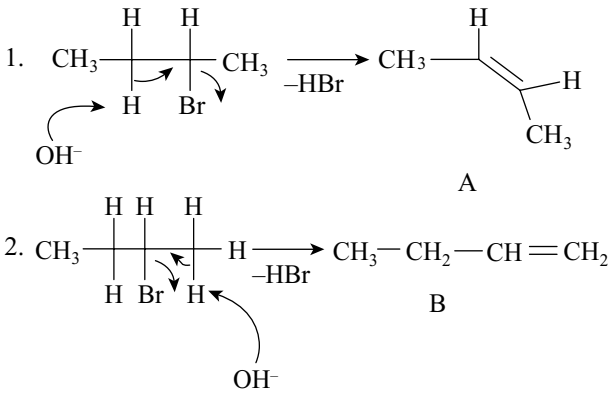
It states that in case of alternative βhydrogen in the charged substrate (4° ammonium); the least substituted alkene is predominantly formed.

Saytzeff Rule

De-hydro halogenation of secondary-and tertiary-alkyl halides proceeds by the preferential removal of the hydrogen from the carbon that has the smallest number of hydrogens.

Or

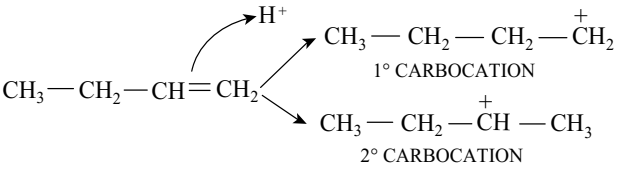
The elimination in which produce more stable alkene (highly substituted) is preferred.



According to Saytzeff's rule, **A** is more substituted alkene which is more stable and easily formed.

Markonikov's Rule

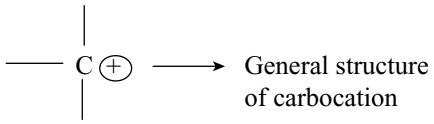
When an acidic reagent is added to –C=C-than the positive portion of reagent goes to the side of double bond or triple bond contain more H.



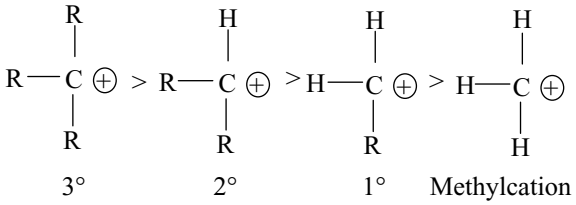
- So according to the rule, 2° carbocation can easily formed compared to 1° carbocation.

Reactive Intermediate in Organic Chemistry

Carbocation/Carbenium ion Carbon having positive charge is known as Carbocation.

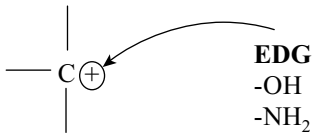


Stability of Carbocation 3° > 2° > 1° > Methylcation

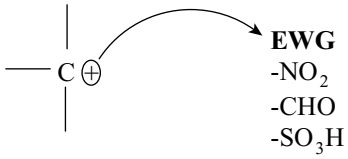


- Because of 3° Carbocation can easily form so it is more stable than 2° and 1°.
- 3° Carbocation directly attached with three partially electron donating alkyl group. So it will increase the stability of Carbocation.

Effect of electron donating/withdrawing group on carbocation



EDG donate the electron to cationic carbon and increase the stablity of it.

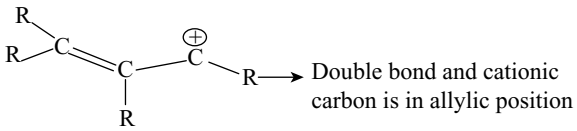


EDG withdraws the electron and destabilizes carbocation, decrease its stability.

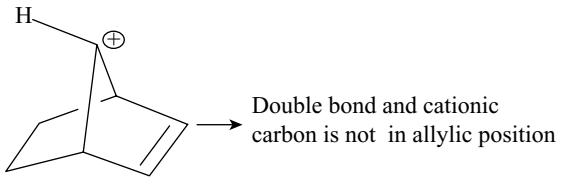
Classical Carbocation: +ve charge located on one carbon atom/delocalized by resonance involving unshared pair of electrons/or double or triple bonds in allylic position.

Non-classical Carbocation: +ve charge is delocalized by double or triple bonds that is not in allylic position is known as non-classical carbocation.

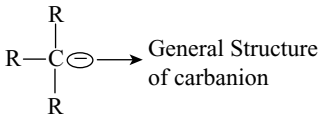
Classical Carbocation



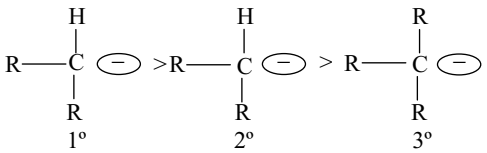
Non classical carbocation



Carbanions: It contains an unshared pair of electrons or negative charge is known as carbanion. Therefore it acts as base/nucleophile.



Stability of Carbanions: 1° > 2° > 3°



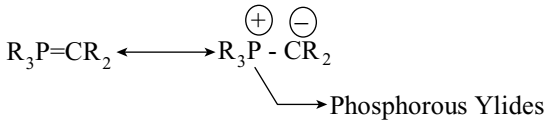
Effect of electron donating/withdrawing group on carbanion

Stability of carbanion increase by

- When carbanion carbon conjugated with –C=O, –C=N etc.
- Carbanion increases its stability with an increase in the amount of s character at carbanion carbon.
- Carbanion is stabilized by sulphur/phosphorus atom due to pϖ-dϖ bonding
- pϖ-dϖ bonding: filled p orbital of O atom overlaps with empty d orbital of sulphur/phosphorus.

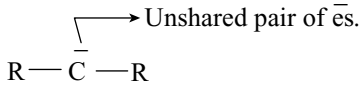
Ylides

It may be defined as compound in which +ve charged atom from group 15/16 (Sulphur/Phosphorus) of periodic table is directly connected to the carbon carrying unshared pair of electrons due to pϖ-dϖ bonding.



Carbene Carbon having open sextet is known as carbene or divalent carbon is known as carbene.

Carbene are very reactive species.



General Structure of carbene

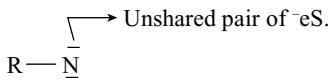
In carbene, these two electrons are paired or unpaired.

Singlet carbene: Two non-bonding electrons are in paired, present in SP_2 hybridized orbitals.

Singlet carbene electrons are in paired | Triplet carbene electrons are not in paired

Triplet carbine: Electrons are unpaired one electron present in SP_2 hybridized orbitals and other presents in vacant unhybridized p-orbital.

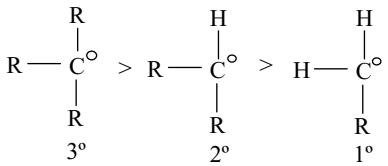
Nitren Nitrogen analogus of carbene is known as Nitrene.



General Structure of Nitrene

Free Radicals: Carbon having single electron is known as free radicals

Stability of free radicals: 3° > 2° > 1° > Methyl radicals



Nitrenium Ion: Nitrogen analogus of carbocation is known as Nitrenium ion.

General Structure of Nitrenium Ion

Stereochemistry

Stereochemistry is the study of the three dimensional shape of molecules and the effects of shape upon the properties of molecules.

- Isomers are compounds that have the same molecular formulas but different structural arrangements of atoms.

They fall into two categories: Constitutional isomers and stereo isomers.

- Constitutional isomers are isomers that have different atomic connectivity.

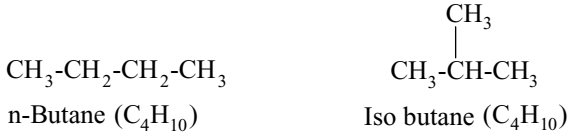
  Examples of constitutional isomers include butane and isobutane (both have the molecular formula C_4H_{10}, but different structures and ethanol and dimethyl ether (both have the formula C_2H_6O, but again the two differ structurally.
- Stereo isomers are isomers whose constituent atoms are connected in the same sequence, but in different **spatial** patterns.

A molecule can have more than one **stereogenic carbon**. The number of stereoisomers can be determined by the 2^n rule, where n equals the number of stereogenic carbons. Thus, if one stereogenic carbon is present, there are two possible stereoisomers; with two stereogenic carbons, there are four possible stereoisomers.

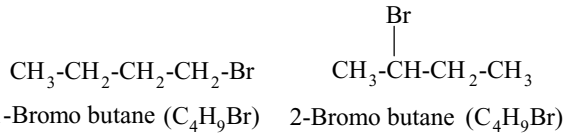
Stereo isomers can be further subdivided into: enantiomers and diastereomers.

Structural Isomers

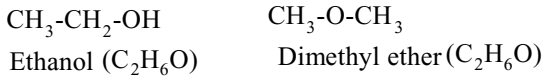
1. **Chain Isomers:** Structures having a similar molecular formula but differ in arrangement of carbon chain are known as chain isomer.



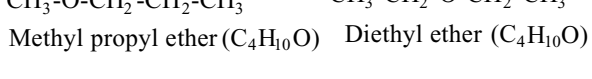
2. **Positional Isomers:** Structures having a similar molecular formula but differ in position of functional group are known as positional isomers.



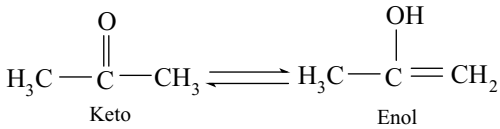
3. **Functional Isomers:** Structures having a similar molecular formula but differ in functional group are known as functional isomer.



4. **Metamerism:** Unequal distribution of carbon chain on either side of functional group is known as Metamerism.



5. **Tautomerism:** The existence of two or more chemical compounds that are capable of facile interconversion is known as Tautomerism.



Optical isomer (d and l)

Optically active compound: A compound which rotates the plane polarized light is known as optically active compound.

- Chiral compounds are optically active; they rotate the plane of polarized light.
- Achiral compounds do not rotate the plane of polarized light. They are optically inactive.
- If the compound rotates the plane polarized light to the right side, then it known as ***Dextrorotatory*** compound. **[d or (+)].**
- If the compound rotates the plane polarized light to left side, then it known as ***laevorotatory*** compound. **[l or (–)].**
  - Ordinary light is converted into plane polarized light by Nicol prism (Polarizer), and it is made up of calcite crystals or crystalline $CaCO_3$.
  - Light Source: D-line Sodium lamp at $\lambda = 5830\ A^0$
- A polarizer measures the degree of optical rotation of a compound

$$[\alpha]_{\lambda}^{T} = \frac{\alpha}{1xc}$$

- T is the temp in °C
- λ is the wavelength
- α is the measured rotation in degrees
- l is the path length in decimeters
- c is the concentration in grams per mL

Each optically active compound has a characteristic specific rotation.

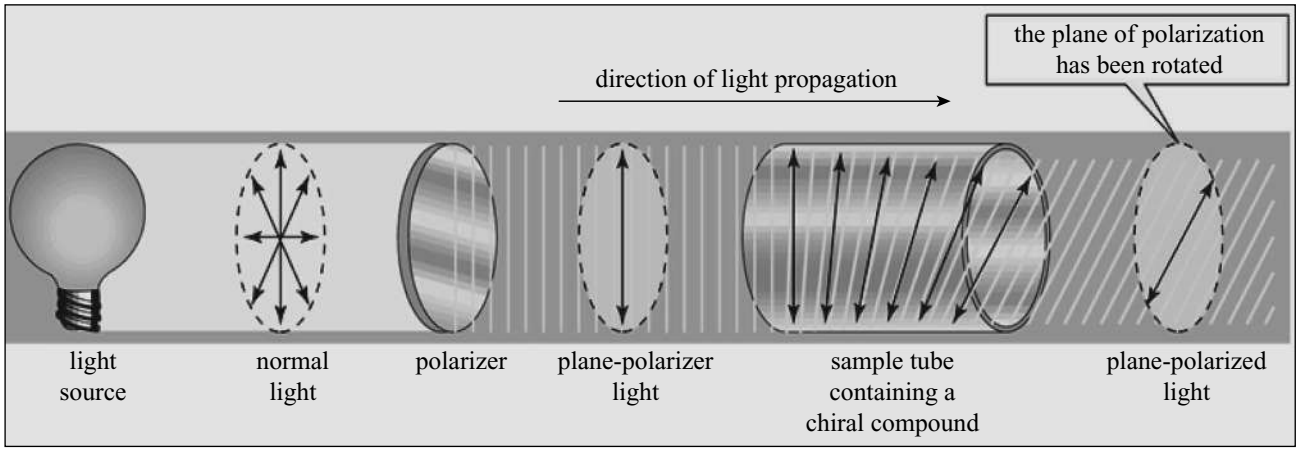


Figure 2.3 Polarimeter-to measure optical activity

Optical Purity = Observed Specific rotation/Specific rotation of pure enantiomer

Enantiomer Excess = Excess of a single a_{λ}^{T} = specific rotation enantiomer/Entire mixture

Racemic mixture, which contains an equal amount (equi-molar mixture) of the two enantiomers, is optically inactive

Absolute configuration (R, S system)

- Rank the groups (atoms) bonded to the chirality center

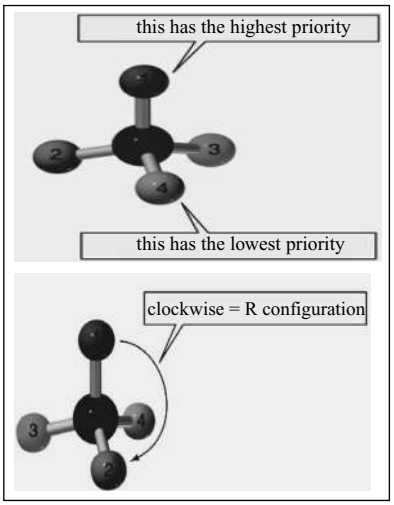


Figure 2.4 Absolute configuration (R, S system)

- Orient the lowest priority (4) away from you
- Clockwise = R configuration, Counterclockwise = S configuration

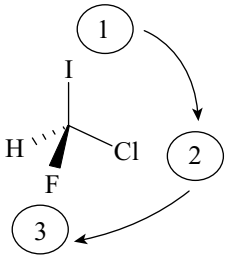
Cahn-Ingold-Prelog (CIP system)–R/S Notation

The Cahn-Ingold-Prelog R/S rules are used for naming enantiomers and diastereomers.

1. Identify the chiral centres (most commonly an sp^3 C with 4 different groups attached)
2. Assign the priority to each group (high = 1, low = 4) based on atomic number of the atom attached to the chiral center (remember the first point of difference rule)
3. Position the lowest priority group *away from you* as if you were looking along the C-(4) s bond.
4. For the other 3 groups, determine the direction of high to low priority (1 to 3)
5. If this is clockwise, then the center is R. (Latin: *rectus* = right)
6. If this is counter clockwise, then it is S. (Latin: *sinister* = left)

   Example: Chlorofluoroiodomethane

The chirality center is easy to spot, and the four attached groups are I, Br, F and H listed in priority order, highest to to lowest.



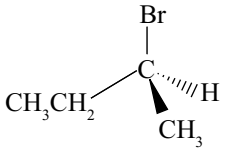
So this is the **R** enantiomer.

Sub-rules

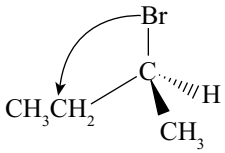
- Isotopes: H vs D? Since isotopes have identical atomic numbers, the mass number is used to discriminate them, so D > H.
- Same atom attached? By moving out one unit at a time, locate the first point of difference and apply rules there.

Naming from the perspective formula

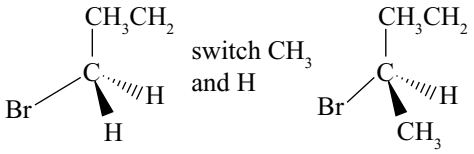
1. Rank the groups bonded to the asymmetric carbon.



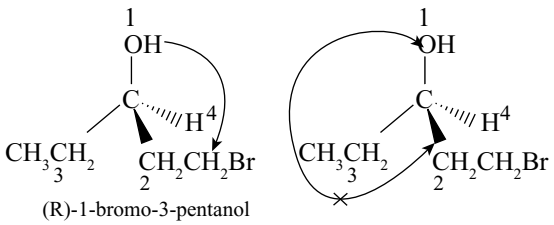
2. If the group (or atom) with the lowest priority is bonded by hatched wedge.



3. If necessary, rotate the molecule so that the lowest priority group (or atom) is bonded by a hatched wedge.



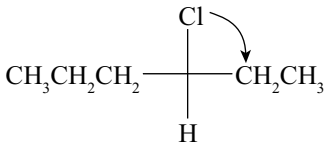
4. You can draw group 1 to group 2, passing group 4, but never 3.



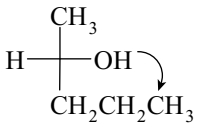
(R)-1-bromo-3-pentanol

Naming from the Fischer projection

1. Rank the groups (or atom) that are bonded to the asymmetric carbon and draw an arrow with the highest priority to the lowest priority.

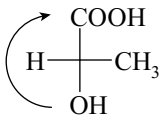


2. If the lowest priority is on a horizontal bond, the naming is opposite to the direction of the arrow.



S-2-Pentanol

3. The arrow can go from group 1 to 2, passing group 4, but not group 3.

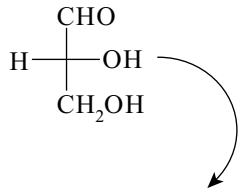


S-Lactic acid

4. A Fischer projection can only be rotated 180° in the plane of the paper to yield the same molecule.

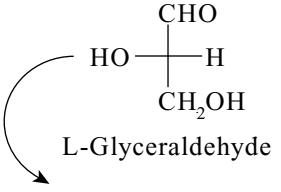
Relative configuration (D/L configuration)

D-Glyceraldehyde



-OH group is right side to CH_2OH So, D-Glyceraldehyde is relative Configuration

L-Glyceraldehyde

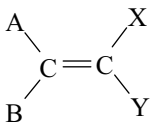


L-Glyceraldehyde

-OH group is left side to CH_2OH So, L-Glyceraldehyde is relative Configuration

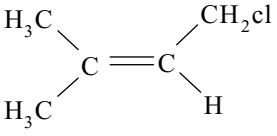
- Relative configuration has been seen in protein, carbohydrate and alkaloids.

Geometrical isomer A type of isomer which restricts the rotation around –C=C–is known as geometrical isomer.

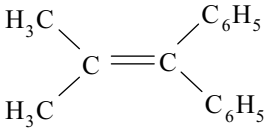


Condition for existance of geometrical

if $A \neq B$ & $X \neq Y$



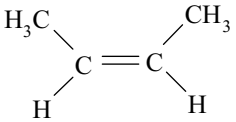
A



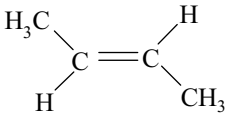
B

In structure A and B, one carbon is attached with two similar groups so there is no possibility to exist geometrical isomer.

Cis-Trans system



Cis isomer

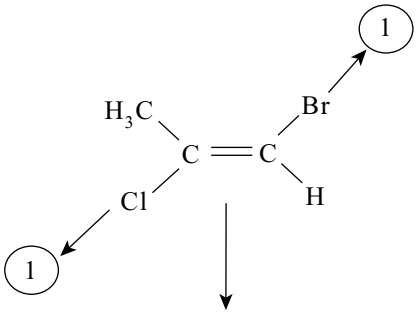


Trans Isomer

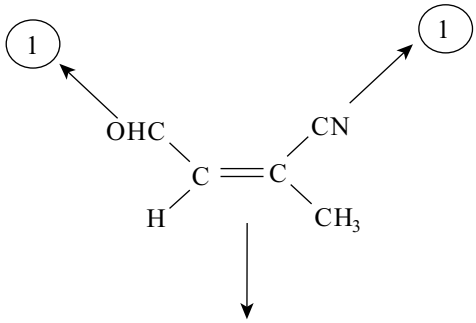
- **Cis** means two similar groups are on same side.
- **Trans** means two similar groups are on opposite direction.
- Trans isomer is more stable than Cis isomer due to steric hindrance is more with cis isomer because two bulky groups are in same side.
- Trans isomer having Dipole moment $\mu = 0$

E/Z system: In alkenes, if carbon is attached with four different groups than it will be nomenclatured by E/Z system.

- **E means Entegegen-Opposite side**
- **Z means Zusammen-Same side**



E isomer because two prior group are on opposite side

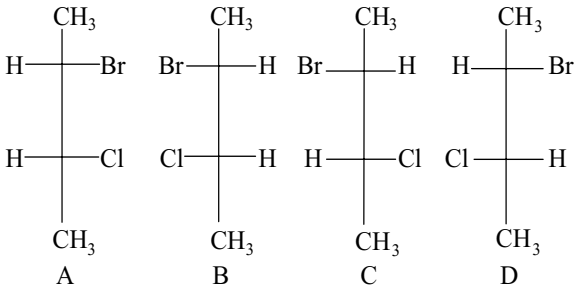


Z isomer because two prior group are on Same side

Enantiomer and Diastereomer

Enantiomer The stereoisomer of compounds which are non-superimposable mirror image of each other are known as enantiomers.

- Enantiomers are often referred as a optical isomer.
- Chirality is necessary and sufficient condition for existence of an enantiomer.
- Non-superimposabilty on its mirror image is necessary and sufficient condition for existence of enantiomerism.
- It is also a necessary but not sufficient condition for optical activity.
- E.g., Racemic mixture is optically inactive.
- All enantiomer have similar physical property (exception is specific rotation) while different chemical property.



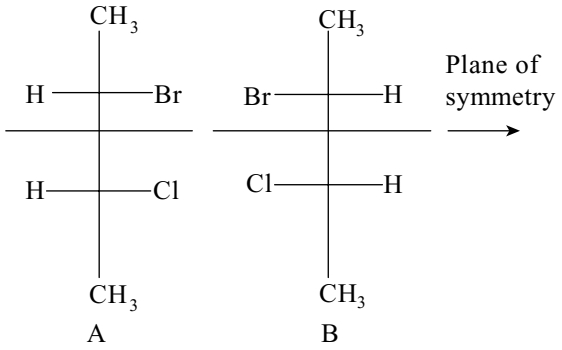
A B C D

- A and B and C and D are pair of **enantiomer**
- While A and C, A and D, B and C and B and D are pair of **diastereomer.**

Diastereomer: The stereoisomer of compound which are not mirror image of each other are known as diastereomers.

- All diastereomers have similar chemical property and different physical property.
- Diastereomer is possible if the molecule is having two or more than two chiral centre.

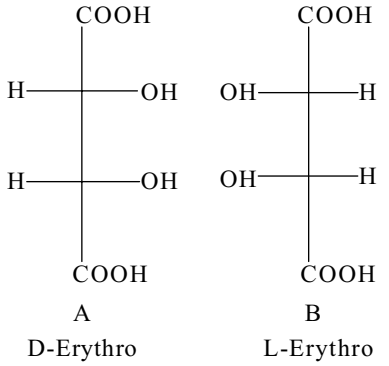
Meso compounds: These are the ones which are superimposable on their mirror image even though they contain chiral carbon. Because it has a plane of symmetry in its structure, so it is optically inactive.

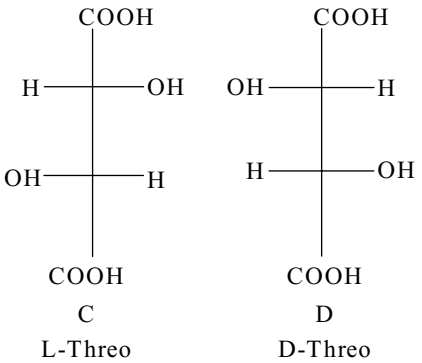


Erythro/Threo

Erythro: If two similar groups are on the same side of carbon chain.

Threo: If two similar groups are on the opposite side of carbon chain.

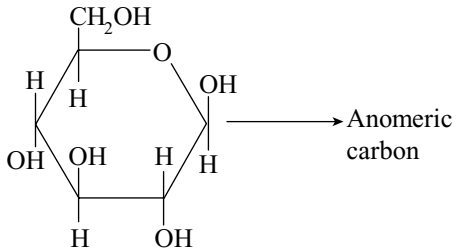




Epimer When two diastereomers differ in the stereochemistry at only one stereocentre then these are epimers of each other.

- E.g., Glucose and galactose are epimer at C-4
- Glucose and mannose are epimer at C-2

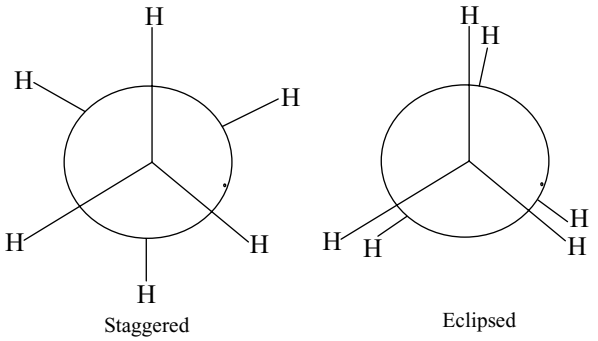
Anomer If diastereomers differ in their configuration at C-1 (anomeric carbon), then these are called anomers.



- β-anomer: If –OH group is in upward direction to anomeric carbon.
- α-anomer: If –OH group is in downward direction to anomeric carbon.

Conformation Different three dimensional arrangements of atoms results due to free rotation about C-C single bond, this is known as conformation.

Conformation in ethane



Staggered forms are more stable than eclipsed because all atoms are arranged opposite to each other so it reduces steric hindrance among them.

Anti It is a type of staggered conformation dihedral angle between two bulky groups is 180°.

Gauche: It is a type of staggered conformation dihedral angle between two bulky groups is 60°.

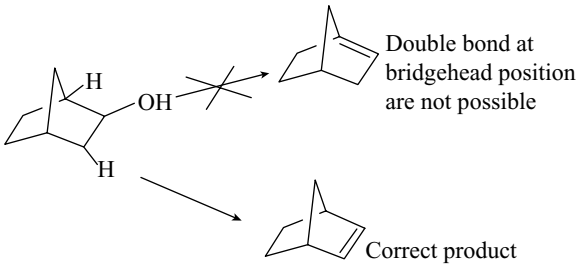
NOTE

Conformation In Cyclohexane: Stability order

Chair conformation > Twist boat conformation > boat conformation >half chair conformation

- *Chair conformation: It is most stable because all H atoms are in staggered form.*
- *Twist-boat conformation: Where it twists, two H atoms are at staggered position.*
- *Boat form: All H-atoms are at eclipsed form.*
- *Half-Chair form: Because at one end of ring are planar.*

Bredt's Rule: In bridgehead bicyclic compound, double bond at the bridgehead position are impossible in small system.



Stereoselectivity

Any chemical reaction that yields predominantly, one stereoisomer, out of several stereoisomer possibilities is said to be a stereoselective reaction.

It is the property of a chemical reaction in which a single reactant forms an unequal mixture of stereoisomers during the non-stereospecific creation of a new stereocenter or during the non-stereospecific transformation of a pre-existing one.

The selectivity arises from the differences in steric effects and electronic effects in the mechanistic pathways leading to the different products. Stereoselectivity can vary in degree but it can never be total since the activation energy difference between the two pathways is finite. However, in favourable cases, the minor stereoisomer may not be detectable by the analytic methods used.

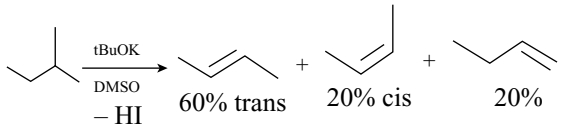
An **enantioselective reaction** is the one in which one enantiomer is formed in preference to the other, in a reaction that creates an optically active product from an achiral starting material, using either a chiral catalyst, an enzyme or a chiral reagent. The degree of selectivity is measured by the enantiomeric excess. An important variant is kinetic resolution, in which a pre-existing chiral center undergoes reaction with a chiral catalyst, an enzyme or a chiral reagent such that one enantiomer reacts faster than the other and leaves behind the less reactive enantiomer, or in which a pre-existing chiral center influences the reactivity of a reaction center elsewhere in the same molecule.

A **diastereoselective reaction** is the one in which one diastereomer is formed in preference to another (or in which a subset of all possible diastereomers dominates the product mixture), establishing a preferred relative stereochemistry. In this case, either two or more chiral centers are formed at once such that one relative stereochemistry is favoured, or a pre-existing chiral center (which needs not be optically pure) biases the stereochemical outcome during the creation of another. The degree of relative selectivity is measured by the diastereomeric excess.

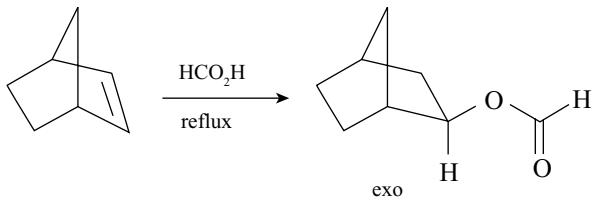
Stereoconvergence can be considered an opposite of stereoselectivity, when the reaction of two different stereoisomers yields a single product stereoisomer.

Examples

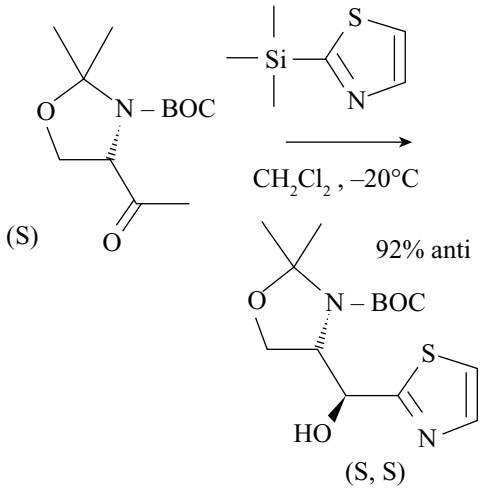
An example of modest stereoselectivity is the dehydrohalogenation of 2-iodo-butane which yields 60% *trans*-2-butene and 20% *cis*-2-butene. Since alkene geometric isomers are also classified as diastereomers, this reaction would also be called diastereoselective.



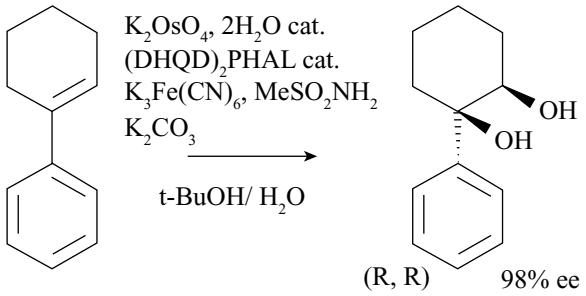
The addition of formic acid to norbornene is also stereospecific because the exo isomer is formed exclusively without any of the endo isomer.



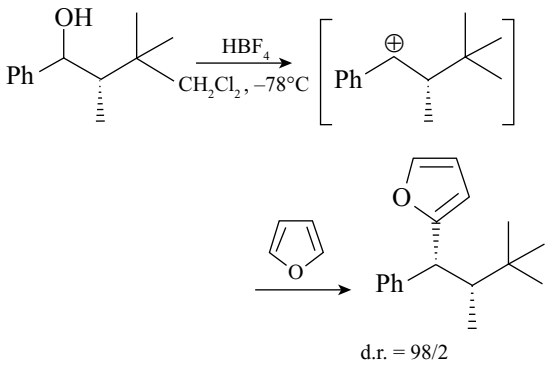
Cram's rule predicts the major diastereomer resulting from the diastereoselective nucleophilic addition to a carbonyl group next to a chiral center. The chiral center need not be optically pure, as the relative stereochemistry will be the same for both enantiomers. In the example below, the (S)-aldehyde reacts with a thiazole to form the (S, S) diastereomer but only a small amount of the (S, R) diastereomer.



The sharpless epoxidation is an example of an enantioselective process, in which an achiral allylic alcohol substrate is transformed into an optically active epoxyalcohol. In the case of chiral allylic alcohols, kinetic resolution results. Another example is sharpless asymmetric dihydroxylation. In the example below, the achiral alkene yields only one of possible four stereoisomers.



With a stereogenic center next to the carbocation, the substitution can be stereoselective in intra and intermolecular reactions. In the reaction depicted below, the nucleophile (furan) can approach the carbocation formed from the least shielded side away from the bulky t-butyl group resulting in high facial diastereoselectivity:



Stereospecificity

Stereospecificity is the property of a reaction mechanism that leads to different stereoisomeric reaction products from different stereoisomeric reactants, or which operates on only one (or a subset) of the stereoisomers.

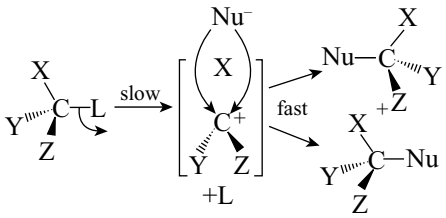
In contrast, stereoselectivity is the property of a reactant mixture where a non-stereospecific mechanism allows for the formation of multiple products, but where one (or a subset) of the products is favoured by factors, such as steric access, that are independent of the mechanism.

A stereospecific mechanism *specifies* the stereochemical outcome of a given reactant, whereas a stereoselective reaction *selects* products from those made available by the same, non-specific mechanism acting on a given reactant. Given a single, stereoisomerically pure starting material, a stereospecific mechanism will give 100% of a particular stereoisomer (or no reaction), although loss of stereochemical integrity can easily occur through competing mechanisms with different stereochemical outcomes. A stereoselective process will normally give multiple products even if only one mechanism is operating on an isomerically pure starting material.

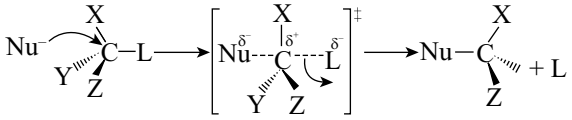
Examples

Nucleophilic substitution at sp^3 centres can proceed by the stereospecific S_N2 mechanism, causing only inversion, or by the non-specific S_N1 mechanism, the outcome of which can show a modest selectivity for inversion, depending on the reactants and the reaction conditions to which the mechanism does not refer. The choice of mechanism adopted by a particular reactant combination depends on other factors (steric access to the reaction centre in the substrate, nucleophile, solvent, temperature).

Stereospecificity in substitution reactions



S_N1 mechanism non-stereospecific

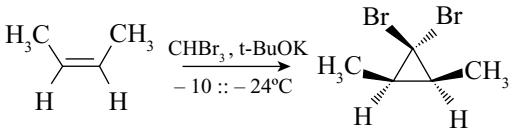


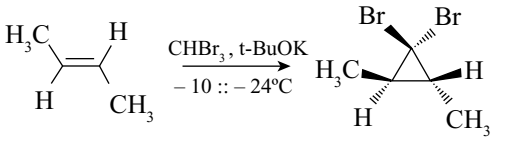
S_N2 mechanism stereospecific

For example, tertiary centres react almost exclusively by the S_N1 mechanism whereas primary centres (except

neopentyl centres) react almost exclusively by the S_N2 mechanism. When a nucleophilic substitution results in incomplete inversion, it is because of a competition between the two mechanisms, which often occurs at secondary centres, or because of double inversion (as when iodide is the nucleophile).

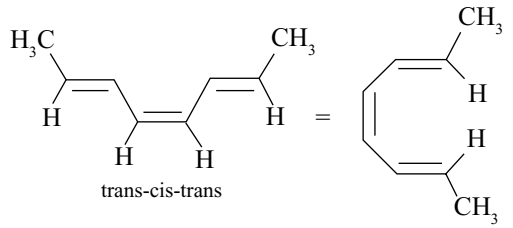
The addition of carbenes to alkenes is stereospecific in that the geometry of the alkene is preserved in the product. For example, dibromocarbene and *cis*-2-butene yield *cis*-2, 3-dimethyl-1, 1-dibromocyclopropane, whereas the *trans* isomer exclusively yields the *trans* cyclopropane.

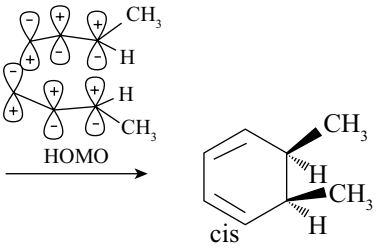




This addition remains stereospecific even if the starting alkene is not isomerically pure, as the products stereochemistry will match the reactants.

The disrotatory ring closing reaction of conjugated trienes is stereospecific in that isomeric reactants will give isomeric products. For example, *trans, cis, trans*-2, 4, 6-octatriene gives *cis*-dimethylcyclohexadiene, whereas the *trans, cis, cis* reactant isomer gives the *trans* product and the *trans, trans, trans* reactant isomer does not react in this manner.





Important Organic Reactions Mechanism

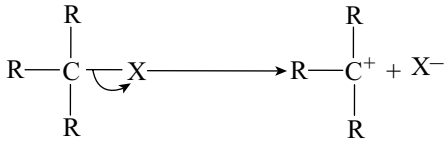
1. SN1 mechanism

SN1 indicates a ***substitution***, ***nucleophilic***, ***unimolecular*** reaction,

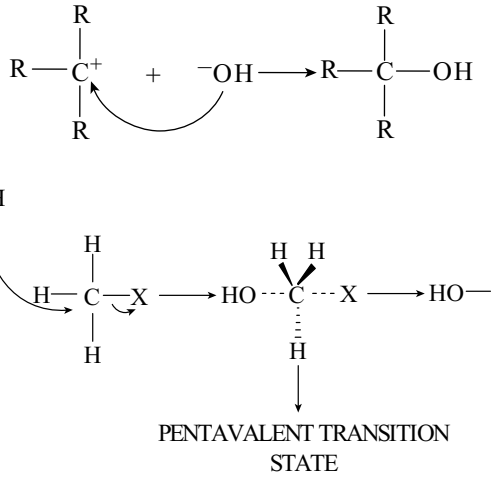
Rate = k[R–X] follows first order kinetics

This implies that the rate determining step of the mechanism depends on the decomposition of a single molecular species.

Step-1 Generation of carbocation, slow step, rate determining step.



Step-2 Rapid attack of nucleophile on carbocationic carbon.



This pathway is a concerted process (single step) as shown by the following reaction coordinate diagrams, where there is simultaneous attack of the nucleophile and displacement of the leaving group.

Reactivity order 3° >2°>1° alkyl halides

Stereochemitry Inversion plus partial racemization

Solvent Polar protic solvent increases the rate of SN1 reaction because it increases the rate of ionization of the alkyl halide.

2. SN2 mechanism

SN2 indicates a ***substitution***, ***nucleophilic***, ***bimolecular*** reaction, described by the expression

Rate = k [**Nu**][**R**–**X**]. It follows second order kinetics.

Reactivity order $1^0 > 2^0 > 3^0$ alkyl halides

Stereochemitry Total inversion of configuration

Halides Nucleophilicity in protic solvent: F < Cl <Br < I, because nucleophile is solvated.

Halides Nucleophilicity in Aprotic solvent: F > Cl >Br > I, because nucleophile is not solvated.

3. E1 mechanism

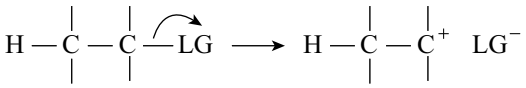
E1 indicates an ***elimination***, ***unimolecular*** reaction,

Where rate = k [**R–LG**].

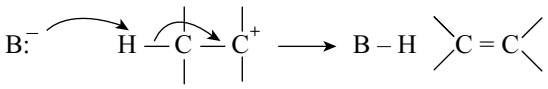
This implies that the rate determining step of the mechanism depends on the decomposition of a single molecular species.

Overall, this pathway is a multi-step process with the following two critical steps:

Step-1: Loss of the leaving group, LG, to generate a carbocation intermediate.



Step-2: Loss of a proton, H^+, from the carbocation to form the –C=C–bond.



Reactivity order $(CH_3)_3C \rightarrow (CH_3)_2CH \rightarrow CH_3CH_2 \rightarrow CH_3–$

4. Orientation of E1 mechanism follows Saytzeff's rule

Selectivity E1 reactions usually favours the more stable alkene as the major product: more highly substituted and trans → cis-

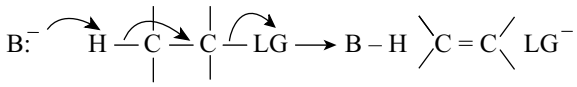
In an E1 reaction, the rate determining step is the loss of the leaving group to form the intermediate carbocation. The more stable the carbocation is, the easier it is to form, and the faster the E1 reaction will be carried out.

This E1 mechanistic pathway is most common with:

- Good leaving groups
- Stable carbocations
- Weak bases

5. E2 mechanism

E2 indicates an ***elimination***, ***bimolecular*** reaction, where rate = k [**B**][**R-LG**]. This implies that the rate determining step involves an interaction between these two species, the base and the organic substrate.



This pathway is a concerted process with the following characteristics:

Simultaneous removal of the proton, H^+, by the base, loss of the leaving group, LG, and formation of the double-bond.

Reactivity Rate of reaction increase as more branched alkene is formed.

Orientation of E2 mechanism follows Saytzeff's rule.

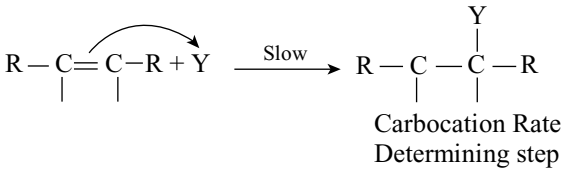
6. Electrophilic addition reactions

- It is an important class of reactions that allow the inter conversion of C=C and C≡C into a range of important functional groups.
- Addition reaction is the reverse of elimination
- An electrophile, Y^+, is an electron deficient species that will react with an electron rich species (the C=C).
- The following pointers may aid your understanding of these reactions:
- Intermediate is carbocation, so rearrangement takes place

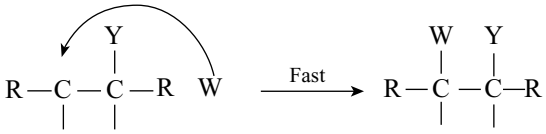
Reactivity

- Electron withdrawing group at "–C=C–"decrease reaction because intermediate is carbocation.
- Electron donating group at "–C=C–"increase reaction because Intermediate is carbocation so EDG stabilize carocation.
- Orientation of electrophilic addition reactions follows Markonikov's rule.
- If the two new σ bonds form at the same time from the same species, then syn-addition is observed.
- If the two new σ bonds form at different times from different species, then anti-addition is observed.

Step-1 Addition of electrophile toward alkene



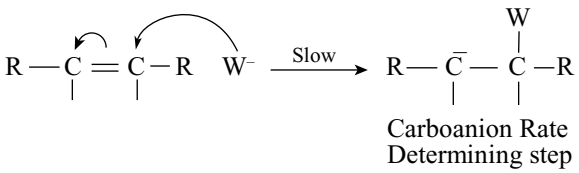
Step-2 Addition of nucleophile to carbocation



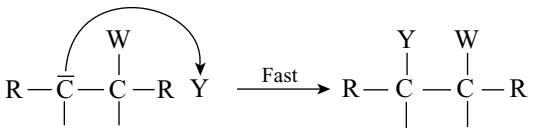
7. Nucleophilic addition reactions

In nucleophilic addition reactions, first, attack of nucleophile takes place then addition of electrophile takes place.

Step-1 Attack of nucleophile towards alkene



Step-2 Addition of electrophile to carbanion



The following pointers may aid your understanding of these reactions:

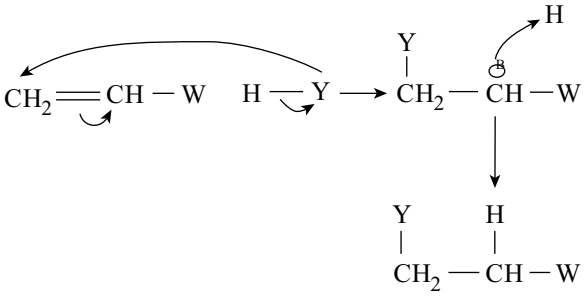
- Intermediate is carbanion, so rearrangement cannot take place.

Reactivity

- Electron withdrawing group at "–C=C–"increases reaction rate because the intermediate is carbanion, so it will stabilize carbanion.
- Electron donating group at "–C=C–"decreases reaction rate because intermediate is carboanion so EDG increases the electron density and destabilizes the carbanion.
- Orientation of nucleophilic addition reactions follows

Micheal addition rule:

- Attack of nucleophile to the "–C=C–" bond occurs in such a way that it attacks the side away from carbon having electron withdrawing group.



W = Electron withdrawing groups like –CHO, –COOR, –COOH, $–NO_2$

8. Mechanism of addition to –C=X (X=hetero atom) multiple bond

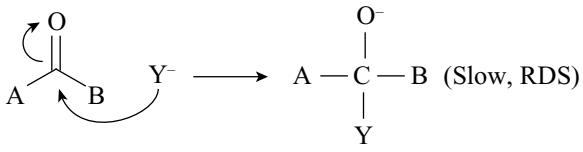
(Electrophilic addition to –C=O and Nucleophilic addition to –C=O)

It is concerned with addition to –C=O, –C=N, –C=S, –C≡N, so these all are stronger and polar bonds hence only ionic mechanism can operate. No free radical mechanism can operate.

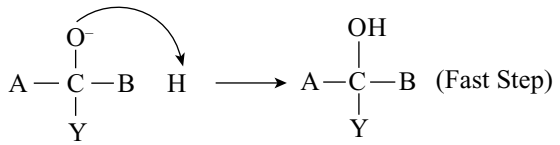
In this reaction, nucleophile always goes with carbon atom and electrophile always goes with hetero atom.

Nucleophillic addition reaction

Step-1 Addition of nucleophile to –C=O

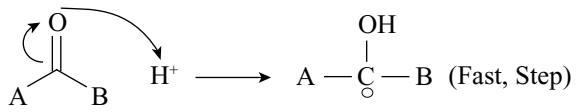


Step-2 Addition of electrophile to O (Hetero atom)

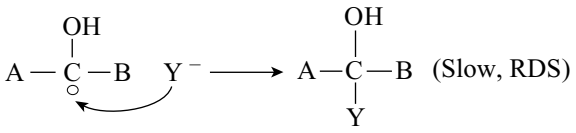


Electrophillic addition reaction

Step-1 Addition of electrophile to O (Hetero atom)



Step-2 Addition of nucleophile



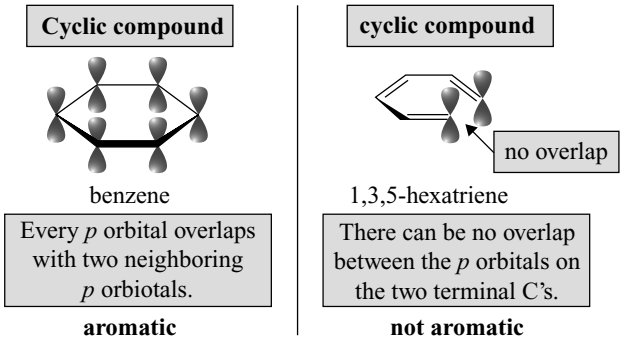
In both the mechanisms, the rate limiting step is the attack of nucleophile reactivity.

- Electron donating groups (A/B): Decrease the reaction rate, nucleophile cannot attack on carbonyl carbon because electron density at carbonyl carbon (–C=O) is increased.
- Electron withdrawing groups (A/B): Increase the reaction rate, nucleophile can easily attack on carbonyl carbon because the electron density at carbonyl carbon (–C=O) is decreased so –C=O becomes more positive.
- Steric hindrance near –C=O group also decrease the reactivity.
- Aryl group or ϖ bond in conjugation with –C=O also decrease the reactivity by releasing electron through resonance.

Criteria for Aromaticity—Hückel's Rule

Four structural criteria must be satisfied for a compound to be aromatic.

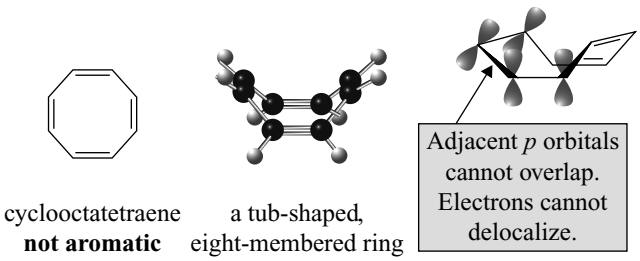
(1) A molecule must be cyclic:



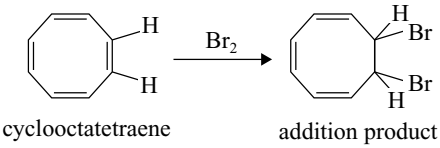
To be aromatic, each *p* orbital must overlap with *p* orbitals on adjacent atoms.

(2) A molecule must be planar:

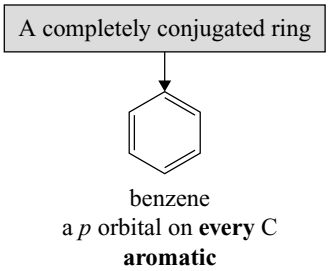
All adjacent *p* orbitals must be aligned so that the π electron density can be delocalized.

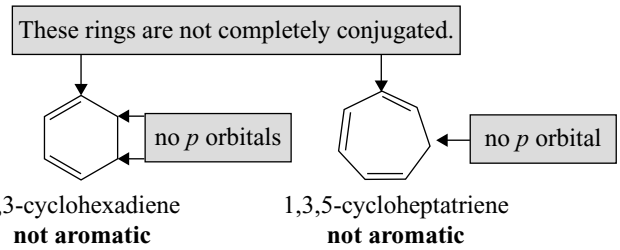


Since cyclo octatetraene is non-planar, it is not aromatic, and it undergoes addition reactions just like those of other alkenes.



(3) A molecule must be completely conjugated:

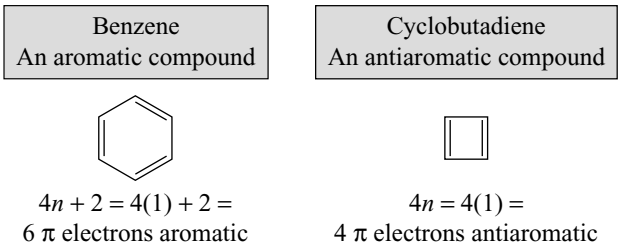




(4) A molecule must satisfy Hückel's rule, and contain a particular number of π electrons.
Hückel's rule:

- An aromatic compound must contain 4n+2π electrons (n = 0, 1, 2, 3 and so forth).
- Cyclic, planner and completely conjugated compounds that contain 4n π electrons are especially unstable, and are said to be anti aromatic.

Benzene is aromatic and especially stable because it contains 6 π electrons. Cyclobutadiene is antiaromatic and especially unstable because it contains 4 π electrons.

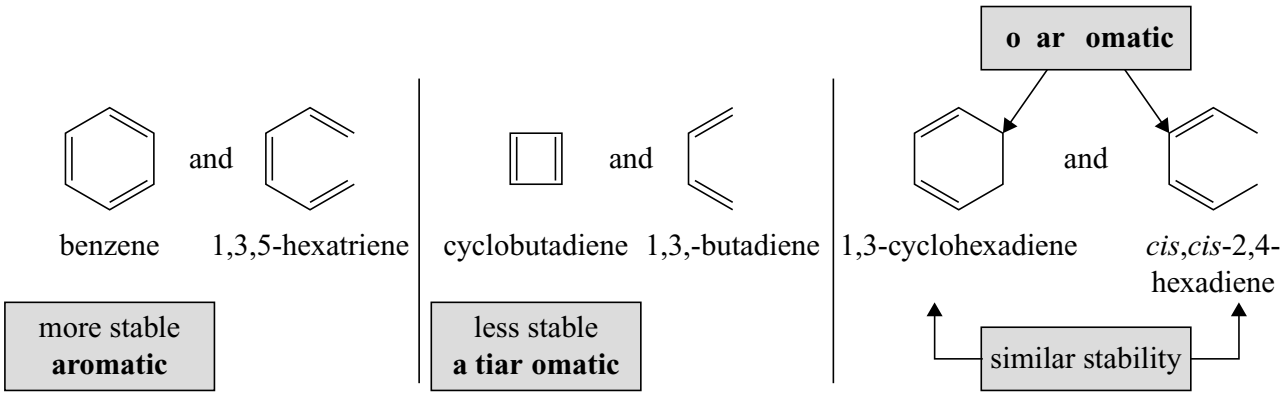


Note that Hückel's rule refers to the number of π electrons, not the number of atoms in a particular ring.

Where *n*	The no of π electrons that obey the huckel's rule
0	2
1	6
2	10
3	14
4	18

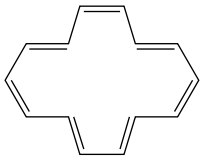
Considering aromaticity, a compound can be classified in one of three ways:

1. **Aromatic**—A cyclic, planar, completely conjugated compound with $4n + 2$ π electrons**.**
2. **Anti-aromatic**—A cyclic, planar, completely conjugated compound with $4n\pi$ electrons.
3. **Not aromatic (nonaromatic)**—A compound that lacks one (or more) of the following requirements for aromaticity: being cyclic, planar, and completely conjugated.
   - An aromatic compound is *more* stable than a similar acyclic compound having the same number of ϖ electrons. Benzene is more stable than 1,3,5-hexatriene.
   - An antiaromatic compound *less* stable than an acyclic compound having the same number of ϖ electrons. Cyclobutadiene is less stable than 1,3-butadiene.
   - A compound that is not aromatic is *similar* in stability to an acyclic compound having the same number of ϖ electrons. 1,3-Cyclohexadiene is similar in stability to *cis,cis*-2-4-hexadiene, so it is not aromatic.

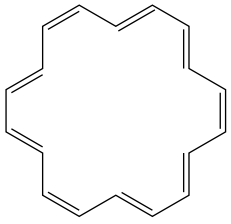


Annulene:

- To name an annulene, indicate the number of atoms in the ring in brackets and add the word annulene



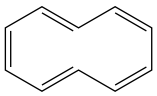
[14]-annulene
$4n + 2 = 4(3) + 2 =$
14 π electrons
aromatic



[18]-annulene
$4n + 2 = 4(4) + 2 =$
18 π electrons
aromatic

- [10]-Annulene has 10 π electrons, which satisfies Hückel's rule, but a planar molecule would place the two H atoms inside the ring too close to each other. Thus, the ring puckers to relieve this strain.
- Since [10]-annulene is not planar, the 10 π electrons can't delocalize over the entire ring and it is notaromatic.

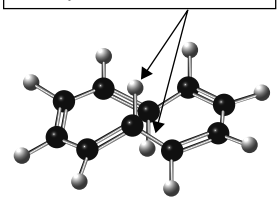
[10]-Annulene fits Hückel's rule, but it's **not planer**.



[10]-annulene
10 π electrons
not aromatic

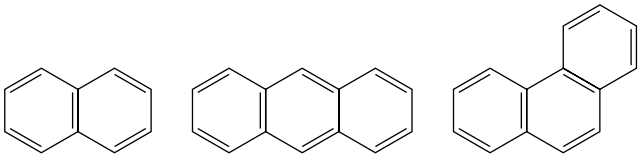
=

The molecule puckers to keep these H's further away from each other.



3-D representation

- Two or more six-membered rings with alternating double and single bonds can be fused together to form polycyclic aromatic hydrocarbons (PAHs).
- There are two different ways to join three rings together, forming anthracene and phenanthrene.



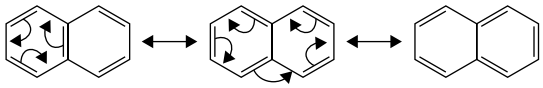
naphthalene
10 π electrons

anthracene
1 π electrons

phenanthrene
1 π electrons

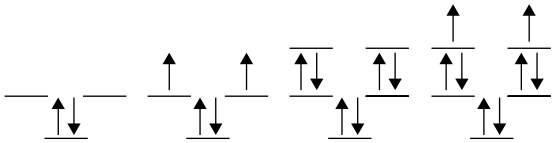
- As the number of fused rings increases, the number of resonance structures increases. Naphthalene is a hybrid of three resonance structures whereas benzene is a hybrid of two.

Three resonance structures for naphthalene



Annulenes:

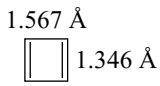
Monocyclic, completely conjugated polyenes. According to the HMO, the 4n + 2 = 2,6,10,14…π-electron annulenes are aromatic, while the 4n = 4,8,12,16…π-electron annulenes are anti-aromatic (paratropic compound: a presence of paramagnetic ring current).



Duet (aromatic) | Quartet (anti-aromatic, diradical) | Sextet (aromatic) | Octet (anti-aromatic, diradical)

Note

- That according to the Huckel rule, the first pair of π-electrons goes to the π-orbital of the lowest energy. After that the bonding orbitals are degenerate and occur in pairs of equal energy. According to the Hund's rule, these orbitals are filled first with unpaired π- electrons (diradical structure), and then paired (sextet structure). The degeneracy may be removed by a distortion of a molecule and the resulting loss of symmetry.

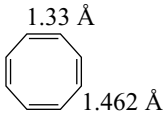


[4]annulene
antiaromatic

π 2 × 2 (anti)

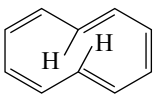
[6]annulene
aromatic

1 × 4 + 2



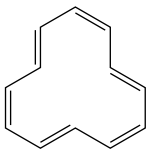
[8]annulene
nonaromatic
distorted

4 × 2 (anti)



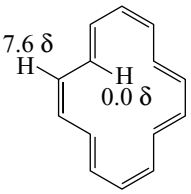
[10]annulene (*ZEZZE)*
3 isomers - all non-aromatic (non planar)

2 × 4 + 2



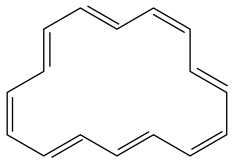
[12]annulene
non-aromatic
(non-planar)

4 × 3 (anti)



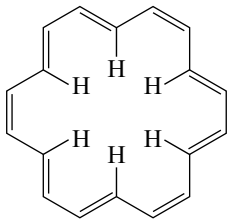
[14]annulene
aromatic (NMR)

3 × 4 + 2



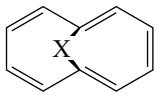
[16]annulene
nonaromatic
(non-planar)

4 × 4 (anti)



[18]annulene
aromatic (NMR)

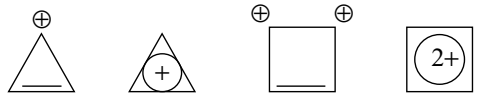
4 × 4 + 2



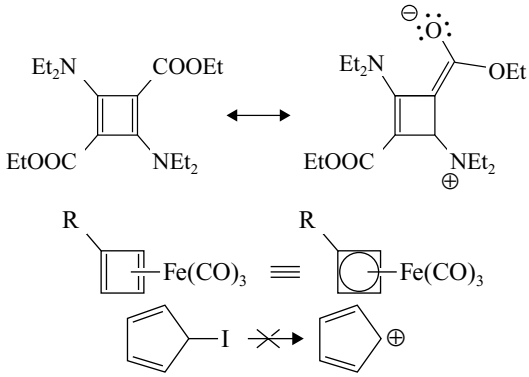
X=CH_2, O, NH are planarized and are aromatic

Aromaticity in charged rings

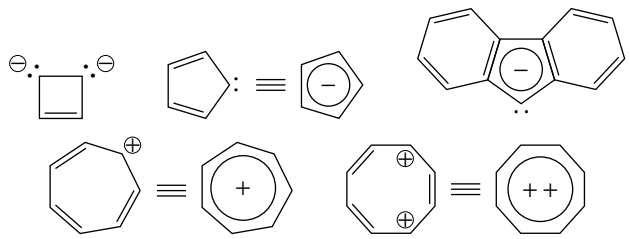
Aromatic systems with two ϖ-electrons:



Four π-electrons are generally unstable (anti-aromatic).



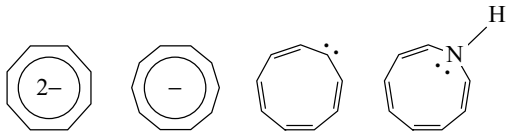
Six π-electron systems; aromatic and stable:



Eight π-electron systems: anti-aromatic and unstable:

Ten π-electron systems: may be aromatic

[10]annulene –non-aromatic due to its deviation from planarity (NMR:all hydrogens are of the alkene type). Two isomers (ZZZZZ, ZEZZE) were prepared. Recent calculations suggest that the last one, EZZZZ may be aromatic.



Examples of other aromatic systems:

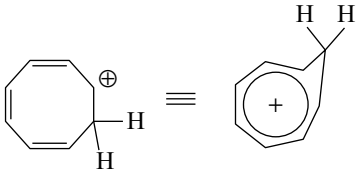
Super large systems:

"Normal" annulenes are aromatic according to the Huckel's rule (4n+2). The presence of the Mobius twist and resulting phase discontinuity of the atomic orbitals would cause the reversal of the aromaticity/antiaromaticity rules.

Huckel orbital array	Mobius orbital array
Aromatic: 4n+2	Aromatic: 4n
Antiaromatic: 4n	Antiaromatic: 4n+2

Homoaromaticity:

Homoaromatic systems are that contain conjugated delocalized systems that bypass one of the atoms (saturated), or alternatively, that have a saturated atom (usually carbon) interrupting the π-system.



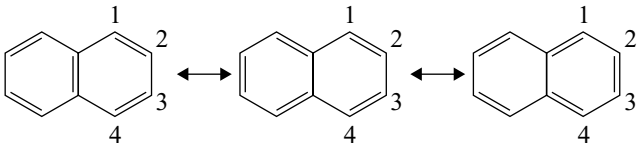
Fused ring systems:

Numerous completely conjugated hydrocarbons can be derived from annulenes. These fused annulenes may be represented by several resonance structures.

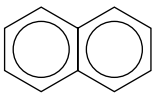
For example

Naphthalene: 3 resonance structures may be drawn (without considering Dewar forms).

The 1,2 bond has more of C=C character than 2,3 C/C bond.



Bond order (length) 1.724 (1.36 Å)



1.603 (1.415 Å)

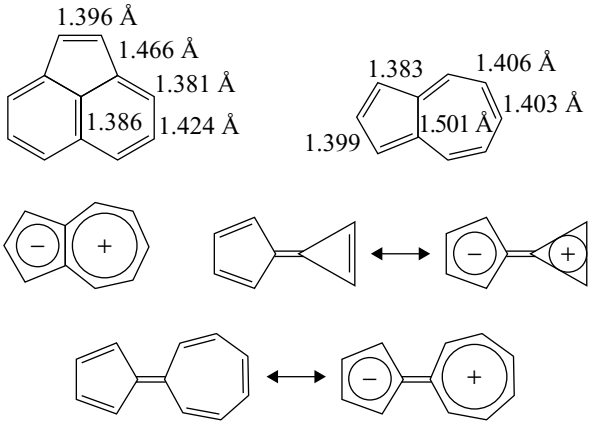
We observe so called "partial bond fixation", which is typical for the reactivity of fused annulenes. In the case of naphthalene, we observe that 1,2-bond reacts more like a double bond: epoxidation, ozonolysis, etc. Note also that the major resonance contributor is the structure with a double bond at the ring fusion, the first structure.

Several interesting cases:

Acenaphthylene: the additional C=C has very much character of the regular C=C (does not contribute significantly to the delocalization energy).

Azulene: the bond between two cycles has enhanced C-C

character. Aromaticity is believed to be caused by the dipolar structure (+ –) composed of the cyclopentadiene anion and the cycloheptatriene cation (both aromatic). In agreement is the large dipole moment of azulene (0.8D).

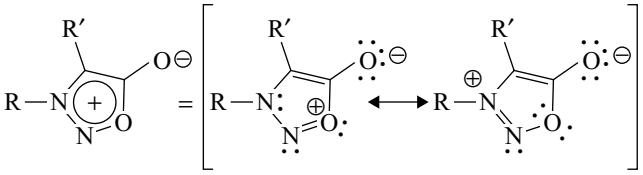


Similarly to azulene, there are bicyclic aromates, that may be stabilized by their dipolar forms. Interestingly, they do not have to be fused. Such compounds too have large dipoles

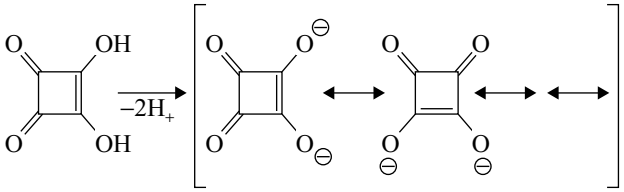
Conjugated heterocyclic compounds are in many cases isoelectric with the aromatic

Other aromatic compounds

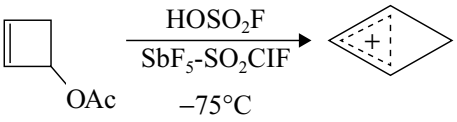
1. Mesoionic compounds: their structure cannot be explained/described by Lewis structures that do not involve a charge separation. Most of them are five-membered heterocycles. Example: sydnones



2. The dianion of squaric acid (squarate) and the corresponding five-membered species.



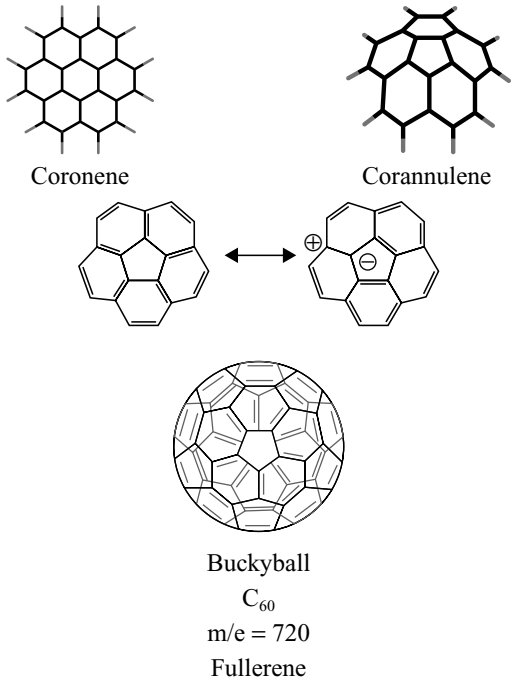
3. Homoaromatic species (vide supra): Another example that is reasonably stabile is the cyclobutenium cation, which is explained by the formation of the homoaromatic acyclopropenium carbocation loop.



2. Fullerenes (Bucky balls and bowels)

Fullerenes are spherical conjugated polyenes that display aromatic properties. These recently discovered forms of carbon are related to bowl-shaped aromatic hydrocarbons whose parent is the bowl-shaped hydrocarbon corannulene. If aromatic systems are constructed of a two-dimensional array of fused six-membered rings, a planar aromatic system results that upon its ultimate extension is called graphite. On the other hand, if the aromatic system is constructed five- and six-membered rings where every fivemembered ring is isolated from other five-membered rings by circles of six-membered rings, then a curved aromatic surface results. Upon ultimate extension, this pattern of construction results in carbon nanotubes and fullerenes.

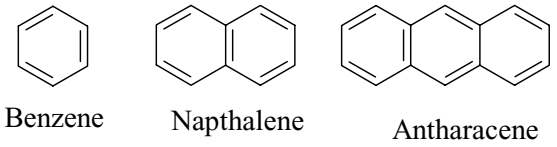
Example: Corannulene compared with coronene.



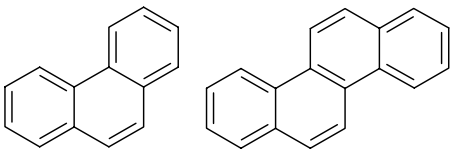
NOTE

- That even though corannulene is not planar, it can be view as being composed of concentric aromatic rings, the inner ring bearing a negative charge and the outer one a positive charge.

Aromatic carbocyclic compounds

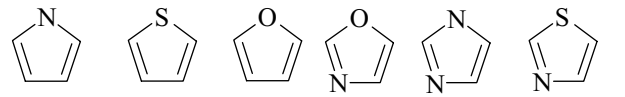


Benzene Napthalene Antharacene

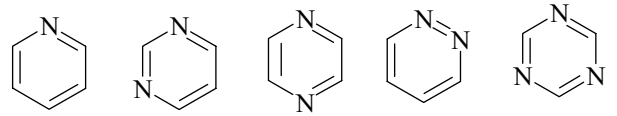


Phenanthrene Chrysene

Aromatic heterocyclic compounds



Pyrrole Thiophene Furan Oxazole Pyrazole Thiazole



Pyridine Pyrimidine Pyrazine Pyridazine Triazine

Anti-aromatic A compound is anti-aromatic if it is a planar, cyclic compound with an uninterrupted ring of ϖ cloud, but it contains even number of pairs of ϖ electrons.

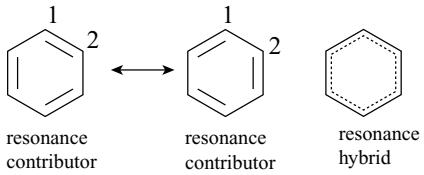
Relative stabilities

Aromatic compound > Cyclic compound with localized electrons >Antiaromatic compound

Increasing Stability

Benzene

- A planar molecule has six identical carbon–carbon bonds.
- Each ϖ electron is shared by all six carbons.
- The ϖ electrons are delocalized.



Resonance contributors are imaginary, but the resonance hybrid is real.

Rules for drawing resonance contributors

- Only electrons move.
- Only p electrons and lone-pair electrons move.
- The total number of electrons in the molecule does not change.
- The numbers of paired and unpaired electrons do not change.

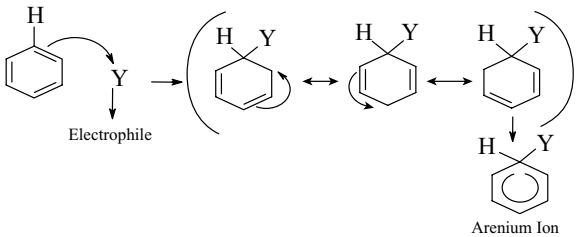
The electrons can be moved in one of the following ways

- Move ϖ electrons toward a positive charge or toward a ϖ bond.
- Move lone-pair electrons toward a ϖ bond.
- Move a single nonbonding electron toward a ϖ bond.

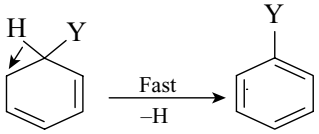
General mechanism for electrophilic aromatic substitution of benzene

EAS mechanism/SE2 mechanism

Step-1 Generation of Arenium ion

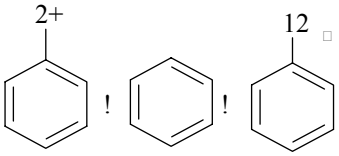


Step-2 Loss of Proton

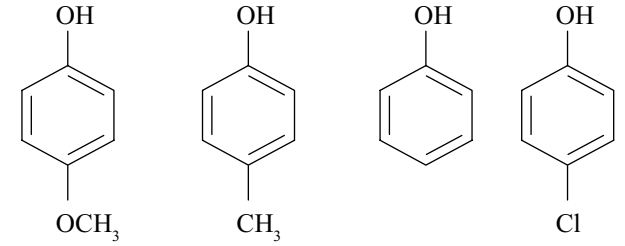


Step 1: It is a slow step and hence a rate determining step

- Intermediate is arenium ion or benzonium ion or whel-and intermediates
- Reactivity of EAS
- EDG on benzene ring increases the reactivity towards electrophillic aromatic substitution.
- EWG on benzene ring decreases the reactivity towards electrophillic aromatic substitution. e.g., of reactivity order



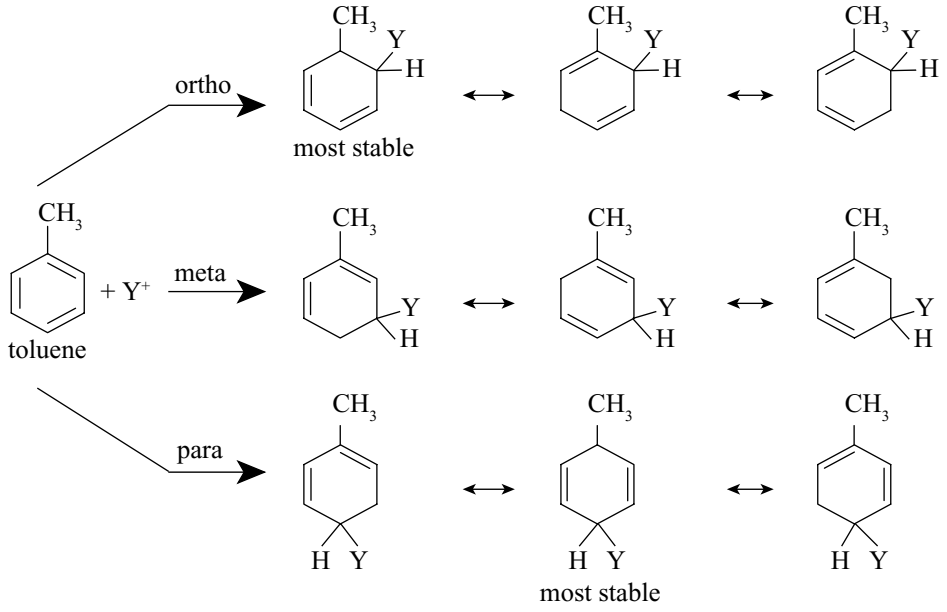
- Electron withdrawal decreases reactivity towards electrophilic substitution and increases acidity
- Electron donation increases reactivity towards electrophilic substitution and decreases acidity.



$pK_a = 10.20$ $pK_a = 10.19$ $pK_a = 9.95$ pK_a

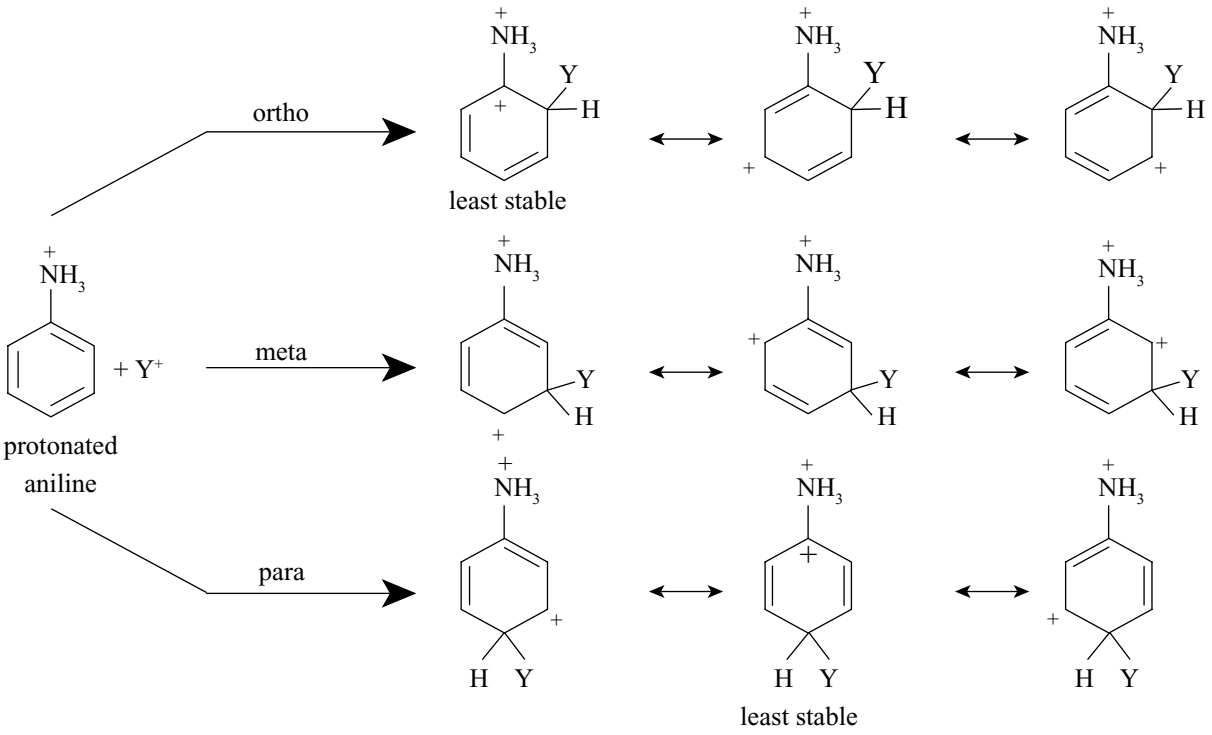
Orientation

Why EDG are o/p directing?



In the above example, methyl group of toluene acts as a partially electron donating group, so in the above example, the positive charge genaration is on carbon where methyl group is attached so it stabilizes the positive charge. This happens with only o/p isomer, it is not seen in m isomer that is why all activating group are o/p directing group.

Why EWG are m-directing?



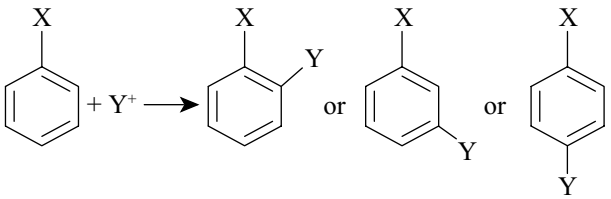
In the above example (4° Ammonium group) on ring acts as an electron withdrawing group, so in the above example, the positive charge genaration is on carbon where 4° Ammonium group is attached, so it destabilizes the positive charge because it wihdraws the electron. This happens with only o/p isomer, it is not seen in m isomer, that is why all deactivating group are m-directing group.

List of electron donating and withdrawing groups

Activating Substituents (EDG) ↓	Most activating		Ortho-Para Directing ⇒
	-NH_2, -NHR, -NR_2, -OH, -OR →	Strongly activating	
	-NHCOR, -OCOR →	Moderately activating	
	-R, Ar, -CH=CH_2 →	Weakly activating	

Standard of comparision Deactivating Substituents (EWG) ↓	-H		
	-F -Cl -Br -I →	Weakly deactivating	Meta Directing
	-CHO -COR -COOR -COOH -COCl →	Moderately deactivating	
	-CN -SO_3H -NO_2 -NR_3^+ →	Strongly deactivating	

The substituent already attached to the benzene ring determines the location of the new substituent.



ortho isomer meta isomer para isomer

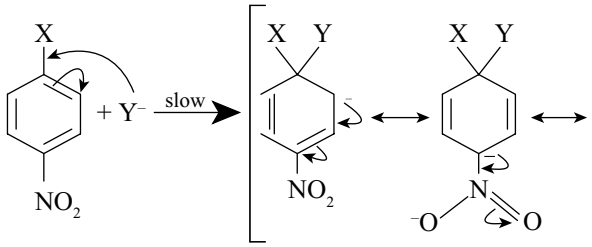
All activating substituents and the weakly deactivating halogens are ortho–para directors.

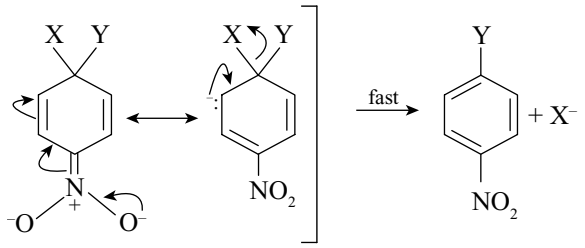
All substituents that are more deactivating than halogens are meta directors.

- Any substituent that donates electrons inductively is an ortho–para directors.
- All substituents that donate electrons by resonance are ortho–para directors.

Nucleophillic Aromatic Substitution Reaction (Bimolecular displacement mechanism or S_N Ar mechanism)

General mechanism for nucleophilic aromatic substitution





Step 1 Intermediate is carbanion generation or meisenheimer complex formation.

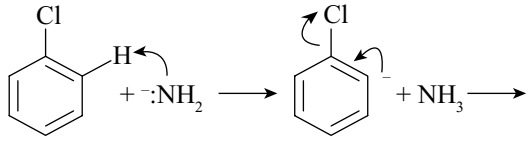
Step 2 is loss of leaving group (X^-) to stabilize carbanion.

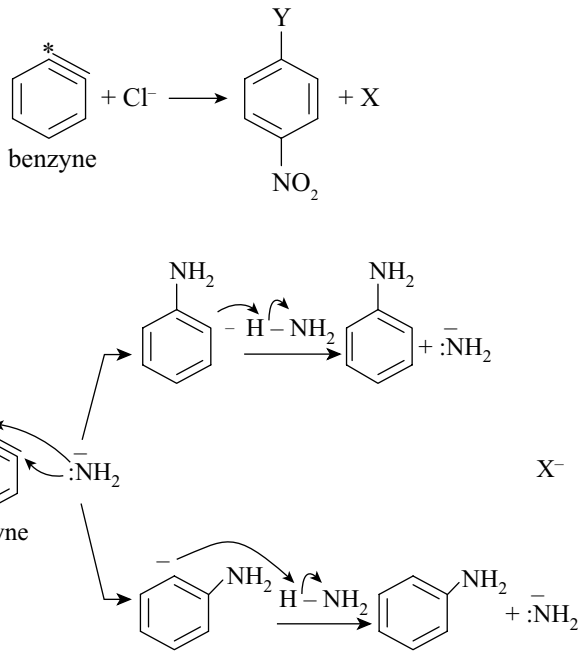
Reactivity

The electron-withdrawing substituents at ortho or para to the site of nucleophile attack increase the S_N Ar reaction, while electron withdrawing substituents decrease the S_N Ar reaction.

Benzyne mechanism or aryne mechanism or benzyne mechanism

It requires strong basic condition.

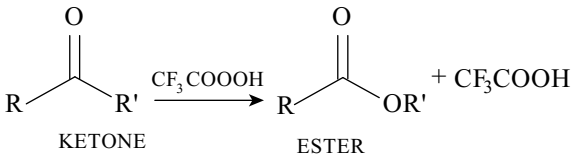




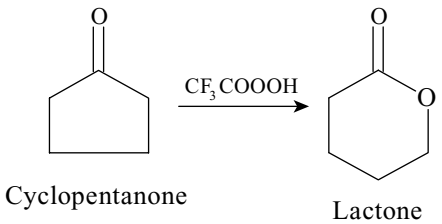
Rearrangements

1. Baeyer-villiger rearrangements

- Baeyer-Villiger rearrangements is an example of the migration of a group from carbon to electron deficient oxygen.
- The reaction involves oxidation of ketones to esters by treatment with paracids such as per benzoic acid, pertrifluoroacetic acid etc.



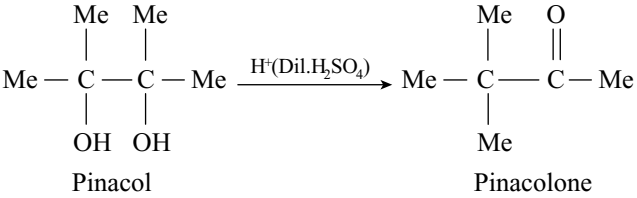
Cyclic ketone is converted into the lactone with ring expansion.



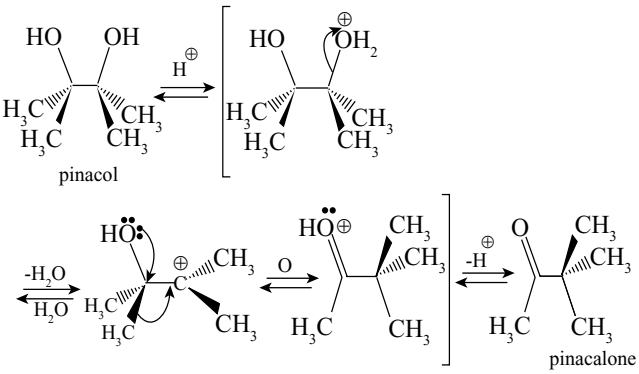
- The overall reaction is an insertion of oxygen atom between carbonyl carbon and the adjacent carbon in ketone.
- Commonly used solvents are glacial acetic acid and chloroform.

2. Pinacole-pinacolone rearrangements

The acid catalysed rearrangements of vic. diols (1, 2-diols) to ketone or aldehyde with elimination of water is known as pinacol-pinacolone rearrangement.



Mechanism of pinacole-pinacolone rearrangements

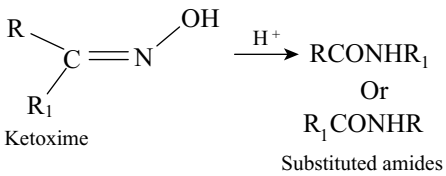


3. Beckmann rearrangement

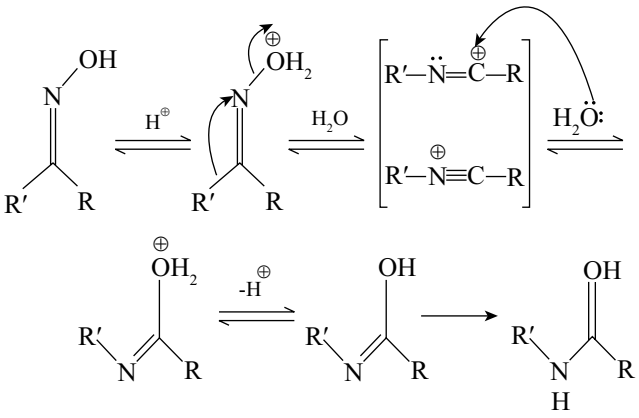
The acid catalysed conversion of ketoxime to N-substituted amides is known as Beckmann rearrangement.

The reaction is catalysed by acidic reagents such as H_2SO_4, $SOCl_2$, P_2O_5, PCl_5, C_6H_5, SO_2Cl.

The reaction involves migration of group from carbon to nitrogen.



Mechanism of beckmann rearrangement



The migration of group depends not on migration aptitude but upon the orientation of the group in relation to –OH group. It is found that the migration group is always anti to –OH group. Thus the reaction is stereospecific.

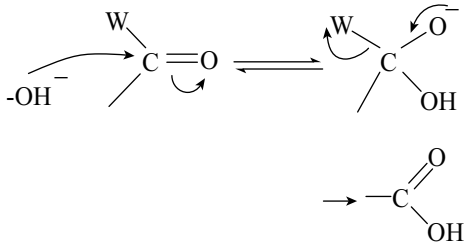
Application

Synthesis of isoquinoline and lactams.

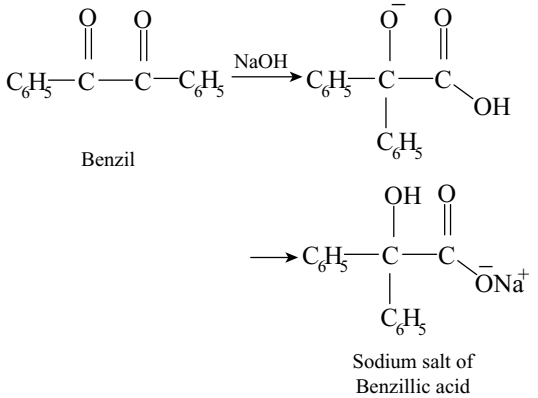
4. Benzillic acid rearrangement

The addition of a strong base to a carbonyl group results in the formation of an anion. The reversal of the anionic charge may cause removing of attached group W.

e.g.,



In 1, 2-diketone the group W may migrate to the adjacent electron-deficient carbonyl carbon, forming βhydroxy acid.



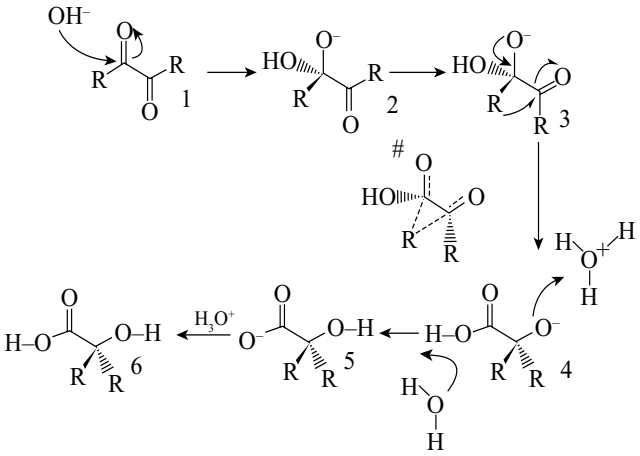
Benzil

Sodium salt of Benzillic acid

Application

Synthesis of citric acid, furillic acid.

Mechanism of benzillic acid rearrangement



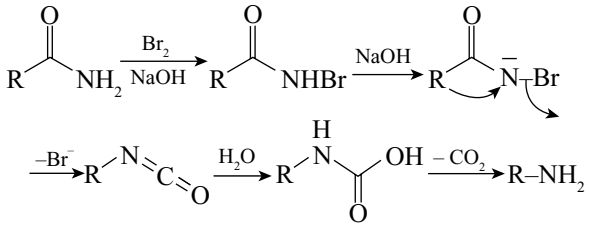
5. Hofmann rearrangement or Hofmann bromamide reaction

The reaction involves the conversion of an ***amide to a primary amine (1°)*** with one carbon less, by the action of alkaline hypohalite (NaOH solution + Br_2 or Cl_2).

$$RCONH_2 + Br_2 + {}_4NaOH \rightarrow RNH_2 + {}_2NaBr + Na_2CO + {}_2H_2O$$

Bromine is mostly used in this reaction and the intermediate is ***N-bromamide***.

Mechanism of Hofmann rearrangement



Application

Synthesis of amino acid, β-amino pyridine from nicotinamide, urea to hydrazine

Some important terminology

(a) Cheletropic reaction A retrocycloaddition in which a small molecule such as CO or SO_2 is lost.

(b) Concerted reaction Any reaction in which all bond breaking and bond making occurs in a single step.

(c) Cycloaddition reaction Any addition reaction that results in the formation of a new ring.

(d) Electrocyclic reaction An intramolecular reaction of a single conjugated pi electron system in which a ring is formed or broken.

(e) HOMO **H**ighest **O**ccupied **M**olecular **O**rbital. The highest energy molecular orbital that bears an electron pair.

(f) LUMO **L**owest (energy) **U**noccupied **M**olecular **O**rbital.

(g) Pericyclic reaction Any reaction that occurs by a concerted shift of electrons in a cyclic transition state.

(h) Sigmatropic reaction Any pericyclic reaction in which the σ bond at one end of the molecule is broken while a new σ bond is formed at the other end.

(i) Woodward-Hoffmann rules Orbital combination rules that define the number of atoms and orbitals involved in pericyclic reactions.

Pericyclic reaction Any reaction that occurs by a concerted shift of electrons in a cyclic transition state.

Types of pericyclic reactions:

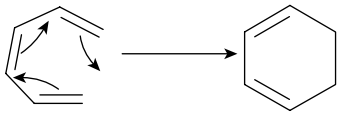
- **Electrocyclic reaction**
- **Cycloaddtion reaction**
- **Sigmatropic reaction**

Electrocyclic reaction Under the influence of light/heat, a conjugated polyene can undergo isomerization to form a cyclic compound with a single bond between the terminal carbon of the original conjugated system.

Or

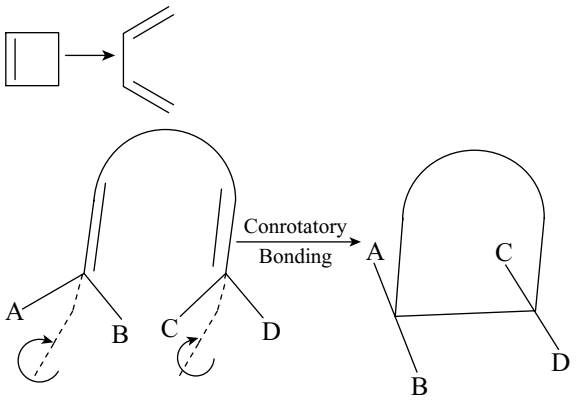
An intramolecular reaction of a single conjugated electron system in which a ring is formed or broken.

E.g., 1, 3, 5 hexatriene to 1, 3 cyclohexadiene



The reverse process can also take place.

Cyclobutane to 1, 3 cyclobutadiene



Conrotatory means rotate the bond in same direction.

Disrotatory means rotate the bond in opposite direction.

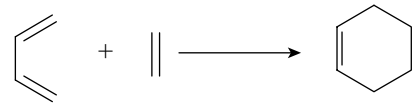
The electrocyclic reaction is completely stereospecific and stereo selective.

Woodword–Hoffmann Rules for Electrocyclic Reaction

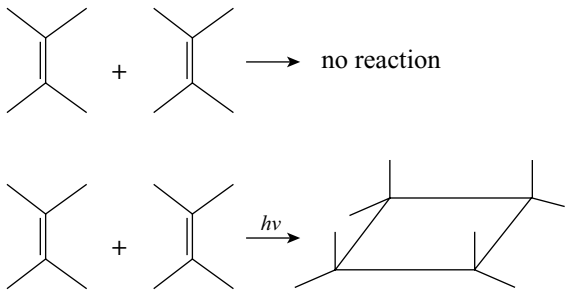
No of pi electron	Types of cleavage	Motion
4n+2	Thermal	Disrotatory
4n+2	Photochemical	Conrotatory
4n	Thermal	Conrotatory
4n	Photochemical	Disrotatory

Cycloaddition Reaction Any addition reaction that results in the formation of a new ring. Or two unsaturated compounds combine to form a cyclic compound.

(4+2) Cycloaddition reaction:



A[2 +2] Cycloaddition Reaction



Woodword–Hoffmann Rules for Cycloaddition Reaction

I + j	Thermal Cleavage	Photochemical cleavage
4n	Supra, Antra Antra, Supra	Supara, Supara Antara, antara
4n + 2	Supra, Supra Antara, Antara	Supra, Antra Antra, Supra

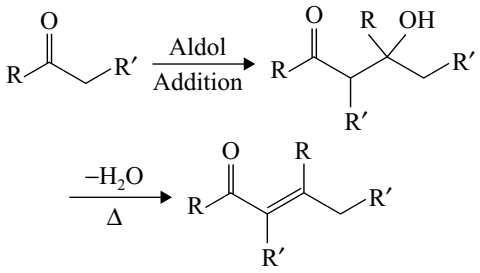
Name Reaction

1. Aldol Condensation

The two mole aldehyde/ketone with α-hydrogen undergoes self condensation on heating with dilute base to give β-hydroxy aldehydes/ketone is called aldol (aldehyde and alcohol).This reaction is known as aldol condensation reaction, which later on dehydration to give α, β unsaturated carbonyl compound.

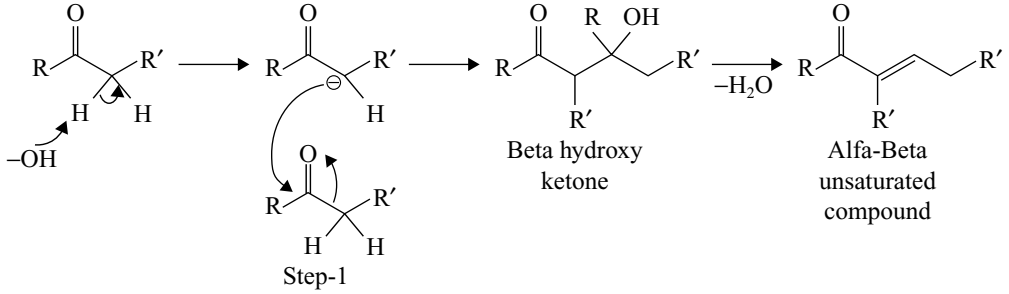
Various basic reagents like ***dilute sodium hydroxide, aqueous alkali carbonate and alkali metal alkoxide*** can be used.

The aldol condensation can be applicable on two identical/different aldehyde or ketone or an aldehyde and ketone.



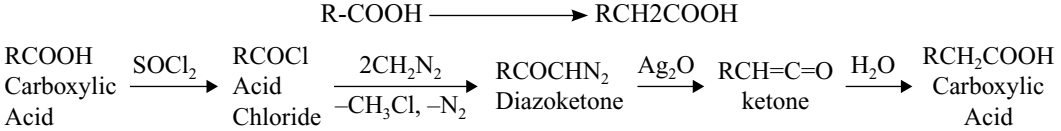
Reaction Mechanism

The base abstract the acidic proton (α-H) to generate resonance stabilized carbanion intermediate and generated carbanion attack on carbonyl carbon of another mole of aldehyde/ketone which leads to form alkoxide anion. The latter then takes up a proton to form β-hydroxy aldehydes/ketone, which later on dehydration to give α, β unsaturated carbonyl compound.



2. Arndt Eistert Reaction

The reaction involves the increase the length of carbon chain by one methylene group in carboxylic acid is known as Arndt Eistert Reaction.

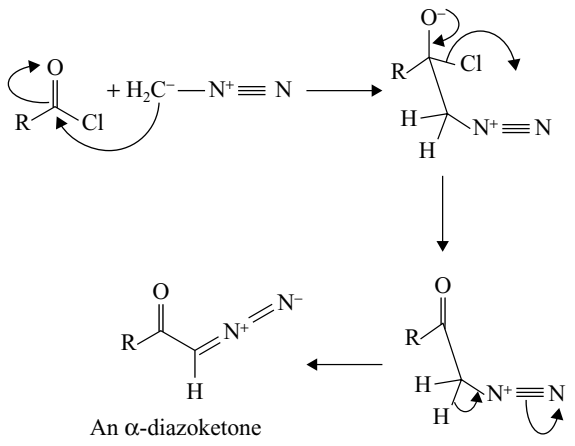


Steps of Reaction

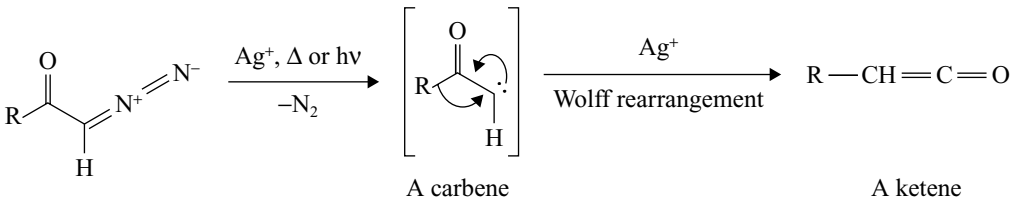
- Carboxylic acid converts into the acid chloride by thionyl chloride.
- The acid chloride reacts with diazomethane to give diazoketone.
- The diazoketone catalysed by Ag2O in presence of water split off nitrogen and rearrange to give ketene intermediate.(Other than Ag2O, reacto
- The ketene then reacts with water, alcohol and amine to form a higher homologue of carboxylic acid, ester and amide.

Reaction Mechanism

The diazomethane is acylated by the acid chloride to give a diazoketone.

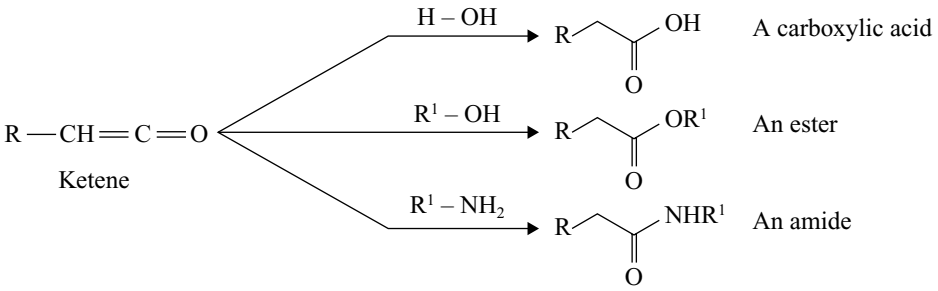


The generated diazoketone is rearranged to a ketene. This is called **Wolff-rearrangement.**



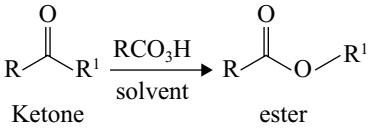
Silver salts like $PhCO_2Ag$, Ag_2O along with heat or light catalyze the Wolff rearrangement. Where the configuration of 'R' group during Wolff rearrangement is retained.

The ketene is immediately attacked by an appropriate nucleophile in the solution.



3. Baeyer–Villiger Rearrangement

It is an organic reaction in which a ketone is oxidized to an ester by treatment with peroxy acids or hydrogen peroxide. It is an example of reaction in which migration of alkyl group from carbon to electron deficient oxygen.

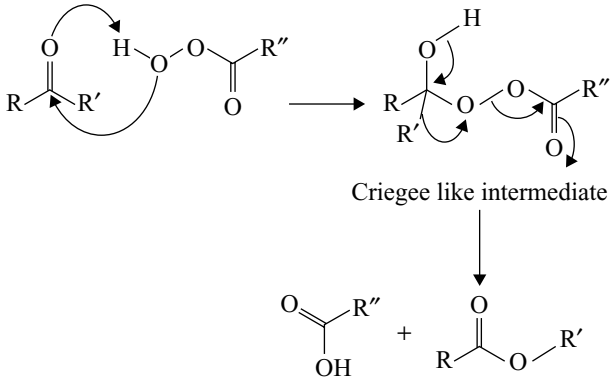


The reagents can be used in Baeyer villiger oxidation include:

- Metachloroperbenzoic acid (MCPBA),
- Peroxyacetic acid (PAA),
- Peroxytrifluoroacetic acid (TFPAA)
- Hydrogen peroxide/BF_3,
- Caro's acid buffered with disodium hydrogen phosphate
- Sodium percarbonate ($Na_2CO_3.1.5H_2O_2$),
- Magnesium salt of monoperoxyphthalic acid (MMPP),
- Potassium peroxomonosulphate (potassium caroate) supported on hydrated silica also known as "reincarnated caro's acid".
- Baeyer villager monooxygenase (an enzyme abbreviated as BVMO).

Reaction Mechanism

Initially the peroxy group is added to the carbonyl carbon to give a **Criegee** like intermediate. Then one of the group attached to carbonyl carbon is migrated on to the electron deficient oxygen atom in a **concerted step**, which is the rate determining step.



The substituents which can stabilize the positive charge can migrate readily. The migratory aptitude of various substituents is approximately:

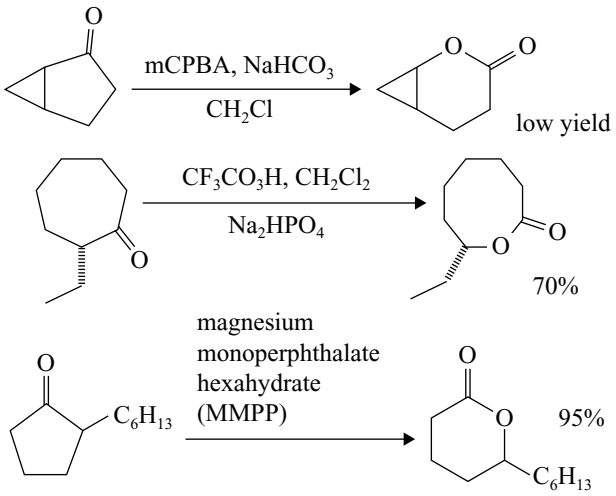
3°-alkyl > cyclohexyl > 2°- alkyl > benzyl > aryl > 1° - alkyl > methyl

The electron withdrawing groups (-I groups) on peroxy acids enhance the rate of the reaction.

As the rearrangement is a concerted process, the con-

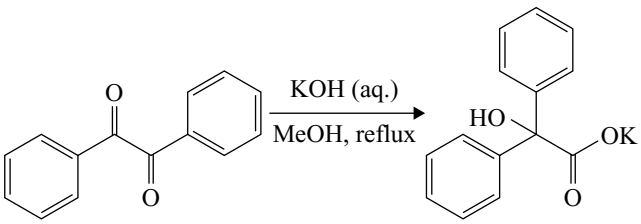
figuration of the migrating chiral substituent is retained.

Reactive or strained ketones react with peroxy benzoic acid to form lactones.

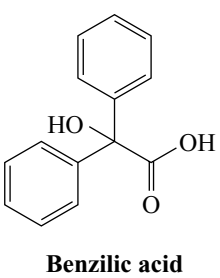


4. Benzilic Acid Rearrangement

The **benzilic acid rearrangement** is the rearrangement reaction of benzil with potassium hydroxide to benzilic acid. The addition of strong base to carbonyl carbon (–C=O) of di ketone results in formation of an anion and react with acid it will convert to carboxylic acid.



Benzil **Potassium salt of benzilic acid**

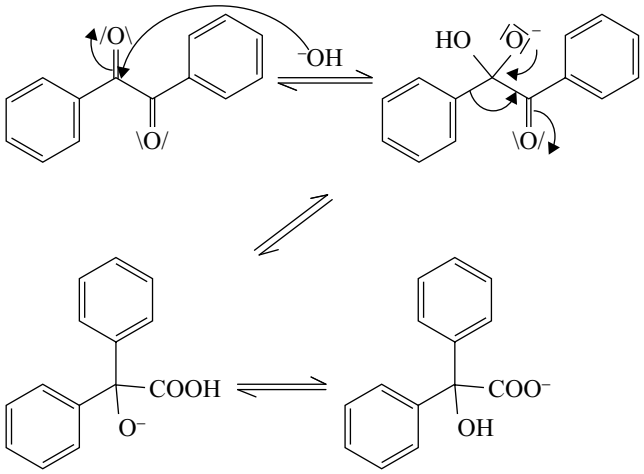


Benzilic acid

Reaction Mechanism

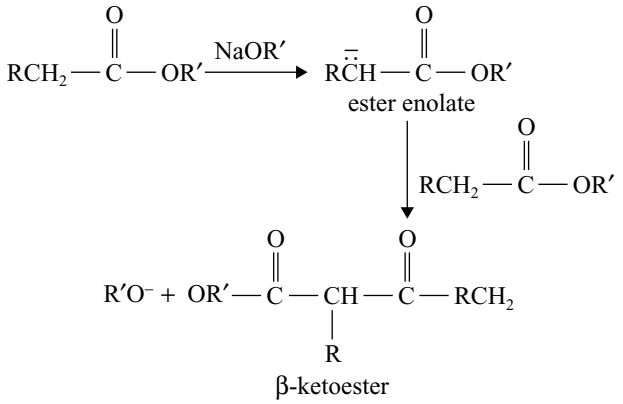
Ist Step: Reversible nucleophillic attack occurs at carbonyl carbon (–C=O).

IInd Step: It is a rate determining step in which migration of phenyl ring to carbonyl carbon occurs. (Migration of Ar to Carbonyl carbon).



5. The Claisen Condensation

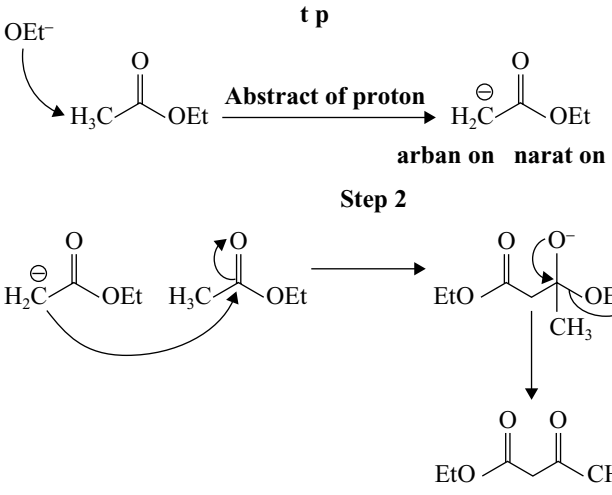
The Claisen condensation is a carbon–carbon bond forming reaction that occurs between two esters or one ester and another carbonyl compound in the presence of a strong base, (C_2H_5ONa-Sodium ethoxide) resulting in a β-keto ester or a β-diketone. This reaction is totally differ to Claisen rearrangement.



Reaction Mechanism (Nucleophilic Acyl Substitution)

Step-1: In reaction mechanism the ethoxide act as a nucleophiles and abstract the acidic proton on methyl group of ester and generate a carbanion.

Step-2: Generated carbanion attack on carbonyl carbon of another molecule of ester to generate anion and finally removal of ethoxy to form a β-keto ester and ethanol.

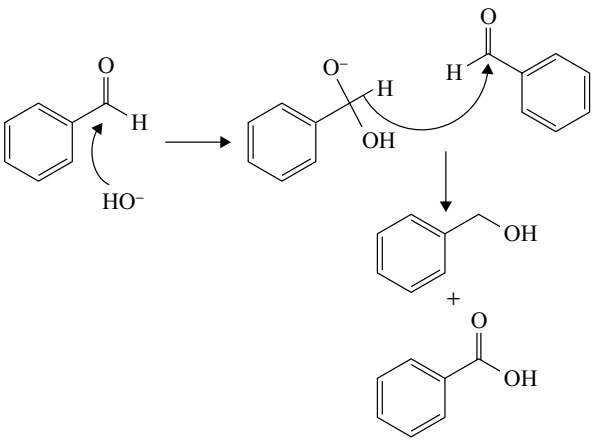


The Claisen condensation is the ester analogue of the condensation. The most commonly the base would be the alkoxide, **R'O**- The reaction involves an ester enolate reacting with another molecule of the ester. In this reaction enolates are act as a good nucleophiles and the ester carbonyl **C** are act as a electrophilic. The products of these reactions are β-ketoesters which are important, useful synthetic intermediates.

6. The Cannizzaro Reaction

The base-induced disproportionation reaction of aldehydes without α-hydrogens in presence to furnish an alcohol and a carboxylic acid is called Cannizzaro reaction. One molecule of aldehyde is reduced to the corresponding alcohol, while a second one is oxidized to the carboxylic acid. The oxidation product is a salt of a carboxylic acid and the reduction product is an alcohol.

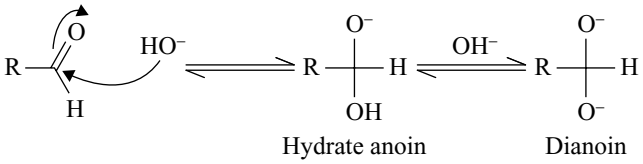
$$2\ C_6H_5CHO + KOH \rightarrow C_6H_5CH_2OH + C_6H_5CO_2K$$



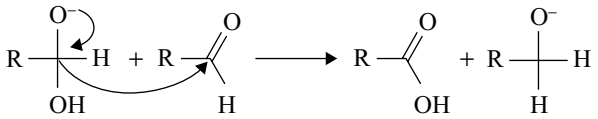
For aldehydes with a hydrogen atom alpha to the carbonyl, i.e. R_2CHCHO, the preferred reaction is an aldol condensation, originating from deprotonation of this hydrogen. This reaction restricts the scope of the Cannizzaro reaction.

Reaction Mechanism

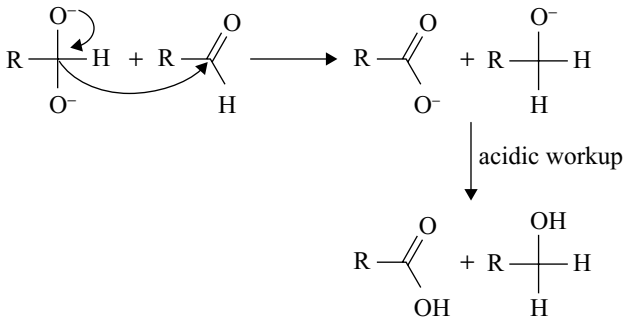
The cannizzaro reaction is initiated by the nucleophilic attack of a hydroxide ion to the carbonyl carbon of an aldehyde molecule by giving a hydrate anion. This hydrate anion can be de-protonated to give dianion in a strongly alkaline medium.



Hydride (H^-) is transferred either from the mono anionic species or dianionic species onto the carbonyl carbon of another aldehyde molecule. The strong electron donating effect of O^- groups facilitates the hydride transfer and drives the reaction further. This is the rate determining step of the reaction.



Under acidic workup it is converted into carboxylic acid and alcohol.

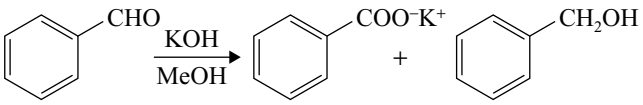


Some examples of cannizaro reaction:

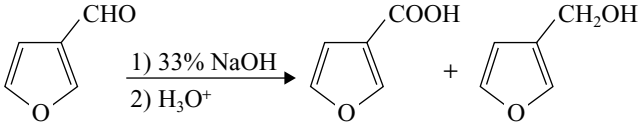
Formaldehyde is disproportionated to formic acid and methyl alcohol in strong alkali.

$$2\ HCHO \xrightarrow{NaOH} HCOO^-Na^+ + CH_3OH$$

Benzaldehyde can be converted to benzoic acid and benzyl alcohol.



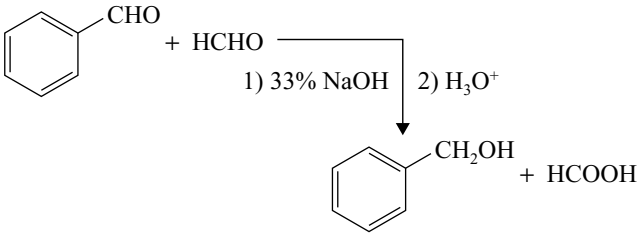
Furfural gives furoic acid and furfuryl alcohol in presence of strong alkali.



7. Crossed Cannizzaro Reaction

When a mixture of formaldehyde and a non enolizable aldehyde is treated with a strong base, the later is preferentially reduced to alcohol while formaldehyde is oxidized to formic acid. This variant is known as crossed cannizzaro reaction.

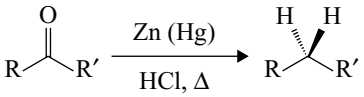
E.g. Benzyl alcohol and formic acid are obtained when a mixture of benzaldehyde and formaldehyde is treated with alkali.



The reason may be: the initial nucleophilic addition of hydroxide anion is faster on formaldehyde as there are no electron donating groups on it. The preferential oxidation of formaldehyde in crossed Cannizzaro reactions may be utilized in the quantitative reduction of some aldehydes.

8. Clemmensen Reduction

The carbonyl groups of aldehydes and ketone (mainly) undergo reduction to methylene groups with amalgamated zinc and concentrated HCl acid is known as **Clemmensen reduction.** The Clemmensen Reduction allows the deoxygenation of aldehydes or ketones, to produce the corresponding hydrocarbon.

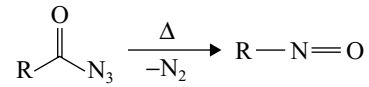


Reaction Mechanism

The reduction takes place at the surface of the zinc catalyst. In this reaction, alcohols are not postulated as intermediates, because subjection of the corresponding alcohols to these same reaction conditions does not lead to alkanes. In the mechanism two time carbanions are generated and accept the proton and converted into alkane.

9. Curtius Rearrangement

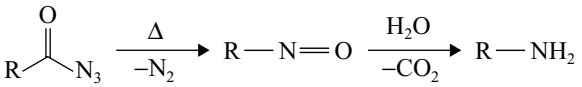
The Curtius Rearrangement involves decomposition of acid azides (R-CON_3) to isocyanates (R-N=C=O) and nitrogen (N_2) in inert solvents like benzene and chloroform is known as the Curtius rearrangement.



Acid Azides Isocynate

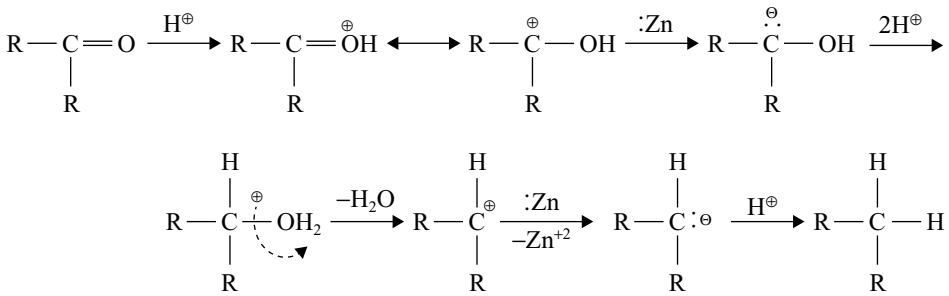
The reaction is a preparative method for isocyanates, ureas, amides, and amines.

The reaction including subsequent reaction with water which leads to amines - is named the Curtius Reaction. This reaction is similar to the Schmidt Reaction with acids, differing in that the acyl azide in the present case is prepared from the acyl halide and an azide salt.

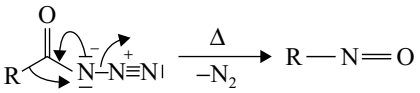


Mechanism of the Curtius Rearrangement

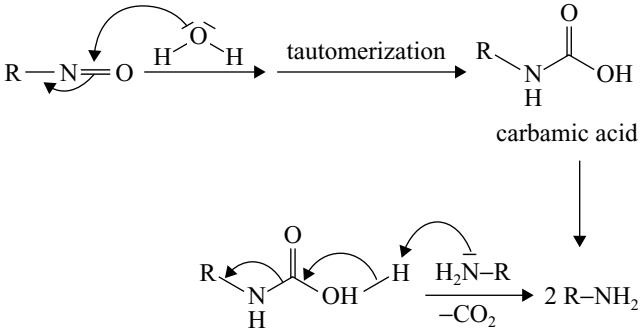
Preparation of azides: Acid azides are commonly prepared by treating hydrazides in cold, aqueous solution with nitrous acid.

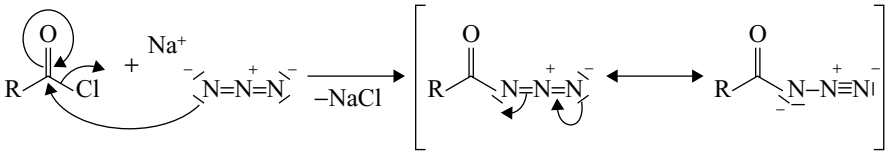


Decomposition to Isocynate and Nitrogen

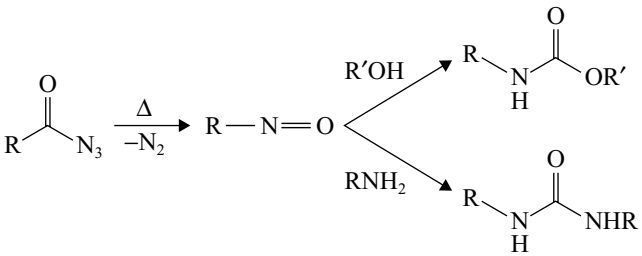


Reaction with water to isocynate intermediate generate the unstable carbamic acid derivative which will undergo spontaneous decarboxylation to amine derivative:



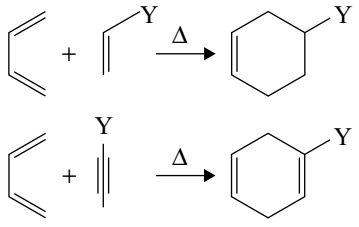


From Isocyanates intermediate we can synthesize various amine as well as alkyl substituted urea derivative.



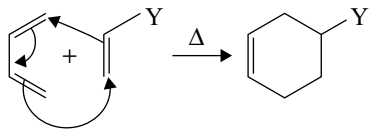
10. Diels-Alder Reaction

It is a type of cyclo addition reaction in which 1,4-addition of an alkene to conjugated diene to form an adduct of six membered ring. The double/triple bond containing group is known as dienophile. So it is a reaction between diene and dienophile to get adduct (product). The reaction initiated thermally or by lewis acid catalyst with or without the use of solvents.



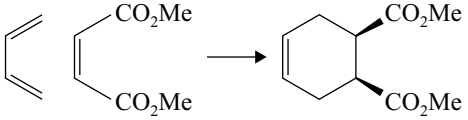
The [4+2]-cycloaddition of a conjugated diene and a dienophile (an alkene or alkyne), an electrocyclic reaction that involves the 4 ϖ-electrons of the diene and 2 ϖ-electrons of the dienophile. The driving force of the reaction is the formation of new σ-bonds, which are energetically more stable than the ϖ-bonds.

Mechanism of the Diels-Alder Reaction

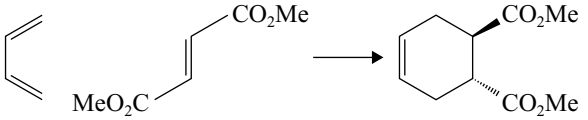


Stereoselectivity

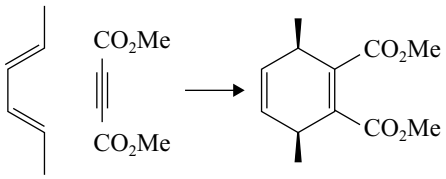
- The Diels-Alder reaction is stereospecific with respect to both the diene and the dienophile.
- Addition is syn on both components (bonds form from same species at the same time)
- This is illustrated by the examples below:
- a *cis*-dienophile gives *cis*-substituents in the product



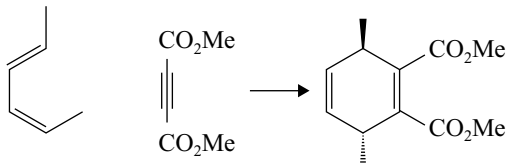
- a *trans*-dienophile gives *trans*-substituents in the product.



- If the diene substituents have the same stereochemistry (here they are both E), then both end up on the same face of the product

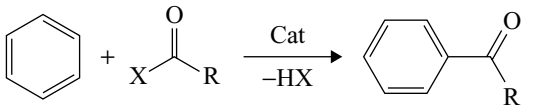


- If the diene substituents have opposite stereochemistry (here one is E and one Z), then they end up on opposite faces of the product



11. Friedel-Crafts Acylation

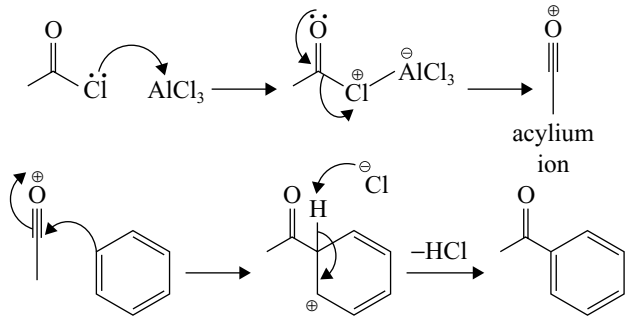
Friedel–Crafts acylation involves the acylation of an aromatic ring with an Acyl chloride halide using a strong Lewis acid catalyst ($AlCl_3$). This electrophilic aromatic substitution allows the synthesis of monoacylated products from the reaction between arenes and acyl chlorides or anhydrides.



X = Cl or RCOO

Reaction Mechanism

Step-1: Formation of electrophile (Acylium Ion)
Step-2: Electrophilic Aromatic substitution reaction-In which benzene ring's pi electron act as a neucleophile and attack on acylium ion (electrophile).



Summary of Limitations of Friedel-Crafts Acylations:

- Acylation can only be used to give ketones. This is because HCOCl decomposes to CO and HCl under the reaction conditions.
- Deactivated benzenes are not reactive to Friedel-Crafts conditions, the benzene needs to be as or more reactive than a mono-halobenzene
- The Lewis acid catalyst $AlCl_3$ often complexes to aryl amines making them very unreactive.
- Amines and alcohols can give competing N or O acylations rather than the require ring acylation

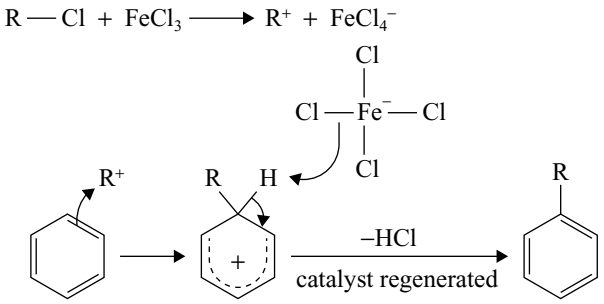
12. Friedel–Crafts Alkylation

The reaction involves the alkylation of an aromatic ring with an alkyl halide using a strong Lewis acid catalyst. With anhydrous ferric chloride as a catalyst, the alkyl group attaches at the former site of the chloride ion.

Reaction Mechanism

Step-1: Formation of carbocation by the reaction between Alkyl halide and $FeCl_3$.

Srep-2: Electrophilic aromatic substitution reaction takes place.



Limitations of Friedel-Crafts Alkylation

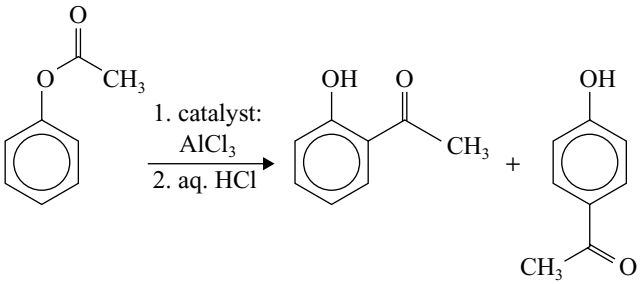
Carbocation Rearrangement: Only certain alkyl benzenes can be made due to the tendency of cations to rearrange.

Compound Limitations: Friedel-Crafts fails when used with compounds such as nitrobenzene and other strong deactivating systems.

Polyalkylation: Products of Friedel-Crafts are even more reactive than starting material. Alkyl groups produced in Friedel-Crafts Alkylation are electron-donating substituents meaning that the products are more susceptible to electrophilic attack than what we began with.

13. Fries Rearrangement

The reaction of an aryl ester with a Lewis acid catalyst followed by an aqueous acid to give phenols is known as Fries rearrangement.



Reaction Mechanism

The reaction is catalyzed by Brønsted or Lewis acids such as HF, $AlCl_3$, BF_3, $TiCl_4$ or $SnCl_4$. The acids are used in

excess of the stoichiometric amount, especially the Lewis acids, since they form complexes with both the starting materials and products

The complex can dissociate to form an **acylium ion**. Depending on the solvent, an ion pair can form, and the ionic species can react with each other within the solvent cage. However, reaction with a more distant molecule is also possible: After hydrolysis, the product is liberated.

The reaction is *ortho*,*para*-selective so that, for example, the site of acylation can be regulated by the choice of temperature. Only sterically unhindered arenes are suitable substrates, since substituents will interfere with this reaction.

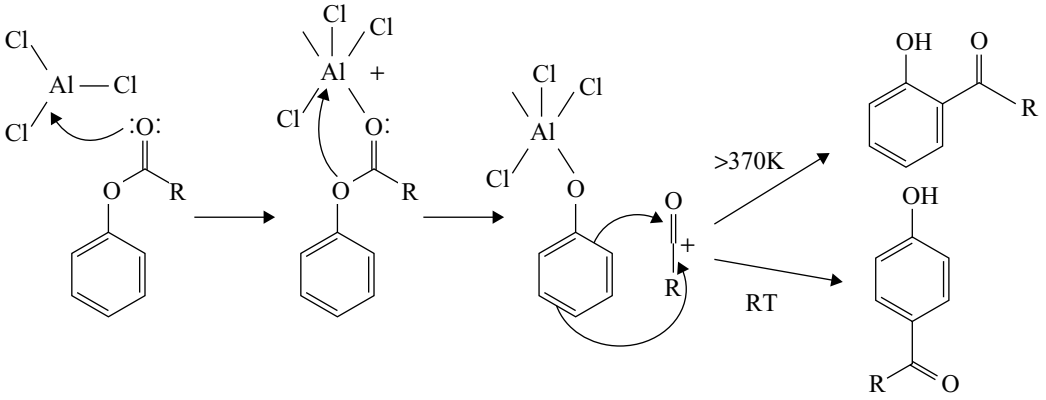
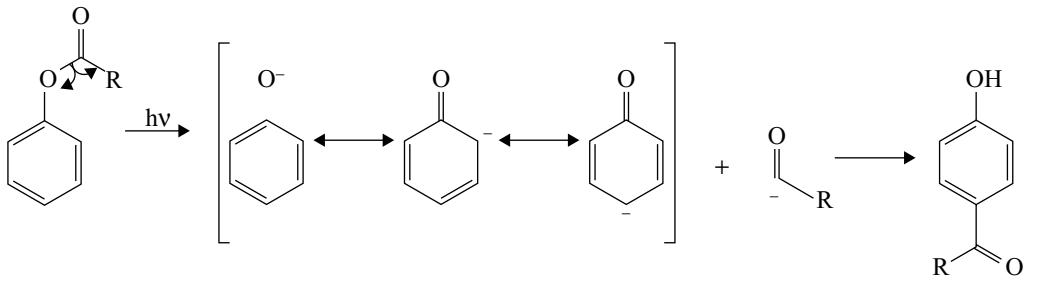


Photo-Fries Rearrangement

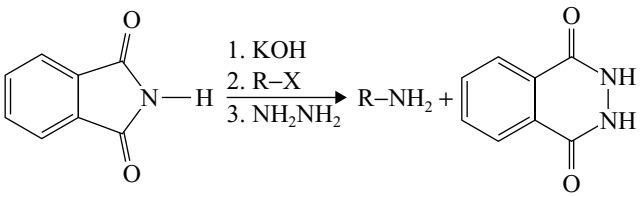
Photo-Fries rearrangement exists that involves free radical reaction mechanism. This reaction is also pos-sible with deactivating substituents on the aromatic group.

Because the yields are low this procedure is not used in commercial production.



14. Gabriel Synthesis

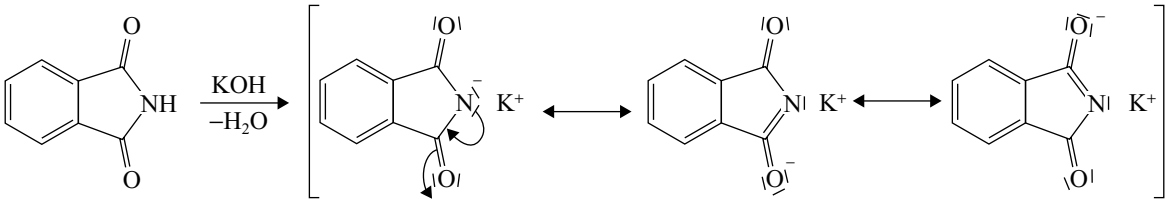
The Gabriel synthesis is named for the German chemist Siegmund Gabriel. Traditionally, it is a chemical reaction that convert primary alkyl halides into primary amines using potassium phthalimide The Gabriel reaction has since been generalized to include the alkylation of sulfonamides and imides, followed by deprotection to obtain amines. The utility of the method is based on the fact that the alkylation of ammonia is an unselective and inefficient route to amines in the laboratory The conjugate base of ammonia, sodium amide ($NaNH_2$), is more basic than it is nucleophilic



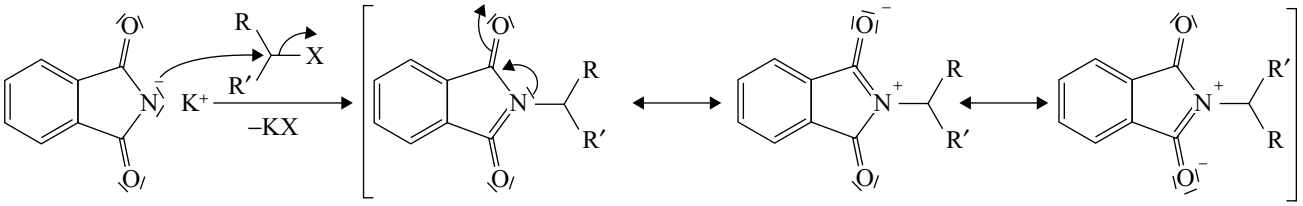
Pthalimide

Reaction Mechanism

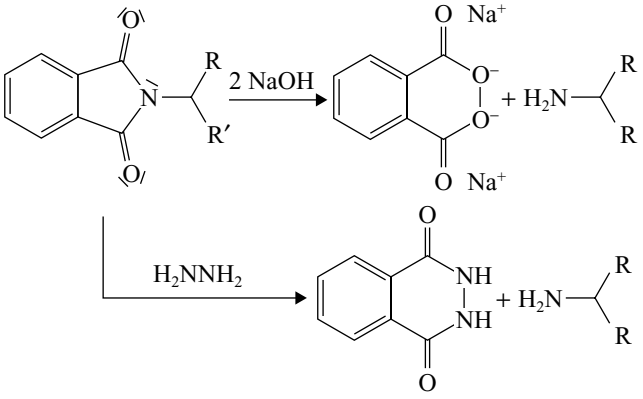
Step-1: Reaction between Pthalimide and Potassium Hydroxide removes the N-H proton giving an imide ion, a good nucleophile to get potassium phthalimide



Step-2: Attack of imide ion to alkyl halide (Nucleophilic substitution by the imide ion on the alkyl halide generates an intermediate, N-alkyl phthalimide)

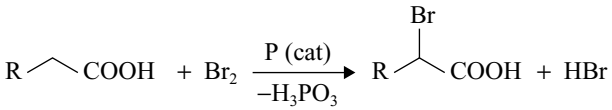


Step-3: Clavage by base and hydrazine(Hydrolysis or hydrazinolysis liberates a primary alkyl amine)



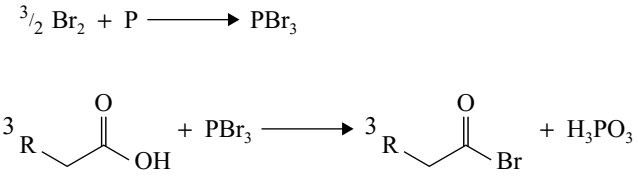
15. Hell-Volhard-Zelinsky Reaction

Treatment with bromine and a catalytic amount of phosphorus leads to the selective α-bromination of carboxylic acids.

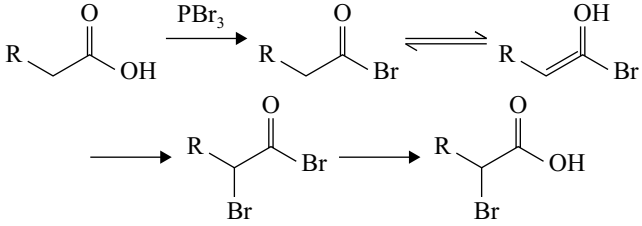


Reaction Mechanism

Phosphorus reacts with bromine to give phosphorus tribromide, and in the first step this converts the carboxylic acid into an acyl bromide.

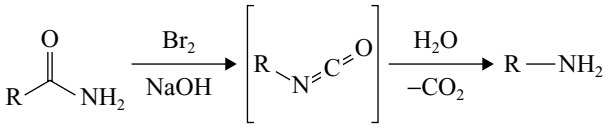


An acyl bromide can readily exist in the enol form, and this tautomer is rapidly brominated at the α-carbon. The monobrominated compound is much less nucleophilic, so the reaction stops at this stage. This acyl intermediate compound can undergo bromide exchange with unreacted carboxylic acid via the anhydride, which allows the catalytic cycle to continue until the conversion is complete.



16. Hofmann Rearrangement

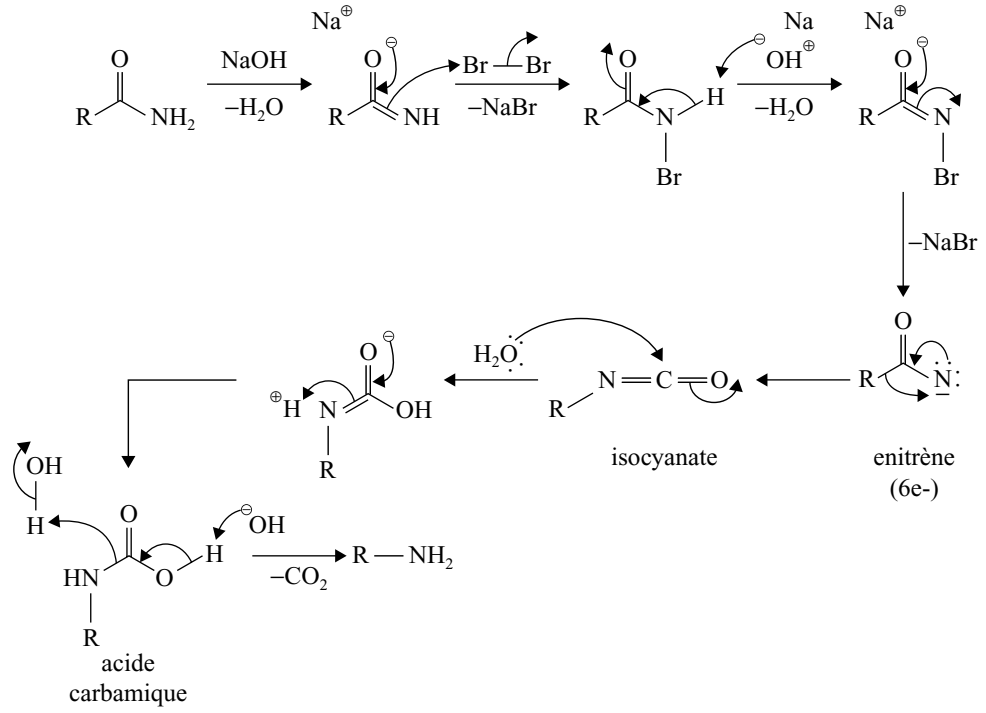
It is organic reaction which convert of a primary amide to a primary amine with one carbon atom loss by using of sodium bromamide (NaOBr) prepared by NaOH and Br_2.



The reaction is named after its discoverer: August Wilhelm von Hofmann. This reaction is also sometimes called the **Hofmann degradation** or the **Harmon Process**, and should not be confused with the Hofmann elimination.

Reaction Mechanism

Step-1: N-Bromination takes place.
Step-2: Formation of Nitrene.
Step-3: Formation of Isocynate intermediate.
Step-4: Decarboxylation to yield a 1^0 amine.

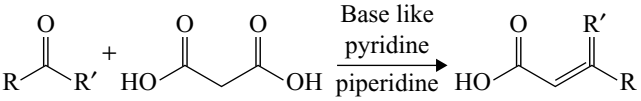


Application

- Aliphatic and Aromatic amides are converted into aliphatic and aromatic amines, respectively.
- In the preparations of Anthranilic Acid from Phthalimide
- Nicotinic acid is converted into 3-Amino pyridine.

17. Knoevenagel Reaction

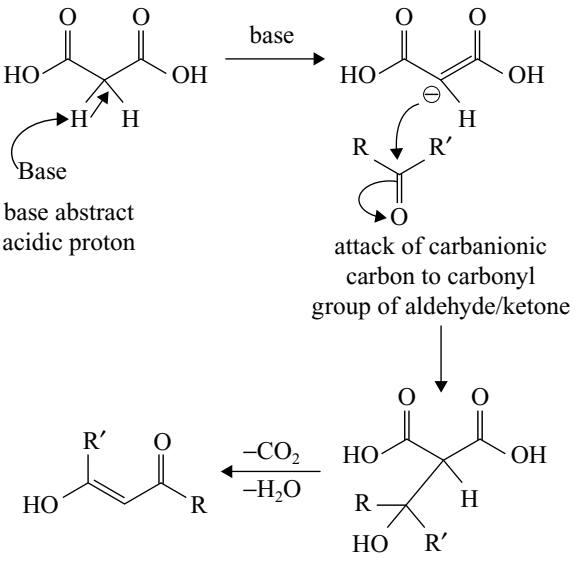
The condensation of aldehyde/ketone with the compounds having active methylene group in the presence of basic catalyst to give α, β unsaturated carbonyl compound is called Knoevenagel Reaction.The basic catalyst may be ammonia and its derivative like pyridine or piperidine.



Reaction Mechanism

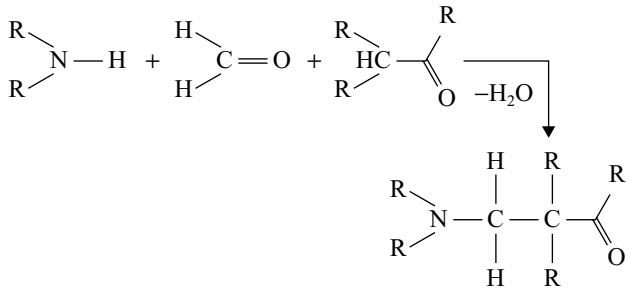
The initial stage is base catalysed aldol condensation with subsequent dehydration and decarboxylation yield α, β unsaturated carbonyl compound.

The reaction starts with the base catalysed methylene proton abstraction from dicarboxylic acid group and generate carbanion, the generated carbanion attack on the carbonyl carbon of aldehyde and ketone to β hydroxy formation and then subsequently dehydration and decarboxylation yield α, β unsaturated carbonyl compound.



18. Mannich Reaction

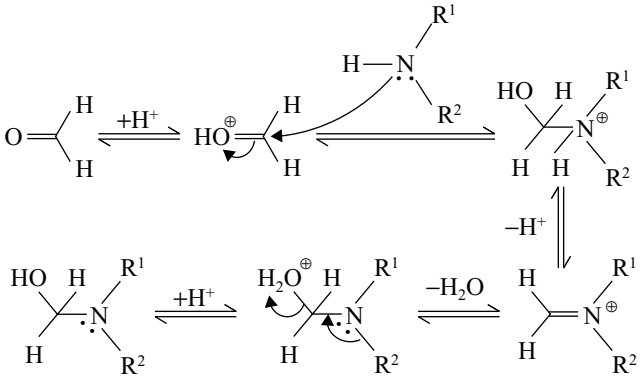
The Mannich reaction is the aminoalkylation reaction, involving the condensation of an enolizable carbonyl compound (α-CH acidic compound) with a nonenolizable aldehyde (like formaldehyde) and ammonia; or a primary or a secondary amine to furnish a β-aminocarbonyl compound, also known as Mannich base. The Mannich reaction is also considered a condensation reaction. The Mannich reaction is an example of nucleophilic addition of an amine to a carbonyl group followed by dehydration to the Schiff base. The Schiff base is an electrophile which reacts in the second step in a electrophilic addition with a compound containing an acidic proton. Instead of formaldehyde, other aliphatic or aromatic aldehydes or ketones can be employed.



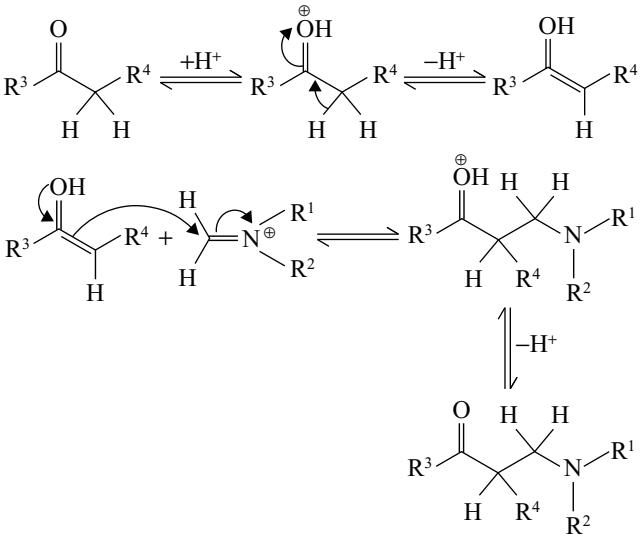
The amine used may be ammonia or 1° or 2° aliphatic amine. Mostly dimethyl amine is used. The aromatic amines do not undergo Mannish reaction. 3° amine can not give this reaction positive because of lacking of proton. The reaction is usually carried out with the hydrochloride salt of amine. This salt exists in equilibrium with the free amine and proton. Hence the acidic conditions are maintained in Mannich reaction. The **Eschenmoser's salt**, $[(CH_3)_2N{=}CH_2]^+I^-$ is used as a source of formaldehyde and dimethyl amine for Mannich reactions. The reactions are usually carried out in aqueous or alcoholic solutions.

Reaction Mechanism

Step-1: The reaction starts with the formation of an iminium ion from the amine and the formaldehyde.



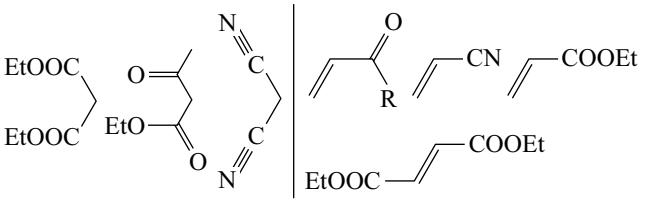
Step-2: The compound with the carbonyl functional group (in this case a ketone) can tautomerize to the enol form, after which it can attack the iminium ion.



19. Michael Reaction/Michael Addition

It is the nucleophilic addition of a carbanion or another nucleophile to an α,β-unsaturated carbonyl compound. It belongs to the larger class of conjugate additions. This is one of the most useful methods for the mild formation of C–C bonds. It is also known as conjugate addition type of reaction.

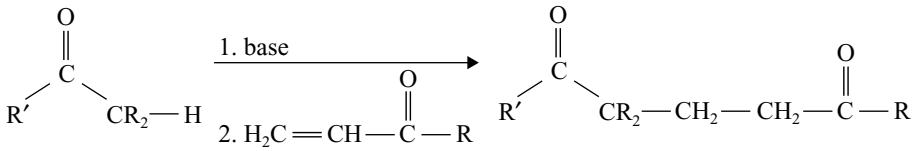
Michael Donors: The Michael donors contain active $–CH_2$ (methylene) group or –CH group. The acidic nature of methylene group is enhanced by the electron withdrawing groups (EWG) like: keto, cyano, nitro, carboxylic acid derivatice etc.



Michael donors Michael acceptors

Michael Acceptors: Not only α,β-unsaturated ketones, however, and also esters; nitriles; sulfones; and compounds with activated double bonds can act as Michael acceptors. Vinyl ketones, alkyl acrylates, acrylo nitrile, fumarates etc., are some examples.

Reaction: In michael addition reaction carbanion always add to the α,β-unsaturated position of the α,β-unsaturated carbonyl compound it is known as Michael addition rule.

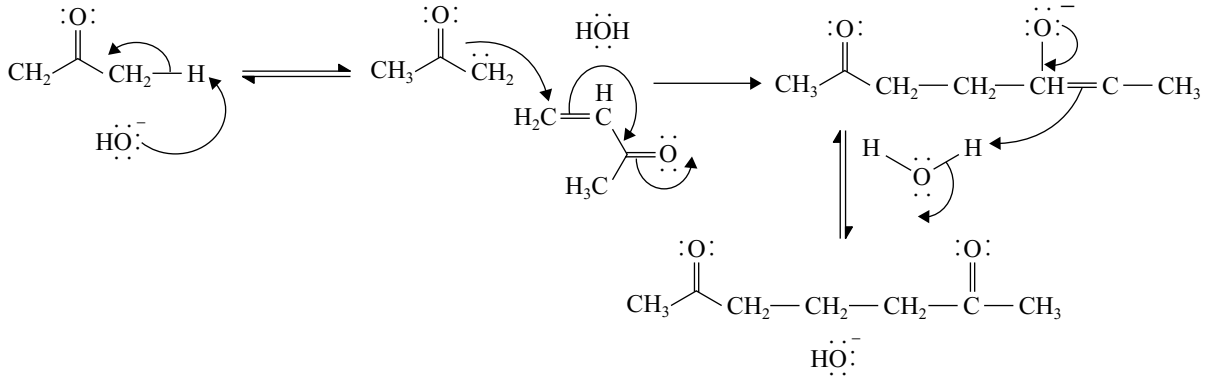


Reaction Mechanism

Step 1: In first step of the mechanism, an acid-base reaction. Hydroxide anion act as a base and removes the acidic βhydrogen giving the reactive enolate.

Step 2: In this step, the carbanionic carbon attacks the conjugated ketone at the electrophilic alkene (C=C) in a nucleophilic addition type process with the electrons being pushed through to the electronegative O, giving an intermediate enolate.

Step 3: In this step, an acid-base reaction. The enolate deprotonates a water molecule recreating hydroxide and the more favourable carbonyl group.

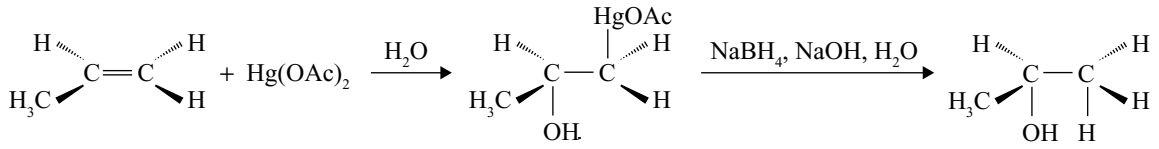


20. Oxymercuration/Demercuration

In oxymercuration reaction addition of mercury and hydroxyl group to alkene takes place whie in demercuration, it is the process which involves the removal of mercury using Sodium Hydroboride. of the hydrogens (a hydride) of Borohydride will do a backside displacement (S_N2 type reaction) on the least substituted carbon kicking off the mercury.

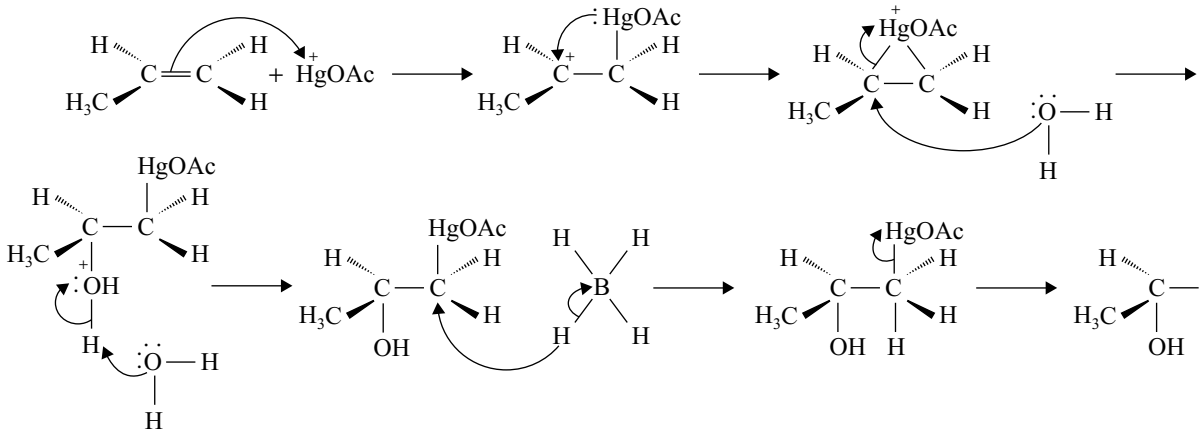
Oxymercuration - Demercuration Mechanism follows Markovnikov's Regioselectivity. Markovnikov's Regioselectivity is the process in which the OH group is attached to the most substituted carbon and the H is attach to the least substituted carbon.

Oxymercuration/Demercuration Reaction



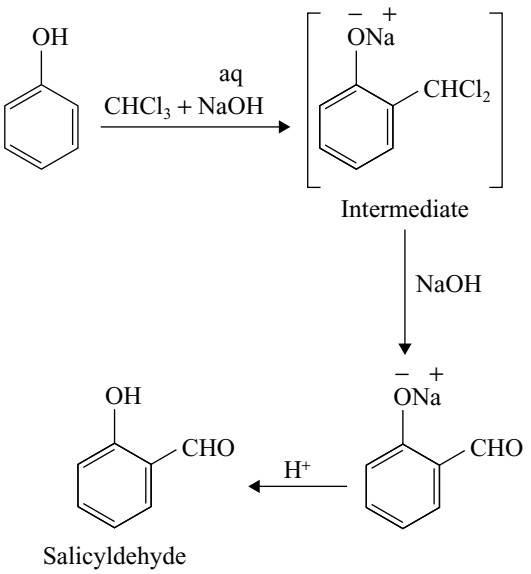
Reaction Mechanism

Mechanism of Oxymercuration/Demercuration



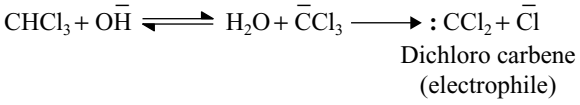
21. Reimer-Tiemann Reaction

Formylation of phenol with chloroform in alkaline solution is known as Reimer-Tiemann reaction.The chemical reaction used for the ortho-formylation of phenols.

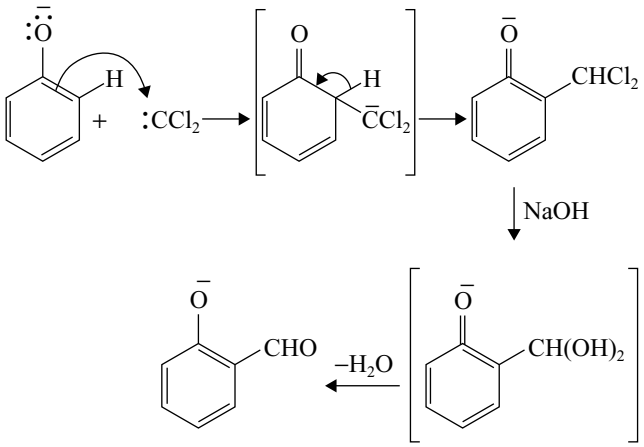


Reaction Mechanism

Reimer Tiemenn reaction is an electrophilic substitution reaction. The first step is generation of electrophile (Dichloro carbene). Dichlorocarbene contains a sextet of electrons and thus is a strong electrophile.



Attack of ring's electron to dichlorocarbene to form banzal chloride,which later on hydrolysed in presence of alkali to produce salicylaldehyde.



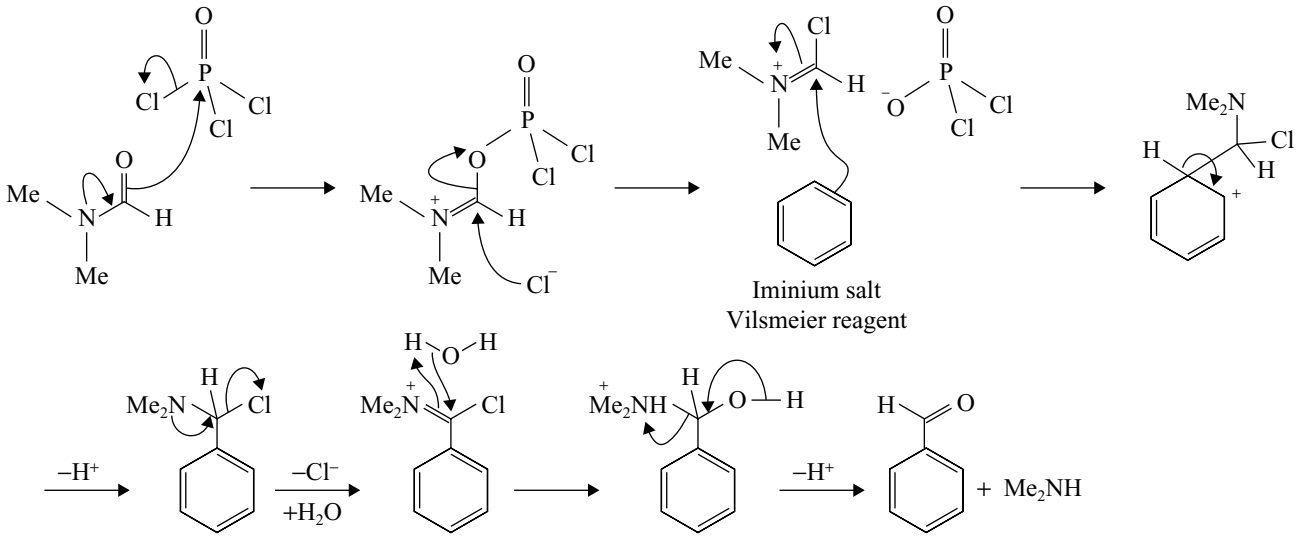
22. Vilsmeier-Haack Reaction

The Vilsmeier-Haack reaction is an organic reaction involves convenient methods for formylation of electron rich aromatic ring to an aryl aldehyde using DMF, an acid chloride, and aqueous work-up.

Reaction Mechanism

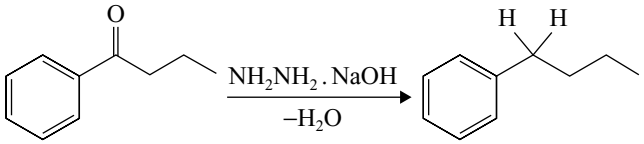
The mechanism begins with the reaction of DMF with the acid chloride to form an iminium salt known as the "***Vilsmeier reagent***".

The electron rich aromatic ring then attacks the iminium ion with loss of aromaticity. A deprotonation step restores aromaticity, which is followed by the release of a chloride ion to form another iminium intermediate. Aqueous work-up then leads to the aryl aldehyde.



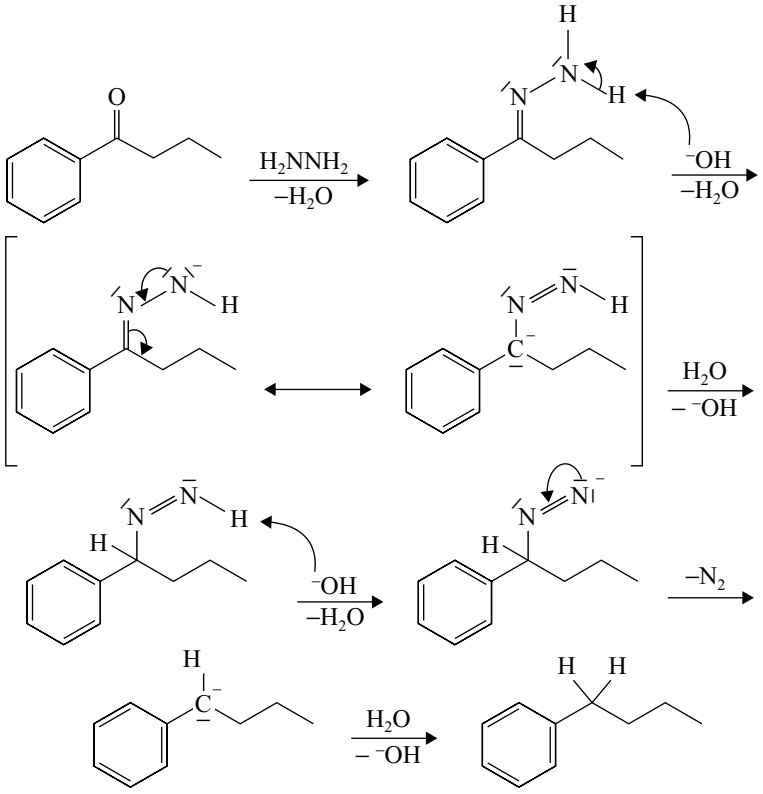
23. Wolff-Kishner Reduction

Condensation of the carbonyl compound with hydrazine forms the hydrazone, and treatment with base induces the reduction of the carbon coupled with oxidation of the hydrazine to gaseous nitrogen, to yield the corresponding alkane. The wolff Kishner reduction yield aldehydes and ketones to alkanes.



Reaction Mechanism

In the mechanism, hydrazine molecule act as a neucleophile and attack on carbonyl carbon of ketone and by loosing



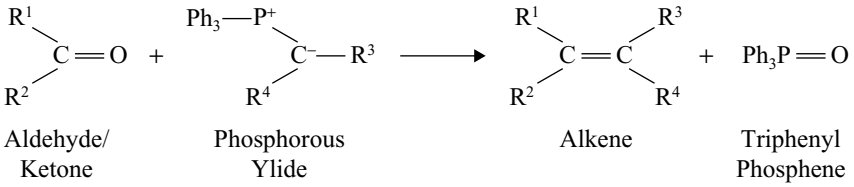
of water molecule convert in to imine function group. In subsequent steps by loosing of two mole water and nitrogen molecule via carbanion intermediate it will generate alkane.

24. Wittig Reaction

It is a reaction of an aldehyde or ketone with a triphenyl phosphonium ylide (often called a Wittig reagent) to give an alkene and triphenylphosphine oxide (Ph_3PO). The reaction also known as Wittig Olefination.

Wittig reactions are most commonly used to couple aldehydes and ketones to singly substituted phosphine ylides. With simple ylides this results in almost exclusively the Z-alkene product.

Ylides: It may be defined as the group 15 and 16 of periodic table having positive charge directly attached to carbon containing negative charge (extra unshared pair of electron) due to pϖ-dϖ bonding is known as ylides.

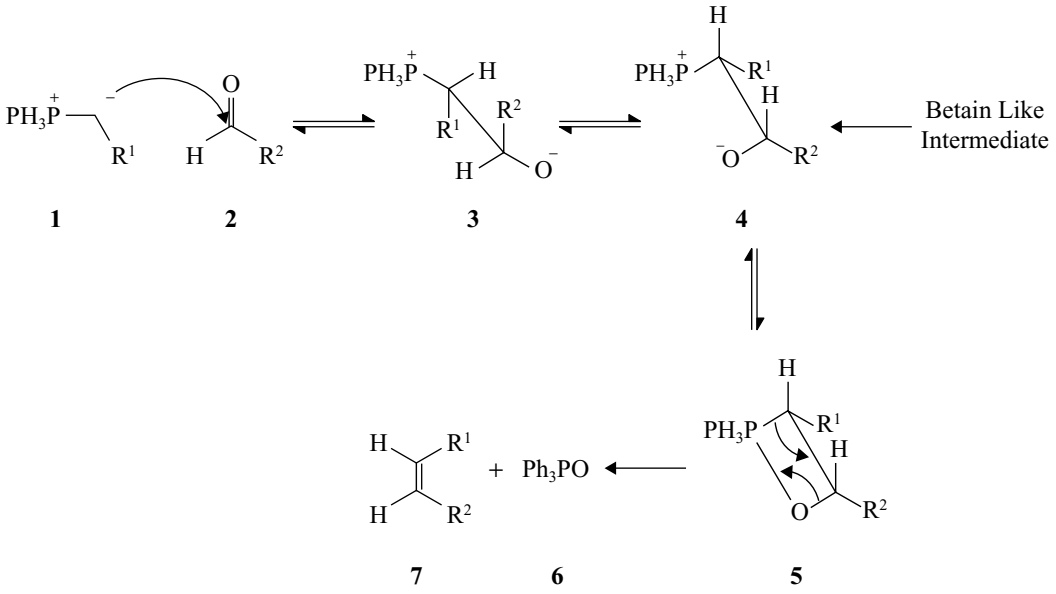


Reaction Mechanism: Nucleophilic Addition then Elimination

In the mechanism the first step is an addition of the phosphorous ylide to the carbonyl icarbon of Aldehyde/ketone lead to the zwitterionic intermediate betaine.

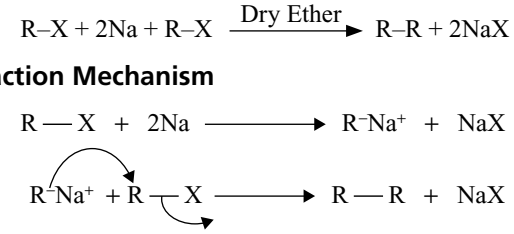
Than the extra electron on oxygen atom attack on electrodeficient phosphorous atom to form a four-membered cyclic intermediate, an oxaphosphetane.

The four membered ring clave (due to ring strain) to form stable alkene and stable tri phenyl phosphene.



25. Wurtz Reaction

In this reaction, two alkyl halide molecules are coupled in presence of sodium metal (Na) in anhydrous ether or Tetrahydrofuran to form a new carbon carbon bond and thus by giving a symmetrical alkane. The Wurtz reaction must be performed under anhydrous conditions because the alkyl free radical formed.



Reaction Mechanism

26. Williamson Method

In the reaction sodium methoxide act as a base and it is proceeds via an SN_2 mechanism, in which an alkoxide ion attack on the alkyl group of alkyl halide and displaces a halogen ion.

$$CH_3^-ONa^+ + CH_3Cl \longrightarrow CH_3OCH_3 + NaCl$$

This method cannot be used with tertiary alkyl halides due to the steric hindrance, SN_2 mechanism is not operated. An S_N1 mechanism is likewise unfavored, because as the 3° carbon attempts to become a carbocation, the hydrogens on the adjacent carbons become acidic. Under these conditions, the alkoxide ion begins to show less nucleophilic character and, correspondingly, more basic character. This basic character leads to an acid-base reaction, which results in the generation of an elimination product (an alkene).

Nomenclature of Hetrocyclic Compounds

Table 2.1A Prefix for Hetero Atoms

Hetero atom	Valence	Prefix
O	2	Oxa
N	3	Aza
S	2	Thia
Se	2	Selena
Te	2	Tellura
P	3	Phospha
As	3	Arsa
Si	4	Sila
Ge	4	Germa

Table 2.1B Common Suffix used for Hetero Compounds

Ring size	Suffixes for fully unsaturated compounds		Suffixes for fully saturated compounds	
	With N	Without N	With N	Without N
3	-irine	-irene	Iridine	-irane
4	-ete	-ete	Etidine	-etane
5	-ole	-ole	Olidine	-olane
6	-ine	-in	-	-ane
7	-epine	-epin	-	-epane
8	-ocine		ocin	-ocane

Heterocyclic Chemistry: Structure and Property

Heterocyclic compounds are organic compounds that contain a ring structure containing atoms in addition to carbon, such as sulfur, oxygen or nitrogen, as the heteroatom.

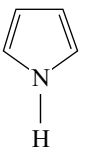
Carbocyclic compounds are organic compounds that contain ring system made up entirely of carbon atoms.

π-Excessive heterocyclic system have an e^- - donating heteroatom

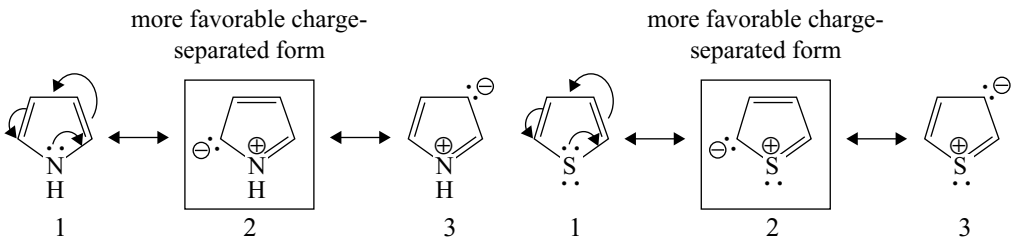
a heteroatom donates a pair of π-electrons to the π-system (pyrrole, thiophene, furan)

Five member ring containing O, NH, S are π-Excessive system because of in ring system total six electron are distributed in only five atom so each atom having a more than one electron that's why it is π-Excessive heterocyclic system.

E.g. Pyrrole



Pyrrole

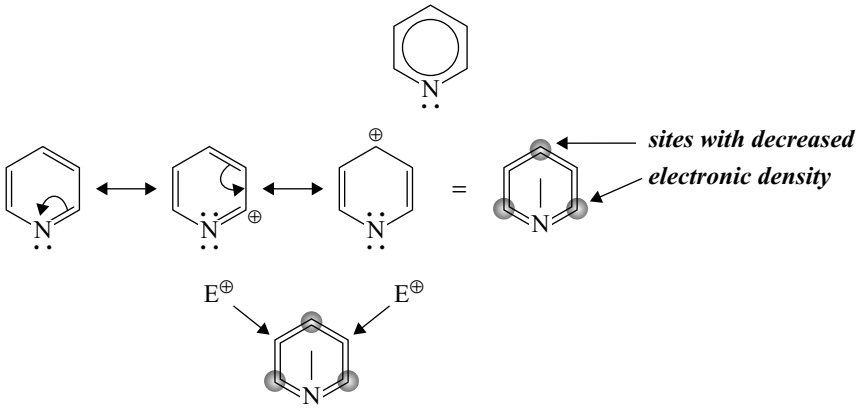


preference: 2 > 3

π-Deficient heterocyclic have an e⁻ - accepting heteroatom eg. N or N+

Six member ring system has N atom is an example of π-Deficient heterocyclic system due to electronegativity of N atom is more compare to carbon so electron density is more at N atom so each carbon has less one electron that's why it is π-Deficient heterocyclic system.

E.g. Pyridine



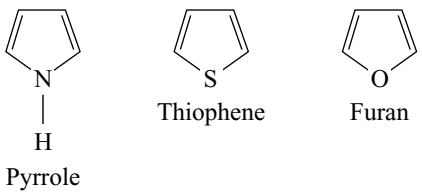
Reactivity order towards electrophilic aromatic substitution reaction in pyrrole, pyridine and benzene.

- **Towards S_EAR reaction:** Pyrrole > Benzene > Pyridine

Heterocyclic Compounds and Benzene: A Comparison

- Both are aromatic because it obeys 4n + 2 π e Hückel's rule.
- Delocalization gives rise to resonance resulting in stability of compounds, benzene is more stable than heterocyclic compounds.
- Both undergo electrophilic as well as nucleophilic substitution.
- Reactions are regioselective.

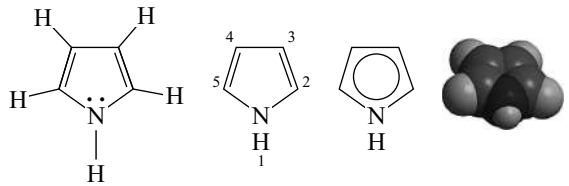
Five member heterocyclic ring system contains one hetero atom; Pyrrole, Furan and Thiophene



All rings have following characteristics;

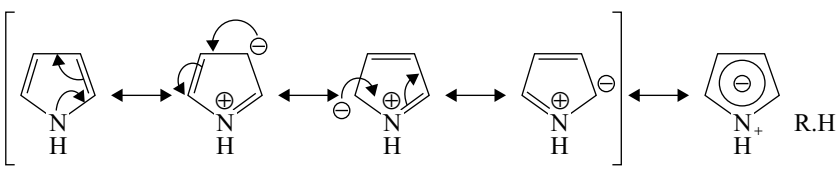
- All are aromatic: Thus, 6π electrons
- Sp^2 hybridised and planar
- Lone pair electrons on hetero atom is in p-orbital so it is overlaps with the carbon p-orbital
- Thus, electrophilic aromatic substitution is easy.
- Nucleophilic Substitution is Difficult

Pyrrole



Structure of Pyrrole

- It having a 6π electrons, conjugated system and delocalization of π electron takes place.
- Overlapping p orbital.
- In pyrrole, each of the 4-C contribute 1π electron and the sp^2hybdridised nitrogen contributes 2 e that's why obey the 4n + 2 π e Hückel's rule.
- Lone pair electrons on nitrogen atom are in p-orbital so it is overlaps with the carbon p-orbital.
- Electron movement thus results in resonance.
- Lone pair on N a part of aromatic sextet.

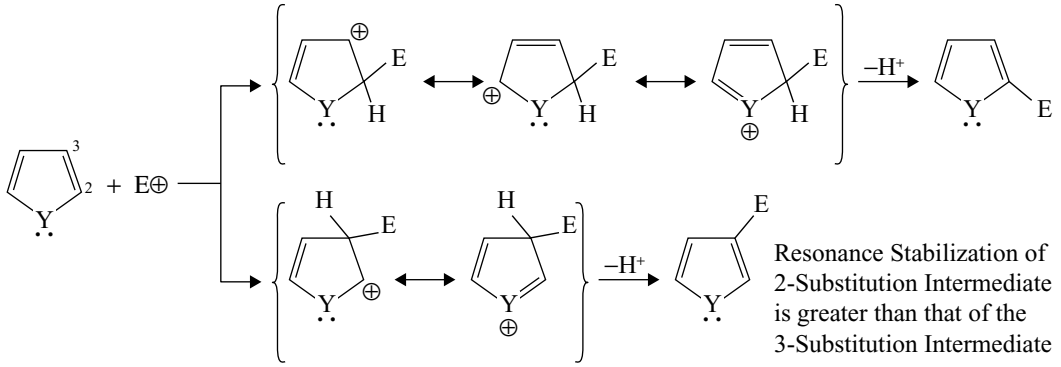


Delocalization of electron in pyrrole ring

Basicity and Reactvity of Pyrrole

- Lone pair on N-atom is part of aromatic sextet, therefore, less available for bonding with acids. Thus Pyrrole - less basic, less Nucleophilic than aliphatic amines. Weakly basic but has greater aromatic character
  - Electron pair NOT available to act as base
  - Protonation would destroy aromaticity

Electrophilic aromatic substitution reaction in pyrrole

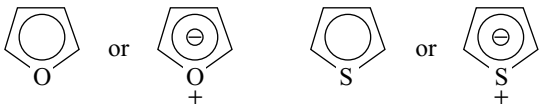


In pyrrole, Electrophilic aromatic substitution reaction occurs at C-2 position because of it having more no of resonating structure compare to attack of electrophile at C-3 of pyrrole ring, and the positive charge in accommodate in three atom rather than two atom, if attack of electrophile occur at C-3.

Same like pyrrole in furan and thiophene EAS reaction takes place on C-2.

Other Properties of Pyrrole

Pyrrole having more boiling point than furan and thiophene, because of in pyrrole structure inter molecular hydrogen bonding takes place due to the N-H group in ring system. Due to intermolecular H-bonding pyrrole has more b.p than furan and thiophene.



Pyrrole and Furan Is Least Aromatic Than Thiophene

Because of electronegativity of sulphur in less than O and N containing heterocycles (Furan and Pyrrole) so it can easily delocalized electron in ring system that's why thiophene is more aromatic than pyrrole and furan.

Six Member Heterocyclic System: Pyridine

- Aromatic
- Pyridine replaces the CH of benzene by a N atom (and a pair of electrons)
- Flat planner molecule with bond angle 120^0 (SP^2 Hybridization)with similar resonance stabilization energy
- Lone pair of electrons not involved in aromaticity like pyrrole
- It undergoes Substitution reaction rather than addition reaction.
- The molecule has a dipole moment as the e^- - distribution is uneven.
- The C-C bond lengths > the C-N bond lengths.

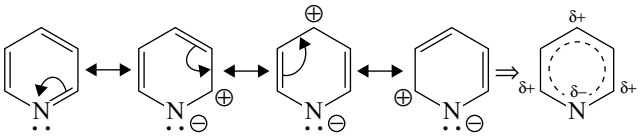
Basicity of Pyridine

- Pyridine is more basic than pyrrole because of K_b of pyridine is 2.3×10^{-9} and K_b of pyridine is 2.5×10^{-14}.
- Pyridine has more K_b value than pyrrole, so more basic.
- Another reason to more basicity of pyridine is, in pyrrole the lone pair on N atom is involved in aromaticity while in pyridine it is not a case.

Electrophilic Aromatic Substitution Reaction in Pyridine

- Pyridine is highly deactivating ring because of π-Deficient heterocyclic system.
- EAS reaction is least readily than benzene, because of N is more electronegative than C and is a net acceptor of π-density and so makes the π-cloud less available.
- In other words, N deactivates the ring, especially in positions 2 and 4.
- So electrophilic aromatic substitution (EAS) reaction occur at C-3 position.
- In the below figure it is clearly shown that in pyridine the positive charge is generate at C-2 and C-4 that's why EAS reaction is not possible on it so EAS reaction is possible on C-3 only because there is no any positive charge generate on C-3.
- Nucleophilic Aromatic Substitution reaction occurs at C-2 and C-4 , because of positive charge is generate at

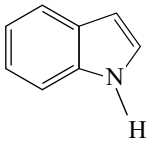
C-2 and C-4 so neucleophile can easily attack on electron deficient center.



Fused Heterocycles

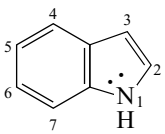
eg. Indole, Benzofuran and Benzothiophene

Indole

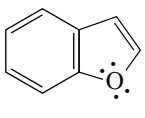


Indole

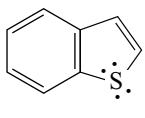
- It is a fusion of benzene and pyrrole ring it is also known as banzopyrrole.
- Aromatic because cyclic conjugated, planar
- Aromatic due to 10 π-electrons and obey Huckel's rule (8π-electrons from the double bond and 2π-electrons from the hetero atom) lone pair of e from N delocalizes to give the aromatic character.
- Benzene part of indole is non-reactive.
- Electrophilic aromatic substitution occurs at the 3-position because of more canonical structures are form if attack occur at C-3 position compare to attack of electrophile at C-2.
- Analogous compounds derived by fusion of a benzene ring to a pyrrole, furan or thiophene nucleus called indole, benzofuran and benzothiophene.
- For all analogues: Rings numbered in a way that it gives lowest possible number to the heteroatom



indole



en o n



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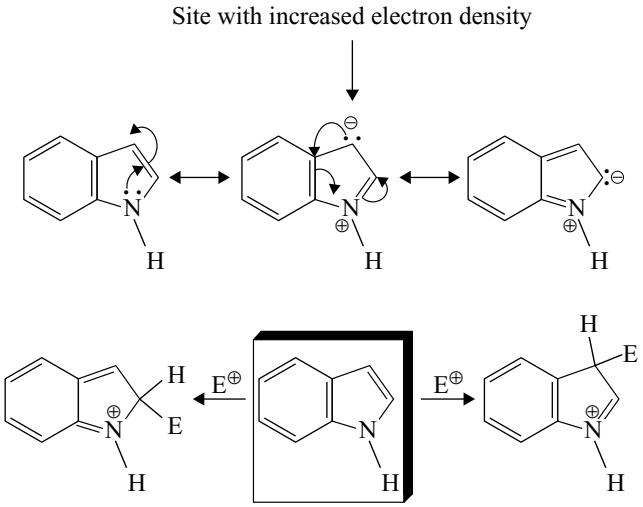
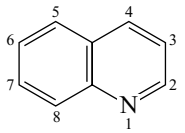
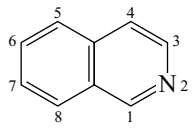
Electrophilic Aromatic Substitution in Indole



Quinoline and Isoquinoline

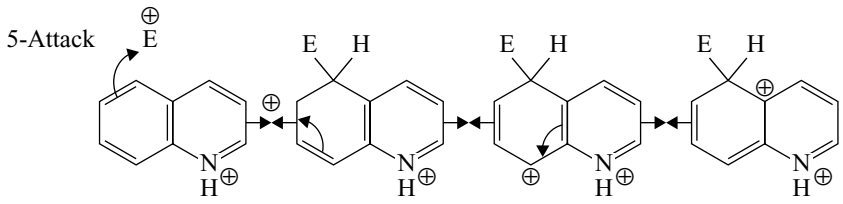


Quinoline

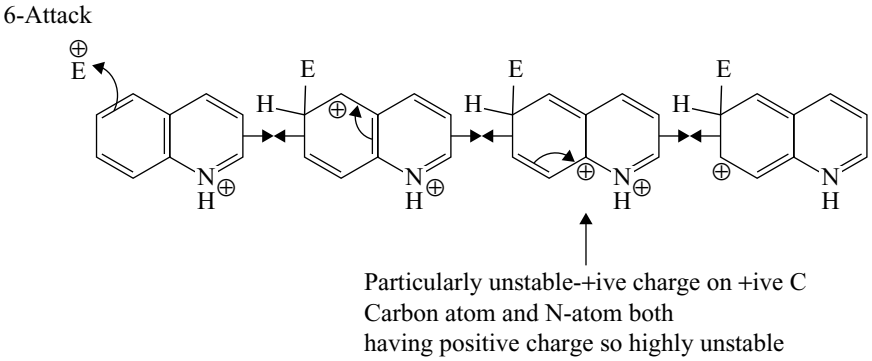


Isoquinoline

- It is also known as benzopyridine: due to fusion of one benzene and one pyridine ring
- Aromatic because cyclic conjugated, planar
- Aromatic due to 10 π-electrons and obey Huckel's rule.
- Electrophilic aromatic substitution occurs at the benzene ring giving a mixture of substitution products – C-5 and C-8
- Nucleophilic aromatic substitution occurs at the pyridine ring giving substitution at C-2 and C-4 for quinoline and C-1 for isoquinoline
- Electrophilic subsitution in quinoline and isoquinoline: explanation
- Attack at C5 and C8; Compare two scenarios: attack at C5 and C6



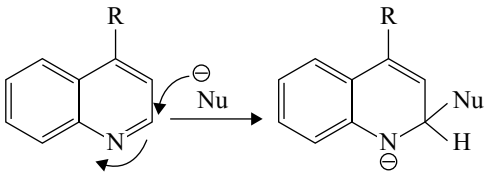
These are more stable



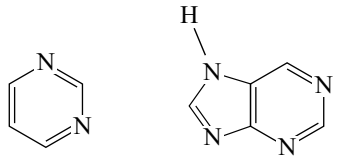
Intermediates for substitution at C-5 and C-8 more resonance stabilized than attack at C-6 because if we look at the structure than both C and N atoms having positive charge on it.

Nucleophilic substitution reaction occurs at C-2 and C-4 position same like pyridine.

- Explain by looking at the anionic intermediates
- Hydride can be displaced at the 2- and 4- positions
- Stable intermediate from attack at position 2- and 4-, negative charge on nitrogen atom



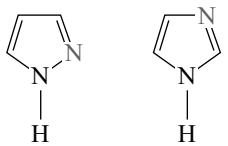
Purines and Pyrimidines



Pyrimidine **P rine**

- Most important heterocyclic ring system from biological point of view, nucleic acids
- Pyrimidine: Contains 2 pyridine-like N in a 6-membered aromatic system
- Purine: Contains 4 N in a fused ring system, 3 of these N are basic and pyridine-like with their l.p. e in sp^2 orbitals in the plane of the ring while remaining 1 N is nonbasic and pyrrole-like with l.p. e as part of aromatic π e system.

Diazole: Pyrazole and Imidazole



Pyrazole Imidazole

Replacing a CH group in the pyrrole ring with a nitrogen atom can give rise to two compounds: pyrazole and imdazole.

Only one nitrogen atom can contribute two electrons to the aromatic sextet. It is the nitrogen with the hydrogen and it is described as pyrrole-like nitrogen. While the second nitrogen (2^{nd} position) which has no hydrogen is described as pyridine-like.

The lone pair on pyrrole-like nitrogen is delocalized round the ring while that on the pyridine-like nitrogen is localized in sp^2 orbital on nitrogen. Thus these compounds have properties *intermediate* between those of pyrrole and pyridine.

Physical Properties of Imidazole and Pyrazole

Solubility

- Imidazole and pyrazole are water soluble solids and insoluble in aprotic solvent.
- They have very much higher boiling point:256 and 187 °C respectively, this difference is due to imidazole has an extensive hydrogen bonding than pyrazole thus imidazole molecules can exist as oligommers, consequently more energy is required to break these bonds to bring the molecules from one phase to another.
- On the other hand pyrazole molecules can form dimers only thus lesser energy is required to break these molecules.
- N-subsituted imidazole and pyrazole have lower boiling and melting points than the unsubstituted compounds due to inability to form H-bonds.

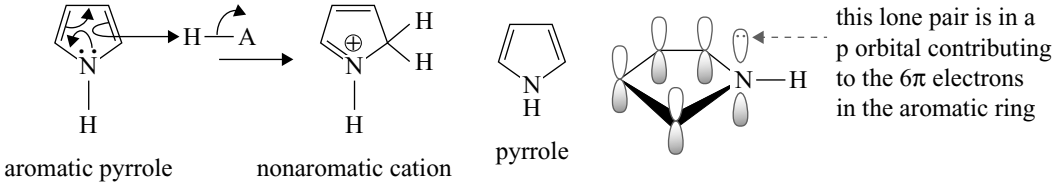
Basicity

Imidazole is a stronger base than pyrazole or pyridine and of course pyrrole. Thus imidazole and pyrazole are more stabilized than pyrrole in acidic medium.

> **Basicity order:** Imidazole > Pyrazole > Pyridine > Pyrrole

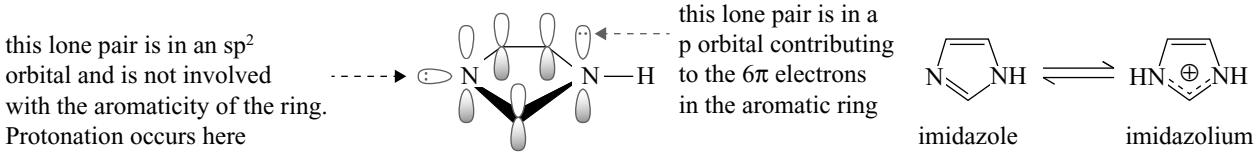
This can be explained as follows:

Pyrrole is not basic because the lone pair on the only nitrogen is needed to complete the aromatic pi system and protonation if occurs at all occurs at carbon rather than on nitrogen and the resulting cation is not aromatic.



aromatic pyrrole nonaromatic cation pyrrole

Both of imidazole and pyrazole have two nitrogen atoms and on protonation the positive charge can be delocalized over them. However, pyrazoles are much weaker bases than imidazoles. This difference is due to the fact that the positive charge in pyarzolium ion is less delocalized than in the imidazolium ion.



the aromaticity of imidazole imidazole imidazolium

Effect of substitution on basicity

- Generally E.D.G groups on the ring increase the basicity while E.W.G. decrease it.
- N-methyl imidazole is more basic than imidazole itself.
- However, N-methylpyrazole is less basic than pyrazole which can be attributed to steric hindrance effect which cause difficulty in accessing the lone pair of electron by the proton.
- Imidazoles unsubstituted in the 1-position are weak acids. Its acidity is greater than that pyrrole and equals that of pyrazole.
- Diazoles are less reactive than 5-membered heterocycles with one heteroatom (pyrrole and its analogs) in electrophilic aromatic substitution due to the inductive electron-withdrawing effect of the second heteroatom.
- However, they are more reactive than pyridine due to delocalization of the lone pair of electrons on the N-atom make the C- atoms bear negative charges while in pyridine the N- atom exerts inductive electron withdrawing effect only.
- The orientation in pyrazole, is at the 4-position due to the deactivation effect of the pyridine-like nitrogen
- The orientation in imidazole, is at 5-position, due to the additional N-atom deactivates its vicinal positions
- However, if the position 5 is occupied the electrophiles will be directed to 4-position.

Multiple Choice Questions

1. Which of the following intermediates has a positive charge?
(a) Carbocation (b) Carbanion
(c) Carbene (d) Nitrene

2. Which of the following intermediates has a negative charge?
(a) Carbocation (b) Carbanion
(c) Carbene (d) Nitrene

3. Which of the following is a nitrogen analog of carbene?
(a) Carbocation (b) Carbanion
(c) Carbene (d) Nitrene

4. Which of the following groups comes under EDG?
(a) Nitro (b) Chloro
(c) Amino (d) Aldehyde

5. Which of the following groups comes under EWG?
(a) Nitro (b) Methyl
(c) Amino (d) Anilide

6. Which of the following rules is not used to determine the electronic configuration?
(a) Pauli's (b) Saytzeff
(c) Hund's (d) Aufbau

7. All statements are correct for SN-1 reaction, except
(a) Follows first-order kinetic
(b) Rearrangement is possible
(c) Inversion of configuration takes place
(d) Two-step reaction

8. All statements are correct for SN-2 reaction, except
(a) Follows second-order kinetic
(b) Rearrangement is possible
(c) Inversion of configuration takes place
(d) Single step reaction

9. All statements are correct for E-2 reaction, except
(a) Follows first-order kinetic
(b) Reactivity order is $3° > 2° > 1°$
(c) Always βhydrogen abstracted
(d) Single-step reaction

10. Orientation of elimination reaction follows …
(a) Markoniov's rule (b) Saytzeff rule
(c) Micheal addition (d) Hoffmann rule

11. Orientation of addition reaction follows …
(a) Markoniov's rule
(b) Saytzeff rule
(c) Micheal addition
(d) a and c

12. In polar aprotic solvent the nucleophilicity of halides is
(a) $F^- > Cl^- > Br^- > I^-$
(b) $F^- < Cl^- < Br^- < I$
(c) $F^- = Cl^- = Br^- = I^-$
(d) None of the above

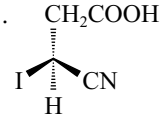
13. In polar protic solvent the basicity of halides is
(a) $F^- > Cl^- > Br^- > I^-$
(b) $F^- < Cl^- < Br^- < I^-$
(c) $F^- = Cl^- = Br^- = I^-$
(d) None of the above

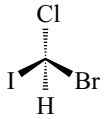
14. Which of the following is a polar aprotic solvent?
(a) DMF (b) Etahanol
(c) Water (d) All

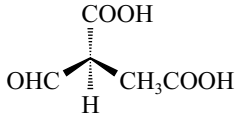
15. Which of the following is a polar protic solvent?
(a) Acetic acid (b) Etahanol
(c) Water (d) All

16. In which of the following structures, geometrical isomer is not possible?
(a) Ethene (b) Propene
(c) 2-Pentene (d) a and b

17. Find out the absolute configuration of following structure:

1. 

2. 

3. 

(a) 1-S,2-R,3-S (b) 1-S,2-R,3-S
(c) 1-R,2-R,3-S (d) 1-S,2-S,3-S

18. How many isomers are present in the structure of glucose?
(a) 12 (b) 16
(c) 10 (d) 4

19. Which form is more stable in conformation of n-butane?
(a) Skew staggered
(b) Skew eclipsed
(c) Totally staggered (anti)
(d) Fully eclipsed

20. All statements are correct for enantiomer, except
(a) It must be a chiral
(b) Not superimposable on its mirror image
(c) Gives optical activity
(d) All enantiomer are optically active

21. Which of the following bonds is the weakest bond?
(a) Coordinate bond
(b) Covalent bond
(c) Van der Walls' force
(d) H-Bond

22. Compound A is highly volatile and insoluble in water so bonding in A is
(a) Coordinate bond (b) Ionic bond
(c) Covalent bond (d) Polar covalent bond

23. Which substance has a dipole moment?
(a) CCl_4 (b) CH_2Cl_2
(c) C_2Cl_2 (d) C_2Cl_4

24. Which form is more stable in conformation of cyclohexane?
(a) Chair (b) Boat
(c) Twist boat (d) Half chair

25. Which of the following has a zero dipole moment?
(a) CO (b) SO_2
(c) SO_3 (d) H_2O

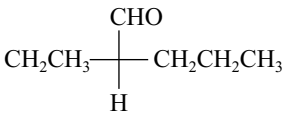
26. Mixture of amino acid can be separated by
(a) Sublimation (b) Chromatography
(c) Distillation (d) None

27. Spraying reagent used in detection of amino acid is
(a) Iodine solution (b) Benedict reagent
(c) Molisch reagent (d) Ninhydrin reagent

28. $C_3H_6 + H_2 = C_3H_8$ The above reaction is an example of?
(a) Substitution (b) Addition
(c) Polymerization (d) Esterification

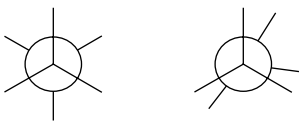
29. The number of optically active isomers of tartaric acid is
(a) 2 (b) 3
(c) 4 (d) 5

30. The chiral carbon in the following compound has _____ configuration



(a) R (b) S
(c) a and b (d) None

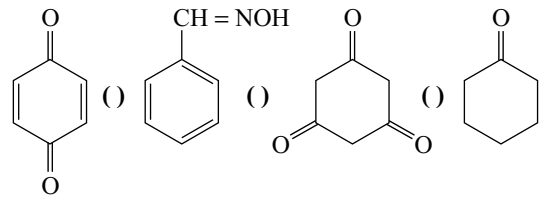
31. Which types of conformation are shown by A and B?



A B

(a) A is eclipsed and B is staggered
(b) B is eclipsed and A is staggered
(c) Both are in staggered form
(d) Both are in eclipsed form

32. Tautomerism is not exhibited by

(a) 

33. The term atropiisomerism is used for isomers
(a) That can be interconverted by rotation about single bonds
(b) That are geometrical isomers
(c) That are optical isomers
(d) That are enantiomers

34. The separation of racemic mixture into the pure enantiomer is
(a) Racemization
(b) Resolution
(c) Isomerization
(d) All of the above

35. A meso compound
(a) Is an achiral molecule that contains chirality centre
(b) Contains plane of symmetry
(c) Is optically inactive
(d) Is characterized by all of these

36. D and L are a pair of _____ configuration.
(a) Relative (b) Absolute
(c) Cis-trans (d) None of above

37. R and S are a pair of _____ configuration.
(a) Relative (b) Absolute
(c) E-Z (d) None of above

38. d and l are a pair of _____ configuration.
(a) Relative (b) Absolute
(c) E-Z (d) Optical isomer

39. A bond in which atoms share a pair of electrons is
(a) Ionic bond
(b) Covalent bond
(c) Electrovalent bond
(d) Binary compound bond

40. Which statement best explains why carbon tetrachloride (CCl_4) is non-polar?
(a) Each carbon chloride bond is polar
(b) Carbon and chlorine are both nonmetals
(c) Carbon tetrachloride is an organic compound
(d) The carbon tetrachloride molecule is symmetrical.

41. _____ is a heterocyclic compound with three-membered ring.
(a) Furans (b) Pyrroles
(c) Ethylene oxide (d) Cyclo propane

42. _____ is a heterocyclic compound with five-membered ring.
(a) Aziridine (b) Azoletine
(c) Azole (d) Azoline

43. 1,2-postion with six member heterocyclic contain two nitrogen atom is called
(a) Pyrimidine (b) Pyridine
(c) Pyrazine (d) Pyridazine

44. 1,3-postion with six member heterocyclic contain two nitrogen atom is called
(a) Pyrimidine (b) Pyridine
(c) Pyrazine (d) Piperazine

45. A gas whose molecule is monatomic is
(a) Oxygen (b) Helium
(c) Nitrogen (d) Chlorine

46. A molecule of ethane is similar to a molecule of methane in that they both have the same
(a) Structural formula
(b) Molecular formula
(c) Number of carbon atoms
(d) Number of hydrogen atoms

47. A reaction between an acid and an alcohol produces an ester and
(a) Carbon dioxide (b) Water
(c) Glycerol (d) Ethanol

48. Removal of hydrogen from alkene produces a/an
(a) Alcohol (b) Alkane
(c) Alkyne (d) Protein

49. Secondary alcohols
(a) Have two hydroxy groups on the carbon chain
(b) Have a –OH group bonded to a carbon that is bonded to two other carbon atoms.
(c) Have hydroxy groups at both ends of the carbon chain
(d) Have a hydroxy group on the last carbon of the hydrocarbon chain.

50. Substances having the same molecular formulas but different structural formulas are known as
(a) Dimers (b) Isomers
(c) Polymers (d) Allotropes

51. The carbon-carbon bond length in benzene is
(a) Longer than a double bond
(b) Shorter than a single bond
(c) Both a and b
(d) Neither a nor b

52. A compound has the empirical formula CH_2O and the molecular mass is 180 grams per mole. What is its molecular formula?
(a) CH_8O_{10} (b) $C_{12}H_4O_2$
(c) $C_6H_{12}O_6$ (d) $C_{12}H_{24}O_{12}$

53. The highest electronegativity atom from following is
(a) Fluorine (b) Neon
(c) Lithium (d) Cesium

54. The oxidation of ethyl alcohol results in the formation of
(a) Formic acid (b) Propyl alcohol
(c) Acetic acid (d) Acetone

55. The process by which heated iodine crystals form a vapour without passing through the liquid state is
(a) Evaporation (b) Sublimation
(c) Condensation (d) Distillation

56. Which compound is a trihydroxy alcohol?
(a) Ethylene glycol (b) Glycerol
(c) Butanol (d) Isopropyl alcohol

57. Trichloromethane is another name for
(a) Methyl chloride
(b) Chloroform
(c) Carbon tetrachloride
(d) Freon

58. The general formula RCOOR' represents a(n)
(a) Ester (b) Ketone
(c) Aldehyde (d) Ether

59. Diels Alder comes under _____ reaction
(a) Cycloaddition
(b) Electrocyclic
(c) Sigmatropic
(d) All of above

60. Which of the following is/are pericyclic reaction?
(a) Cycloaddition
(b) Electrocyclic
(c) Sigmatropic
(d) All of above

61. As per Woodward–Hoffman rules for electrocyclic reaction, for 4n system under thermal condition rotation direction for bonding is _____
(a) Conrotation (b) Disrotation
(c) a and b (d) None of the above

62. As per Woodward–Hoffman rules for electrocyclic reaction, for 4n system under photochemical condition rotation direction for bonding is _____
(a) Conrotation (b) Disrotation
(c) a and b (d) None of above

63. As per Woodward–Hoffman rules for electrocyclic reaction, for 4n + 2 system under photochemical condition rotation direction for bonding is _____
(a) Conrotation (b) Disrotation
(c) a and b (d) None of above

64. Anchimeric assistance is associated with _____
(a) Neighbouring group mechanism
(b) SN2 mechanism
(c) SN1 mechanism
(d) Elimination mechanism

65. Which of the following is a homogeneous catalyst?
(a) Nickel (b) Platinum
(c) Palladium (d) Wilkinson catalyst

65. In branching at α and β position of alkyl halide following sentence is true.
(a) Rate of SN_1 and SN_2 reaction is increased
(b) Rate of SN_1 reaction is increased
(c) Rate of SN_2 reaction is increased
(d) None of the above

66. Betain Shape intermediate is generated in _____ reaction
(a) Wittig (b) Aldol
(c) Hofmann (d) None of the above

67. Dichloro carbene as an intermediate is generated in _____ reaction
(a) Wittig (b) Aldol
(c) Hofmann (d) Reimer Tiemann

68. In Hoffmann rearrangement
(a) Nitrene is an intermediate
(b) Nucleophillic rearrangement of alkyl group takes place
(c) Products have one carbon less compared to starting material
(d) All are true

69. Correct thing in case of crossed aldol condensation is _____
(a) Both aldehyde/ketone have an α hydrogen
(b) Only one aldehyde/ketone has an α hydrogen
(c) It does not have α hydrogen
(d) All of the above

70. Which of the following is an oxidizing reagent?
(a) $KMnO_4$ (b) Concentrated HNO_3
(c) H_2O_2 (d) All

71. Which of the following is a reducing reagent?
(a) H_2/Ni (b) Fe/HCl
(c) $NaBH_3$ (d) All

72. SN2 reaction fast with
(a) 1° Alkyl halide (b) 2° Alkyl halide
(c) 3° Alkyl halide (d) All

73. SN1 reaction fast with
(a) 1° Alkyl halide (b) 2° Alkyl halide
(c) 3° Alkyl halide (d) All

74. Which of the following reagent is used in oppenauer oxidation?
(a) Aluminiun t-butoxide
(b) Liithium aluminium hydride
(c) Sodium borohydride
(d) Sodium hydroxide

75. Which of the following is a correct formula of Grignard reagent?
(a) RMgX (b) RMg_2X
(c) $RMgX_2$ (d) All

76. Bond angle in case of SP2 hybridization is _____
(a) 120 (b) 180
(c) 90 (d) 109.5

77. Shape in case of SP3 hybridization is _____
(a) Tetragonal (b) Trigonal
(c) Linear (d) Octagonal

78. Bond angle in case of water molecule is _____
(a) 105 (b) 120
(c) 107 (d) 109.5

79. Hybridization is case of water molecule is _____
(a) SP2 (b) SP3
(c) SP and SP3 (d) SP

80. Bond angle in case of ammonia molecule is _____
(a) 105 (b) 120
(c) 107 (d) 109.5

81. All statements are true in case of electronegativity, except
(a) From downward to upward in periodic table electronegativity is increased
(b) From right to left to periodic table electronegativity is increased
(c) From left to right in periodic table electronegativity is increased
(d) From upward to downward in periodic table electronegativity is decreased

82. Which of the following is a correct order of electronegativity?
(a) F > O > N > C (b) F > Cl > Br > I
(c) F > O > N > S (d) All of the above

83. Dipole moment of molecule is measured in _____ unit.

(a) Debye (b) Dyne/Cm
(c) Dyne (d) Poise

84. Following have zero dipole moment except
(a) H_2 (b) CH_4
(c) CCl_4 (d) CH_3Cl

85. Which of the following is not inter molecular forces?
(a) Repulsion and attraction
(b) Dipole–dipole interaction
(c) Van der Waals forces
(d) H-bonding

86. Bredt's rule is applicable for _____
(a) Aliphatic system
(b) Heterocyclic system
(c) Bridgehead bicyclic system
(d) Spirocyclic system

87. Cahn Ingold and prologue rule is used for determining _____
(a) The R and S configuration
(b) The D and L configuration
(c) The Cis and Trans configuration
(d) The E and Z configuration

88. Which of the following is an example of cyclic ether?
(a) Oxiran (b) Epoxide
(c) Cyclobutane (d) a and b

89. The nomenclature of geometrical isomer is done by
(a) E and Z configuration
(b) Cis- and trans configuration
(c) All of the above
(d) None

90. Which of the following is a type of structural isomer?
(a) Tautomerism
(b) Metamerism
(c) Functional isomerism
(d) All of the above

91. Higher ring strain is associated with
(a) Cyclopropane (b) Cyclobutane
(c) Cyclopentane (d) Cyclohexane

92. Staggered and eclipsed is a type of
(a) Conformational isomer
(b) Geometrical isomer
(c) Enantiomer
(d) Optical isomer

93. Which of the following statement is not correct for benzene?
(a) Heat of hydrogenation and combustion are lower than expected value
(b) Benzene undergoes addition reaction rather than substitution reaction
(c) All C=C in benzene have an intermediate bond length between C–C and C=C
(d) Benzene follows Huckel's rule

94. Which of the following is ortho-para directing group?
(a) Nitro (b) Ester
(c) Methyl (d) 4° ammonium compound

95. Which of the following is a meta directing group?
(a) Chloro
(b) Cyno
(c) Anilide
(d) Alkoxy

96. Which of the following is not aromatic?
(a) Cyclopentadiene anion
(b) Cyclopentadine
(c) Anthracene
(d) Napthalene

97. The migration of a group from carbon to electron-deficient oxygen is an example of _____ reaction.
(a) Baeyer–Villiger rearrangements
(b) Pinacole–Pinacolone rearrangements
(c) Beckmann rearrangement
(d) Benzillic acid rearrangement

98. The acid catalysed conversion of ketoxime to N-substituted amides is known as _____
(a) Baeyer–Villiger rearrangements
(b) Pinacole–Pinacolone rearrangements
(c) Beckmann rearrangement
(d) Benzillic acid rearrangement

99. Which reaction involves migration of group from carbon to nitrogen?
(a) Baeyer–Villiger rearrangements
(b) Pinacole–Pinacolone rearrangements
(c) Beckmann rearrangement
(d) Benzillic acid rearrangement

100. Which reaction involves the conversion of an amide to a primary amine (1°) with one carbon less?
(a) Baeyer–Villiger rearrangements
(b) Pinacole–Pinacolone rearrangements
(c) Beckmann rearrangement
(d) Hofmann rearrangement

101. Hexane and 3-methylpentane are examples of:
(a) Enantiomers
(b) Stereoisomers
(c) Diastereomers
(d) Constitutional isomers

102. A reaction between an acid and an alcohol produces an ester and?
(a) Water (b) Carbon dioxide
(c) Ethanol (d) Oxygen

103. The quantity of heat evolved when one molecule of hydrogen is burned to carbon dioxide and water is called
(a) Heat of sublimation
(b) Enthalpy
(c) Heat of combustion
(d) Entropy

104. Which of the following reagent is used for diazotization?
(a) $NaNO_2$ + dilute HCI
(b) $KNO_3 + H_2SO_4$
(c) $NaNO_2 + K_2SO_4$
(d) $NaNO_3$ + Dilute HCI

105. What is the bond angle in SP hybridization?
(a) 109.5 (b) 120
(c) 180 (d) 119.5

106. Which of the following is not having dipole moment?
(a) Methyl chloride (b) Water
(c) Ammonia (d) Methane

107. When you treat phenol with dilute HNO_3 at 20°C, you will get _____
(a) Orthonitro phenol
(b) Paranitro phenol
(c) Mixture of ortho and para nitro phenol
(d) Meta nitro phenol

108. What is the reactivity order of SN_2 reaction?
(a) Primary > secondary > tertiary
(b) Secondary > primary > tertiary
(c) Tertiary > secondary > primary
(d) Tertiary > secondary > primary > methane

109. What is the reactivity order of E_1 reaction?
(a) Primary > secondary > tertiary > methane
(b) Secondary > primary > tertiary
(c) Primary > secondary > tertiary
(d) Tertiary > secondary > primary

110. Which test is used to differentiate primary, secondary and tertiary amines?
(a) Hinsberg's test (b) Carboline test
(c) Osazone test (d) Hydroxylamine test

111. "Only two electrons can occupy any atomic orbital" Which principle is this?
(a) Aufbau's principle
(b) Pauli's principle
(c) Hund's principle
(d) None of the above

112. The compound that is not a Lewis acid is:
(a) BF_3 (b) $AICI_3$
(c) $BeCI_2$ (d) $SnCl_4$

113. Which aldehyde undergoes Cannizzaro reaction?
(a) Acetaldehyde (b) Benzaldehyde
(c) Formaldehyde (d) Propionaldehyde

114. What is the degree of unsaturation of compound with formula $C_3H_6O_2$?
(a) 0 (b) 3
(c) 1 (d) 2

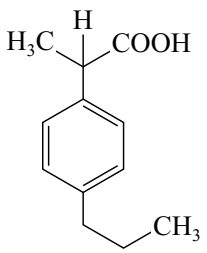
115. In nitration of the aromatic compounds the nitrating species is
(a) NO^- (b) NO_2^+
(c) NO_3 (d) NO

116. The pyrolysis of alkanes present in petroleum is known as?
(a) Thermal cracking
(b) Cracking
(c) Combustion
(d) None of the above

117. Bayer's reagent is?
(a) $KMnO_4$ (b) $K_2Cr_2O_7$
(c) $NaNO_2$ + HCl (d) HNO_3 15: $2Cr_2O_7$

118. Which of the following would not be a reasonable neucleophile in a SN_2 reaction?
(a) NH_3 (b) NC^-
(c) H_2O (d) HO^-

119. How many isomers does above compound will have?

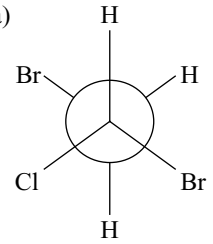


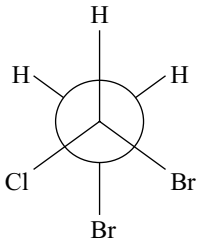
(a) 4 (b) 1
(c) 3 (d) 2

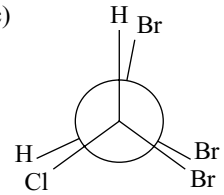
120. Different arrangements of atoms that can be converted into one another by rotation about single bonds are?
(a) Enantiomer (b) Diastereomer
(c) Conformations (d) Configuration

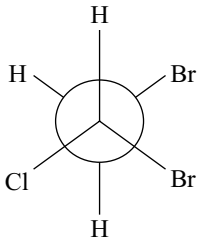
121. Dipole movement between two atoms is mainly
(a) Because of sharing of bonding electron pairs not equal
(b) Due to steric hindrance
(c) Because of change in polyhedral bonds
(d) None of the above

122. Which Newman projection shows the most stable conformation of the following compound?

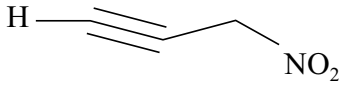
(a)


(b)


(c)


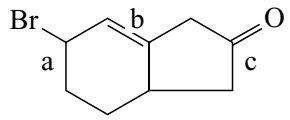
(d)


123. What is the total number of pi bonds found in the following compound?



(a) 1
(b) 2
(c) 3
(d) 4

124. Which of the functional groups on the following molecule are susceptible to nucleophilic attack?



(a) a
(b) b
(c) c
(d) a and c

125. Each member of the alkane series differs from the preceding member by one additional carbon atom and
(a) 1 hydrogen atom
(b) 2 hydrogen atoms
(c) 3 hydrogen atoms
(d) 4 hydrogen atoms

ANSWER KEYS

1. (a)	**2.** (b)	**3.** (d)	**4.** (c)	**5.** (a)	**6.** (b)	**7.** (c)	**8.** (b)	**9.** (a)	**10.** (b)
11. (a)	**12.** (a)	**13.** (a)	**14.** (a)	**15.** (d)	**16.** (d)	**17.** (d)	**18.** (b)	**19.** (c)	**20.** (d)
21. (c)	**22.** (c)	**23.** (b)	**24.** (a)	**25.** (c)	**26.** (b)	**27.** (d)	**28.** (b)	**29.** (a)	**30.** (a)
31. (b)	**32.** (a)	**33.** (a)	**34.** (b)	**35.** (d)	**36.** (a)	**37.** (b)	**38.** (d)	**39.** (b)	**40.** (d)
41. (c)	**42.** (c)	**43.** (d)	**44.** (a)	**45.** (b)	**46.** (d)	**47.** (b)	**48.** (c)	**49.** (b)	**50.** (b)
51. (c)	**52.** (c)	**53.** (a)	**54.** (c)	**55.** (b)	**56.** (b)	**57.** (b)	**58.** (a)	**59.** (a)	**60.** (d)
61. (a)	**62.** (b)	**63.** (a)	**64.** (a)	**65.** (d)	**66.** (b)	**67.** (a)	**68.** (d)	**69.** (b)	**70.** (d)
71. (b)	**72.** (a)	**73.** (c)	**74.** (a)	**75.** (a)	**76.** (a)	**77.** (a)	**78.** (a)	**79.** (b)	**80.** (c)
81. (b)	**82.** (d)	**83.** (a)	**84.** (d)	**85.** (a)	**86.** (c)	**87.** (a)	**88.** (a)	**89.** (d)	**90.** (c)
91. (d)	**92.** (a)	**93.** (b)	**94.** (c)	**95.** (b)	**96.** (b)	**97.** (a)	**98.** (c)	**99.** (c)	**100.** (d)
101. (d)	**102.** (a)	**103.** (c)	**104.** (a)	**105.** (c)	**106.** (d)	**107.** (c)	**108.** (a)	**109.** (d)	**110.** (a)
111. (b)	**112.** (c)	**113.** (b)	**114.** (c)	**115.** (b)	**116.** (b)	**117.** (a)	**118.** (c)	**119.** (b)	**120.** (c)
121. (a)	**122.** (a)	**123.** (c)	**124.** (d)	**125.** (b)					

CHAPTER 3

ANALYTICAL CHEMISTRY

PHARMACEUTICAL ANALYSIS

Electromagnetic Radiation

Electromagnetic (EM) radiation is a periodically changing or oscillating electric field propagating in a certain direction with a magnetic field oscillating at the same frequency but perpendicular to the electric field.

EM radiation may be considered as a travelling wave or as a stream of massless elementary particles, often called **photons.**

Characteristics of wave

- **Wavelength** λ (the length of one wave)
  - Expressed in nm/ A°/μm
- **Frequency** ν **(**the number of waves per unit time)
  - Expressed in cycle per second (cps)/Hertz/Fresnel
  - V = c/λ = c * wave number
- **Wave number *k*** (the number of waves per unit length)
  - Wave number =1/λ
  - Expressed in cm^{-1} or Kaiser

Max-Plank Equation

$$E = h\nu = h\,c/\lambda$$

Where E is energy of photon

ν is frequency of EM radiation = c/λ hence ν is inversly proportional to λ

h is Plank constant (6.6×10^{-27} erg-sec)

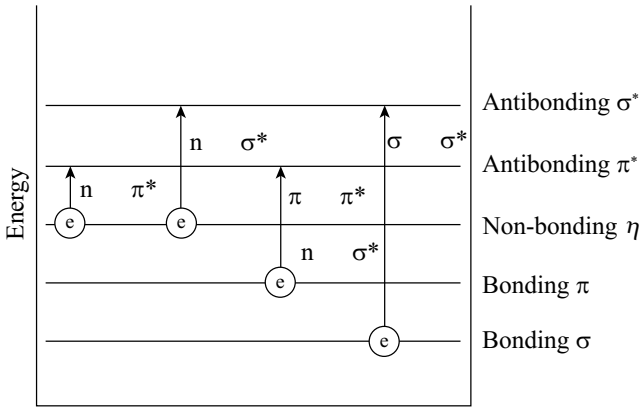
c is velocity of light

λ is wavelength of EM radiation

UV-Visible Spectroscopy (Electronic Spectroscopy)

Basic principle Valence shell electronic transition.

Graph Plotted between absorbance and wavelength.



Energy value order for transition

$$n \rightarrow \varpi^* < n \rightarrow \sigma^* < \varpi \rightarrow \varpi^* < \sigma \rightarrow \sigma^*$$

Transition probablity

1. Allowed–extinction coefficient value 10^4 or greater
2. Forbidden–extinction coefficient value 10^2 or less

Absorption band

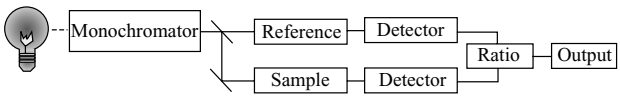
1. K band–due to $\varpi \rightarrow \varpi^*$ transition
2. R band–due to $n \rightarrow \varpi^*$ transition

Cut-off wavelength Above which solvent behaves as transparent

Methanol	210 nm	Hexane	199 nm	Water	190 nm	Diethyl ether	205 nm
Ethanol	207 nm	Benzene	280 nm	Heptane	200 nm	THF	220 nm
Chloroform	247 nm	Carbon tetrachloride	257 nm	Acetone	331 nm	Dichloromethane	233 nm

Instrumentation

1. Sources (UV and visible)
2. Wavelength selector (monochromator)
3. Sample containers
4. Detector
5. Signal processor and readout



- Most widely used radiation source in UV deuterium discharge lamp and in visible tungsten halogen lamp.
- Most widely used detector in UV-visible spectroscopy is PMT (photo multiplier tube).

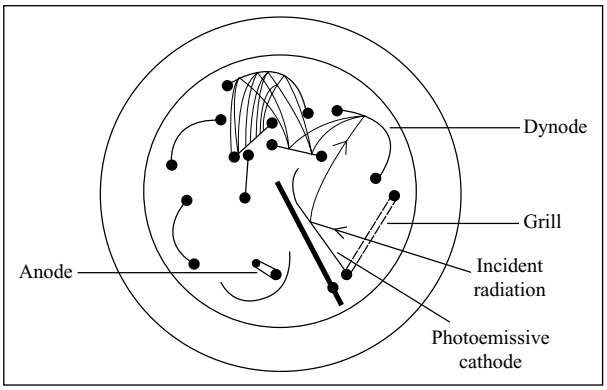


Figure 3.1 UV-Visible Spectroscopy

Wavelength selector

- It should provide narrow band of radiation and maximum throughput.
- Wavelength isolation can be done using filter, monochromator and interferometer.

Filter A wavelength selector that uses either absorption, or constructive and destructive interference to control range of selected wavelength.

A. Absorption Filter Narrow effective bandwidth 30 to 250 nm and Maximum throughput 10%.

B. Interference Filter Narrow effective bandwidth 10 to 20 nm and Maximum throughput 40%.

Monochromator

A wavelength selector that uses diffraction grating or prism, and that allows continuous variation of nominal wavelength.

Advantages of monochromator over filter

1. It provide continuous variation of nominal wavelength.
2. Provides narrow effective bandwidth with increased output.

Construction of monochromator

1. Entrance slit
2. Collimating mirror (Provide parallel beam of radiation to prism or grating)
3. Diffracting grating
4. Focussing mirror
5. Exit slit

Basically, monochromator converts polychromatic light (EM radiation of more than one wavelength) into monochromatic light (EM **radiation** of single wavelength).

Interferometer

Instead of filtering or dispersing the EM radiation, it simultaneously allows source radiation of all wavelengths to reach detector.

Construction of interferometer

1. Fixed mirror
2. Moving mirror
3. Beam splitter (Transmit half of the radiation to fixed mirror and half of the radiation (which are reflected) to movable mirror). It is a semi reflecting device and made up of silicon or germanium coated on metal halide plate.

Isobestic point common point to every absorption curve which is obtained in the spectrum of compound taken at different pH.

IR Spectroscopy

Basic principle Vibrational level changes

Graph Plotted between % transmittance and wave number.

Selection rule in IR

Only those compounds are IR active which show change in dipole moment upon interaction with IR radiation.

Fundamental frequency of Vibration $\gamma = 1/2\varpi * (K/\mu)^{1/2}$

Region	Wavelength range (Micron)	Wavenumber range (cm^{-1})
Near/Harmonic/Overtone	0.78–2.5	12800–4000
Middle/Fundamental	2.5–50	4000–200
Far/Rotational	50–1000	200–10

Bending Change in angle between two bonds. There are four types of bends:

- Rocking
- Scissoring
- Wagging
- Twisting

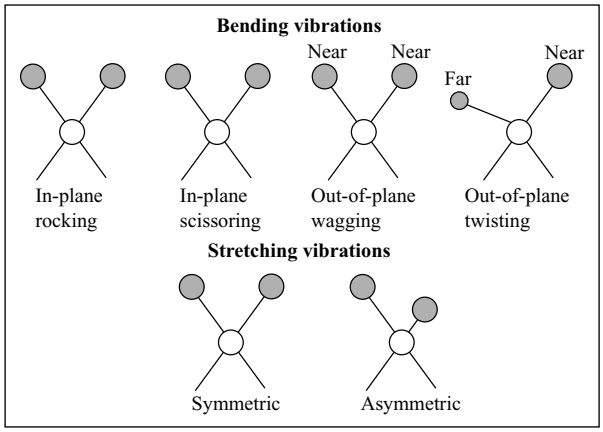


Figure 3.2 Types of Bending and Stretching Vibrations

Factors affecting vibration frequency

1. Nature of bond present
2. Masses of atoms
3. Force constant of bond
4. Electronic effect
5. Bond angle
6. Hydrogen bonding
7. Symmetry of molecule

Type of degree of freedom	Linear	Non-linear
Transitional	3	3
Rotational	2	3
Vibrational	3N-5	3N-6
Total	3N	3N

Finger print region

1. 8 μ to 16 μ or 1500 cm^{-1} to 500 cm^{-1}
2. Absorption is unique and complex.

Fermi resonance

Energy of harmonic or overtone region coincides with fundamental mode of vibration. Instead of one band, two bands of almost equal intensity results. It is normally observed in carbonyl compounds.

Sampling techniques

1. Mull technique

Nujol (mineral oil) is a mixture of paraffin hydrocarbons. To avoid Nujols band in spectrum sometimes hexachlorobutadiene or chlorofluorocarbon oil is added.

2. Pressed pellet/KBr

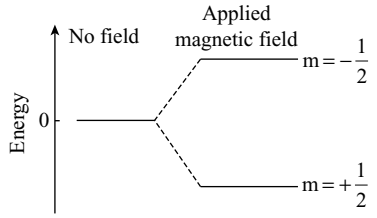
KBr is used 100 times to sample quantity. This technique can be used for quantitative analysis.

NMR Spectroscopy

Basic principle Nuclear spin changes.

Nuclear-zeeman effect Splitting of nuclei spin state in applied external magnetic field.

Energy levels for a nucleus with spin quantum number 1/2



Larmor equation It is fundamental equation of NMR spectroscopy.

W (Angular Precessional Frequency) = γH

$$2\varpi v = \gamma H$$

Precessional frequency (v) = $\gamma/2\varpi$

where H = Applied magnetic field

γ = Magnogyretic ratio or Gyromagnetic ratio = $2\varpi\mu/hI$

where h is Plank constant and I is Spin Quantum Number. μ is Magnetic moment of spinning nuclei.

Magnetic moment = γ * Spin angular moment ($h/2\varpi$ * spin quantum number I)

Note only those Nuclei show NMR absorption signal having spin quantum number (I) greater or equals to ½.

1. If the number of neutrons **and** the number of protons are both even, then the nucleus has **no** spin.
2. If the number of neutrons **plus** the number of protons is odd, then the nucleus has a half-integer spin (i.e., 1/2, 3/2, 5/2)
3. If the number of neutrons **and** the number of protons are both odd, then the nucleus has an integer spin (i.e., 1, 2, 3)

Element	H^1	H^2	C^{12}	C^{13}	N^{14}	O^{16}	O^{17}	P^{31}	Cl^{35}	F^{19}
Spin quantum number (I)	1/2	1	0	1/2	1	0	5/2	1/2	3/2	1/2
No. of spin states (2I + 1)	2	3	1	2	3	1	6	2	4	2

Nucleus	Spin (I)	Natural Abundance/%	Magnetogyric Ratio (γ) /10^7 $kg^{-1}{\cdot}s{\cdot}A$	Relative Frequency (ν) /MHz
^1H	1/2	99.985	26.752196	100.00
^2H	1	0.015	4.106625	15.35
^{13}C	1/2	1.10	6.72828	25.15
^{15}N	1/2	0.366	–2.712621	10.14
^{17}O	5/2	0.037	–3.62808	13.56
^{19}F	1/2	100.0	25.18147	94.13
^{29}Si	1/2	4.67	–5.319	19.88
^{31}P	1/2	100.0	10.8394	40.52
^{119}Sn	1/2	8.58	–10.0318	37.27

Population Densities of Nuclear Spin States

Saturation of signal If population densities of upper and lower spin states becomes exactly equals then we observe no net signal. This is called saturation of signal. Saturation of signal can be achieved by intense RF signal.

Saturation should be avoided in during NMR experiment.

Boltzmann distribution

In the presence of an external magnetic field, different m_I nuclear spin states have different energies. At thermal equilibrium, they will also have different populations according to the Boltzmann equation

$$\frac{N_{high}}{N_{low}} = e^{-\Delta E/kT} = \frac{1}{e^{-\Delta E/kT}}$$

where N_{high} and N_{low} are the populations of the upper and lower states respectively, $\Delta E = E_{high} - E_{low}$ is the energy difference between the two states, k is the Boltzmann constant, and T is the absolute temperature.

Relaxation Processes

It is the process by which nuclei undergo (return back) from higher energy state to the lower state.

Ideally, Relaxation rates to be fast–but not too fast. If the relaxation rate is fast, then saturation is reduced. If the relaxation rate is too fast, line-broadening in the resultant NMR spectrum is observed.

There are two major relaxation processes:

- Spin-lattice (longitudinal) relaxation
- Spin-spin (transverse) relaxation

Spin-lattice-relaxation

Nuclei in an NMR experiment are in a sample. The sample in which the nuclei are held is called the *lattice*. Nuclei in the lattice are in vibrational and rotational motion, which creates a complex magnetic field. The magnetic field caused by motion of nuclei within the lattice is called the *lattice field*. This lattice field has many components. Some of these components will be equal in frequency and phase to the Larmor frequency of the nuclei of interest. These components of the lattice field can interact with nuclei in the higher energy state, and cause them to lose energy (returning to the lower state). The energy that a nucleus loses increases the amount of vibration and rotation within the lattice (resulting in a tiny rise in the temperature of the sample).

Spin-spin-relaxation

Spin-spin relaxation describes the interaction between neighbouring nuclei with identical precessional frequencies but differing magnetic quantum states. In this situation, the

nuclei can exchange quantum states; a nucleus in the lower energy level will be excited, while the excited nucleus relaxes to the lower energy state. There is no **net** change in the populations of the energy states, but the average lifetime of a nucleus in the excited state will decrease. This can result in line-broadening.

Chemical shift It is a dimensionless quantity and does not depends on applied external field. It is expressed in parts per million (ppm).

δ = Frequency shift (In Hz) X 10^6/Operating frequency (MHz)

Reference for measurement of chemical shift

TMS (tetra methyl silane) is used as reference in proton NMR. Because

1. TMS has 12 equivalent protons
2. Chemically inert and very low B.P.
3. Miscible with all organic substances
4. Electron negativity of silicon is very low so shielding of protons in TMS are most shielded compared to other organic compounds.

TMS is not soluble in aqueous solution hence 2,2 dimethyl-2-2-silapentane-5-sulphonate.

Shift reagent These are paramagnetic substances used to spread the NMR absorption pattern without increasing the magnetic field strength.

Example-Lanthanide Fluorinated β-di ketones

Splitting of signal

- The multiplicity of a multiplet is given by the number of equivalent **protons** in **neighbouring** atoms plus one, i.e., *the n + 1 rule*
- Equivalent nuclei do not interact with each other.

Type of Multiplet	Relative Intensity	No. of Vicinal Protons
Doublet	1:1	1
Triplet	1:2:1	2
Quartet	1:3:3:1	3
Quintet (Pentet)	1:4:6:4:1	4
Sextet	1:5:10:10:5:1	5

Coupling constant (J)

- Distance of centre of peaks in a given multiplet. It is expressed in Hz or cycle per second.
- Normal range 0–20. Ratio of J for trans to cis alkene is approximately 2.

- **Chemical shift equivalent protons**-Nuclei having identical chemical shift.
- **Magnetically equivalent protons**-Nuclei having identical coupling constant.

NMR instrumentation

1. **Magnet-**To provide magnetic field

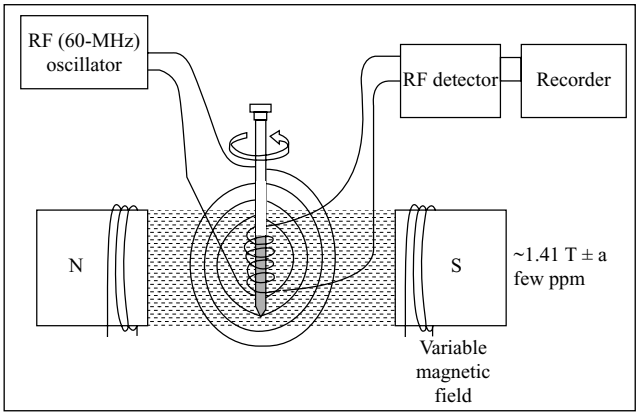


Figure 3.3 NMR instrumentation

2. **Sweep generator**–To vary the field strength. There are two methods, one is field sweep another is frequency sweep method.
3. **Rf transmitter**–To provide Rf radiation for NMR phenomenon
4. **Rf receiver**

Magnet

Earlier, NMR magnets were iron core permanent or electromagnets producing magnetic fields of less than 1.5 T. Today, most NMR magnets are of the superconducting type. Superconducting NMR magnets range in field strength from approximately 6 to 23.5 T.

A superconducting magnet has an electromagnet made of superconducting wire. Superconducting wire has a resistance approximately equal to zero when it is cooled to a temperature close to absolute zero (–273.15° C or 0 K) by immersing it in liquid helium. Once current is caused to flow in the coil, it will continue to flow for as long as the coil is kept at liquid helium temperatures.

The superconducting elements of the wire are made of $(NbTaTi)_3Sn$. This material is brittle and therefore is embedded in copper for strength. The Cu has a high resistance compared to the superconductor which is carrying the current.

This wire is wound into a multi-turn solenoid or coil. The coil of wire is kept at a temperature of 4.2K or less by immersing it in liquid helium. The coil and liquid helium are kept in a large dewar. This dewar is typically surrounded

by a liquid nitrogen (77.4K) dewar, which acts as a thermal buffer between the room temperature air (293K) and the liquid helium.

There is a vacuum region followed by a liquid nitrogen reservoir. The vacuum region is filled with several layers of a reflective mylar film. The function of the mylar is to reflect thermal photons, and thus diminish heat from entering the magnet.

Shim Coils

The purpose of shim coils on a spectrometer is to correct minor spatial inhomogeneities in the B_o magnetic field. These inhomogeneities could be caused by the magnet design, materials in the probe, and variations in the thickness of the sample tube, sample permeability, and ferromagnetic materials around the magnet. A shim coil is designed to create a small magnetic field which will oppose and cancel out an inhomogeneity in the B_o magnetic field.

Shim Coil function: by passing the appropriate amount of current through each coil, a homogeneous B_o magnetic field can be achieved.

Sample Probe

The sample probe is the name given to that part of the spectrometer which accepts the sample, sends RF energy into the sample, and detects the signal emanating from the sample. It contains the RF coil, sample spinner, temperature controlling circuitry, and gradient coils.

The purpose of the sample spinner is to rotate the NMR sample tube about its axis. In doing so, each spin in the sample located at a given position along the Z axis and radius from the Z axis, will experience the average magnetic field in the circle defined by this Z and radius. The net effect is a narrower spectral linewidth.

RF Coils

RF coils create the B_1 field which rotates the net magnetization in a pulse sequence. They also detect the transverse magnetization as it precesses in the XY plane.

Most RF coils on NMR spectrometers are of the saddle coil design and act as the transmitter of the B_1 field and receiver of RF energy from the sample. You may find one or more RF coils in a probe.

Chemical Shift Equivalence

If a set of nuclei exists in identical environments, they are expected to have the same chemical shift. Such nuclei are called chemical shift equivalent or chemically equivalent.

Pair of nuclei in a molecule is chemically equivalent if they are **interchangeable** through any symmetry operation of the molecule OR if they interchange by a rapid process (rapid with respect to the NMR timescale).

If a pair of nuclei can be interchanged by rotation about an axis of symmetry of the molecule, then they are chemically equivalent and are called homotopic. E.g., the pair of protons in dichloromethane are chemically equivalent.

If a pair of nuclei can be interchanged by an improper rotational symmetry operation of the molecule, then they are chemically equivalent and are called enantiotopic. E.g., pair of protons attached to the alpha-Carbon in glycine amino acid (they are not chemically equivalent if glycine is part of a polypeptide chain).

If a pair of geminal protons (CH_2) cannot be interchanged through a symmetry operation of the molecule, then these protons are diastereotopic and are not chemically equivalent. E.g., the β-methylene protons of amino acids where the methylene group is attached to chiral Cα atom.

Chemical shift equivalence by rapid interconversion of structures may occur due to rapid rotation about bonds or due the rapid chemical changes such as keto-enol tautomerism.

Magnetic Equivalence (Spin Coupling Equivalence)

If in a set of chemically equivalent nuclei, each member of the set has exactly the same interaction (J-coupling) to every other magnetically active nucleus in the molecule, then the nuclei are also magnetically equivalent. E.g., the pair of protons in dichloromethane are chemically as well as magnetically equivalent.

A set of nuclei that are magnetically equivalent will also be chemically equivalent; however, chemical equivalence does not guarantee magnetic equivalence. e.g., the two protons ortho to hydroxy group in tyrosine are chemically equivalent but they are not magnetically equivalent.

Nuclear Overhauser Effect (NOE)

Nuclear Overhauser Effect (NOE) is the transfer of nuclear spin polarization from one nuclear spin population to another via cross-relaxation.

When a proton is saturated or inverted, spatially-close protons may experience an intensity enhancement, which is termed the Nuclear Overhauser Effect (NOE). The NOE is unique among NMR methods because it does not depend upon through-bond J couplings but depends only on the spatial proximity between protons. In other words, the strength of the NOE gives information on how close two protons are. For small molecules, an NOE may be observed between protons that are up to 4Å apart, while the upper limit for large molecules is about 5Å.

The NOE differs from the application of spin-spin coupling in that the NOE occurs through space, not through chemical bonds. Thus, atoms that are in close proximity to each other can give a NOE, whereas spin coupling is observed only when the atoms are connected by 2-3 chemical bonds. The inter-atomic distances derived from the observed NOE can often help to confirm a precise molecular conformation, i.e., the three-dimensional structure of a molecule.

Magic Angle NMR

In nuclear magnetic resonance, **magic angle spinning** (MAS) is a technique often used to perform experiments in solid-state NMR spectroscopy.

By spinning the sample (usually at a frequency of 1 to 70 kHz) at the magic angle θ_m (ca. 54.74°, where $\cos^2\theta_m = 1/3$) with respect to the direction of the magnetic field, the normally broad lines become narrower, increasing the resolution for better identification and analysis of the spectrum.

In any condensed phase, a nuclear spin experiences a great number of interactions. The main three interactions (dipolar, chemical shift anisotropy, quadrupolar) often lead to very broad and featureless lines. However, these three interactions in solids are time-dependent and can be averaged by MAS.

Shielding

All atoms in a molecule are surrounded by electrons that occupy core and valence orbitals. The permanent magnetic field $\vec{\beta}_0$ induces a current in the surrounding electrons, which in turn generates an induced magnetic field $\vec{\beta}_{ind}$. According to Lenz's Law, the induced field is proportional to the permanent magnetic field but is opposite in direction.

In general, the amount of shielding is proportional to the local electron density, i.e., higher electron density causes more shielding and results a lower Larmor frequency. However, it is possible for some chemical groups with circular πelectron systems, most notably aromatic rings and triple bonds, to cause induce chemical shifts which are not the same for all orientations in space, a phenomenon known as chemical shift anisotropy.

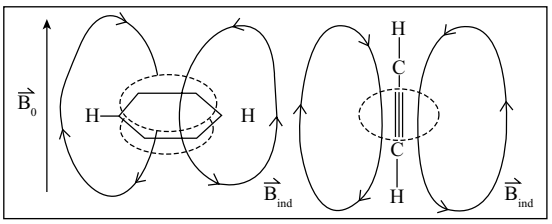


Figure 3.4 Shielding

Mass Spectroscopy

Basic principle

Molecules are bombarded with high energetic electron beam, positive ion fragments are sorted out depending upon their m/z ratio. (No EM radiation used)

Graph Plotted between Relative Abundance and m/z.

Mass Spectrometer	Sorting out mechanism
Conventional MS	Energy and momentum
Time of Flight (TOF) MS	Energy and Velocity
FT-MS	Momentum and Velocity

Ionization mode in MS

A. Gas Phase

1. Electron impact ionization (Unimolecular)–Tungsten filament (50–80 ev) used as electron source.
2. Chemical mode (Bi molecular)–Methane (mostly used gas), Isobutane, Ammonia and inert gases (He, N_2 Ar_2).

B. Desorption/Condensed Phase

1. Field desorption or Laser desorption
2. Plasma desorption or californium fission fragments
3. FAB (Fast Atom Bombardment)–Solvent used is Glycerol

   Argon gas ionized ⟶ $Ar^{+\cdot}$ ions are accelerated ↓ Again strike to argon gas (Ar) ⟵ Accelerated Ar molecule ↓ Strike to sample dissolved in polar solvent E.g., Glycerol ↓ Fragmentation of sample result.
4. Electron Spray Ionization (ESI)

Sorting out system or sector analyser

1. **Magnetic Sector Analyser**

   $m/z = H^2 r^2/2V$

   Where, H is magnetic field strength
   r is ion tranjectory
   V is applied Voltage
2. **TOF analyser**

   Ions are allowed to travel in a field free path, each ion will take different time to travel a particular distance

depending upon their m/z ratio. This time is known as time of flight.

3. **Quadruple analyser**
   Both TOF and Quadruple analysers are used in interfacing with GC.

Detector system in MS Electron multiplier tube

Types of peak in MS

1. **Molecular ion or Parent peak**–Comes at molecular weight of compound. Peaks at M+1 and M+2 are due to isotopic abundance.
   Relative intensity ratio for Br and Cl form and M+2 are 1:1 and 1:3 respectively.
2. **Base Peak**
   (a) It is considered as 100%
   (b) Most abundant peak
3. **Metastable peak**

   M^+ (Origional ion) $\longrightarrow$ N^+ (daughter ion) + Z (Neutral molecule)
   Meta stable peak $M^* = (N^+)^2/M^+$

   (a) arise due to decomposition of ions in field free path
   (b) appears as weak, diffuse (humped shape) and at non-integral mass
   (c) relative low abundance and broader peak

Maclafferty rearrangement

Migration of γ-hydrogen followed by β bond cleavage and elimination of ethylene or substituted ethylene neutral molecule.

Instrumentation of Mass spectrometer

1. Sample inlet system
2. Molecular leak–It is pin-hole restriction (0.01 to 0.05 mm diameter) and made up of gold foil. It is used for metering the sample to ionization chamber.
3. Ionization Chamber
4. Ion separation (Sector analyser)
5. Ion collector (Detector)

Recorder 5 separated galvanometers can be used to record simultaneously, the peaks for fragment ions and parent ions.

Nitrogen Rule It states that organic compound having:

1. an even integral molecular weight must contains either none or even number of nitrogen atoms.
2. odd molecular weight must contain odd number of nitrogen atoms.

NOTE

- Operation of Mass spectrometer requires a collision free path for ions to prevent arching due to high voltage and to avoid recombination of fragmented ions.
- For this, Vacuum Systems are used.
- Vacuum in 1. Ionization Source (10^{-5} to 10^{-6} torr) 2. Sector Analyser (10^{-6} to 10^{-7} torr)

Luminescence

Luminescence is the emission of light by a substance. It occurs when an electron returns to the electronic ground state from an excited state and loses its excess energy as a photon.

Luminescence spectroscopy is a collective name given to *three* related spectroscopic techniques. They are:

- Molecular fluorescence spectroscopy
- Molecular phosphorescence spectroscopy
- Chemiluminescence spectroscopy

Fluorescence and phosphorescence (photoluminescence)

The electronic states of most organic molecules can be divided into *singlet* states and *triplet* states.

Singlet state All electrons in the molecule are spin-paired

Triplet state One set of electron spins is unpaired.

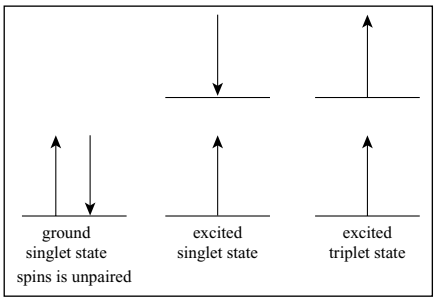


Figure 3.5 Triple Set

Fluorescence

Absorption of UV radiation by a molecule excites it from a vibrational level in the electronic ground state to one of the

many vibrational levels in the electronic excited state. This excited state is usually the first excited *singlet* state.

A molecule in a high vibrational level of the excited state will quickly fall to the lowest vibrational level of this state by losing energy to other molecules through collision.

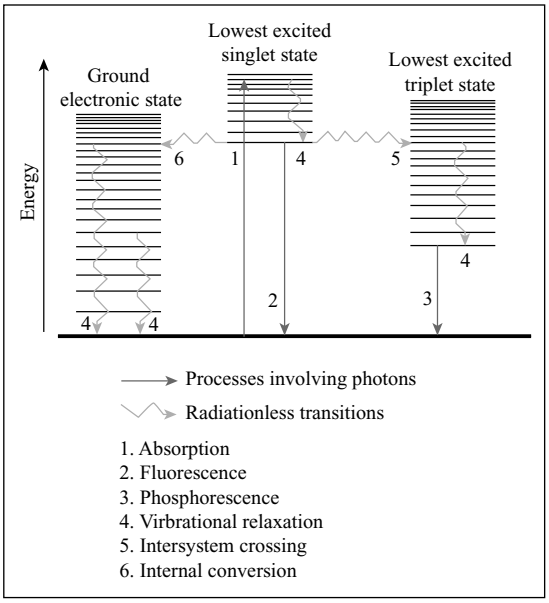


Figure 3.6 Possible physical process following absorption of a photon by a molecule

Phosphorescence

A molecule in the excited triplet state may not always use intersystem crossing to return to the ground state. It could lose energy by emission of a photon. A triplet/ singlet transition is much less probable than a singlet/singlet transition. The lifetime of the excited triplet state can be up to 10 seconds, in comparison with 10^{-5} s to 10^{-8} s average lifetime of an excited singlet state. Emission from triplet/singlet transitions can continue after initial irradiation. Internal conversion and other radiationless transfers of energy compete so successfully with phosphorescence that it is usually seen only at low temperatures or in highly viscous media.

Chemiluminescence

Chemiluminescence occurs when a chemical reaction produces an electronically excited species which emits a photon in order to reach the ground state. These sort of reactions can be encountered in biological systems; the effect is then known as *bioluminescence*. The number of chemical reactions which produce chemiluminescence is small. A good example of chemiluminescence is the determination of nitric oxide:

$$NO + O_3 \rightarrow NO_2^* + O_2$$
$$NO_2^* \rightarrow NO_2 + h\nu \quad (\ell = 600\text{–}2800\ \text{nm})$$

Jablonski Diagram (Relaxation Mechanism for Excited State Molecules)

Once a molecule has absorbed energy in the form of electromagnetic radiation, there are a number of routes by which it can return to ground state (the statistically most common energy state for room temperature chemical species). The following graphic, termed a Jablonski diagram, shows a few of these processes.

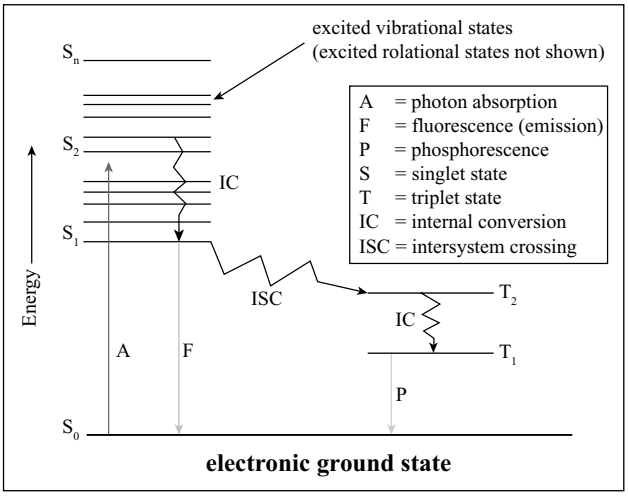


Figure 3.7 Jablonski Diagram

If the photon emission occurs between states of the same spin state, (e.g., S_1 ---> S_0) this is termed fluorescence.

If the spin state of the initial and final energy levels are different (e.g., T_1 --> S_0), the emission (loss of energy) is called phosphorescence.

Since fluorescence is statistically much more likely than phosphorescence for most molecules, the lifetimes of fluorescent states are very short (1×10^{-5} to 10^{-8} seconds) and phosphorescence somewhat longer (1×10^{-4} seconds to minutes or even hours).

Three non-radiative deactivation processes are also significant here: internal conversion (IC), intersystem crossing (ISC) and vibrational relaxation.

Internal conversion is the **radiation less** transition between energy states of the same spin state (compare with fluorescence-a radiative process).

Intersystem crossing is a radiationless transition between different spin states (compare to phosphorescence).

Vibrational relaxation, the most common of the three—for most molecules, occurs very quickly (<1×10^{-12} seconds) and is enhanced by physical contact of an excited molecule

with other particles with which energy, in the form of vibrations and rotations, can be transferred through collisions. This means that most excited state molecules never emit any energy because in liquid samples the solvent or, in gas phase samples, other gas phase molecules that are present "steal" the energy before other deactivation processes can occur.

Fluorescence (fluorimetry) and phosphorescence (phosphorimetry)

Absorption followed by emission i.e., $\lambda_{emitted} > \lambda_{incident}$

Fluorescence	Phosphorescence
Average life time of electron in excited state is 10^{-5}–10^{-8} sec. Decay rapidly after excitation source is removed.	Average life time for phosphorescence ranges from 10^{-4}–10^{4} sec. Phosphorescence may continue for sometime after removing excitation source.
No change in spin state Excited singlet state (Multiplicity = 1)	Change in spin state Excited triplet state (Multiplicity = 3)
⇑	⇑
Ground state (Multiplicity=1)	Ground state (Multiplicity=1)
Fluorescence spectrum is a mirror image	Not a mirror image because excited triplet energy levels lies lower than corresponding excited singlet level

Factor affecting fluorescence and phosphorescence

1. Nature of molecule
2. Nature of substitutents
   a. **Substituents that delocalize the ϖ electrons such as $-NH_2$, –OH, –OR etc., enhance the fluorescence.**
   b. **Substituents which withdraw electrons such as $-NO_2$, –Cl, –Br etc., quench the fluorescence.**
3. Rigidity of molecule
4. Viscosity
5. Temperature
6. pH

X-ray Diffraction

Basic principle Inner shell electron transition

K_α line (transition from shell L to Shell K)
K_β line (transition from shell M to Shell K)
K_γ line (transition from shell N to Shell K)

Target material used Co, Ni, Cu, Mn, Mo etc.

Brag's equation

$$n\lambda = 2d \sin\theta$$

Where
n = order of diffraction
d = lattice spacing or inter planner distance
θ = angle between direction of incident beam and that of diffracted beam

NOTE

Diffraction from crystal is only possible when λ is equal to or less than d.

Detectors

1. Photographic film method
2. Counter method
   (a) Geiger-muller tube
   (b) Proportional counter
   (c) Scintillation detector
   (d) Solid state semiconductor

Nephelometry	Turbidimetry
1. Intensity of scattered light measured as a function of concentration of dispersed phase	1. Intensity of transmitted light measured as a function of concentration of dispersed phase
2. Most suitable for dilute suspension	2. Most suitable for concentrated suspension
3. Similar to fluorimetry because both measure scattered radiations but elastic scattering in fluorimetry while non-elastic scattering in nephelometry.	3. Similar to colorimetry because both measure transmitted radiations but light intensity decreased by scattering in turbidimetry while by absorption in colorimetry.

Flame Photometry (Flame Emission Spectroscopy)

1. Mainly used for Alkali metal like Li, Na, K and Alkali earth metals like Mg, Ca, Ba, Sr**.**
2. **Principle**
   Nebulization (breakdown of liquid into smaller droplets) → Evaporation → Atomization in Flame → Excitation followed by Emission

Electro Analytical Methods

1. Conductometry

Conductivity cell

1. Made up of Pyrex glass and Quartz
2. Two platinum electrode system: To avoid polarization, Pt electrodes are coated with Pt black (Chloro platinic acid and lead acetate mixture).
3. Cell constant (x=specific conductivity/observed conductivity) is determined using N/50 KCl.

Specific conductance

- Conductivity offered by 1 ml or cm^3 solution.
- It is the reciprocal of specific resistance (ρ). It has unit ohm^{-1} cm^{-1} or mho cm^{-1}

$$\Pi = 1/\rho = 1/R * L/A$$

$$= \text{Conductance} * \text{cell constant } (L/A)$$

$$\pi_{eq} = \Pi(\text{Specific conductance}) * V \text{ (dilution)}$$

K decreases but there is much greater increment in V hence overall equivalent conductance increases.

2. Potentiometry

Nernst equation

$$E = E^0\text{-}RT/nF \log_e (P)/(R)$$

Where E = electrode potential of the cell

E^0 = standard electrode potential

n = No. of electron consumed in 1 mol oxidation or reduction of electro active species

(P), (R) = product and reactant concentration

3. Polargraphy

1. **Polarogram**–Graph between current and applied voltage
2. **Polarograph**–Apparatus used for polarography
3. **Residual/Charging/Capacitance current =** Faradic current (due to impurity) + Condenser current (due to supporting electrolyte)
4. **Electrode system:**
   a. **Indicator/Working electrode–DME (dropping mercury electrode)**
   b. **Reference electrode–Large mercury pool**

   Supporting Electrolyte
   a. It neither reacts with material under investigation nor with DME. It has higher discharge potential compared to material under investigation.
   b. Quantity of supporting electrolyte taken as 100 times to material.
   c. It carries almost all the current of the solution and raise the conductivity of the solution, thus suppress the migration current.
5. **Ilkovic equation** $\mathbf{I_d = 607\ n\ CD^{1/2}\ m^{2/3}\ t^{1/6}}$
   I_d = Diffusion current = Limiting current–residual current
   D = diffusion coefficient
   C = concentration
   m = flow rate of mercury from DME
   t = drop time
6. **Half wave potential ($E^{1/2}$)**
   Potential corresponding to point of inflexion of polar graphic wave. It is a characteristic of nature of reacting material.
7. **Polar graphic Maxima-**Developed due to streaming movement of diffusion layer at interface.
8. **Maxima suppressor**
   Gelatin (0.002–0.01 %) and triton-x-100 (0.02–0.01 %) are used as maxima suppressor.

Special Note

1. **Salt Bridge–**It is made up of inert, hot, concentrated, aqueous solution of KCl, KNO_3, NH_4NO_3 in gelatine or agar-agar solution. Only those salts can be used in preparation of Salt bridge formation which have equal cations and anions mobility.
2. Saturated KCl solution mostly used compared to molar or decimolar solution in the preparation of reference electrodes because it minimize the liquid-liquid junction potential.

Chromatography

Chromatography terms

- **Analytical chromatography** is used to determine the existence and possibly also the concentration of analyte (s) in a sample.
- **Preparative chromatography** is used to purify sufficient quantities of a substance for further use, rather than analysis.

- A **bonded phase** is a stationary phase that is covalently bonded to the support particles or to the inside wall of the column tubing.
- A **chromatogram** is the visual output of the chromatograph. In the case of an optimal separation, different peaks or patterns on the chromatogram correspond to different components of the separated mixture.
- A **chromatograph** is an equipment that enables a sophisticated separation e.g., gas chromatographic or liquid chromatographic separation.
- **Chromatography** is a physical method of separation in which the components to be separated are distributed between two phases, one of which is stationary (stationary phase) while the other (the mobile phase) moves in a definite direction.
- The **eluate** is the mobile phase leaving the column.
- The **eluent** is the solvent that will carry the analyte.
- An **eluotropic series** is a list of solvents ranked according to their eluting power.

Chromatogram development technique

1. **Frontal analysis**–A large volume of sample mixture is continuously passed through the column. Most weakly retained component of the mixture emerges first.
2. **Displacement analysis**–Sample mixture is dissolved in large volume of solvent and applied to the top of the column. Mobile phase containing displacement agent is passed through the column.
3. **Elution Analysis**–Most widely used technique. It can be used for quantitative applications.
   A. **Isocratic elution** (Solvent composition or strength is not changed during column development)
   B. **Gradient elution** (Solvent composition or strength is changed during column development).It is also known as solvent programming.

Introduction

Chromatography involves a sample (or sample extract) being dissolved in a *mobile phase* (which may be a gas, a liquid or a supercritical fluid). The mobile phase is then forced through an immobile, immiscible *stationary phase*.

The phases are chosen such that components of the sample have differing solubilities in each phase. A component which is quite soluble in the stationary phase will take longer to travel through it than a component which is not very soluble in the stationary phase but very soluble in the mobile phase.

As a result of these differences in mobilities, sample components will become separated from each other as they travel through the stationary phase.

Distribution of analytes between phases

The distribution of analytes between phases can often be described quite simply. An analyte is in equilibrium between the two phases;

$$A_{mobile} \rightleftharpoons A_{stationary}$$

The equilibrium constant, K, is termed the *partition coefficient*; defined as the molar concentration of analyte in the stationary phase divided by the molar concentration of the analyte in the mobile phase.

The time between sample injection and an analyte peak reaching a detector at the end of the column is termed the *retention time* (t_R). Each analyte in a sample will have a different retention time. The time taken for the mobile phase to pass through the column is called t_M.

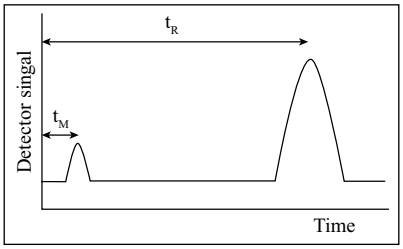


Figure 3.8 Distribution of analyses between phases

A term called the *retention factor, k′*, is often used to describe the migration rate of an analyte on a column. You may also find it called the *capacity factor*. The retention factor for analyte A is defined as;

$$k'_A = t_R - t_M/t_M$$

t_R and t_M are easily obtained from a chromatogram. When an analytes retention factor is less than one, elution is so fast that accurate determination of the retention time is very difficult. High retention factors (greater than 20) mean that elution takes a very long time. Ideally, the retention factor for an analyte is between one and five.

We define a quantity called the *selectivity factor*, α, which describes the separation of two species (A and B) on the column;

$$\alpha = k'_B/k'_A$$

When calculating the selectivity factor, species A elutes faster than species B. The selectivity factor is always greater than one.

Band broadening and column efficiency

To obtain optimal separations, sharp, symmetrical chromatographic peaks must be obtained. This means that band broadening must be limited. It is also beneficial to measure the efficiency of the column.

Theoretical plate model of chromatography

The plate model supposes that the chromatographic column is contains a large number of separate layers, called *theoretical plates*. Separate equilibrations of the sample between the stationary and mobile phase occur in these "plates". The analyte moves down the column by transfer of equilibrated mobile phase from one plate to the next.

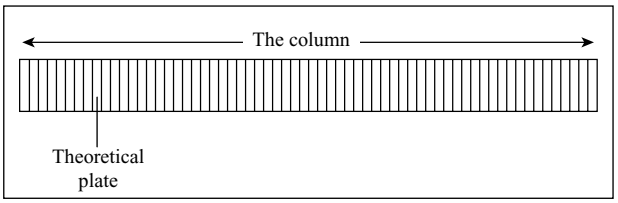


Figure 3.9 Theoretical plate model of chromatography

It is important to remember that the plates do not really exist; they are a figment of the imagination that help us understand the processes at work in the column. They also serve as a way of measuring column efficiency, either by stating the number of theoretical plates in a column, N (the more plates the better), or by stating the plate height; the Height Equivalent to a Theoretical Plate (the smaller the better).

If the length of the column is L, then the HETP is

$$\text{HETP} = L/N$$

The number of theoretical plates that a real column possesses can be found by examining a chromatographic peak after elution;

$$N = \frac{5.5t_R^2}{w_{1/2}^2}$$

where $w_{1/2}$ is the peak width at half-height.

As can be seen from this equation, columns behave as if they have different numbers of plates for different solutes in a mixture.

Rate theory of chromatography

A more realistic description of the processes at work inside a column takes account of the time taken for the solute to equilibrate between the stationary and mobile phase (unlike the plate model, which assumes that equilibration is infinitely fast). The resulting band shape of a chromatographic peak is therefore affected by the rate of elution. It is also affected by the different paths available to solute molecules as they travel between particles of stationary phase. If we consider the various mechanisms which contribute to band broadening, we arrive at the Van Deemter equation for plate height;

$$\text{HETP} = A + B/u + C\,u$$

Where u is the average velocity of the mobile phase. A, B, and C are factors which contribute to band broadening.

A. Eddy diffusion

The mobile phase moves through the column which is packed with stationary phase. Solute molecules will take different paths through the stationary phase at random. This will cause broadening of the solute band, because different paths are of different lengths.

B. Longitudinal diffusion

The concentration of analyte is less at the edges of the band than at the center. Analyte diffuses out from the center to the edges. This causes band broadening. If the velocity of the mobile phase is high then the analyte spends less time on the column, which decreases the effects of longitudinal diffusion.

C. Resistance to mass transfer

The analyte takes a certain amount of time to equilibrate between the stationary and mobile phase. If the velocity of the mobile phase is high, and the analyte has a strong affinity for the stationary phase, then the analyte in the mobile phase will move ahead of the analyte in the stationary phase. The band of analyte is broadened. The higher the velocity of mobile phase, the worse the broadening becomes.

Van Deemter plots

A plot of plate height vs average linear velocity of mobile phase.

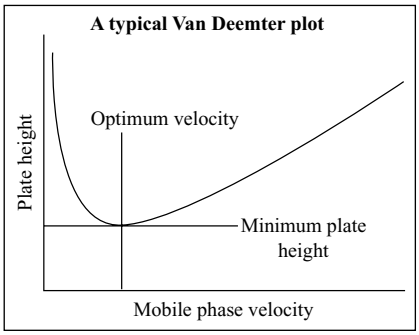


Figure 3.10 Van Deemter plots

Such plots are of considerable use in determining the optimum mobile phase flow rate.

Resolution

Although the selectivity factor, R, describes the separation of band centres, it does not take into account peak widths.

Another measure of how well species have been separated is provided by measurement of the *resolution*. The resolution of two species, A and B, is defined as

$$R = \frac{2\left[(t_R)_B - (t_R)_A\right]}{W_A + W_B}$$

Baseline resolution is achieved when $R = 1.5$

It is useful to relate the resolution to the number of plates in the column, the selectivity factor and the retention factors of the two solutes;

$$R = \frac{\sqrt{N}}{4}\left(\frac{--1}{-}\right)\left(\frac{1+K'_B}{K'_B}\right)$$

To obtain high resolution, the three terms must be maximized.

An increase in N, the number of theoretical plates,

By lengthening the column leads to an increase in retention time

By increasing band broadening—which may not be desirable.

Instead, to increase the number of plates, the height equivalent to a theoretical plate can be reduced by reducing the size of the stationary phase particles.

It is often found that by controlling the capacity factor, k', separations can be greatly improved. This can be achieved by changing the temperature (in Gas Chromatography) or the composition of the mobile phase (in Liquid Chromatography).

The selectivity factor, α, can also be manipulated to improve separations. When α is close to unity, optimising k' and increasing N is not sufficient to give good separation in a reasonable time. In these cases, k' is optimised first, and then R is increased by one of the following procedures:

1. Changing mobile phase composition
2. Changing column temperature
3. Changing composition of stationary phase
4. Using special chemical effects (such as incorporating a species which complexes with one of the solutes into the stationary phase)

NOTE

Column chromatography is used to separate and purify components of a mixture.

TLC and GC are usually used only to analyse mixtures: to determine the number of components and to see if a desired component is present.

TLC is often used to determine the "ideal solvent system" for a column chromatography or flash chromatography.

The ideal system is the one that moves the desired component of the mixture to a TLC R_f of 0.25–0.35 and will separate this component from its nearest neighbour by difference in TLC R_f values of at least 0.20. Therefore, a mixture is analysed by TLC to determine the ideal solvent (s) for a flash chromatography procedure.

Gas Chromatography

Principle Adsorption (GSC) or partition (GLC)

Main requirement Thermal stability and volatile nature of compound.

Derivatization in GC

1. To improve thermal stability of compound (polar compound to non-polar compound).
2. To introduce a detector oriented tag in molecule.
3. For purposeful adjustment of volatility.

Instrumentation

Gas chromatography Specifically, gas-liquid chromatography–involves a sample being vaporized and injected onto the head of the chromatographic column. The sample is transported through the column by the flow of inert, gaseous mobile phase. The column itself contains a liquid stationary phase which is adsorbed onto the surface of an inert solid.

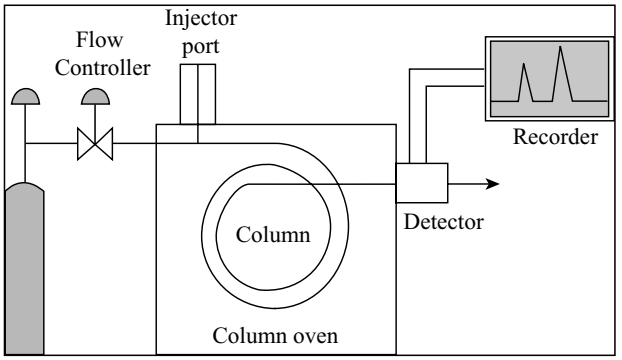


Figure 3.11 Gas Chromatography

Most common stationary phases

1. Separation of mixture of polar compounds

   Carbowax 20M (polyethylene glycol)

2. Separation of mixtures of non-polar compounds

   OV101 or SE-30 (polymer of methylsilicone)

3. Methylester of fatty acids

   DEGS (diethylene glycol succinate)

Instrumental Components

Carrier gas

The carrier gas must be chemically inert. Commonly used gases include nitrogen, helium, argon, and carbon dioxide. The choice of carrier gas often depends upon the type of detector used.

Sample injection port

The most common injection method is where a micro syringe is used to inject sample through a rubber septum into a flash vaporizer port at the head of the column. The temperature of the sample port is usually about 50°C higher than the boiling point of the least volatile component of the sample.

For packed columns, sample size ranges from tenths of a microliter up to 20 microliter.

Capillary columns, on the other hand, need much less sample, typically around 10^{-3} microliter. For capillary GC, split/splitless injection is used.

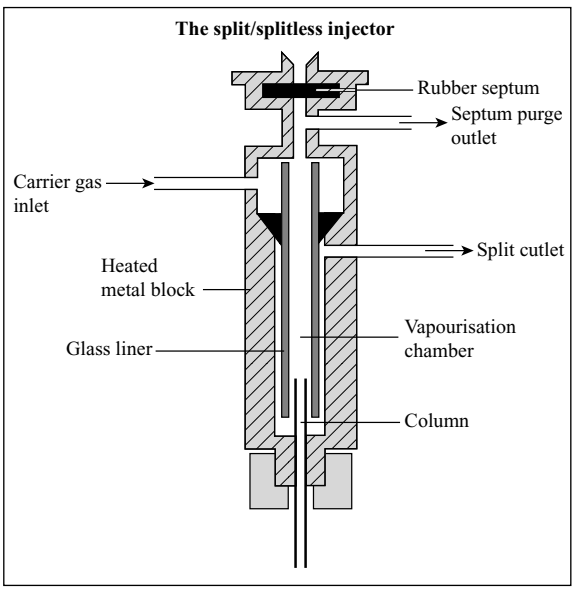


Figure 3.12 Capillary columns

The injector can be used in one of the two modes; split or splitless. The injector contains a heated chamber containing a glass liner into which the sample is injected through the septum. The carrier gas enters the chamber and can leave by three routes (when the injector is in split mode). The sample vapourises to form a mixture of carrier gas, vapourized solvent and vapourised solutes. A proportion of this mixture passes onto the column, but most exits through the split outlet. The septum purge outlet prevents septum bleed components from entering the column.

Columns

There are two general types of column, *packed* and *capillary* (also known as *open tubular*).

Packed columns contain a finely divided, inert, solid support material (commonly based on *diatomaceous earth*) coated with liquid stationary phase. Most packed columns are 1.5–10m in length and have an internal diameter of 2–4mm.

Capillary columns have an internal diameter of a few tenths of a millimeter. They can be of one of the two types: *wall-coated open tubular* (WCOT) or *support-coated open tubular* (SCOT).

Wall-coated columns consist of a capillary tube whose walls are coated with liquid stationary phase.

In support-coated columns, the inner wall of the capillary is lined with a thin layer of support material such as diatomaceous earth, onto which the stationary phase has been adsorbed. SCOT columns are generally less efficient than WCOT columns. Both types of capillary column are more efficient than packed columns.

A new type of WCOT column was devised–the *Fused Silica Open Tubular* (FSOT) column;

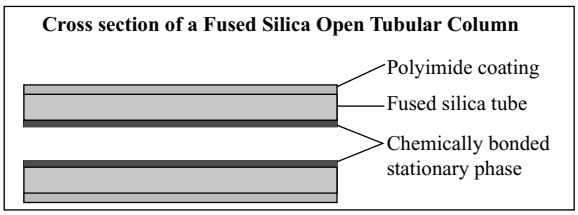


Figure 3.13 Cross section of a Fused Silica Open Tubular Column

These have much thinner walls than the glass capillary columns, and are given strength by the polyimide coating. These columns are flexible and can be wound into coils. They have the advantages of physical strength, flexibility and low reactivity.

Column temperature

For precise work, column temperature must be controlled to within tenths of a degree. The optimum column temperature is depends upon the boiling point of the sample. As a rule of thumb, a temperature slightly above the average

boiling point of the sample results in an elution time of 2–30 minutes. Minimal temperatures give good resolution, but increase elution times. If a sample has a wide boiling range, then **temperature programming** can be useful. The column temperature is increased (either continuously or in steps) as separation proceeds.

Detectors

A *non-selective* detector responds to all compounds except the carrier gas, a *selective detector* responds to a range of compounds with a common physical or chemical property and a *specific detector* responds to a single chemical compound.

Detectors can also be grouped into *concentration dependant detectors* and *mass flow dependant detectors*. The signal from a concentration dependant detector is related to the concentration of solute in the detector, and does not usually destroy the sampled dilution of with make-up gas will lower the detectors response. Mass flow dependant detectors usually destroy the sample, and the signal is related to the rate at which solute molecules enter the detector. The response of a mass flow dependant detector is unaffected by make-up gas.

Detector	Type	Support gases	Selectivity	Detectability	Dynamic range
Flame ionization (FID)	Mass flow	Hydrogen and air	Most organic compounds	100 pg	10^7
Thermal conductivity (TCD)	Concentration	Reference	Universal	1 ng	10^7
Electron capture (ECD)	Concentration	Make-up	Halides, nitrates, nitriles, peroxides, anhydrides, organometallics	50 fg	10^5
Nitrogen-phosphorus	Mass flow	Hydrogen and air	Nitrogen, phosphorus	10 pg	10^6
Flame photometric (FPD)	Mass flow	Hydrogen and air possibly oxygen	Sulphur, phosphorus, tin, boron, arsenic, germanium, selenium, chromium	100 pg	10^3
Photoionization (PID)	Concentration	Make-up	Aliphatics, aromatics, ketones, esters, aldehydes, amines, heterocyclics, organosulphurs, some organometallics	2 pg	10^7
Hall electrolytic conductivity	Mass flow	Hydrogen, oxygen	Halide, nitrogen, nitrosamine, sulphur		

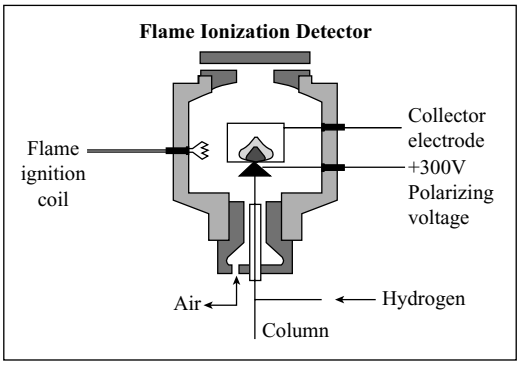


Figure 3.14 Flame Ionization Detector

The effluent from the column is mixed with hydrogen and air, and ignited. Organic compounds burning in the flame produce ions and electrons which can conduct electricity through the flame. A large electrical potential is applied at the burner tip, and a collector electrode is located above the flame. The current resulting from the pyrolysis of any organic compounds is measured. FIDs are mass sensitive rather than concentration sensitive; this gives the advantage that changes in mobile phase flow rate do not affect the detector's response. The FID is a useful general detector for the analysis of organic compounds; it has high sensitivity, a large linear response range, and low noise. It is also robust and easy to use, but unfortunately, it destroys the sample.

Thermal conductivity detector

Principal When a compound elutes, the thermal conductivity of the gaseous mixture of carrier gas and compound gas is lowered, and the filament in the sample column becomes hotter than the other control column.

Its resistance increases, and this imbalance between control and sample filament resistances is measured by a simple gadget and a signal is recorded.

Electron capture detector

For pesticide analysis (picogram).^{3}H or ^{63}Ni which emits β particles. Accept electrons of carrier gas.

Ionization: N_2 (Nitrogen carrier gas) + β (e) = $N_2^+ + 2e$

These N_2^+ establish a "base line"

X (F, Cl and Br) containing sample + β (e) → X^-

Ion recombination: $X^- + N_2^+ = X + N_2$

The "base line" will decrease and this decrease constitutes the signal. Insecticides, pesticides, vinyl chloride, and fluorocarbons.

HPLC

Derivatization in HPLC

1. To improve sensitivity of the method such as formation of fluorescent derivative of amino acids.
2. To improve resolution by adding functional group that enhances interaction of solute with stationary phase.

Instrumentation

1. **Pump**
   a. Pneumatic pump
   b. Reciprocating pump
   Pressure up to 6000 psi but most of the analytical work done in 400 to 1500 psi.
2. **Sample Injector**
   a. Micro litre syringe
   b. Rotary valve
   c. Loop Injector
3. **Precolumn/Guard/Support column**
   - It is similar to analytical column but differs in particle size (30–50 μ) from analytical column (Size below 5μ).
   - Function
     (a) Prevents dissolution of silica gel (Column Bleeding) by previously saturating the mobile phase.
     (b) Removes irreversibly, adsorption of particulate matter.
4. **Analytical Column**
   - Made up of stainless steel or fused silica
   - Particle size below 5 μm
   - Mostly used silica gel as stationary phase. (NP-HPLC)
   - Mostly used bonded phase silica gel as stationary phase. (RP-HPLC)
     E.g., RP 18 (ODS), RP 8, RP 2
   - Type of material used for column packing
     (a) Totally porous
     (b) Superficially porous/pellicular type
5. **Detector**
   A. UV-Visible spectrometer–(**Most widely used**)
      (a) Fixed wavelength (254 nm)
      (b) Diode array detector
   B. Refractive Index Detector
      Temperature sensitive detector and cannot be used in case of gradient elution method.
   C. Fluorescent Detector
   D. Conductrometric Detector

Ion Exchange Chromatography

Principle

Ionic compounds of solute are selectively separated by forming temporary electrostatic chemical bond with counter ion of stationary phase.

$$\text{Resin.....}SO_3H + Na^+ \longrightarrow \text{Resin.....}SO_3Na + H^+$$

$$\text{Resin.....}N(CH_3)_3OH + Cl^- \longrightarrow \text{Resin.....}N(CH_3)_3Cl + OH^-$$

Cation exchanger

Strong – ..... SO_3H Weak – ..... COOH

Anion exchanger

Strong – ..... NR_3Cl Weak – ..... NR_2H

Stationary phase

Polymeric Matrix e.g., **Styrene (Vinyl benzene)-Divinyl Benzene (DVB) Copolymer**

Divinyl Benzene is added to cross-link the chains formed from Styrene polymerization and gives a three-dimensional bead structure.

Size Exclusion Chromatography

Principle Molecular sieve basis i.e., larger molecule unable to fit into pores are eluted first while small molecules enters into pores and are eluted later.

Two types

1. **Gel Filtration-**S.P. used are cross-linked carbohydrates (Soft gel)
   E.g., Sephadex (Cross linked dextran), Agarose (Sepharose), Polyacrylamide (Bio-gel)
2. **Gel Permeation-**S.P. used are semi-rigid or rigid gel
   E.g., Cross-linked polystyrene, Alkylated Dextran, Controlled porosity Glass beads

Chiral Chromatography

Principle

Separation of particular isomer from enantionmeric mixture involves formation of Diastereomers.

Methods

1. Chiral Stationary Phase
   e.g., Naphthyl Alanine, Naphthyl Leucine, Dinitro benzoyl phenyl glycine, β-Cyclodextrin
2. Chiral mobile phase

Affinity chromatography

1. Affinity ligand is immobilized by covalent attachment with inert support E.g., Silica or polysaccharide matrix. Affinity ligands selectively adsorb a single molecular species which is complementary to it, from a mixture of solute.
2. Adsorption is reversible and non-covalent.
3. It exploit lock and key binding.
4. It is specially used for purification and separation of biological macromolecules.

Analyte	Affinity ligand
Enzyme	Coenzyme or inhibitor
Antigen	Antibody
Lectin	Carbohydrate
Hormone	Carrier

Super critical fluid chromatography

Supercritical point is a point at which a gas cannot be Liquified no matter how high is the pressure. The resulting liquid has density, viscosity and diffusivity characteristics midway between gaseous and liquid states.

The most commonly used mobile phase, carbon dioxide has a critical temperature of 31 degree C at 73 atm pressure.

Thin layer chromatography (TLC)

Principle may be adsorption, partition, ion exchange or molecular sieve depending upon the stationary phase used.

Paper Chromatography

Principle Partition

Stationary phase Bound water in pores of cellulose filter paper act as S.P.

R_f Value = distance travelled by solute/distance travelled by Solvent front

R_f Value cannot be greater than 1.

Derivatization in TLC

Compound class	Derivatizing Agent
General	Iodine Vapor
General	Sulphuric acid (50%)
Acids	Bromo cresol green
Aldehyde and Ketones	2, 4-dinitro phenyl hydrazine
Amines and amino acids	Ninhydrin
Alkaloids	Mercuric nitrate
Barbiturates	Diphenylcarbazone
Lipids	Bromo thymol blue
Steroids	Antimony trichloride
Carbohydrate	Aniline Phthalate

Important Table: Pharmaceutical Analysis

Spectral Region	Frequency (Hertz)	Wavelength	Wave number (cm^{-1})	Special Phenomenon
Gamma Rays	$3 \times 10^{18} - 3 \times 10^{20}$	–	–	Nuclear reaction and Mossbauer spectroscopy
X Rays	$3 \times 10^{16} - 3 \times 10^{18}$	0.01–2 nm	–	Inner shell electron transition
Vacuum or Far UV	$1.5 \times 10^{15} - 3 \times 10^{16}$	2nm–200 nm	–	Ionization of atoms or molecule

Spectral Region	Frequency (Hertz)	Wavelength	Wave number (cm^{-1})	Special Phenomenon
UV	$8 \times 10^{14} - 1.5 \times 10^{15}$	200–400 nm	50, 000–25, 000	Outer or valence shell electron transition
Visible	$4 \times 10^{14} - 4 \times 10^{14}$	400–800 nm	25, 000–12, 500	Outer or valence shell electron transition
IR	$10^{12} - 4 \times 10^{14}$	0.8 μm–1 mm	12, 500–20	Molecular vibration
Micro wave	$10^{10} - 10^{12}$	1 mm–30 cm	–	Molecular rotation
Radio wave	$10^{6} - 10^{10}$	10 m–2000 m	–	Nuclear spin change

Spectroscopy	Sample Window or Sample cell
UV	Quartz or Fused silica
Visible	Glass or plastic
IR	Metal halide salts e.g., NaCl, KBr, CsBr (for Non-Aqueous samples) LiF, CaF_2 (For Aqueous samples)
ATR-IR (Attenuated total Reflectance)	Silicon, Germanium, Sapphire (single crystal of Al_2O_3)
NMR	Cylindrical Glass Tube

Detector	Composition	Principle
Bolometer	Pt strip in Evacuated vessel	Resistance change
Thermocouple and Thermopile	Two dissimilar metals e.g., Bismuth and Antimony	Voltage or EMF Change at junction
Thermister	Oxide of Mn, Co, Ni	Resistance change
Goley cell (Pneumatic)	Xenon gas	Membrane displacement or Expansion of gas
Pyroelectric	Non-centrosymmetric crystal below its Curie point. TGS (Tri glycine sulphate) used as medium	Electric polarization producing current

Spectroscopy	Radiation Source	Detector
UV	1. Hydrogen discharge lamp 2. Deuterium discharge lamp 3. Xenon arc lamp	1. Barrier layer cell (Photo Voltaic Cell) 2. Photo Emissive Cell 3. Photo Multiplier Tube (PMT) 4. Silicon Diode 5. Charge coupled device (CCD) 6. Photo Diode Array
Visible	Tungsten halogen lamp	Same as UV
IR	1. Nernst glower operates at 1500 degree C (Rod of fused or sintered mixture of rare earth oxide e.g., Zirconium, Ytterbium, Erbium or Thorium) 2. Globar source operates at 1300°C (Rod of Silicon carbide) 3. Nichrome wire or coil	1. Bolometer 2. Themocouple or Thermopile 3. Thermister 4. Golay cell 5. Pyroelectric 6. Semiconductor 7. Photo conductivity detector
NMR	Radio Frequency Oscillator or Generator	Radio Frequency Receiver or Phase Sensitive Detector

Spectroscopy	Radiation Source	Detector
Fluorescence and Phosphorescence	1. Mercury vapour Lamp 2. Xenon Arc lamp	PMT (Photo Multiplier Tube)

Type of Potentiometric Titration	Indicator Electrode	Reference Electrode
Acid-base (Neutralization)	Glass electrode	Calomel (Hg/Hg_2Cl_2) or Ag/AgCl
Complexometric or Chelometric	Mercury-Mercury (II) electrode	Calomel (Hg/Hg_2Cl_2) or Ag/AgCl
Precipitation	Silver Electrode	Calomel (Hg/Hg_2Cl_2) or Ag/AgCl
Redox	Pt electrode	Calomel (Hg/Hg_2Cl_2) or Ag/AgCl

Electro-Analytical Method	Basic principle
Conductometry	Conductance V/S volume of Titrant added
Potentiometry	Potential V/S volume of Titrant added (No current flow i.e., I = 0)
Amperometry	Current V/S volume of Titrant added (V=Constant)
Polargraphy	Current V/S Applied Potential

Bathochromic shift (Red Shift)	Shift towards longer wavelength or lower energy
Hypsochromic shift (Blue Shift)	Shift towards shorter wavelength or higher energy
Hyper chromic shift	Increase in intensity
Hypo chromic shift	Decrease in intensity
Auxochrome	A group which extend the conjugation of a chromophore by sharing of non-bonding electrons.
Chromophore	Structural unit responsible for absorption
max	The molar absorption at λ_{max}

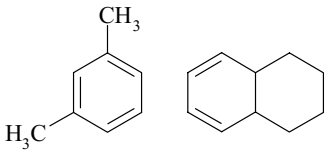
Bathochromic shift (Red Shift)	Shift towards longer wavelength or lower energy
λ_{max}	The wavelength at maximum absorption

Electrode System	Construction
Standard Hydrogen electrode (SHE)	It is a primary reference electrode. It consists of Pt electrode immersed in a solution whose hydrogen ion activity is 1.0 and in which H_2 gas is bubbled at 1 atm Pressure.
Calomel ((Hg/Hg_2Cl_2) electrode	Solid mercury surrounded with Hg, Hg_2Cl_2 Paste and kept in saturated solution of KCl.
Ag/AgCl electrode	Silver wire is coated with thin film of silver chloride and kept in saturated solution of KCl.
Glass electrode	Most widely used H^+ ion sensitive electrode used in pH metre. Calibration of pH metre carried out in following buffers 7.0, 4.0, 10.0 (sequence order). It is made up of 22%Na_2O, 6%CaO, and 72% SiO_2.

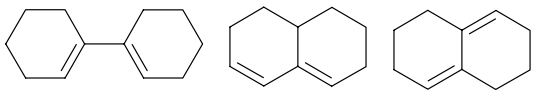
Woodward Fieser Rule for conjugated Diene, triene systems		
Parent Values	Homoannular conjugated diene	253 nm
	Heteroannular conjugated diene	214 nm
	Acyclic conjugated diene	217 nm
	Acyclic triene	245 nm
Increment	Each alkyl substituent or Ring residue	+ 5 nm
	Exocyclic double bond	+ 5 nm
	Double bond extending conjugation	+ 30 nm
Auxochromes	-Cl, -Br	+ 5 nm
	-OH/-OR/-SH	+ 6 nm
	-SR	+ 30 nm
	$-NR_2$	+ 60 nm
	$-OCOCH_3$	+ 0 nm

Important Terminology

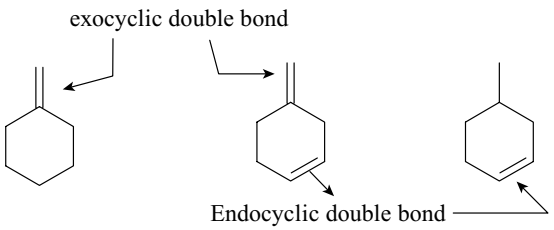
1. Homoannular Diene: It is a cyclic diene having conjugated double bond in the same ring.
   For example,

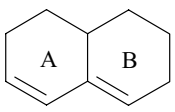


2. Heteroannular diene: It is a cyclic diene in which double bonds in conjugation are present in different rings.
   For example,



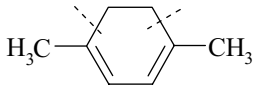
3. Endocyclic double bond: A double bond present in a ring as shown in the example.
4. Exocyclic double bond: A double bond in which one of the double bond is a part of a ring system shown in ring B.



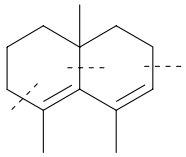


Ring A has one endocyclic and one exocyclic double bond.
Ring B has only one endocyclic double bond

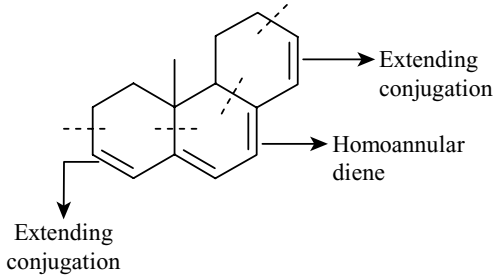
Question: Calculate λ_{max} of following examples of Dienes.



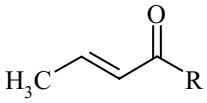
- Parent value for homoannular diene = 253 nm
- Two alkyl substituents = 2 × 5 = 10 nm
- Two ring residue = 2 × 5 = 10 nm
- **Total calculated λ_{max} = 253 + 10 + 10 = 273 nm**



- Parent value for heteroannular diene = 214 nm
- Two alkyl substituents = 2 × 5 = 10 nm
- Three ring residue = 3 × 5 = 15 nm
- One exocyclic double bond = 5 nm
- **Total calculated λ_{max} = 214 + 10 + 15 + 5 = 244 nm**

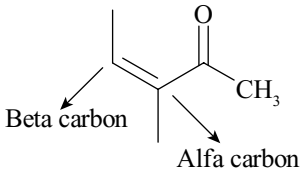


- Parent Value for homoannular diene = 253 nm
- Four ring residue = 4 × 5 = 20 nm
- Two exocyclic double bond = 10 nm
- Two double bond extanding conjugation = 2 × 30 = 60 nm
- **Total calculated λ_{max} = 253 + 20 + 10 + 60 = 343 nm**

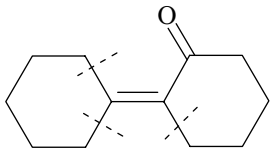
Woodward Fieser Rule for α, β-unsaturated carbonyl compounds		
Parent		215 nm
Values	R = H (Aldehyde) X = OH, OR (Acid or Ester) X = alkyl (Ketone) or six membered ring	207 nm 193 nm 215 nm
Increment	Homoannular conjugated diene Exocyclic double bond Double bond extending conjugation	+ 39 nm + 5 nm + 30 nm

Woodward Fieser Rule for α, β-unsaturated carbonyl compounds					
Auxochromes	Alkyl group or ring residue	α +10 nm	β +12 nm	γ +18 nm	Δ/higher + 18 nm
	–Cl	+15 nm	+12 nm	+12 nm	+ 12 nm
	–OH	35 nm	+ 30 nm	+ 30 nm	+ 50 nm
	–SR	–	85 nm	–	–
	$-NH_2$	–	95 nm	–	
	$-OCOCH_3$	+ 6 nm	+ 6nm	+ 6 nm	+ 6 nm
	–Br	+ 25 nm	+ 30 nm	+18 nm	+31 nm
	–OR	+ 35 nm	+ 30 nm	+18 nm	+31 nm

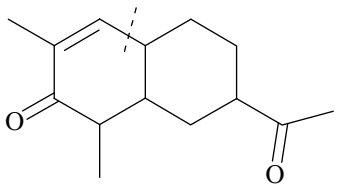
Examples:



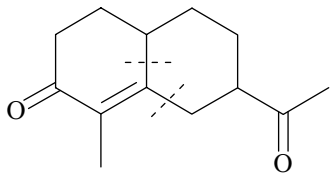
- Parent value for α, β uusaturated acyclic compound = 215 nm
- One alkyl substituents on α carbon = 10 nm
- One alkyl substituents on β carbon = 12 nm
- **Total calculated λ_{max} = 215 + 10 + 12 = 237 nm**



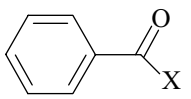
- Parent value for α, β uusaturated 6 membered cyclic compound = 215 nm
- One ring residue on α carbon = 10nm
- Two ring residue on β carbon = 2 ×12 =24 nm
- Double bond exocyclic to two (both) ring = 2 × 5 = 10 nm
- **Total calculated λ_{max} = 215 + 10 + 24 + 10 = 259 nm**



- Parent value for α, β uusaturated 6 membered cyclic compound = 215 nm
- One alkyl substituent on α carbon = 10 nm
- One ring residue on β carbon = 12 nm
- **Total calculated λ_{max} = 215 + 10 + 12 = 237 nm**



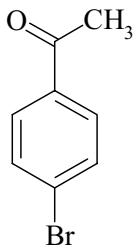
- Parent value for α, β uusaturated 6 membered cyclic compound = 215 nm
- One alkyl substituent on α carbon = 10 nm
- Two ring residue on β carbon = 2 × 12 = 24 nm
- One exocyclic double bond = 5
- **Total calculated λ_{max} = 215 + 10 + 24 + 5 = 254 nm**



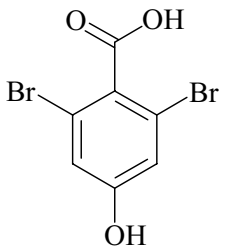
Woodward Fieser Rule for Acyl Benzene derivatives		
Parent Value	X= Alkyl	246 nm
	X= H	250 nm
	X= OH/OR	230 nm

Auxochromes			
	Ortho	Meta	Para
Alkyl	+3nm	+3nm	+10nm
OH/OR	+7nm	+7nm	+25nm
Cl	0nm	0nm	+10nm
Br	+2nm	+2nm	+15nm
NH_2	+13nm	+13nm	+58nm
$NHOCOCH_3$	+20nm	+20nm	+45nm

Examples:



- Parent value for acyl benzene (Ketone) derivative = 246 nm
- -Br atom at para position = 15 nm
- **Total calculated λ_{max} = 246 + 15 = 261 nm**



- Parent value for aromatic carboxylic acid derivative = 230 nm
- -Br atom at two ortho position = 2 × 2 = 4 nm
- -OH group at para position = 25
- **Total calculated λ_{max} = 230 + 04 + 25 = 259 nm**

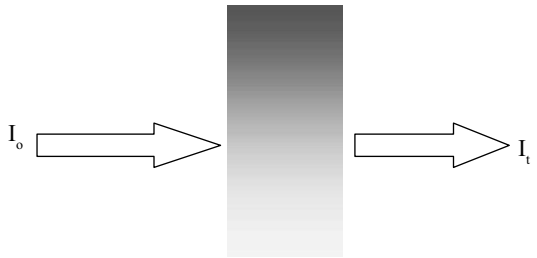
Karl Fisher Titration (Coulometric end point detection)

- It determines water content (moister content) in pharmaceuticals.
- Reagent consists of mixture of anhydrous methanol, anhydrous pyridine, and iodine and sulphur dioxide.
- End point detection-presence of water causes conversion of iodine to iodide through its reduction by sulphur dioxide.
- Sodium tartarate dihydrate is used in standardization of Karl-Fisher reagent.

Standard reference materials used in calibration of spectroscopic instrument

SRM	Parameter checked
Potassium dichromate	Absorbance in UV/Visible
Quartz cuvett	Path length in UV/Visible
Toluene in Hexane	Resolution in UV/Visible
Potassium iodide	Stray Light in UV/Visible
Didymium or Holomium Oxide	Wavelength in UV/Visible
Polystyrene Film	Wavelength in IR

Beer-Lambert Law



It states that the proportion of the light absorbed by the solute in a homogenous, transparent medium is independent of the intensity of the incident light and proportional to the number of absorbing molecules and path length.

$A = \epsilon Cl = \log (I_O/I_t) = \log 1/T = -\log T = 2 - \log \% T$

A directly proportional to path length (Lambert law)

A directly proportional to concentration (Beer's law)

Where A = Absorbance

Є = molar absorptivity/molar extinction coefficient

C = concentration (mol per litre)

l = path length

$T = \text{Transmittance} = I_t/I_O$

If concentration is taken in g per litre, then the formula becomes

$A = aCl$

a = absorptivity or extinction coefficient

When molecular weight of absorbing molecule is not known, the $A_{1cm}^{1\%}$ is used to compare absorption intensity instead of Є.

$A_{1cm}^{1\%} = A/Cl$

Where C = concentration (gm per 100 ml)

Thus $\epsilon = (A_{1cm}^{1\%} \times \text{mol.wt})/10$

Proton (H^1) NMR V/S Carbon (C^{13}) NMR

1. Gyro magnetic (Magnogyretic) Ratio for proton NMR is 4 times than carbon-13 NMR.
2. Proton NMR provide information of periphery while C-NMR about Backbone.
3. Chemical shift normal range for Proton NMR (0–10) while for C-NMR (0–200).
4. Proton NMR spectrum is more complex than C-NMR because homo (H^1-H^1) as well as hetero (H^1-H^2) nuclear coupling are possible in PMR but in C-NMR hetero nuclear coupling is not possible due to spin quantum number of C^{12} is zero and probability of homo nuclear coupling is very low due to natural isotopic abundance of C^{13} is only 1.1%.
5. PMR is more sensitive than C^{13}-NMR.

Information from PMR

Number of Signals	Different sets of equivalent protons in molecule
Intensity of Signal	Relative number of protons of different kinds
Splitting or Multiplicity of Signal	Environment of proton with respect to neighbouring proton
Area of Peak	Number of absorbing protons giving rise to a signal

Flame Temperature in Kelvin (K)

Fuel	Oxidant		
	Air	Nitrous Oxide (N_2O)	Oxygen (O_2)
Acetylene	2400 K	3200K	3400K
Hydrogen	2300K	2900K	2900 K
Propane	2200K	3000K	3100K

Normal Phase Chromatography (NPC)

Stationary Phase (S.P.) Polar
Mobile Phase (M.P.) Non-Polar

Elution Order-Alkane → Olefins → Aromatics → Organic halides → Sulfide → Ether → nitro compounds → Ester/Aldehyde/Ketone → Alcohol/Amines → Sulfone → Sulfoxide → Amides → Carboxylic Acids

Non-polar compound will elute first and most polar will elute last in the NPC.

Reverse Phase Chromatography (RPC)

Stationary Phase (S.P.) Non-Polar
Mobile Phase (M.P.) Polar

Eluotropic Series–Increasing order of Solvent Polarity

Hexane/Pentane < Petroleum ether < Cyclo Hexane < Xylene <Toluene < Diethyl ether < Chloroform < Dichloromethane < THF < Acetone <Dioxane < Acetonitrile < Methanol <Water

List of important Chemical Shift Values (δ)

Protons on unsaturated carbons next to oxygen e.g., Aldehyde	Protons on unsaturated carbons e.g., Benzene, Aromatic Hydrocarbons	Protons on unsaturated carbons e.g., Alkenes	Saturated CH_3, CH_2, and CH protons next to oxygen e.g., CH_3O, CH_2O	Saturated CH_3, CH_2, CH protons not next to oxygen

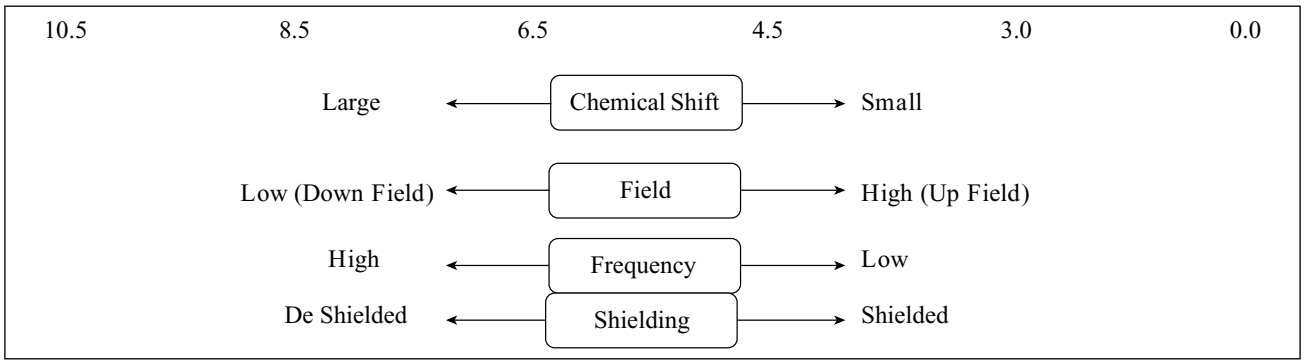


Figure 3.16

1. System Suitability Parameters for HPLC Method development

Parameters	Acceptance criteria
Capacity factor	The peak should be well resolved from other peaks.
Resolution (R_s)	Rs > 2 between the peak of interest
Tailing factor (T)	T is less than or equal to Two.
Theoretical plate (N)	In general should be greater than 2000

2. Analytical method validation parameters

Specificity	Specificity is the ability to assess unequivocally the analyte in the presence of components which may be expected to be present. Typically these might include impurities, degradants, matrix, etc. The specificity of the method is determined by comparing the spectra (for UV) and chromatogram (for RP-HPLC) of the standard and sample solutions of analyte and both are spectra/chromatogram are overlap.
Precision (n=6)	Repeatability(n=6): Repeatability expresses the precision under the same operating conditions over a short interval of time.
	Reproducibility: Reproducibility expresses the precision between laboratories
	Intermediate precision (n=3): Intermediate precision expresses within-laboratories variations: different days, different analysts, different equipment, etc. The intermediate precision of the method was confirmed by intraday (variation of results within the same day) and interday (variation of results between days) analysis. The intraday and interday precision of the proposed methods were performed by analyzing the corresponding responses three times on the same day for intraday precision and over a period of three days for inter day with three different concentrations of standard tertiary mixture solutions.
LOD (Limit of Detection)	The detection limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be detected but not necessarily quantitated as an exact Value.
LOQ (Limit of Quantification)	The quantitation limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be quantitatively determined with suitable precision and accuracy. The quantitation limit is a parameter of quantitative assays for low levels of compounds in sample matrices, and is used particularly for the determination of impurities and/or degradation products.
	The LOD and LOQ can be determine as per following LOD = 3.3 σ / S and LOQ = 10 σ / S Where, σ = standard deviation of y intercept of calibration curve (n = 6) S = slope of a regression equation.
Linearity (n=6)	The linearity of an analytical procedure is its ability (within a given range) to obtain test results which are directly proportional to the concentration (amount) of analyte in the sample. Linearity is checked by diluting standard stock solution at six different concentrations and correlation coefficients (r^2) is greater than 0.995.

Range	The range of an analytical procedure is the interval between the upper and lower concentration (amounts) of analyte in the sample (including these concentrations) for which it has been demonstrated that the analytical procedure has a suitable level of precision, accuracy and linearity.
Accuracy (n=3)	The accuracy of an analytical procedure expresses the closeness of agreement between the value which is accepted either as a conventional true value or an accepted reference value and the value found. This is sometimes termed trueness. The accuracy of the method will be carried out at three levels 80, 100 and 120 % of the working concentration of sample. This procedure was repeated for three times for each concentration.
Robustness(n=3)	The robustness of an analytical procedure is a measure of its capacity to remain unaffected by small, but deliberate variations in method parameters and provides an indication of its reliability during normal usage. Robustness of the method will be determined by changes in following parameters. • pH ± 0.2 • Flow rate ± 10 % • Wavelength ± 2 nm • Change in mobile phase ratio ± 2 %

*For all validation parameters, % RSD value should not be more than 2.

3. List of Indicator used in different titration methods

Titration	Indicators
Complexometric	Murexide, solochrome black, Patton and Reedder's indicator, Calcon or solochrome dark blue, Xylenol orange, bromopyrogallol, thymolphthalexone, methylthymol blue, zincon, variamine blue
Precipitation	Eosin , fluorescin, Rose Bengal, tartrazine, alizarin red S, rhodamine 6G, Phenosafranine
Nonaqueous	Crystal violet, methyl red, 1- napthol benzein, oracet blue
Aqueous	Methyl orange, phenolphthalein, methyl red, thymol phthalein, methyl yellow, neutral red, congo red etc.

4. List of ICH Guidelines

Quality Guidelines
Q1A - Q1F: Stability
• Q1A(R2)Stability Testing of New Drug Substances and Products
• Q1BStability Testing : Photostability Testing of New Drug Substances and Products
• Q1A(R2)Stability Testing of New Drug Substances and Products
• Q1BStability Testing : Photostability Testing of New Drug Substances and Products
• Q1A(R2)Stability Testing of New Drug Substances and Products
• Q1BStability Testing : Photostability Testing of New Drug Substances and Products

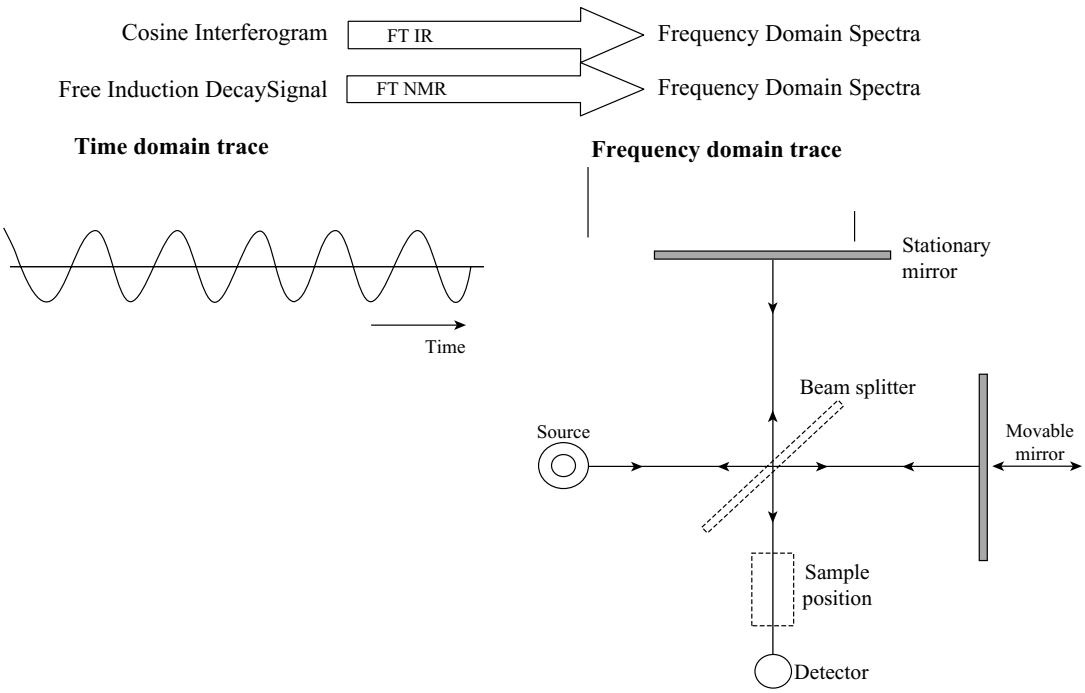
Q2(R1): Validation of Analytical Procedures: Text and Methodology
Q3A - Q3D: Impurities
• Q3A(R2)Impurities in New Drug Substances
• Q3B(R2)Impurities in New Drug Products
• Q3C(R5)Impurities: Guideline for Residual Solvents
• Q3DGuideline for Elemental Impurities
• Q3d Training Implementation of Guideline for Elemental Impurities
Q4 - Q4B: Pharmacopoeias
• Q4Pharmacopoeias
• Q4APharmacopoeial Harmonisation
• Q4BEvaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions
Q5A - Q5E: Quality of Biotechnological Products
• Q5A(R1)Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin
• Q5BAnalysis of the Expression Construct in Cells Used for Production of r-DNA Derived Protein Products
• Q5CStability Testing of Biotechnological/Biological Products
• Q5DDerivation and Characterisation of Cell Substrates Used for Production of Biotechnological/ Biological Products
• Q5EComparability of Biotechnological/Biological Products Subject to Changes in their Manufacturing Process
Q6A- Q6B: Specifications
• Q6ASpecifications : Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances
• Q6BSpecifications : Test Procedures and Acceptance Criteria for Biotechnological/Biological Products
Q7 : Good Manufacturing Practice
Q8 : Pharmaceutical Development
Q9 : Quality Risk Management
Q10: Pharmaceutical Quality System
Q11: Development and Manufacture of Drug Substances
Q12: Lifecycle Management

Safety Guidelines
S1A - S1C: Carcinogenicity Studies
• S1Rodent Carcinogenicity Studies for Human Pharmaceuticals
• S1ANeed for Carcinogenicity Studies of Pharmaceuticals
• S1BTesting for Carcinogenicity of Pharmaceuticals
• S1C(R2)Dose Selection for Carcinogenicity Studies of Pharmaceuticals
S2: Genotoxicity Studies
S3A - S3B: Toxicokinetics and Pharmacokinetics
• S3ANote for Guidance on Toxicokinetics: The Assessment of Systemic Exposure in Toxicity Studies
• S3A Q&AsQuestions and Answers: Note for Guidance on Toxicokinetics: The Assessment of Systemic Exposure - Focus on Microsampling
• S3BPharmacokinetics: Guidance for Repeated Dose Tissue Distribution Studies
S4: Toxicity Testing
S5: Reproductive Toxicology
S6: Biotechnological Products
S7A - S7B: Pharmacology Studies
• S7ASafety Pharmacology Studies for Human Pharmaceuticals
• S7BThe Non-Clinical Evaluation of the Potential for Delayed Ventricular Repolarization (QT Interval Prolongation) by Human Pharmaceuticals
S8: Immunotoxicology Studies
S9: Nonclinical Evaluation for Anticancer Pharmaceuticals
S10: Photosafety Evaluation
S11: Nonclinical Safety Testing
Efficacy Guidelines
E1: Clinical Safety for Drugs used in Long-Term Treatment
E2A - E2F: Pharmacovigilance
• E2A:Clinical Safety Data Management: Definitions and Standards for Expedited Reporting
• E2B(R3):Clinical Safety Data Management: Data Elements for Transmission of Individual Case Safety Reports

• E2B(R3): Implementation: Electronic Transmission of Individual Case Safety Reports
• E2C(R2):Periodic Benefit-Risk Evaluation Report
• E2C(R2:) Questions & Answers: Periodic Benefit-Risk Evaluation Report
• E2D:Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting
• E2E:Pharmacovigilance Planning
• E2F:Development Safety Update Report
E3: Clinical Study Reports
E4: Dose-Response Studies
E5: Ethnic Factors
E6: Good Clinical Practice
E7: Clinical Trials in Geriatric Population
E8: General Considerations for Clinical Trials
E9: Statistical Principles for Clinical Trials
E10: Choice of Control Group in Clinical Trials
E11: Clinical Trials in Pediatric Population
E12: Clinical Evaluation by Therapeutic Category
E14: Clinical Evaluation of QT
E15: Definitions in Pharmacogenetics / Pharmacogenomics
E16: Qualification of Genomic Biomarkers
E17: Multi-Regional Clinical Trials
E18: Genomic Sampling
Multidisciplinary Guidelines
M1: MedDRA Terminology
M2: Electronic Standards
M3: Nonclinical Safety Studies
M4: Common Technical Document
M5: Data Elements and Standards for Drug Dictionaries
M6: Gene Therapy
M7: Genotoxic Impurities
M8: Electronic Common Technical Document (eCTD)

Fourier transform (F.T.) concept

It is a mathematical operation which converts Time Domain Spectra into Frequency Domain Spectra.



Advantage of FT

1. Fellgett or Multiplex–Increase in S/N ratio
2. Jacquinot–Increased energy throughput
3. High resolution
4. High sensitivity

Michelson interferometer

It acts as modulating device. **Modulation** means conversion of high frequency signals to measurable ones.

Radiation source is He-Ne laser lamp.

Laser beam positioning It tells about Sampling Interval time.

Zero position referencing (White light system) It indicates starting point of data sampling for each scan.

Stretching Vibrational Frequencies (cm^{-1})					
O-H C-H N-H	C-C, C-N (Triple bond) X=C=Y X, Y=C, O, N, S	Transparent Region	C=O	C=N C=C	C-X C-O C-N C-C

4000 2500 2000 1800 1650 1550 500

Alkane – (-C-C-)	-C-$H_{stretch}$ (3000 cm^{-1}) Isopropyl (1375 cm^{-1})	-C-H_{bend} (1440, 1375 cm^{-1}) t-Butyl (1375 cm^{-1})
Alkene – (-C=C-)	C-H_{bend} in Cis alkene (700 cm^{-1})	Trans alkene (970cm^{-1})
Alkynes –	C-H in triple bonded carbon atom (3300 cm^{-1}) C triple bond C (2150 cm^{-1})	

Aromatics –	$C\text{-}H_{bend}$ in	O-disubstituted 750, 690 cm^{-1} m-disubstituted 690, 780 cm^{-1} p-disubstituted 800–850 cm^{-1}
Alcohols –	O-H stretching at	3500–3700 cm^{-1} (without hydrogen bonding) 3200–3500 cm^{-1} (hydrogen bonding)
	C-O stretching at	1100–1300 cm^{-1}
Carbonyl and Acid derivatives –	$C{=}O_{stretch}$ order	

Anhydride I band (1810 cm^{-1}) > Acid Halide (1800 cm^{-1}) > Anhydride II band (1760 cm^{-1}) > Esters (1735 cm^{-1}) > Aldehydes (1725 cm^{-1}) > Ketones (1715 cm^{-1}) > Carboxylic Acid (1710 cm^{-1}) > Amides (1690 cm^{-1})

Aldehyde can be differentiated from Ketone due to presence of doublet of $C\text{-}H_{stretch}$ at 2750 cm^{-1} and 2850 cm^{-1}

C-N stretching in Nitriles at 2250 cm^{-1}
N=O stretching at 1550 and 1650 cm^{-1}
S-H stretching at 2550 cm^{-1}
S=O stretching at 1350 and 1150 cm^{-1}

Analytical method based on different properties

Measured Property	Analytical Methods
Mass	Gravimetric
Volume	Volumetric
Electrical potential	Potentiometry, Chronopotentiometry
Electrical Conductance	Conductometry,
Electrical current,	Polarography, Amperometry
Quantity of electricity	Coulometer
Absorption of radiation	Spectrophotometry (UV, Visible, IR, X-ray), Calorimetry, Atomic absorption spectroscopy, NMR and ESR
Emission of radiation	Emission spectroscopy (UV, Visible, X-ray), Flame photometry, Fluorescence, Radiochemical methods
Refraction of radiation	Refrectometry, Interferometry
Scattering of radiation	Turbidimetry, Nephelometry, Raman Spectroscopy
Diffraction of radiation	X-ray electron diffraction methods
Mass to charge ratio	Mass Spectroscopy
Rotation of radiation	Polarimetry, Optical rotatory dispersion (ORD) and Circular Dichroism (CD)
Thermal Properties	Thermal conductivity and enthalpy methods

Titrimetic Analysis

Titration A measured amount of a solution of unknown concentration is added to a known volume of a second solution until the reaction between them is just complete; the concentration of the unknown solution (the titer) can then be calculated.

Analyte (Titrant) An analyte is a weak base or acid. Its structure is made from any compound that can be converted to a strong acid or base.

Titrant The titrant is a strong acid or base that is slowly added to the analyte until it reaches any visible change in the colour of the solution under observation.

Indicator It is a pH marker added to the analyte that triggers a change in colour when equilibrium is reached. It should have a weaker acid/base concentration than the analyte.

Acidimetry Volumetric analysis using standard solutions of acids to measure the amount of a base present.

Alkalimetry Volumetric analysis using standard solutions of alkali to measure the amount of acid present.

Standards

Certain chemicals which are used in defined concentrations as reference materials.

- Primary standards
- Secondary standards

Primary standards

Available in pure form, stable and easily dried to a constant known composition.

- Stable in air.
- High molecular weight.
- Readily soluble.
- Undergoes stoichiometric and rapid reactions.

Titration Method	Primary Standards
Acid-base reactions	Na_2CO_3, $Na_2B_4O_7$, KH ($C_8H_4O_4$), HCl
Complex formation reactions	$AgNO_3$, NaCl
Precipitation reactions	$AgNO_3$, KCl
Redox reactions	$K_2Cr_2O_7$, $Na_2C_2O_4$, I_2

Secondary standards

A substance that can be used for standardisations, and whose concentration of active substance has been determined by comparison to a primary standard.

Standard solution

It is a solution of accurately known concentration prepared from a primary standard (a compound which is stable, of high purity, highly soluble in water and of a high molar mass to allow for accurate weighing) that is weighed accurately and made up to a fixed volume.

Types of volumetric titrations

There are three types of volumetric titration, which are classified based on the rate of their reaction. Direct titration method (DTM) is a one-step titration process. Indirect method (ITM) involves a two-step titration process. Back titration method (BTM) uses a three-step titration process.

Back titration

The term back titration is used when a titration is done "backwards"; instead of titrating the original analyte, one adds a known excess of a standard reagent to the solution, then titrates the excess. A back titration is useful if the endpoint of the reverse titration is easier to identify than the endpoint of the normal titration. They are also useful if the reaction between the analyte and the titrant is very slow.

Types of titrations

1. Acid-base titration

Indicators for Acid-Base titration

Indicator	Colour on Acidic Side	Range of Colour Change	Colour on Basic Side
Methyl Violet	Yellow	0.0–1.6	Violet
Bromophenol Blue	Yellow	3.0–4.6	Blue
Methyl Orange	Red	3.1–4.4	Yellow
Methyl Red	Red	4.4–6.2	Yellow
Litmus	Red	5.0–8.0	Blue
Bromothymol Blue	Yellow	6.0–7.6	Blue
Phenolphthalein	Colorless	8.3–10.0	Pink
Alizarin Yellow	Yellow	10.1–12.0	Red

pH meter and Conductivity metre can be used for end point detection.

2. Redox titration

Most commonly, a potentiometer or a redox indicator is used to determine the end point of the titration. For example, when one of constituents of the titration is the oxidizing agent potassium dichromate, the colour change of the solution from orange to green is not definite and thus an indicator such as sodium diphenylamine is used. The analysis of wines for their sulfur dioxide content requires the use of iodine as an oxidizing agent. In this case, starch is used as an indicator; a blue starch-iodine complex is formed once an excess of iodine is present, thus signalling the endpoint of the titration.

Some redox titrations do not require an indicator, due to the intense colour of some of the constituents. For instance, in a titration where the oxidizing agent potassium permanganate (permanganometry) is present, a slightly faint persisting pink colour signals the endpoint of the titration, and no particular indicator is therefore required.

Standardization of Potassium Permanganate or Cerium IV sulphate done by Sodium Oxalate or Arsenic III oxide. Standardization of Potassium Dichromate is done by metallic iron. Standardization of Iodine is done by Sodium Thiosulphate or Arsenic III oxide.

Application–Determination of Copper, Dissolved oxygen, Chlorine, Arsenic IV, Sulphides.

3. Complexometric titration

These titrations are based on the formation of a complex between the analyte and the titrant. The chelating agent EDTA is very commonly used to titrate metal ions in solution. These titrations generally require specialized indicators that form weaker complexes with the analyte. A common example is Eriochrome Black T for the titration of calcium and magnesium ions. Indicators-Murexide, Solochrome Black, Xylenol orange, Eriochrome Black etc.

Application Determination of cations and hardness of water.

4. Zeta potential titration

These titrations characterize heterogeneous systems, such as colloids. Zeta potential plays role of indicator. One of the purposes is determination of iso-electric point when surface charge becomes 0.

5. Iodometry

Usual reagents are sodium thiosulfate as titrant, starch as an indicator (it forms blue complex with iodine molecules—though polyvinyl alcohol has started to be used recently as well), and an iodine compound (iodide or iodate, depending on the desired reaction with the sample).

The principal reaction is the reduction of iodine to iodide by thiosulfate:

$$I_2 + 2S_2O_3^{2-} \rightarrow S_4O_6^{2-} + 2I^-$$

6. Precipitation reactions

1. **Mohr method-**Using Ag^+ as a titrant in chlorides (or bromides) determination.
   End point detection-small amount of sodium or potassium chromate
2. **Volhard method**-Titration with thiocyanates, can be used for Ag^+ determination, or for indirect determination (thorough back titration) of chlorides.
   End point detection-Iron (III) thiocyanate complex
3. **Kjeldahl method** or **Kjeldahl digestion**
   Quantitative determination of nitrogen in chemical substances.

The method consists of heating a substance with sulphuric acid, which decomposes the organic substance by oxidation to liberate the reduced nitrogen as ammonium sulphate. In this step, potassium sulphate is added in order to increase the boiling point of the medium. Chemical decomposition of the sample is complete when the medium has become clear and colourless (initially very dark).

The solution is then distilled with sodium hydroxide (added in small quantities) which converts the ammonium salt to ammonia. The amount of ammonia present (hence the amount of nitrogen present in the sample) is determined by back titration. The end of the condenser is dipped into a solution of boric acid. The ammonia reacts with the acid and the remainder of the acid is then titrated with a sodium carbonate solution with a methyl orange pH indicator.

Degradation $\text{Protein} + H_2SO_4 \rightarrow (NH_4)_2SO_4(aq) + CO_2(g) + SO_2(g) + H_2O(g)$

Liberation of ammonia $(NH_4)_2SO_4(aq) + 2NaOH \rightarrow Na_2SO_4(aq) + 2H_2O(l) + 2NH_3(g)$

Capture of ammonia $B(OH)_3 + H_2O + NH_3 \rightarrow NH_4^+ + B(OH)_4^-$

Back-titration $B(OH)_3 + H_2O + Na_2CO_3 \rightarrow NaHCO_3(aq) + NaB(OH)_4(aq) + CO_2(g) + H_2O$.

Precipitation Titration

Titrations with precipitating agents are useful for determining certain analytes. E.g., Cl^- can be determined when titrated with $AgNO_3$.

Detection of end point

- **Chemical**
  - Precipitation Type–Mohr's method
  - Adsorption–Fajan's method
  - For silver analysis–Volhard method
- **Sensors–Potentiometric or amperometric**

The chemical types are also classified into:

1. Indicators reacting with titrant forming specific colour.
2. Adsorption indicators.

Indicators reacting with the titrant

Two methods will be discussed where this type of indicators are applied; namely: Mohr and Volhard.

I) Mohr method for determining chloride

Chloride is titrated with $AgNO_3$ solution. A soluble chromate salt is added as the indicator. This produces a yellow colour solution. When the precipitation of the chloride is complete, the first excess of Ag^+ reacts with the indicator to precipitate red silver chromate:

$$2\,Ag^+(aq) + CrO_4^{2-}(aq) \rightarrow Ag_2CrO_4(s)$$

Yellow red ppt

The Mohr method must be performed at a pH about 8. This method is useful for determining Cl^- in neutral or unbuffered solutions such as drinking water.

II) Volhard titration

This is an indirect titration procedure for the determination of anions that precipitate with silver like Cl^-, Br^-, I^-, SCN^-, and it is preferred in acid (HNO_3) solution. A measured excess of $AgNO_3$ is added to precipitate the anion, and the excess of Ag+ is determined by back titration with standard potassium thiocyanate solution:

$$Ag^+(aq) + Cl^-(aq) \rightarrow AgCl(s) + \text{excess } Ag^+$$

$$\text{excess } Ag^+(aq) + SCN^-(aq) \rightarrow AgSCN(s)$$

The end point is detected by adding iron III (Fe^{3+}) as ferric ammonium sulfate which forms a soluble red complex with the first excess of titrant.

$$Fe^{3+}(aq) + SCN^-(aq) \rightarrow [FeSCN]^{2+}(aq)$$

These indicators must not form a compound with the titrant that is more stable than the precipitate or the colour reaction would occur on addition of the first drop of titrant.

Adsorption indicators

The indicator reaction takes place on the surface of the precipitate. The indicator, which is a dye, exists in solution as the ionized form, usually an anion.

Principle of adsorption

Consider the titration of Cl^- with Ag^+. Before the equivalent point, Cl^- is in excess and the primary layer is Cl^- (go back to precipitation process in gravimetry). This repulses the indicator anions; and the more loosely held the secondary (counter) layer of adsorbed ions is cations, such as

$$Na^+ \quad : \quad AgCl \quad : \quad Cl^- \; : \; : \; Na^+$$

Beyond the equivalent point (end point as well), Ag^+ is in excess and the surface of the precipitate becomes positively charged, with the 1° layer being Ag^+. This will now attract the indicator anion and adsorb it in the 2° (counter) layer:

$$AgCl \quad : \quad Ag^+ \; : \; : \; \text{indicator}^-$$

The colour of the adsorbed indicator is different from that of the unadsorbed indicator, and this difference signals the completion of the titration. The degree of adsorption of the indicator can be decreased by increasing the acidity.

The titration of chloride using this kind of indicator is called **Fajan's Method.**

Fajan's method is the most recent and most accurate silverhalide method. It is based on the adsorption of dichlorofluorescein (DCF) on the surface of the positively charged silver chloride particles formed in the precipitation titration when Ag+ ion is in excess.

Application of PPtion Titration Determination of anions such as halides, divalent anions, mercaptans.

Non-aqueous titration

Non-aqueous titration is the titration of substances dissolved in non-aqueous solvents. It is the most common titrimetric procedure used in pharmacopoeial assays and serves a double purpose: it is suitable for the titration of very weak acids and very weak bases, and it provides a solvent in which organic compounds are soluble.

The most commonly used procedure is the titration of organic bases with perchloric acid in *anhydrous* acetic acid.

Non-aqueous solvents

Aprotic solvents

These are neutral, chemically inert substances such as benzene and chloroform. They have a low dielectric constant, do not react with either acids or bases and therefore do not favour ionization. Since dissociation is not an essential preliminary to neutralization, aprotic solvents are often added to 'ionizing' solvents to depress solvolysis (which is comparable to hydrolysis) of the neutralization product and so sharpen the endpoint.

Protophilic solvents

These are basic in character and react with acids to form solvated protons.

$$HB + Sol. \rightleftharpoons Sol.H^+ + B^-$$

Acid + Basic solvent ⇌ Solvated proton + Conjugate base of acid

A weakly basic solvent has less tendency than a strongly basic one to accept a proton. Similarly, a weak acid has less tendency to donate protons than a strong acid. As a result a strong acid such as perchloric acid exhibits more strongly acidic properties than a weak acid such as acetic acid when dissolved in a weakly basic solvent.

On the other hand, all acids tend to become indistinguishable in strength when dissolved in strongly basic solvents owing to the greater affinity of strong bases for protons. This is called the **leveling effect**. Strong bases are leveling solvents for acids, weak bases are differentiating solvents for acids.

Protogenic solvents

These are acidic substances, e.g., sulphuric acid. They exert a levelling effect on bases.

Amphiprotic solvents

They have both protophilic and protogenic properties. Examples are water, acetic acid and the alcohols. They are dissociated to a slight extent. The dissociation of acetic acid, which is frequently used as a solvent for titration of basic substances, is shown in the equation below:

$$CH_3COOH \rightleftharpoons H^+ + CH_3COO^-$$

Here, the acetic acid is functioning as an acid. If a very strong acid such as perchloric acid is dissolved in acetic acid, the latter can function as a base and combine with protons donated by the perchloric acid to form protonated acetic acid, an onium ion:

$$HClO_4 \rightleftharpoons H^+ + ClO_4^-$$

$$CH_3COOH + H^+ \rightleftharpoons CH_3COOH_2^+ \text{ (onium ion)}$$

Since the $CH_3COOH_2^+$ ion readily donates its proton to a base, a solution of perchloric acid in glacial acetic acid functions as a strongly acidic solution.

When a weak base, such as pyridine, is dissolved in acetic acid, the acetic acid exerts its levelling effect and enhances the basic properties of the pyridine. It is possible, therefore, to titrate a solution of a weak base in acetic acid with perchloric acid in acetic acid, and obtain a sharp endpoint when attempts to carry out the titration in aqueous solution are unsuccessful.

Visual indicators for non-aqueous titration

Indicator	Colour change basic	Colour change neutral	Colour change acidic
Crystal violet (0.5 per cent in glacial acetic acid)	violet	blue-green	yellow-ish-green
α-Naphtholbenzein (0.2 per cent in glacial acetic acid)	blue or blue-green	orange	dark-green
Oracet Blue B (0.5 per cent in glacial acetic acid)	blue	purple	pink
Quinaldine Red (0.1 per cent in methanol)	magenta		almost colo

Gravemetric Analysis

Gravimetric analysis, which by definition is based upon the measurement of mass, can be generalized into two types: precipitation and volatilization.

The quantitative determination of a substance by the precipitation method of gravimetric analysis involves isolation of an ion in solution by a precipitation reaction, filtering, washing the precipitate free of contaminants, conversion of the precipitate to a product of known composition, and finally weighing the precipitate and determining its mass by difference. From the mass and known composition of the precipitate, the amount of the original ion can be determined.

Steps involved in gravemetric analysis

1. Coprecipitation

This is anything unwanted which precipitates with the thing you do want. Coprecipitation occurs to some degree in every gravimetric analysis (especially barium sulfate and those involving hydrous oxides). You cannot avoid it—all you can do is minimize it by careful precipitation and thorough washing.

2. Surface adsorption

Here unwanted material is adsorbed onto the surface of the precipitate. Digestion of a precipitate reduces the amount of surface area and hence the area available for surface adsorption. Washing can also remove surface material.

3. Occlusion

This is a type of coprecipitation in which impurities are trapped within the growing crystal.

4. Postprecipitation

Sometimes a precipitate standing in contact with the mother liquor becomes contaminated by the precipitation of an impurity on top of the desired precipitate.

5. Washing and filtering

Problems with coprecipitation and surface adsorption may be reduced by careful washing of the precipitate. With many precipitates, **peptization** occurs during washing. Here part of the precipitate reverts to the colloidal form e.g.,

$$AgCl \text{ (colloidal)} \rightleftharpoons AgCl \text{ (s)}$$

This results in the loss of part of the precipitate because the colloidal form may pass through on filtration. By washing with ice cold water, this can be minimized.

6. Drying of solid

Generally, the solids are dried at about 120°C but conditions for drying can vary considerably. To determine the correct drying regime, a thermogravimetric balance may be used.

Commercial Acids and Bases

Solution	Formula Weight	Molarity	Normality	Weight (%)	Specific Gravity
Acetic acid [CH_3COOH]	60.05	17.4	17.4	99.8	1.05
Ammonia [NH_4OH]	35.05	14.8	14.8	57	0.90
Hydrochloric acid [HCl]	36.46	12.1	12.1	37	1.19
Nitric acid [HNO_3]	63.01	15.8	15.8	70	1.42
Sulfuric acid [H_2SO_4]	98.08	18.0	36.0	96	1.84
Phosphoric acid [H_3PO_4]	97.1	14.8	44.6	85	1.70

Pharmaceutical Impurities

Impurities in pharmaceuticals are the unwanted chemicals that even in small amounts may influence the efficacy and safety of the pharmaceutical products. Impurity profiling is the identity as well as the quantity of impurity in the pharmaceuticals.

Sources of Impurities

Associated with API	Related to Formulation	Upon Aging
1. Organic Impurities	1. Process /Method Related	1. Ingredient interaction
2. Inorganic Impurities	2. Dosgae form related	2. Functional group degradation
3. Residual Solvents	3. Environment related	

ICH Guideline on Impurities

Q3A	Impurities in New Drug Substances
Q3B(R2)	Impurities in New Drug Products
Q3C	Guidelines for Residual solvents
Q3D	Guidelines for Elemental impurities

Drug Substances Impurities thresholds

Maximum daily Dose (x)	Reporting threshold (y, z)	Identification Threshold (z)	Qualification threshold
< 2g/day	0.05%	0.1% or 1 mg per day intake (whichever is lower)	0.15% or 1 mg per day intake (whichever is lower)
> 2g/day	0.03%	0.05%	0.05%

x. The amount of drug substance administered per day.
y. Higher reporting thresholds should be scientifically justified.
z. Lower thresholds can be appropriate if the impurity is unusually toxic.

Thresholds for degradation products in Drug Products

Maximum daily dose (a)	Reporting threshold (b,c)
≤1 g	0.1%
>1 g	0.05%
Maximum daily dose (a)	**Reporting threshold (b,c)**
<1 mg	1.0% or 5 µg TDI, whichever is lower
1 mg–10 mg	0.5% or 20 µg TDI, whichever is lower
>10 mg–2 g	0.2% or 2 mg TDI, whichever is lower
x>2 g	0.10%
Maximum daily dose (a)	**Reporting threshold (b,c)**
<10 mg	1.0% or 50 µg TDI, whichever is lower
10 mg–100 mg	0.5% or 200 µg TDI, whichever is lower
>100 mg–2 g	0.2% or 3 mg TDI, whichever is lower
>2 g	0.15%

a The amount of drug substance administered per day.
b Thresholds for degradation products are expressed either as a percentage of the drug substance or as total

daily intake (TDI) of the degradation product. Lower thresholds can be appropriate if the degradation product is unusually toxic.

c Higher thresholds should be scientifically justified

Residual Solvents

Class I solvents: Solvents to be Avoided Known human carcinogens strongly suspected human carcinogens Environmental hazards.

Residual solvent	Concentration limit (ppm)
Benzene	2 (Carcinogenic)
Carbon tetrachloride	4 (Toxic)
1,1 Dichloro ethene	8 (Toxic)
1,2 Dichloro ethene	5 (Toxic)
1,1,1 trichloro ethane	1500 (Environmental hazard)

Class II solvents: Solvents to be Limited Nongenotoxic animal carcinogens or possible causative agents of other irreversible toxicity, such as neurotoxicity or teratogenicity. Solvents suspected of other significant but reversible toxicities.

Solvent	Permissible daily exposure (mg/day)	Concentration limit (ppm)
Acetonitrile	4.1	410
Chlorobenzene	3.6	360
Chloroform	0.6	60
Cyclohexane	38.8	3880
1,2-Dichloroethene	18.7	1870
Dichloromethane	6	600
1,1-Dimethoxy-ethane	1	100
N,N-Dimehtyl acetamide	10.9	1090
N,N-Dimethyl formamide	8.8	880
1,2-Dioxane	3.8	380
2-Ethoxyethanol	1.6	160
Ethylene glycol	6.2	620
Formamide	2.2	220
Hexane	2.9	290
Methanol	30	3000
N-methyl pyrrol-idone	48.4	4840
Pyridine	2	200
Toluene	8.9	890
Xylenes	21.7	2170
Methyl cyclo hex-ane	11.8	1180
Methyl butyl ketone	0.5	50
Nitromethane	0.5	50
Sulfolane	1.6	160
Tetralin	1	100
1,1,2-Trichloro ethane	0.8	80

Class III Solvents: These are less toxic and possess lower risk to human health than class I or class II solvents. Long-term toxicity or carcinogenicity not reported, which is evident from the available data for the solvents under this category. The use of class III solvents in pharmaceuticals does not have any serious health hazard.

Solvents with Low Toxic Potential Solvents with low toxic potential to humans; no health-based exposure limit is needed. [NOTE—Class 3 residual solvents may have PDEs of up to 50 mg or more per day.]

Acetic acid	Dimethyl sulfoxide	Isobutyl acetate
Acetone	Ethanol	Isopropyl acetate
Anisole	Ethyl acetate	Methyl acetate
1-butanol	Ethyl ether	Propyl acetate
2-butanol	Ethyl formate	Pentane
Butyl acetate	Formic acid	Methyl ethyl ketone
Cumene	Heptane	Methyl isobutyl ketone
1- pentanol	1-propanol	2-propanol

Class IV Solvents: Class IV solvents, adequate toxicological data is not available. The manufacturers should justify the residual levels for these solvents in pharmaceutical products. The solvents under class IV are1, 1-diethoxy propane, 1-1-dimethoxy propane, 2-2-dimethoxy propane, methyl isopropyl ketone, isooctane, isopropyl ether, methyl tetrahydrofuran, petroleum ether, trichloro acetic acid.

Guideline for Elemental Impurities ICH Q3D
Three Class based on their Toxicity (PDE) and Occurrence

Type of Class	Elemental Impurities
Class 1	As, Cd, Hg & Pb
Class 2A	Co, Ni & V
Class 2B	Ag, Au, Ir, Os, Pd, Pt, Rh, Ru, Se & Tl
Class 3	Ba, Cr, Cu, Li, Mo, Sb & Sn

* PDE-Permitted daily exposure

Class 1: The elements, As, Cd, Hg, and Pb, are human toxicants that have limited or no use in the manufacture of pharmaceuticals. Their presence in drug products typically comes from commonly used materials (e.g., mined excipients). Because of their unique nature, these four elements require evaluation during the risk assessment, across all potential sources of elemental impurities and routes of administration. The outcome of the risk assessment will determine those components that may require additional controls which may in some cases include testing for Class 1 elements. It is not expected that all components will require testing for Class 1 elemental impurities; testing should only be applied when the risk assessment identifies it as the appropriate control to ensure that the PDE (permitted daily exposure) will be met.

Class 2: Elements in this class are generally considered as route-dependent human toxicants. Class 2 elements are further divided in sub-classes 2A and 2B based on their relative likelihood of occurrence in the drug product.

- Class 2A elements have relatively high probability of occurrence in the drug product and thus require risk assessment across all potential sources of elemental impurities and routes of administration (as indicated). The class 2A elements are: Co, Ni and V.
- Class 2B elements have a reduced probability of occurrence in the drug product related to their low abundance and low potential to be co-isolated with other materials. As a result, they may be excluded from the risk assessment unless they are intentionally added during the manufacture of drug substances, excipients or other components of the drug product. The elemental impurities in class 2B include: Ag, Au, Ir, Os, Pd, Pt, Rh, Ru, Se and Tl.

Class 3: The elements in this class have relatively low toxicities by the oral route of administration (high PDEs, generally > 500 µg/day) but may require consideration in the risk assessment for inhalation and parenteral routes. For oral routes of administration, unless these elements are intentionally added, they do not need to be considered during the risk assessment. For parenteral and inhalation products, the potential for inclusion of these elemental impurities should be evaluated during the risk assessment, unless the route specific PDE is above 500 µg/day. The elements in this class include: Ba, Cr, Cu, Li, Mo, Sb, and Sn.

Other elements: Some elemental impurities for which PDEs have not been established due to their low inherent toxicity and/or differences in regional regulations are not addressed in this guideline. If these elemental impurities are present or included in the drug product they are addressed by other guidelines and/or regional regulations and practices that may be applicable for particular elements (e.g., Al for compromised renal function; Mn and Zn for patients with compromised hepatic function), or quality considerations (e.g., presence of W impurities in therapeutic proteins) for the final drug product. Some of the elements considered include: Al, B, Ca, Fe, K, Mg, Mn, Na, W and Zn.

Permitted Daily Exposures(PDEs) for Elemental Impurities

Element	Class	Oral PDE µg/day	Parenteral PDE, µg/day	Inhalation PDE, µg/day
Cd	1	5	2	2
Pb	1	5	5	5
As	1	15	15	2
Hg	1	30	3	1
Co	2A	50	5	3
V	2A	100	10	1
Ni	2A	200	20	5
Tl	2B	8	8	8
Au	2B	100	100	1
Pd	2B	100	10	1
Ir	2B	100	10	1
Os	2B	100	10	1
Rh	2B	100	10	1
Ru	2B	100	10	1
Se	2B	150	80	130
Ag	2B	150	10	7
Pt	2B	100	10	1
Li	3	550	250	25
Sb	3	1200	90	20
Ba	3	1400	700	300
Mo	3	3000	1500	10
Cu	3	3000	300	30
Sn	3	6000	600	60
Cr	3	11000	1100	3

Multiple Choice Questions

1. Bending vibrations include all following except
(a) Rocking (b) Stretching
(c) Twisting (d) Wagging

2. For calibration of wave number scale in IR _____ is used.
(a) Holmium filter (b) Polystyrene film
(c) Polyvinyl film (d) None

3. For obtaining IR radiation Nernst filament should be heated to _____°C.
(a) 500–1000 (b) 1000–1500
(c) 2000–2500 (d) 1000–1800

4. CO_2 not identified by IR spectroscopy it's due to
(a) CO_2 has no dipole moment although C=O is polar
(b) CO_2 has no dipole moment since C=O is non-polar
(c) Optical activity of the system
(d) Both a and b

5. Which of the following requires the most energy in IR?
(a) Wagging (b) Asymmetric bend
(c) Twisting (d) Asymmetric stretch

6. Lasers are nowadays used as radiation source in visible and IR regions because
(a) It emits highly monochromatic light.
(b) It emits coherent light
(c) Little or no spreading of radiation as it propagates
(d) All the above are correct

7. In far infrared region the radiation sources use is
(a) Incandescent lamp (b) Nernst glower
(c) Globar sources (d) Mercury Arc

8. In XY_2 molecule vibration of atom is take place in same plan and only bond angle is change then it is called
(a) Stretching vibration
(b) Bending vibration
(c) Scissoring vibration
(d) Rocking vibration

9. SiC rod heated to a high temperature is used as
(a) Source of light in IR
(b) Detector in IR
(c) Source of light in UV
(d) Source of light in florimetry

10. The IR spectrum of an organic liquid can be taken by placing it between a pair of polished plates made of
(P) NaCl
(Q) eSO_4
(R) KBr
(S) $AlCl_3$
(a) P, Q (b) P, S
(c) R, S (d) P, R

11. The region mostly used for IR spectroscopy is
(a) Near IR (b) Mid-IR
(c) Far IR (d) Very far IR

12. Hexachlorobutadiene is preferred over Nujol as a mulling agent because
(a) It is non toxic
(b) It does not give C–H vibration bands
(c) It is transparent over IR range
(d) It has very high boiling point.

13. The band width in IR _____ due to H bonding.
(a) Increases
(b) Decreases
(c) Remains unchanged
(d) Cannot be predicted

14. Homo molecular molecules are IR inactive because
(a) They cannot give vibrational spectra
(b) They have only stretching vibrations
(c) They have no bending vibrations
(d) The dipole moment does not change during vibration

15. Which of the following transitions will require more wavelengths?
(a) Vibrational
(b) Rotational
(c) Electronic
(d) Vibrational – Rotational

16. Which of the following prisms will you use for IR spectroscopy?
(a) Glass prism
(b) Fused silica prism
(c) Prism coated with NaCl
(d) All can be used

17. Which of the following is not a thermal detector that used in IR spectroscopy?
(a) Thermocouple
(b) Photoconductive detector

(c) Bolometer
(d) Golay pneumatic detector

18. IR spectroscopy generally used to determine
(a) Molecular structure
(b) Functional group
(c) Number of protons
(d) All of the above

19. Pressed disk techniques for the sample preparation in IR involve the use of
(a) Salt plate (b) Nujol
(c) KBr (d) All of the above

20. Why is the oxygen–hydrogen absorption of CH_3OH is such a broad band in the infrared?
(a) Rotational energy levels broaden the absorption
(b) Hyperconjugation resonance broadens the absorption
(c) Resonance broadens the absorption
(d) Hydrogen bonding broadens the absorption

21. Which of the following bonds would show the strongest absorption in the IR?
(a) Carbon–hydrogen
(b) Oxygen–hydrogen
(c) Nitrogen–hydrogen
(d) Sulfur–hydrogen

22. Normally graph plotted in IR spectroscopy?
(a) % T vs frequency
(b) % T vs wave number
(c) Absorbance vs wave number
(d) Absorbance vs wavelength

23. The solvent not used in IR spectroscopy is
(a) Chloroform (b) Carbon tetra chloride
(c) Carbon disulfite (d) Water

24. FT IR instrument does not contain
(a) Monochromator
(b) Grattings are covering entire IR range
(c) Quartz made prism acts as monochromator
(d) None of the above

25. Which of the following sequence is the correct order of C=O stretching in descending order?
(a) Ester, ketone, acid, amide
(b) Acid, amide, ketone, ester
(c) Ester, ketone, amide, acid
(d) Amide, acid, ketone, ester

26. Fermi resonance is often observed in
(a) Carbonyl compounds
(b) Azo compounds
(c) Halogenated compounds
(d) Nitro compounds

27. Sample window suitable for IR of aqueous solution of a compound is
(a) KBr (b) CsBr
(c) CaF_2 (d) NaCl

28. In IR spectra, C–H stretching of aldehyde is at
(a) 2850–2750 cm^{-1} (b) 1750–1725 cm^{-1}
(c) 2250–2150 cm^{-1} (d) 2100 cm^{-1}

29. In Raman spectroscopy optical system is made up of
(a) Glass or quartz (b) NaBr or CaF_2
(c) KBr or NaBr (d) All of the above

30. Conjugation of C=C with C=O causes what effect on frequency of C=O bond in IR spectrum?
(a) Lower the frequency
(b) Increase the frequency
(c) No change in frequency
(d) None of the above

31. Mercury lamp is used as radiation source in which technique?
(a) Colorimetry
(b) Flourimetry
(c) UV visible spectroscopy
(d) Infrared

32. Which following source is used in Raman spectrometry?
(a) Hydrogen (b) Deuterium lamp
(c) Xenon arc lamp (d) Helium/neon laser

33. C=O bond in IR spectrum of acetic anhydride gives peak at which frequency (in cm^{-1})?
(a) 1760 (b) 1725
(c) 1810 (d) (a) and (c)

34. Which of following gas is present in Golay detector?
(a) Xenon (b) rgon
(c) Helium (d) Hydrogen

35. Rod of sintered silicon is present in which of following?
(a) Incandescent lamp (b) Nernst glower
(c) Globar source (d) Carbon dioxide laser

36. Which is the right frequency (cm^{-1}) order for O–H bond IR spectrum?
(a) Phenols < 1º alcohol < 2º alcohol < 3ºalcohol
(b) 1º alcohol> 2º alcohol> 3ºalcohol> phenols

(c) Phenols> 1º alcohol > 2ºalcohol> 3ºalcohol
(d) 1ºalcohol < 2º alcohol < 3º alcohol < phenols

37. In IR spectra, alkyne has characteristic peak at
(a) 1680 cm^{-1} (b) 2150 cm^{-1}
(c) 2750 cm^{-1} (d) 1810 cm^{-1}

38. What is Nujol?
(a) Hexachlorobutadiene
(b) Hexachloropentadiene
(c) Mineral oil
(d) Heptachlorobutadiene

39. Wavelength 780 nm = _____wave number
(a) 7800 cm^{-1} (b) 12800 cm^{-1}
(c) 25000 cm^{-1} (d) 4000 cm^{-1}

40. Wavelength 2.5 μm =_____ wave number
(a) 400 cm^{-1} (b) 4000 cm^{-1}
(c) 250 cm^{-1} (d) 2500 cm^{-1}

41. In IR, pyroelectric detector is constructed from
(a) Mercury cadmium telluride
(b) Triglycine sulphate
(c) Lead and telluride
(d) Both (a) and (c)

42. Which is the right frequency (cm^{-1}) order for C–O bond IR spectrum?
(a) Phenols < 1° alcohol < 2" alcohol < 3° alcohol
(b) 1° alcohol > 2° alcohol > 3° alcohol > phenols
(c) Phenols > 1° alcohol > 2° alcohol > 3° alcohol
(d) 1° alcohol < 2 alcohol < 3° alcohol < phenols

43. In a photo emissive tube, the following coating material is used:
(a) Silver
(b) Gold
(c) Oxides of K, Ag or Cs
(d) KBr

44. One of the following wavelength regions is used for near IR:
(a) 400 nm–800 nm (b) 800 nm–2.5 μm
(c) 2.5 μm–25 μm (d) 25 um–0.04 cm

45. What is the wavelength of mid-IR?
(a) 800–2500 nm (b) 2500–4000 nm
(c) 4000–25000 nm (d) 25000–50000 nm

46. Hook's law is associated with
(a) IR (b) NMR
(c) Mass (d) UV

47. In IR photo conducting detector can be constructed from
(a) Lead sulfide
(b) Lead telluride
(c) Mercury cadmium telluride
(d) All of the above

48. Which of following compound is used Mull technique instead of Nujol?
(a) Hexachlorobutadiene
(b) KBr
(c) Hexabromobutadiene
(d) NaCl

49. In IR spectra, alkene have C=C stretching at
(a) 1280–1220 cml^{-1} (b) 1360–1300 cm^{-1}
(c) 1680–1620 cm^{-1} (d) 2180–2150 cm^{-1}

50. What is the frequency range (in cm^{-1}) for the carbonyl group of lactum ring in IR spectra?
(a) 1620–1660 (b) 1720–1780
(c) 1660–1720 (d) 1780–1840

51. Following are the frequency range (in cm^{-1}) in IR spectra for different groups containing (–C=O) Which of following pair is not true?
(a) Aldehyde: 1740–1720
(b) Ketone: 1700–1650
(c) Amide: 1680–1630
(d) Acid chloride: 1800

52. Which of following technique is used to detect the hydrogen bonding in compound?
(a) UV visible spectroscopy
(b) Infrared
(c) Flourimetry
(d) Colorimetry

53. In IR spectra, alkyne has characteristic peak at
(a) 1680 cm^{-1} (b) 2150 cm^{-1}
(c) 2750 cm^{-1} (d) 1810 cm^{-1}

54. Fourier transform is
(a) A mathematical function
(b) Used to convert from the time domain to the frequency domain
(c) Used in many modern analytical techniques
(d) All of the above

55. Hexachlorobutadiene is preferred over Nujol as a mulling agent because
(a) It is non toxic
(b) It does not give C–H vibration bands

(c) It is transparent over IR range
(d) It has very high boiling point

56. Gratings are generally preferred over prisms for dispersive IR because:
(a) Better resolution is possible
(b) Linear dispersion is achieved
(c) Gratings are resistant to attack by water
(d) All are correct

57. The grating in IR spectrophotometer is made up of
(a) Glass (b) Quartz
(c) Alkyl halides (d) Polystyrene

58. The most commonly used mulling reagent in IR is
(a) $CHCl_3$
(b) Nujol
(c) Hexachlorobutadienc
(d) Chlorofluoro carbon oil

59. In alcohol, the –OH stretches approximately
(a) 1725 cm^{-1} (b) 1660 cm^{-1}
(c) 3345 cm^{-1} (d) 2300 cm^{-1}

60. The region of an infra-red spectrum where many absorptions take place is known as the _____
(a) Thumbprint region
(b) Handprint region
(c) Footprint region
(d) Fingerprint region

61. Bolometer is made up of
(a) Two dissimilar metals
(b) Non-centro-symmetric crystal
(c) Fused mixture of metal oxide
(d) Pt strip in evacuated vessel

62. Which is used in calibration of IR instrument?
(a) TMS (b) Glass
(c) Metal halide (d) Polystyrene

63. Which material is used in pressed pellet technique?
(a) Cholorofluoro carbon oil
(b) NaCl
(c) Hexacholoro butadiene
(d) KBr

64. What is multiplex advantage?
(a) Decreased energy throughput
(b) Increased energy throughput
(c) Increased N/S ratio
(d) Increased S/N ratio

65. Basic principle underlying FT-IR is?
(a) Polarization (b) Diffraction
(c) Refraction (d) Interference

66. Which solvent is normally used in IR spectroscopy?
(a) DMSO–D_6 (b) CS_2 or CCl_4
(c) H_2O (d) Methanol

67. What is the normal range of fingerprint region in IR?
(a) 8000–4000 cm^{-1} (b) 4000–1500 cm^{-1}
(c) 1500–500 cm^{-1} (d) 4000–500 cm

68. What is selection rule for a molecule to become IR active in I.R. spectroscopy?
(a) Must show change in dipole moment
(b) Must show dipole moment
(c) Must show change in magnetic moment
(d) Must show magnetic moment

69. Compound A with formula C_2H_7N shows the following important bands in the IR spectra: (i) 3423 cm^{-1} (ii) 3236 cm^{-1}
(a) $–CH_3$ (b) $–NH_2$
(c) –CN (d) =C=N

70. In IR Spectroscopy the changes in electronic energy is always associated with charges in
(a) Rotational energy
(b) Vibrational and rotational
(c) Vibrational, rotational and translational
(d) All

71. In Raman spectroscopy physical properties measured is
(a) Absorption of radiation
(b) Scattering of radiation
(c) Emission of radiation
(d) Rotation of radiation

72. Globar sources is made of
(a) Earth oxide Zirconia
(b) Mercury
(c) Silicon dioxide
(d) Silicon carbide

73. In aldehydes, the C=O stretch approximately
(a) 1725 cm^{-1} (b) 1660 cm^{-1}
(c) 2750 cm^{-1} (d) 3300 cm^{-1}

74. Which of the following statements are correct?
(a) An IR detector which responds to heat changes is more efficient than a photocell.
(b) A photocell detector is more useful in UV and visible regions.

(c) All the optical components of the instrument used in optical regions of EM spectrum must be transparent towards the region being studied.
(d) All are correct

75. Gratings are generally preferred over prisms for dispersive IR because
(a) Better resolution is possible
(b) Linear dispersion is achieved
(c) Gratings are resistant to attack by water
(d) All are correct

76. NMR signal is obtained in 1,4-dioxane
(a) 3 peaks (b) 2 peaks
(c) 1 peak (d) 4 peaks

77. Reference compound used in NMR spectroscopy is
(a) Silane (b) Trimethylsilane
(c) Dimethylsilane (d) Tetramethylsilane

78. What is the delta value for TMS in NMR?
(a) 0 (b) 10
(c) 5 (d) 7

79. Radiofrequency radiation is associated with
(a) NMR (b) IR
(c) Mass spectroscopy (d) UV

80. Number of NMR signal generated by acetone is
(a) 2 (b) 6
(c) 3 (d) 1

81. The unit of magnetic field strength in NMR is
(a) Cycles/second (b) Gauss
(c) Pulse/second (d) Debye

82. Solvent commonly used in NMR is
(a) Chloroform
(b) Methanol
(c) Carbon tetrachloride
(d) Acetone

83. Rotation of electrons about the protons generates a secondary magnetic field which opposes the applied magnetic field. The proton is said to be
(a) Shielded (b) H-bonded
(c) Deshielded (d) Shifted

84. What is δ value of aldehyde proton in PMR spectrum?
(a) 1–2 (b) 4–5
(c) 7–8 (d) 9–10

85. Which is the unit of magnetic field?
(a) Gauss (b) esla
(c) Weber (d) All of the above

86. Position of signal in NMR spectrum indicates
(a) Number of different kind of the proton present in different environment
(b) Electronic environment of each kind of proton
(c) Relative number of protons of each kind
(d) Number of neighbouring proton present

87. Which compound is used as an internal reference standard for aqueous solution in NMR?
(a) DMSO-d_6
(b) $CDCl_3$
(c) 2,2-dimethy-l,2-silapentane-5-sulphonate
(d) Hexachloro acetone

88. Intensities in NMR spectrum indicate
(a) Number of different kinds of the protons present in different environment
(b) Electronic environment of each kind of protons
(c) Relative number of protons of each kind
(d) Number of neighbouring proton present

89. Wave length used in the NMR (nuclear magnetic resonance) is
(a) 10^{10} nm to 10^{12} nm
(b) 10^{8} nm to 10^{10} nm
(c) 10^{10} μm to 10^{11} μm
(d) 10^{8} μm to 10^{10} μm

90. Magic angle NMR is carried out at which angle?
(a) 52.7 (b) 54.7
(c) 56.7 (d) 58.7

91. The number of signals in NMR spectrum indicates _____
(a) Number of different kinds of protons present in different environment
(b) Electronic environment of each kind of proton
(c) Relative number of protons of each kind
(d) Number of neighbouring protons present

92. Which of following has the highest chemical shift (PPM)value?
(a) CH_3I (b) CH_3Br
(c) CH_3F (d) CH_3Cl

93. How many PMR peaks are given by 1, 2- dichloro propane?
(a) 2 (b) 3
(c) 4 (d) 5

94. Splitting of signal in NMR spectrum indicates

(a) Number of different kinds of protons present in different environment
(b) Electronic environment of each kind of proton
(c) Relative number of protons of each.
(d) Number of neighbouring protons present

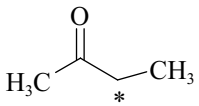
95. Allyl alcohol has how many NMR peaks?
(a) 2 (b) 3
(c) 4 (d) 5

96. Unit of coupling constant is
(a) Cycle per second (b) Hertz
(c) Both (d) None of the above

97. PMR of 2-methyl 1-pentene gives how many peaks?
(a) 3 (b) 4
(c) 5 (d) 6

98. Presence of Si in TMS causes
(a) Deshielding and upfield
(b) Deshielding and downfieJd
(c) Shielding and upfield
(d) Shielding and downfield

99. What is the multiplicity expected in the hydrogen NMR spectrum for the hydrogen atoms marked by a "star" in the following compound?

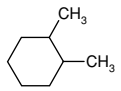


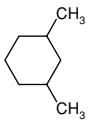
(a) Singlet (b) Triplet
(c) Quartet (d) Heptet

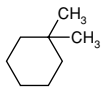
100. Which of following is universal solvent in NMR?
(a) CCI_4 (b) DMSO-d_6
(c) $CDCI_3$ (d) Hexachloroacetone

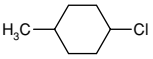
101. Unit of chemical shift δ is
(a) Hz (b) ppm
(c) Cps (d) Unit less

102. The C^{13} NMR spectrum of an unknown compound shows 4 absorptions and the H^1 NMR spectrum shows 4 absorptions. Which of the following compounds is the unknown compound?

(a) 

(b) 

(c) 

(d) 

103. m-dibromo benzene has how many PMR peaks?
(a) 1 (b) 2
(c) 3 (d) 4

104. Presence of electronegative atom on NMR spectra cause
(a) Deshielding and upfield
(b) Deshielding and downfield
(c) Shielding and upfield
(d) hielding and downfield

105. Coupling causes the peaks in ^1H NMR spectra to be split _____
(a) Into two peaks
(b) Into multiple peaks equal to the number of hydrogen on surrounding atoms
(c) Into multiple peaks equal to the number of surrounding carbon atoms
(d) Into multiple peaks equal to the number of hydrogen on surrounding atoms, plus one

106. Environmental effects that occur in NMR is
(a) Chemical shift (b) hemical exchange
(c) Spin spin splitting (d) Both (a) and (b)

107. The pressure inside a mass spectrometer is
(a) Lower than atmospheric pressure
(b) Almost nil
(c) Higher than atmospheric pressure
(d) Equal to atmospheric pressure

108. Telsa is a unit to express
(a) Frequency (b) Pressure
(c) Voltage (d) Magnetic field strength

109. One of the following compounds gives 3 signals in NMR spectroscopy.
(a) CH_3–COOH (b) CH_3–CH_2–NH_2
(c) CH_3–O–CH_3 (d) CH_3–CH_2–Cl

110. Benzene gives _____ NMR signal.
(a) 1 (b) 2
(c) 3 (d) 6

111. The number of peaks shown by diethyl ether in an NMR spectrum are is
(a) Four (b) Two
(c) One (d) Five

112. Nuclear magnetic moment is not shown by
(a) ^{13}C (b) ^{16}O
(c) ^1H (d) ^{15}N

113. In NMR spectroscopy radiation source used is

(a) Radiofrequency source transmitter
(b) Tungsten lamp
(c) Xenon arc lamp
(d) Mercury vapour lamp

114. The method of expressing magnetic field strength is
(a) Cycles/second (b) Pulses/second
(c) Debye units (d) Gauss

115. A solvent used in NMR studies is
(a) Chloroform
(b) Acetone
(c) Carbon tetrachloride
(d) Ethanol

116. Rotation of electrons about the proton generates a secondary magnetic field which may oppose the applied magnetic field. The proton is then said to be
(a) Shielded (b) Shifted
(c) Hydrogen bonded (d) Deshielded

117. Coupling constant (J) value
(a) Depends upon magnetic field
(b) Is independent of field strength
(c) Depends upon reference standard used
(d) Depends on solvents used

118. Anisotropic effect means
(a) Shielding of protons through space by counter magnetic field
(b) Shielding or deshielding of protons through space by counter magnetic field
(c) Shielding or deshielding of protons through space by applied magnetic field
(d) Shielding of protons through space by applied magnetic field

119. Spin quantum number I of ^{13}C is
(a) 0 (b) 1
(c) 1/2 (d) 3/2

120. 1 Telsa is equal to _____ gauss.
(a) 10^4 (b) 10^5
(c) 10^6 (d) 10^3

121. Cyclo butane have NMR signal is
(a) 1 (b) 2
(c) 4 (d) 3

122. Coupling constant (J) value is expressed in unit is
(a) Hertz (b) Cycle per cm
(c) Cycle into second (d) cm

123. Isotopic composition of ^{13}C in carbon is
(a) 1.1% (b) 1.6%
(c) 10% (d) 0.99%

124. In NMR greater the deshielding of proton,
(a) Larger the value of δ or smaller value of τ
(b) Smaller the value of δ or larger value of τ
(c) Larger the value of δ and larger value of τ
(d) Smaller the value of δ and smaller value of τ

125. 2-bromo propene gives NMR signal is
(a) 2 (b) 3
(c) 4 (d) 6

126. The most intense peak in the mass spectrum is called
(a) Mass peak (b) Metastable peak
(c) Base peak (d) M + 1 peak

127. What is nuclear-Zeeman effect in NMR?
(a) Transition from lower energy spin state to higher energy spin state
(b) Splitting of spin states in applied external magnetic field
(c) Splitting of spin states in absence of field
(d) Precessional motion of nuclei in applied magnetic field

128. Which is not a correct statement about chemical shift?
(a) Depends on applied external magnetic field
(b) Does not depend on applied external magnetic field
(c) Dimensionless
(d) Expressed in ppm

129. Correct formula for gyro-magnetic ratio (γ) is
(a) γ = magnetic moment/spin quantum number
(b) γ = magnetic moment/spin angular moment
(c) γ = spin angular moment/magnetic moment
(d) γ = spin quantum number/magnetic moment

130. How many PMR signals will come in NMR spectra of iso-butylene.
(a) 5 (b) 2
(c) 3 (d) 4

131. What is range of chemical shift (δ) in PMR spectra?
(a) 0 to 100 (b) 0 to 200
(c) 0 to 20 (d) 0 to 10

132. How many PMR signals will come in NMR spectra of vinylchloride?
(a) 2 (b) 3
(c) 4 (d) 5

133. Proton NMR is useful for investigating the structure of organic compounds because _____
(a) Organic compounds contain carbon atoms
(b) Organic compounds are mostly covalent
(c) Hydrogen atoms are found in nearly all organic compounds
(d) Organic compounds have low boiling points

134. Which of the following statements about tetramethylsilane is incorrect?
(a) It produces a single peak at $\delta = 10$
(b) It is inert
(c) It is used to provide a reference against which other peaks are measured
(d) It is volatile and can be easily distilled off and used again

135. In a triplet, the relative peak areas are in the ratio _____
(a) 1:1:1 (b) 1:2:1
(c) 1:3:1 (d) 1:4:1

136. All solvents are used to record NMR spectra except:
(a) $CDCI_3$ (b) DMSO-d_6
(c) C_2H_5 OH (d) Deutariated benzene

137. In mass spectrometry ^{81}Br shows:
(a) M+1 peak (b) M+2 peak
(c) M+3 peak (d) M+4 peak

138. Klystron is used as radiation source in
(a) X-ray diffraction
(b) Electron spin resonance
(c) Mass spectrometry
(d) None of above

139. In mass spectra, the most intense peak is the
(a) Base peak
(b) Metastable ion peak
(c) Fragment ion peak
(d) Rearrangement ion peak

140. Which of following ionization technique is used in molecular weight determination of large biomolecule by using mass?
(a) Electron impact (b) Chemical ionization
(c) MALDI (d) None of the above

141. A mass spectrometer bombards molecules with a high energy electron beam in
(a) Colloidal Phase (b) Liquid Phase
(c) Solid State (d) Vapour Phase

142. The inert gas used in the ionization stage of mass spectrometry is
(a) Helium (b) rgon
(c) Xenon (d) Methane

143. The correct order for the basic features of a mass spectrometer is _____
(a) Acceleration, deflection, detection, ionization
(b) Ionisation, acceleration, deflection, detection
(c) Acceleration, ionisation, deflection, detection
(d) Acceleration, deflection, ionisation, detection

144. Principal involved in mass spectrometer is
(a) Excitation of electron
(b) Electron impact bombardment
(c) Molecular vibration
(d) Splitting of electrons magnetic energy

145. A mixture of the following gases can be used in flame photometry to get a temperature of 3125°C:
(a) Hydrogen and nitrous oxide
(b) Acetylene and oxygen
(c) Hydrogen and air
(d) Hydrogen and oxygen

146. In mass spectroscopy positively charged ions can be produced by
(P) Heating the sample
(Q) Bombarding the sample with high energy electrons
(R) Bombarding the sample with high energy protons
(S) Chemical oonization
(a) Q, S (b) Q, R
(c) P, R (d) P, S

147. In mass spectrum M-18 peak indicates loss of
(a) Hydroxyl group (b) Hydrogen
(c) Methyl group (d) Water molecule

148. In mass spectrum of yoluene, widely the meta stable peak appear at
(a) 91 m/e (b) 77 m/e
(c) 46.6 m/e (d) 64.5 m/e

149. Metastable peaks have following all characteristics except
(a) These peaks are much broader that is they spread over mass units
(b) These peaks are of high intensity
(c) These peaks appear in the mass spectrum usually at non-integral m/e value
(d) The meta stable ions can be detected by a double focusing mass spectrometer

150. Removal of a single electron from a molecule results in the formation of
(a) Fragment ion (b) Metastable ion
(c) Molecular ion (d) Rearrangement ion

151. The reference electrode in potentiometry is _____
(a) Dropping mercury electrode
(b) Saturated calomel electrode
(c) Platinum electrode
(d) Glass electrode

152. Nitrogen estimation is done by
(a) Kjeldahl method (b) Gasometry
(b) Karl Fischer (d) None of the above

153. TGA curve is a plot
(a) Weight vs temperature
(b) eight vs volume of titrant
(b) eight vs current
(d) Weight loss vs temperature

154. Diazotisation titration is used for the assay of
(a) NSAIDs (b) Sulpha drugs
(b) teroids (d) All of the above

155. Rotating platinum electrode used in amperometry rotates at _____ rpm.
(a) 6 (b) 600
(c) 60 (d) 6000

156. The end point of complexometric titrations is shown by
(a) Acid–base indicators
(b) pM indicators
(c) Colorimeter
(d) pH meter

157. For conjugated acid-base pairs, following equation is correct.
(a) p*K*a = p*K*w – p*K*b (b) p*K*w = p*K*a – p*K*b
(c) p*K*w = p*K*a + p*K*b (d) p*K*a = p*K*b

158. Analytical Method Validation is mention in _____ guidelines.
(a) EMEA (b) ICH
(b) WHO (d) GMP

159. Robustness in used to determine
(a) Minor deliberate changes
(b) Inter- intraday studies
(c) Interference from excipients
(d) Major changes

160. Conformation of drugs is commonly determined by:
(a) NMR (b) Polarimetry
(c) Mass spectrometry (d) pH determination

161. Dropping mercury electrode is an important component of
(a) HPLC (b) Spectrophotometer
(c) Polarograph (d) Potentiometer

162. Conductivity cells are made up of
(a) Copper rods
(b) Two parallel sheets of platinum
(c) Glass membranes with Ag/AgCl
(d) Sb-SbP3

163. Quantitative analysis by polarography is based on
(a) Electrode potential (b) Half-wave potential
(c) Migration current (d) Limiting current.

164. Nernst equation is used to measure

$E = E^{\ominus} + (RT/nF) \ln a_{M^{n+}}$

(a) Conductance (b) Potential difference
(c) Current (d) Resistance

165. Glass transition temperature is detected through
(a) X-Ray diffractometery
(b) Solution calonmetery
(c) Differential scanning calorimeter
(d) Thermogravimetric analysis

166. Iodine number of fat is determining to know:
(a) Free fatty acid
(b) Average molecular size
(c) Relative unsaturation
(d) All of the above

167. 100 ppm solution =
(a) 100 µg/ml (b) 10% w/w
(c) 10 µg/ml (d) 10 mg/ml.

168. In MOHR'S method of precipitation titration which indicator is used?
(a) Fluorescein (b) Potassium chromate
(c) Ferric ion (d) NaCl solution

169. $SnCl_4$ acts as Lewis acid because
(a) It has six electrons and so need two electrons to complete octet
(b) It has eight electrons but can accept two more electrons
(c) It has positive charge
(d) None of the above

170. Specific conductance (conductivity 'k') unit is

(a) Ohm cm^{-1} (b) Mho cm^{-1}
(c) Ohm cm (d) hm^{-1} cm^{-1}

171. Ammonium purpurate (murexide) is used for determination of
(a) Sodium (b) Calcium
(c) Silver (d) Iron

172. Which of following primary standards used to standardize perchloric acid?
(a) Potassium hydrogen phthalate
(b) Sodium carbonate
(c) KBr
(d) Oxalic acid

173. What is the reagent used for diazotization?
(a) $NaNO_2$ + dilute HCl
(b) KNO_3 + dilute H_2SO_4
(c) Zn + dilute H_2SO_4
(d) Tin + H_2SO_4

174. How many grams of NaOH is required to prepare 100 ml 1M solution of NaOH?
(a) 400 mg (b) 4 g
(c) 200 mg (d) 2 g

175. How many significant figures in 0.002500?
(a) 7 (b) 5
(c) 4 (d) 2

176. In polymerase chain reaction renaturation is carried out at what condition (temperature and time)?
(a) At 95ºC for 1 min (c) At 55ºC for 2 min
(b) At 95ºC for 2 min (d) At 55ºC for 1 min

177. In polarography, half-wave potential indicates
(a) Quality of compound
(b) Quantity of compound
(c) Both of the above
(d) None of the above

178. Sulphafurazole is assayed by
(a) 0.1 M NaOH (b) 0.1 M TBAH
(c) 0.1M $NaNO_2$ (d) 0.1M $HClO_4$

179. Which of following is protogenic solvent?
(a) Sulphuric acid (b) Formic acid
(c) Both (d) None of the above

180. 10 Faraday = _____ Coulomb.
(a) 96500 (b) 965000
(c) 94600 (d) 946000

181. Which of following drug is analysed by gravimetry?
(a) $BaSO_4$
(b) NaCl
(c) Paracetamol
(d) Ascorbic acid

182. In thermogravimetric titration which of following property is measured with ml of titrant?
(a) Heat absorbed
(b) Heat evolved
(c) Change in temperature
(d) All of the above

183. Angle between source and detector in calorimeter is
(a) 90° (b) 45°
(c) 180° (d) 60°

184. IS0 9000 Series has five main type (ISO 9000, ISO 9001, ISO 9002, ISO 9003, ISO 9004). Which of them are descriptive documents?
(a) ISO 9000 & ISO 9002
(b) ISO 9001 & ISO 9002
(c) ISO 9003 & ISO 9004
(d) ISO 9000 & ISO 9004

185. 10 gauss = _____
(a) 100 Tesla (b) 1000 Tesla
(c) 10000 Tesla (d) 100000 Tesla

186. Polarogram of a solution containing an electro-reducible substance is obtained by plotting
(a) Current vs Volume
(b) Current vs Potential
(c) Resistance vs Time
(d) Potential vs Volume

187. Paracetamol is assayed by
(a) Ceric ammonium sulphate
(b) I_2
(c) HPLC
(d) KIO_3

188. Which of following is aprotic solvent?'
(a) Benzene (b) Glacial acetic acid
(c) Pyridine (d) Ethylenediamine

189. Which of following used as precipitating agent for Ca^{2+} ion in gravimetric analysis?
(a) $BaCl_2$ (b) HNO_3
(c) NH_4SCN (d) $H_2C_2O_4$

190. HCl reacts with $Ba(OH)_2$ to give water and $BaCl_2$. If 25.00 mL of an HCI solution reacts with 25.00 mL of

a 0.2000 M Ba(OH)2 what is the molarity of the HCl solution?(hint: write out the reaction!)

(a) 0.2000 M (b) 0.4000 M
(c) 0.1000 M (d) None of these

191. In polarography, to eliminate migration current which the of following is used?

(a) NaCI (b) KCI
(c) NaOH (d) KOH

192. Diclofenac sodium is assayed by

(a) 0.1M NaOH (b) 0.1 M TBAH
(c) 0.1 M $NaNO_2$ (d) 0.1 M $HClO_4$

193. Which of the following is used as indicator in non-aqueous titration?

(a) Crystal violet (b) Quinaldine red
(c) Orcet blue (d) All of the above

194. Which of following is not a primary standard?

(a) Sodium carbonate (b) KBr
(c) Oxalic acid (d) NaOH

195. For determination of the growth of bacteria in culture media which technique is used?

(a) X ray diffraction (b) Infrared
(c) Turbidometry (d) All of the above

196. In redox titration, indicator electrode is

(a) Pt wire (b) Ag wire
(c) Glass electrode (d) Hg electrode

197. Assay of aspirin is carried out by

(a) Back titration with NaOH
(b) Direct titration with NaOH
(c) Back titration with HCI
(d) Direct titration with HCl

198. Specifically used technique for identification of DNA is

(a) Northern Blotting (b) Southern Blotting
(c) Dot Blotting (d) Western Blotting

199. Saccharimetry is the practical application of

(a) Alkalimetry (b) Potentiometry
(c) Polarimetry (d) Aquametry

200. Which source is used for DNA polymerase in PC?

(a) *E.coli*
(b) *Staphylococcus species*
(c) *Thermos aquaticus*
(d) *Plasmodium species*

201. Circular dichromism is due to

(a) Right circularly polarized ray absorbed from left circularly polarized ray
(b) Right circularly polarized ray absorbed same as left circularly polarized ray
(c) Only right circularly polarized ray is absorbed
(d) Only left circularly polarized ray is absorbed

202. Propranolol is assayed by

(a) 0.1 M NaOH (b) 0.1 M TBAH
(c) 0.1 M $NaNO_2$ (d) 0.1M $HClO_4$

203. Protogenic solvent causes

(a) Enhance acidity of weak acid
(b) Enhance basicity of weak base
(c) Enhance basicity of weak acid
(d) Enhance acidity of weak base

204. Fluorescein dye is used as adsorption indicator in Fajan's method, what is its nature?

(a) Acidic (b) Basic
(c) Amphoteric (d) Neutral

205. What is pH range of methyl orange?

(a) 3.1–4.4 (b) 1.2–2.8
(c) 4.5–6.3 (d) 6.3–8.5

206. Assay of furosemide is carried out by

(a) Back titration with NaOH
(b) Direct titration with NaOH
(c) Back titration with HCI
(d) Direct titration with HCl

207. The analyte is used in the form of a solution in flame photometry because it should undergo

(a) Evaporation (b) Condensation
(c) Nebulisation (d) Precipitation

208. Specifically used technique for identification of RNA is

(a) Northern Blotting (b) Southern Blotting
(c) Dot Blotting (d) Western Blotting

209. In polarography apparatus _____ is generated.

(a) Polarogram (b) Polarograph
(c) Polarometer (d) Polaroscope

210. Ascorbic acid injection assayed by

(a) CAS (b) 2,6- Dichloro indophenol
(c) I_2 (d) KIO_3

211. Protophilic solvent is of _____ nature

(a) Acidic (b) Basic
(c) Neutral (d) Both (a) and (b)

212. Calorimeter is used to:

(a) Determine the heat of a reaction
(b) Determine the heat given off/absorbed during some process
(b) Store the heat from a chemical reaction
(d) None of the above

213. In Limit of Quantitation (LOQ), signal to noise ratio is
(a) 2:1 (b) 3:1
(c) 8:1 (d) 10:1

214. In refractometry, D line from sodium vapour lamp is used. What is the wavelength of it?
(a) 435.3 nm (b) 469.3 nm
(c) 589.3 nm (d) 653.6 nm

215. What is included in the Karl Fischer reagent?
(a) odine, Pyrimidine, SO_2
(c) odine, Pyridine, SO_2
(b) Iodine, Pyridine, SO_2, Methanol
(d) Iodine, Pyridine, SO_2, Ethanol

216. What is the pH range of phenolphthalein?
(a) 3.1–4.4 (b) 8.3–11.0
(c) 4.5–6.3 (d) 6.3–8.3

217. A litre of ethanol solution which contains 1.5 microlitres of ethanol has concentration of _____ ethanol.
(a) 1.5 ppb (b) 1.5 ppm
(c) 1.5 ppt (d) None of these

218. 10 curie = _____
(a) 3.7×10^{11} dps (b) 3.7×10^{9} becquerel
(c) 3.7×10^{11} RAD (d) 3.7×10^{10} REM

219. In thermogravimetric titration which of following property is measured with ml of titrant?
(a) Heat absorbed
(b) Heat evolved
(c) Change in temperature
(d) All of the above

220. In gel electrophoresis, DNA travels
(a) Cathode to Anode
(b) Anode to Cathode
(c) Positive to Negative
(d) Can not say

221. IP assay of ferrous gluconate tablet is carried out by
(a) Ceriometry (b) Iodometry
(c) Iodimetry (d) argentometry

222. Precision is calculated by
(a) Standard deviation (b) Mean
(c) Mode (d) Median

223. Nernst equation is used to measure
(a) Current (b) Conductance
(c) Potential (d) Resistance

224. Which indicator is not used for weak base and strong acid titration?
(a) Methyl orange (b) Methyl red
(c) Bromocresol green (d) Thymol blue

225. _____ method involves use of indicator like acidic or basic dyes.
(a) Volhard's method (b) Mohr's method
(c) Fajan's method (d) Gay-Lussac method

226. 1000 becquerel = _____
(a) 2.7×10^{-11} curie (b) 2.7×10^{-11} dps
(c) 10^3dps (d) 2.7×10^{11} curie

227. Which technique involves the identification of proteins?
(a) Northern Blotting (b) Southern Blotting
(c) Dot Blotting (d) Western Blotting

228. Assay of the chloride ion in intraperitoneal dialysis fluid is carried out by
(a) Complexometric titration
(b) Gravimetric method
(c) Mohr's method
(d) Karl Fischer titration

229. Which of following titrant is self indicator?
(a) $KMnO_4$
(b) Potassium dichromate
(c) Cerric ammonium sulphate
(d) Both (a) and (c)

230. Saccharimetry is used for determination of sugars. Which of following technique is used in it?
(a) Polarography (b) Refractometry
(c) Polarimetry (d) Iodometry

231. In diazotization titration, reference electrode is
(a) Glass electrode
(b) Saturated calomel electrode
(c) Ag–AgCl electrode
(d) Hydrogen electrode

232. Refrective index can be determined by using?
(a) Abbe's refrectometer (b)Refrecto calimeter
(c) Colorimeter (d)None of the above

233. Compared to the rate of inorganic reactions, the rate of organic reactions generally is?
(a) Slower because organic particles are ions
(b) Slower because organic particles contains covalent bonds
(c) Faster because organic particles are ions
(d) Faster because organic particles contains covalent bonds

234. In polymerase chain reaction denaturation is carried out at what condition (temperature and time)?
(a) At 95°C for 1 min (b) At 95°C for 2 min
(c) At 55°C for 2 min (d) At 55°C for 1 min

235. Faraday is unit of
(a) Charge (b) Current
(c) Potential (d) Capacitance

236. Which of following is right sequence in polymerase chain reaction?
(a) 1. Denaturation 2. DNA synthesis 3. Renaturation
(b) 1. Denaturation 2. Renaturation 3. DNA synthesis
(c) 1. Renaturation 2 DNA synthesis 3. Denaturation
(d) 1. DNA synthesis 2 Denaturation 3. Renaturation

237. Assay of sulpha drugs by nitrite titration using potentiometric end point detection is also known as
(a) Sigmoidal end point method
(b) External end point method
(c) Dead-stop end point method
(d) odometric end point method

238. Solubility of AgCl is 0.0019 g/litre. Molecular weight of AgCl is 143.3. The calculated solubility product constant (Ksp) of AgCl is _____.
(a) 1.33×10^{-5} (b) 1.80×10^{-5}
(c) 1.33×10^{-10} (d) 1.80×10^{-10}

239. The solution of slightly soluble electrolyte will be precipitated if
(a) Ion concentration product is less than its Ksp.
(b) Ion concentration product is greater than its Ksp.
(c) Ion concentration product is equal to its Ksp.
(d) It follows any of the above conditions.

240. Mohr's method involves
(a) Formation of coloured precipitates at the end point
(b) Formation of soluble coloured compound at the end point
(c) Formation of turbidity at the end point
(d) Use of adsorption indicator

241. Mohr's method is not applicable
(a) In alkaline condition – pH > 9.0.
(b) In acidic condition
(c) For titration of iodide and thiocyanate
(d) In all above conditions

242. Gay-Lussac method is also called
(a) Clear point method
(b) Argentiometric method
(c) Adsorption indicator method
(d) Volhard's method

243. The colour change for methyl red is _____ when pH changes from acidic to alkaline.
(a) Colourless to pink (b) Yellow to red
(c) Red to blue (d) Red to yellow

244. _____ is self-indicator and acidic primary standard compound.
(a) Potassium permanganate
(b) Potassium hydrogen phthalate
(c) Sulfamic acid
(d) 2,4,6-trinitrobenzoic acid

245. _____ is assayed by acid–base back titration.
(a) Zinc oxide (b) Aspirin
(c) Lactic acid (d) All

246. _____ indicator shows blue colour at the end point.
(a) Potassium permanganate
(b) Starch paste
(c) Iodine
(d) Diphenyl amine

247. _____ acid is not used to perform redox titration using $KMnO_4$ in acidic medium.
(a) HCl (b) HNO_3
(c) Both (d) None

248. Purity of water is determined by
(a) Conductometer (b) HPLC
(c) Potentiometer (d) UV

249. Indicator used for complexometric titration
(a) Solochrome black (b) EDTA
(c) Phenolphthalein (d) Methylene red

250. Which equation is used for quantification of a substance by Polarography?
(a) Ilkovic equation
(b) Vandeemter
(c) Langmuir equation
(d) Hilderband Scott equation

251. The most commonly used detector in liquid chromatography is
(a) UV
(b) Electrical conductivity detector
(c) Refractive index
(d) Polarography detector

252. What useful information can be found from a Van Deemeter plot?
(a) Optimum column temperature
(b) Optimum mobile flow rate
(c) Selectivity factor
(d) All of above

253. Condition maintained in programmed temperature GC
(a) Temperature of entire column is raised
(b) Temperature of detector is raised
(c) Temperature of sample injector is raised
(d) Temperature of recorder is raised

254. In anion exchange chromatography what is the charge of counter ion?
(a) Negative (b) Positive
(c) Both of above (d) Cannot say

255. In gel filtration chromatography which compound is elute first?
(a) Larger molecule
(b) Smaller molecule
(c) Molecule with intermediate size
(d) Cannot say

256. Indicate the HPLC detector that is most sensitive to change in temperature:
(a) PDA detector
(b) Refractive Index detector
(c) Fluorescence detector
(d) Electrochemical detector

257. What is the correct order of the retention in mixture of four compounds in normal phase chromatography?
(a) Acetic acid > Ethanol > Acetone > Petroleum ether
(b) Acetic acid < Ethanol < Acetone < Petroleum ether
(c) Ethanol > Acetic acid > Acetone > Petroleum ether
(d) Ethanol < Acetic acid < Petroleum ether < Acetone

258. Which carrier gas is use in GC containing electron capture detector?
(a) Hydrogen (b) elium
(c) Oxygen (d) Argon

259. Tailing of peak in GLC is reduced by using
(a) Dimethyl silane
(b) etramethyl silane
(c) Hexamethyl disilazane
(d) Trimethyl silane

260. Derivatisation techniques in HPLC are intended to enhance
(a) Molecular weight (b) Detectability
(c) Reversibility (d) Reproducibility

261. Which of following has strongest absorbent?
(a) Cellulose (b) Calcium carbonate
(c) Fuller's Earth (d) Silica gel

262. The stationzry phase used in gel permeation chromatography
(a) Alumina
(b) Charcoal
(c) Squalene
(d) Styrene divinyl benzene copolymer

263. Band broadening is:
(a) Directly proportional to column efficiency
(b) Inversely proportional to solvent efficiency
(c) Directly proportional to solvent efficiency
(d) Inversely proportional to column efficiency

264. Which of the following detector of gas chromatography is destructive type?
(a) Kathetormeter
(b) Argon ionization detector
(c) Flame ionization detector
(d) Electon capture detector

265. Which of following HPLC detectors is not a solute property detector?
(a) UV–Visible detector
(b) Photo diode array detector
(c) Fluorescence detector
(d) Refractive index detector

266. Band (peak) separation is
(a) Directly proportional to solvent efficiency
(b) Inversely proportional to solvent efficiency
(c) Directly proportional to column efficiency
(d) Inversely proportional to column efficiency

267. Choose the correct semirigid get used for exclusion chromatography

(a) Sephadex (b) Gelatin
(c) Cellulose (d) Alumina

268. In limit of detection (LOD), signal to noise ratio is
(a) 2:1 (b) 3:1
(c) 8:1 (d) 10:1

269. The length of analytical column is_____.
(a) 5–25 cm (b) 10–100 cm
(c) 1–10 m (d) 40–50 cm

270. One of the following statements is NOT true:
(a) Precision represents reproducibility of measurement
(b) Accuracy expresses the correctness of measurement
(c) Specificity means ability of method to detect the lowest possible concentration
(d) Limit of quantization is ability of method to quantify the lowest possible concentration

271. The parameter in the elution curve that is proportional to the concentration of a compound in gas chromatographic effluent is the
(a) Number of peaks
(b) Width of the peaks
(c) Area under the peak
(d) Shape of the peak

272. The number of theoretical plates depends on
(a) Length of the column
(b) HETP
(c) Both (a) and (b)
(d) None of the above

273. Derivatizing agent for TLC of steroidal compound?
(a) Diphenylcarbazone
(b) Bromothymol blue
(c) Antimony trichloride
(d) Ninhydrin

274. Silica gel G contains which of following binder?
(a) Starch (b) Gelatin
(c) Cellulose (d) Gypsum

275. For base line separation value of R (resolution)
(a) $R > 0.5$ (b) $R > 1.5$
(c) $R \geq 0.5$ (d) $R \leq 1.5$

276. Derivatizing agent for TLC of lipid compound is
(a) Antimony trichloride
(b) Bromothymol blue
(c) Ninhydrin
(d) Diphenyl carbazone

277. Silica gel H has:
(a) Starch as binder (b) Gelatin as binder
(c) Gypsum as binder (d) No binder

278. Tailing occurs due to
(a) Sample overloading
(b) Impurity
(c) More than one ionic species of compound
(d) All of the above

279. The mobile phase used in ion exchange chromatography is
(a) Polar solvent
(b) Non-polar solvent
(c) Buffer solutions
(d) All of the above methods

280. Qualitative analysis in GLC is based on
(a) Time required for peaks to appear
(b) Peak height
(c) Peak area
(d) All of the above

281. In reverse phase chromatography which compound is most retained?
(a) Intermediate polar compound
(b) Least polar compound
(c) More polar compound
(d) Cannot say

282. Which of following is not a masking agent?
(a) Triethanolamine
(b) Potassium citrate
(c) Ormaldehyde-acetic acid solution
(d) Ammonium fluoride

283. Tailing of peak in GLC is reduced by using
(a) Dimethyl silane
(b) Tetramethyl silane
(c) Hexamethyl disilazane
(d) Trimethyl silane

284. Which of following HPLC detector is a bulk property detector?
(a) Refractive index detector
(b) UV detector
(c) Photo diode array detector
(d) Flouresence detector

285. ΔR_m number is a chromatographic parameter used to find out whether the compound belonging to homologous series or not.

(a) R_f value (b) Homologous series
(c) Both (a) and (b) (d) None of the above

286. Quantitative analysis in GLC is based on
(a) Time required for peaks to appear
(b) Peak height
(c) Peak area
(d) Both (b) and (c)

287. In normal phase chromatography which compound is eluted first
(a) More polar compound
(b) Least polar compounds
(c) Intermediate polar compound
(d) Cannot say

288. Silica gel 60 F_{254} contains
(a) Gypsum as binder
(b) Fluorescent indicator
(c) 254 μm particle size
(d) Both (a) and (b)

289. Which of following is used as a mobile phase in super-critical fluid?
(a) Carbon dioxide (b) Water
(c) Acetic acid (d) Both (a) and (b)

290. What can be used to reduce tailing in gas chromatography?
(a) Hexa methyl silane (b) Tetra methyl silane
(c) Glacial acetic acid (d) Trimethylamine

291. The principle of separation in GSC is
(a) Gel permeation (b) Adsorption
(c) Partition (d) Ion exchange

292. In gas chromatography sample must be in
(a) Solid state (b) Gas state
(c) Liquid state (d) Crystal

293. In gas chromatography, derivatisation is desirable to
(P) Improve the thermal stability of compounds
(Q) Enable interaction with carrier gas
(R) Introduce a detector oriented tag into the molecule
(S) Removes contaminants
(a) P, Q (b) Q, R
(c) P, R (d) P, S

294. In HPLC the analytical performance improves when
(a) Particle diameter is increased
(b) Particle diameter is decreased
(c) Coarser particles are paired with shorter columns
(d) Low temperature is used

295. In size exclusion chromatography the stationary phase used are
(a) Alumina (b) Dextrose
(c) Agarose (d) Styrene

296. For amino acid analysis by HPLC derivatisation reagent used by UV absorption detector is
(a) 4-Nitrobenzyl-N-propylamine hydrochloride
(b) 4-Nitrobenzyloxyamine hydrochloride
(c) 3,5-Dinitro benzoyl chloride
(d) 4-Nitrobenzyl-N-N'-disopropylisourea

297. The mobile phase in column chromatography acts as a
(a) Solvent for sample (b) Developer and as eluent
(c) As eluent only (d) Both (a) and (b)

298. In a normal phase mode, the following component is eluted first
(a) Hydrocarbons (b) Primary alcohol
(c) Salicylic acid (d) Primary amine

299. Chlorine or bromine substitution in aromatic compound
(a) Enhances fluorescence
(b) Does not change the fluorescence
(c) Quenches the fluorescence
(d) Removes the fluorescence

300. The separation of components because of distribution of components between two immiscible liquid phases occurs in
(a) Paper chromatography
(b) Ion exchange chromatography
(c) High pressure thin layer chromatography
(d) HPLC

301. In chromatography if column length is constant and the height of theoretical plate is decreases, then
(a) Peak width increases
(b) Column separation efficiency decreases
(c) Number of theoretical plate decreases
(d) Olumn separation efficiency increases

302. In chromatography compound X has retention time 10.5 min and peak width is 0.7 min and compound Y has retention time 15.5 min and peak width is 0.4 min then resolution is
(a) 9.09 (b) 0.909
(c) 4.54 (d) 5.5

303. In TLC Kiesleguhr material _____ is used as coating material
(a) Acidic nature (b) Alkaline nature
(c) Neutral nature (d) Amphoteric nature

304. Principle of paper chromatography is
(a) Adsorption (b) Partition
(c) Ion exchange (d) Affinity

305. Calculate the length of column if height of theoretical plate 0.234 cm and number of theoretical plate is 3550
(a) 15170.94 (b) 13291.2
(c) 830.7 (d) 1120

306. Steroid separation is by paper chromatography then paper used is
(a) Carboxyl paper (b) Acetylated paper
(c) Kieselguhr paper (d) Silica paper

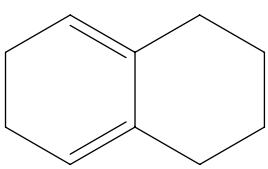
307. In chromatography capacity factor related to
(a) Polarity of solvent
(b) Number of theoretical plate
(c) The migration rate of solute
(d) Resolution

308. In radial paper chromatography sample is placed
(a) Near to outer surface of paper
(b) At the centre of the paper
(c) At the bottom of the paper
(d) On the top of the paper

309. In TLC silica-G is used as coating material 'G' means
(a) Gelatin and used to improve solubility of silica
(b) Gelatin and used as a binder
(c) Gypsum and used to improve solubility of silica
(d) Gypsum and used as a binder

310. RP-HPLC method contains
(a) Stationary phase is polar and mobile phase is non-Polar
(b) Stationary phase is non-polar and mobile phase is polar
(c) Stationary phase is non-polar and mobile Phase is non-polar
(d) Stationary phase is polar and mobile phase is polar

311. Which of following compounds shows peak in vacuum UV region?
(a) Benzene (b) Butadiene
(c) Methane (d) Naphthalene



312. What is the λmax for the following compound? Use the provided parameters for your calculation?
(a) 234 nm (b) 244 nm
(c) 273 nm (d) 283 nm

313. Material used in sample handling of X-ray diffraction is
(a) Glass (b) Quartz
(c) KBr (d) KHP

314. Which of following conditions leads to decrease in fluorescence intensity?
(a) Increase in temperature or increase in viscosity
(b) Increase in temperature or decrease in viscosity
(c) Decrease in temperature or decrease in viscosity
(d) Decrease in temperature or increase in viscosity

315. Water shows which transition?
(a) n – > ϖ* (b) ϖ – > ϖ*
(c) σ – > σ* (d) n – > σ*

316. Increase in conjugation causes
(a) Hypsochromic shift
(b) Hyperchromic shift
(c) Bathochromic shift
(d) Hypochromic shift

317. In UV 1,3-butadiene shows which transition?
(a) n – > ϖ* (b) ϖ – > ϖ*
(c) σ – > σ* (d) n – > σ*

318. Which isomer of olefine has high λmax?
(a) rans
(b) Cis
(c) Both have same λmax
(d) Can not say

319. Turbidity is carried out at wavelength
(a) 450 nm (b) 680 nm
(c) 530 nm (d) 600 nm

320. Which of the following techniques has the highest sensitivity?
(a) UV spectroscopy (b) Colorimetry
(c) Infrared (d) Flourimetry

321. X-ray is generated by cathode tube. Which filament is used as cathode in it?
(a) Copper (b) Tungsten
(c) Mercury (d) None of the above

322. Most widely used radiation source in visible spectroscopy is:
(a) Tungsten–halogen lamp
(b) Hydrogen-discharge lamp

(c) Deuterium lamp
(d) Nernst glower

323. Which of the following techniques is based on Tyndall effect?
(a) Turbidimetry
(b) Nephelometry
(c) Raman spectroscopy
(d) All of the above

324. Which transition requires the highest energy?
(a) $n \rightarrow n^*$ (b) $\varpi \rightarrow \mu^*$
(c) $\sigma \rightarrow \sigma^*$ (d) $n \rightarrow \sigma^*$

325. Flame photometry cannot be used for:
(a) Barium (b) Calcium
(c) Selenium (d) Sodium

326. In Raman spectroscopy optical system is made up of:
(a) Glass or Quartz (b) NaBr or CaF2
(c) KBr or NaBr (d) All of above

327. Transmittance is defined as
(a) log Io/It (b) og I_t/I_o
(c) I_t/I_o (d) Io/It

328. Which of following detectors has the most sensitivity?
(a) Flame ionization detector
(b) Argon ionization detector
(c) Electron capture detector
(d) Kathetormeter

329. Angle between source and detector in flourimeter is
(a) 90° (b) 45°
(c) 180° (d) 60°

330. Sample window used in UV is made up of
(a) Quartz (b) Glass
(c) Metal halide (d) Both (a) and (b)

331. Which of following source is used fluorescence spectrometry?
(a) Tungsten (b) Deuterium arc lamp
(c) Xenon arc lamp (d) Helium/neon laser

332. Conjugated diene shows which band?
(a) K (b) B
(c) E (d) R

333. In ESR which waves are used?
(a) Radiowaves (b) Near UV
(c) Far IR (d) Microwaves

334. Wavelength used in X-ray diffraction spectroscopy
(a) 0.1 to 1 nm (b) 0.01 to 10 nm
(c) 10 to 100 nm (d) 0.1 to 10 nm

335. R-band associated with which transition?
(a) $n - \varpi^*$ (b) $\varpi - \varpi^*$
(c) $\sigma - \sigma^*$ (d) $n - \sigma^*$

336. Kirchhoff's law associated with
(a) IR (b) NMR
(c) AAS (d) Raman spectroscopy

337. B, E and K bands are associated with which transition?
(a) $n - \varpi^*$ (b) $\varpi - \varpi^*$
(c) $\sigma - \sigma^*$ (d) $n - > \sigma^*$

338. Fluorescence is due to which transition?
(a) $n - \varpi^*$ (b) $\varpi - \varpi^*$
(c) $\sigma - \sigma^*$ (d) $n - \sigma^*$

339. For study of the free radicals which of following techniques is used?
(a) Infrared spectroscopy
(b) Electron spin resonance spectroscoy
(c) Flourimetry spectroscopy
(d) UV spectroscopy

340. X-ray effect is based on
(a) Outer shell electron transition
(b) Inner shell electron transition
(c) Rotation of molecule
(d) None of the above

341. Toluene shows transition of_____ .
(a) $n\text{-}\varpi^*$ (b) $\varpi\text{-}\varpi^*$
(c) $\sigma\text{-}\sigma^*$ (d) $n\text{-}\sigma^*$

342. A compound (mol wt.-200g/mol) has specific absorbance 100 at its A = 257. Find the molar absorptivity of compound.
(a) 200 (b) 2000
(c) 1000 (d) 100

343. Value of λ_{max} for a particular compound
(a) Increases with increase in concentration
(b) Decreases with decrease in concentration
(c) Does not change
(d) Both of (a) and (b)

344. In fluorimetry which of following is true:
(a) Excitation wavelength > florescence wavelength
(b) Excitation wavelength < florescence wavelength

(c) Excitation wavelength = florescence wavelength
(d) None of the above

345. Which wave is used in densitometer?
(a) UV–Visible (c) Microwave
(b) Infrared (d) None of the above

346. Riboflavin can be easily analysed by which method?
(a) Nephelometry
(b) Fluorimetry
(c) Flame photometry
(d) Phosphorimetry

347. Pyridine shows which transition in UV region?
(a) n – ϖ* (b) ϖ – ϖ*
(c) Both (a) and (b) (d) n – σ*

348. Which of following compound has the highest λ_{max}?
(a) $CH_3F < CH_3CI < CH_3I$
(b) $CH_3I < CH_3F < CH_3CI$
(c) $CH_3CI < CH_3I < CH_3Br$
(d) $CH_3I < CH_3Br < CH_3CI$

349. In naphthalene, which type of absorption band is observed?
(a) R (b) B
(c) E (d) K

350. Angle between source and detector in turbidimeter is
(a) 90° (b) 45°
(c) 180° (d) 60°

351. Absolute configuration of a compound is determined by which technique?
(a) UV–Visible spectroscopy
(b) Infrared
(c) Mass
(d) X ray diffraction

352. In case of carbonyl compound which of following is a forbidden transition?
(a) n–σ* (b) ϖ–ϖ*
(c) σ–σ* (d) n–ϖ*

353. ESR spectra only given by molecule have
(a) Paired electron (b) Unpaired electron
(c) Positive proton (d) None of the above

354. For determination of the growth of bacteria in culture media which technique is used?
(a) X ray diffraction (b) Infrared
(c) Turbidometry (d) All of the above

355. Angle between source and detector in nephalometer is
(a) 90° (b) 45°
(c) 180° (d) 60°

356. Xenon arc lamp is source of light in
(a) Spectrofluorimeter
(b) IRspectroflurometer
(c) Flame photometer
(d) Calorimeter

357. Match the following:

(P) UV	(1) Precessional motion
(Q) IR	(2) Electronic transitions
(R) NMR	(3) Fragmentation
(S) MASS	(4) Vibrational motion

(a) P2, Q4, R1, S3 (b) P2, Q4, R3, S1
(c) P2, Q1, R3, S4 (d) P4, Q2, R1, S3

358. X-ray spectral line Kα doublet arises from transition of electrons from
(a) M shell to K shell (b) L shell to M shell
(c) L shell to K shell (d) M shell to L shell

359. A mixture of the following gases can be used in flame photometry to get a temperature of 2045°C
(a) Hydrogen and nitrous oxide
(b) Acetylene and oxygen
(c) Hydrogen and air
(d) Hydrogen and oxygen

360. The process undergo by the analyte in flame photometry is
(a) Evaporation (b) Nebulization
(c) Condensation (d) Precipitation

361. Base value of benzaldehyde is 250 nm. What would be λmax of p-hydroxybenzalaldehyde
(a) 253 nm (b) 261 nm
(c) 275 nm (d) 270 nm

362. For calibration of resolution in UV _____ is used
(a) Holmiun filter
(b) Polystyrene
(c) Potassium dichromate
(d) Toluene and hexane

363. Flame photometry is an example of
(a) Atomic absortion spectrometry
(b) Atomic emission spectrometry
(c) Both (a) and (b)
(d) None

364. The phenomena of scattering of light occurs in
(a) Aquamtery (b) Colorimetry
(c) Spectrophotometry (d) Nephlometry

365. Resolution of a spectrophotometer is
(a) Its wavelength range
(b) Its ability to distinguish adjacent absorption bands
(c) Its capacity for its continuous use
(d) All of the above

366. The formula is
(a) Molar Absorptivity(ε) = $A^{1\%}_{1cm}$ × mol.wt/1000
(b) olar Absorptivity(ε) = $A^{1\%}_{1cm}$ × mol.wt/10
(c) Molar Absorptivity(ε) = $A^{1\%}_{1cm}$ × eq.wt/1000
(d) Molar Absorptivity(ε) = $A^{1\%}_{1cm}$ × eq.wt/100

367. A compound has a molecular weight of 297; an equivalent of 148.5 and an $A^{1\%}_{1cm}$ of 742 at 309nm. Its molar absorptivity is
(a) 220.37 (b) 1101.857
(c) 110.18 (d) 22037.4

368. Increase in the extent of conjugation of a double-bonded system results in
(a) Hyperchromic shift
(b) Hypochromic shift
(c) Hypsochromic shift
(d) Bathochromic shift

369. In Bragg's equation $n\lambda = 2d \sin\theta$, θ is the angle between
(a) The direction of the incident beam and the reflected beam
(b) The surface of the crystal and the incident fluorescent beam
(c) The direction of the incident beam and the diffracted beam
(d) Two incident beams

370. The electronic transition possible in Br2 is
(a) $\sigma \rightarrow \sigma^*$
(b) $\sigma \rightarrow \sigma^*$ and $n \rightarrow \sigma^*$
(c) $\sigma \rightarrow \varpi^*$ and $\varpi \rightarrow \varpi^*$
(d) $\sigma \rightarrow \varpi^*$ and $n \rightarrow \varpi^*$

371. In UV spectroscopy the lowest energy is required for transition of
(a) $\sigma \rightarrow \sigma^*$ (b) $n \rightarrow \sigma^*$
(c) $\varpi \rightarrow \varpi^*$ (d) $n \rightarrow \varpi^*$

372. An organic compound 'X' has an absorption maxima at 217 nm. Its E_{max} is 16,000. The absorbance is 0.64 when the cell length is 1 cm. Then molar concentration is
(a) 5×10^{-5} (b) 4×10^{-5}
(c) 4×10^{-4} (d) 5×10^{-2}

373. Bathchromic shift involves
(a) Increase in intensity of absorption
(b) Decrease in intensity of absorption
(c) Increase in wavelength of maxima absorption
(d) Decrease in wavelength of maxima absorption

374. Benzene shows the following transition in UV spectra:
(a) $\sigma \rightarrow \sigma^*$ (b) $\varpi \rightarrow \varpi^*$
(c) $n \rightarrow \sigma^*$ (d) $n \rightarrow \varpi^*$

375. Which one of the following can be used as target material for X-ray production?
(a) Sodium (b) Aluminium
(c) Copper (d) Xenon

376. ESR is applied to only those substances showing paramagnetism which is due to the magnetic moment
(a) Neutrons (b) Protons
(c) Paired electrons (d) Unpaired electrons

377. n à ϖ* is also known as
(a) K-bands (b) R-bands
(c) P-bands (d) B-bands

378. In UV spectroscopy propane shows the following transition:
(a) $\sigma \rightarrow \sigma^*$ (b) $n \rightarrow \sigma^*$
(c) $\varpi \rightarrow \varpi^*$ (d) $n \rightarrow \varpi^*$

379. Emission of radiation is measured by _____ method.
(a) Raman spectroscopy
(b) Flame photometry
(c) Interferometer
(d) Calorimetry

380. Scattering of radiation is not measured by _____method.
(a) Raman Spectroscopy
(b) Spectrophotometer
(c) Turbidometry
(d) Nephalometry

381. The conjugation increases the l_{max} by
(a) 5 nm (b) 10 nm
(c) 20 nm (d) 30 nm

382. The transition from excited state to ground state is called
(a) Excitation (b) Absorption
(c) Relaxation (d) Scattering

383. The relationship between absorbance (A) and trasmittance (T) can be given by
(a) A = 2 – log% T (b) T = 2 – log A
(c) A = 2 + log T (d) T = 2 + log A

384. The following is the example of absorption spectra:
(a) Flourimetry (b) Flame photometry
(c) X-ray diffraction (d) UV spectra

385. The following is the example of emission spectra:
(a) IR spectra (b) UV spectra
(c) NMR spectra (d) Flourimetry

386. The following light is measured in nephalometry
(a) Scattered (b) Reflected
(c) Dispered (d) Transmitted

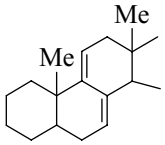
387. The following light is measured in turbidimetry:
(a) Scattered (b) Reflected
(c) Dispered (d) Transmitted

388. The following gas has got a higher thermal conductivity value:
(a) Nitrogen (b) Helium
(c) Argon (d) Carbon

389. The following is an example for atomic spectra:
(a) UV spectra (b) Colorimetry
(c) Flourimetry (d) Flame photometry

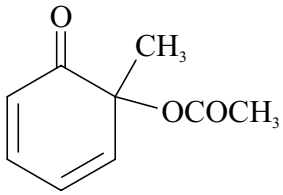
390. Types of sources materials in UV–Visible spectroscopy is
(a) Hydrogen–deuterium lamp
(b) Tungsten lamp
(c) Xenon arc lamp
(d) All

391. What will be the absorption maxima (λ_{max}) as per Woodward–Fieser rule?



(a) 234 nm (b) 229 nm
(c) 244 nm (d) 239 nm

392. What will be the absorption maxima (λ_{max}) as per Woodward–Fieser rule**?**



(a) 257 nm (b) 263 nm
(c) 233 nm (d) 302 nm

393. Bathochromic shift depends on:
(a) Isolated double bonds
(b) Conjugated double bond
(c) Thermal conductivity
(d) Absorption of light

394. The value of extinction coefficient more than 100 is known as:
(a) Absorbed transition
(b) Allowed transition
(c) Curved transition
(d) Bonded transition

395. When a molecule is excited by the absorption of radiation it soon returns to its ground state by losing its excess of energy emitted as radiation. This phenomenon is known as:
(a) Phosphorescence (b) Bathochromic shift
(c) Electron emission (d) Fluorescence

396. When excitation of electrons by chemicals, the phenomena is called
(a) Chemiluminescence
(b) Photoluminescence
(c) Electro chemiluminescence
(d) Phosphorescence

397. 'n' electrons are present in
(a) Methane (b) Ethylene
(c) Acetylene (d) Propanol

398. Which transition is more susceptible towards hydrogen bonding?
(a) $n \rightarrow \varpi^*$
(b) $\varpi \rightarrow \varpi^*$
(c) $n \rightarrow \sigma^*$
(d) $\sigma \rightarrow \sigma^*$

399. Correct energy value order for electronic transition in UV is
(a) $n \rightarrow \varpi^* < n \rightarrow \sigma^* < \varpi \rightarrow \varpi^* < \sigma \rightarrow \sigma^*$
(b) $n \rightarrow \varpi^* < \varpi \rightarrow \varpi^* < \sigma \rightarrow \sigma^* < n \rightarrow \sigma^*$
(c) $\varpi \rightarrow \varpi < n \rightarrow \varpi^* < n \rightarrow \sigma^* < \sigma \rightarrow \sigma^*$
(d) $n \rightarrow \varpi^* < \varpi \rightarrow \varpi^* < n \rightarrow \sigma^* < \sigma \rightarrow \sigma^*$

400. Most widely used detector in UV spectroscopy is
(a) Bolometer
(b) Photomultiplier tube
(c) Photoemissive cell
(d) Pyroelectric detector

ANSWER KEYS

1. (b)	**2.** (b)	**3.** (d)	**4.** (a)	**5.** (d)	**6.** (d)	**7.** (d)	**8.** (a)	**9.** (a)	**10.** (d)
11. (b)	**12.** (c)	**13.** (a)	**14.** (d)	**15.** (b)	**16.** (c)	**17.** (b)	**18.** (b)	**19.** (c)	**20.** (d)
21. (b)	**22.** (b)	**23.** (d)	**24.** (d)	**25.** (a)	**26.** (a)	**27.** (a)	**28.** (a)	**29.** (a)	**30.** (a)
31. (d)	**32.** (d)	**33.** (d)	**34.** (a)	**35.** (c)	**36.** (b)	**37.** (b)	**38.** (c)	**39.** (b)	**40.** (b)
41. (b)	**42.** (d)	**43.** (c)	**44.** (b)	**45.** (c)	**46.** (a)	**47.** (d)	**48.** (a)	**49.** (c)	**50.** (c)
51. (b)	**52.** (b)	**53.** (b)	**54.** (d)	**55.** (b)	**56.** (d)	**57.** (c)	**58.** (b)	**59.** (c)	**60.** (d)
61. (d)	**62.** (d)	**63.** (d)	**64.** (d)	**65.** (d)	**66.** (b)	**67.** (c)	**68.** (a)	**69.** (b)	**70.** (c)
71. (b)	**72.** (d)	**73.** (a)	**74.** (d)	**75.** (a)	**76.** (c)	**77.** (b)	**78.** (a)	**79.** (a)	**80.** (d)
81. (b)	**82.** (c)	**83.** (a)	**84.** (d)	**85.** (d)	**86.** (b)	**87.** (c)	**88.** (c)	**89.** (a)	**90.** (b)
91. (a)	**92.** (c)	**93.** (c)	**94.** (d)	**95.** (d)	**96.** (c)	**97.** (d)	**98.** (c)	**99.** (c)	**100.** (b)
101. (b)	**102.** (d)	**103.** (c)	**104.** (b)	**105.** (d)	**106.** (d)	**107.** (b)	**108.** (d)	**109.** (b)	**110.** (a)
111. (b)	**112.** (b)	**113.** (a)	**114.** (d)	**115.** (c)	**116.** (a)	**117.** (b)	**118.** (c)	**119.** (c)	**120.** (b)
121. (a)	**122.** (a)	**123.** (a)	**124.** (a)	**125.** (b)	**126.** (c)	**127.** (b)	**128.** (a)	**129.** (b)	**130.** (b)
131. (d)	**132.** (b)	**133.** (c)	**134.** (a)	**135.** (b)	**136.** (c)	**137.** (b)	**138.** (c)	**139.** (a)	**140.** (c)
141. (d)	**142.** (d)	**143.** (b)	**144.** (b)	**145.** (b)	**146.** (a)	**147.** (d)	**148.** (c)	**149.** (b)	**150.** (c)
151. (b)	**152.** (a)	**153.** (d)	**154.** (b)	**155.** (b)	**156.** (b)	**157.** (c)	**158.** (b)	**159.** (a)	**160.** (b)
161. (c)	**162.** (b)	**163.** (b)	**164.** (b)	**165.** (c)	**166.** (c)	**167.** (a)	**168.** (b)	**169.** (b)	**170.** (b)
171. (b)	**172.** (a)	**173.** (a)	**174.** (b)	**175.** (c)	**176.** (d)	**177.** (a)	**178.** (b)	**179.** (c)	**180.** (b)
181. (a)	**182.** (c)	**183.** (c)	**184.** (d)	**185.** (d)	**186.** (b)	**187.** (a)	**188.** (a)	**189.** (d)	**190.** (b)
191. (b)	**192.** (d)	**193.** (d)	**194.** (d)	**195.** (c)	**196.** (a)	**197.** (c)	**198.** (b)	**199.** (c)	**200.** (c)
201. (a)	**202.** (a)	**203.** (b)	**204.** (a)	**205.** (a)	**206.** (a)	**207.** (c)	**208.** (a)	**209.** (b)	**210.** (b)
211. (b)	**212.** (b)	**213.** (d)	**214.** (c)	**215.** (b)	**216.** (b)	**217.** (a)	**218.** (a)	**219.** (c)	**220.** (a)
221. (a)	**222.** (a)	**223.** (c)	**224.** (d)	**225.** (c)	**226.** (c)	**227.** (d)	**228.** (c)	**229.** (d)	**230.** (c)
231. (b)	**232.** (a)	**233.** (b)	**234.** (a)	**235.** (a)	**236.** (b)	**237.** (c)	**238.** (d)	**239.** (a)	**240.** (a)
241. (d)	**242.** (a)	**243.** (d)	**244.** (d)	**245.** (d)	**246.** (b)	**247.** (c)	**248.** (a)	**249.** (a)	**250.** (a)
251. (a)	**252.** (b)	**253.** (a)	**254.** (b)	**255.** (a)	**256.** (b)	**257.** (a)	**258.** (d)	**259.** (c)	**260.** (b)
261. (c)	**262.** (d)	**263.** (d)	**264.** (c)	**265.** (d)	**266.** (a)	**267.** (a)	**268.** (b)	**269.** (a)	**270.** (c)
271. (c)	**272.** (c)	**273.** (c)	**274.** (d)	**275.** (c)	**276.** (b)	**277.** (d)	**278.** (d)	**279.** (c)	**280.** (a)
281. (b)	**282.** (c)	**283.** (c)	**284.** (a)	**285.** (c)	**286.** (d)	**287.** (b)	**288.** (d)	**289.** (d)	**290.** (a)
291. (b)	**292.** (b)	**293.** (c)	**294.** (b)	**295.** (d)	**296.** (c)	**297.** (d)	**298.** (a)	**299.** (c)	**300.** (a)
301. (d)	**302.** (a)	**303.** (b)	**304.** (b)	**305.** (c)	**306.** (b)	**307.** (c)	**308.** (b)	**309.** (d)	**310.** (b)
311. (c)	**312.** (c)	**313.** (d)	**314.** (b)	**315.** (d)	**316.** (c)	**317.** (b)	**318.** (a)	**319.** (c)	**320.** (d)
321. (b)	**322.** (a)	**323.** (d)	**324.** (c)	**325.** (c)	**326.** (a)	**327.** (c)	**328.** (c)	**329.** (a)	**330.** (b)
331. (c)	**332.** (a)	**333.** (d)	**334.** (b)	**335.** (a)	**336.** (c)	**337.** (b)	**338.** (b)	**339.** (b)	**340.** (b)
341. (b)	**342.** (b)	**343.** (c)	**344.** (b)	**345.** (a)	**346.** (b)	**347.** (c)	**348.** (a)	**349.** (b)	**350.** (c)
351. (d)	**352.** (d)	**353.** (b)	**354.** (c)	**355.** (a)	**356.** (a)	**357.** (a)	**358.** (c)	**359.** (c)	**360.** (b)
361. (c)	**362.** (d)	**363.** (c)	**364.** (d)	**365.** (b)	**366.** (b)	**367.** (d)	**368.** (d)	**369.** (c)	**370.** (b)
371. (d)	**372.** (c)	**373.** (c)	**374.** (b)	**375.** (c)	**376.** (d)	**377.** (b)	**378.** (a)	**379.** (b)	**380.** (b)
381. (d)	**382.** (c)	**383.** (a)	**384.** (d)	**385.** (d)	**386.** (a)	**387.** (d)	**388.** (b)	**389.** (d)	**390.** (d)
391. (c)	**392.** (d)	**393.** (b)	**394.** (b)	**395.** (d)	**396.** (a)	**397.** (d)	**398.** (c)	**399.** (d)	**400.** (b)

CHAPTER 4

BIOCHEMISTRY

CARBOHYDRATES

Carbohydrates may be defined as **polyhydroxyaldehyde** or **ketones** or compounds which produce them on hydrolysis.

Classification of Carbohydrates

1. Monosaccharides The monosaccharides is also called simple sugar, compound which possessing free aldehyde (–CHO) or ketone (–C=O) group and 2 or more (–OH) group.

The general formula of Monosaccharides is $\mathbf{C_n\ (H_2O)_n}$ or $\mathbf{C_nH_{2n}O_n}$.

Monosaccharide	General formula	Aldose Sugar (–CHO)	Ketose sugar (–C=O)
Trioses	$C_3H_6O_3$	Glyceraldehyde	Dihydroxyacetone
Tetroses	$C_4H_8O_4$	Erythrose	Erythrulose
Pentose	$C_5H_{10}O_5$	D-Ribose D-Xylose	D-Ribulose D-Xylulose
Hexoses	$C_6H_{12}O_6$	D-Glucose D-Galactose D-Mannose	Fructose
Heptoses	$C_7H_{14}O_7$	Glucoheptose	Sedoheptulose D-Sedoheptulose

Structural aspects of monosaccharides

Stereoisomers Are compounds that have the same structural formula but differ in their spatial arrangement of atoms. It is an important character of monosaccharides.

Asymmetric carbon A carbon attached to four different groups is called asymmetric carbon. And number of asymmetric carbon determines the possible number of isomers of given compound which is equal to 2^n.

E.g., Glucose has four chiral (asymmetric) centres so it has a total of 16 isomers.

Glyceraldehyde has been chosen as the reference carbohydrate to represent the structure of all other carbohydrates.

2. Oligosaccharides It is a compound sugar which yields two to ten molecules of same or different monosaccharides on hydrolysis.

Accordingly, an oligosaccharide yeilding two molecules of monosaccharides on hydrolysis is designed as a disaccharide, and the one yielding three molecules of monosaccharides as a trissaccharides.

The general formula of disaccharides is $\mathbf{C_n(H_2O)_{n-1}}$ and trisaccarides is $\mathbf{C_n(H_2O)_{n-2}}$.

- **Disaccharides:** Sucrose, Lactose, Maltose, Cellobiose, Trehalose, Gentiobiose, Melibiose.
- **Trisaccharides:** Rhamninose, Gentianose, Raffinose (=Malitose)

- **Tetrasaccharides:** Stachyose, Scorodose
- **Pentasaccharides:** Verbascose

Reducing sugar	Non-reducing sugar
• Carbohydrate with a free aldehyde (at-1) or free ketone (at-2) group. (Aldehyde or ketone group is free)	• Aldehyde or ketone group is not free.
• They are in hemiacetal or hemiketal form.	• They are in acetal or ketal form.
• Do exhibit mutarotation.	• Do not exhibit mutarotation.
• Do form osazones with phenyl hydrazine.	• Do not form osazones.
• Do form oximes with hydroxylamine.	• Do not form oximes.
E.g., Glucose, Fructose, Lactose, Maltose, Cellobiose	E.g., Sucrose (Invert sugar), Glycogen, Inulin

- Sucrose is also known as cane sugar, mostly produced by sugarcane and sugar beats and made up of **α-D-Glucose** and **β-D-fructose**.
- Sucrose is also known as **Invert sugar** because of sucrose, as such is in dextrorotatory (+66.5°) but when hydrolysed, sucrose becomes levorotatory (–28.2°). This process of change in optical rotation is known as inversion, that is why sucrose is known as invert sugar.
- Lactose (milk sugar) is made up of **β-D-Glucose** and **β-D-Galactose**.
- Maltose is made up of two molecule of **α-D-Glucose.**

3. Polysaccharides Polysaccharides (or simply glycan) consist of repeat units of monosaccharides or their derivative held together by glycosidic bonds.

The main function of polysaccharide is structural and storage of energy.

Polysaccharides are linear or branched polymers.

The general formula of polysaccharide is $(C_6H_{10}O_5)_x$.

Types of polysaccharides

Homopolysaccharides On hydrolysis, it gives only a single type of monosaccharide.

E.g., Starch, Glycogen, Inulin, Cellulose, Pectin, Chitin, Dextrin

Heteropolysaccharides When polysaccharides are made up of different types of sugar or their derivatives, they are referred as heteropolysaccharides.

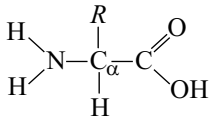
E.g., Hyaluronic acid, Chondrotin, Heparin, Keratan Sulfate

Amino Acids and Proteins

Chemical nature of the amino acids

The α-amino acids in peptides and proteins (excluding proline) consist of a carboxylic acid (–**COOH**) and an amino (–$\mathbf{NH_2}$) functional group attached to the same tetrahedral carbon atom. This carbon is the α-carbon. Distinct R-groups, that distinguish one amino acid from another, also are attached to the alpha-carbon (except in the case of glycine where the R-group is hydrogen). The fourth substitution on the tetrahedral α-carbon of amino acids is hydrogen.

The carboxyl group and amino group are attached to the same carbon atom, hence amino acids are termed as α-amino acids.



Classification of Amino acids

Amino Acid	Symbol
Amino Acids with Aliphatic R-Groups	
Glycine	Gly–G
Alanine	Ala–A
Valine	Val–V
Leucine	Leu–L
Isoleucine	Ile–I
Non-Aromatic Amino Acids with Hydroxyl R-Groups	
Serine	Ser–S
Threonine	Thr–T
Amino Acids with Sulphur-containing R-Groups	
Cysteine	Cys–C
Methionine	Met–M
Acidic Amino Acids and their Amides	
Aspartic Acid	Asp–D
Asparagine	Asn–N
Glutamic Acid	Glu–E
Glutamine	Gln–Q

Basic Amino Acids	
Arginine	Arg–R
Lysine	Lys–K
Histidine	His–H
Amino Acids with Aromatic Rings	
Phenylalanine	Phe–F
Tyrosine	Tyr–Y
Tryptophan	Trp–W
Imino Acids	
Proline	Pro–P

There are two types of amino acids as per the nutritional requirement.

- **Essential amino acids** are those that are not synthesized by the body and are needed in the diet. Methionine, threonine, tryptophan, valine, isoleucine, leucine arginine histidine and phenylalanine are the essential amino acids.
- **Non-essential amino acids** are those that are synthesized in the body and are not necessary in the diet. Glycine, alanine, serine, cysteine, tyrosine, proline, aspartic acid and glutamic acid are the non-essential amino acids.

Acid-base properties of the amino acids

Amino acids can undergo an intramolecular acid–base reaction. Transfer of the H from the –COOH group to the $–NH_2$ group forms a neutral dipolar ion, an ion that has one (+) charge and one (–) charge. Neutral dipolar ions are known as zwitterions.

$$R\text{-}COOH \longleftrightarrow R\text{-}COO^- + H^+$$

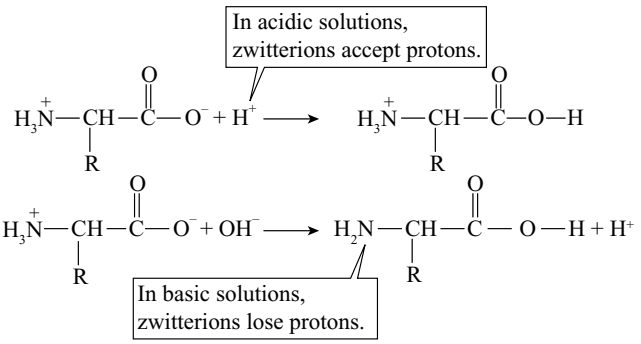
$$R\text{-}NH_3^+ \longleftrightarrow R\text{-}NH_2 + H^+$$

The equilibrium reactions, as written, demonstrate that amino acids contain at least two weakly acidic groups. However, the carboxyl group is a far stronger acid than the amino group. At physiological pH, (around 7.4) the carboxyl group will be unprotonated and the amino group will be protonated. An amino acid with no ionizable R-group would be electrically neutral at this pH. This species is termed a **zwitterion**.

When the net charge of an amino acid or protein is zero, the pH will be equivalent to the **isoelectric point pI**.

Optical properties of the amino acids

A tetrahedral carbon atom with four distinct constituents is said to be **chiral**. The one amino acid not exhibiting chirality is glycine since its "R-group" is a hydrogen atom. Chirality describes the handedness of a molecule that is observable by the ability of a molecule to rotate the plane of polarized light either to the right (**dextrorotatory**) or to the left (**levorotatory**).

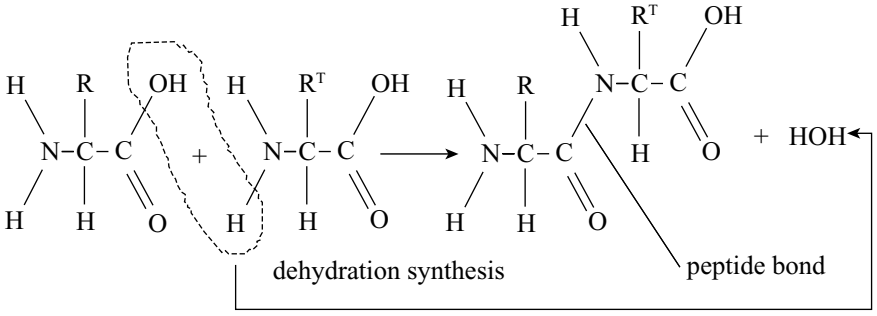


All of the amino acids in proteins exhibit the same absolute steric configuration as L-glyceraldehyde. Therefore, they are all L-α-amino acids. D-amino acids are never found in proteins, although they exist in nature. D-amino acids are often found in polypeptide antibiotics.

Aromatic R-groups in amino acids absorb ultraviolet light with an absorbance maximum in the range of 280nm. The ability of proteins to absorb ultraviolet light is predominantly due to the presence of the tryptophan which strongly absorbs ultraviolet light.

Peptide bond

Peptide bond formation is a condensation reaction leading to the polymerization of amino acids into peptides and proteins. Peptides are small chains consisting of few amino acids. A number of hormones and neurotransmitters are peptides. Additionally, several antibiotics and antitumor agents are peptides. Proteins are polypeptides of greatly divergent length. The simplest peptide, a **dipeptide**, contains a single peptide bond formed by the condensation of the carboxyl group of one amino acid with the amino group of the second with the concomitant elimination of water. The presence of the carbonyl group in a peptide bond allows electron resonance stabilization to occur such that the peptide bond exhibits rigidity not unlike the typical –C=C– double bond. The peptide bond is, therefore, said to have partial double-bond character.



Proteins

They are complex molecules made up of carbon, hydrogen, oxygen and nitrogen (sometimes sulphur and phosphorus).

Proteins are used to synthesize enzymes (E.g., pepsin, trypsin), hormones (E.g., insulin, adrenaline), carrier proteins (E.g., haemoglobin), contractile proteins (E.g., myosin, actin), structural proteins (E.g., collagen) and protective proteins (antibodies). They also form skin pigments like melanin and nucleic acids of the genetic material, DNA and RNA-purines and pyrimidines.

Structure of proteins

- Their **Primary** structure is the amino acid sequence of the polypeptide chain.
- **Secondary** structure is the local spatial arrangement of a polypeptide's backbone atoms. Common secondary structures are alpha-helices and beta-strands. In both, hydrogen bonding between backbone atoms holds the polypeptide chain in place. Alpha confirmation (Helical coil) and Beta confirmation (Pleated sheet).
- **Tertiary structure** The overall three-dimensional shape that results from the folding of a protein chain is the protein's tertiary structure.
- In contrast to secondary structure, which depends mainly on attraction between backbone atoms, tertiary structure depends mainly on interactions of amino acid side chains that are far apart along the same backbone. The fourth and final level of protein structure, and the most complex, is **quaternary protein structure**—the way in which two or more polypeptide subunits associate to form a single three-dimensional protein unit.
- The individual polypeptides are held together by the same non-covalent forces responsible for tertiary structure. In some cases, there are also covalent bonds and the protein may incorporate a non-amino acid portion.

Denaturation The loss of secondary, tertiary, or quarternary protein structure due to disruption of non-covalent interactions and/or disulfide bonds that leaves peptide bonds and primary structure intact.

Lipids

Saponification Value

- Saponification is the base-catalysed hydrolysis of an ester.
- Products of the reaction are–an alcohol and an ionized salt which is a soap.

Acid value

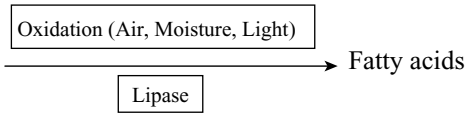
- Number of mgs of KOH required to neutralize the free fatty acids in 1g of fat, that number indicates degree of rancidity.

Iodine Value

- Number of iodine (g) absorbed by 100 g of oil.
- Molecular weight and iodine number can calculate the number of double bonds.

Rancidity

- Due to long exposure to air, a foul odour or smell comes known as rancidity.
- Triglyceride



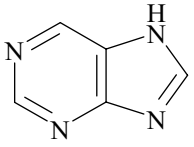
Especially, C_4 butyric acid and other short chain fatty acids in butter are the real problem.

Fatty Acids	No. of Carbons (Double bonds)
Palmitic acid	16 (0)
Stearic Acid	18 (0)
Oleic acid	18 (1)
Myristic acid	14 (0)
Linoleic acid	18 (2)

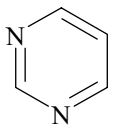
Fatty Acids	No. of Carbons (Double bonds)
Linolenic acid	18 (3)
Arachidonic acid	20 (4)
Lauric Acid	12 (0)
Capric Acid	10 (0)

$$\text{AV} = \frac{\text{ml of KOH} \times \text{N} \times 56}{\text{Weight of Sample}} \text{ mg of KOH}$$

Nucleoside and Nucleotide Structure and Nomenclature

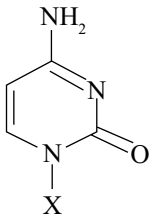
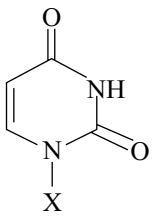
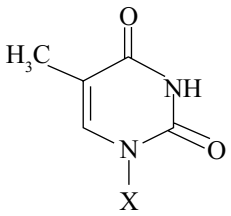
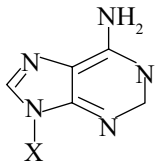
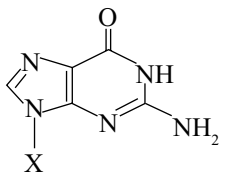


Purine



Pyrimidine

The derivatives of purine are called adenine and guanine, and the derivatives of pyrimidine are called thymine, cytosine and uracil. The common abbreviations used for these five bases are, A, G, T, C and U.

Base Formula	Base (X=H)	Nucleoside X=ribose or deoxyribose	Nucleotide X=ribose phosphate
	Cytosine, C	Cytidine, C	Cytidine monophosphate, CMP
	Uracil, U	Uridine, U	Uridine monophosphate, UMP
	Thymine, T	Thymidine, T (only deoxyribose)	Thymidine monophosphate, TMP
	Adenine, A	Adenosine, A	Adenosine monophosphate, AMP
	Guanine, G	Guanosine, G	Guanosine monophosphate, GMP

- The purine and pyrimidine bases in cells are linked to pentose sugar and in this form are termed, nucleosides.
- The nucleosides are coupled to D-ribose or 2′-deoxy-D-ribose through a β-*N*-glycosidic bond between the anomeric carbon of the ribose and the N^9 of a purine or N^1 of a pyrimidine.
- The base can exist in two distinct orientations about the *N*-glycosidic bond. These conformations are identified as, *syn* and *anti*. It is the anti-conformation that predominates in naturally occurring nucleotides.

DNA	RNA
1. Found in nucleus 2. sugar is deoxyribose 3. Bases are A, T, C, G	1. Found in nucleus and cytoplasm 2. Sugar is ribose. 3. Bases are A, U, C, G
DNA is a long polymer with a deoxyribose and phosphate backbone and four different bases: adenine, guanine, cytosine and thymine	RNA is a polymer with a ribose and phosphate backbone and four different bases: adenine, guanine, cytosine, and uracil Chargaff's rule is not obeyed due to single stranded nature
Typically a double-stranded molecule with a long chain of nucleotides	Single-stranded molecule in most of its biological roles and has a shorter chain of nucleotides
Pairing of Bases: A-T (Adenine-Thymine), G-C (Guanine-Cytosine)	A-U (Adenine-Uracil), G-C (Guanine-Cytosine)
Deoxyribose sugar in DNA is less reactive because of C-H bonds. Stable in alkaline conditions. DNA has smaller grooves where the damaging enzyme can attach which makes it harder for the enzyme to attack DNA.	Ribose sugar is more reactive because of C-OH (hydroxyl) bonds. Not stable in alkaline conditions. RNA on the other hand has larger grooves which make it easier to be attacked by enzymes.
The helix geometry of DNA is of β-Form.	The helix geometry of RNA is of α-Form.
Storage and transmission of genetic information.	Transfer the genetic code needed for the creation of proteins from the nucleus to the ribosome.

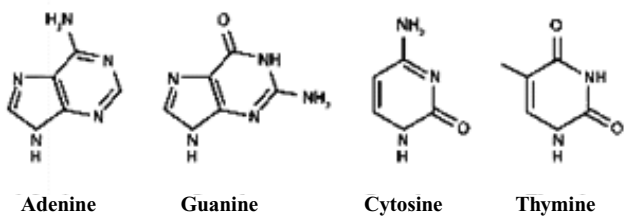
- Nucleosides are found in the cell primarily in their phosphorylated form. These are termed nucleosides. The most common site of phosphorylation of nucleosides found in cells is the hydroxyl group attached to the 5′-carbon of the ribose The carbon atoms of the ribose present in nucleotides are designated with a prime (′) mark to distinguish them from the backbone numbering in the bases. Nucleotides can exist in the mono-, di-, or tri-phosphorylated forms.

Chargaff's rules

It was known that DNA is composed of nucleotides, each of which contains a nitrogen-containing base, a five carbon sugar (deoxyribose), and a phosphate group. In these nucleotides, there is one of the four possible bases: adenine (A), guanine (G), cytosine (C), or thymine (T) . Adenine and guanine are purine bases, and cytosine and thymine are pyrimidine bases.

Erwin Chargaff (1905-2002), an Austrian-American biochemist from Columbia University, analyzed the base composition of the DNA of various species. This led him to propose two main rules that have been appropriately named Chargaff's rules.

Nitrogen Bases in DNA



Adenine **Guanine** **Cytosine** **Thymine**

Rule 1: Chargaff determined that in DNA, the amount of one base, a purine, always approximately equals the amount of a particular second base, a pyrimidine. Specifically, that in any double-stranded DNA the number of guanine units equals approximately the the number of cytosine units and the number of adenine units equals approximately the number of thymine units. Human DNA is 30.9% A and 29.4% T, 19.9% G and 19.8% C. The rule constitutes the basis of base pairs in the DNA double helix: A always pairs with T, and G always pairs with C. He also demonstrated that the number of purines (A+G) always approximates the number of pyrimidines (T+C), an obvious consequence of the base-pairing nature of the DNA double helix.

Rule 2: In 1947 Chargaff showed that the composition of DNA, in terms of the relative amounts of the A, C, G and T bases, varied from one species to another. This molecular diversity added evidence that DNA could be the genetic material.

Bonding

There are three different kinds of chemical bonds:

1. Ionic bonds (also called electrovalent bonds) are formed between atoms when one or more electrons are completely transferred from one atom to the other.
2. Covalent bonds are formed between atoms when two atoms share one or more pairs of electrons.
3. Hydrogen bonds are formed between the positively-charged hydrogen atom in one covalently-bonded molecule and the negatively-charged area of another covalently-bonded molecule.

DNA bases are held together by hydrogen bonds. There are two hydrogen bonds between A and T and three hydrogen bonds between C and G.

Protein Synthesis

1. Transcription

It is the process of creating a complementary RNA copy from sequence of DNA. Both RNA and DNA are nucleic acids, which use base pairs of nucleotides as a complementary language that can be converted back and forth from DNA to RNA by the action of the correct enzymes. During transcription, a DNA sequence is read by RNA polymerase, which produces a complementary, antiparallel RNA strand. As opposed to DNA replication, transcription results in an RNA complement that includes uracil (U) in all instances where thymine (T) would have occurred in a DNA complement.

Transcription can be explained easily in four or five simple steps, each moving like a wave along the DNA.

1. DNA unwinds/"unzips" as the hydrogen bonds break.
2. The free nucleotides of the RNA, pair with complementary DNA bases.
3. RNA sugar-phosphate forms backbone. (Aided by RNA Polymerase.)
4. Hydrogen bonds of the untwisted RNA+DNA "ladder" break, freeing the new RNA.
5. If the cell has a nucleus, the RNA is further processed and then moves through the small nuclear pores to the cytoplasm.

2. Translation

"Biosynthesis of a protein or polypeptide in a living cell is known as Translation"

The ribosome binds to the mRNA at the start codon (AUG) that is recognized only by the initiator tRNA. The ribosome proceeds to the elongation phase of protein synthesis. During this stage, complexes, composed of an amino acid linked to tRNA, sequentially bind to the appropriate codon in mRNA by forming complementary base pairs with the tRNA anticodon. The ribosome moves from codon to codon along the mRNA. Amino acids are added one by one, translated into polypeptidic sequences dictated by DNA and represented by mRNA. At the end, a release factor binds to the stop codon, terminating translation and releasing the complete polypeptide from the ribosome.

Genetic Code

The genetic code consists of 64 triplets of nucleotides. These triplets are called codons. With three exceptions, each codon encodes for one of the 20 amino acids used in the synthesis of proteins. That produces some redundancy in the code: most of the amino acids being encoded by more than one codon.

One codon, AUG serves two related functions:

- it signals the start of translation
- it codes for the incorporation of the amino acid methionine (Met) into the growing polypeptide chain

The genetic code can be expressed as either RNA codons or DNA codons. RNA codons occur in messenger RNA (mRNA) and are the codons that are actually "read" during the synthesis of polypeptides (the process called translation).

Properties of genetic codes

- Genetic code is degenerate The occurrence of more than one codon per amino acid is called degeneracy. All amino acids except methionine and tryptophan have more than one codon, so that all the possible triplets have a meaning, despite there being 64 triplets and only 20 amino acids. Leucine, Serine and Arginine have six different codons.
- Code contains punctuation codons Three codons do not code for specific amino acids. These codons are called as nonsense codons. These nonsense codons cause termination of protein synthesis. AUG codon codes for starting of the gene and position where translation should begin. AUG codes for the initiation codon and because it codes for methionine, almost all newly synthesized polypeptides have this amino acid at the start.
- Codon is commaless. There are no commas or some specific nucleotide sequences to separate the codons, i.e., CCCAAAUUUGGG has four code words and upon translation, we have a tetrapeptide chain of pro-lys-phen-gly. So all the letters are used to code for one or other amino acid.
- Codon is Triplet in nature.

Myoglobin

- Myoglobin and hemoglobin are hemeproteins whose physiological importance is principally related to their ability to bind molecular oxygen.
- Myoglobin is a monomeric heme protein found mainly in muscle tissue where it serves as an intracellular storage site for oxygen. The tertiary structure of myoglobin is that of a typical water soluble globular protein. Its secondary structure is unusual in that it contains a very high proportion (75%) of α-helical secondary structure. A myoglobin polypeptide is comprised of 8 separate right handed α-helices, designated A through H, that are connected by short non helical regions.
- Each myoglobin molecule contains one heme prosthetic group inserted into a hydrophobic cleft in the protein. Each heme residue contains one central coordinately bound iron atom that is normally in the Fe^{2+}, or ferrous, oxidation state.
- The oxygen carried by hemeproteins is bound directly to the ferrous iron atom of the heme prosthetic group. Oxidation of the iron to the Fe^{3+}, ferric, oxidation state renders the molecule incapable of normal oxygen binding.
- Hydrophobic interactions between the tetrapyrrole ring and hydrophobic amino acid R groups on the interior of the cleft in the protein strongly stabilize the heme protein conjugate. In addition, a nitrogen atom from a histidine R group located above the plane of the heme ring is coordinated with the iron atom further stabilizing the interaction between the heme and the protein.
- Carbon monoxide also binds coordinately to heme iron atoms in a manner similar to that of oxygen, but the binding of carbon monoxide to heme is much stronger than that of oxygen. The preferential binding of carbon monoxide to heme iron is largely responsible for the asphyxiation that results from carbon monoxide poisoning.

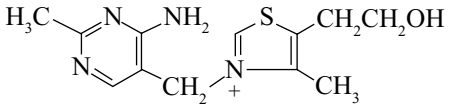
Hemoglobin

Adult hemoglobin is a [α(2):β(2)] tetrameric hemeprotein found in erythrocytes where it is responsible for binding oxygen in the lung and transporting the bound oxygen throughout the body where it is used in aerobic metabolic pathways.

6. Vitamins

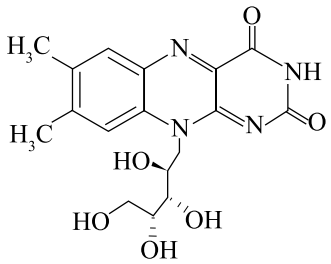
Water Soluble vitamin	Water insoluble vitamin
Thiamin (B_1),	Vitamin A
Riboflavin (B_2)	Vitamin D
Niacin (B_3)	Vitamin E
Pyridoxal, Pyridoxamine Pyridoxine	Vitamin K
Biotin (B_7)	
Cobalamin (B_{12})	
Folic Acid, Pantothenic acid	
Ascorbic Acid	

Thiamine



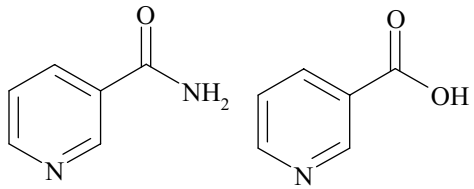
- Thiamin is derived from a substituted pyrimidine and a thiazole which are coupled by a methylene bridge. Thiamin is rapidly converted to its active form, thiamin pyrophosphate, TPP, by thiamin diphosphotransferase.
- TPP is necessary as a cofactor for the pyruvate dehydrogenase and α-ketoglutarate dehydrogenase catalysed reactions as well as the transketolase catalysed reactions of the pentose phosphate pathway.
- Thiamin deficiency causes Beriberi, Wernicke-Korsakoff syndrome.

Riboflavin



Riboflavin is the precursor for the coenzymes, flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD). The enzymes that require FMN or FAD as cofactors are termed flavoproteins. Both classes of enzymes are involved in a wide range of redox reactions e.g., succinate dehydrogenase and xanthine oxidase.

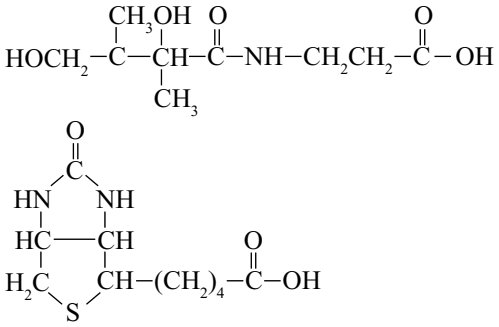
Niacin



Nicotinamide Nicotinic acid

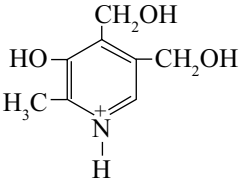
- Niacin is required for the synthesis of the active forms of vitamin B_3, nicotinamide adenine dinucleotide (NAD^+) and nicotinamide adenine dinucleotide phosphate ($NADP^+$). Both NAD^+ and $NADP^+$ function as cofactors for numerous dehydrogenases e.g., lactate dehydrogenase and malate dehydrogenase.
- Niacin is not a true vitamin.
- Niacin deficiency causes pellagra.

Pantothenic acid

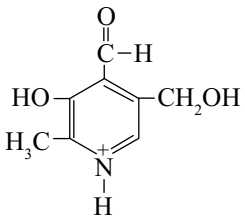


- Pantothenic acid is formed from β-alanine and pantoic acid.
- Pantothenate is required for synthesis of coenzyme A.

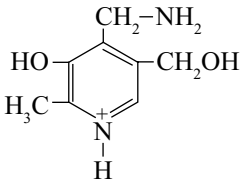
Vitamin B_6



Pyridoxine



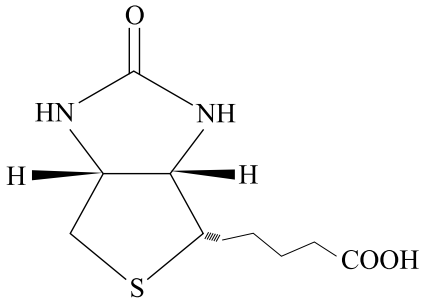
Pyridoxal



Pyridoxamine

- Pyridoxal, pyridoxamine and pyridoxine are collectively known as vitamin B_6. All three compounds are efficiently converted to the biologically active form of vitamin B_6, pyridoxal phosphate (PLP). This conversion is catalysed by the ATP requiring enzyme, pyridoxal kinase. Pyridoxal kinase requires zinc for full activity thus making it a metaloenzyme.
- Pyridoxal phosphate functions as a cofactor in enzymes involved in transamination reactions required for the synthesis and catabolism of the amino acids as well as in glycogenolysis as a cofactor for glycogen phosphorylase and as a co-factor for the synthesis of the inhibitory neurotransmitter γ-aminobutyric acid (GABA).
- Isoniazid (see niacin deficiencies above) and penicillamine (used to treat rheumatoid arthritis and cystinurias) are two drugs that complex with pyridoxal and PLP resulting in a deficiency of this vitamin.

Biotin

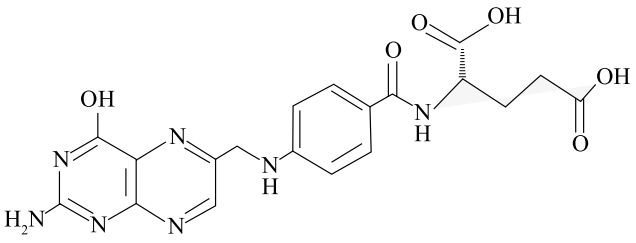


Biotin is the cofactor required of enzymes that are involved in carboxylation reactions e.g., acetyl-CoA carboxylase and pyruvate carboxylase.

Cobalamin

- Cobalamin is more commonly known as vitamin B_{12}. Vitamin B_{12} is composed of a complex tetrapyrrol ring structure (corrin ring) and a cobalt ion in the center.
- The reaction requiring vitamin B_{12} catalyses the conversion of homocysteine to methionine and is catalysed by methionine synthase. This reaction results in the transfer of the methyl group from N^5-methyltetrahydrofolate to hydroxycobalamin generating tetrahydrofolate (THF) and methylcobalamin during the process of the conversion.
- B_{12} deficiency-Pernicious anemia is a megaloblastic anemia resulting from vitamin B_{12} deficiency.

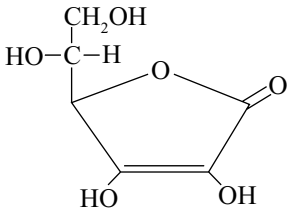
Folic acid



Positions 7 and 8 carry hydrogens in dihydrofolate (DHF)
Positions 5–8 carry hydrogens in tetrahydrofolate (THF)

- Folic acid is a conjugated molecule consisting of a pteridine ring structure linked to para-aminobenzoic acid (PABA) that forms pteroic acid. Folic acid itself is then generated through the conjugation of glutamic acid residues to pteroic acid.
- The function of THF derivatives is to carry and transfer various forms of one carbon units during biosynthetic reactions. The one carbon units are either methyl, methylene, methenyl, formyl or formimino groups.
- Folate deficiency–The most pronounced effect of folate deficiency on cellular processes is upon DNA synthesis. This is due to an impairment in dTMP synthesis which leads to cell cycle arrest in S-phase of rapidly proliferating cells, in particular hematopoietic cells. The result is megaloblastic anemia as for vitamin B_{12} deficiency.
- The inability to synthesize DNA during erythrocyte maturation leads to abnormally large erythrocytes termed macrocytic anemia.

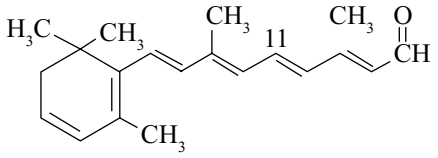
Ascorbic acid



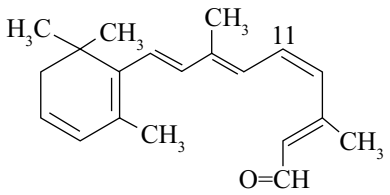
- Ascorbic acid is more commonly known as vitamin C. Ascorbic acid is derived from glucose via the uronic acid pathway. The enzyme L-gulonolactone oxidase is responsible for the conversion of gulonolactone to ascorbic acid.
- The active form of vitamin C is ascorbic acid itself. The main function of ascorbate is as a reducing agent in a number of different reactions.
- Ascorbate is the cofactor for Cu^{+}–dependent monooxygenases and Fe^{2+}–dependent dioxygenases.
- Ascorbate has the potential to reduce cytochromes *a* and *c* of the respiratory chain as well as molecular oxygen.
- The most important reaction requiring ascorbate as a cofactor is the hydroxylation of proline residues in collagen. Vitamin C is, therefore, required for the maintenance of normal connective tissue as well as for wound healing since synthesis of connective tissue is the first event in wound tissue remodeling.
- Vitamin C also is necessary for bone remodeling due to the presence of collagen in the organic matrix of bones.
- Ascorbic acid also serves as a reducing agent and an antioxidant. When functioning as an antioxidant, ascorbic acid itself becomes oxidized to semidehydroascorbate and then dehydroascorbate.
- Deficiency of vitamin C leads to the disease called scurvy.

Vitamin A

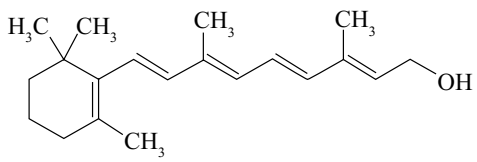
Vitamin A consists of three biologically active molecules, retinol, retinal (retinaldehyde) and retinoic acid.



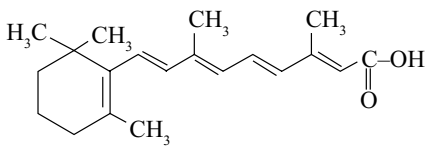
All-*trans*-retinal



11-*cis*-retinal



Retinol



Retinoic Acid

- Each of these compounds are derived from the plant precursor molecule, β-carotene. Beta-carotene, which consists of two molecules of retinal linked at their aldehyde ends, is also referred to as the provitamin form of vitamin A.
- Vision and the role of Vitamin A
  The photosensitive compound of most mammalian eyes is a protein called opsin to which is covalently coupled an aldehyde of vitamin A. The opsin of rod cells is called scotopsin. The photoreceptor of rod cells is specifically called rhodopsin or visual purple. This compound is a complex between scotopsin and the 11-*cis*-retinal (also called 11-*cis*-retinene) form of vitamin A. Rhodopsin is a serpentine receptor imbedded

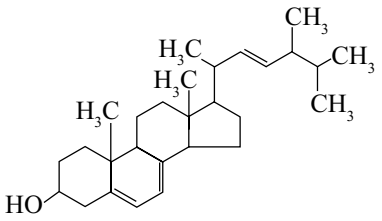
in the membrane of the rod cell. Coupling of 11-*cis*-retinal occurs at three of the transmembrane domains of rhodopsin. Intracellularly, rhodopsin is coupled to a specific G-protein called transducin.

When the rhodopsin is exposed to light it is bleached releasing the 11-*cis*-retinal and opsin. Absorption of photons by 11-*cis*-retinal triggers a series of conformational changes on the way to conversion all-*trans*-retinal.

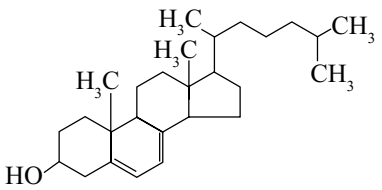
- Vitamin A deficiency: It causes night blindness, hyperkeratinosis, keratinization of the cornea, a condition known as xerophthalmia.

Vitamin D

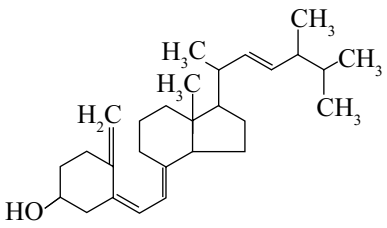
Vitamin D is a steroid hormone that functions to regulate specific gene expression following interaction with its intracellular receptor. The biologically active form of the hormone is 1, 25-dihydroxy vitamin D_3 (1, 25-$(OH)_2D_3$, also termed calcitriol). Calcitriol functions primarily to regulate calcium and phosphorous homeostasis.



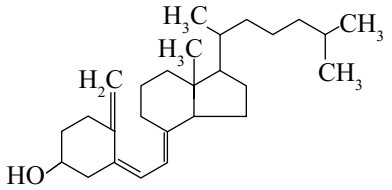
Ergosterol



7-Dehydrocholesterol



Vitamin D2



Vitamin D3

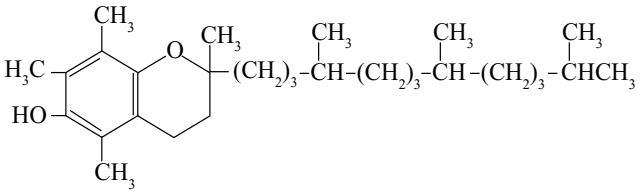
Active calcitriol is derived from ergosterol (produced in plants) and from 7-dehydrocholesterol (produced in the skin). Ergocalciferol (vitamin D_2) is formed by uv irradiation of ergosterol. In the skin 7-dehydrocholesterol is converted to cholecalciferol (vitamin D_3) following *uv* irradiation.

Cholecalciferol (or ergocalciferol) are absorbed from the intestine and transported to the liver bound to a specific vitamin D-binding protein. In the liver, cholecalciferol is hydroxylated at the 25 position by a specific D_3-25-hydroxylase generating 25-hydroxy-D_3 [25-$(OH)D_3$] which is the major circulating form of vitamin D. Conversion of 25-$(OH)D_3$ to its biologically active form, calcitriol, occurs through the activity of a specific D_3-1-hydroxylase present in the proximal convoluted tubules of the kidneys, and in bone and placenta.

Calcitriol functions in concert with parathyroid hormone (PTH) and calcitonin to regulate serum calcium and phosphorous levels.

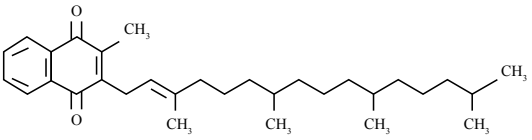
Vitamin D deficiency: The main symptom of vitamin D deficiency in children is rickets and in adults is osteomalacia.

Vitamin E

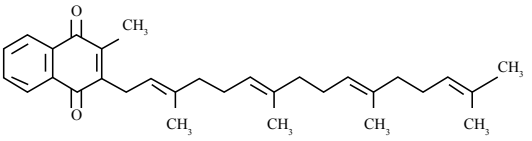


- Vitamin E is a mixture of several related compounds known as tocopherols. The α-tocopherol molecule is the most potent of the tocopherols.
- The major site of vitamin E storage is in adipose tissue.
- The major function of vitamin E is to act as a natural antioxidant by scavenging free radicals and molecular oxygen.
- In particular, vitamin E is important for preventing peroxidation of polyunsaturated membrane fatty acids.
- The vitamins E and C are interrelated in their antioxidant capabilities.
- Vitamin E deficiency-The major symptom of vitamin E deficiency in humans is an increase in red blood cell fragility.

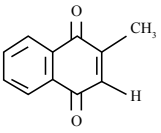
Vitamin K



Phylloquinone (vitamin K_1)



Menaquinone-4 (vitamin K_2)



Menadione (vitamin K_3)

Human use 6, 7 or 9 isoprene chains.

The K vitamins exist naturally as K_1 (phylloquinone) in green vegetables and K_2 (menaquinone) produced by intestinal bacteria and K_3 is synthetic menadione. When administered, vitamin K_3 is alkylated to one of the vitamin K_2 forms of menaquinone.

The major function of the K vitamins is in the maintenance of normal levels of the blood clotting proteins, factors II, VII, IX, X and protein C and protein S, which are synthesized in the liver as inactive precursor proteins.

Conversion from inactive to active clotting factor requires a post-translational modification of specific glutamate (E) residues. This modification is a carboxylation and the enzyme responsible requires vitamin K as a cofactor. The resultant modified e residues are γ-carboxyglutamate (*gla*).

During the carboxylation reaction, reduced hydroquinone form of vitamin K is converted to a 2, 3-epoxide form.

Vitamin K deficiency-Malabsorptive diseases can result in vitamin K deficiency.

Important table

Sr. No.	Vitamins	Precursor (Biosynthetic)
1	Vitamin A	Carotenoid
2	Vitamin D	Acetyl-Mevalonic acid
3	Vitamin Bl/Thiamine	Pyrimidine phosphatase + Thiazole moieties
4	Riboflavin/ Vitamin B2	Purine
5	Nicotinic acid	Reaction between Aspartic acid + glutaraldehyde-3-phosphate
6	Pantothenic acid	Beta-alanine + alpha J, ~toisovaleric acid
7	PABA	Shikimic acid
8	Biotin	Pimelic acid
9	Choline	Serine
10	Folic acid	Purine or Purine equivalent

Mutarotation

Mutarotation – change in the optical rotation that occurs by epimerization (that is the change in the equilibrium between two epimers, when the corresponding stereocenters interconvert). Cyclic sugars show mutarotation as α and β anomeric forms interconvert. The optical rotation of the solution depends on the optical rotation of each anomer and their ratio in the solution.

The two stereoisomeric forms of glucose, i.e., α-D-glucose and β-D-glucose exist in separate crystalline forms and thus have different melting points and specific roations. For example α-D-glucose has a m.p. of 419 K with a specific rotation of +112° while β-D-glucose has a m.p. of 424 K and has a specific rotation of +19°. However, when either of these two forms is dissolved in water and allowed to stand, it gets converted into an equilibrium mixture of α-and β-forms through a small amount of the open chain form.

$$\underset{(36\%)}{\alpha\text{-D-Glucose}} \rightleftharpoons \underset{\text{form (0.02\%)}}{\text{Open chain}} \rightleftharpoons \underset{(54\%)}{\beta\text{-D-Glucose}}$$

As a result of this equilibrium, the specific rotation of a freshly prepared solution of α-D-glucose gradually decreases from of +112° to +52.7° and that of β-D-glucose gradually increases from +19° to +52.7°.

$$\underset{[\alpha]_D = +112^\circ}{\alpha\text{-D-Glucose}} \rightleftharpoons \underset{[\alpha]_D = +52.7^\circ}{\text{Equilibrium mixtute}} \rightleftharpoons \underset{[\beta]_D = +19^\circ}{\beta\text{-D-Glucose}}$$

Where $[\alpha]_D$ = specific rotation

This change in specific rotation of an optically active compound in solution with time, to an equilibrium value, is called mutarotation. During mutarotation, the ring opens and then recloses either in the inverted position or in the original position giving a mixture of α-and-β-forms. All reducing carbohydrates, i.e. monosaccharides and disacchardies (maltose, lactose etc.) undergo mutarotation in aqueous solution.

Isoelectric Point

The isoelectric point (pI) - is the pH at which a particular molecule or surface carries no net electrical charge.

Amphoteric molecules called zwitterions contain both positive and negative charges depending on the functional groups present in the molecule. The net charge on the molecule is affected by pH of their surrounding environment and can become more positively or negatively charged due to the loss or gain of protons (H^+). The pI is the pH value at which the molecule carries no net electrical charge or the negative and positive charges are equal.

Surfaces naturally charge to form a double layer. In the common case when the surface charge-determining ions are H^+/OH^-, the net surface charge is affected by the pH of the liquid in which the solid is submerged. Again, the pI is the pH value of the solution at which the surfaces carries no net charge.

The pI value can affect the solubility of a molecule at a given pH. Such molecules have minimum solubility in water or salt solutions at the pH that corresponds to their **pI** and often precipitate out of solution. Biological amphoteric molecules such as proteins contain both acidic and basic functional groups. Amino acids that make up proteins may be positive, negative, neutral, or polar in nature, and together give a protein its overall charge. At a pH below their pI, proteins carry a net positive charge; above their pI they carry a net negative charge. Proteins can, thus, be separated according to their isoelectric point (overall charge) on a polyacrylamide gel using a technique called isoelectric focusing, which uses a pH gradient to separate proteins. Isoelectric focusing is also the first step in 2-D polyacrylamide gel electrophoresis.

Calculation of pI

For an amino acid with only one amine and one carboxyl group, the pI can be calculated from the mean of the pKas of this molecule .

$$pI = \frac{pK_1 + pK_2}{2}$$

For amino acids with more than two ionizable groups, such as lysine, the same formula is used, but this time the two pKa's used are those of the two groups that lose and gain a charge from the neutral form of the amino acid. Lysine has a single carboxylic pKa and two amine pKa values (one of which is on the R-group), so fully protonated lysine has a +2 net charge. To get a neutral charge, we must deprotonate the lysine twice, and therefore use the R-group and amine pKa values (found at List of standard amino acids).

$$pI = \frac{9.06 + 10.54}{2} = 9.80$$

The pH of an electrophoretic gel is determined by the buffer used for that gel. If the pH of the buffer is above the pI of the protein being run, the protein will migrate to the positive pole (negative charge is attracted to a positive pole). If the pH of the buffer is below the pI of the protein being run, the protein will migrate to the negative pole of the gel (positive charge is attracted to the negative pole). If the protein is run with a buffer pH that is equal to the pI, it will not migrate at all. This is also true for individual amino acids

Osazone

Osazones are carbohydrate derivatives formed when sugars are reacted with phenyl hydrazine.

The reaction involves formation of a pair of phenylhydrazone functionalities, concomitant with the oxidation of the hydroxymethylene group adjacent to the formyl center. The reaction can be used to identify monosaccharides. It involves two reactions.

Firstly glucose with phenyl hydrazine gives us glucose phenylhydrazone by elimination of a water molecule from the functional group. The next step involves reaction of one mole of glucose phenylhydrazone with two moles of phenyl hydrazine (excess).

First phenyl hydrazine is involved in oxidizing the alpha carbon to a carbonyl group, and the second phenyl hydrazine involves in removal of one water molecule with the formyl group of that oxidized carbon and forming the similar carbon nitrogen bond. The alpha carbon is attacked here because its more reactive than the others. They are highly colored and crystalline compounds and can be easily detected. Glucose gives broomstick shaped crystals with this whereas maltose gives sunflower shaped crystals.

Carr Price Reaction

A reaction of antimony trichloride and vitamin A in chloroform solution that gives a blue color and is used for the identification and assay of vitamin A.

Classification of Enzyme

1. Oxidoreductases: catalyze the transfer of hydrogen or oxygen atoms or electrons from one substrate to another, also called oxidases, dehydrogenases, or reductases. Note that since these are 'redox' reactions, an electron donor/acceptor is also required to complete the reaction.

Oxidases	Use oxygen as an electron acceptor but do not incorporate in the substrate
Dehydrogenase	Use molecule other than oxygen(e.g. NAD^+) as an electron acceptor
Oxygenases	Directly incorporate oxygen into the substrate
Peroxidase	Use H_2O_2 as an electron acceptor

2. Transferases: catalyze group transfer reactions, excluding oxidoreductases (which transfer hydrogen or oxygen and are EC 1). These are of the general form ($A-X + B \leftrightarrow BX + A$)

Methyltransferase	Transfer of one carbon units between substrates
Aminotransferases	Transfer of NH_2 from amino acid to keto acids
Kinases	Transfer of PO_3 from ATP to a substrate
Phosphorylases	Transfer of PO_3 from inorganic phosphate(P) to a substrate

3. Hydrolases: catalyze hydrolytic reactions. Includes lipases, esterases, nitrilases, peptidases/proteases. These are of the general form ($A-X + H_2O \leftrightarrow X-OH + HA$)

Phosphatase	Removal of PO_3 from substrate
Phosphodiesterases	Cleavage of Phosphodiester bond such as those in Nucleic acid
Protease	Cleavage of amide bond such as those in proteins

4. Lyases: It catalyze non-hydrolytic (covered in EC 3) removal of functional groups from substrates, often creating a double bond in the product; or the reverse reaction, ie, addition of function groups across a double bond. It includes decarboxylases and aldolases in the removal direction, and synthases in the addition direction.

Decarboxylases	Produce CO_2 via elimination reactions
Aldolases	Produce Aldehyde via elimination reactions
Synthases	Link two molecule without involvement of ATP

5. Isomerases: It catalyzes isomerization reactions, including racemizations and cis tran isomerizations.

Racemases	Interconvert L and D stereoisomers
Mutases	Transfer of group between atoms within a molecule

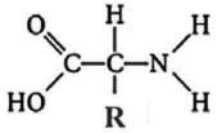
6. Ligases: catalyzes the synthesis of various (mostly C–X) bonds, coupled with the breakdown of energy–containing substrates, usually ATP.

Carboxylases	Use CO_2 as a substrate
Synthetases	Link two molecule via an ATP dependent reaction

Classification of amino acids

I. Chemical classification: According to number of COOH and NH_2 groups i.e. according to net charge on amino acid.

A. Monobasic & monocarboxylic amino acids i.e. neutral or uncharged:



1. Glycine R= H
2. Alanine R= CH_3
3. Branched chain amino acids: R is branched such as in:
   a. Valine R= isopropyl group
   b. Leucine R= isobutyl group
   c. Isoleucine R = is isobutyl group
4. Neutral Sulfur containing amino acids: e.g. Cysteine and Methionine. Cysteine, not involved in proteins. It is dimer of cysteine linked by S-S bond (oxidized form)
5. Neutral, hydroxyl amino acids: e.g. Serine and Threonine
6. Neutral aromatic amino acids:
   a. Phenyl alanine
   b. Tyrosine: - it is p- hydroxy phenyl alanine
   c. Tryptophan:
7. Neutral heterocyclic amino acids:
   a. Tryptophan: contains indole ring
   b. Proline: In proline, amino group enters in the ring formation being α-imino group so proline is an α-imino acid rather than α-amino acid

B. Basic amino acids: Contain two or more NH groups or nitrogen atoms that act as base i.e. can bind proton. At physiological pH, basic amino acids will be positively charged.

e.g. Lysine, Arginine: contains guanido group, Histidine

C. Acidic Amino acids: at physiological pH will carry negative charge.

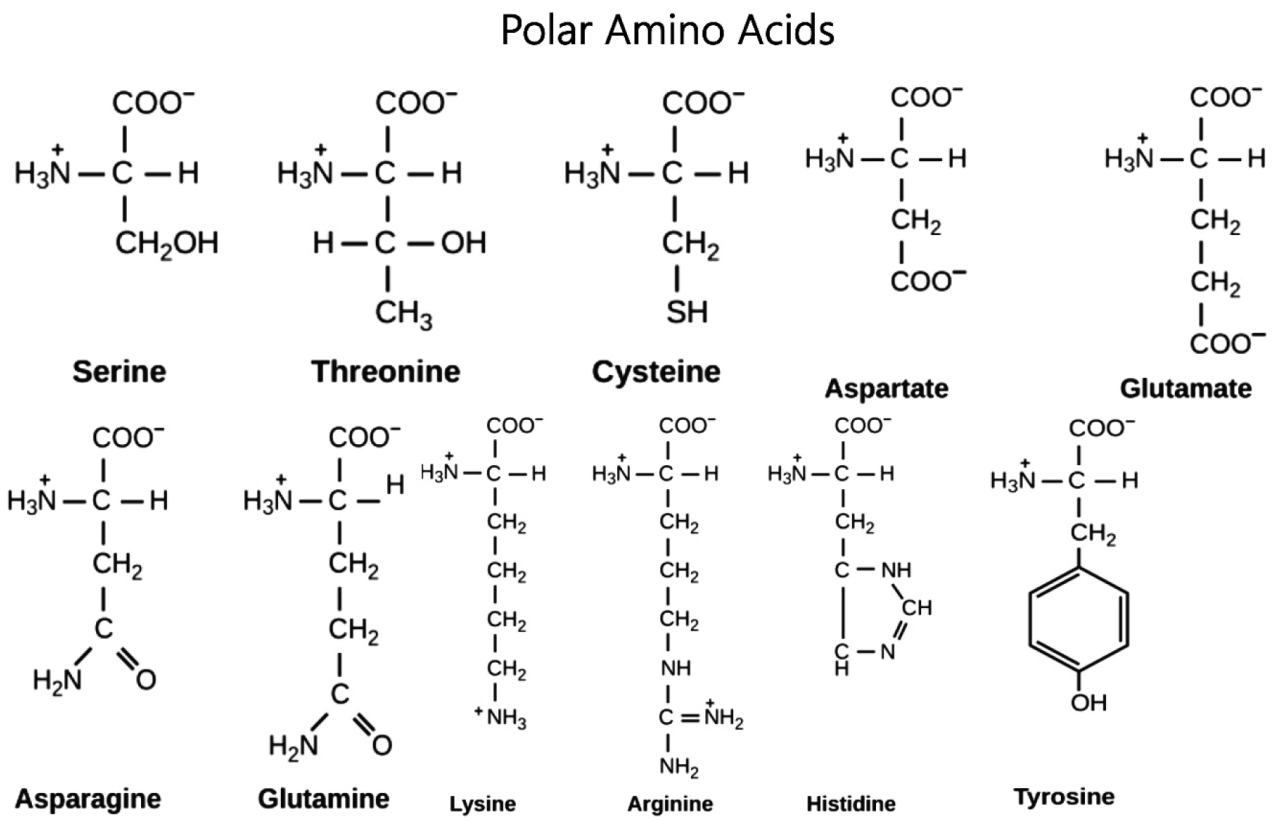
e.g. Aspartic acid (aspartate) and Glutamic acid (glutamate). Aspargine and Glutamine: They are amide forms of aspartate and glutamate in which side chain COOH groups are amidated. They are classified as neutral amino acids.

II. Classification according to polarity of side chain (R):

A. Polar amino acids: in which R contains polar hydrophilic group so can forms hydrogen bond with H

O. In those amino acids, R may contain:

1. OH group : as in serine, threonine and tyrosine
2. SH group : as in cysteine
3. amide group: as in glutamine and aspargine
4. NH_2 group or nitrogen act as a base (basic amino acids) : as lysine, arginine and histidine
5. COOH group (acidic amino acids): as aspartic and glutamic acid



B. Non polar amino acids:

R is alkyl hydrophobic group which can't enter in hydrogen bond formation. 9 amino acids are non-polar (glycine, alanine, valine,leucine, isoleucine, phenyl alanine, tryptophan, proline and methionine)

III. Nutritional classification:

1. Essential amino acids: These amino acids can't be formed in the body and so, it is essential to be taken in diet. Their deficiency affects growth, health and protein synthesis.

2. Semiessential amino acids: These are formed in the body but not in sufficient amount for body requirements especially in children.

Summary of essential and semi-essential amino acids:

[V= valine i= isoleucine l= lysine l= leucine A = arginine* H= histidine* M= methionine

T= tryptophan Th= threonine P= phenyl alanine (*= arginine and histidine are semiessential)]

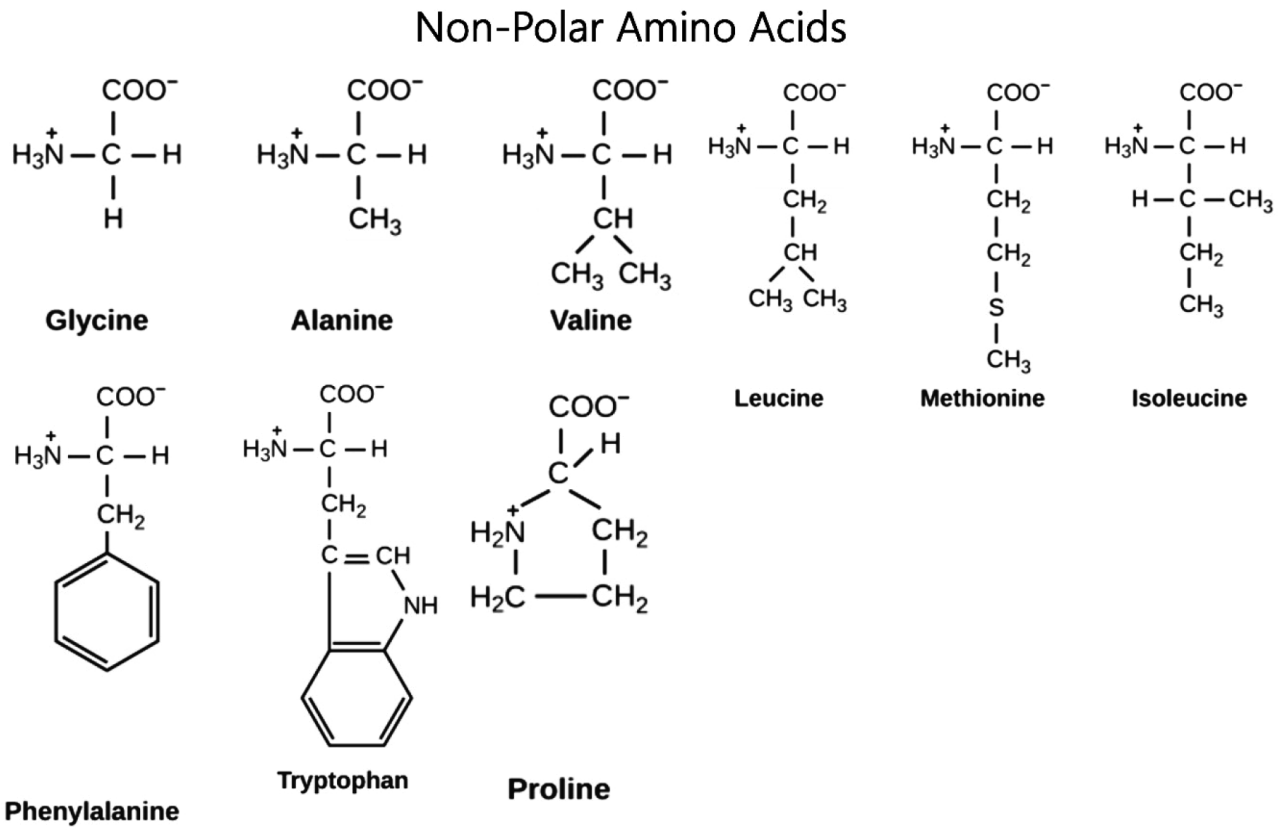
3. Non essential amino acids: These are the rest of amino acids that are formed in the body in amount enough for adults and children. They are the remaining 10 amino acids.

IV. Metabolic classification: according to metabolic or degradation products of amino acids they may be:

1. Ketogenic amino acids: which give ketone bodies . Lysine and Leucine are the only pure ketogenic amino acids.

2. Mixed ketogenic and glucogenic amino acids: which give both ketonbodies and glucose.These are: isoleucine, phenyl alanine, tyrosine and tryptophan.

3. Glucogenic amino acids: Which give glucose. They include the rest of amino acids. These amino acids by catabolism yields products that enter in glycogen and glucose formation.



Classification of Lipids

1. Simple Lipids: Esters of fatty acids with alcohols. These are mainly of two types

a. **Fats** & **Oils** (**Triacyglycerols**)**:** These are esters of fatty acids with glycerol. The difference between at and oil is only physical. Thus, oil is a liquid while fat is a solid at room temperature

b. **Waxes:** Esters of fatty acids (usually long chain) with alcohols other than glycerol. These alcohols may be liphatic or alicyclic. Cetyl alcohol is most commonly found in waxes.

2. Complex (**or compound**) **lipids:** These are esters of fatty acids with alcohols containing additional groups such as phosphate, nitrogenous base, carbohydrate, protein etc They are further divided as follows;

(a) Phospholipids: They contain phosphoric acid and frequently a nitrogenous base This is in addition to alcohol and Fatty acids.

I. Glycerophospholipids: These phospholipids contain glycerol as the alcohol e.g. lecithin, cephalin

II. Sphingophospholipids: Sphingosine is the alcohol in this group of phospholipids

e.g., sphingomyelin

(**b**) **Glycolipids:** These lipids contain a fatty acid, carbohydrate and nitrogenous base. The alcohol is sphingosine, hence they are also called as glycosphingolipids. Glycerol and phosphate are absent e.g., cerebrosides, ganglioside

(**c**) **Lipoproteins:** Macromolecular complexes of lipids with proteins.

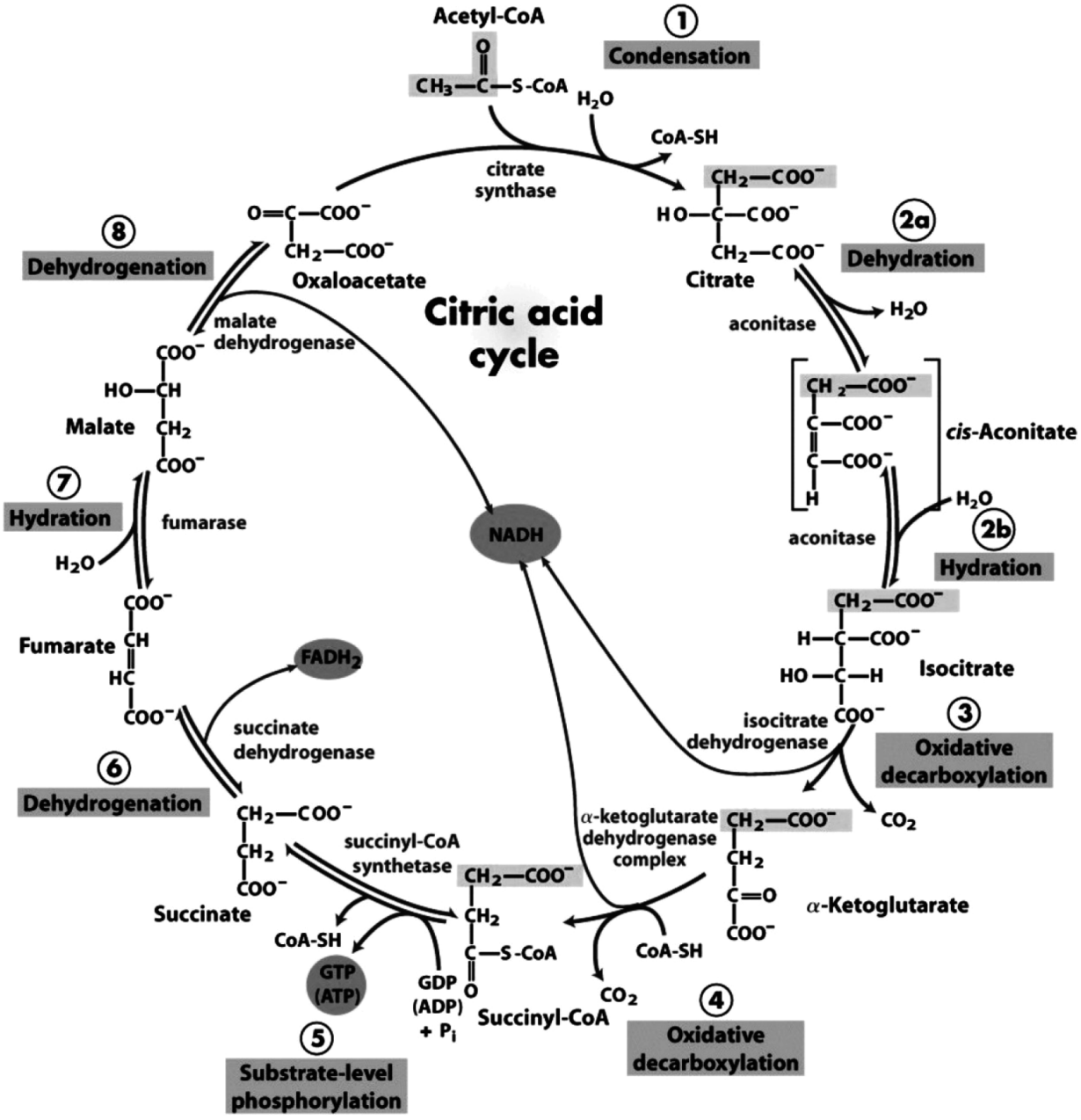
(**d**) **Other complex lipids:** Sulfolipids, aminolipids and lipopolysaccharides are among the other complex lipids.

3. Derived lipids: These include glycerol and other alcohols, fatty acids, mono and diacylglycerols, lipid (fat) soluble vitamins, steroid hormones, hydrocarbons and ketone bodies.

4. Miscellaneous lipids: These include a large number of compounds possessing the characteristics of lipids e.g., carotenoids, squalene, hydrocarbons such as pentacosane (in bees wax), terpenes etc

IMPORTANT BIOCHEMISTRY PATHWAY (CYCLE)

1. Citric acid cycle (Krebs cycle, TCA cycle)



Summary of TCA cycle:

- The citric acid cycle (Krebs cycle, TCA cycle) is a nearly universal central catabolic pathway in which compounds derived from the breakdown of carbohydrates, fats, and proteins are oxidized to CO_2, with most of the energy of oxidation temporarily held in the electron carriers $FADH_2$ and NADH. During aerobic metabolism, these electrons are transferred to O_2 and the energy of electron flow is trapped as ATP.
- **Acetyl-CoA** enters the citric acid cycle (in the mitochondria of eukaryotes, the cytosol of prokaryotes) as citrate synthase catalyzes its condensation with oxaloacetate to form **citrate**.
- In seven sequential reactions, including two decarboxylations, the citric acid cycle converts citrate to oxaloacetate and releases two CO2.The pathway is cyclic in that the intermediates of the cycle are not used up; for each oxaloacetate consumed in the path, one is produced.
- For each acetyl-CoA oxidized by the citric acid cycle, the energy gain consists of three molecules of NADH, one FADH2, and one nucleoside triphosphate (either ATP or GTP).
- Besides acetyl-CoA, any compound that gives rise to a four- or five-carbon intermediate of the citric acid cycle - for example, the breakdown products of many amino acids—can be oxidized by the cycle.

The citric acid cycle is amphibolic, serving in both catabolism and anabolism; cycle intermediates can be drawn off and used as the starting material for a variety of biosynthetic products.

When intermediates are shunted from the citric acid cycle to other pathways, they are replenished by several anaplerotic reactions, which produce four-carbon intermediates by carboxylation of three-carbon compounds; these reactions are catalyzed by pyruvate carboxylase, PEP carboxykinase, PEP carboxylase, and malic enzyme. Enzymes that catalyze carboxylations commonly employ biotin to activate CO2 and to carry it to acceptors such as pyruvate or phosphoenol pyruvate.

TCA cycle regulatory enzymes

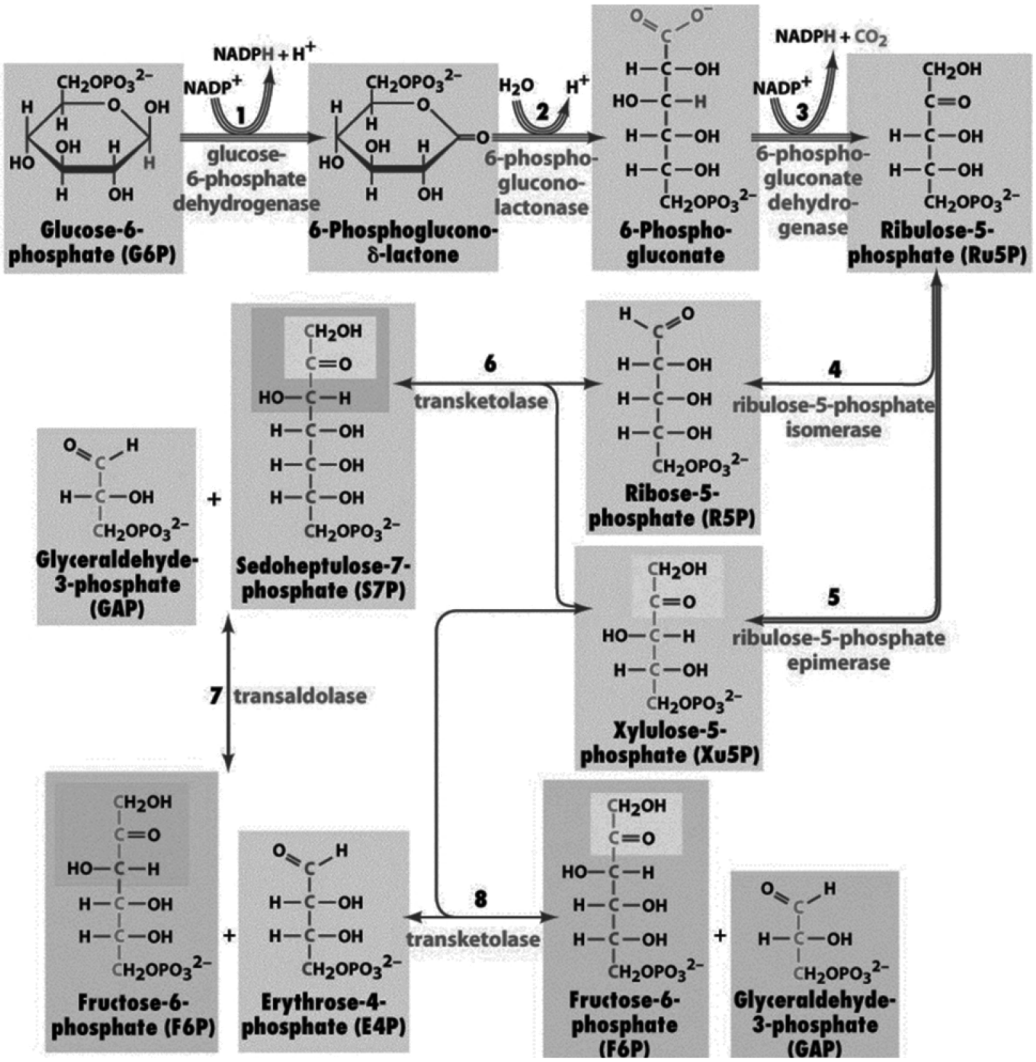
Enzyme	Stimulators	Inhibitors	Comments
Pyruvate carboxylase	Acetyl-CoA	ADP	Several hormones alter the amount of this enzyme: Insulin ↓, Cortisol ,Glucagon
Pyruvate dehydrogenase	CoA, NAD, Ca^{2+},Mg^{2+}, pyruvate, insulin	Acetyl-CoA, NADH, phosphorylation and ATP	Effect of Mg^{2+}: ATP binds Mg^{2+} with higher affinity than ADP; high free Mg^{2+} means low ATP Concentration. Mg and Ca activate the phosphatase.
Citrate synthase	NAD, CoA, ADP High [oxaloacetate] and [acetyl-CoA],	Citrate, Long chain acyl-CoA, ATP, NADH, succinyl-CoA	--
Isocitrate dehydrogenase	Ca^{2+}, ADP	ATP, NADH	Isocitrate dehydrogenase is probably the most important regulatory enzyme in the TCA cycle.
α-Ketoglutarate dehydrogenase	Ca^{2+}	NADH, succinyl-CoA	--

2. HMP SHUNT

Also known as:

- Pentose shunt
- Hexose monophosphate shunt
- Phosphogluconate pathway
- It occurs in the cytosol.

The pentose phosphate pathway (also called Phosphogluconate Pathway, or Hexose Monophosphate Shunt [HMP shunt]) is a process that serves to generate NADPH and the synthesis of pentose (5-carbon) sugars. There are two distinct phases in the pathway. The first is the oxidative phase, in which NADPH is generated, and the second is the non-oxidative synthesis of 5-carbon sugars. This pathway is an alternative to glycolysis. While it does involve oxidation of glucose, its primary role is anabolic rather than catabolic. For most organisms it takes place in the cytosol; in plants most steps take place in plastids.



Functions

The primary functions of the pathway are:

1. To generate reducing equivalents, in the form of NADPH, for reductive biosynthesis reactions within cells.

2. To provide the cell with ribose-5-phosphate (R5P) for the synthesis of the nucleotides and nucleic acids.

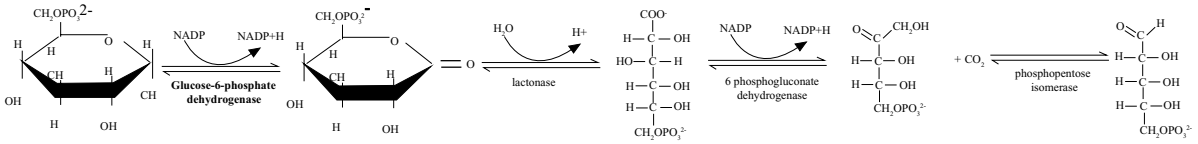
3. Although not a significant function of the PPP, it can operate to metabolize dietary pentose sugars derived from the digestion of nucleic acids as well as to rearrange the carbon skeletons of dietary carbohydrates into glycolytic/gluconeogenic intermediates.

Located exclusively in the cytoplasm, the pathway is one of the three main ways the body creates molecules with reducing power, accounting for approximately 60% of NADPH production in humans. One of the uses of NADPH in the cell is to prevent oxidative stress. It reduces the coenzyme glutathione, which converts reactive H2O2 into H2O. If absent, the H2O2 would be converted to hydroxyl free radicals, which can attack the cell. Significantly, erythrocytes utilize the reactions of the PPP to generate large amounts of NADPH used in the reduction of glutathione It is also used to generate hydrogen peroxide for phagocytes

Phases of HMP shunt

Oxidative phase

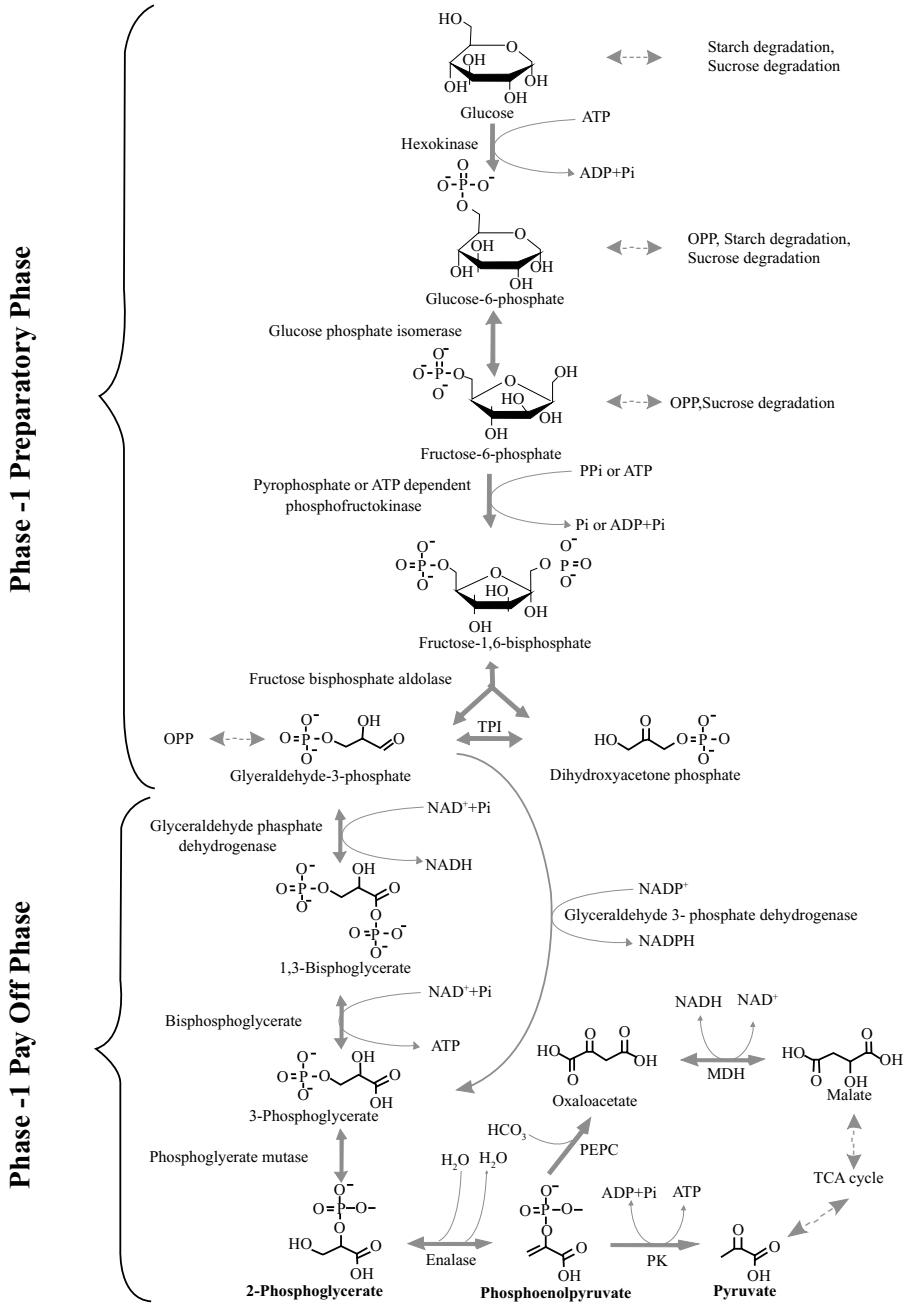
In this phase, two molecules of NADP+ are reduced to NADPH, utilizing the energy from the conversion of glucose-6-phosphate into ribulose 5-phosphate.



Regulation

Glucose-6-phosphate dehydrogenase is the rate-controlling enzyme of this pathway. It is allosterically stimulated by NADP+. The ratio of NADPH:NADP+ is normally about 100:1 in liver cytosol. This makes the cytosol a highly-reducing environment. Formation of NADP+ by a NADPH-utilizing pathway, thus, stimulates production of more NADPH.

3. Glycolysis Pathway (Embden-Meyerhof Pathway)



Glycolysis

- The Glycolytic pathway describes the oxidation of glucose to pyruvate with the generation of ATP and NADH.
- It is also called as the **Embden-Meyerhof Pathway**
- Glycolysis is a universal pathway; present in all organisms: from yeast to mammals.
- In eukaryotes, glycolysis takes place in the cytosol
- Glycolysis is anaerobic; it does not require oxygen
- In the presence of O_2 pyruvate is further oxidized to CO_2
- In the absence of O_2, pyruvate can be fermented to lactate or ethanol.

The 3 stages of Glycolysis

- Stage 1 is the investment stage. 2 mols of ATP are consumed for each mol of glucose.
- Glucose is converted to fructose-1,6-bisphosphate.
- Glucose is trapped inside the cell and at the same time converted to an unstable form that can be readily cleaved into 3-carbon units.
- In stage 2 fructose-1,6-bisphosphate is cleaved into 2,3carbon units of glycerladehyde-3-phosphate.
- Stage 3 is the harvesting stage. 4 mols of ATP and 2 mols of NADH are gained from each initial mol of glucose. This ATP is a result of substrate-level phosphorylation
- Glyceraldehyde-3-phosphate is oxidized to pyruvate.

Keeping in mind that each molecule of glucose yields 2 molecules of glyceraldehyde 3-phosphate, the total inputs and the outputs of all the 10 glycolytic reactions may be written as follows

Net Reaction: Glucose + 2**NAD**$^+$ + 2 **Pi** + 2 **ADP** = 2 **pyruvate** + 2**ATP** + 2**NADH** + 2$\mathbf{H_2O}$

Thus, three things happen simultaneously in glycolysis:

(a) Glucose is oxidized to pyruvate.
(b) NAD+ is reduced to NADH.
(c) ADP is phosphorylated to form ATP.

There can be no EMP pathway without all 3 events which means that NAD, ADP and Pi, as well as glucose, must be present. Further, 2 moles of ATP are generated in glycolysis. A summary of the steps in which ATP is consumed or formed is given in Table.

Step	*Reaction*	*Consumption of ATP*	*Gain of ATP*
1	Glucose ⟶ Glucose 6-phosphate	1	
3	Fructose 6-phosphate ⟶ Fructose 1, 6-diphosphate	1	
7	1, 3-diphosphoglycerate ⟶ 3-phosphoglycerate		$1 \times 2 = 2$
10	Phosphoenolpyruvate ⟶ Pyruvate		$1 \times 2 = 2$
		2	4
		Net gain of ATP = $4 - 2 = 2$	

4. Cholesterol Biosynthesis Pathway

Cholesterol is biosynthesized from 2-carbon metabolic intermediate, acetyl-CoA hooked end to end involving a number of enzymatic reactions and finally get converted into the 27-carbon molecule of cholesterol.

The process of cholesterol synthesis has five major steps:

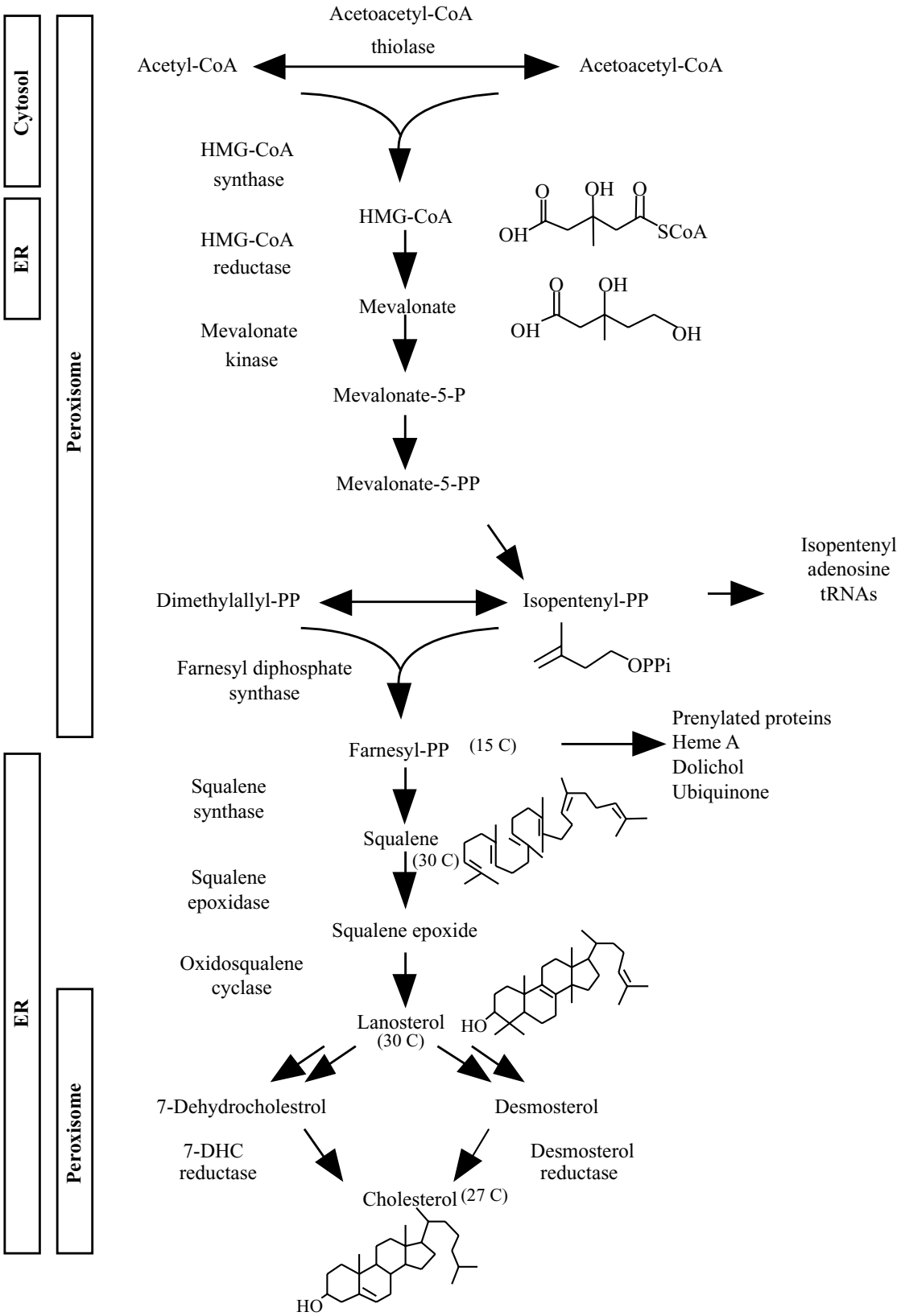
1. Acetyl-CoAs are converted to 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) Cholesterol.
2. HMG-CoA is converted to mevalonate.
3. Mevalonate is converted to the isoprene based molecule, isopentenyl pyrophosphate (IPP), with the concomitant loss of CO2
4. IPP is converted to squalene.
5. Squalene is converted to cholesterol.

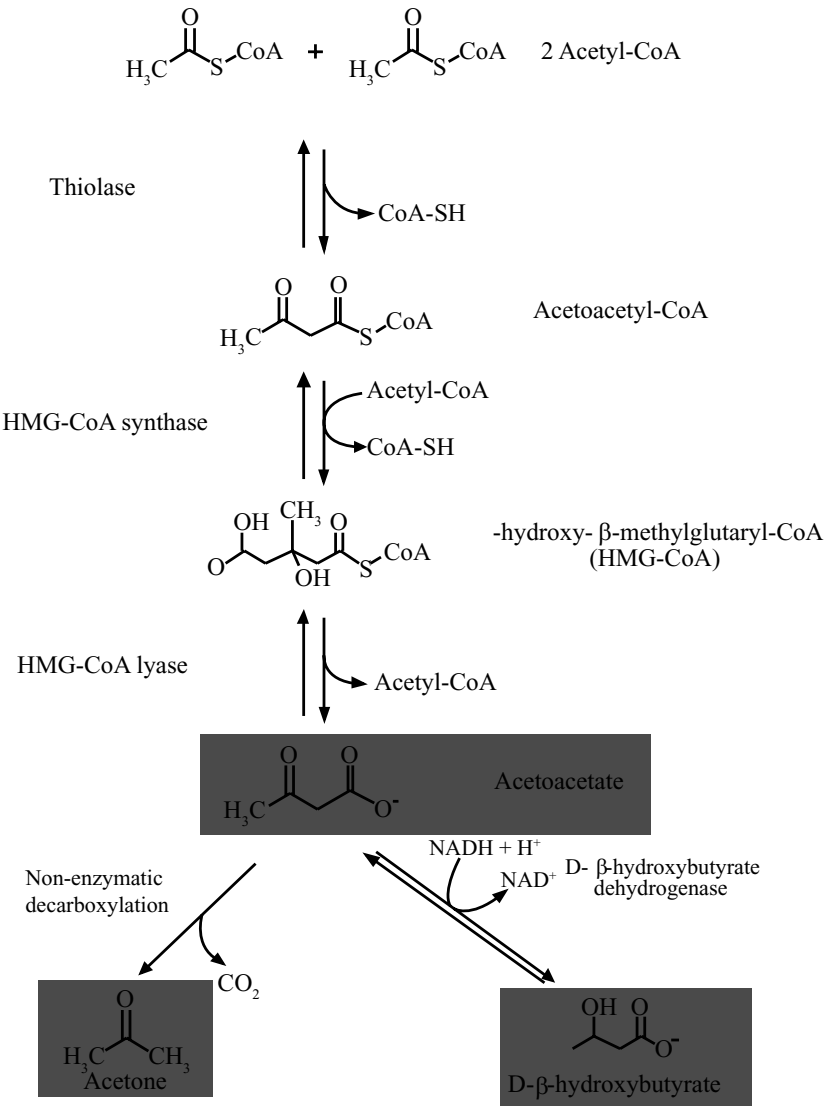
5. KETOGENESIS

Ketogenesis is the biochemical process by which organisms produce a group of substances collectively known as ketone bodies by the breakdown of fatty acids and ketogenic amino acids.

Ketone bodies are three chemicals that are produced when fatty acids are broken down in excess. Production of these compounds is called "ketogenesis", and this is necessary in small amounts. Ketone bodies are produced from acetyl-CoA, mainly in the mitochondrial matrix of liver cells when carbohydrates are so scarce that energy must be obtained from breaking down of fatty acids.

The three ketone bodies, each synthesized from acetyl-CoA molecules, are:


Cytosol
ER
Peroxisome
ER
Peroxisome
Acetoacetyl-CoA
thiolase
Acetyl-CoA
Acetoacetyl-CoA
HMG-CoA
synthase
HMG-CoA
HMG-CoA
reductase
Mevalonate
Mevalonate
kinase
Mevalonate-5-P
Mevalonate-5-PP
Isopentenyl
adenosine
tRNAs
Dimethylallyl-PP
Isopentenyl-PP
OPPi
Farnesyl diphosphate
synthase
Prenylated proteins
Heme A
Dolichol
Ubiquinone
Farnesyl-PP (15 C)
Squalene
synthase
Squalene
(30 C)
Squalene
epoxidase
Squalene epoxide
Oxidosqualene
cyclase
Lanosterol
(30 C)
HO
7-Dehydrocholestrol
Desmosterol
7-DHC
reductase
Desmosterol
reductase
Cholesterol (27 C)
HO



- **Acetoacetate**, which can be converted by the liver into β-hydroxybutyrate, or spontaneously turn into acetone
- **Acetone**, which is generated through the decarboxylation of acetoacetate, either spontaneously or through the enzyme acetoacetate decarboxylase. It can then be further metabolized either by CYP2E1 into hydroxyacetone (acetol) and then via propylene glycol to pyruvate, lactate and acetate (usable for energy) and propionaldehyde, or via methylglyoxal to pyruvate and lactate.
- β-hydroxybutyrate (not technically a ketone according to IUPAC nomenclature) is generated through the action of the enzyme D-β-hydroxybutyrate dehydrogenase on acetoacetate.

Regulation:

Ketogenesis may or may not occur, depending on levels of available carbohydrates in the cell or body. This is closely related to the paths of acetyl-CoA

- When the body has ample carbohydrates available as energy source, glucose is completely oxidized to CO_2; acetyl-CoA is formed as an intermediate in this process, first entering the citric acid cycle followed by complete conversion of its chemical energy to ATP in oxidative phosphorylation.
- When the body has excess carbohydrates available, some glucose is fully metabolized, and some of it is stored in the form of glycogen or, upon citrate excess, as fatty acids. (CoA is also recycled here.)
- When the body has no free carbohydrates avail-

able, fat must be broken down into acetyl-CoA in order to get energy. Acetyl-CoA is not being recycled through the citric acid cycle because the citric acid cycle intermediates (mainly oxaloacetate) have been depleted to feed the gluconeogenesis pathway, and the resulting accumulation of acetyl-CoA activates ketogenesis.

6. Urea Cycle

The urea cycle (also known as the ornithine cycle) is a cycle of biochemical reactions occurring in many animals that produces urea ($(NH2)_2CO$) from ammonia (NH_3). This cycle was the first metabolic cycle discovered (Hans Krebs and Kurt Henseleit, 1932), five years before the discovery of the TCA cycle. The urea cycle consists of five reactions: two mitochondrial and three cytosolic. The cycle converts two amino groups, one from NH4+ and one from ASP, and a carbon atom from HCO_3^-, to the relatively nontoxic excretion product urea at the cost of four "high-energy" phosphate bonds (3 ATP hydrolyzed to 2 ADP and one AMP). Ornithine is the carrier of these carbon and nitrogen atoms.

Reactions of the urea cycle

Step	Reactants	Products	Catalyzed by	Location
1	NH_3 + HCO_3^- + 2ATP	carbamoyl phosphate + 2ADP + Pi	CPS1	mitochondria
2	carbamoyl phosphate + ornithine	citrulline + Pi	OTC	mitochondria
3	citrulline + aspartate + ATP	argininosuccinate + AMP + PPi	ASS	cytosol
4	argininosuccinate	Arg + fumarate	ASL	cytosol
5	Arg + H_2O	ornithine + urea	ARG1	cytosol

In the first reaction, $NH_4^+ + HCO_3^-$ is equivalent to $NH_3 + CO_2 + H_2O$.
Thus, the overall equation of the urea cycle is:

$NH_3 + CO_2$ + aspartate + 3 ATP + 2 $H_2O \rightarrow$ urea + fumarate + 2 ADP + 2 Pi + AMP + PPi

Since fumarate is obtained by removing NH_3 from aspartate (by means of reactions 3 and 4), and PPi + H2O $\rightarrow$ 2 Pi, the equation can be simplified as follows:

2 $NH_3 + CO_2$ + 3 ATP + $H_2O \rightarrow$ urea + 2 ADP + 4 Pi + AMP

Note that reactions related to the urea cycle also cause the production of 2 NADH, so the urea cycle releases slightly more energy than it consumes. These NADH are produced in two ways:

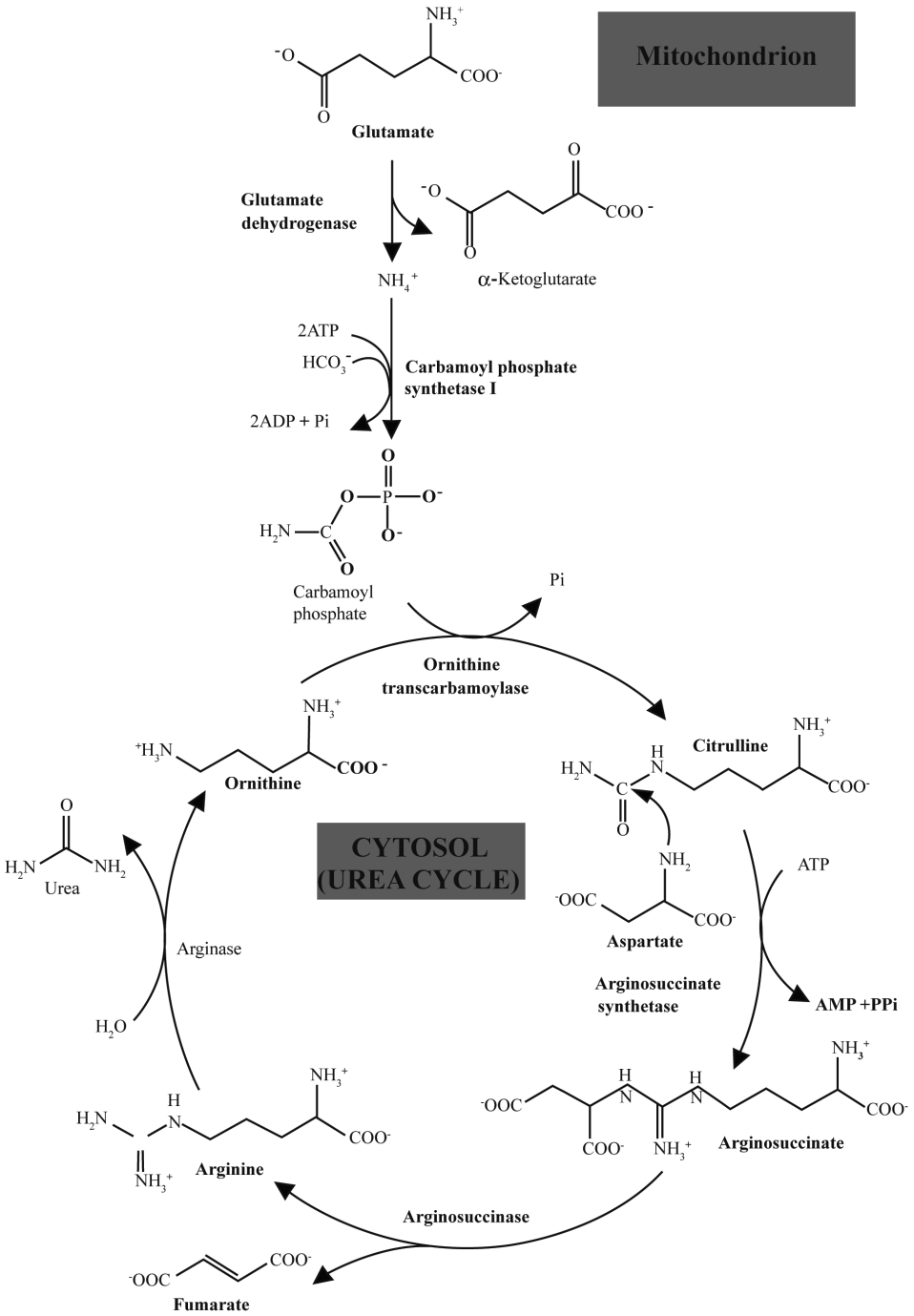
One NADH molecule is reduced by the enzyme glutamate dehydrogenase in the conversion of glutamate to ammonium and α-ketoglutarate. Glutamate is the non-toxic carrier of amine groups. This provides the ammonium ion used in the initial synthesis of carbamoyl phosphate.

The fumarate released in the cytosol is converted to malate by cytosolic fumarase. This malate is then converted to oxaloacetate by cytosolic malate dehydrogenase, generating a reduced NADH in the cytosol. Oxaloacetate is one of the keto acids preferred by transaminases, and so will be recycled to aspartate, maintaining the flow of nitrogen into the urea cycle.

The two NADH produced can provide energy for the formation of 4 ATP (cytosolic NADH provides only 1.5 ATP due to the glycerol-3-phosphate shuttle who transfers the electrons from cytosolic NADH to FADH2 and that gives 1.5 ATP), a net production of one high-energy phosphate bond for the urea cycle. However, if gluconeogenesis is underway in the cytosol, the latter reducing equivalent is used to drive the reversal of the GAPDH step instead of generating ATP.

The fate of oxaloacetate is either to produce aspartate via transamination or to be converted to phosphoenolpyruvate, which is a substrate for gluconeogenesis.

Regulation:
N-Acetylglutamic acid (NAG): The synthesis of carbamoyl phosphate and the urea cycle are dependent on the presence of NAcGlu, which allosterically activates CPS1. NAcGlu is an obligate activator of Carbamoyl phosphate synthase. Synthesis of NAcGlu by NAGS is stimulated by both Arg, allosteric stimulator of NAGS, and Glu, a product in the transamination reactions and one of NAGS's substrates, both of which elevated when free amino acids are elevated. So Glu not only is a substrate for NAGS but also serves as an activator for the urea cycle.



Substrate concentrations:
The remaining enzymes of the cycle are controlled by the concentrations of their substrates. Thus, inherited deficiencies in cycle enzymes other than ARG1 do not result in significant decreases in urea production (if any cycle enzyme is entirely missing, death occurs shortly after birth). Rather, the deficient enzyme's substrate builds up, increasing the rate of the deficient reaction to normal.

The anomalous substrate buildup is not without cost, however. The substrate concentrations become elevated all the way back up the cycle to NH_4^+, resulting in hyperammonemia (elevated $[NH_4^+]$P).

Although the root cause of NH_4^+ toxicity is not completely understood, a high $[NH_4^+]$ puts an enormous strain on the NH_4^+-clearing system, especially in the brain (symptoms of urea cycle enzyme deficiencies include intellectual

disability and lethargy). This clearing system involves GLUD1 and GLUL, which decrease the 2-oxoglutarate (2OG) and Glu pools. The brain is most sensitive to the depletion of these pools. Depletion of 2OG decreases the rate of TCAC, whereas Glu is both a neurotransmitter and a precursor to GABA, another neurotransmitter.

7. Biosynthesis of Catecholamines

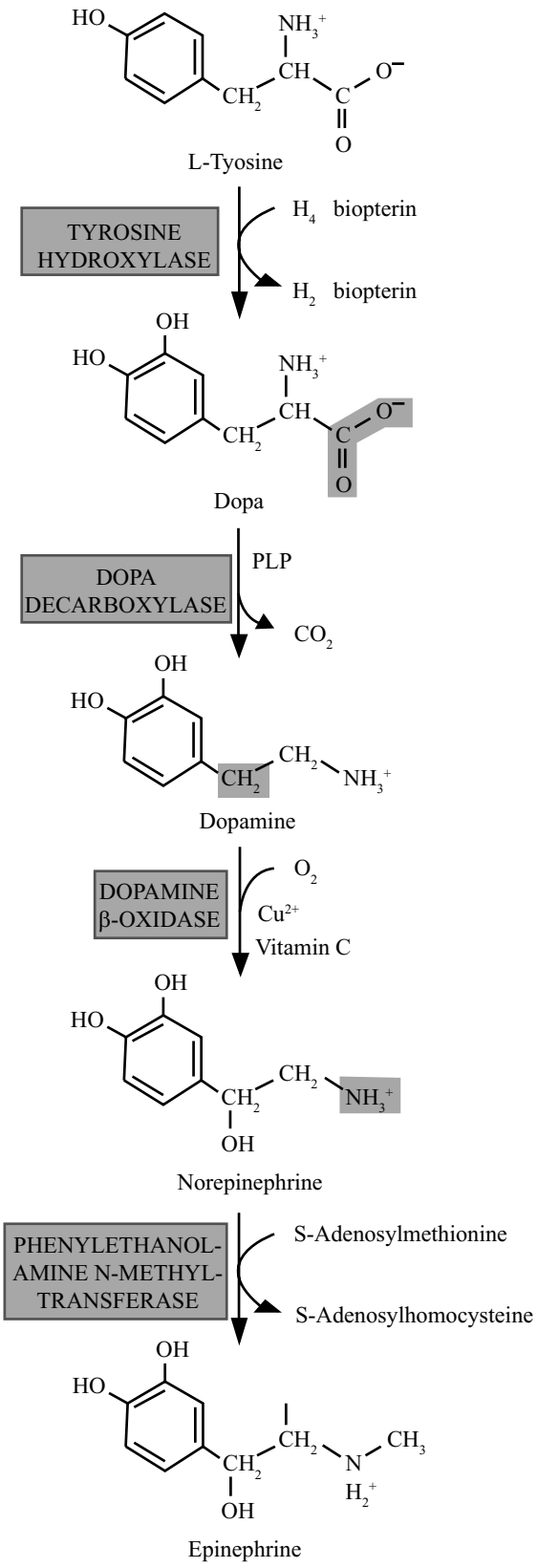
Catecholamines are derived from the amino acid tyrosine. catecholamines are epinephrine (adrenaline), norepinephrine (noradrenaline), and dopamine, all of which are produced from phenylalanine and tyrosine. Release of the hormones epinephrine and norepinephrine from the adrenal medulla of the adrenal glands is part of the fight-or-flight response.

Tyrosine is created from phenylalanine by hydroxylation by the enzyme phenylalanine hydroxylase. Tyrosine is also ingested directly from dietary protein. Catecholamine-secreting cells use several reactions to convert tyrosine serially to L-DOPA and then to dopamine. Depending on the cell type, dopamine may be further converted to norepinephrine or even further converted to epinephrine.

Catecholamines are produced mainly by the chromaffin cells of the adrenal medulla and the postganglionic fibers of the sympathetic nervous system. Dopamine, which acts as a neurotransmitter in the central nervous system, is largely produced in neuronal cell bodies in two areas of the brainstem: the substantia nigra and the ventral tegmental area. The similarly melanin-pigmented cell bodies of the locus ceruleus produce norepinephrine.

Steps for Biosynthesis of different catecholamine:

1) Tyrosine is hydroxylated to Dihdroxy Phenyl Alanine(DOPA) by Tyrosine Hydroxylase enzyme, that require BH4(Tetra hydrobiopterine) and NADPH. The reaction is similer to hydroxylation to Phenylalanine to form Tyrosine. Tyrosine hydroxylase (Tyrosinase) meant for catecholamine synthesis is different for the one require for melanin synthesis.
2) DOPA Decarboxylase, a pyridoxal phosphate (BP-6-) dependent enzyme, forms Dopamine from decarboxylation of DOPA.
3) Subsequent hydroxylation of Dopamine by Dopamine- β-oxidase then forms norepinephrine. The enzyme requires molecular oxygen, vitamin C and copper ion for its activity.
4) In Adrenal medulla, Phenyl ethanolamine-N- methyltransferase utilizes S-adinosyl methionine(SAM) to methylate the primary amine of Norepinephrine, forming Epinephrine.



Multiple Choice Questions

1. α-D-glucose and β-D-glucose both are
(a) Keto-aldo pairs (b) Anomers
(c) Epimers (d) Stereoisomers

2. Compounds that have the same structural formula but different spatial configuration are called
(a) Epimers (b) Anomers
(c) Stereoisomers (d) Optical isomers

3. One of the following is a reducing sugar:
(a) Isomaltose (b) Sucrose
(c) Trehalose (d) None of the above

4. An L-isomer of monosaccharide formed in human body during uronic acid pathway is
(a) L-Xylulose (b) L-Erythrose
(c) L-Ribulose (d) L-Fructose

5. Which of the following is an epimeric pair?
(a) Glucose and fructose
(b) Lactose and maltose
(c) Galactose and mannose
(d) Glucose and mannose

6. One of the following is an enzyme required for glycolysis pathway:
(a) Pyruvate carboxylase
(b) Pyruvate kinase
(c) Fructose-6-phosphatase
(d) Phosphokinase

7. Glucose tolerance is decreased in one of the following disease:
(a) Diabetes insipidus (b) Addison's disease
(c) Hypo pituitarisme (d) Diabetes mellitus

8. In carbohydrate metabolism all of the following hormones is involved except:
(a) Glucagon (b) ACTH
(c) Vasopressin (d) Insulin

9. For converting glucose to glycogen in liver an essential component is
(a) UTP (b) GTP
(c) GLU-1 (d) Lactic acid

10. Phenylalanine is the precursor of
(a) Histamine (b) Dopamine
(c) Tyrosine (d) Thyroxin

11. One of the following amino acids contains special group pyrrolidine:
(a) Proline (b) Tyrosine
(c) Tryptophan (d) Phenylalanine

12. The cyclic hemiacetal formation in D-Glucose involves bond formation between
(a) C-1 and C-4 (b) C-1 and C-5
(c) C-2 and C-5 (d) C-1 and C-2

13. Cori cycle is
(a) Reuse of glucose (b) Synthesis of glucose
(c) Uptake of glucose (d) Both (a) and (b)

14. Invert sugar is
(a) Galactose
(b) Mannose
(c) Fructose
(d) Hydrolytic product of sucrose

15. Generally all proteins contain
(a) More than 50 amino acids
(b) Different amino acids less than 50
(c) Only a few amino acids
(d) 300 amino acids occurring in nature

16. An example of sulphur-containing amino acid is
(a) 3-Amino butanoic acid
(b) 2-Amino-3-methylbutanoic acid
(c) 2-Amino-3-thiobutanoic acid
(d) 2-Amino-3-mercaptopropanoic acid

17. At isoelectric pH, a mixture of amino acids in solution would be predominantly:
(a) Zwitter ions (b) Nonpolar molecules
(c) Hydrophilic (d) Positive and monovalent

18. Dispensible amino acids
(a) Can not be synthesized by the body
(b) May be synthesized in the body to meet biological needs.
(c) Have no role in the metabolism
(d) May be synthesized in the body in diseased states

19. The technique for purification of proteins that can be made specific for a given protein is
(a) Gel filtration chromatography
(b) Thin layer chromatography
(c) Affinity chromatography
(d) Electrophoresis

20. Amino acid tryptophan could be considered as precursor of

(a) Meltonin (b) Thyroid hormones
(c) Methionine (d) Phenylephrine

21. The enzyme dopamine β-hydroxylase which catalyses conversion of dopamine to norepinephrine requires
(a) Vitamin C (b) Vitamin A
(c) Vitamin K (d) Vitamin B1

22. Pulses are deficient in _____ amino acid.
(a) Lysine (b) Tyrosine
(c) Methionine (d) Crystine

23. _____, a water-soluble vitamin is absent in eggs.
(a) Biotin (b) Niacin
(c) Ribofalvin (d) Ascrobic acid

24. Primary structure of a protein is formed by
(a) Disulphide bonds (b) Hydrogen bonds
(c) Peptide bonds (d) Amine bonds

25. Semi-essential amino acid is
(a) Valine (b) Histidine
(c) Asparagine (d) Serine

26. Alanine can be synthesized from
(a) Pyruvate and glutamate
(b) Glycine and α-ketoglutarate
(c) Pyruvate and α ketoglutarate
(d) Asparate and pyruvate

27. Glycine can be synthesized from
(a) Serine (b) Threonine
(c) Betaine (d) All of these

28. Non-protein amino acids are
(a) Ornithine
(b) β-alanine
(c) γ-amino butyric acid
(d) All of these

29. Allergic reactions are mediated by
(a) IgE (b) IgG
(c) IgA (d) IgD

30. A Zwitter ion is a
(a) Molecule containing negative ion
(b) Molecule containing positive ion
(c) Molecule containing positive and negative ionic group
(d) None of these

31. Synthesis of calcitonin takes place in
(a) Parathyroid glands
(b) Anterior pituitary glands
(c) Thyroid gland
(d) Adrenal medulla

32. The basic amino acid is
(a) Lysine (b) Proline
(c) Leucine (d) Tyrosine

33. For adrenaline synthesis the precursor amino acid is
(a) Alanine (b) Proline
(c) Phenylalanine (d) Cystine

34. Amino acids are soluble in
(a) Ammonia (b) Water
(c) Chloroform (d) Benzene

35. Optically active compounds are capable of
(a) Rotating plane of polarized light
(b) Emitted the light radiation
(c) Showing same chemical properties
(d) Different chemical reaction

36. SGOT level in an adult is
(a) 15–45 units/dl (b) 10–50 units/dl
(c) 5–15 units/dl (d) 5–40 units/dl

37. Zymogen is
(a) An inactivated enzyme
(b) An activated enzyme
(c) An intracellular enzyme
(d) An extracellular enzyme

38. Xanthoproteic test is positive for
(a) Sulphur amino acids
(b) Indole ring containing amino acids
(c) Aromatic amino acids
(d) α-amino acids

39. Michaelis–Menton equation is used to explain the effect of substrate concentration on
(a) Carbohydrate (b) Protein
(c) Lipid (d) Enzyme

40. Low plasma level of tryptophan and other neutral amino acid leads to the disorder is known as
(a) Maple syrup disease
(b) Wilson's disease
(c) Hartnup's disease
(d) Wolman's disease

41. A dietary deficiency in the quantity of protein results in
(a) Alkaptonuria
(b) Marasmus
(c) Richner–Hanhart syndrome
(d) Kwashiorkar

42. The normal range of total serum bilirubin is
(a) 0.2–1.2 mg/100 ml
(b) 1.5–1.8 mg/100 ml
(c) 2.0–4.0 mg/100 ml
(d) Above 7.0 mg/100 ml

43. A test to evaluate the detoxifying function of liver is
(a) Serum albumin: globulin ratio
(b) Galactose tolerance test
(c) Hippuric acid test
(d) Prothrombin time

44. Fat-soluble vitamins have properties like
(a) Stored in liver
(b) One or more propene units
(c) Soluble in alcohol
(d) All these

45. Precursor of vitamin A, β-carotene is oxidatively cleaved by
(a) Hydroxylase
(b) Oxygenase
(c) β-Carotene dioxygenase
(d) Reductase

46. Carr–Price reaction is used to detect
(a) Vitamin E (b) Vitamin B_{12}
(c) Aspartic acid (d) Vitamin A

47. Deficiency of vitamin D causes
(a) Tuberculosis of bone
(b) Ricket and osteomalacia
(c) Pellagra
(d) Beri-beri

48. Vitamin D absorption is increased in
(a) Contents of diet
(b) Alkaline pH of intestine
(c) Neutral pH of stomach
(d) Acid pH of intestine

49. One international unit (IU) of vitamin D is defined as the biological activity of
(a) 0.025 μg of ergosterol
(b) 0.025 μg of 7-dehydrocholecalciferol
(c) 0.025 μg of cholecalciferol
(d) 0.025 μg of ergocalciferol

50. One of the following vitamins is synthesized by bacteria in the intestine
(a) Vitamin A (b) Vitamin K
(c) Vitamin D (d) Vitamin E

51. Due to the riboflavin deficiency _____ is caused.
(a) Pellagra (b) Mental deterioration
(c) Cheilosis (d) Dermatitis

52. Vitamin B6 deficiency may occur during tuberculosis therapy with
(a) Isoniazid (b) Rifampicin
(c) Sulpha drugs (d) Thamibutole

53. Xanthurenic Acid Index' is a reliable criterion for the deficiency of vitamin
(a) Pantothenic acid (b) Thiamin
(c) Pyridoxal (d) Riboflavin

54. For determination of amino acid sequence of a protein _____ is used.
(a) Ninhydrin reagent (b) Biuret reagent
(c) Milons reagen (d) Sanger reagent

55. The deficiency of folate causes
(a) Pernicious anaemia
(b) Megaloblastic anaemia
(c) Macrocytic anaemia
(d) Hemolytic anaemia

56. Folic acid contains
(a) Pteridine (b) p-Amino benzoic acid
(c) Glutamic acid (d) All of these

57. Vitamin A is synthesized from
(a) γ-Carotene (b) β-Carotene
(c) α-Carotene (d) All of these

58. The molecule of vitamin A1 contains
(a) β-Carotene ring (b) β-Lonone ring
(c) Naphthalene ring (d) α-Lactone ring

59. A chemical name of vitamin K_3 is
(a) Phylloquinone (b) Menadione
(c) Menaquinone (d) Napthoquinone

60. The rhodopsin contain non-protein part is
(a) Retinal (b) Retinol
(c) Carotene (d) Retinoic acid

61. Vitamin K regulates the synthesis of blood clotting factors:
(a) VII (b) IX
(c) X (d) All of these

62. Vitamin which has anti-oxidant properties is
(a) Vitamin A (b) Vitamin C
(c) Vitamin D (d) Vitamin E

63. Severe deficiency of _____ causes xerophthalmia.
(a) Vitamin D (b) Vitamin B2

(c) Vitamin B6 (d) Vitamin A

64. Antisterility vitamin is
(a) Biotin (b) Riboflavin
(c) Vitamin E (d) Vitamin K

65. Thymine is characterized as a
(a) Water-soluble vitamin
(b) Fat-soluble vitamin
(c) Purine base
(d) Pyrimidine base

66. All of following is antagonist for folic acid except
(a) Aminopterin (b) Trimethoprim
(c) Sulfonamides (d) Isoniazid

67. Calcitriol is
(a) 1,25-dihydroxy cholecalciferol
(b) 1-hydroxy cholecalciferol
(c) 25,26-dihydroxy cholecalciferol
(d) 25-hydroxy cholecalciferol

68. Which of the following vitamin act as a respiratory catalyst?
(a) Riboflavin (b) Pyridoxine
(c) Niacin (d) Vitamin E

69. Vitamin B12 contains _____ metal.
(a) Copper (b) Iron
(c) Cobalt (d) Lead

70. Nonsteroidal antiinflammatory drugs, such as aspirin act by inhibiting the activity of the enzyme:
(a) Lipoxygenase (b) Cyclooxygenase
(c) Phospholipase A2 (d) Lipoprotein lipase

71. Holoenzyme is
(a) Functional unit of enzyme
(b) Made of apoenzyme
(c) Coenzyme
(d) All of these

72. Enzymes, which are produced in inactive form in the living cells, are called
(a) Co-enzyme (b) Apoenzymes
(c) Proenzymes (d) Isozymes

73. Vitamin B2 is the precursor for
(a) Co enzyme pyridoxal phosphate
(b) Co enzyme thiamine pyrophosphate
(c) Co enzyme FMN
(d) Co enzyme NADP

74. In reversible non-competitive enzyme activity inhibition
(a) V_{max} value is increased
(b) K_m value is increased
(c) K_m value is decreased
(d) Concentration of active enzyme is decreased

75. The specificity of the enzyme is mostly dependent on
(a) Glucose
(b) Pyruvate
(c) Xanthurenic acid
(d) Thiamine pyro phosphate

76. The specificity of the enzyme is mostly dependant on
(a) Co-enzyme (b) Apoenzymes
(c) Proenzymes (d) Isozymes

77. How many number of net ATP generated during oxidation of one molecule of palmitate?
(a) 14 (b) 21
(c) 129 (d) 96

78. Factors affecting enzyme activity is
(a) Temperature (b) pH
(c) Concentration (d) All of these

79. Glucose absorption is promoted by
(a) Vitamin A (b) Vitamin E
(c) Ascorbic acid (d) Thiamin

80. Zellweger syndrome occurs due to the:
(a) Absence of peroxisomes
(b) Deficiency of vitamin B_{12}
(c) Deficiency of acyl CoA dehydrogenase
(d) Overproduction of ketone

81. Ketosis is generally associated with the disease:
(a) Nephritis (b) Diabetes Insipidus
(c) Edema (d) Diabetes mellitus

82. Conversion of HMG-CoA to the mevalonate by the reduction is catalysed by
(a) HMG-CoA reductase
(b) HMG-CoA synthetase
(c) Thiolase
(d) Mevalonate kinase

83. One of the following amino acids is used as an antibiotic
(a) Thyroxine (b) Ornithine
(c) Homoserine (d) Azaserine

84. Sulfur-containing B-complex vitamin is
(a) Biotin (b) Niacin
(c) Pyridoxine (d) Riboflavin

85. One of the following vitamins is known as pellagra preventive factor of Goldberg:
(a) Biotin (b) Niacin
(c) Riboflavin (d) Pyridoxine

86. Adenylate cyclase is activated by
(a) Insulin
(b) Vitamin K
(c) Prostaglandin E1
(d) Glucagon

87. Coenzyme A is derived from the vitamin:
(a) Niacin (b) Pantothenic acid
(c) Pyridoxine (d) Biotin

88. The Michaelis–Menten constant, K_m is defined as
(a) Substrate concentration to produce half maximal velocity in an enzyme catalysed reaction
(b) Dependent on the enzyme concentration
(c) Substrate concentration to produce half minimal velocity in an enzyme catalysed reaction
(d) Numerically equal to $\frac{1}{2}V_{max}$

89. 'Lock and key' theory was proposed by
(a) Koshland (b) Emil Fischer
(c) Mehler (d) Sanger

90. Allosteric inhibitor of hexokinase enzyme is
(a) Glucose-6-phosphate
(b) Palmitate
(c) AMP
(d) ATP

91. The non-protein, organic and low molecular weight substance, bound to an enzyme and essential for the activity of enzyme is known as
(a) Holoenzyme (b) Coenzyme
(c) Isoenzyme (d) Apoenzyme

92. When in enzyme inhibition K_m value is unchanged and V_{max} is value is decreased then it known as
(a) Allostreric inhibition
(b) Reversible non-competitive inhibition
(c) Reversible competitive inhibition
(d) Irreversible inhibition

93. If two monosaccharides differ from each other in their configuration around single specific carbon atom other than anomeric carbon they are known as
(a) Epimers (b) Enediols
(c) Stereoisomers (d) Optical isomers

94. Chemically Barfoed's reagent is
(a) Copper acetate and glacial acetic acid
(b) Resorcinol in hydrochloric acid
(c) Copper sulphate in sulphuric acid
(d) Phenylhydrazine in hydrochloric acid

95. Poisoning of morphine causes
(a) Metabolic acidosis (b) Respiratory alkalosis
(c) Metabolic alkalosis (d) Respiratory acidosis

96. Which enzyme hydrolyses starch?
(a) Invertase (b) Amylase
(c) Sucrase (d) Maltase

97. One of the following amino acid is nonessential
(a) Arginine (b) Valine
(c) Glutamate (d) Lysine

98. The oxidation of glucose to pyruvate and lactate is known as
(a) Glycolysis (b) Gluconeogenesis
(c) Glycogenesis (d) Glycogenolysis

99. Citric acid cycle is also known as
(a) Uronic acid cycle
(b) Reductive pathway of carbohydrate
(c) Krebs cycle
(d) Synthesis of glucose from non-carbohydrate precursor

100. Embden–Meyerhof pathway is also known as
(a) Hexose monophosphate shunt
(b) Oxidative pathway of carbohydrate
(c) Krebs cycle
(d) Glycolysis

101. One of the following is oxidative pathway of glucose
(a) Gluconeogenesis
(b) Hexose mono phosphate shunt
(c) Glycogenolysis
(d) Lipogenesis

102. Generation of ATP during citric acid cycle is
(a) 8 (b) 22
(c) 24 (d) 30

103. Glycolysis reaction is regulate by catalyze the irreversible reaction by all of the following enzyme except
(a) Hexokinase (b) Phosphofructokinase
(c) Pyruvate kinase (d) Phosphoglycerate kinase

104. The inhibition of glycolysis by oxygen is known as
(a) Crabtree effect
(b) Pasteur effect

(c) Rapaport–Leubering effect
(d) Krebs effect

105. In citric acid cycle citrate is convertinged in to isocitrate by
(a) Aconitase (b) Isocitrate dehydrogenase
(c) Citrate synthase (d) Succinate dehydrogenase

106. In tricarboxylic acid cycle citrate synthase enzyme is inhibited by
(a) ADP (b) AMP
(c) NAD^+ (d) Succinyl Co-A

107. The enzymes of tricarboxylic acid cycle are located in
(a) Cytosol
(b) Mitochondrial matrix
(c) Cytosomal fraction of the cell
(d) Liver

108. All of the following are precursors for gluconeogenesis except
(a) Lactate (b) Pyruvate
(c) Acetyl Co-A (d) Glycerol

109. Gluconeogenesis is regulated by
(a) ACTH (b) Glucagon
(c) Progesterone (d) Insulin

110. Glycogen synthesis is increased in one of the following conditions:
(a) If insulin level is increased
(b) If glucagon level is increased
(c) If norepinephrine level is increased
(d) If glucose level is increased

111. Van Gierke's disease occurs because of
(a) Glucose level is decreased
(b) Glucagon level is decreased
(c) Glycogen accumulates in hepatocytes and renal cells
(d) Lactic acid level is increased

112. In hexose mono phosphate shunt glucose 6-phosphate is converted in to 6-phosphogluconolactone by
(a) Glucose 6-Phosphate dehydrogenase
(b) Transketolase
(c) Gluconolactone hydrolase
(d) Phosphogluconate dehydrogenase

113. Uronic acid pathway is concerned with synthesis of
(a) Vitamin A (b) Vitamin D
(c) Vitamin C (d) Glucose

114. The process of shifting of hydrogen atom from one carbon atom to another to produce enediols is known as
(a) Anomers (b) Epimers
(c) Mutarotaiton (d) Tautomerization

115. Krebs Cycle is known as amphibolic because
(a) Catabolic in nature
(b) Anabolic in nature
(c) Both anabolic and catabolic in nature
(d) Either anabolic or catabolic in nature

116. Lyase means
(a) Enzymes specialized in the addition or removal of water, ammonia, etc.
(b) Enzymes that brings about hydrolysis of various compound
(c) Enzymes that catalyse the transfer of functional groups
(d) Enzymes involved in all the isomerization reaction

117. Multienzyme complexes means
(a) It is made up of a single polypeptide
(b) Some of the enzymes which possess more than one polypeptide chain
(c) Possessing specific site to catalyse different reaction in a sequence
(d) Enzymes made up of apoenzyme and coenzyme

118. Hexokinase is classified as a
(a) Oxidoreductases enzyme
(b) Transferases enzyme
(c) Hydrolases enzyme
(d) Lyases enzyme

119. Most of the enzymes of the higher organism show optimum activity around
(a) pH 1–2 (b) pH 10–11
(c) pH 6–8 (d) pH 4–6

120. Thiamin pyrophosphate is derived from
(a) Thyroxine (b) Thiamine
(c) Tryptophan (d) Niacin

121. As per IUB enzyme activity is expressed in
(a) Micromol (b) Katal
(c) Miligram (d) Mcrogram

122. Serum glutamate pyruvate transminase is used for diagnose of
(a) Hepatitis
(b) Acute pancreatics
(c) Myocardial infarction
(d) Rickets

123. For cancer of prostate gland one of the following enzymes is used
(a) Amylase (b) Alkaline phosphate
(c) Acid phosphate (d) Aldolase

124. Indole ring is present in _____amino acid
(a) Tyrosine (b) Proline
(c) Tryptophan (d) Lysine

125. Gaucher's disease occurs due to the deficiency of
(a) Ceramidase (b) Hexosaminidase
(c) Sphingomyelinase (d) βGlucosidase

126. One of the following hormones decreases the cholesterol synthesis
(a) Insulin (b) Thyroxine
(c) Glucagon (d) Growth hormone

127. The protein component of lipoprotein is known as
(a) Chylomicron (b) Apoprotein
(c) Phophoprotein (d) None of the above

128. According to the Frederickson's classification of hyperliporoteinemias in Type IV
(a) Increased IDL level
(b) Increased LDL level
(c) Increased VLDL level
(d) Increased HDL level

129. In HDL _____ of triacylglycerol is present.
(a) 88% (b) 55%
(c) 12% (d) 98%

130. The two products in the βoxidation of odd chain fatty acids are
(a) Acetyl CoA and malonyl CoA
(b) Propionyl CoA and acyl CoA
(c) Succinyl CoA and malonyl CoA
(d) Propionyl CoA and acetyl CoA

131. Hypocholesterolemia is observed in the disorder
(a) Diabetes mellitus (b) Thyrotoxicosis
(c) Hyperthyrodism (d) Nephrotic syndrome

132. One of the following amino acids contains hydroxyl group:
(a) Threonine (b) Leucine
(c) Valine (d) Glutamine

133. Acidic amino acid is
(a) Lysine (b) Arginine
(c) Histidine (d) Glutamic acid

134. DNA and RNA differ in their structure:
(a) DNA contains Cytosine and RNA contains Adenine
(b) RNA contains Adenine and RNA contains Cytosine
(c) DNA contains Thymine and RNA contains Uracil
(d) RNA contains Guanine and RNA contains Adenine

135. In DNA structure width of double helix is
(a) 5 nm (b) 8 nm
(c) 1 nm (d) 2 nm

136. Structure of polydeoxyribonucleotide segment is held by
(a) Peptide bonds
(b) Phospho bonds
(c) Phosphodiester bonds
(d) Amide bond

137. In DNA structure aAdenine makes the hydrogen bond only with
(a) Thiamine (b) Guanine
(c) Cytosine (d) Uracil

138. In Z-DNA confirmation of DNA helix the number of base pairs present in each turn is
(a) 10 (b) 11
(c) 12 (d) 13

139. The sugar present in RNA is
(a) Ribose (b) Deoxyribose
(c) Fructose (d) Pentose

140. In RNAs cellular composition of ribosomal RNA is
(a) 5–10% (b) 10–20%
(c) 50–80% (d) 20–50%

141. rRNA function is to
(a) Transfer genetic information from genes to ribosomes
(b) Provide structural framework for ribosomes
(c) Trnasfer aminoacid to mRNA
(d) Involve in the selection of protein for export

142. Which of the following enzymes is NADPH dependent?
(a) Malic enzyme
(b) HMG CoA reductase
(c) Lactate dehyrogenase
(d) Tyramine dehyrogenase

143. By the non-oxidative deamination process enzyme histidase act on histidine to convert in
(a) Threonine (b) Pyruvate
(c) Urocanate (d) Homoserine

144. Oxidative amination mostly takes place in

(a) Liver and kidney
(b) Liver and intestine
(c) Kidney and urinary tract
(d) Brain

145. In transamination process all transaminase require _____ co-enzyme.
(a) Lipoic acid (b) TPP
(c) FMN (d) PLP

146. Urea cycle is known as
(a) Embden–Meyerhof pathway
(b) Krebs–Henseleit cycle
(c) Krebs cycle
(d) Kurt Henseleit cycle

147. Tocopherols prevents the oxidation of
(a) Vitamin D (b) Vitamin A
(c) Vitamin C (d) Vitamin B_{12}

148. For the synthesis of creatine all of the following amino acids are required except
(a) Glycine (b) Arginine
(c) Cysteine (d) Methionine

149. Hypervitaminosis of vitamin A causes
(a) Xeropthalmia (b) Pernicious anemia
(c) Keratomalacia (d) Dermatitis, loss of hair

150. Storehouse of ammonia in biological system is
(a) Glutamine (b) Glutamate
(c) Creatine (d) Urea

151. Lesch–Nyhan syndrome occurs due to deficiency of which enzyme?
(a) PRPP synthetase (b) Xanthine oxidase
(c) HGPRT (d) Glucose-6-phosphatase

152. Orotic aciduria can be treated by a diet rich in
(a) Adenine (b) Guanine
(c) Uridine (d) All of the above

153. Menke's disease is due deficiency of which of the following?
(a) Iron (b) Copper
(c) Molybdenum (d) Sodium

154. Which is the storage form of iron?
(a) Ferritin (b) Hemosiderin
(c) Both (a) and (b) (d) None of the above

155. Krebs–Henseleit cycle occurs in
(a) Mitochondria (b) Cytosol
(c) Both (a) and (b) (d) Kidney

156. Citrullinemia is due to defect in which of the following enzyme?
(a) Carbamoyl phosphatase synthase
(b) Arginase
(c) Ornithin transcarbomylase
(d) Arginosuccinate synthase

157. Which amino acid is the precursor of melanine?
(a) Alanine (b) Tyrosine
(c) Aspartic acid (d) Lysin

158. Hyperlipoproteinemia type III is due to elevated plasma level of which of the lipoproteins?
(a) LDL (b) VLDL
(c) IDL (d) Chylomicrone

159. Jamaican vomiting sickness disease is due to
(a) Hypoglycin C (b) Haemoglobin
(c) Hypoglycin A (d) Both (a) and (b)

160. Krabbe's disease occurs due to defect in
(a) βglucosidase
(b) βgalactocidase
(c) Sphingomylein metabolism
(d) Hexosaminidases A

161. HMP shunt occurs in
(a) Mitochondria (b) Cytosol
(c) Both (a) and (b) (d) None of the above

162. The reaction catalysed by hexokinase in glycolysis is dependent on
(a) ATP (b) Mg^{+}
(c) Both (a) and (b) (d) ADP

163. In Krebs cycle oxalosuccinate is converted to βketoglutarate by which enzyme?
(a) βketoglutarate dehydrogenase
(b) **Isocitrate dehydrogenase**
(c) Succinate dehydrogenase
(d) Aconitase

164. Fluroacetate is the inhibitor of which enzyme in Krebs cycle?
(a) βketoglutarate dehydrogenase
(b) Isocitrate dehydrogenase
(c) Succinate dehydrogenase
(d) Aconitase

165. Cori's disease is due to defect in which of the following enzyme?
(a) Glucose-6-phosphatase
(b) Amylo-β1,6-glucosidase

(c) Phospho fructokinase
(d) Liver glycogen phosphorylase

166. What is the starting material of retinol?
(a) Butyraldehyde and formic acid
(b) Beta-ionone and methylvinyllactone
(c) Ribulose
(d) Beta -ionone and methyl lactone

167. What is the starting material of pantothenic acid?
(a) Ribose
(b) Beta ionone and methyl lactone
(c) Benzaldehyde and l-o-Butraldehyde
(d) Formaldehyde and isobutyraldehyde

168. According to the chemical and biological classifications of fatty acids, we can classify palmitic acid as:
(a) Monounsaturated and essential
(b) Polyunsaturated and essential
(c) Saturated and essential
(d) Saturated and non- essential

169. A premature baby, shortly after birth, presents with rapid breathing, intercostal retractions, and grunting sound while breathing. A blood gas analysis reveals low oxygen and acidosis. A diagnosis of respiratory distress syndrome is quickly made. This syndrome is seen in newborns with immature lungs whose pneumocytes do not synthesize enough:
(a) Phosphatidyl choline
(b) Phosphatidyl inositol
(c) Sphingosin
(d) Sphingomyelin

170. The following compounds are phospholipids:
(a) Lecithin and sphingomyelin
(b) Plasmalogens and cerebrosides
(c) Diacylglycerols and cephalins
(d) Glycerol and gangliosides

171. Name the enzymes involved in conversion of oxaloacetate to βketoglutarate
(a) Isocitrate dehydrogenase
(b) Fumarase
(c) Aconitase
(d) Thiolase

172. Which kind of enzymes catalyses the activation or inactivation of other proteins and enzymes by phosphorylation of specific amino acid residues in the protein that acts as substrate:
(a) Cyclases (b) Kinases
(c) Proteases (d) Phosphatase

173. This carbohydrate acts as lubricant of synovial fluid and contributes to tensile strength and elasticity of cartilages and tendons. It is also an important component of skin.
(a) Cellulose (b) Glycogen
(c) Starch (d) Hyaluronic acid

174. It is the most important polysaccharide in human diet:
(a) Heparine (b) Starch
(c) Glycogen (d) Cellulose

175. In which form glucose is stored in muscle and liver?
(a) Cellulose (b) Glycogen
(c) Starch (d) Condroitin sulfate

176. The compound 5,7,8-trimethyltocol is commonly known as ..
(a) α-tocopherol (b) ß-tocopherol
(c) γ-tocopherol (d) Menaquinone

177. L-amino acid dehydrogenase is an enzyme that can catalyse the oxidation of different L-amino acids. It cannot catalyse the oxidation of D-amino acids or other L-compounds. Based on these characteristics we can say that this enzyme shows:
(a) Absolute specificity over substrate
(b) Allosteric regulation
(c) Relative specificity over substrate
(d) Specificity of action

178. Inactive precursors of some enzymes that are activated through hydrolysis reactions are called:
(a) Apoenzyme (b) Holoenzymes
(c) Prosthetic groups (d) Zymogens

179. These enzymes have different structure but the same catalytic function. Frequently they are oligomers made from different polypeptide chains. These enzymes are called:
(a) Allosteric enzymes (b) Isozymes
(c) Lyases (d) Proenzymes

180. The necessary coenzyme for transamination reactions is
(a) Aminotransferases (b) FAD
(c) Transcatalase (d) FMN

181. In glucose metabolism, name the enzymes catalysing the following step: Conversion of **glucose to glucose-6-phosphate?**
(a) Hexokinase
(b) Glucokinase
(c) Glucose-6-phosphate dehydrogenase
(d) Phosphofructokinase

182. The amino acid lysine is symbolized as

(a) K (b) R
(c) L (d) H

183. Which of the following residue in DNA exists predominantly as the keto tautomer?
(a) Cytosine (b) Guanine
(c) Alanine (d) Thymidine

184. D-galactose upon reduction gives
(a) D-sorbitol (b) D-Ribitol
(c) D-Dulcitol (d) D-Mnnitol

185. Glycoprotein laminin functions as
(a) Transporter
(b) Blood clotting
(c) Antigens
(d) Cell recognition and adhesion

186. What is the common name of cis-9-octadecanoic acid?
(a) Oleic acid (b) Linoleic acid
(c) Lauric acid (d) Palmitoleic acid

187. For vitamin D1
(a) 1 IU is contained in 7 6mg of standard preparation
(b) 1 lU is present in 0.344 μg of standard preparation
(c) 1 IU is contained in 0.025 μg of standard preparation
(d) 1 lU is present in 7 μg of standard preparation

188. Tyrosine gives the entire test positive except _____
(a) Xanthoprotic reaction
(b) Folin-Coicalteau's test
(c) Millons reaction
(d) Hopkins-Cole reaction

189. Which of the following test is specific for the ketone bodies?
(a) Rothera's test (b) Gammelin's test
(c) Hay's test (d) Fouchet's test

190. Which of the following tests are positive for bile salts?
(a) Hay's test (b) Patternkofer's test
(c) Both (a) and (b) (d) None of the above

191. Which method is used for blood glucose estimation?
(a) Alkaline picrate method
(b) Diacyl monoxime method
(c) Folin Wu method
(d) Bromocresol green dye method

192. Which of the following does not cause haemolysis in GP6D?
(a) Primaquine (b) Sulfonamide
(c) Asprin (d) Penicillin

193. Which of the following conjugations is not done by microsomal enzyme?
(a) Sulfate conjugation
(b) Gultathione conjugation
(c) Acetylation
(d) Glucuronidation

194. Which vitamin deficiency causes cheilosis?
(a) Thiamine (b) Riboflavin
(c) Pyridoxine (d) Biotin

195. Which of the following tests is specific for ketohexoses?
(a) Molisch test (b) Benedict's test
(c) Barfoed's test (d) Seliwanoff's test

196. Hopkins-Cole reaction is for which type of amino acid?
(a) Aromatic amino acid
(b) Imidazole ring
(c) Indole ring
(d) None of the above

197. The following protein/polypeptide has a quaternary structure.
(a) Chymotrypsin (b) Haemoglobin
(c) Insulin (d) Myoglobin

198. Maltose is composed by
(a) Glucose + Galactose
(b) Fructose + Galactose
(c) Glucose + Fructose
(d) Glucose + Glucose

199. Protein X is formed by two chains with 80 amino acids in one chain and 58 in the other. These two chains are linked by disulfide bonds and all the essential amino acids are present in the structure, but not all the non-essential amino acids. With this information, we can say that this protein is:
(a) A globular protein
(b) A fibrous protein
(c) A conjugated protein
(d) A complete protein

200. An amino acid that yields acetoacetyl CoA during the catabolism of its carbon skeleton would be considered:
(a) Glycogenic
(b) Ketogenic
(c) Glycogenic and ketogenic
(d) Neither glycogenic nor ketogenic

201. The NH_3 produced in muscle degradation of nitrogenated compounds is transported through blood to the liver using _____ as carriers.

(a) Alanine and glutamine
(b) Urea and alanine
(c) NH_4 and glutamate
(d) Glutamate and glutamine

202. Nitric oxide and urea have in common _____ as an immediate precursoramino acid.
(a) Aspartate (b) Arginine
(c) Glutamate (d) Phenylalanine

203. The correct conformation of complex proteins is achieved with the help of
(a) Chaperones (b) Hing domain
(c) Zinc figures (d) None of the above

204. Which of the following immunoglobulins has B-cell receptor as major function?
(a) IgA (b) IgE
(c) IgD (d) IgG

205. What is the starting material of biotin?
(a) Bisbenzyl succinic acid
(b) Ribulose
(c) Beta-ionone and methylvinyl lactone
(d) Beta -ionone and methyl lactone

206. What is the starting material of ascorbic acid?
(a) Beta -ionone and methyl lactone
(b) Benzaldehyde and isobutraldehyde
(c) Ribose
(d) Ribulose

207. Which of the following occurs due to defect in uroporphyrinogen decarboxylase?
(a) Protoporphyria
(b) Hereditary coporphyria
(c) Porphyria cutaneatarda
(d) Acute intermittant porphyria

208. The P:O ratio for oxidation of FADH2 is?
(a) 1 (b) 2
(c) 3 (d) 4

209. Which of the following is the sulfur-containing compound involved in decarboxylation reaction?
(a) Choline (b) Lipoic acid
(c) Inositol (d) Niacin

210. Which one is described as "vitamin in search of disease"?
(a) Vitamin A (b) Vitamin C
(c) Vitamin E (d) Vitamin H

211. Wernicke–Korsakoff syndrome is due to deficiency of vitamin?
(a) B1 (b) Riboflavin
(c) B7 (d) Niacin

212. Which vitamin decreases circulatory free fatty acid in adipose tissue?
(a) Riboflavin (b) Ascorbic acid
(c) Biotin (d) Niacin

213. Which vitamin is only synthesized by microorganism and not by plant or animal?
(a) Riboflavin (b) Ascorbic acid
(c) Biotin (d) Cobalamin

214. The reaction given by two or more peptide linkages is?
(a) Biuret test (b) Ninhydrin test
(c) Xanthoproteic test (d) Pauley's test

215. How many base pairs are present in each turn of β-form of DNA helix?
(a) 9 (b) 10
(c) 11 (d) 12

216. Which of the following is the inhibitor of isocitrate dehydrogenase in Krebs cycle?
(a) ATP (b) AMP
(c) ADP (d) NAD

217. In muscular dystrophy serum level of which enzyme is elevated?
(a) Acid phosphatase
(b) Creatinine phosphokinase
(c) Amylase
(d) Aldolase

218. In Wilson's disease serum level of which enzyme decreases?
(a) Amylase
(b) Ceruloplasmin
(c) Glucose-6-phosphate dehydrogenase
(d) Creatine phosphokinase

219. In visual cycle, iodopsin gives which pigment?
(a) Red
(b) Green
(c) Yellow
(d) Blue

220. Caprylic acid chemically is
(a) $CH_3[CH_2]_4COOH$
(b) $CH_3[CH_2]_6COOH$
(c) $CH_3[CH_2]_8COOH$
(d) $CH_3[CH_2]_{10}COOH$

ANSWER KEYS

1. (b)	**2.** (c)	**3.** (a)	**4.** (a)	**5.** (d)	**6.** (b)	**7.** (d)	**8.** (c)	**9.** (a)	**10.** (c)
11. (a)	**12.** (b)	**13.** (d)	**14.** (d)	**15.** (a)	**16.** (d)	**17.** (a)	**18.** (b)	**19.** (c)	**20.** (a)
21. (a)	**22.** (c)	**23.** (d)	**24.** (c)	**25.** (b)	**26.** (a)	**27.** (d)	**28.** (a)	**29.** (a)	**30.** (c)
31. (c)	**32.** (a)	**33.** (c)	**34.** (b)	**35.** (a)	**36.** (d)	**37.** (a)	**38.** (c)	**39.** (d)	**40.** (c)
41. (d)	**42.** (a)	**43.** (c)	**44.** (d)	**45.** (c)	**46.** (d)	**47.** (b)	**48.** (d)	**49.** (c)	**50.** (b)
51. (c)	**52.** (a)	**53.** (c)	**54.** (d)	**55.** (b)	**56.** (d)	**57.** (d)	**58.** (a)	**59.** (b)	**60.** (a)
61. (d)	**62.** (d)	**63.** (d)	**64.** (c)	**65.** (d)	**66.** (d)	**67.** (a)	**68.** (a)	**69.** (c)	**70.** (b)
71. (d)	**72.** (c)	**73.** (c)	**74.** (d)	**75.** (b)	**76.** (b)	**77.** (c)	**78.** (d)	**79.** (d)	**80.** (a)
81. (d)	**82.** (a)	**83.** (d)	**84.** (a)	**85.** (b)	**86.** (d)	**87.** (b)	**88.** (a)	**89.** (b)	**90.** (a)
91. (b)	**92.** (b)	**93.** (a)	**94.** (a)	**95.** (d)	**96.** (b)	**97.** (c)	**98.** (a)	**99.** (c)	**100.** (d)
101. (b)	**102.** (c)	**103.** (d)	**104.** (b)	**105.** (a)	**106.** (d)	**107.** (b)	**108.** (c)	**109.** (b)	**110.** (a)
111. (c)	**112.** (a)	**113.** (c)	**114.** (d)	**115.** (c)	**116.** (a)	**117.** (c)	**118.** (b)	**119.** (c)	**120.** (b)
121. (b)	**122.** (a)	**123.** (c)	**124.** (c)	**125.** (d)	**126.** (c)	**127.** (b)	**128.** (c)	**129.** (a)	**130.** (d)
131. (a)	**132.** (a)	**133.** (d)	**134.** (c)	**135.** (d)	**136.** (c)	**137.** (a)	**138.** (c)	**139.** (a)	**140.** (c)
141. (b)	**142.** (b)	**143.** (c)	**144.** (a)	**145.** (d)	**146.** (b)	**147.** (b)	**148.** (c)	**149.** (d)	**150.** (a)
151. (c)	**152.** (c)	**153.** (b)	**154.** (c)	**155.** (c)	**156.** (d)	**157.** (b)	**158.** (c)	**159.** (c)	**160.** (b)
161. (b)	**162.** (c)	**163.** (b)	**164.** (d)	**165.** (b)	**166.** (b)	**167.** (d)	**168.** (b)	**169.** (a)	**170.** (a)
171. (a)	**172.** (b)	**173.** (d)	**174.** (b)	**175.** (b)	**176.** (a)	**177.** (c)	**178.** (d)	**179.** (b)	**180.** (a)
181. (a)	**182.** (a)	**183.** (d)	**184.** (c)	**185.** (d)	**186.** (a)	**187.** (c)	**188.** (d)	**189.** (a)	**190.** (c)
191. (c)	**192.** (d)	**193.** (d)	**194.** (b)	**195.** (d)	**196.** (a)	**197.** (b)	**198.** (d)	**199.** (d)	**200.** (b)
201. (a)	**202.** (b)	**203.** (a)	**204.** (c)	**205.** (a)	**206.** (c)	**207.** (c)	**208.** (b)	**209.** (b)	**210.** (c)
211. (a)	**212.** (d)	**213.** (d)	**214.** (a)	**215.** (b)	**216.** (a)	**217.** (d)	**218.** (c)	**219.** (b)	**220.** (b)

CHAPTER 5

MEDICINAL CHEMISTRY

DRUGS ACTING ON ANS

Adrenergic System

- **Adrenergic neurotransmitter:** Chemically, it is catecholamine like Adrenaline, Noradrenaline, Dopamine.
- **Biosynthesis:** L-tyrosine use as bioprecursor.
- **Type of receptor:**
  (1) α-adrenergic receptor: α_1 and α_2
  (2) β-adrenegic receptor: β_1, β_2, β_3
- **Metabolism:** Catecholamine metabolism occurs by two enzymes:
  (1) COMT – Catechol-O-methyltransferase
  (2) MAO – Monoamine oxidases

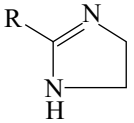
Direct acting agent

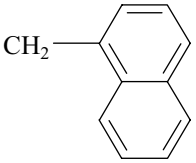
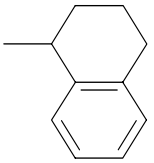
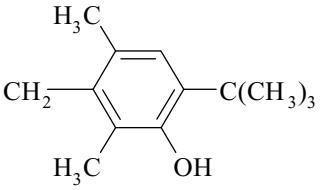
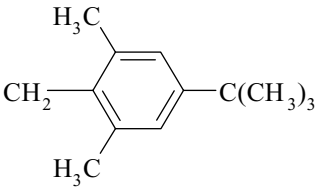
(1) Selective α_1 agonist:

Sr. no	Name of drug	Characteristics	Side effects
1	Phenyephrine	Used as mydriatic when cyclopegia is not require and nasal decongestant	Bradycardia
2	Methoxamine	Used as nasal decongestant	Bradycardia
3	Midodrine	N-glycyl prodrug of desglymidodrine.	–

(2) Non-selective α agonist:

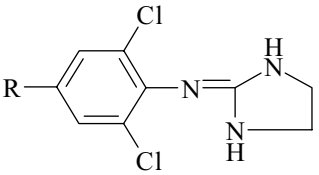
General structure



Sr. no	Name of drug	R
1	Naphazoline	
2	Tetrahydrozoline	
3	Oxymetazoline	
4	Xylometazoline	

Selective α_2 agonist

General structure:



Sr. no	Name of drug	R	Characteristic
1	Clonidine	–H	Used in migraine, glaucoma, opioid withdrawal syndrome
2	Apraclonidine	$–NH_2$	Used in glucoma
3	Brimonidine	–	Used in glucoma
4	Guanabenz	–	–
5	Guanafacine	–	–

Dual α and β agonist

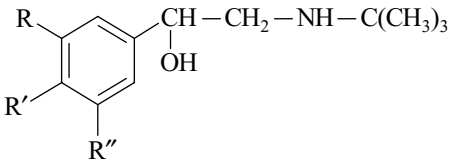
- **Example is Dobutamine:** It exists as a pair of enantiomer.
- **(+) enantiomer:** β_1 and β_2 agonist and **(–) enantiomer:** α_1 agonist.
- It is a racemic mixture used in CHF as I.V.

β-Adrenergic agonist

(1) Non selective:
Example is Isoproterenol: It is a powerful bronchodialator used in asthma.

(2) Selective β_2 agonist:

General structure:



(Pirbuterol contain pyridine ring instead of phenyl ring)

Sr. no	Name of drug	R	R′	R″
1	Salbutamol	CH_2OH	OH	H
2	Terbutaline	OH	H	OH
3	Pirbuterol	CH_2OH	OH	H
4	Orciprenaline (Metoproterenol)	–	–	–

(5) Clenbuterol

(6) Salmeterol, Formoterol, Levabuterol are long acting agent.

- **Use:** It is used in Asthma and as uterine relaxant to delay premature labour.

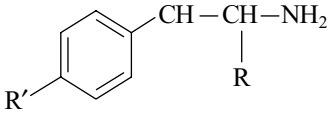
Common side effect:

- Tachycardia, Arrythmia, Vasodialation

Indirect acting agent

It acts by release of endogenous catecholamines.

General structure:



Sr. no	Name of drug	R	R′	Character-istic
1	Amphetamine	CH_3	H	It is MAO inhibitor and CNS stimulant and appetite suppressant
2	Hydroxyamphetamine	CH_3	OH	It gives with atropine to produce Mydriasis.
3	p-tyramine	H	OH	Not used clinically.

- ***L-pseudoephedrine*** which is threo isomer of ephedrine and nasal decongestant.

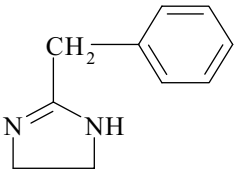
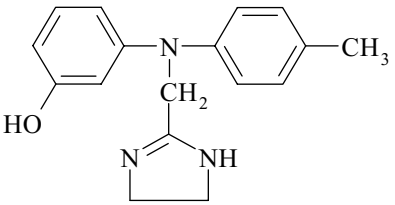
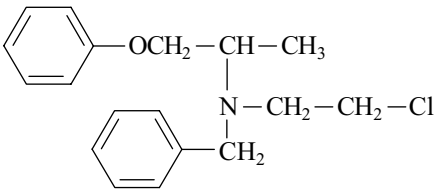
Sympathomimetic agent with mix mechanism of action

(1) D-ephedrine It is erythro racemate of ephedrine and used in asthma, nasal decongestant.

(2) Metaramenol It is given parenterally during spinal anaesthesia to prevent acute hypotensive state.

α-Adrenergic Antagonist

(1) Non-selective blocker:

Sr. no	Name of drug	Characteristics	Side effects
1	Tolazoline 	It is imidazoline derivatives.	–
2	Phentolamine 	It is imidazoline derivatives.	–
3	Phenoxybenamine 	It forms aziridinium ion which irreversibely block receptor.	Miosis, nasal congestion, postural hypotension.

Use: Management of hypertension associate with pheochromocytoma.

(2) Selective α_1 blocker:

- **Tamsulosin:** It aryl sulfonamide uro selective drug.
- **Side effect:** Failure of ejaculation.
- Prazosin, Terazosin, Doxazosin, Trimzosin etc.

(3) Selective α_2 blocker:

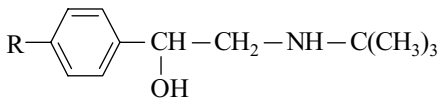
(1) Rauwolscine and Yohimbine obtain from Rauwolfia alkaloids.
(2) Mirtazepine: It is an antidepressant which also block 5-HT receptor

The ergot alkaloid like ergocrystin, ergocryptine, ergocornine are derivatives of lysergic acid which is also α blocker.

β-Adrenergic antagonist-Chemical classification:

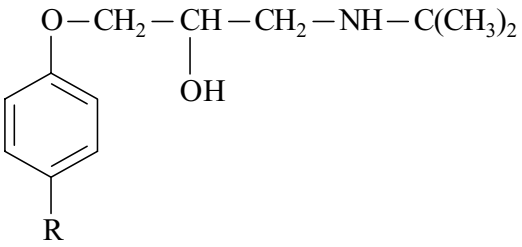
- Arylethanolamine derivatives:

General structure:



Sr. no	Name of drug	R	Characteristics
1	Dichloro-isoproterenol	$(Cl)_2–C_6H_4$	Carcinogenic
2	Pronethanol	C_6H_5	Cause thymic tumour
3	Sotalol	$NH–SO_2–CH_3$	Used in arrhythmia also.

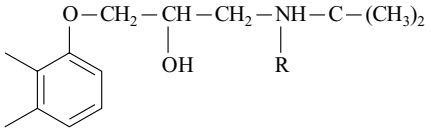
Aryloxy propanolamine derivatives:

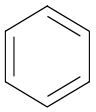
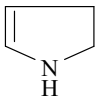
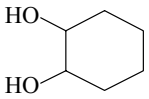


Sr. no	Name of drug	R	Characteristics
1	Practolol	$-NHCOCH_3$	–
2	Metoprolol	$-CH_2-CH_2-OCH_3$	Used in angina, myocardial infaraction
3	Esmolol	$-CH_2-CH_2-COOCH_3$	Ultra short acting agent. (half life-10 min) and use in arrhythmia
4	Atenolol	$-CH_2-CO-NH_2$	Used in angina
5	Betaxolol	$-CH_2-CH_2-O-CH_2$–Cyclopropyl	Used in glaucoma, long acting agent.

Fused ring contains aryloxy propanolamine derivatives:

General structure:



Sr. no	Name of drug	Fused ring	R	Characteristics
1	Propanolol		H	It metabolises to 4-OH propanolol which β blocker with sympathmimetic activity. It causes brnchoconstriction, hypoglycemia.
2	Pindolol		H	–
3	Nadolol		CH_3	It is used in angina and very long acting agent (half life is 20 hr)

- The other is timolol which contain 1, 2, 5 thiadiazole ring and morpholine ring at 4 position.

Use: It is used in migraine and myocardial infaraction.

NOTE

The drugs which used in glaucoma are (1) Carteolol (2) Timolol (3) Levobunolol

All β-blocker use as racemic mixture except Levobunolol, Timolol, Penbutolol.

Cholinergic System

Synthesis and destruction of ACh

It is synthesized from choline acetylase and destruct by cholinesterase.

NOTE

(1) Drug that inhibits ACh synthesis:
e.g., Hemicholinium, Vesamicol.
(2) Drug that inhibits Ach release:
(a) ***Botulinium toxin:*** It causes botulism (food poisioning) and used in eyelid spasm treatment.
(b) ***β-bungarotoxin:*** It contains protein in venom of snake of Cobras family

Acetylcholine receptor

Nicotinic receptor

1. N_M muscle type
2. N_N neurone type

Muscarinic receptor

M1—***Neural type*** cause CNS excitation

M2—***Cardiac type*** cause inhibition

M3—***Glandular*** cause vasodialation and smooth muscle contraction and increase salivery, gastric secretion.

M4—CNS Increase locomotor activity.

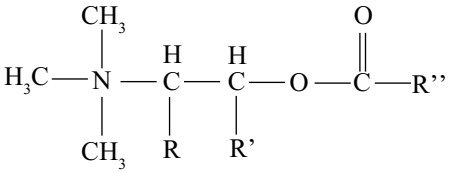
M5—Not clear.

Cholinergic Agonist

Classification

(1) Choline ester derivatives:

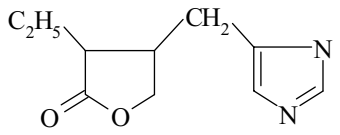
General structure:



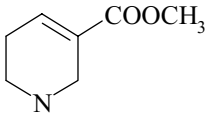
Sr. no	Name of drug	R	R′	R″	Characteristics
1	Methacho-line	CH_3	H	CH_3	S form is active
2	Bethanechol	H	CH_3	NH_2	Use in bladder hypotenia.
3	Carbachol	H	H	NH_2	It is used in glaucoma when response is not obtained by pilocrpine.

The others which do not contain ***quaternary ammonium*** group are

(1) ***Pilocarpine:*** It contains **imidazole** and **tetrahydro-furan** ring, obtained from **Pilocarpus jaborandi and Pilocarpus microphyllus** species.



(2) ***Arecoline:*** It is obtained from ***Areca catechu*** and contains ***1,2,5,6-Tetrahydro Pyridine ring.***



(3) ***Oxotremorine:*** Used in Alzheimer's disease.

Anti-Cholinesteras

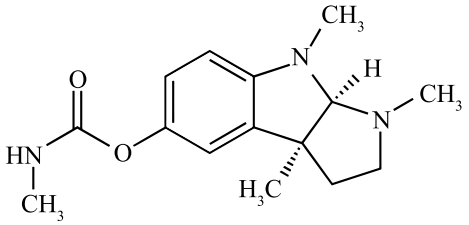
Classification

(1) Reversible Cholinesterase

(a) **Carbamate derivatives**

Physostigmine: It is obtained from ***Physostigma venenosum***

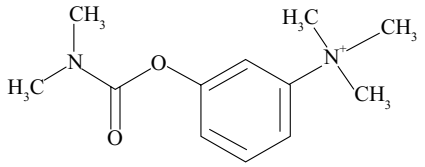
It contains ***tertiary nitrogen*** which is non-polar hence becomes lipid soluble.



Metabolism

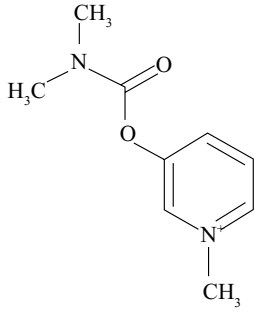
- Hydolysis forms ***eseroline***
- Oxidation forms rubreserine and then serine blue and brown.

Neostigmine It contains ***quaternary nitrogen*** which is made of compound hydrophilic.



Metabolism: Hydrolysis to 3-hydroxy phenyl methyl derivative.

Pyridostigmine



Use: All are acting medium and used in treatment of ***myasthenia gravis.***

Edrophonium

Use: In diagnosis of Myasthenia gravis.

It is potent anti-curare agent use to alleviate overdose of d-tubocurarine.

Ambenonium

All alzheimer's drug like Donepezil, Rivastigmine, Gallantamine, Tacrine (acridine derivative), etc., are ***anti-cholinesterse.***

Irreversible type

Organophsphrous compound

(1) Malathion and Parathion: Both oxidized to Malaoxon and Paraoxon which more potent.

(2) Ecothiophate: It is only hydrophilic organophosphrous compound which use in glaucoma.

(3) Dyflos (Diisopropyl fluoro phosphate):

(4) Isofluorophate

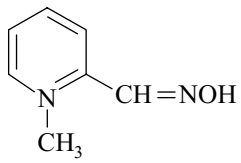
(a) Carbamate derivatives: Carbaryl, Propoxur

NOTE

Malathion, Parathion, Carbaryl, Propoxur, etc., all are used in insecticide and nerve gas for chemical warfare.

Cholinesterase reactivator

- **Pralidoxime:** It is used in organophosphate poisoning and also antagonist Neostigmine and Pyridostigmine.



Anti-cholinergic agent

(1) Naturally occurring

Sr. No	Name of drug	Characteristics
1	Atropine	It is a racemic mixture of hyoscymine. It is used as mydriasis, antispasmodic, anticholinesterase poisoning.
2	Hyoscyamine	Levo form is active. Use in motion sickness.
3	Hyoscine	–

(2) Semisynthetic derivatives

- Homatropine, Hyoscine butyl bromide.
- **Ipratropium and Tiotropium:** It is quaternary ammonium derivative of atropine and used in asthmatic attack.

(3) Synthetic derivatives

(a) Amino alcohol ester derivatives:

Sr. no	Name of the drug	Characteristics
1	Clindinium	It contains **quinclidine** ring Used in peptic ulcer and ulcerative colitis.
2	Cyclopentolate	It is used as Mydriatic and in cyclopegia.
3	Dicyclomine	Used in motion sickness, irritable bowel syndrome.
4	Glycopyrrolate	It is potent M 1 antagonist. Used in peptic ulcer.
5	Methantheline	–
6	Eucatropine	–
7	Oxyphenylcyclimine	–

(b) Amino alcohol ether derivatives: Used in Parkinson disease.

Sr. no	Name of the drug	Characteristics
1	Benztropine	It relieves Tremor and Rigidity.
2	Orphenadrine	It relieves only rigidity.

(c) Amino alcohol derivatives

Sr. no	Name of the drug	Characteristics
1	Biperiden	It blocks nicotinic induced convulsions because of potent nicotinolytic.
2	Procyclidine	It is used in parkinson's disease.
3	Tridihexethyl	It is used in Parkinson disease.

(d) Aminoamide derivatives

Sr. no	Name of the drug	Characteristics
1	Isopropamide	Antispasmodic, antise-cretory
2	Tropicamide	It is potent M-4 antagonist and is used as mydriatic

(e) Miselleneous

Pirenzepine: It is M-1 receptor antagonist.

Drotraverine: Novel agent, used as anti-spasmodic by ***inhibit PDE-4.***

Darcifenacin, Tolterodine, and Oxybutynin: All are ***selective M-3 antagonist*** and used to inhibit micturition.

Drug Acting on CVS

Anti-anginal agent

- **Angina pectoris:** When imbalance between oxygen supply and oxygen demand in myocardium occurs this is called as angina pectoris.
- **Types of angina:**
  1. Classical (stable) angina
  2. Variant (prinzmental) angina
- **Classification of anti anginal drugs:**

1. Nitrate derivative:

(a) short acting drugs:

- **Amyl nitrate/isopentyl nitrate**: Currently used in cyanide poisoning treatment.
- **Glyceryl trinitrate (nitroglycerin):** It is given sub-lingually and duration of action is 30 min.

Specific side effect: Postural hypotension, Methhaemoglo-binemia, Monday morning sickness.

- **Isosorbide nitrate:** It is a bicyclic form of sorbitol.
  - It is given sublingually or as chewable tablet.
  - **Specific side-effect:** Tachycardia
- **Erythrityl tetranitrate**:
- **Pentaerythritol tetranitrate:** It is a powerful explosive and must be diluted with lactose or mannitol.
- **Mechanism of action:** The nitrate release nitric oxide which binds with –SH group of enzyme and carries out dephosphorylation of myosin light chain and relaxation.

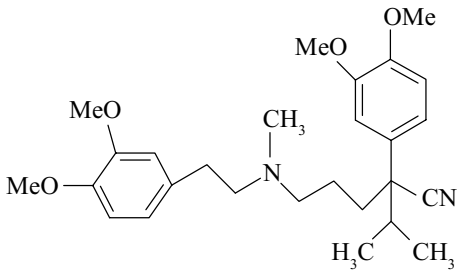
Calcium channel blocker

- **Mechanism of action:** It inhibits phosphorylations of myosin light chain phosphate and prevents binding with actin and prevents contraction.

1. Phenyl alkyl amine derivative:

(a) First generation agent: Verapamil

- **Metabolism:** By N-demethylation to Norverapamil which is active.
- **Specific side-effect:** Bradycardia, constipation.

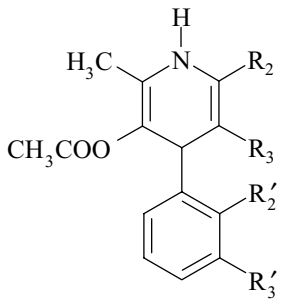


Verapamil

2. 1, 4 dihydropyridine derivatives

Nifedipine is first generation drug, the remaining drugs in below table are second generation.

General structure:



General Structure of
1, 4 Dihydropyridine

Sr no	Name of drug	R_2	R_3	R_2'	R_3'
1	Nifedipine	CH_3	$-COOCH_3$	NO_2	H
2	Amlodipine	$CH_2-O-C_2H_4-NH_2$	$-COOC_2H_5$	Cl	H
3	Felodipine	CH_3	$-COOC_2H_5$	Cl	Cl
4	Nimodipine	CH_3	$-COO-C_2H_4-OCH_3$	H	NO_2
5	Nicardipine	CH_3	$-COO-C_2H_4-N-C_6H_5-CH_2$	H	NO_2
6	Nitrendipine	CH_3	$-COO-C_2H_5$	H	NO_2

Note: Nimodipine can cross BBB, so it is used in cerebral vasospasm

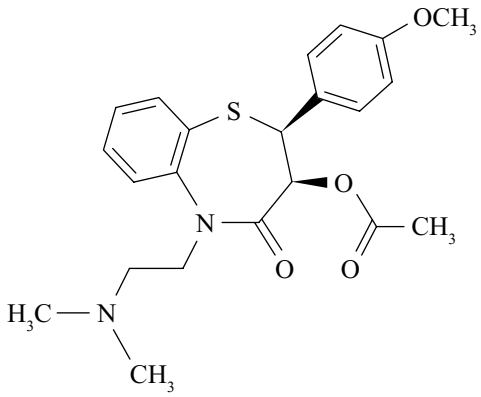
Newer third generation drugs

(1) Lacidipine: It contains additional α blocking activity.

(2) Monatepil: It contains additional anti-artherosclerotic activity.

Common side effect: Ankle odema.

Benzothiazepine derivative: Diltiazem



Potassium (K^+) channel opener

Nicorandil, Pinacidil and Cromakalim are potassium channel opener and bronchodialator which are used in angina as well as in asthma.

Miscellaneous

(1) Khellin: Natural drug obtained from fruits and seeds of ***Ammi visnaga***.

(2) Papaverine: Powerful coronary dialator.

(3) Dipyridamol: It increases adenosine (natural vasodilator) which is a coronary dialator.

Antihyperlipidemic Drugs

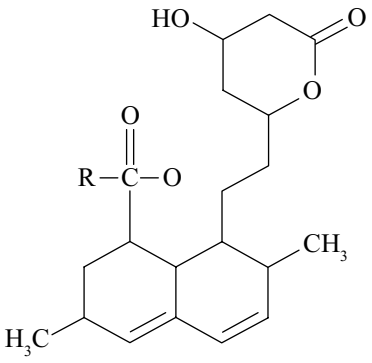
These antihyperlipidemic drugs are specifically used in artherosclerosis.

- **Classification of antihyperlipidemic drugs:**

HMG-CO-A reductase inhibitors

- **Mechanism of action:** They inhibit cholesterol biosynthesis by inhibiting HMG-CO-A.
- They also decrease LDL level by increasing LDL precursor by recognizing apo-B 100.

General structure:

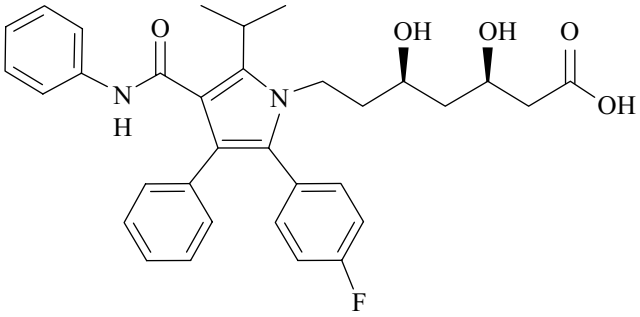


Sr. no	Name of drug	R
1	Lovastatin	$-CH(CH_3)-CH_2-CH_3$
2	Simvastatin	$-C(CH_3)_2-C_5H_{11}$

Note

For obtaining inhibitory activity on HMG-CO-A, lactone ring must hydrolyse to open ring hydroxyl acid.

- **Pravastatin:** It is same in structure as lovastatin, the only difference is that it contains open ring hydroxyl acid instead of lactone ring.
- **Atorvastatin:**

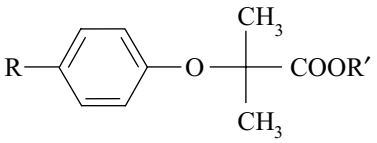


- **Fluvastatin:** It contains indole ring and heptanoic acid as side chain.
- Cerivastatin and Rosuvastatin

Specific side-effects:

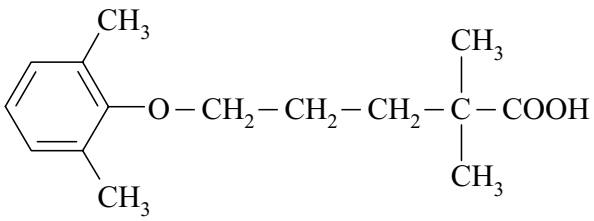
(1) Myalgia
(2) Rhabdomylosis (Myositis)
(3) Angio-odema

Fibric acid derivative: (General structure)



Sr. no	Name of drug	Characteristics	Specific side effects	Metabolism
1	Clofibrate ($R'=-C_2H_5$, $R=-Cl$)	–	Myalgia Rhabdomylosis	Hydrolysis (clofibric acid)
2	Fenofibrate $R=Cl-C_6H_5-C=O$, $R=CH-(CH_3)_2$	More lipophilic	–	–
3	Ciprofibrate $R=CH-(Cl)_2$, $R'=H$	Acid derivative	–	–
4	Beclofibrate $R'=C_2H_5$, $R=Cl-C_6H_5-CH_2-$	–	–	–

- **Gemifibrozil:**



- **Side-effect:** Anaemia, Leukopenia.

Bile acid binding resin

(1) Cholestyramine: It is styrene copolymer of divinyl benzene and quaternary ammonium compound.

- **Side effect:** Constipation

(2) Colestipol: High mol.wt granular copolymer of tetraethyl pentamine and epichlorohydrin.

(3) Cosevelam: Recent drug which does not cause constipation.

- **Mechanism of action:** Bile acid is required for cholesterol absorption so this resin binds with it and decreases cholesterol level in body.

(4) Miscelleneous:

- **Niacin:**
- **Side effect:** Vasodialation, palpitation.
- **Probucol:** It is two tertiary butyl phenol linked to dithio propyl group.
- **Mechanism of action**: It inhibits sterol biosynthesis.
- **Side effect:** Diarrhoea.

Anti-arrythmic agent

Arrhythmia: When there is abnormality of rate, origin or conduction of cardiac muscle, there is lack of rhythm.

Phases of cardiac action potential

- **Phase-0—**Influx of sodium occurs at threshold potential and depolarization occurs.
- **Phase-1—**Initiation of influx calcium occurs.
- **Phase-2—**Calcium influx occurs and contraction takes place.
- **Phase-3—**Potassuim efflux occurs and repolarization occurs and resting potential takes place.
- **Phase-4—**Slowly, depolarization occurs and reaches threshold potential.
- Normal impulse initiated in SA node or pacemaker cell.

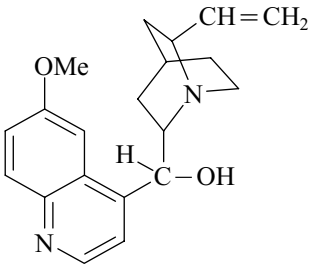
Types of arrhythmia

(1) Extrasystoles: Premature beat from ectopic focus.
(2) Paroxysmal tachycardia: Heart rate increases up to 150–200 beat/min
(3) Atrial flutter: Rapid, regular pulse is 180–300 beat/min
(4) Atrial fibrillation: Rapid, continous, irregular beat.
(5) Ventricular fibrillation:

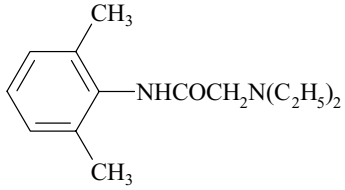
Classification

Class-I: Drug which blocks sodium channel (membrane stabilizing agent)

Class-IA drugs: Drug which slows down depolarization.

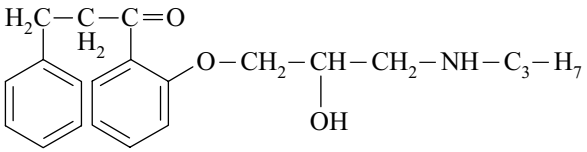
Sr. no	Name and structure of drug	Characteristics	Specific side-effects	Metabolism
1	 Quinidine sulfate	-Dextro isomer of quinine obtained from cinchona. -Increases digoxin toxicity.	Cinchonism Convulsion	Hydroxylation
2	 Procainamide	-Amide derivative of procaine. -Ganlion blocker	Lupus syndrome Agranulocytosis	N-acetylation (NAPA) (active)
3	Disopyramide	It acts by ATP and Pinene receptor.	Anticholinergic side effect.	N-dealkylated

Class-Ib drugs: Mechanism of action: It decreases repolarization.

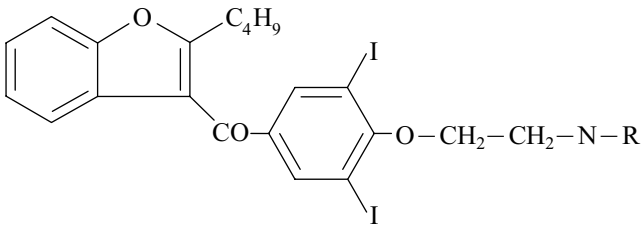
Sr. no	Name of the drug	Characteristics	Specific side-effects	Metabolism
1	 Lidocaine	Used for ventricular arrythmia.	Paresthesias Convulsion	N-dealkylation (active)

2	Phenytoin	It is used for digitalis induced arterial and ventricular arrhythmia.	Hypertrophy Anaemia Osteomalacia	Hydroxylation
3	Mexiletine	–	Bradycardia	Hydroxylation
4	Tocainide	Only used in ventricular type	Agranulosotosis Thrombocytopenia	–
5	Aprinidine	–		–

Class-Ic agent

Sr. no	Name and structure of drug	Characteristics	Metabolism
1	 Propafenone	R and S isomer sodiumchannel Blocker and S is β-blocker.	Hydroxylation (active)
2	Encainide	–	–
3	Flecainide	It contains piperidine ring	O-dealkylated
4	Moricizine	It contains morpholine ring.	–

- **Mechanism of action:** It strongly slows down depolarization in phase-0.
- **Class-II agent:**
- Various β-blockers like Propanolol, Esmolol, Sotalol. It is used as antiarrythmic agent.
- **Class-III agent:**
- **Mechanism of action:** It prolongs repolarization.

Sr. no	Name and structure of drug	Characteristics	Specific side effect
1	 R= $(C_2H_5)_2$ Amiodarone	Due to iodine, it is highly lipophilic and inhibits conversion of T_4 to T_3	Slate-grey or blue skin.
2	Bretylium tosylate	It is used parentrally.	–

Methane sulfonamide derivatives

1	Sotalol.	L-isomer of sotalol having β and K^+ channel blocking activity while D-isomer has only K^+ channel blocking activity	–
2	Dofetlide	–	–
3	Ibutilide	–	–
4.	Azimilide **(Imidazolinedione derivative)**	–	–

Class-IV agent.

1. **Vearapamil:** It is given with digoxin to patients with poor by controlled artrial fibrillation.
2. **Diltiazem:**

Anti-hypertensive agent

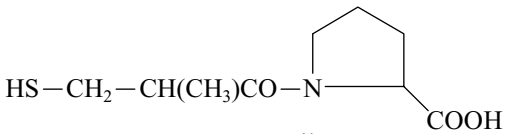
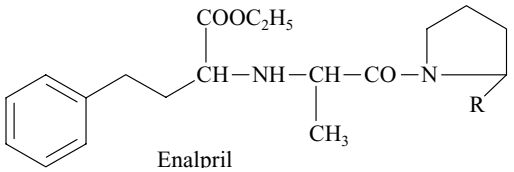
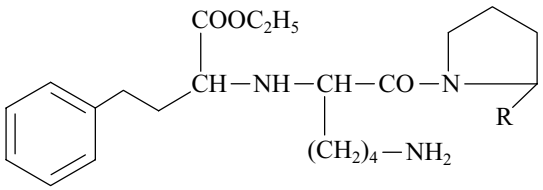
- **Drug acting on Renin angiotensin system:**

(1) Renin inhibitor

Example: Propanolol, Clonidine, Enalkiren, Ramikiren, Terlakiren, Zankiren, Diltiazem.

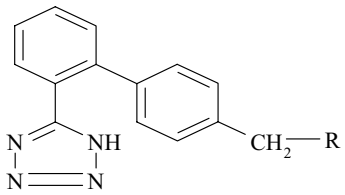
(2) ACE inhibitor

- **Mechanism of action:**
  (1) It inhibits conversion of **angiotensin–I to angiotensin-II**
  (2) It also **increases bradykinin level and vasodialation**.

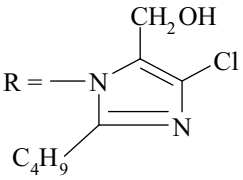
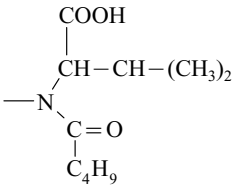
Sr. no	Structure and name of drug	Characteristics	Specific side-effects	Metabolism
1	 Captopril	Thiol group increase bind to zinc of ACE.	Hyperthermia Dysguesia Cough Renal stenosis.	–
2	 Enalpril **Enalpril R=COOH**	Alanine contains prodrug.	Devoid of Dysguesia.	Ester hydrolysis Enalprilate (diacid-form (active)
3	 **Lisinopril R=COOH**	Lysine containing drug not prodrug.	–	–
4	**Benzapril**	It contains Benzazepine ring.	–	–
5	**Quinapril**	It contains Isoquinoline Ring.	–	
6	**Ramipril**	It contains Pyrrolidine ring	–	–
7	**Fosinopril**	Phosphorous Contains ACE inhibitor.		

(3) **Angiotensin-II antagonist with AT_1 receptor blocker:**

General structure:



SAR: It contains ***tetrazole ring which bind to AT_1 receptor***.

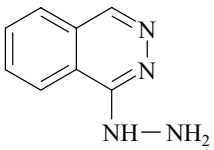
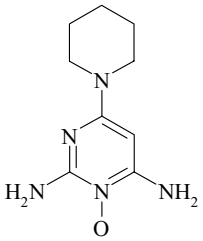
Sr. no	Structure and name of the drug	Characteristics	Specific side-effects	Metabolism
1	**Losartan,** 	It contains Imidazole ring.	–	5–CH_2OH convert into COOH group which is15 times more potent than parent.
2	**Valsartan,** R = 	It is valine containing drug.	–	–
3	**Candesartan**	It contain R= benzimidazole ring with ester group.	–	Ester hydrolysis to acid.
4	**Telmisartan**	It contains R=COOH group … which binds to AT_1 receptor	–	–

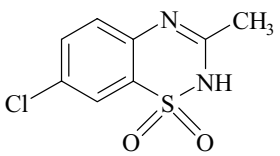
- **Specific side effect:** Fetal damage, Hyperkalemia.

  (4) Only Angiotensin-II inhibitor: Saralasin which need parentral route.

- **Vasodialator**

1. Arteriolar agent

Sr. no	Structure and name of drug	Characteristics	Specific side-effects	Metabolism
1	 **Hydralazine**	It acts by nitrate mechanism.	Lupus syndrome Nasal stuffness.	Benzylic oxidation And acetylation. (inactive)
2	 **Minoxidil**	It requires metabolic activation by sulfotransferase for antihypertensive use.	Hirsutism (So use in alopecia) Tachycardia. Sodium and water retention.	–

Sr. no	Structure and name of drug	Characteristics	Specific side-effects	Metabolism
3	 **Diazoxide**	It is like thiazide diuretic but causes sodium and water retention.	Hyperglycemia.	–

2. Arteriolar and venous dialator:

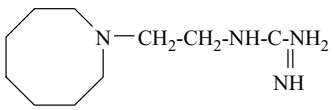
Sr. no	Structure and name of drug	Characteristics	Specific side-effects	Metabolism
1	Sod.nitroprusside	Acts by nitrate mechanism	Thiocynate toxicity. Perspiration.	Metabolized to thiocynate.
2	Pinacidil	It contains pyridine ring.	–	–
3	Cromakalim	It contains cromane ring.	–	Active isomer is lemakalim.

Drug acting on sympathetic system:

1. Central sympatholytic agent:

Sr. no	Structure and name of drug	Characteristics	Specific side-effects	Metabolism
1	α-methyl dopa	It acts on α_2 receptor.	Postural hypotension	–
2	Clionidine	It is α_2 agonist and imidazoline derivative.	Bradycardia Constipation	P-hydroxy derivative.
3	Guanabenz	It is α_2 agonist.	–	–
4	Guanafacine	It contain guanidine ring.	–	–

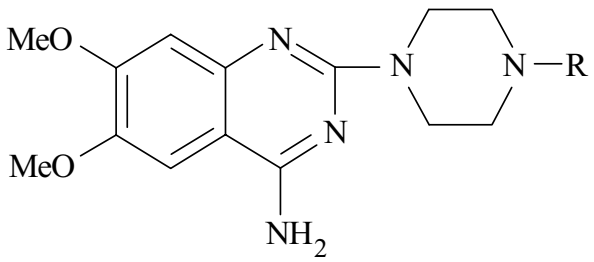
2. Catecholamine depletor and adrenergic neuron blocker:

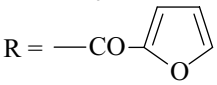
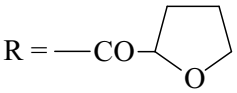
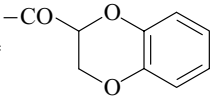
Sr. no	Structure and name of drug	Characteristics	Specific side-effects	Metabolism
1	Reserpine	It depletes catecholamine.	Diarrhoea, Bradycardia	Methyl reserpate and 3, 4, 5 trimethoxy benzoic acid.
2	Guanethidine 	It contain azocine ring.	–	N-oxide. Carboxy derivative.
3	Debrisoquine	–	–	–
4	Guanoxon	–	–	–
5	Bretylium	–	–	–
6	Bethanidine	–	–	–

3. Ganglion blocker

- **Quaternary ammonium compounds:** Hexamethonium, Pentolinium, Chlorocondamine.
- **Secondary amine derivative:** Mecamylamine
- **Tertirey amine derivative:** Pempidine, Trimethophan.
- **Drug acts by reflex mechanism:** Protoveratrine obtained from veratrum alkaloids.

4. Selective α_1 blocker: (General structure)



Sr. no	Structure and name of drug	Characteristics
1	Prazosin, 	–
2	Terazosin, 	Long acting agent.
3	Doxazosin, 	Long acting and water soluble compound.
4	Quinazosin R = $-CH_2-CH=CH_2$	–

Specific side effect: (1) First dose hypertension (2) Postural hypotension (3) Impotence.

Use: Specifically in management of hypertension associated with Pheochromocytoma.

Non selective α blocker

(1) Phenoxybenzamine
(2) Phentolamine
(3) Tolazoline

Use: In pheochromocytoma and clonidine withdrawal syndrome.

5. Mixed α and β blocker

- **Labetalol:** It is used to treat hypertension during pregnancy.
- **Carvadilol:** It contains antioxidant property.

6. β *blocker:* Detailed study in ANS.

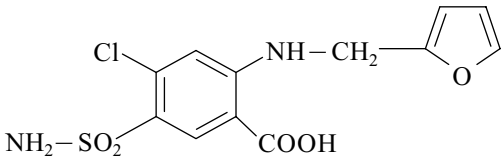
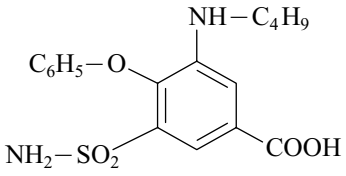
7. *Diuretics:* Thiazide, loop and potassium sparing diuretics also used. (Detail in diuretics)

The compound which promotes flow of urine by increasing excretion of sodium and water is called as diuretics.

Classification:

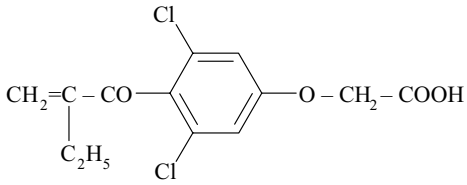
1. High Celling diuretics

a. Sulfamoyl derivative: (loop diuretic because it acts in ascending loop of henle)

Sr. no	Structure and name of drug	Characteristics	Metabolism	Side-effects
1	**Furosemide** 	It is anthrnilic acid derivative. It has 60% bioavailability.	By Glucuronide pathway	–
2	**Bumetanide** 	It has 100% bioavailability. It is meta amino benzoic acid derivatives.	By CPY-450 pathway.	–

3	**Piretanide**	It contains pyrrolidine ring	–	–
4	**Torasemide**	It is inactivate-SH group of enzyme and decreases sodium reabsorption.	–	Hepato Toxicity and Diar-rhoea.

b. Ethacrynic acid (phenoxy acetic acid derivatives)



c. Organomercurial

Example:

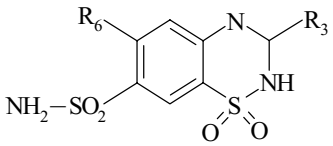
(1) Mersalyl
(2) Merbaphen
(3) Meralluride
(4) Mercaptomerin
(5) Chlormerodrin

- **Mechanism of action:** They first release mercury ion which inactivates –SH group of enzyme.
- **Note:** It is given as I.M or subcutaneously except Chlormerodrin which is given orally.
- **Common side effect** of High celling diuretics: (1) Hypokalemia (2) Hypocalcemia.

(1) Moderately potent diuretics:

(a) Thiazide diuretics/Benzothiadiazine derivative:

General structure:

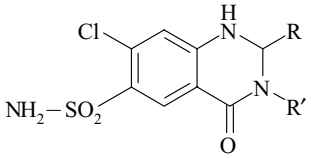


Sr. no	Name of drug	R_3	R_6
1	Hydrochlorthiazide	H	Cl
2	Hydroflumethiazide	H	CF_3
3	Triclomethiazide	$CH–(Cl)_2$	Cl
4	Bendroflumethia-zide	$CH_2–C_6H_5$	CF_3
5	Polythiazide	CH_2-S–$CH_2–CF_3$	Cl

- **Note:** Thiazide diuretics cause lithium and digoxin toxicity.
- **Common side effect:** (1) Gitelmann's syndrome (2) Bartter's syndrome.

(b) Quinazolinone derivative:

General structure:



Sr. no	Name of drug	R	R′
1	Quinethazone	$–C_2H_5$	H
2	Metolazone	$–CH_3$	$–CH_3–C_6H_5$

(c) Pthalimidine derivative/1-oxo isoindole derivative: Example is Chlorthalidone

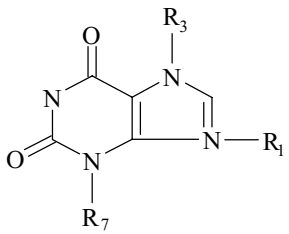
(d) Indole derivative: Example is Indapamide

(2) Weak diuretics:

(a) Osmotic diuretics:

- **Non-electrolyte type:** (1) Mannitol (2) Sorbitol (3) Urea (4) Isosorbide (Bicyclic form of sorbitol)
- **Mechanism of action:** It forms hypertonic solution which causes water to pass from body to kidney tubule.
- **Electrolyte type:**
- Example: NaCl, KCl, Sodium carbonate, Sodium acetate, etc.

(b) Xanthine alkaloids/Purine derivative: General structure:

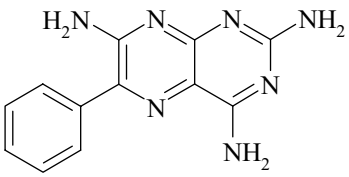
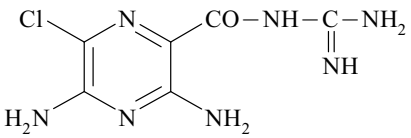
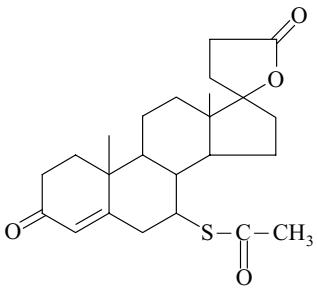


Sr. no	Name of drug	R_1	R_3	R_7
1	Theophylline	CH_3	CH_3	H
2	Theobromine	H	CH_3	CH_3
3	Caffeine	CH_3	CH_3	CH_3

- **Theophyline:** Most active diuretics.

(c) Potassium sparing diuretics:

- **Mechanism of action:** It blocks sodium reabsorption and decrease potassium excretion.

Sr. no	Structure and name of drug	Characteristics	Metabolism	Side-effects
1	**Triamterene** 	It contains pteridine ring. It is given with thiazide is counteract hyperkalemic effect.	In liver, convert, into active metabolite.	It is very photosensitive.
2	**Amiloride** 	It contains pyrazine ring and amidine moiety. It is 10 times more potent than triamterene.	It is not metabolized.	–
3	**Spironolactone** 	It is potent aldosterone antagonist as it prevents it binding. It causes digoxin toxicity.	It is metabolized to canrenone (which does not contain thioacetyl group at 7 position) which is antagonist to aldosterone.	Gynecomastia Atrophy
4	**Eplerenone**	Aldosterone antagonist.	It contains carbomethoxy group at seven positions.	–

(d) Carbonic anhydrase inhibitor

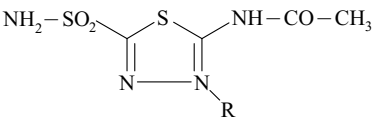
- **Mechanism of action:** Carbonic anhydrase is found in many sites such as renal cortex, eye, CNS, gastric mucosa, and pancreas. This enzyme catalyses the reversible hydration of CO_2 to carbonic acid.

$$\mathbf{CO_2 + H_2O\text{–carbonic anhydrase-----}H^+ + HCO_3^-}$$

- The diuretics inhibit the carbonic anhydrase enzyme at the proximal convoluted tubules cause reduction in H+ ions for Na^+–H^+ exchange CO_2 reabsorption from glamerular filtrate is suppressed and HCO_3^- excretion is increased and facilitates K^+ secretion.

Example:

General structure:



Sr. no	Name of drug	R	Characteristics
1	Acetazolmide	H	It is also use in glaucoma, seizure.
2	Methazolamide	CH_3	–

6. Anti-diabetic agent

Type of diabetes:

(1) Type-1 dibetes (IDDM)/juvenile onset:

Insulin deficiency occurs due to destruction of β cell.

(2) Type-2 diabetes (NDDM)/Maturity onset.

Insulin resistance occurs.

Insulin: It contains 51 amino acids arranged in chain-A 21 and chain-B contains 30 amino acid and both connected by two sulphur bridge, and synthesized from proinsulin (84 amino acid).

Classification

A. *For Type-1 diabetes:* Various insulin preparations are used.

(1) Short acting agent

Sr. no	Insulin preparation
1	Regular insulin
2	Amorphous insulin zinc suspension (Semi-lente)
3	Insulin aspart
4	Insulin lispro

(2) Intermediate acting

Sr. no	Insulin preparation
1	Globin zinc insulin
2	Lente suspension
3	NPH (Neutral protamine hagedorn)

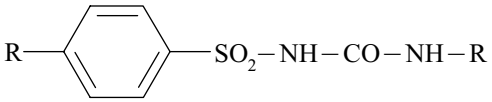
(3) Long acting

Sr. no	Insulin preparation
1	Protamine zinc insulin
2	Ultralente
3	Glargine insulin

For type-2 diabetes

(A) Sulfonylurea derivative

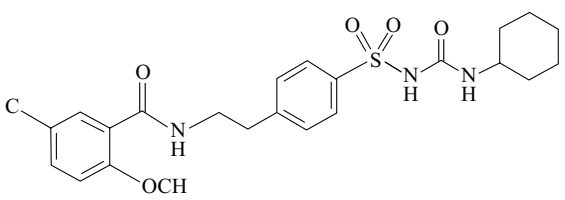
General structure:

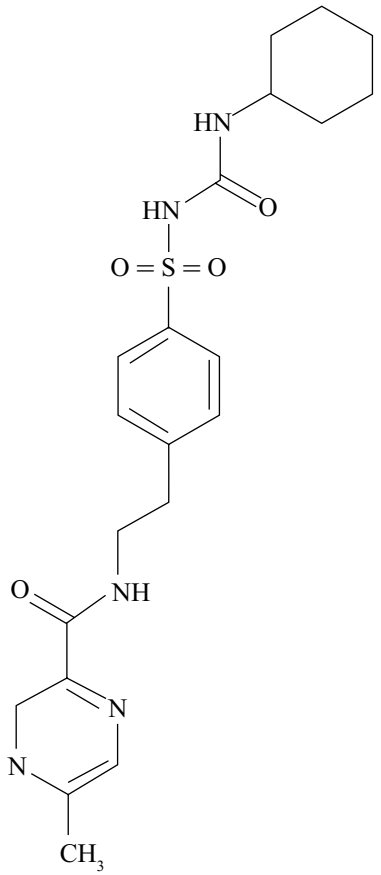


(1) First generation drugs:

Sr. no	Name of drug	Characteristics	Metabolism
1	**Tolbutamide** R=CH_3, R′=C_4H_9	–	P-hydroxy derivatives. (active)
2	**Chloroprop-amide** R=Cl, R′=C_3H_7	Used in diabe-tes insipidus and gives disulfiram like effect, causes jaundice.	Hydroxy derivatives.
3	**Acetohexamide** R=CH_3–CO– R′=Cyclohexane ring	–	Reduction (ketone to alcohol) (inactive) Hydroxyl-ation (active)
4	**Tolazamide** R=CH_3, R′=Azepine ring	–	–

(2) Second generation drugs:

Sr no.	Name of drug	Characteristics	Metabolism
1	**Glibenclamide (glyburide)** 	Inhibiting ATP-sensi-tive potassium channels	4-hydroxy derivatives.

Sr no.	Name of drug	Characteristics	Metabolism
2	**Glipizide** 	Pyrazine containing drug Diuretic action.	N-acetyl derivatives.
3	**Glimepiride**	–	–
4	**Gliclazide**	It has antiplatlet action.	–

(3) Third generation drugs:

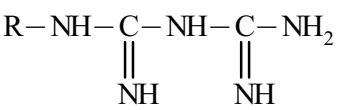
- Glybonuride is more potent than tolbutamide and forms six inactive metabolites.
- Mechanism of action: They act on sulfonylurea receptor on pancreatic cell membrane and block ATP sensitive potassium channel.
- Note: All Sulfonyl urea derivatives except glibenclamide cross placenta and cause hypoglycemia at birth.
- Common side effect: All stimulate appetite, Leukopenia, photosensitivity.

(B) Non-sulfonyl urea derivative or Meglinide derivative: (contain D-phenylalanine)

- Repaglinide
- Nateglinide

(C) Biguanide derivative

General structure:



(1) Phenformin: R = $–C_6H_5–CH_2–CH_2$

(2) Metformin: R = $(CH_3)_2–N–$

- **Mechanism of action:** They increase glucose uptake and decrease insulin resistance.

Common side effect: (1) Lactic acidosis (2) Vit B_{12} deficiency

(D) Alpha glucosidase inhibitors

- **Acarbose:** It is a naturally occurring oligosaccharide.
- **Miglitol:** It is desoxy nojirimycin derivative and chemically piperidinetriol derivative.
- **Varcabose:**

(E) Thiazolidinediones derivative

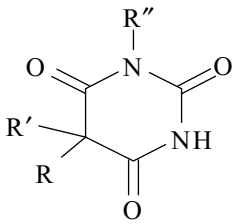
- Rosiglitazone
- Pioglitazone
- **Mechanism of action:** They activate PPAR-γ and enhance transcription of insulin responsive gene and increase insulin sensitivity.
- **Side effect:** Myalgia, Mild anaemia.
- **Interaction:** They inhibit ketoconazole absorption.

Drugs Acting on CNS

1. Sedative and hypnotics

Chemical Classification

(1) Barbiturates: General structure—Chemically, it is tri keto saturated pyrimidine derivative.



Long acting drug (duration of action–>6 hr)

Sr. no	Name of drug	R	R′	R″
1	Mephobarbital	C_2H_5	C_6H_5	CH_3
2	Phenobarbital	C_2H_5	C_6H_5	H
3	Barbital	C_2H_5	C_2H_5	H

Intermediate acting drug (duration of action 3 to 6 h)

Sr. no	Name of drug	R	R′	R″
1	Amobarbital	C_2H_5	$–CH_2–CH_2–CH(CH_3)–CH_3$	H
2	Butabarbital	C_2H_5	$–CH(CH_3)–CH_2–CH_3–$	H

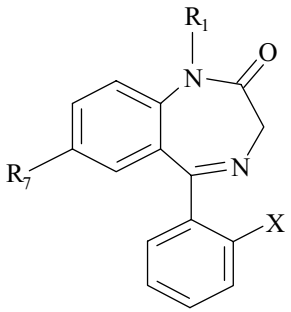
Short acting: (duration of action–< 3h)

Sr. no	Name of drug	R	R′	R″
1	Pentobarbital	$–C_2H_5$	$–CH(CH_3)–CH_2–CH_2–CH_3–$	H
2	Secobarbital	$–CH_2–CH=CH_2$	$–CH(CH_3)–CH_2–CH_2–CH_3$	H
3	Cyclobarbital	$–C_2H_5$	Cyclohexene	H
4	Heptabarbital	$–C_2H_5$	Cycloheptene	H

Ultra short acting: (duration of action <1 h)

Sr. no	Name of drug	R	R′	R_2
1	Thiopental	C_2H_5	$–CH–(CH_3)–CH_2–CH_2–CH_3$	S
2	Thiamylal	$–CH_2–CH=CH_2$	$–CH(CH_3)–CH_2–CH_2–CH_3$	S
3	Hexobarbital	C_2H_5	Cyclohexene	$R″=CH_3$

Benzodiazepine: General Structure



- **Hydroxyl group contains benzodiazepine drug at third position:**

Sr. no	Name of drug	R_1	R_7	X
1	Oxazepam	H	Cl	H
2	Lorazepam	H	Cl	Cl
3	Temazepam	CH_3	Cl	H

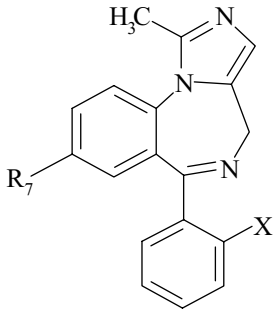
- **Non-hydroxy benzodiazepine drug: Does not contain 3-OH group.**

Sr. no	Name of drug	R_1	R_7	X
1	Diazepam	CH_3	Cl	H
2	Nitrazepam	H	NO_2	H
3	Clonazepam	H	NO_2	Cl
4	Prazepam	CH_2–cyclopropyl	Cl	H
5	Quazepam	CH_2–CF_3	Cl	F

Triazolobenzodiazepine Drug

It contains fused ***triazole*** ring. Except ***midazolam which contains imidazole ring***.

General structure:



Midazolam

Sr. no	Name of drug	R_1	R_7	X
1	Alprazolam	Fused triazole ring	Cl	H
2	Triazolam	Fused triazole ring	Cl	Cl
3	Midazolam	Fused imidazole	Cl	F

Newer benzodiazepine Drug

Example is Zolpidem, Zaleplon.

Mechanism of action: It facilitates GABA activated chloride channel and increase GABA concentration.

Pharmacokinetics profile:

Sr. no	Drug	Plasma half life (h)	Metabolism (Metabolite)	Plasma half life of metabolite
1	Triazolam	2–4	Hydroxylation	< 6 h
	Midazolam	2–4	Hydroxylation	< 6 h
2	Diazepam, Chlordiazepoxide	20–40	Nordazepam	60 h
3	Flurazepam	1	Desmethyl flurazepam	60 h

(2) Ureides derivative:

Example: Apronalide, Bromasuvalum, Capuride, Cabromal.

All are bromine containing compounds are very toxic because of bromism.

(3) Piperidinedione derivative:

Example : Methgyprylon, Glutethimide.

(4) Chloral derivative: Chlorobutanol, Dichlorophenazone.

(5) Carbamate derivative: Meprobamate which is central muscle relaxant and anti-anxiety.

(6) Amide derivative: Triacetamide, Valuoctamide, Oxonamide

(7) Acetylene derivative: Methyl pentynol, Ethchlorovynol, Ethinamate.

Local anesthetics

Chemistry

- All local anaesthetics are weak base and Pka is 8 to 9 so not completely ionized at physiological pH so easily penetrate nerve and axonal membrane.
- All local anaesthetics contains lipophilic group like aromatic ring which attach to hydrophilkc moiety by Ester or Amide linkage.

Aromatic ring-------Ester or amide linkage-----Basic amino side chain

- All above contain moiety except benzocaine which does not contain basic amino group.
- **Mechanism of action:**

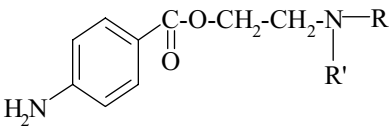
They block increase in sodium conductance by S6 trans-membrane helical domain of channel protein.

Chemical Classification

(A) Ester derivative:

(1) Amino alkyl ester of para amino benzoic acid.

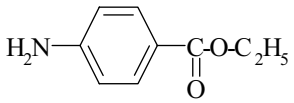
General structure:



Sr. no	Name of drug	Characteristic	Metabolism
1	Procaine R and R′=C_2H_5		Ester hydrolysis
2	Tetracaine (Amethocaine) R and R′= CH_3	It contains butyl additional chain at 4th position	By cholinesterase

(2) Alkyl ester of p-amino benzoic acid.

Example: Benzocaine



(3) Ester of benzoic acid:

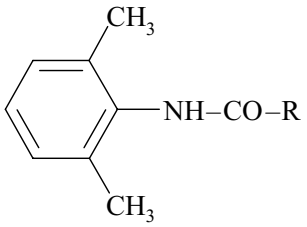
Example:

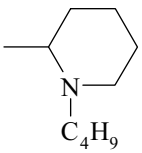
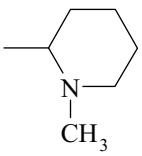
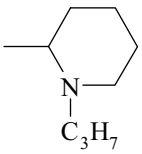
(**1**) **Cocaine:** It is obtained naturally from ***Erythroxylum coca***.

(**2**) **Piperocaine** and **Cyclomethycaine:** Both contain piperidine ring.

(B) Amide derivative

General structure:



Sr. no	Name of drug	Characteristics	Metabolism	Side-effects	R
1	Lidocaine	It is also used in ventricular arrhythmia.	N-dealkylation (glycine xylide) (active)		CH_2–N–$(C_2H_5)_2$
2	Prilocaine		N-dealkylation	Methaemoglobinemia	CH $(CH_3)_2$–NH–C_3H_7
3	Bupivacaine	Levo form is use	N-dealkylation	Cardiotoxic (If racemic mixture is used)	
4	Mepivacaine		N-dealkylatiion		
5	Ropivacaine		N-dealkylation		

Application profile:

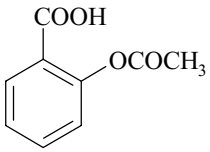
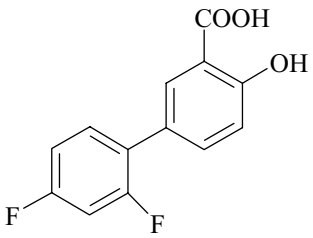
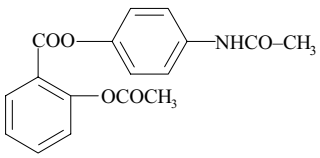
Sr. no	Method	Drugs
1	Surface anaesthesia	Lidocaine, Amethocaine, Benzocaine
2	Infiltration anaesthesia	All
3	IV anaesthesia	Lidocaine, Prilocaine
4	Nerve block anaesthesia	All
5	Spinal anaesthesia	Lidocaine, Amethocaine
6	Epidural anaesthesia	Lidocaine, Bupivacaine

NSAIDS

- It is also called as ***non-opioid analgesic.***
- **Mechanism of action:** It inhibits cyclooxygenase enzyme (COX) so inhibit a production of prostaglandin.

Chemical Classification:

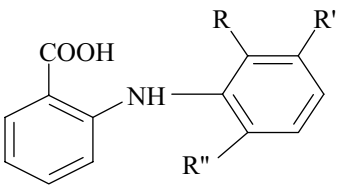
(1) Salicylate and salicylic acid derivative:

Sr. no	Name and structure of drug	Characteristics	Metabolism	Side-effects
1	 Aspirine	-Irreversibly block COX-1 and COX-2 -Also obtained from spirea plant	Ester hydrolysis in 30 min of administration to salicylate (active)	-Reye's syndrome -Gastric irritation
2	 Diflunisal	It contains hydrophobic aryl group provide strongly potent as antiinflammtory Than aspirin.		
3		It is esterification of paracetamol and aspirin which is long acting.		
4	Sulfasalazine	Used in ulcerative colitis		

- **Common side effect: Salicylism**

(2) N-anthranilic acid derivative:

General structure:



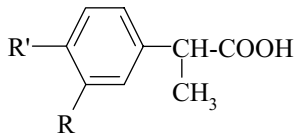
Sr. no	Name of drug	R	R′	R″	Characteristics
1	Mefenamic acid	CH_3	CH_3	H	It is metabolised by oxidation. Diacid form (inactive)

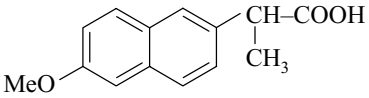
Sr. no	Name of drug	R	R′	R″	Character-istics
2	Flufenamic acid	H	CF_3	H	Five times more potent than mefenamic acid.
3	Meclof-enamic acid	Cl	CH_3	Cl	

- **Common side effect:** Haemolytic anaemia, Diarrhoea

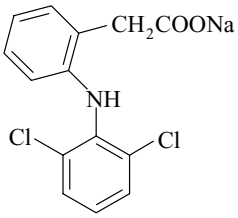
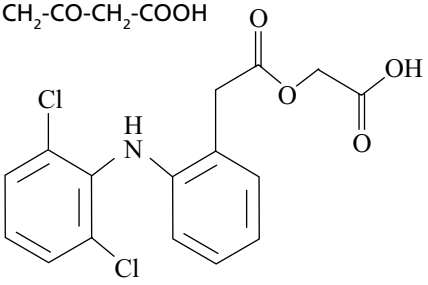
(3) Aryl propionic acid derivative:

General structure:



Sr. no	Name of drug	Characteristic	Metabolism	Side effect
1	Ibuprofen R=H, R′= $CH_2CH(CH_3)_2$	S (+) is active		Hepatotoxicity, Constipation
2	Phenoprofen R= O–C_6H_5, R′=H	S (+) is active (35 times more potent)	Hydroxylation	Anti-platlet
3	Ketoprofen R= C=O–C_6H_5			
4	Flurbiprofen R=F, R′=C_6H_5	Used topically to prevent miosis during ocular surgery.		
5	Indoprofen	Contain 1-oxo iso indole ring.		
6	Naproxen 	Dextrorotatory drug and if re-places COOH by OH/CHO, retains activity.	6-desmethyl Naproxen (inactive)	Used in acute gout also

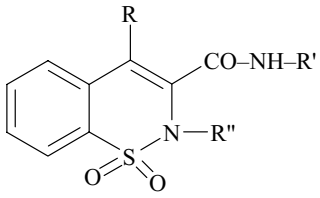
(4) Aryl and Hetero aryl acetic acid derivative:

Sr. no	Drug	Characteristic	Metabolism	Side effects
1	Diclofenac sodium 	It decreases arachidonic acid level in leuko-cyte. It raises lithium and digoxin level in plasma.	–	Acidity
2	Aciclofenac CH_2-CO-CH_2-COOH 	It is prodrug of diclofenac.	–	–

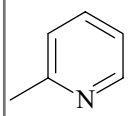
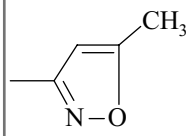
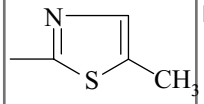
Sr. no	Drug	Characteristic	Metabolism	Side effects
3	Ketorolac	It contains pyrollidine ring.	Used in migraine	Glucuronidation
4	Tolmetin	It is pyrole acetic acid derivative.		Oxidation (diacid) (inactive)

(5) Enolic acid derivative/Benzothiazine derivative:

General structure:

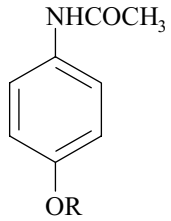


- **Common side effect: Peptic ulcer, toxicity.**

Sr. no	Name of drug	R	R′	R″	Characteristics
1	Piroxicam	OH		CH_3	Long acting Half life (45h) Used in acute gout.
2	Isoxicam	OH		CH_3	
3	Meloxicam	H		H	

(6) Aniline and p-Aminophenol derivative:

General structure:

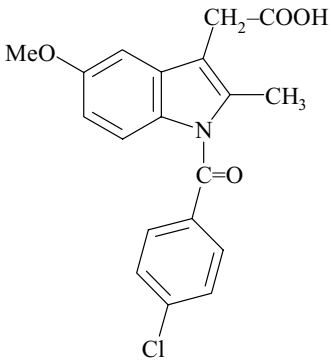


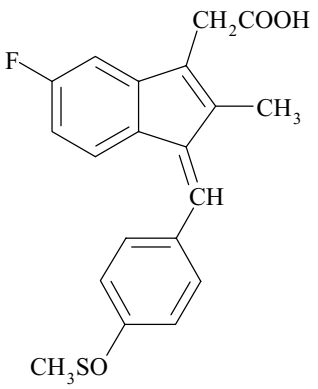
Sr. no	Name of drug	R	Characteristics	Metabolism
1	Phenacetin	C_2H_5	Prodrug of paracetamol	O-dealkylation
2	Paracetamol	H	Cause hepatotoxicity, thrombocytopenia, anaemia	It forms N-acetyl p-benzoquinone (at toxic dose)

(7) Pyrazole/Pyrazoline derivative: (potent analgesic and antipyretic)

- Antipyrine (phenazone): Use as analgesic in otic preparation.
- Aminopyrine
- Analgine (Metamizol)
- **Common side effect:** Agranulocytosis

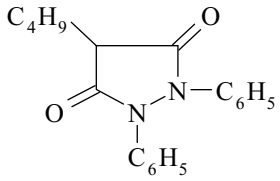
(8) Indole acetic acid derivatives

Sr. no	Structure and name of drug	Characteristics	Side effects
1	Indomethacin 	S (+) is active and given as IV in infants. p-Anisidine (p-methoxy aniline) is used as starting material for synthesis. Contraindicatd in epilepsy, pregnancy.	Leukopenia Hallucinogen Psychosis

Sr. no	Structure and name of drug	Characteristics	Side effects
2	Sulindac 	It is prodrug (half life is 8 h) by reduction to form sulfide metabolite which is active. (half life is 16.4 h). It is contraindicated with aspirin because of decrease in sulfide blood level.	Diarrhoea

(9) 3, 5 pyrazolidinedione derivative.

- Example is Phenylbutazone

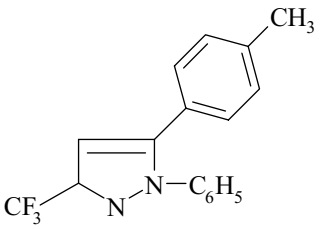


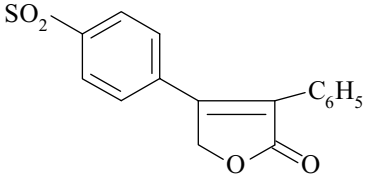
- **Metabolism:** By hydroxylation form, oxyphenylbutazone (active).
- **Side effect:** (1) Agranulocytosis (2) Aplastic anaemia (3) Bone marrow depression (4) Steven Jhonson syndrome (5) With salicylate black stool form.

(10) Nefopam: It is a recently introduced drug which does not inhibit prostaglandin synthesis and as potent as morphine.

(11) Selective COX-II inhibitors: It is potent NSAIDs.

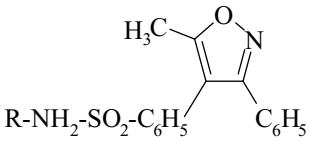
(A) First generation drugs:

Sr. no	Structure and name of drug
1	Celecoxib 

Sr. no	Structure and name of drug
2	Rofecoxib 

(B) Second generation drug/Isoxazole derivative:

General structure:



Sr. no	Name of drug	R	Characteristic
1	Valdecoxib	H	
2	Paracoxib	$-COC_2H_5$	It is given parentrally.

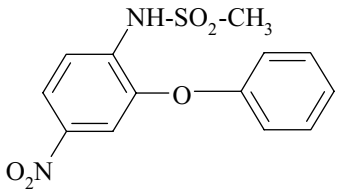
(C) Third generation drug:

Example: (1) Etocoxib (2) Lumaricoxib.

Note: All selective COX-II inhibitor cause CVS toxicity.

(12) Miscelleneous:

Example: (1) Nimesulide: It is aryl sulfonamide derivative.



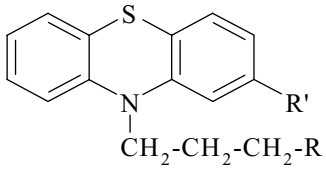
Anti-Psychotic drugs (neuroleptic, major tranquillizer)

Classification

1. Typical antipsychotic drugs

A. Phenothiazine derivative

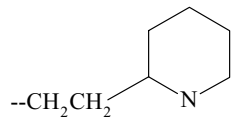
General structure:



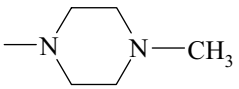
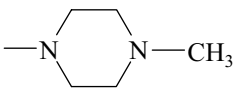
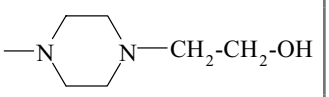
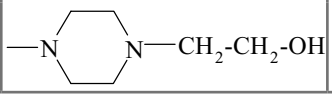
Aliphatic side chain contain drug:

Sr. no	Name of the drug	R	R′
1	Chlorpromazine	N–$(CH_3)_2$	Cl
2	Triflupromazine	N–$(CH_3)_2$	CF_3

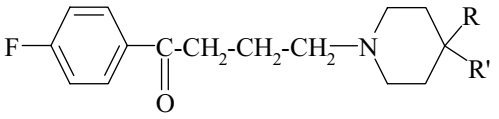
Piperidine side chain drug:

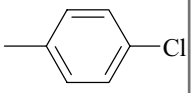
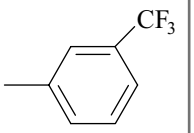
Sr. no	Name of drug	R	R′
1	Thioridazine		SCH_3

Piperazine side chain contain drug:

Sr. no	Name of drug	R	R′
1	Trifluperazine		CF_3
2	Prochlorpera-zine		Cl
3	Perphenazine		Cl
4	Fluphaenazine		CF3

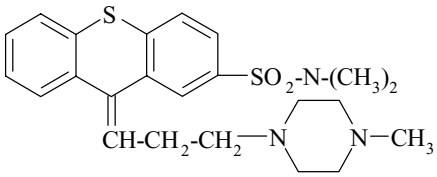
B. Fluorobutyrophenone derivative (General structure)



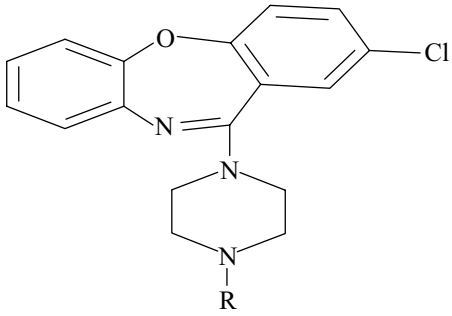
Sr. no.	Name of the drug	R	R′
1	Haloperidol	OH	
2	Trifluperi-dol	OH	
3	Droperidol	Contain fused benz-imidazolinone.	

(C) Thioxanthene derivative:

Example is Thiothixene having Z isomer which is clinically active.



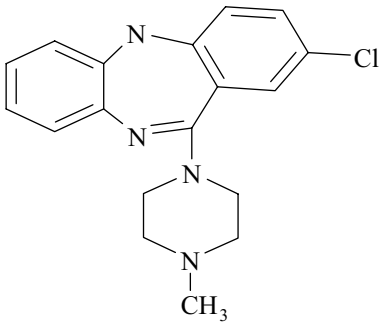
(D) Dibenzoxazepine derivative: (General structure)



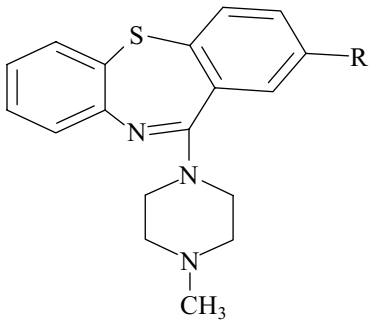
Sr. no	Name of drug	R
1	Loxapine	CH_3
2	Amoxapine	H

B. Atypical antipsychotic:

Dibenzdiazepine derivative: Clozapine which is selective D_2 and 5-HT_{2a} blocker



Dibenzthiazepine derivative: Metiapine, Clothiapine, quetiapine.



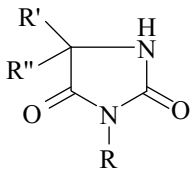
Clothiapine: R = Cl
Metiapine : R = CH_3

- **Indole derivative:** Molindone, Sertindol, oxypertine.
- **Benzoquinoline derivative**: Tetrabenazinre
- **Fluorobutyrophenone derivative:** Risperidone
- **Benzodiazepine derivative:** Olanzapine

5. Anti convulsant

A. Hydantoin derivative

General structure:



Sr. no	Name of drug	= R″	R′	= R
1	Phenytoin	C_6H_5	C_6H_5	H
2	Mephenytoin	C_6H_5	C_2H_5	CH_3
3	Ethotoin	C_6H_5	H	C_2H_5

Mechanism of action: It blocks sodium channel.
Metablosim: Hydroxylation

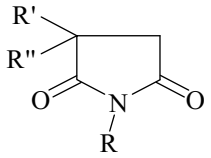
Side effect:

- Gum hypertrophy
- Megaloblastic anaemia
- Osteomalacia
- Hyperglycemia

Use: In all type of seizures except petit-mal type.

B. Succinimide derivative:

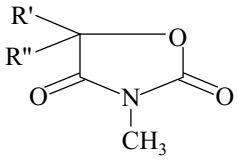
General structure:



Sr. no	Name of the drug	= R″	R′	= R
1	Phensuximide	C_6H_5	H	CH_3
2	Methsuximide	C_6H_5	CH_3	CH_3
3	Ethosuximide	C_2H_5	CH_3	H

- **Side effect:** Bone marrow depression.
- **Use:** Specifically in petit-mal seizure.
- **Mechanism of action:** They block T-type calcium channel.

C. Oxazolidinedione derivative: General structure

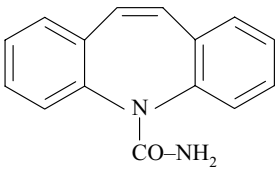


Sr. no	Name of drug	R′	R″
1	Trimethadione	CH_3	CH_3
2	Paramethadione	CH_3	C_2H_5

Metabolism: By N-demethylation trimethadione converts into dimethadione which is T-type calcium channel blocker.

D. Iminostilbene derivative or urea derivative.

Example is Carbamazepine



Metabolism: Oxidation (10, 11 epoxide form) (active) but cause aplstic anaemia also.

Recently, Oxacarbazepine is used which contains oxo group at 10 position and no aplastic anaemia.

E. Aliphatic carboxylic acid derivative: Valproic acid or Sodium valproate

It is dipropyl acetic acid derivative which is used in petit mal seizure.

F. Phenyltriazine derivative

Example is Lamotrigine which contains triazine ring.

G. Benzodiazepine derivative: Clonazepam, Diazepam, Clobazepam.

H. Barbiturates

Desoxybarbiturates: Primidone

I. Miscellaneous

- **Gabapentin:** It is cyclic GABA analogue and block T-type calcium channel.
- **Vigabatrine:** It inhibits GABA transaminase
- **Tiagabine:** It is nipecotic acid derivative and inhibit GABA reuptake.
- **Zonsamide and Topiramate:** It is aryl sulfonamide derivative.
- **Carbonic anhydrase inhibitor:** Acetazolamide

Anti-depressent

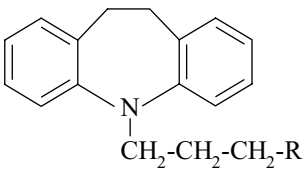
Classification

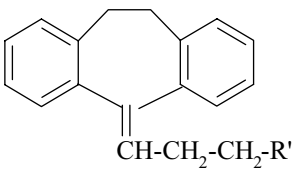
A. Tricyclic antidepressant: (Nor-adrenaline reuptake inhibitor)

i. **Tertiary amine derivative:** Imipramine, Trimipramine, Amitryptyline, Doxepine

ii. **Secondary amine derivative**: Desipramine, Nortryptyline, protryptyline, amoxepine, maprotiline

General structure:





Sr. no	Name of drug	R	R′
1	Imipramine	N $(CH_3)_2$	–
2	Triimipramine	N $(CH_3)_2$, On C-2 of Propyl chain there is a substitution of $–CH_3$ (Methyl) group	–
3	Desipramine	NH–CH_3	
4	Amitriptyline	–	N $(CH_3)_2$
5	Nortriptyline	–	NH–CH_3

- **Common side effect:** Anticholinergic type, postural hypotension.
- **Metabolism**-By N-demethylation of imipramine to desipramine. (ACTIVE)

B. Selective serotonin reuptake inhibitors (SSRI)

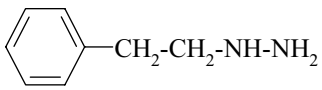
- Examples are Fluoxetine, Fluvoxamine, Citalopram, Sertaline, and Paroxetine.
- General plasma half life is 15–24 h except fluoxetine (96 h)
- **Common side effect:** Anorexia, Insomnia, Anorgasmia.
- **Interaction:** Serotonin reaction with MAO.

C. MAO Inhibitor

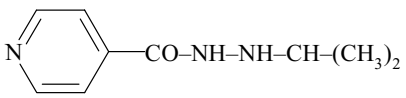
MAO-A inhibitor is **Anti depressant,** MAO-B inhibitor is **Anti pakinsonism**

Classification:

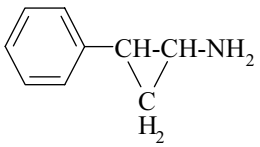
1. **Hydrazine derivative:**
   Phenelzine



   Iproniazid



   Nialamide
   Isocarboxazide: It contains Isoxazole ring.
2. **Cyclopropylamine derivative:**
   - Pargyline
   - Clorgyline
   - Tranylcypromine
   - Selegiline (selective MAO-B inhibitor)



Side effect:

- Cheese reaction
- Postural hypotension.

D. Non-selective uptake inhibitor

- Venlafaxine
- Duloxetine
- Hyperforin: Obtained from natural St Jhon's wart.

Miscellaneous

- Trazodone and Bupropion
- **Raboxetine:** Selective NA reuptake inhibitor, and causes anti cholinergic side effect.
- Mirtazepine

Narcotic-analgesic (Opioid analgesic)

- The narcotic analgesics are also called as opiate analgesics. These are mainly obtained from unripe capsules of ***papaver somniferum*** (Opium poppy) plant. The important alkaloid is isolated from opium is morphine. The other alkaloids isolated from opium are codeine, Papaverine and thebain.

Classification

1. Morphine Analogues:

Morphine Sulphate, Codeine Phosphate, Ethyl Morphine, Diacetyl morphine (Heroin), Hydro morphoneHCl, Oxy morphone.HCl, Apo morphine.HCl, Hydrocodone, Oxy codone, Dihydromorphine, Dihydro codeine

2. Morphinan Analogues:

Levorphanol tartarate, Dextro methorphan, Butorphanol

3. Morphan Analogues:

Metazocine, Cyclazocine, Pentazocine.

4. 4-Phenyl Piperidine Analogues:

Meperidine.HCl (Pethidine.HCl), Di phenoxylate.HCl, Fentanyl citrate, Anileridine.HCl, Phenoperidine, Alphaprodine.HCl, Loperamide.HCl.

5. Phenyl propylamine Analogues:

Methadone.HCl, Dextro propoxyphene.HCl, Metho Trimeprazine.

6. Miscelleneous:

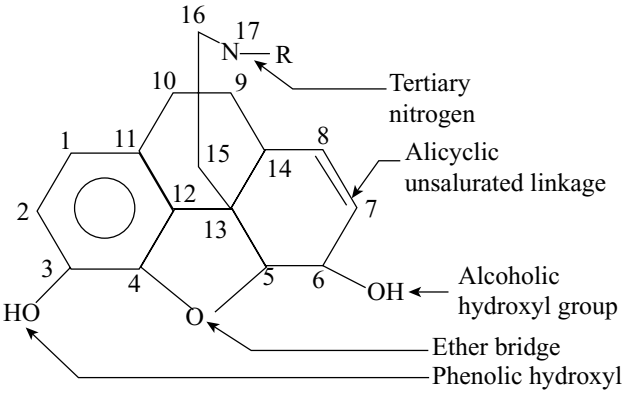
Tramadol, Tilidate, Nexeridine, Sulfentanil.

7. Narcotic Antagonists:

Nalorphine, Naloxone, Levellorphan, Naltrexene, Cyclazocine, Propiram, Profadol

SAR for Morphine like drugs

General Structure



The structural activity relationship is studied due to the modifications of the following parts of morphine.

(1) Modifications on aromatic ring system
(2) Modifications on alicyclic ring system
(3) Modifications of tertiary nitrogen
(4) Modifications of ether Bridge

I. Modifications on aromatic ring system

- An aromatic phenyl ring is essential for activity.
- Modifications of C_3 Phenolic hydroxyl group decreases analgesic activity.
- Making the Phenolic–OH group by etherification to methyl ether (Codeine) and ethyl ether (ethyl morphine) results in about one tenth of analgesic activity of morphine. Because Phenolic –OH group binds with opiate receptor by hydrogen bonding easily. But ethers are not easily hydrolysed.
- Esterification of 3–OH group gives compounds more active than morphine.
- Substances other than 3-position in the aromatic ring results in a reduction of opioid actions. But 1-fluoro codeine possesses some analgesic activity as that codeine.

II. Modifications on alicyclic ring system

- The C-6-α-OH group is methylated, esterified, oxidized, removed or replaced by halogen in order to get more potent analgesics. But there is also a parallel increase in toxicity. Example: Codeine, heroin, chloro morphone.
- The saturation of double bond at C-8 position gives more potent compounds. Example: Dihydromorphine, Dihydrocodeine.
- Introduction of 14 –OH in dihydro from gives more potent 14–hydroxy dihydro codeinone and 14–hydroxy dihydro morphinone.

- Bridging of C6 and C14 through ethylene linkage gives etorphine which is 200 times more potent than morphine.
- Introduction of any new substituents at 5th position does not enhance the activity except 5–methyl dihydro morphine and azidomorphines.

III. Modifications of 3⁰ Nitrogens

- Replacement of N–CH_3 by N–C_2H_5 results in slight fall in analgesic response. More hydrophobic groups such as propyl, pentyl, hexyl and phenylethyl gives an increase in activity.
- N-allyl and N-cycloalkyl methyl functions gives the narcotic antagonistic properties.
- N-Phenyl ethyl group enhances the analgesic activity in desmorphine, codeine and heterocodeine.

IV. Modifications of Ether Bridge

- Breaking of Ether Bridge and opening of piperidine ring decreases the activity.

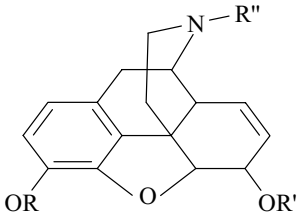
Mechanism of action

The pharmacological actions of opiods are mediated by several types of opiate receptors in the CNS.

1. **There are three major types of opiod receptors:**
   (i) **Mu (m)**–op3 receptors–produce analgesia, respiratory depression, Euphoria and addiction.
   (ii) **Kappa (K)**–op2 receptors–produce dysphoria, Euphoria and addiction.
   (iii) **Delta (d)**–op1 receptors–G–proteins–linked receptors.
2. Morphine binds to m receptor and induces change in shape and opens the ion channel in cell membrane. So K+ ion can flow out of the cell, hyperpolarizes membrane potential. Therefore the frequency of action potential firing is decreased; resulting in a decrease in ion neuron excitability.
3. The increase in permeability decreases the influx of Ca into nerve retinal and reduces neuro transmitter release. Both the effects shut down the nerve and block pain message.
4. Kappa receptor is directly associated with Ca channel. When an agonist binds to K receptor, the Ca channel is closed. Since Ca is necessary for neurotransmitter it cannot pass on pain message.
5. When agonist binds with d (delta) receptor, the receptor changes its shape and triggers a messenger protein (G protein) to carry a message to a neighboring enzyme with catalyses the formation of cyclic adenosine monophosphate. The G protein inactivates the enzyme by preventing the synthesis of cyclic AMP. This acts as a second messenger is the transmission of pain signed and stops the pain.

(1) Morphine like ring contains derivatives:

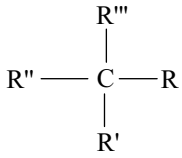
General structure



Sr. no	Name of drug	R	R′	R″
1	Morphine	H	H	CH_3
2	Codeine	$-CH_3$	H	CH_3
3	Heroin	$-CH_3C=O$	$-CH_3-C=O$	CH_3
4	Pholcodeine	H	H	$O-CH_2CH_2-$ Morpholine
5	Nalorphine	H	H	$CH_2-CH=CH_2$
6	Naltrexone	H	H	CH_2–Cyclopropyl
7	Nalbuphine	H	H	CH_2–Cyclobutyl

(2) Methadone derivatives:

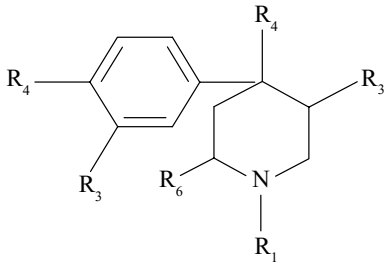
General structure:



Sr. no	Name of drug	R	R′	R″	R‴
1	Methadone	C_6H_5	C_6H_5	$C=O-C_2H_5$	$-CH_2-CH(CH_3)-N(CH_3)_2$
2	propoxyphene	C_6H_5	$CH_2-C_6H_5$	$O-C=O-C_2H_5$	$CH(CH_3)-CH_2-N(CH_3)_2$

(3) Meperidine derivatives:

General structure:



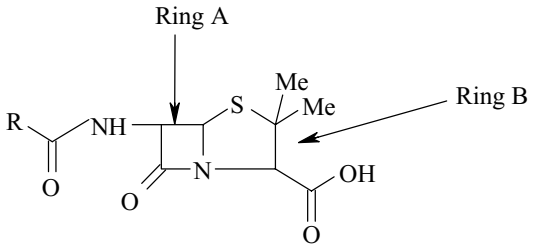
Sr. no	Name of drug	R_1	R_3	R_4	R'_3	R'_4
1	Meperidine	CH_3	H	$COOC_2H_5$	H	H
2	Bemindone	CH_3	H	$COOC_2H_5$	OH	H
3	Trimeperidine	CH_3	CH_3	$OCOC_2H_5$	H	H

CHEMOTHERAPY

Antibiotics

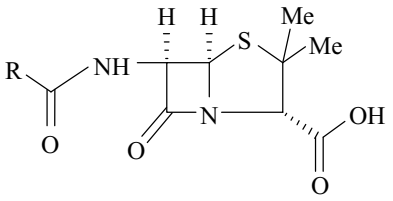
β-Lactam Antibiotics-Penicillin and Cephalosporin Penicillin

It is obtained from ***Penicilin Notatum*** and ***Penicillin Chrysogenam***.

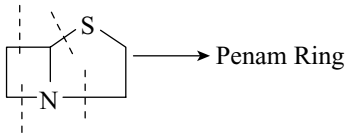


- Ring A is a four membered **β-Lactam ring (cyclic amide)**
- Ring B is a five membered **Thiazolidine ring**
- **Degradation product of penicillin:**
  - At acidic pH-***Penillic Acid***
  - At basic pH-***Penicilloic acid***
- **Certain strands of micro organism destroy β-Lactam antibiotics enzymatically like Penicillanase or β-Lactamase (Open the β-Lactam ring).**

Stereochemistry and IUPAC of β-Lactam ring



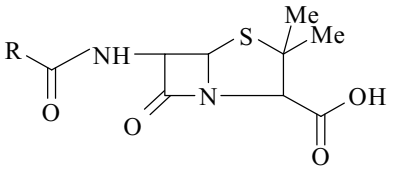
- It has total ***three chiral carbon*** like 3, 5 and 6.
- All synthetic and semi synthetic penicillin having same absolute configuration ***(like 3S and 5R, 6R)***.
- Acyl amino and carboxylic acid ***Trans*** to each other.
- The lead molecule in the discovery of semi synthetic penicillin is ***6 amino penicillinic acid (6-APA)***.
- 6-APA structurally derived from ***L-Valine and L-cysteine***
- All penicillins has **Penam ring** as a basic moiety.

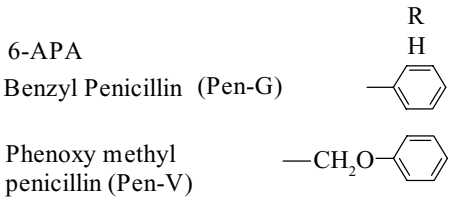


1-Aza-4-thia-Bicyclo [3.2.0] heptane

Classification

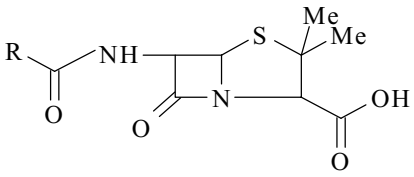
1. Fermentation derived penicillin

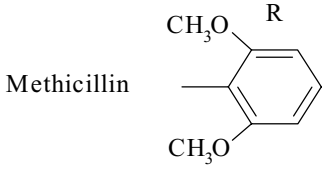


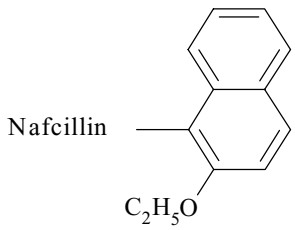


2. Semi synthetic penicillanase resistance penicillin: Parenteral Penicillin

E.g., Methicillin, Nafcillin



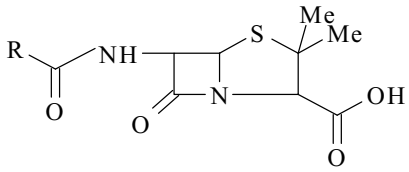




Methicillin-2, 6-Dimethoxy phenyl penicillin
Nafcillin-2-Ethoxy-1-Napthyl-Penicillin

3. Semi synthetic penicillanase resistance penicillin: Oral Penicillin

- It contains isoxazole as a basic moiety.
- 5-Hydroxy methyl penicillin derivative is a metabolite.
- It is applicable to penicillin sensitive patients.



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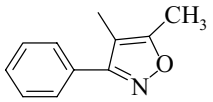
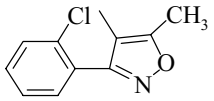
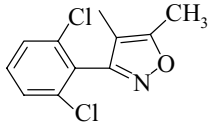
Oxacillin 

Cloxacillin 

Dicloxacillin 

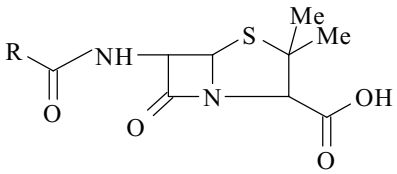
- **Oxacillin-**5-Methyl-3-Phenyl-4-isoxazolyl penicillin
- **Cloxacillin**-5-Methyl-3-(2-chlorophenyl)-4-isoxazolyl penicillin
- **Dicloxacillin-5**-Methyl-3-(2, 6-di chlorophenyl)-4-isoxazolyl penicillin

Note

Extra halogen is responsible for increasing fraction bound to protein in the plasma potentially reduce the concentration of free antibiotics in plasma and tissue.

4. Semi synthetic penicillanase sensitive broad spectrum parental penicillin

(Anti psedomonal penicillin-Ticarcillin, Carbencillin)



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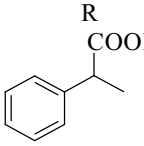
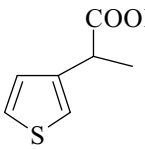
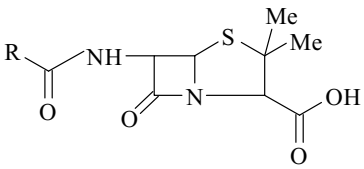
Carbencillin 

Ticarcillin 

Ticarcillin is an isoster of carbencillin, and it having thiophene ring azlocillin.



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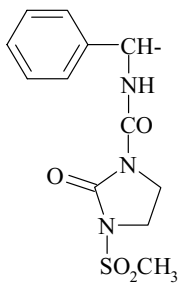
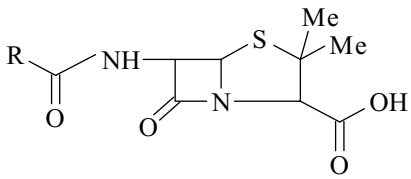
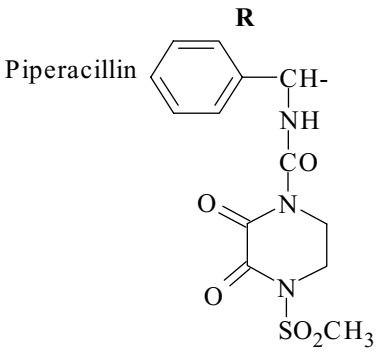
Mezlocillin 

Azlocilin: SO_2CH_3 is replaced by H.

Azlocillin and mezlocillin have **Oxoimidazolidino** basic moiety.

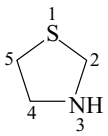
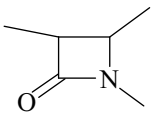
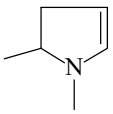
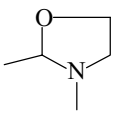
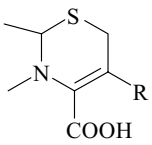
Piperacillin: has dioxo piperizine





SAR of penicillin

- All β-lactam antibiotics contain 4 membered β-lactam rings fused with N atom and tetrahedral carbon to a second heterocyclic ring.

Penicillin (Penam Ring)		**Thiazolidine** 
Thienamycin (Carbapenam)	**β-lactam** 	**Pyrrolidine** 
Clavulanic acid (Oxapenam)		**Oxazolidine** 
Cephalosporin (Cepham Ring)		**Dihydrothiazine** 

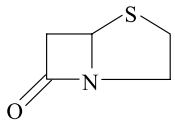
- Penicillin is unstable under acidic and basic condition so manipulation ***of polar amide groups*** leads to increased potency as well as chemical and physical stability.
- Introduction of ***chemical inducer/precursor*** in culture medium leads to increasing quantity as well as quality of penicillin production.
  E.g., ***phenyl acetic acid*** is added as a chemical inducer in production of 6-APA.
- Some bacteria like gram negative bacilli are resistant to action of penicillin due to production of β-lactamase enzyme. So many semi synthetic penicillin were developed by manipulation of C-6 polar amide group.
- Increasing steric hindrance at α carbon of acyl group increases resistance to staphylococcal β-lactamase like substitution of Aromatic (Phenyl, Napthyl) ring or any heterocyclic ring (Isoxazoyl-Oxacillin, Cloxacilln) or ring substitution at ortho position (2, 6 dimethoxy substitution on phenyl ring of methicillin) and (2 ethoxy substitution on napthayl ring of Nafcillin).
- Incorporation of an ionized/polar/acidic substitution on α carbon of side chain of benzyl carbon atom of benzyl penicillin increasing activity against gram negative bacilli.
  E.g., Ampicillin, Amoxicillin, Carbencillin
- All natural penicillins are dextrorotatory.

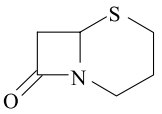
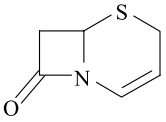
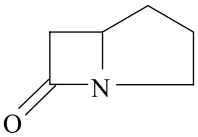
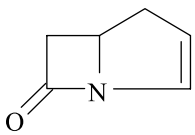
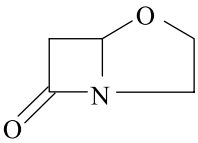
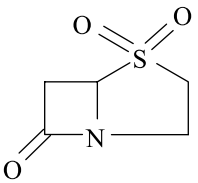
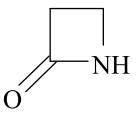
Depot preparation of penicillin-having limited water solubility and release drug over a longer periods.

E.g., Procaine Penicillin-Amine salt of penicillin G with procaine
Benzathin Penicillin
Hydrabamine penicillin

Mechanism of β-lactam antibiotics

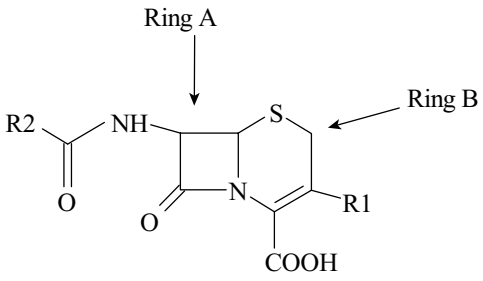
- *Inhibition of bacterial cell wall synthesis by inhibiting the synthesis/production of* ***peptidoglycan****.*
- Cell wall of bacteria is essential for normal growth and development.
- ***Peptidoglycan*** is an essential constitutent of bacterial cell wall, and it is a heteropolymeric components of cell wall responsible for the providing stability.
- ***Glycan chain*** is made up of two alternating amino sugar (NAM-N-Acetyl muramic acid) and (NAG-N-Acetyl Glucosamine) by peptide linkage.

β lactam rings	Name of ring	Examples
	Penam	Penicillin

β lactam rings	Name of ring	Examples
	Cepham	Cephalosporins
	Cephem	.....
	Carbapenam	Thienamycin, Imipenam, Meropenam Biapenam
	Carbapenem	(β lactamase inhibitors)
	Oxapenam	Clavunic acid (β lactamase inhibitors)
	Penam-1, 1-Dioxide	Salbactum, Tazobactam
	Monobactam	Saulfazecin, Aztreonam, Tigemonam (β lactamase resistance agent)

CEPHALOSPORIN

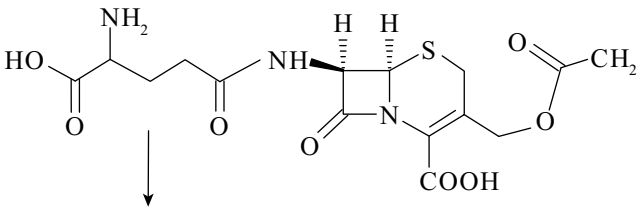
Source: Cephalosporium Acremonium



Cepham ring IUPAC-5-Thia-1-Aza-Bicyclo[4.2.0] Oct-2-ene

- Ring A is a four membered **β-Lactam ring (cyclic amide)**
- Ring B is a six membered **Dihydrothizine ring.**
- Cephalosporin having **cepham** as a basic moiety
- Like 6-APA in penicillin, 7-Amino cephalosporic acid is a lead molecule for synthesis semi synthetic cephalosporin
- **Cephalosporin C-**True cephalosporin or 7-ACA
- **Cephalosporin P-**Acidic antibiotics or Steroidal antibiotic (Fusidin)
- **Fusidin-**It is sodium salt of fusidic acid.
- **Cephalosporin N-**Derivative of 6-APA, Also known as Synnnematin N now a days, it is known as Penicillin N.
- **Semi synthetic cephalosporin prepared by modification in**
- Acylation of 7-Amino cephalosporic acid.
- Reduction of 3-Acetyloxy group.

Cephalosporic Acid (Cephalosporin C)



Alfa amino adipoyl side chain

(If α Amino adipoyl side chain is removed from Cephalosporin C by breaking of amide bond to structure of 7ACA)

MACROLIDE ANTIBIOTICS

Sources: Actinomycetes

Common Structural features of Macrolide antibiotics

- A many membered (12, 14 and16 atoms) lactone ring-hence named Macrolide
- Various ketonic and –OH functional group.
- Glycosidically linked to 6-deoxy sugar

Picromycin first identified drug of Macrolide antibiotics.

- E.g., Spiramycin, Oleanlomycin, Erythromycin
- Semi-synthetic derivative of erythromycin

- Roxithromycin
- Dirithromycin
- Clarithromycin
- Azithromycin

Mechanism of Action

- It binds selectively to a specific site on **50S ribosomal** unit to prevent the translocation step of bacterial protein synthesis.
- It does not bind to mammalian ribosomes.

Pharmacokinetic

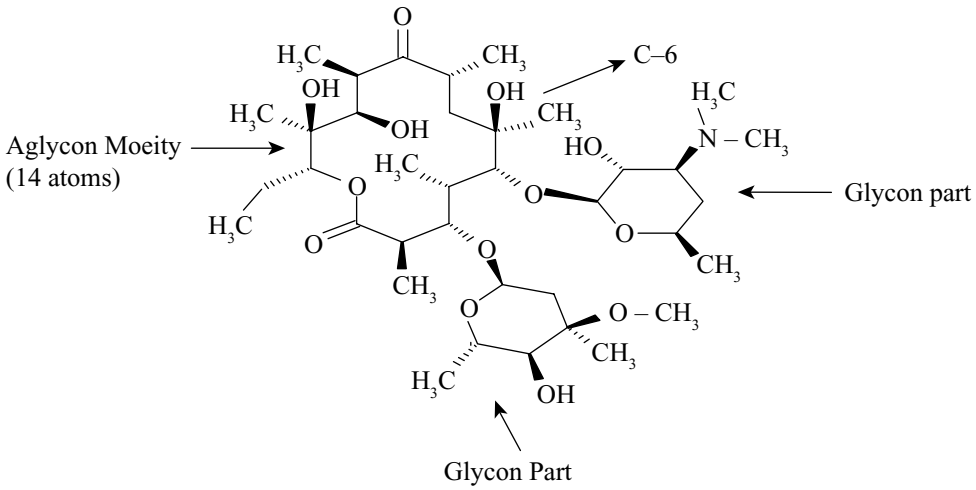
- All macrolides are destroyed by acidic pH so it is always formulated in enteric coated tablet form.

Spectrum of Activity

- Active against gm+ve cocci, bacilli and gm-ve cocci
- Also active against H.Influenza, mycoplasma pneumonia, N.Gonorrhoea and legionella

Erythromycin-*Streptomyces Erythraeus*

Erythromycin



- Commercial product is Erythromycin A which is different from Erythromycin B in having –OH group at 12 position of aglycon.
- Erythronolide-Aglycon part of Erythromycin
- Glycon part-1. Basic ring-Desosamine 2. Neutral ring-cladinose

While in case of Erythromycin C, it has Mycarose as a neutral glycon part instead of Cladinose

- It acts as Enzyme inhibitors (***Cyto-P-450 oxidase***) for other drugs.
- Like Theophylline, Hydroxy coumarine, Benzodiazepine (Alprazolam, Midazolam), carbamazepine. Cyclosporine, Anti histaminic drugs
- While activity of terfenadine and astimizole is potentiate by Erythromycin.
- Stability of Erythromycin is at or neutral pH (7)

Clarithromycin-6-methyl ether derivative of Erythromycin. (6-OH group is methylated to 6-OCH_3).

- It acts as Enzyme inhibitors (***Cyto-P-450 oxidase***) for other drugs.
- Specifically used to treat Lyme disease caused by ***Borrelia Burdorferi.***

Azithromycin, prepared by Beckmann rearrangement of 9-Oxime followed by N-methylation and reduction of resulting ring expanded lactam.

Nitrogen containing 15 membered rings Macrolide is known as Azalides.

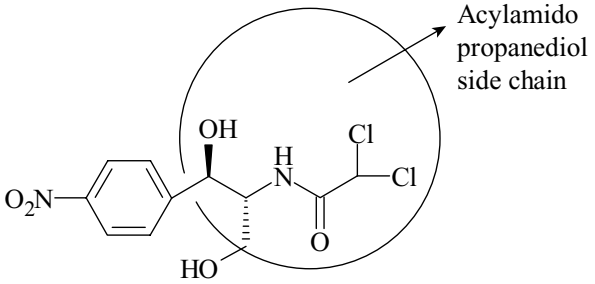
- It does not act as enzyme inhibitors (***Cyto-P-450 oxidase***) for other drugs.
- Removal of 9-keto group-increasing stability of azithromycin to acid catalysed degradation. These change also increase lipid solubility.

Dirithromycin-Having 9N, 11 O-Oxazine ring

CHLORAMPHENICOL

Sources: Streptomyces Venezuelae

- Broad spectrum antibiotic
- Now a days, it is prepared by synthetic route from ***p-Nitro acetophenone***.



Chloramphenicol

- It has two chiral carbons, so a total of four (4) isomers are possible D-erythro, L-erythro, D-threo and L-threo.
- Among these four isomers, ***D-threo*** isomer is most active. The prodrug of Chloramphenicol viz., Chloramphenicol palmitate (USP) which is a tasteless product is intended for pediatric usage.

Metabolism

Major route: Formation of 3-O-Glucrodination
Minor route: Reduction of p-Nitro group to amino

Mechanism of action: Inhibition of protein synthesis by binding with ***50s*** subunits of ribosomes.

Use

- Meningitis
- Active against gm+ve and gm-ve bacteria that is resistant to PenicillinG and ampicillin.
- Active against H.Influenza, S.Typhi, S.Pneumonia, B.fragilis and N.meningitis
- In UTI
- Rickettsial infections as ***"Rocky mountain Spotted Fever"***

Adverse Effect: Grey baby syndrom

Note

Chloramphenicol has a bitter taste so it is always available in Palmitate and Succinate ester form and acts as prodrug.

AMINOGLYCOSIDE

Chemically, it is aminosugar obtained from actinomyces.

Classification:

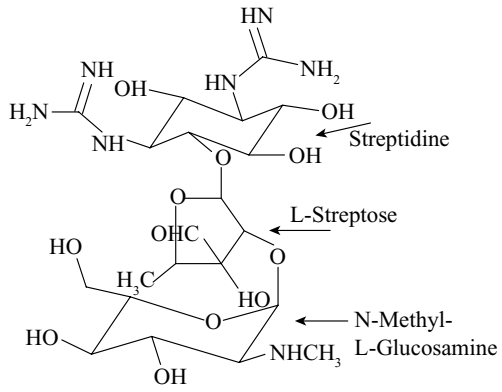
Streptomycin family	Kanamycin family	Gentamycin family	Neomycin family
Streptomycin	Kanamycin	Gentamycin	Neomycin
Dehydro-Streptomycin	Amikacin	Sisomycin	Framycetin
It has 2 amino sugar	Tobramycin	Netilmycin	Paramomycin-Anti amoebic agent
	It has 2 amino sugar		It has 2 amino sugar
			Not given parentraly, is topically applied

Aminoglycosides	Obtained from
Streptomycin	***Streptomyces Griseus***
Kanamycin	***Streptomyces kanamyceticus***
Tobramycin	***Streptomyces tenebrarius***
Gentamycin	***Micromonospora purpurea***
Neomycin	***Streptomyces fradiae***
Framycetin	***Streptomyces decaris***
Paramomycin	***Streptomyces Rimosus***
Amikacin	Semisynthetic derivative of Kanamycin A
Netilmycin	Semisynthetic derivative of Sisomycin
Sisomycin	

Chemistry

- Amino sugar linked glycosidically
- All have at least one amino hexose and some have a pentose lacking an amino group (Streptomycin, Neomycin, Paramomycin).
- 1, 3-Diamino cyclohexane central ring present in Kanamycin, Neomycin, Gentamycin and Tobramycin.
- All aminoglycosides are available in sulphate form.
- They do not enter in CNS, bone or connective tissue because they exist as polycation at physiological pH.

Streptomycin



Streptomycin

- On acid hydrolysis, Streptomycin yields Streptidine and Streptobiosamine (L-Streptose and N-Methyl-L-Glucosamine)
- Streptomycin A having D-ribose and Streptomycin B having mannose sugar part.

Neomycin

- It does not having anti-.bacterial but anti fungal activity.
- Basic Structure: Neosamine C----Deoxystreptamine---D-Ribose------Neosamine C

Paramomycin

- Basic structure: D-glucosamine----Deoxystreptamine -----D-Ribose------Neosamine B/C
- **It is structurally similer to neomycin.**
- **Used in GIT infection by salmonella and anti amoebic agent.**

Amikacin

Acylation of 1-amino group of deoxystreptamine ring of Kanamycin A with L-Amino hydroxyl butyric acid.

Gentamycin

Basic structure: Purpurosamine---Deoxystreptamine---Gasosamine

Used in Tularemia a lymphoid disease.

Netilmycin

Chemically it is 1-N-ethyl sisomycin.

Anti Bacterial Spectrum

- Broad spectrum antibiotics
- Effective on Aerobic gm-ve bacilli and Aerobic gm+ve and gm–ve cocci
- Anerobic bacteria are resistant to aminoglycoside.

Mechanism of action

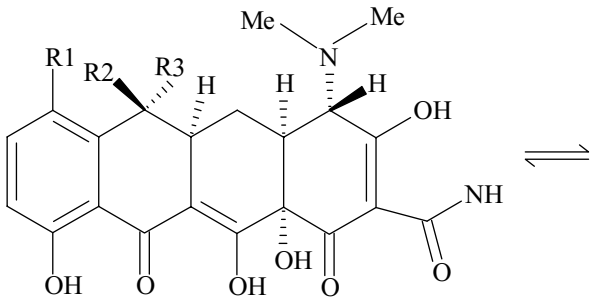
The aminoglycoside acts directly on bacterial 30s ribosomal unit to inhibit the protein synthesis.

Adverse effect

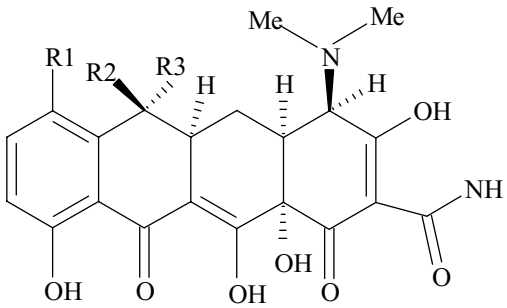
- Ototoxicity
- Nephrotoxicity
- Neuromuscular paralysis due to decrease ach release
- Allergic reaction

Tetracycline

- Carbon atom 4, 4a, 5, 5a, 6 and 12a are potentially chiral.
- Oxytetracycline and doxycycline each with 5α-OH substituents have six asymmetric centres while others have only five asymmetric centres.
- The basic ring present in Tetracycline is polycyclic napthacene carboxamide.
- All Tetracycline are amphoteric in nature.
- At pH-7, it is converted into Zwitterion.
- Ability to undergo epimerization at C-4 in solution of neutral pH range (7).



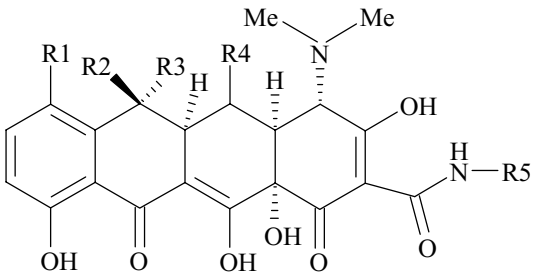
Tetracyclin



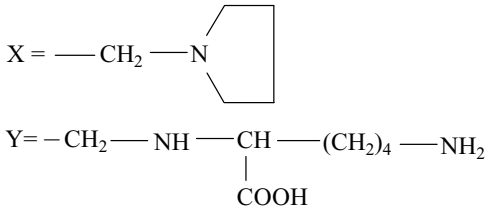
Epi tetracyclin

- Tetracycline forms *chelate complex* with many metals like *calcium, magnesium and iron.* Chelates are usually insoluble in water which impaired absorption of tetracycline in presence of milk, Ca, Mg and Al containing antacids.

- Affinity of tetracycline for calcium causes them to be incorporated into newly forming bones and teeth as tetracycline-calcium orthophosphate complex.
- Deposition of these antibiotics in teeth causes yellow discoloration.
- In pregnancy, Tetracycline is distributed into milk of lactating mother and it crosses the placental barrier into fetus causing harmful effect on bone and teeth of child.



Name	R_1	R_2	R_3	R_4	R_5	Source
7-Chlorotetracyclin	Cl	CH_3	OH	H	H	S.aureofaciens
Oxyetracyclin	H	CH_3	OH	OH	H	S.rimosus
Doxycyclin	H	CH_3	H	OH	H	Semisynthetically from Oxyetracyclin
Tetracyclin	H	CH_3	OH	H	H	Semisynthetically from 7-Chlorotetracyclin
Demeclocyclin	Cl	H	OH	H	H	Mutant strain of S.aureofaciens
Methacyclin	H	$=CH_2$		OH	H	Semisynthetically from Oxyetracyclin
Minocyclin	N $(Me)_2$	H	H	H	H	Semisynthetically from Oxyetracyclin
Rolitetracyclin	H	CH_3	OH	H	X	Semisynthetically from tetracyclin
Lymecycline	H	CH_3	OH	H	Y	Mannich base of tetracyclin



Miscellaneous Class Antibiotics

Lincomycin and clindamycin

- Source: S.lincolnensis
- Sulphar containing antibiotics
- It acts on 50s ribosomal sub unit.
- It having pyrrolidine ring attached with sugar part.

2. Polypeptide Antibiotics

- Source: Bacilli Species
- **Anti TB antibiotics**-Capreomycin, Viomycin
- **Anti tumor antibiotics:** Bleomycin, Actinomycin
- **Glucopeptide:** Vancomycin
- **Others:** Polymixin, Bacitracin, Colistin
- All are in cyclic nature (except: Gramicidine)

3. Novobiocin

- Source: **S.Niveus**
- The structure contains substituted benzoic acid, **Coumarin** and sugar part.
- Glycon part is **Noviose**
- Aglycon part is **Novobiocic acid**

4. Fosfomycin

- Source: S.fradie
- Synthetically, it is **derivative of Phosphoric acid**.
- Mechanism of action: **Interferes in first step in bacterial cell wall**.
- It is having an **epoxy ring** in its structure.

Anti amoebic agent

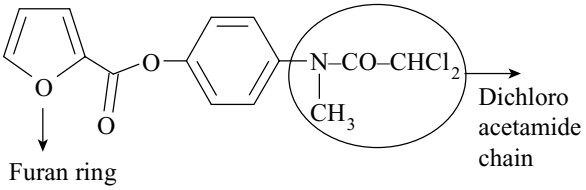
Amoebiasis: It is an infection of the mucous membrane of the large intestine where ***"Entamoeba Histolytica"*** is a causative organism.

Classification:

(1) Luminal Amoebicides

- Effective for organism presents in bowel lumen.

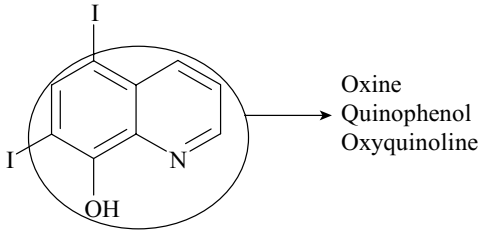
- It is very effective because of poor oral absorption, so drugs remains in intestine for a long time.
  e.g., Diloxamide Furoate, Teclozan, Etofamide



- It is a prodrug, ***dichloro acetamide derivative*** used to treat chronic amoebiasis.
- Adverse effect: Urticaria, Pruritis, Flatulence

8-Hydroxy quinolines Derivative

- Example, Di-iodohydroxyquin (Iodoquinol), Iodochlorohydroxyquin (Clioquinol)
- All are halogenated 8-Hydroxy quinolines derivatives



Iodoquinol

Adverse effect: Optic neuropathy

Contraindication: Drug therapy increases plasma iodine level. This agent must be used with caution in patients hypersensitive to iodine or with thyroid dysfunction.

Mechanism of action: It kills trophozoites and cysts in intestinal tract by chelating ferrous ion which is essential for protozoal metabolism.

Adverse effect

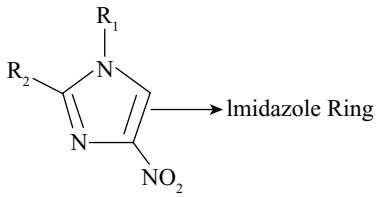
Blurred vision, Optic neuropathy, Peripheral neuropathy

2) Luminal Trophozotocidal Agents:

They attack on intestinal trophozoites and are effectively used to treat invasive intestinal amoebiasis.

E.g., Metronidazole, Tinidazole-***Nitroimidazole dérivatives***

Antibiotics –Tetracycline, Erythromycin, Paramomycin



Drugs	R_1	R_2
Metronidazole	$-CH_3$	$-CH_2CH_2OH$
Tinidazole	$-CH_3$	$-CH_2CH_2SO_2C_2H_5$
Timorazole	H	$-CH_2CH_2$–N O (Morpholine Ring)

Mechanism of action: $-NO_2$ group participates in endogenous reduction as an electrone acceptor. Since its redox potential is lower than protein (Ferredoxin) which is found in anaerobic organism, so nitro group is reduced and reduced form of metronidazole interferes in carbohydrate metabolism and nucleic acid synthesis.

- Antibiotics are not used alone, they are always used along with other amoebicidal agent.
- Except Paramomycin, all antibiotics exert an indirect trophozoitocidal action.

Carbarsone:

- It is an organic arsenical compound used in treatment of acute and chronic amoebiasis.

Mechanism of action: Anti amoebic agents due to the presence of arsenic metal in their structure, exert amoebicidal action by non-specifically inactivating the enzyme containing –SH (Sulfhydral) group.

Glycobiarsol: A bismuth salt of phenyl arsenic acid.

- It is least favoured due to toxicity.

Systemic Amoebiasis

E.g., Metronidazole, Tinidazole, Chloroquin, Emetine and Dehydroemitine

Emetine -It is an alkaloid obtained from the roots of Ipecac plant (Cephalis ipecacuanha).

Dehydroemitine -It is synthetic analog of emetine, having better activity than emetine.

Mechanism of action: It affects the protein synthesis by inhibiting translocation of the peptidyl-t-RNA on ribosomes resulting in the inhibition of polypeptide side chain.

Miscellaneous Agents

E.g., Chlorbetamide, Chlorphenoxamine, Phanquone

Anti Malarial Agents

Malaria in humans is caused by the infection with protozoa parasites of the genus plasmodium. These parasites spend an asexual phase in man and sexual phase in female anopheles

mosquito. Out of several hundred known anopheles species, the four species, the which infect the man are:

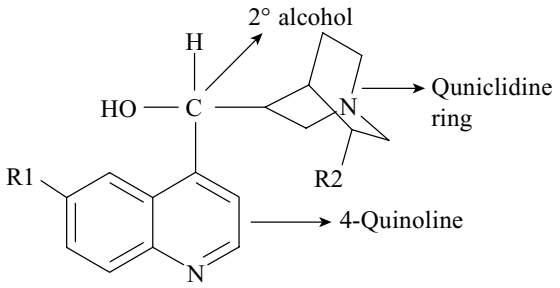
- Plasmodium Falciparum
- Plasmodium Vivax
- Plasmodium Malariae
- Plasmodium Ovale

Classification

1. Quinoline Derivative

Cinchona alkaloids

E.g., Quinine, Quinidine, Cinchonine, Cinchodine



Drugs	R_1	R_2	Optical isomer (d/l)	Absoluate configuration (R/S)
Quinine	$-OCH_3$	$-CH=CH_2$	l (–)	S
Quinidine	$-OCH_3$	$-CH=CH_2$	d (+)	R
Cinchonine	H	$-CH=CH_2$	d (+)	S
Cinchodine	H	$-CH=CH_2$	l (–)	R

All four derivatives of ***4-Quinoline methanol*** which are linked with a substituted quinclidine moiety.

Quinine (l-isomer) having anti-malarial activity while it's ***d-isomer Quinidine*** having anti arrythmatic agent.

Quinine-Most active ingredients (5%) of cinchona bark

- It has schizonticidal and gametocidal for Plasmodium vivex species.
- SC and IM injection form is not used due to local tissue damage.
- Many a times, it is administered with pyrimethamine, sulfadoxine, doxyclcline or mefloquin.
- It is affected against erythrocytic Merozoites.
- It is used in chloroquin resistance plasmodium falciparum infection.
- High dose of quinine may cause quinidine, like depressant effect on heart causes vasodilation and may causes hypotension.

Adverse Effects

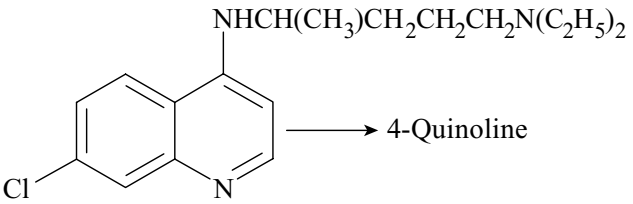
- Cinchonism, Nocturanal leg cramps
- High dose of quinine may produce a quinidine like depressant effect on heart cause vasodilation and may produce hypotension.

SAR

- 2° Alcohol in the structure of quinine alkaloids is responsible for the activity, R_1 ($-OCH_3$) and R_2 ($-CH=CH_2$) group not responsible for activity.
- Quinine antagonizes the action of ***physostigmine*** on skeletal muscle by exerting Curare like effect.
- Due to low therapeutic index, it is not used alone and is always used in combination (***Primaquin, Pyrimethamine and Sulphonamide***)

4-Amino quinoline derivatives

E.g., Chloroquine, Hydroxychloroquine, Amodiaquine



Chloroquin

Mechanism of action: It is concerted in parasitized red cells where it binds to double strand DNA. This results in inhibition of DNA and RNA polymerases function.

- It is used for treatment of all types of malaria except ***"Chloroquin resistance plasmodium falciparum"***.

SAR: 7-chloro, 3^0 Amine and amino alkyl side chain is required for activity

Metabolite: Desethyl chloroquin, Bidesethyl chloroquin

Adverse effect

- Bone marrow depression, Ratinopathy
- Hemolysis in patients with glucose-6-phosphate dehydrogenase deficiency
- Photo allergic dermatitis since it accumulates into the skin

Amodiaquin

Mechanism of action: Ferriprotoporphyrin IX, which is released by plasmodium containing erythrocytes acting as chloroquin receptor. The combination of Ferriprotoporphyrin IX and chloroquin cause lysis of parasite's and/or erythrocyte membrane.

- The quinone imine system is similar to the acetaminophen toxic metabolite.

Hydroxychloroquin:-OH group on ethyl group of diethyl amino group.

8-Amino quinoline

E.g., Primaquin, Pamaquin, Quinocide-having asymmetric center in their structure but Pentaquin does not have it.

Adverse effect

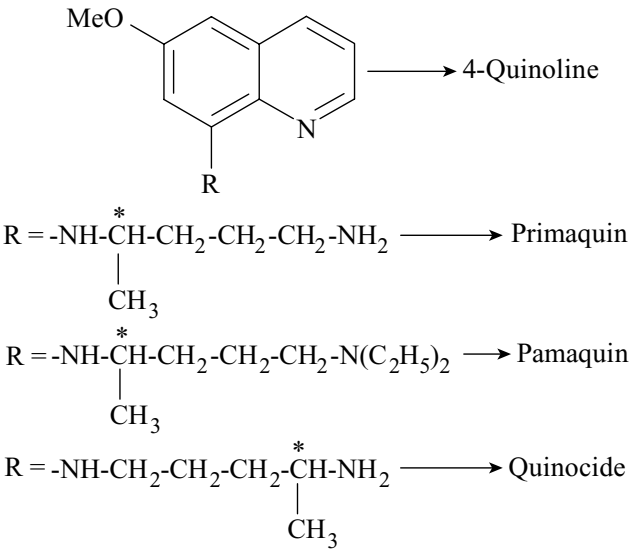
- Hemolytic anemia
- Leucopenia
- Methemoglobinemia

Metabolite

5-Hydroxy primaquin and 5-Hydroxy 6-desmethyl primaquin

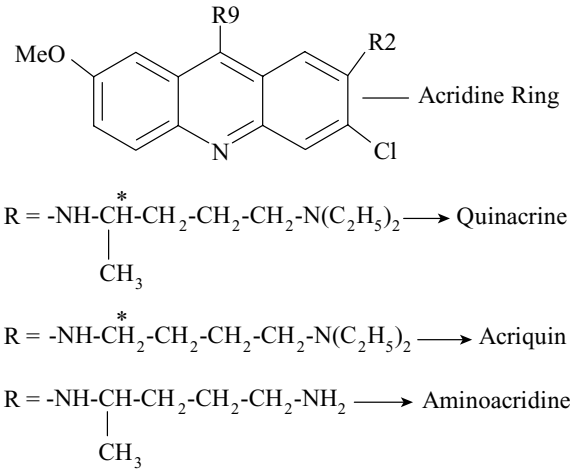
Mechanism of action: Interferes in protein synthesis with enzyme and with erythrocyte phospholipids metabolism in parasite.

- Primaquin inhibits gametocyte stage, leavo isomer is less active than dextro isomer.



2. 9-Aminoacridines derivatives

Quinacrine, Acriquin, Aminoacrichin



Quinacrine, Pamaquin and Chloroquin having similer side chain

- They all have acridine ring in their structure.
- Yellow pigmentation of skin and yellow colour appears in the urine along with acridine dye.

Adverse effect:

- Aplastic anemia

Mechanism of action:

- It acts at many sites within the cells including intercalation of DNA strands
- It is tumorigenic and mutagenic in nature and used as sclerosing agent.

3. 2, 4-Diaminnopyrimidine Derivative

- Pyrimethamine, Trimethoprim
- Used in exoerythrocytic and erythrocytic phase of disease

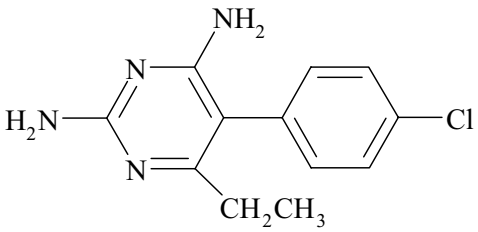
Mechanism of action

It causes selective inhibition of the protozoal enzyme DHFR (Dihydro folate reductase) to disturb the protozoal DNA synthesis and finally death of Protozoal cells.

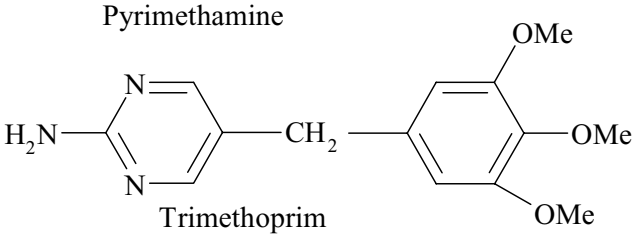
SAR points

- Electron donating group at C-6 position
- Cl at Para position
- Two rings are not separated by carbon atom.

Pyrimethamine: Used in chloroquin resistant falciparum malaria



Pyrimethamine



Trimethoprim

4. Bigunides

- It is a prodrug and is not active until it is not metabolized in-vivo to dihydrio triazine.
- ***Prongunil (Chloroguanil)*** is metabolized to ***active triazine ring*** having anti malarial activity.

5. Atovaquone: It is ***napthoquinone derivative*** used in combination of prongunil administered in ratio (2.5:1)

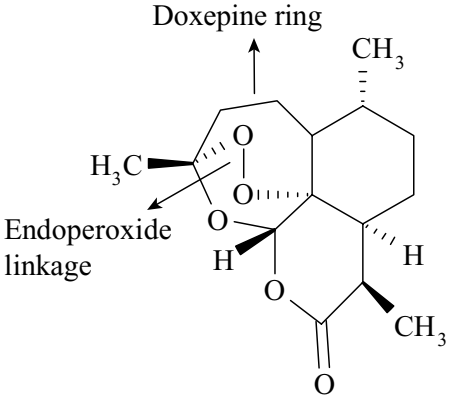
Mechanism of action: It interferes with ***deoxythymidylate synthesis*** by inhibiting dihydro folate reductase enzyme.

6. Sulphone and sulphonamide

- Long acting sulphonamide used in combination with Pyrimethamine/Trimethoprim.
  E.g., Dapson

7. Miscellaneous

- **Mefloquin**
- **Antibiotics:** Doxycycline, Clindamycin, lincomycin, Chloramphenicol
- **Halofantrine:** It is phenanthrene derivative
- **Artimisinin:** It is a natural product excreted from the dry leaves of Artemisia anna.
- Key structure to be "Trioxane" ring consisting endoperoxide and doxepine oxygen.
- Artimisinin is reduced to dihydroartemisinin, having an asymmetric carbon forms.



Artimisinin

- Artemether and artemotil are oil soluble/non-polar methyl/ethyl salt of artimisinin.
- Artesunate is water soluble/polar hemisuccinate salt of Artemisinin.

Anti Fungal Agent

Classification

1. Inhibition of fungal cell wall synthesis:
E.g., Capsofungin

2. Bind to fungal cell membrane ergosterol

E.g., Amphotericin-B, Nystatin, Natamycin-**Polyene Antibiotics**

- As the name indicates; Polyene, so the structure contains many double bonds.
- A series of –OH group on acid derived portion of the ring.
- A glycosidically linked deoxyaminohexose called Myosamine.
- 28 membered polyene antibiotics: *Natamycin* (Pentene-5 double bond)
- 36 membered polyene antibiotics: *Nystatin* (Hexene-Six double bond, *Amphotericin-B*-Heptane-Seven double bond)

Amphotericin-B-"streptomyces nodosus"

Side effect:

- Nephrotoxicity
- Hypokalemia
- Pain at site of injection and thrombophlebitis

Cryptococcosis: Fungal inspection of CNS.

Drug Interaction

- Flucytosin has synergistic action with Amphotericin B, because it facilitates the penetration of flucytosin through fungal cell wall.
- Aminoglycoside and other nephrotoxic drugs enhance toxicity of Amphotericin B
- Concomitant use of Diuretic should be avoided.

*Nystatin:-**"streptomyces noursei"***

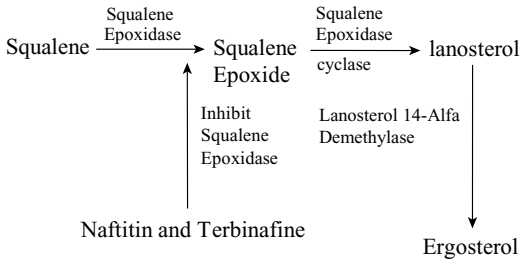
Aglycon part of nystatin is known as Nystatinolide and glycon part is myosamine.

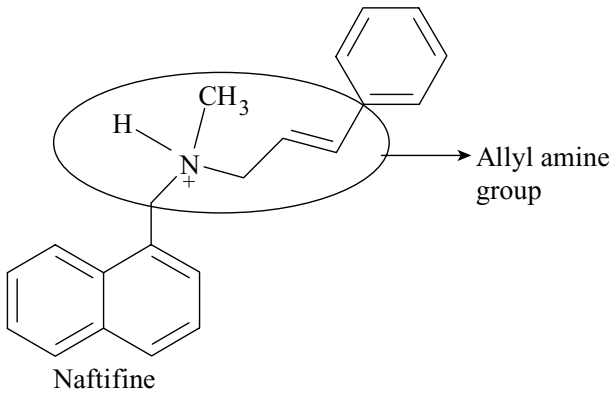
*Natamycin:-**'streptomyces natalensis'***

3. Inhibition of ergosterol + lanosterol synthesis

E.g., Terbinafine, Naftifine, Butenefine.

Mechanism of Action



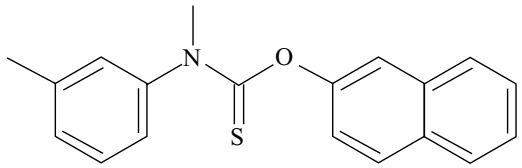


Allyl amine derivative: Terbinafine, Naftifine

- Tolnaftate is not allyl amine but inhibits the squalene epoxidase, that is why it is considered under allyl amine group.
- Terbinafine is more potent than Naftifine, and also has oral activity against onychomycosis (Ringworms of nails).

Tolnaftate:

- It is thioester of β-Napthol. It inhibits Squalene Epoxidase enzyme.



4. Inhibition of ergosterol synthesis

Example, Miconazole, Clotrimazole, Ketoconazole, Fluconazole, Itraconazole, Voriconazole

Basic moiety is imidazole, except **Itraconazole** and **Fluconazole** having two triazole ring.

Mechanism of Action: Azole group of antifungal agent binds to fungal cytochrome P-450-dependant 14α-demethylase enzyme that is responsible for the demethylation lanosterol to ergosterol.

Ketoconazole

Cis-2S, 4R is 4.5 times more active than 2R, 4S

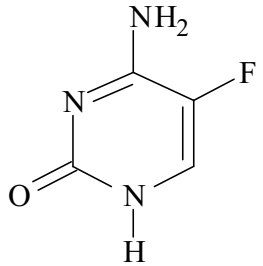
Drug Interaction: H2 receptor antagonist and anti cholinergic agents that inhibit gastric secretion and interfere with its oral absorption.

Amphotericin B and Ketoconazole antagonize each other.

Fluconazole: Inhibits cyt-P-450 oxidase causes increase in plasma level of cyclosporine, Phenytoin, Oral hypoglycaemic agent (Tolbutamide, Glipizide, Glyburide)

5. Inhibition of nucleic acid synthesis

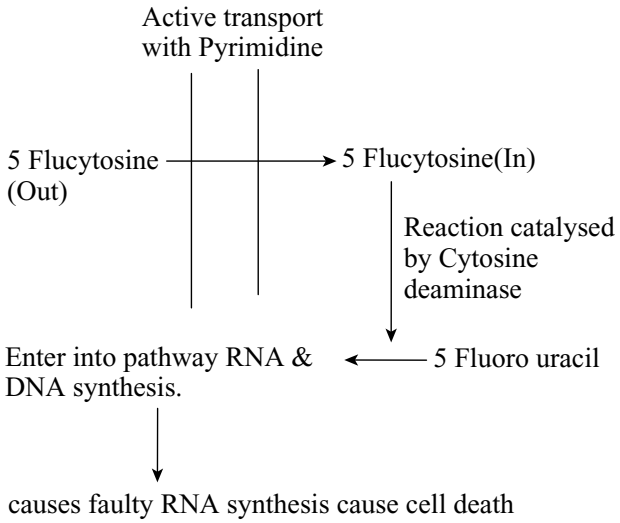
Flucytosine



4-amino-5-fluoro-2(1H)-pyrimidone

- Orally active antifungal agent.
- Used for the infection of candida and cryptococcus.

Mechanism of Action:



Adverse Effect: Bone marrow depression leading to leucopenia and thrombocytopenia.

6. Disruption of mitotic spindle and inhibition of fungal mitosis.

E.g., Griseofulvin

- It is obtained from Fungus ***Penicillium Griseofulvum***.
- It has ***Benzofuran derivative***.

Use: Ring worm infection of body, hair, feet and nails caused by species of dermatophytic fungi including trichophyton, Epidermophyton.

- Fungistatic agent
- Allergic reaction: Rash, urticaria, Git upset

7. Miscellaneous agents: Ciclopirox, Haloprongin, Undecylenic agent

8. Topical agents for dermatophytosis

Keratolytic agent: salicylic acid, α-Hydroxy compound

- Adult have an acidic, fatty substance in or on the skin known as Sebum which having anti fungal activity. So that's why, fatty acids like propionic acid, undecylenic agent, Triacetin is used as anti-fungal agent.
- **Whitfield Ointment: 6% Benzoic acid + 3% Salicylic acid.**

Anti-Tuberculosis Agent

Tuberculosis: It is a disease of respiratory transmission. A person gets infected when he comes in contact with the environment contaminated with viable tuberculi bacilli. It spreads through coughing, sneezing and shouting of infected person.

Causative Organism: ***Mycobacterium Tuberculosis***

Classification

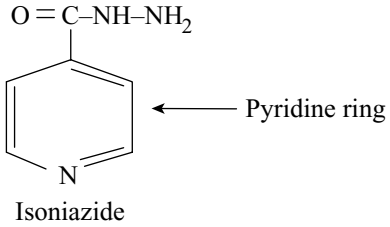
First Line Agent	Second Line Agent
Pyrazinamide Rifampicin Isoniazide Streptomycin Ethambutol	p-Amino salicylic acid (PAS) Capreomycin Cycloserine Ethionamide Prothionamide Macrolide antibiotics Fluoroquinolones

Isoniazide: (INH)

- It is hydrazide of iso nicotinic acid.
- Structure of INH is similer to Pyridoxine (Vit B_6).
- Bacteriostatic in action

Mechanism of action

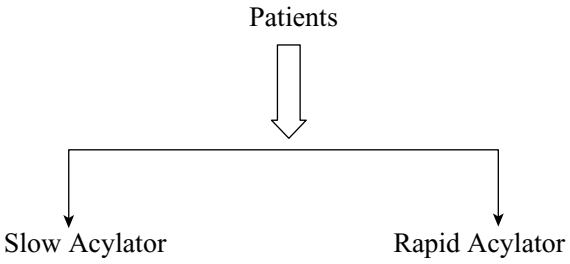
INH inhibits ***Mycolase Synthase***, an enzyme necessary for the biosynthesis of mycolic acid (essential constitute of mycobacterial cell wall).



Isoniazide

Metabolism: N-Acetylation, depends upon transfer of acetyl group from coenzyme A by N-Acetyl transferase.

Rate of acetylation is genetically controlled.



- Rate of INH metabolism is slow
- Prolong plasma level of INH

Acetyl hydrazine: Toxic metabolite of INH which is responsible for hepatotoxicity.

Adverse Effect

- Peripheral Neuritis-Co administration of Pyridoxine (Vit B6) with INH prevents the symptom of peripheral neuritis.
- GIT disturbance (Constipation, Loss of appetite)
- Hepatotoxicity

- Dryness of mouth (xerostomia)

Drug Interaction

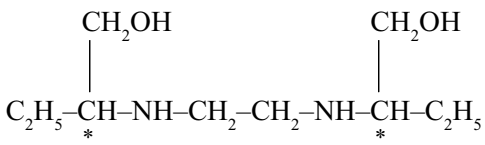
- Antacid (Aluminum Hydroxide)-Inhibits the absorption of INH.
- PAS-Inhibits metabolism.
- INH also inhibits the metabolism of Phenytoin and carbamazepine.

Stereptomycin-Aminoglycoside antibiotic

- Bacteriostatic in action
- Used always in combination
- Nephrotoxicity and ototoxicity are major side effects.
- Sterptomycin resistance strain treated with kanamycin and viomycin.

Ethambutol/EMB/Myambutol

Ethambutol



ETHYLENE-DIAMINO-DI-1-BUTANOL

- Activity of EMB is streospecific, dextro isomer having maximum activity than leavo form.
- It has two chiral centres.

Mechanism of action

- It inhibits "Arabinosyl transferase enzyme" to prevent polymerization of arabinoglycan in mycobacterial cell wall.
- Ethambutol if used in dose of 25 mg/kg/day for more than 9 months can cause **Reterobulbar Neuritis**-impairement of visual activity and **red green colour discrimination.**
- Ethambutol decreases renal excretion and it may produce gouty arthritis.
- Contraindicated in pregnancy and children below 2 years.
- Monthly eye examination of patient is necessary when patient is treated with EMB.

Rifampicin

- It is orally active bactericidal ***semi synthetic derivative of rifamycin B.***
- It is obtained from ***Streptomyces mediterranei.***
- It is also known as ***Ansamycin antibiotics***.

Mechanism of action

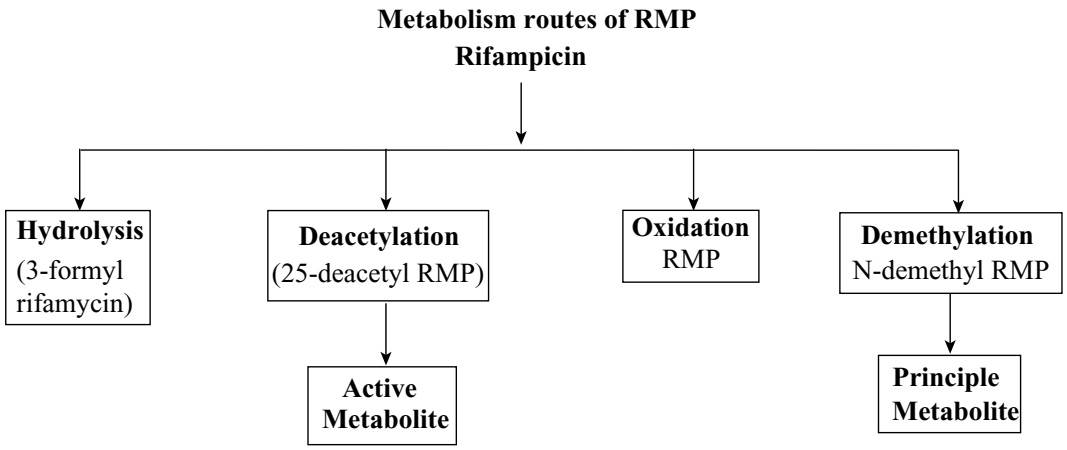
- It strongly binds to the β ***subunit of bacterial 'DNA dependent RNA polymerase'*** enzyme. Thereby inhibits the RNA synthesis of bacteria. Mammalian RNA polymerase does not bind to rifampicin.

Adverse effect

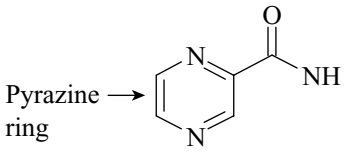
- Hepatitis-risk may increase when used in combination with INH.
- Flu like syndrome characterized by fever, chills, myalgias and thrombocytopenia.
- Rifampicin imparts a harmless red orange colour to urine.

Drug Interaction

- Rifampicin has enzyme induction property hence accelerates the metabolism of several drugs like oral contraceptive, anti-coagulants and protease enzyme.



Pyrazinamide: (PZA)



Pyrazine carboxamide

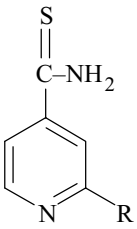
- It is pyrazine analog of ***nicotinamide.***
- Principle metabolite is ***Pyrazinoic acid (Active metabolite) and 5-Hydroxy pyrazinoic acid.***

Mechanism of Action

- PZA enters the cell wall of M.tuberculosis via passive diffusion and it is converted to pyrazinoic acid (Active metabolite) by pyrazinamidase enzyme. Then later it inhibits myco bacterial fatty acid synthase-I enzyme and disturpts mycolic acid synthesis needed for mycobacterium cell wall synthesis.

Second line Agent

Ethionamide



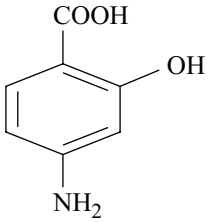
R = $–C_2H_5$ = Ethionamide-2 ethyl thiosonicotinamide
R = $–C_3H_7$ = Prothionamide-2-propyl thiosonicotinamide

- Prothionamide/Ethionamide are congeners of thionicotinamide.
- It is also known as Thioamide analog of Isoniazide.

Mechanism of Action

- It may interfere in peptide synthesis by acting as antimetabolite and inhibiting the incorporation of sulfur (-SH) containing amino acid. (Cysteine, methionine)

p-Amino Salicylic acid: (PAS)



- Because of sour taste and irritant nature, this drug is mainly used in form of its Na^+, K^+ and Ca^+ salts.

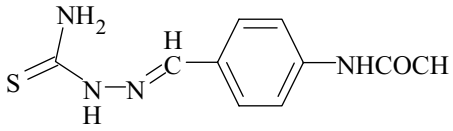
Mechanism of action: Same as sulphonamide

Adverse effect

- Crystalluria
- Lupas like syndrome
- GIT irritation

Thiacetazone

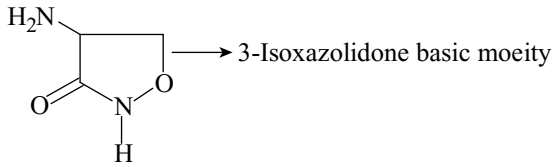
Thiacetazone



Chemically, it is ***thiosemicarbazone derivative***.

Cycloserine

Cycloserine



- Analog of D alanin
- Chemically, D-4-amino3-isoxazolidone.
- Broad spectrum antibiotics.
- Steriochemically similar to D-Serine.

Adverse Effects

- Peripheral Neuritis
- Tremors
- Psycotic
- Behavioral changes

Capreomycin and Viomycin: Peptide Antibiotics

- Both antibiotics are ***basic peptides in nature.***
- **Capreomycin**-Streptomyces capreolus
- **Viomycin-**Streptomyces pumilus
- Capreomycin is more potent and less toxic than viomycin.
- Nephrotoxicity, skin rashes and ototoxicity are major side effects.

Anti Leprotic Agent

- **Leprosy** is a chronic disease caused due to acid fast bacilli which produce nodules in the skin and loss of sensation in affected region.
- It is also known as Hansen's disease.

- Lepra reaction-It is hypersensitivity reaction not occuring as a result of allergy to drug but they should considered as allergic reaction to metabolite product of infected microorganism.

Types of leprosy

1. **Tuberculoid Leprosy:** Presence of infection in restricted area. Dapson treatment is required.
2. **Lepromatous Leprosy:** Infection is spread in wide area of body, so multi-drug treatment is required.
3. **Indeterminate Leprosy:** It is the early stage of disease, m.o are not multiplied to the extent to induce lepra reaction.
4. **Borderline leprosy**: Tuberculoid leprosy and Lepromatous leprosy are two extreme forms of the disease. All forms that lie in between these two forms is known as borderline leprosy.

Treatment

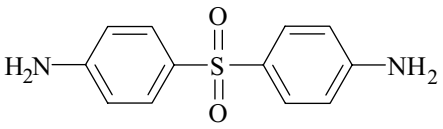
Dapson, clofazimine, Rifampicin, Thicetazone, Prothionamice, Ethionamide, Chaulmogric acid

Cytotoxic antibiotics: Actinomycin, Mitomycin

Dapsone

- Mechanism of action: It inhibits folic acid synthesis.
- Bacteriostatic in action.

Dapsone

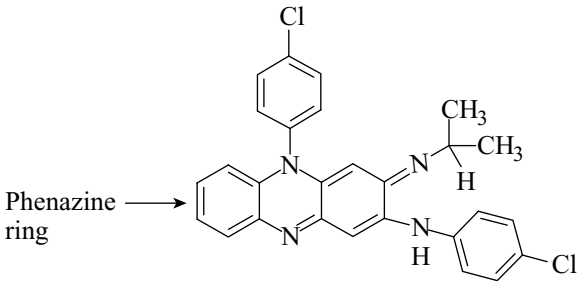


4,4'-Diamino phenyl sulfone

- It may produce methanoglobunaemia in person having Glucose-6-phosphate defiance.
- Sulfone Syndrome-If dapson is used for more than two months.
- Acedapsone: N-acetyl derivative of Dapson.

Clofazimine:

Clofazimine



- It is orally active phenazine dye with bactericidal action.
- The imino group directly attached with phenazine ring is known as ***Riminophenazine***.
- Mechanism of action: Interfering with replication of bacteria.
- Used in ***dasone resistant leprosy***.

Adverse effects

- Red brown discoloration of skin.
- Abdominal pain with loose stool due to deposition of clofazimine crystal in intestinal mucosa.
- Conjunctiva pigmentation
- Photo toxicity

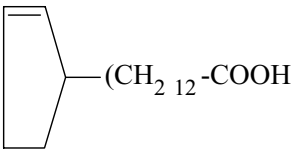
Antibiotic used in Leprosy

- **Fluoroquinolone:** Ofloxacin, Sparfloxacin
- **Macrolide:** Clarithromycin
- **Tetracyclin:** Minocycline

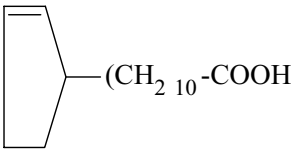
Chaulmogric acid

- The oil of chaulmoogra and hydnocarpus are used since ancient times in treatment of leprosy.
- The oil is extracted from the ripe seed of ***Hydnocarpus anthelmintica and Hydnocarpus heterophylla***.
- It contains ***Glycerides of chaulmogric acid and hydnocarpic acid***.

Chaulmogric Acid



Hydnocarpic Acid



Anti Cancer Agent

Cancer: It refers to a disease of cells that show uncontrolled proliferation, dedifferentiation, invasiveness and the ability to metastasis (Spread to distal part of body).

Causes of cancer

- Exposure to carcinogenic hydrocarbon or excessive radiation.
- Hereditary factors involved in chromosomal abnormalities, enzyme, defence mechanism, hormonal imbalance.
- Cultural factors: like diet, smoking, drinking, sexual habits
- Occupational Factors: including ionization radiation, chemicals and other carcinogenic substance like coal tar, Mustard gas, chromium, Nickel and asbestos
- Virus: can cause cancer in animal but not in humans.

Tumor

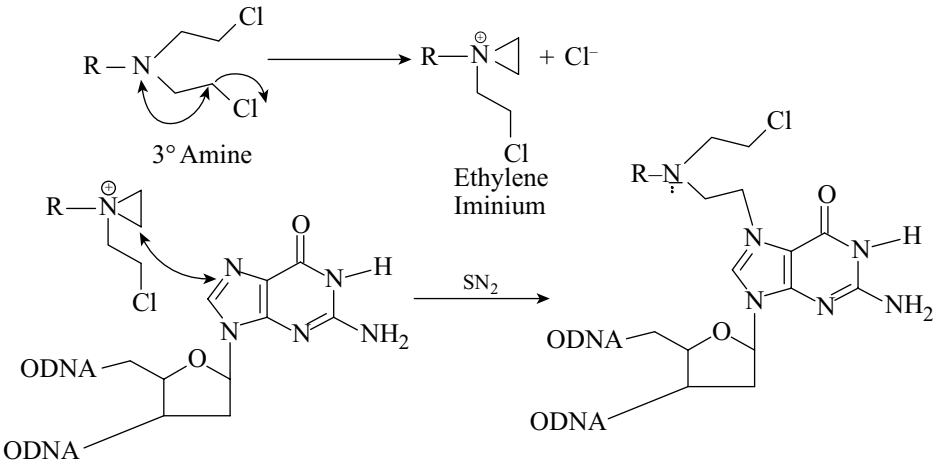
1. **Benign Tumor:** Slow growing, resembles to normal cell, remain localized and not harmful.
2. **Malignant Tumor:** Proliferate rapidly, Manifest dedifferentiation, invasiveness-attacking to other cells. Ability to metastasis and damages to surrounding cells.

Classification

1. Alkylating Agent

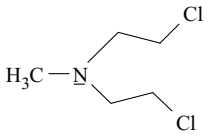
A. Nitrogen mustard derivative

E.g., Cyclophosphamide, Chlorambucil
Mechanism of alkylating agent



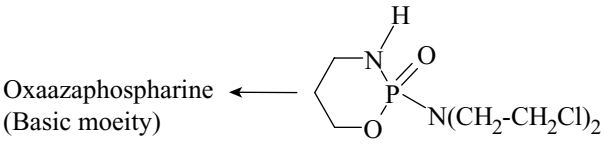
- The chemotherapeutic agent having the common properties of becoming strong electrophile through formation of carbonium ion, which in turn reacts with nucleophile moiety of target molecule (DNA).
- That means N-7 of guanine is particularly susceptible to the formation of a covalent bond with Alkylating agents.

Mechlorthamine



- Effective in Hodgkin's disease.
  Adverse effect: Bone marrow depression and hair loss

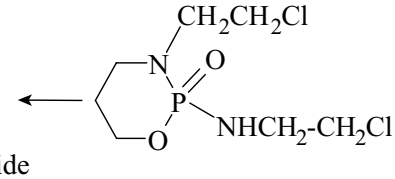
Cyclophosphamide: ***(Latent Drug)***



- **Metabolite:** Phosphoramide Mustard (Having Antitumor activity) and Acrolein (Toxic to urinary bladder)
- **Acreloin toxicity** is decreased by IV/Oral administration of sodium salt of 2-mercaptoethane sulphonic acid (MESNA)
- **Adverse Effect:** Alopecia, Leukopenia

Ifosfamide

2 chloro ethyl substituton on rings N atom in the structure of Cyclophosphsmide

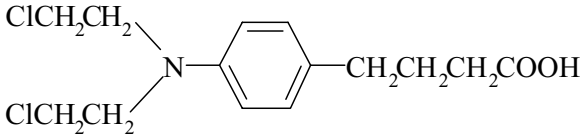


Melphalan: Phenylalanine analogues alkylating agent.

Busulfan: Alkyl Sufonate derivative

- **Use:** Chronic myelogenous leukemia
- **Sulphar Stripping:** In which interaction with Thio (-SH) compounds such as Glutathion or cystein residue results in loss of two equivalent methan sulfonic acid.

Chlorambucil



- **Adverse Effect:** Dose related and rapidly reversible neutropenia.

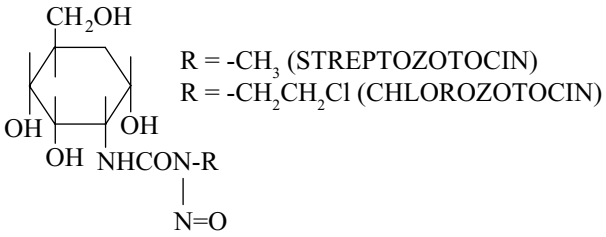
Nitrosourea derivative

Carmustine, Lomstine, Semustine, Chlorozotocin, Streptozotocin

Carmustine: It crosses BBB, so it is used to treat brain tumour.

Adverse Effect: Delayed myosupression, Thrombocytopenia

Chlorozotocin, Streptozotocin



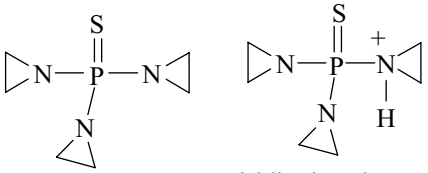
- It is broad spectrum antibiotics containing Nitrosourea.

Mechanism of action:

- At physiological conditions, it will produce chemically reactive species like ISOCYNATE which may cause carbamylation of amino acid and protein resulting inhibition of DNA replication.

Aziridines

Thitepa, Benzotepa, Altretamine



Thiotepa

Aziridinyl Cation act as Electrophile

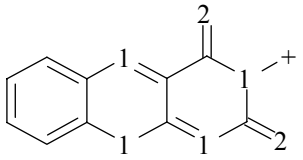
Precaution: Thitepa is highly toxic to bone marrow so high blood count is necessary during the therapy.

Antimetabolite agent

Amino acid inhibitors: Tyrosine analogues

Vitamin and coenzyme antagonists

E.g., Riboflavin analogues



6, 7-Dimethyl-10-D-ribityl=Isoriboflavin
7, 8-Dimethyl-10-d-ribityl=Galactoflavin

- Isoriboflavin and Galactoflavin causes deficiency of riboflavin and controls Lymphosarcoma.

Antagonist of metabolite involved in nucleic acid synthesis:

(a) Glutamate antagonist:

E.g., Azaserine, DON

Mechanism of action

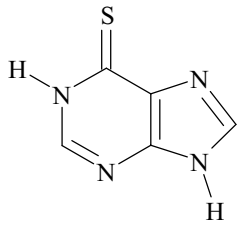
5-phosphoribosyl pyrophosphate (5-PRPP)
↓ Glutamate as cofactor
5-phosphoribosylamine cytidine triphosphate (5-PRCTP)
↓ Glutamate as cofactor
Uridine Triphosphate (UTP)

- DON is more potent since it resembles the normal cofactor L-glutamine than azaserine
- Use: Sarcoma and Leukemias

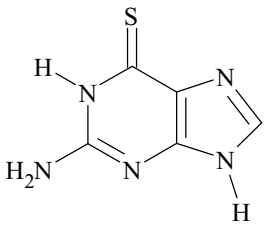
(b) Folic acid antagonist or Antifolics:

- E.g., Aminopterin, Methotrexate, Trimetrexate–All of these have Pteridine as basic nucleus.
- **Mechanism of action:** Competative inhibition of Dihydrofolate reductase.
- Ionosonic acid-required for RNA synthesis and Thymidylic acid-required for DNA synthesis.
- **Toxicity:** Stomatitis, Hepatic dysfunction and thrombocytopenia

Purin base antagonists: E.g., 6-Thioguanine, 6-Mercaptopurin-Purin as basic ring



6-Mercaptopurin



6-Thioguanine

Mechanism of action

Metabolic degradation of 6-MP
↓ Guanase
6-Thioxanthin
↓ Oxidize by xanthin oxidase
Thiouric acid

- **Allopurinol:** Xanthine oxidase inhibitors potentiate the activity of 6-MP and also increases the toxicity.

- **Azathiopurin:** Anti tumor agent but not active than 6-MP-So it is used as immunosuppressive agent in organ transplant.
- **Fludrabin and vidrabine:** Anti-viral agent

Vidrabine

Mechanism of action

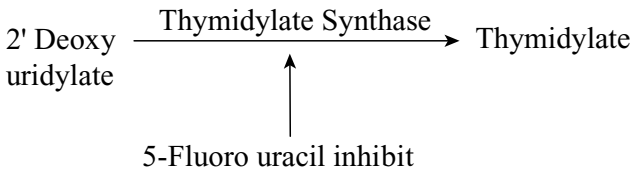
- Adenine arabinside ⟶ Hypoxanthine arabinoside derivative ⟶ Resistance to tumor
- It is also known as Adenine arabinoside-Streptomyces Arabinoside
- Sugar part-D-arabinose

Fludrabin: 2-fluoro derivative of vidrabine is also known as fludrabine.

Pyrimidine Antagonist

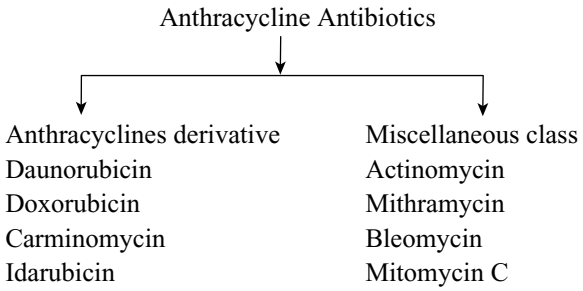
E.g., 5-Fluorouracil (Antimetabolite of uracil), Cytrabin

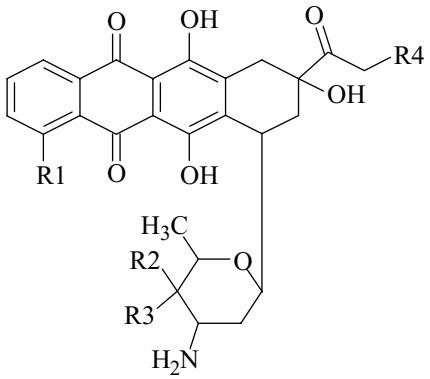
Mechanism of action:



- Resulting in diminishing of the DNA biosynthesis.
- Fluorouracil is anabolized to 2' deoxy ribose mono phosphate which is potent inhibitors of thymodylate synthase.
- **Tegafur:** It is a prodrug, after metabolism, it is converted into 5-Fluoro uracil.
- **Capcitabine:** Tumor selective and tumor activated prodrug of 5-Fluorouracil.
- **Gamcitabine:** It inhibits Ribonucleotide reductase and compate 2-deoxy xytidine triphospahte for incorporation into DNA. These effect producing cell specific cytotoxicity.
- **Use:** Adenocarcinoma of pancreas.
- **Cytrabine:** Cytosine arabinoside
- **Mechanism of action:** Cytrabine anabolized to triphosphate derivative inhibits the conversion of cytidylic acid to 2' deoxy cytidylic acid.
- It also inhibits the DNA dependant DNA polymerase enzyme and miscoding following incorporation into DNA and RNA.

Cytotoxic antibiotics

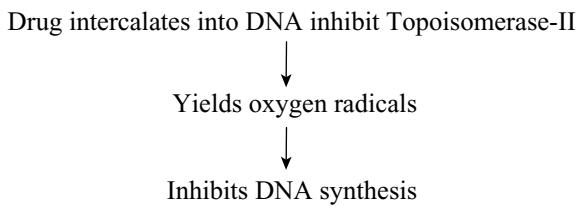




Drugs	R_1	R_2	R_3	R_4
Daunorubicin	$-OCH_3$	H	–OH	H
Doxorubicin	$-OCH_3$	H	–OH	–OH
Carminomycin	–OH	H	–OH	–OH
Idrabicine	H	H	–OH	H
Epirubicin (Epimer of Doxorubicin)	$-OCH_3$	–OH	H	–OH

- Anthracycline occurs as a glycosides of anthracyclinone.
- The glycosidic linkage usually involves the 7-OH group of anthracyclinone and β anomer of a sugar with L-configuration.
- Anthracyclinone-Aglycon containing anthraquinone chromophore within linear hydrocarbon skeleton.

Mechanism of action



- Daunorubicin and Doxorubicin is obtained form S.Pencetium.
- Daunorubicin-It is a glycoside formed between daunomycinone and L-Daunosamine, and Doxorubicine is its 14-OH derivative.

Metabolism

- Daunorubicin ⟶ 13-OH derivative (Daunorubicinol) ⟶ Clave to aglycon
- Doxorubicin ⟶ 13-OH derivative (Adriamycinol)

Miscellaneous

Actinomycin: Having Phenoxazine nucleus.
Source: S.antibioticus

It is also known as dactinomycin.

Mechanism of action: Drug inhibits DNA-dependant RNA polymerase that inhibits the DNA and RNA synthesis.

Bleomycin

- Source: S.verticillus
- Bleomycin and their analogues occur naturally as blue copper chelates.

Mechanism of action: Bleomycin forms a complex with Fe(II) converts into the hydroxy and superoxide radicals that will clave Phosphodiestarase bond of DNA and ultimately cause degradation of DNA strand.

Mitomycin C

Source: S.Caespitosus

This compound has three carcinostatic functions like

- Quinone
- Carbamate
- Aziridine

Mechanism of action: The quinine, carbamate ang aziridine arranged in its natural state so by chemical and enzymatically reduced to hydroquinone derivative followed by loss of methanol resulting formation of Indohydroquinone becoming bifunctional Alkylating agent capable of cross linking double helical DNA.

Mithramycin

- Aurolic acid derivative obtained from S.Plicatus.

Mechanism of action: It inhibits "DNA dependant RNA polymerase enzyme".

Plant Products

Vinca alkaloids:

- It is dimeric indole alkaloid obtained from Catharanthus Roseus, family Apocynaceae.
- Indole containing moiety known as Cathranthine
- Indoline containing moiety known as Vindoline
- E.g., Vincristine, Vinblastine, Vinrosidine and Vinleuroside.
- **Mechanism of action:** It causes mitotic arrest by promoting the dissolution of microtubule in cell.
- **Use:** Acute leukaemia, Hodkin's Disease, lymphocyte lymphoma, Breast carcinoma.

Hetrocyclic Amine as an anti cancer agent

- Isolated from Chinese tree Camptotheca acuminate.
- E.g., Camptothecin, Hydroxy Camptothecin
- Use: Colorectal and Ovarian cancer.

Lactone (Alkaloids) as an anti cancer agent

- Podophylotoxin and Deoxypodophylotoxin are obtained from Himalaya shrub Podophyllam Emodi and P.Peltatum.
- Mechainism of action: It inhibits mitosis by destroying the structural organization of mitotic apparatus.

Taxol derivative

- E.g., Paclitaxel and Docetaxel
- It is obtained from western yew tree Taxus Bravifolia.
- M/A: It binds with β-Tubulin subunit of microtubule and appears to antagonize the disassembly of the key cytoskeletal protein and arrest in mitosis follows.

Colchicine:

- Main use: Terminating acute attack of Gout
- M/A: It inhibits mitosis at metaphase by disorienting the organization of spindle and esters.

Etoposide and Teniposide:

- It is a semisynthetic derivative of Podophyllotoxins.
- It has cytotoxic effect on G2 phase.
- It causes protein linked DNA strand breaks by inhibiting Topoisomerase-II.

Hormones and Their Antagonists

Tamoxifen

- Selective estrogen receptor modulator
- Anti estrogen drugs
- Use: Advanced breast cancer in post menopausal women.

Flutamide

- It is non-steroidal anti-androgen drugs.
- Use: Prostate cancer

Aminoglutethimide

- It inhibits Desmolase enzyme which prevent the conversion of cholesterol to pregnalone.
- Use: Adrenocortical carcinoma, Cushing's Syndrome

Mitotane

- Highly selective effect on adrenal gland.

Aromatase Inhibitors

Generation	Steroidal	Non steroidal
First	Testolactone	Aminoglutethimide
Second	Formestane	Fedrozole
Third	Exemastane	Anstrazole, Letrozole, Vorazole

Leuprolide: Synthetic non-peptide analogue of naturally occurring gonadotrophin-relesing hoemones, (LnRH)

Signal Tranduction Inhibitors

- Microbial product Staurosporin

Immunotherapy

- Levamisole is used in colon cancer

Interferon α-2a/2b

- Highly purified protein containing 165 amino acids.
- Interferon α-n3: It is glycoprotein.

BCG: Bacillus calmette Guerin

- Connaught BCG: It is freeze dried suspension of attenuated strains of Mycobacterium Bovis.

Hydroxy Urea

Cisplatin

- It is potent inhibitor of DNA polymerase.
- Cisplatin is Cis-dichlorodiamineplatinum II
- E.g., Oxaliplatin and Ormaplatin

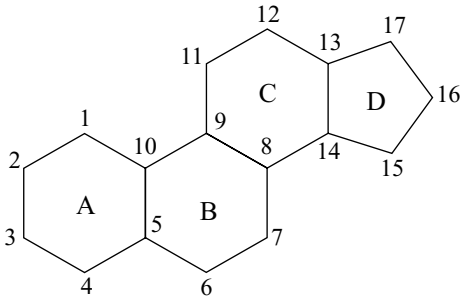
Enzyme as an Anticancer

- L-Asparginase and Pegaspagenase
- Potent immunosuprresive agent.

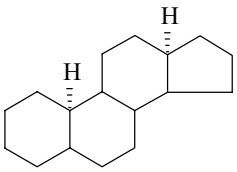
STEROIDS

Steroids: Saturated derivatives of Phenanthrene and Ring D is Cyclopentane ring.

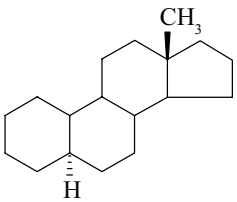
Basic Moiety in Steroids



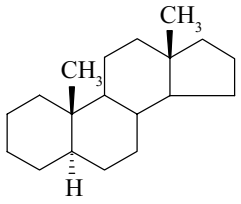
Cyclopentano Perhydro Phenanthrene



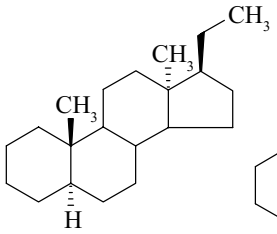
Gonane (C = 17)



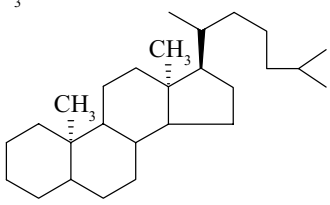
5 .-Estrane (C = 18)



5 . -Androstane (C = 19)



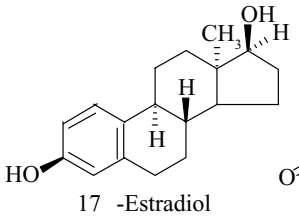
5 . -Pregnane (C = 21)



Cholastane (C=27)

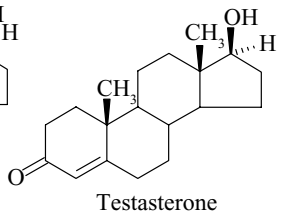
- Meaning of α-Behind the plane
- Meaning of β-Above the plane

Nomenclature and Numbering of Some Steroids



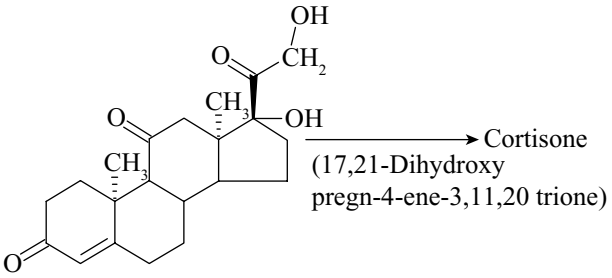
17 -Estradiol

(Estra-1, 3, 5 (10)-triene-3, 17 β diol)



Testasterone

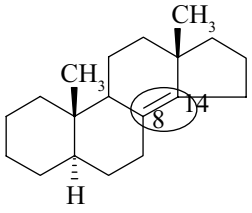
(17 β-Hydroxy androst-4-ene-3one)



Cortisone

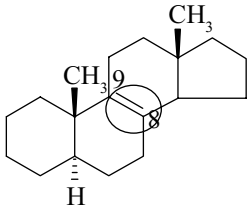
(17,21-Dihydroxy pregn-4-ene-3,11,20 trione)

Nomenclature of Steroids



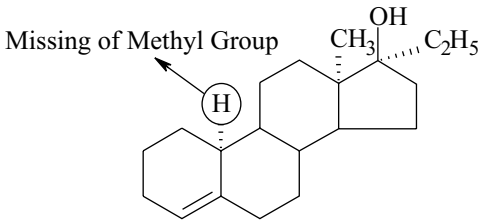
5 . -Androst-8(14)-ene

(Double bond is not In sequence)



5 . -Androst-8-ene

(When double bond is in sequence, we only mention the number at d.b starts)



17 . -ethyl-19-norandrost-4-en-17 -ol

When methyl group is missing from basic moiety, then we have to write **nor** at which number of carbon is the methyl group removed.

Stereochemistry

- In 5α steroids-A/B rings are in Trans form
- In 5 β steroids-A/B rings are in Cis form
- Cholastane, Androstane and Pregnane exist in two conformation

1. Chair form
2. Boat Form

Chair form are more stable than boat form due to less angle strain hence all steroids are exist in chair form.

Classification of Steroid

(1) Anti-inflammatory agent: Cortisone
(2) Sex hormone: Estrogen, Progesterone, Testosterone
(3) Oral Contraceptive: Norethisterone
(4) Cardiac Steroids: Digitoxigenin
(5) Diuretics:Spironolactone, K-Prorenoate
(6) Antibiotic: Fusidic acid
(7) Neuromuscular blocker: Pancuronium
(8) Vitamin-D precursor: Ergosterol

Biosynthesis of Steroidal Hormones

- Steroids are secreted from **endocrine gland** like ovaries, testes and adrenal gland
- Female sex hormone-**Estrogen and Progesterone**
- Male sex hormone-**Androgen**
- Adrenocorticoids-**Glucocorticoids and Minerocorticoids**
- Starting material for all steroid synthesis is ***Cholesterol***
- And overall mechanism of steroid hormone action in ***regulation of gene expression***.

Sex Hormone: Oestrogen

- Hormone activity is controlled by GnRH hormones like FSH, LH/ICSH and Luteoprin/Prolactin
- LHRh agonist-**Nafarelin**

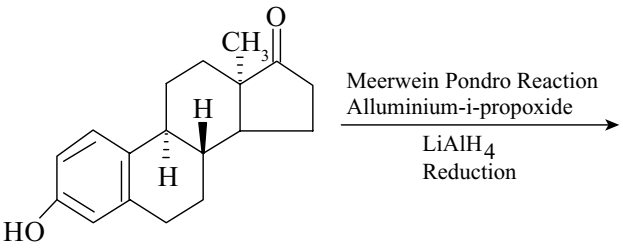
Function of sex hormone:

- Regulate ovulation in women
- Spermatogenesis in men

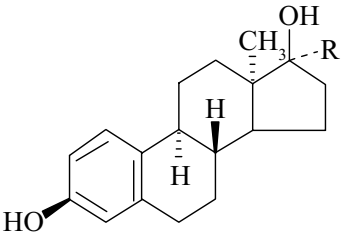
(a) Naturally occurring estrogens: *Estradiol, Estriol and Estrone*

- **Starting Material**

Testosterone----------Estradiol
Androstenedione----------Estrone



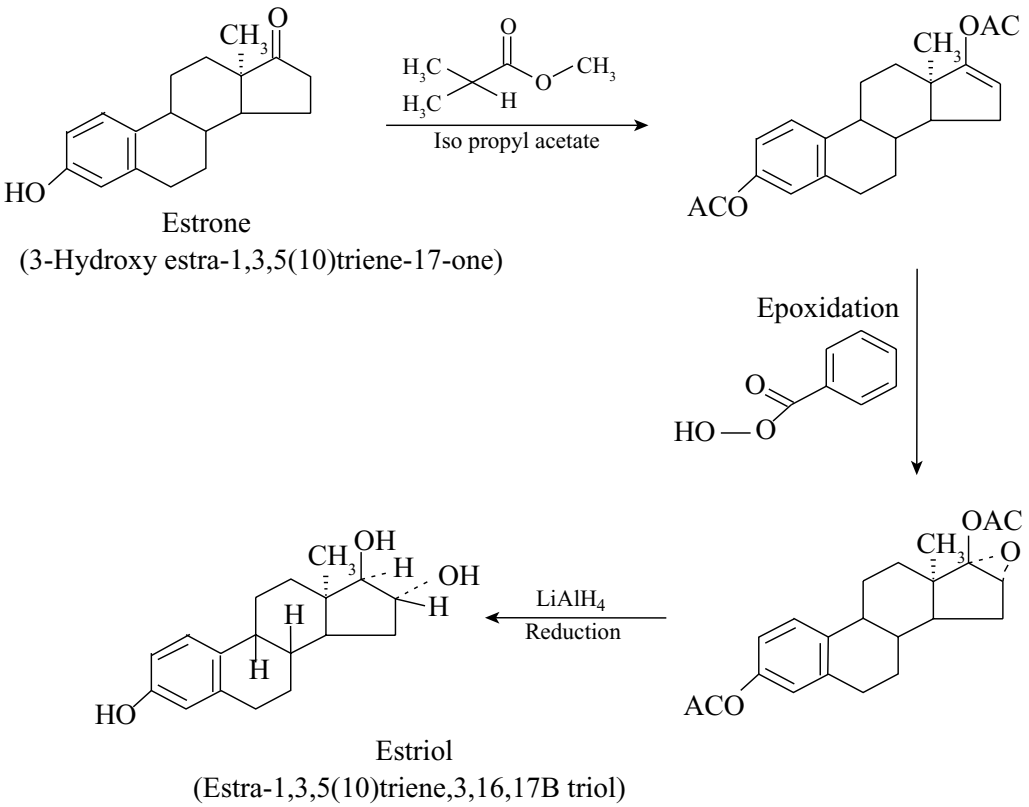
Estrone
(3-Hydroxy estra-1,3,5(10)triene-17-one)



R = H ⟶ 17B-Estadiol

R = C ≡ CH ⟶ Ethinyl Estradiol

Synthesis of Estriol

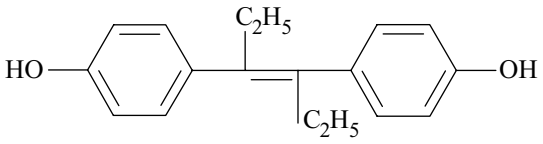


Estrone
(3-Hydroxy estra-1,3,5(10)triene-17-one)

Estriol
(Estra-1,3,5(10)triene,3,16,17B triol)

(b) Stallion Estrogen: equilenin and equilin

(c) Synthetic and Non-steroidal Oestrogen:



Diethyl Stilbesterol
(E)- . -Diethyl Stilbene-4,4 diol

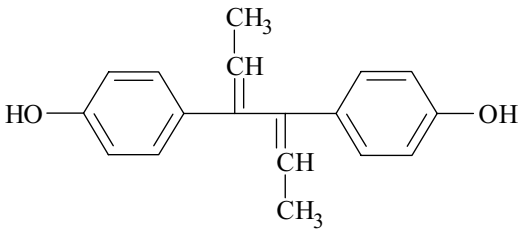
Trans diethyl stibesterol is potent estrogenic activity than Cis-diethyl stibesterol

It is synthesized from Anisaldyhyde and Anethol

Uses

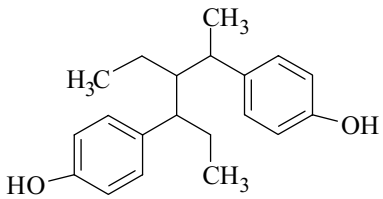
- Inhibition of lactation
- Breast and prostate cancer
- Secondary amenorrhoea due to ovarian insufficiency

Dienosterol

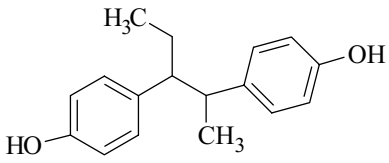


Dienestrol
((E,E)-4,4' di(ethylidene)ethylene diphenol)

- The starting material for synthesis of dienosterol is p-Hydroxy propiophenone.

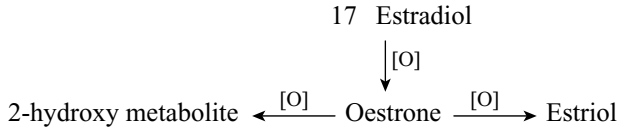


Benzestrol



Hexestrol

Metabolism

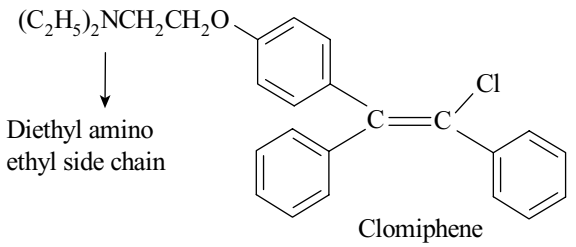


Uses

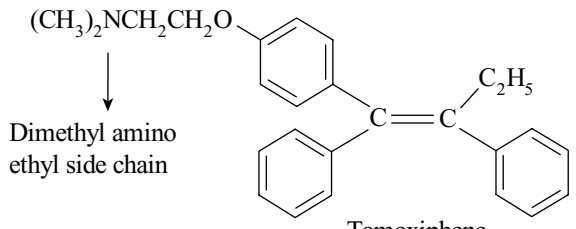
- Oral contraceptive
- In case of Menopause
- In abdominal watering bleeding
- Influences ovarian development

Anti Estrogen/Ovulation Stimulant:/Fertility drugs or Anti Tumor agent

E.g., Clomiphene, Tamoxiphen, Ethamoxytriphetol



Clomiphene



Tamoxiphene

- **Ethamoxytriphetol**-Strong anti oestrogenic activity
- **Danazol-**Weak androgenic activity
- Tamoxiphene and clomiphene are ***aminoether derivative of stilbene***
- Cis isomer of tamoxiphene is estrogenic rather than ant estrogenic
- Tamoxiphene and clomiphene are used in estrogen dependent mammary (breast) carcinoma

Side effects

- Enlargement of ovaries and visual disturbance

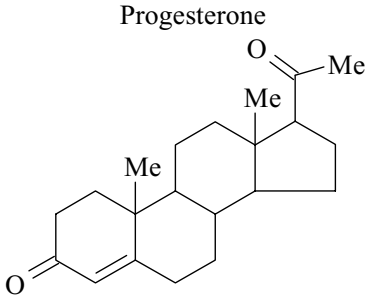
Progestin (Gestagens)

E.g., Progesterone, 19-nor testosterone

This class of hormones is secreted from ***corpus luteum*** and it is responsible to maintain the vascularity of uterine endometrium, and also inhibit oxytocin release.

Mechanism of action

It increases the level of FSH and LH production by hypothalamus by blocking of feedback inhibition of ovary produced estrogen.



4-Pregnene-3,20-dione

Synthesis of progesterone

Disogenin--------Pregnenolone------Progesterone
Chelesterol--------Pregnenolone------Progesterone

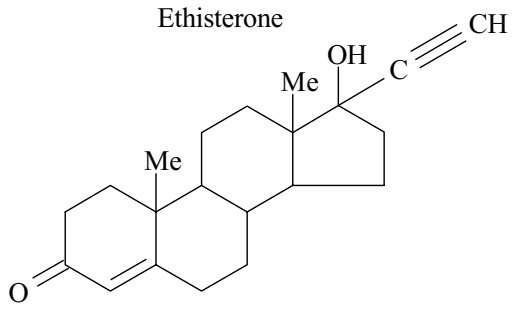
Metabolism: Progesterone is metabolized to 5β-pregnanediol glucronide

(a) C-6 Substituted 17α-acetoxy Progesterone
Medroxy progesterone acetate and Megastrol acetate

(b) Dehydrogesterone
Chlormadione acetate

(c) Derivative of testosterone: Ethisterone, Norethisterone

Ethisterone First synthetic progestin and orally active androgen



17 . -Ethynyl testosterone

(d) Derivative of 19-Nor testosterone:

E.g., : 19-nor testosterone, nor ethynodrel, Norgestrel, Lynesterol

Norgestrel Leavo isomer is actively known as levonorgestrel used as an oral contraceptive.

Androgen and Anabolic Agent

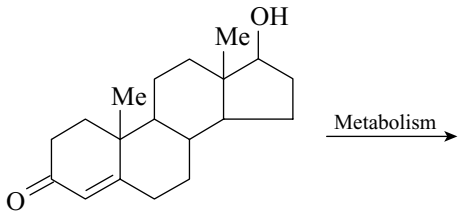
- It is a male sex hormone synthesized from cholesterol.
- E.g., Testosterone

Androgenic/Male Sex Characteristic

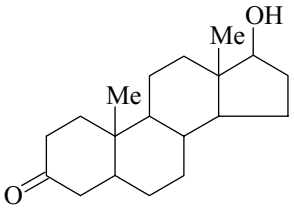
- Normal development
- Functioning and maintenance of male sex organ and male sex characteristic.

Anabolic/Muscle Building Activity

- It causes nitrogen retention by increasing the rate of protein synthesis and decreasing the rate of protein catabolism and ultimately promote the new tissue formation.



Testosterone



Dehydrotestosteron

↓

Active form of testosterone

IUPAC of Testosterone: 17β-Hydroxy-4-androstene-3-one

Dehydrotestosterone: Reduction of C-4-C-5 bond from testosterone.

Steroidal skeleton having minimum requirement to have androgenic activity.

SAR

- 5α-Androstane has androgenic activity, ring expansion and contraction leads to loss of activity.
- Introduction of SP^2 hybridized carbon atom in Ring A renders rings more planner resulting greater anabolic activity. Eg. Methandrosterone.

Metabolism

- Oxidation of 17β –OH group → Androstenedione → Reduction to give Androsterone
- Testosterone → 5α dihydrotestosterone which acts as invivo androgens

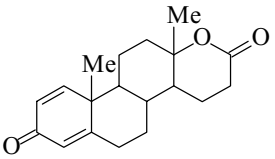
Side Effects

- Musculinization in women-growth of facial hair
- Edema
- On chronic treatment, anabolic steroids can suppress the production of testosterone.

Testolactone

- First generation steroidal aromatase inhibitors
- Used in Breast cancer
- Purely anabolic but minimum androgenic activity

Testolactone



Anti Androgen

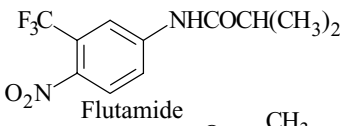
E.g., Cyproterone, BOMT, Nonsteroidal Flutamide

Mechanism of action: They do not prevent dihydrotestosterone formation but inhibit the nuclear retention of dihydrotestosterone in prostate.

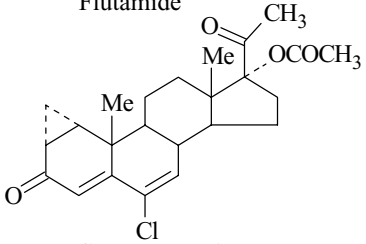
Cyproterone: It competes with receptor at receptor site.

Oral Contraceptive

Noretynodrel, Mestranol, EthinylEstradiol, Trans diethylstilbesterol, Ethisterone, Lybesterol



Flutamide



Cyproterone Acetate

Vaginal Contraceptive

1. Surface active agent/-SH binding agent:
   - Nonoxynol-9, otoxynol
2. Bactericides:
   - Phenyl mercuric acetate, Benzethonium chloride
3. Acids: Boric acid, Tartric acid, Phenol

Interceptive/Abortifacients

- PGE_2 and $PGF_2\alpha$

Mifepristone Progesterone antagonists

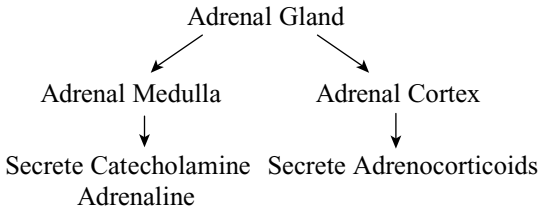
Danazol A gonadotropin inhibitor in females.

Gossypol Phenolic compound isolated from cotton seed oil having directly spermatogenic activity. Only leavo isomer of gossypol is active as a male fertility regulating agent.

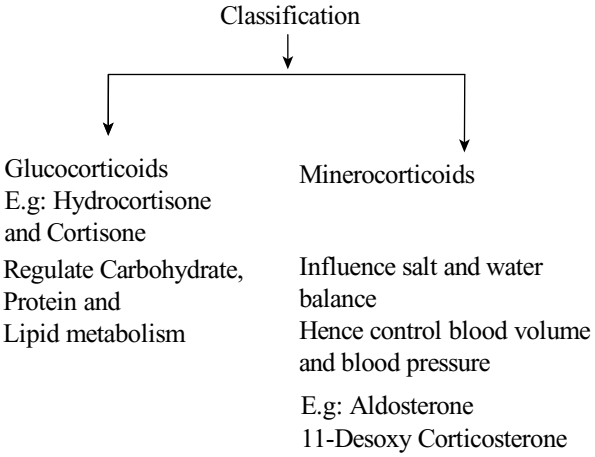
Miscellaneous Contraceptive Methods

Male-Vasoctomy, Female-Tubectomy

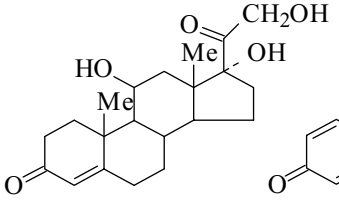
Adrenal Cortex hormones



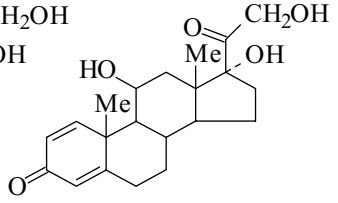
- Adrenal Cortex is regulated by ***Hypothalamus-pitutary gland***.



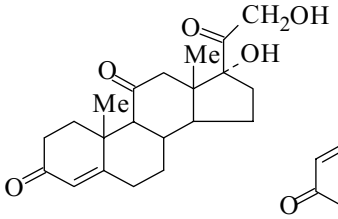
Hydrocortisone



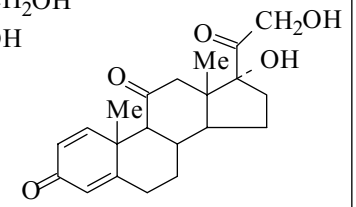
Prednisolone



Cortisone



Prednisone



Cortisone IUPAC: 4-Pregnene-17α, 21-diol-3, 11, 20-trione

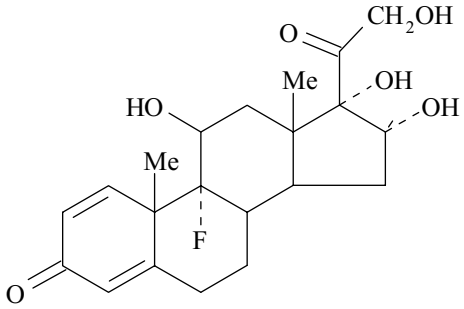
Hydrocortisone/Cortisol: 4-Pregnene-17α, 11, 21-triol-3, 20-dione

Prednisone and prednisolone is 1-Dehydro derivative of cortisone and hydrocortisone.

SAR

- Substituent's (16 α-OH, 16 α-Methyl, 16 β-Methyl, 16 α, 17 α-Ketals) like on cortisone ***decrease minerocorticoid activity***.
- Substituent's (9 α-F, 21-OH, 2 α-Methyl, 9 α –Chloro) like on cortisone ***increase minerocorticoid and glucocorticoid activity***.
- 9 α-F substitutions increase the anti-inflammatory activity.
- Triamacinalone have 9α-F, 16α-OH substitution in the structure of Prednisolone.
- ***Dexamethasone***-In the structure of Triamacinalone, 16α-OH group is substituent with 16α-methyl group. It is 5 times more potent anti inflammatory agent.

Trimcinolone



- Fluprednisolone, Fludrenolone, Fluoromethalone and Flucinolone are potent anti-inflammatory agent.

Minerocorticoids

- Reabsorption of Na^+ from distal tubule of kidney.
- Increase urinary excretion of both K^+/H^+ ions.

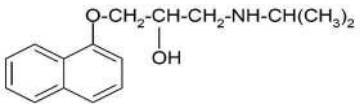
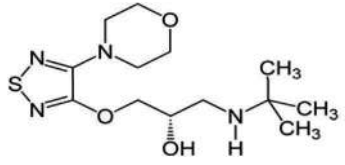
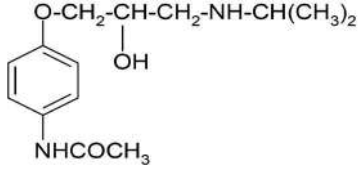
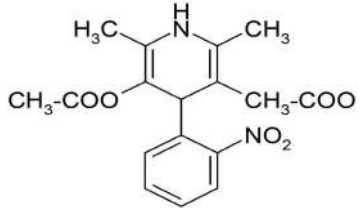
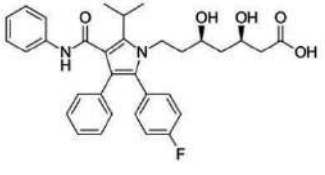
Glucocrticoids

- Glucocrticoids inhibits the action of Vitamin D and inhibits the formation of new tissue.
- In CVS, overdose of corticosteroids leads to hypertension due to high Na^+ concentration.
- Skelatal Muscle: Overdose of corticosteroids causes hypokalemia which leads to muscle weakness.

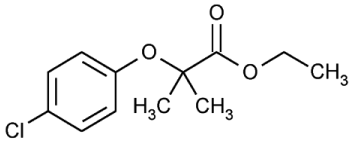
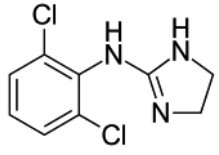
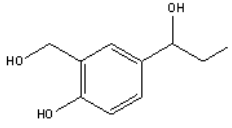
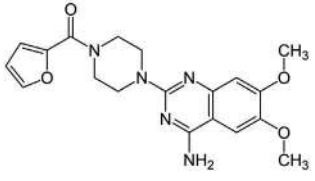
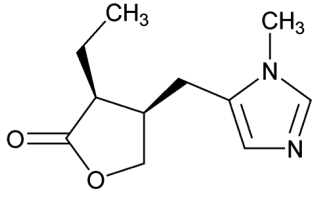
Contraindication

- Peptic ulcer
- Glucoma
- Diabetes
- Psychoses
- Heart disease

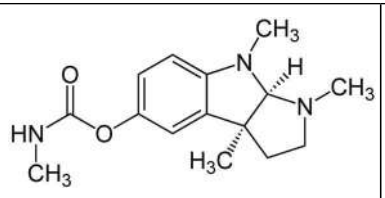
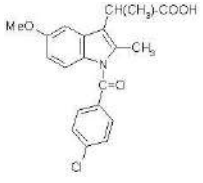
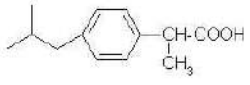
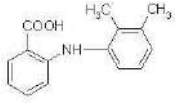
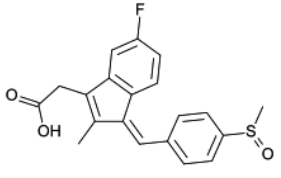
Important Medicinal Agent with its structure, basic ring, IUPAC name, Starting material for synthesis and special properties

Name of Drug	Structure	Basic Ring Present in structure	IUPAC Name	Starting Material For Synthesis	Remarks
Propanolol		**Basic Moiety:** Napthalene Aryloxy propanolamine derivatives	(R,S)-1-isopropylamino-3- (1- naphthyloxy) propan-2-ol	α-Napthol + Epichlorhydrine	**Side Effect:** 1. Bronchitis, 2. Hypoglycemia Contraindicating in Bronchial Asthma **Other Uses:** Migraine, Anxiety
Timolol		**Basic Moiety:** 1,2,5-Thiadiazole and Morpholin	(S)-1-((1,1-Dimethylethyl)amino)-3-((4-(4-morpholinyl)-1,2,5-thiadazol-3-yl)oxy)-2-propanol	Cynoamide + Supur-monochloride	Use in Migraine, Glaucoma and Myocardial Infarction
Atenolol		**Basic Moiety:** Aryloxy propanolamine	(R, S)-4-(2-hydroxy-3- isopropylaminopropoxy) - phenylacetamide.	4-Hydroxyphenyl acetamide + Epichlorhydrine	Use in angina
Nifedipine		**Basic Moiety:** Dihydropyridine	Dimethyl 1,4-dihydro-2,6-dimethyl-4- (2- nitrophenyl) pyridine-3,5-dicarboxylate	Methylacetoacetate+2- nitro Benzaldehyde + Ammonia	Angio edema 1st generation calcium channel blocker
Atorvastatin		**Basic Moiety:** Pyrrole	(3R,5R)-7-[2-(4-Fluorophenyl)-3-phenyl-4-(phenylcarbamoyl)-5-propan-2-ylpyrrol-1-yl]-3,5-dihydroxyheptanoic acid	---	**Side Effect:** 1. Myalgia 2. Rhabdomylosis 3. Angio-odema

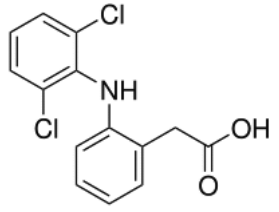
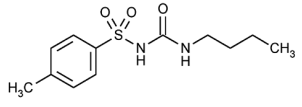
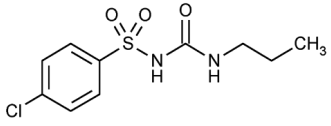
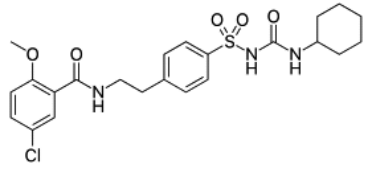
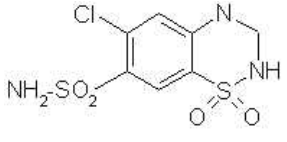
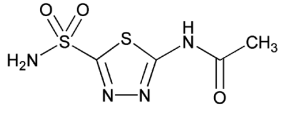
Important Medicinal Agent with its structure, basic ring, IUPAC name, Starting material for synthesis and special properties

Clofibrate		**Basic Moiety:** Phenoxy ester	**2-(4-Chlorophénoxy)-2-méthylpropanoate**	4-Chlorophenol+ Acetone+ Chloroform	**Side Effect:** Lithogenicity of Bile Gall stone formation **Metabolite:** Clofibric acid
Clonidine		**Basic Moiety:** Imidazoline	2-[(2,6-dichlorophenyl) imino]- imidazolidine hydrochloride	2,6-dichloroaniline +NH_4SCN + N-(2,6-dichlorophenyl) thiourea	**Side Effect:** 1. Dizziness, 2. Drowsiness 3. Impotence
Salbutamol		**Basic Moiety:** Phenol	(RS)-1-(4-hydroxy-3- hydroxymethylphenyl)-2-(tert-butylamino) ethanol	4-Hydroxy-3- Hydroxyl Methyl Benzaldehyde	**Side Effect:** 1. Flushing, 2. Muscle cramps β -Adrenergic agonist
Prazosin		**Basic Moiety:** Quinazoline + Piperazine + Furan	2-[4-(2-furoyl)piperazin-1-yl]- 6,7- dimethoxyquinazolin-4-ylamine hydrochloride	2,4-Dichloro-6,7- Dimethoxyquinazoline	**Side Effect:** 1. First dose Hypotension, 2. Failure of ejaculation(Impotency) Selective α1 blocker
Pilocarpine		**Basic Moiety:** Imidazole and Tetrahydrofuran	3S,4R)-3-ethyldihydro-4-[(1-methyl- 1H-imidazol- 5-yl) methyl]furan-2(3H)-one nitrate	2-Ethyl-3-Carboxy-2-Butyrolactone + Thionyl Chloride + Diazomethane	Made from leaves of the tropic plant *Pilocarpus jaborandi and Pilocarpus microphyllus* species Use in Glaucoma and Dryness of mouth (Xerostomia)

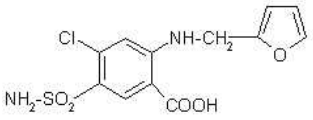
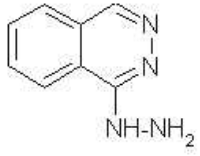
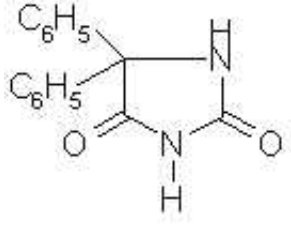
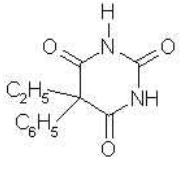
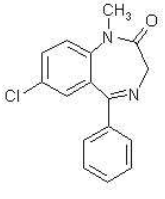
Important Medicinal Agent with its structure, basic ring, IUPAC name, Starting material for synthesis and special properties

Physostigmine		**Basic Moiety:** Pyrrolidine+ Carbamate	**(3aS,8aR)-1,3a,8-Trimethyl-1,2,3,3a,8,8a-hexahydropyrrolo[2,3-b] indol-5-yl methylcarbamate**	Pethoxymethyl aniline + α-Bromo propionyl bromide	Alkaloid isolated from *Physostigma venenosum* **Metabolism:** Hydolysis form eseroline , Oxidation forms rubreserine and then serine blue and brown.
Indomethacin		**Basic Moiety:** Indole derivatives	1-(4-chlorobenzoyl)-5-methoxy-2- methylindol-3-ylacetic acid	p-Anisidine +$NaNO_2$/HCl	S (+) is active Contraindicated in epilepsy, pregnancy.
Ibuprofen		**Basic Moiety:** Phenyl 1-methyl acetic acid	(R,S)-2-(4-isobutylphenyl) propionic acid	Isobutyl Benzene	S(+) is active,
Mefenamic Acid		**Basic Moiety:** N-phenyl Anthranilic acid	N-2,3-Xylyl anthranilic acid	2,3- Xylidine + 2-Chlorobenzoic acid	Contraindicate with Aspirin
Sulindac		**Basic Moiety:** Indane Derivative	(Z)-5-Fluoro-2-methyl-1-[p-(methylsulfinyl)benzylidene]indene-3-acetic acid	Glyoxalic acid	It is prodrug (half life is 8 hr) by reduction to form sulfide metabolite which is active.(half life is 16.4 hr). **Side Effect:** Diarrhoea

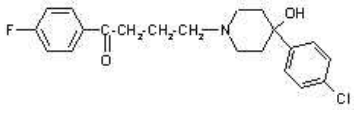
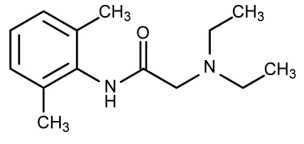
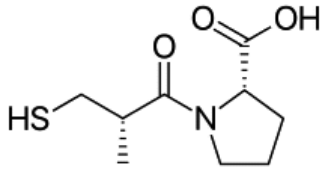
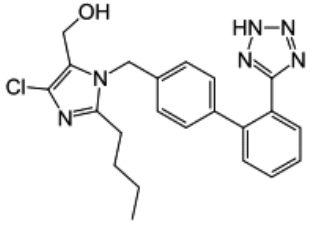
Important Medicinal Agent with its structure, basic ring, IUPAC name, Starting material for synthesis and special properties

Diclofenac		**Basic Moiety:** Biphenyl ring	2-[(2, 6-dichlorophenyl)-amino] phenyl acetate	2-Chlorobenzoic acid and 2,6-Dichloroaniline	It raise lithium and digoxin level in plasma It decreases arachidonic acid level in leukocyte.
Tolbutamide		**Basic Moiety:** Sulphonylurea Derivative	1-butyl-3-p-toluenesulfonyl urea	p- Toluene Sulfonylamide + Butyl isocyanate	**Metabolite:** Form hydroxyl active derivative
Chlorpropamide		**Basic Moiety:** Sulphonylurea Derivative	1-(p-Chlorophenyl sulfonyl)-3-propylurea	p- Chloro Benzene Sulfonylamide+ Propylisocyanate	Use in Diabetes insipidus and give Disulfiram like effect, Cause jaundice
Glibenclamide		**Basic Moiety:** Sulphonyl urea derivatives	1-[4-{2-(5-chloro-2- methoxybenzamido)- ethyl} benzenesulphonyl]-3-cyclohexylurea	2-Methoxy-5-Chlorobenzoic acid chloride + Phenylethylamine	Inhibiting ATP-sensitive potassium channels 2nd generation Sulfonylurea derivative
Chlorthiazide		**Basic Moiety:** Benzothiadiazine	6-chloro-1,1-dioxo-2H-1,2,4-benzothiadiazine-7-sulfonamide	3-Chloroaniline + Chlorosulphonic acid	**Side Effect:** 1. Gitelmann's syndrome 2. Bartter's syndrome
Acetazolamide		**Basic Moiety:** 1,3,4-Thiadiazole	N-(5-sulphamoyl-1,3,4-thiadiazol-2-yl)- acetamide	Hydrazine Hydrate **Or** 5-Amino, 2 Mercapto- 1,3,4-thiadiazole	Carbonic Anhydrase Inhibitor, Used in Glaucoma

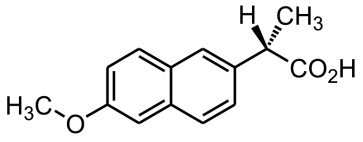
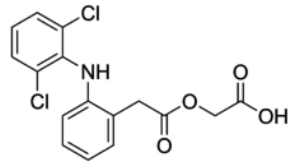
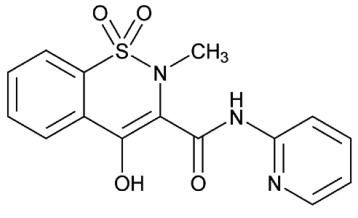
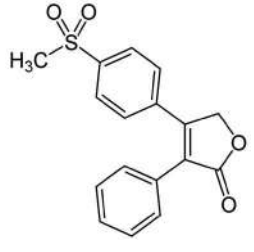
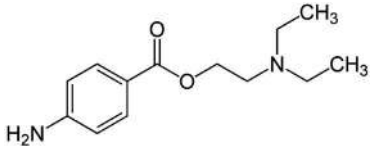
Important Medicinal Agent with its structure, basic ring, IUPAC name, Starting material for synthesis and special properties

Furosemide		**Basic Moiety:** Anthranilic acid derivative	4-Chloro-N-Furfuryl-5-Sul-phamoyl Anthranilic acid	2,4- Dichloroacetic acid+$ClSO_2OH$ By amidation reaction	Loop Diuretics
Hydralazine Hydrochloride		**Basic Moiety:** Pthalazine It acts by nitrate mechanism.	1-hydrazinona phthalazine	Phthalide/ Hy-droxyphthalide	**Side Effect:** 1. Lupus syndrome 2. Nasal stiffness 3. Drug of choice in hypertensive emergency
Phenytoin Sodium		**Basic Moiety:** Imidazolidine-2,4-dione It blocks sodium channel	5,5-Diphenyl imidazolidine-2,4-dione sodium	α-Bromo diphenyl acetyl urea + Alcoholic ammonia	**Side Effect:** Gum Hypertrophy Megaloblastic anemia Osteomalacia Hyperglycemia In all type of sei-zures except petit-mal type.
Phenobarbi-tone		**Basic Moiety:** 2,4,6 Tri Oxo Py-rimidine or 2,4,6 – Pyrimidone	**5-Ethyl-5-phenyl-2,4,6(1H,3H,5H)-pyrimidi-netrione**	Diethyl malonate + Urea	**Side Effect:** 1. Hangover effect 2. Drowsiness 3. Dizziness Long acting drug
Diazepam		**Basic Moiety:** Benzodiazepine	7- Chloro-1,3-Dihydro-1-Methyl-5-Phenyl- 1,4-Benzodiazepin-2-one	2-Amino 5-Chloro-benzophenone	**Metabolite:** Form active Nordazepam by N-demethyl-ation Skeletal muscle relaxants

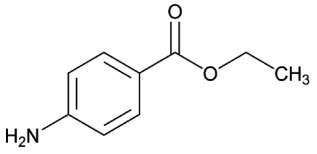
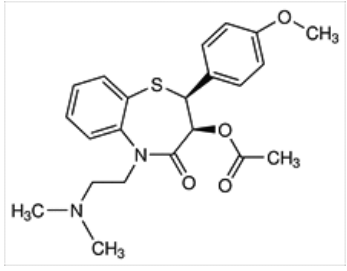
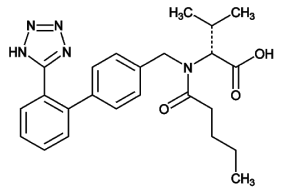
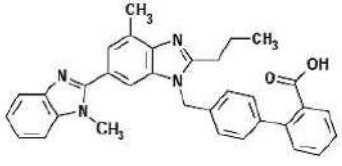
Important Medicinal Agent with its structure, basic ring, IUPAC name, Starting material for synthesis and special properties

Chlorproma-zine		**Basic Moiety:** Phenothiazine	[3-(2-chloropheno- thia-zin-10- yl)propyl]dimethyl amine hydrochloride	m-Chloro aniline + O-Chloro benzoic acid	**Side Effect:** 1. Insomina, 2. Anxiety, 3. Impotence 4. Extrapyramidal Typical antipsy-chotic drugs
Haloperidol		**Basic Moiety:** Fluorobutyrophe-none	4-[4-(4-chlorophenyl)-4-hy-droxy-piperidino]- 4`-fluo-robutyrophenone	4-chlorobutyryl Chloride + p- Chloro methyl styrene	**Side Effect:** 1. Insomnia, 2. Anxious
Lignocaine		**Basic Moiety:** Xylene	2- Diethylamino-2,6-Di-methylacetanilide	2,6-Dimethylaniline + Chloroacetic acid	Lignocaine ad-ministered with adrenaline
Captopril		**Basic Moiety:** Carboxy Proline	1-[(2S)-3-mercapto-2-methylpropionyl]-L- proline	tert- Butylprolinate + 3-thio-2-methyl propionic acid	**Side Effect:** 1. Hyperthermia 2. Dysguesia (Metallic taste) 3. Brassy Cough 4. Renal stenosis. It also increases bradykinin level and vasodilation
Losartan		**Basic Moiety:** Bi-pheyl + Tetrazole + Imidazole	2-butyl-4-chloro-1-{[2'-(1H-tetrazol-5-yl)biphenyl-4-yl] methyl}-1H-imidazol-5-yl) methanol	--	**Metabolism:** 5-CH_2OH Convert into COOH Group, Which is 15 time more potent than parent.

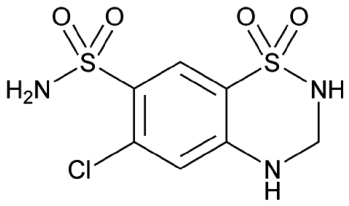
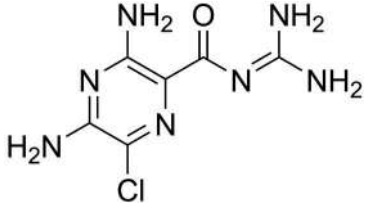
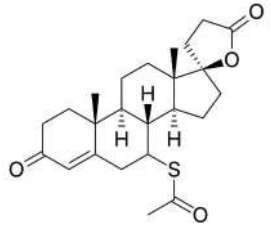
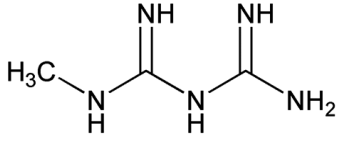
Important Medicinal Agent with its structure, basic ring, IUPAC name, Starting material for synthesis and special properties

Naproxen		**Basic Moiety:** Naphthalene (Propionic Acid derivative)	(2S)-2-(6-methoxynaphtha-len-2-yl)propanoic acid	α Chloromethyl-6-methoxynaphtha-lene	COX-I and II inhibitors, Dextrorotatory drug Used in acute gout
Aceclofenac		**Basic Moiety:** Diphenyl amine or Phenyl acetic acid derivative	2-[2-[2-(2,6-dichloroanilino) phenyl]acetyl]oxyacetic acid	2-[(2, 6-dichlorophe-nyl)- amino] phenyl acetate (Diclofenac) and Benzyl bromo-acetate	It is prodrug of Diclofenac.
Piroxicam		**Basic Moiety:** 1,1 Dioxo Benzothi-azine and Pyridine	4-hydroxy-2-methyl-1,1-dioxo-N-pyridin-2-yl-{6},2-benzothiazine-3-carbox-amide	----	Oxicam derivative **Common side ef-fect:** 1. Peptic ulcer 2. Long acting Half-life (45h) Used in acute gout
Rofecoxib		**Basic Moiety:** Furan-5-one	3-(4-methyl sulfonylphenyl)-4-phenyl-2H-furan-5-one	Phenyl acetic acid + Ethylbromoacetate	Selective cyclooxy-genase-2 (COX-2) inhibitor All selective COX-II inhibitor (Celecox-ib, Valdecoxib and Etoricoxib) cause CVS toxicity
Procaine		**Basic Moiety:** Benzoic acid derivative Amino alkyl ester of para amino benzoic acid	2-(diethyl amino) ethyl 4-aminobenzoate	4- Amino benzoic acid ethyl ester+ 2-Diethyl amino ethanol+ Sodium ethoxide	Benzoic acid derivative with local anesthetic and antiarrhythmic properties, it is me-tabolized to PABA

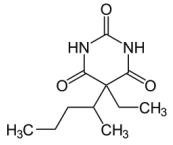
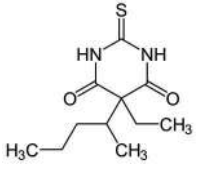
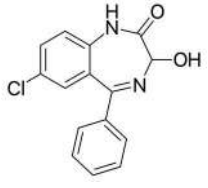
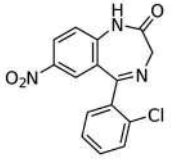
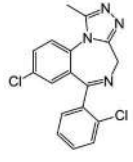
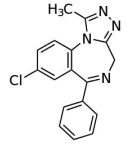
Important Medicinal Agent with its structure, basic ring, IUPAC name, Starting material for synthesis and special properties

Benzocaine		**Basic Moiety:** Benzoic acid derivative Alkyl ester of p-amino benzoic acid	Ethyl 4-aminobenzoate	PABA + Ethanol	Benzocaines is an ester of paraaminobenzoic acid, lacking the terminal diethylamino group of procaine
Diltiazem		**Basic Moiety:** Benzothiazepine	[(2S,3S)-5-[2-(dimethylamino)ethyl]-2-(4-methoxyphenyl)-4-oxo-2,3-dihydro-1,5-benzothiazepin-3-yl] acetate	4- Methoxy Benzaldehyde + Methyl chloro acetate	Calcium-channel blocker. It inhibits phosphorylation of myosin light chain phosphate and prevents binding with actin and prevents contraction
Valsartan		**Basic Moiety:** Biphenyl and Tetrazole	(2S)-3-methyl-2-[pentanoyl-[[4-[2-(2H-tetrazol-5-yl)phenyl]phenyl]methyl]amino] butanoic acid	L- Valine methyl ester HCl via Suzuki coupling reaction	Valsartan is a specific and selective type-1 angiotensin II receptor (AT1) antagonist It is valine containing drug.
Telmisartan		**Basic Moiety:** Benzimidazoles and Biphenyl system	2-[4-[[4-methyl-6-(1-methylbenzimidazol-2-yl)-2-propylbenzimidazol-1-yl] methyl]phenyl]benzoic acid	4-(Hydroxymethyl) phenyl boronic acid + 2- (2- bromophenyl)- 4, + 4-dimethyl 2 Oxazoline	Non-peptide angiotensin II receptor antagonist It contains tetrazole ring which bind to AT1 receptor

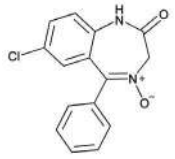
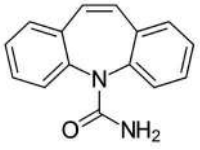
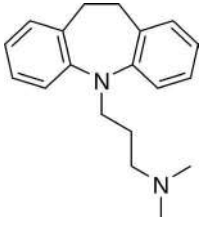
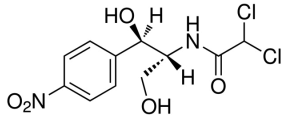
Important Medicinal Agent with its structure, basic ring, IUPAC name, Starting material for synthesis and special properties

Hydrochloro-thiazide		**Basic Moiety:** Benzothiadiazine-7-sulfonamide	6-chloro-1,1-dioxo-3,4-di-hydro-2H-1{6},2,4-benzothi-adiazine-7-sulfonamide	3-Chloroaniline + Chlorosulphonic acid	Short acting thia-zide diuretic It inhibit Na^+/Cl^- reabsorption from the distal convo-luted tubules in the kidneys **Side effect:** Hypo-glycemia
Amiloride		**Basic Moiety:** Pyrazine Ring and amidine moiety.	3,5-diamino-6-chloro-N-(diaminomethylidene) pyrazine-2-carboxamide	5,6-diaminouracil + Glyoxal	Antikaliuretic-diuretic agent Potassium-sparing diuretic It is 10 times more Potent than triam-terene.
Spironolac-tone		**Basic Moiety:** 17 - Spironolac-tone corticosteroid	S-[(7R,8R,9S,10R, 13S, 14S,17R)-10,13-dimethyl-3,5'-dioxospi ro[2,6,7,8,9,11,12,14,15,16-decahydro-1H-cyclopenta[a]phenan-threne-17,2'-oxolane]-7-yl] ethanethioate	Androstenolone - 3R - hydroxy-5-andro-sten-17-one+ So-dium amide in liquid ammonia	Competitive aldo-sterone antagonist **Metabolite:** Can-renone - It causes digoxin toxicity. **Side Effect:** 1. Gynecomastia 2. Atrophy
Metformin		**Basic Moiety:** Guanidine / Bigu-anide	3-(diaminomethyl idene)-1,1-dimethylguani-dine	Dimethyl amine + dicyanodiamide	Metformin is an oral antihypergly-cemic agent that improves glucose tolerance in pa-tients with NIDDM, **Side effect:** Weight gain

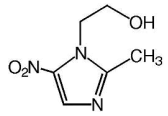
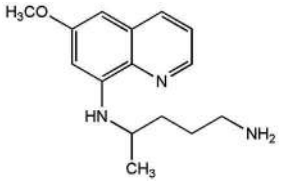
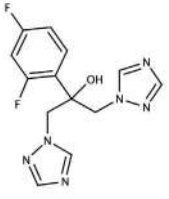
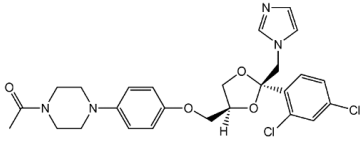
Important Medicinal Agent with its structure, basic ring, IUPAC name, Starting material for synthesis and special properties

Pentobarbitone		**Basic Moiety:** 2,4,6 Tri Oxo Pyrimidine or 2,4,6 – Pyrimidone	5-ethyl-5-pentan-2-yl-1,3-diazinane-2,4,6-trione	1-methyl butyl-ethyl malonic ester + urea	Short acting Barbiturates
Thiopental		**Basic Moiety:** 2-sulfanylidene-1,3-diazinane-4,6-dione	5-ethyl-5-pentan-2-yl-2-sulfanylidene-1,3-diazinane-4,6-dione	Diethyl malonate+ sodium metal	Ultra short acting Barbiturates General Anesthetics agent
Oxazepam		**Basic Moiety:** Benzodiazepin-2-one	7-chloro-3-hydroxy-5-phenyl-1,3-dihydro-1,4-benzodiazepin-2-one	6-chloro-2-chloromethyl-4-phenylquinaphenylquinazolin-3-oxide + Sodium hydroxide	Hydroxyl group contains benzodiazepine drug at third position
Clonazepam		**Basic Moiety:** Benzodiazepin-2-one	5-(2-chlorophenyl)-7-nitro-1,3-dihydro-1,4-benzodiazepin-2-one	2-chloro-2'nitrobenzophenon + 2-bromoacetyl bromide + Ammonia	Non-hydroxy benzodiazepine
Triazolam		**Basic Moiety:** Benzodiazepine fused with Traizole	8-chloro-6-(2-chlorophenyl)-1-methyl-4H-[1,2,4]triazolo[4,3-a][1,4]benzodiazepine	2- Glycylamino-2,5-dichlorobenzenophenone + Pyridine	Use in insomnia
Alprazolam		**Basic Moiety:** Benzodiazepine fused with Traizole	8-chloro-1-methyl-6-phenyl-4H-[1,2,4]triazolo[4,3-a][1,4]benzodiazepine	2,6-dichloro-4-phenylquinoline + hydrazine	Use in insomnia

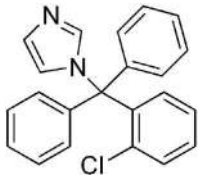
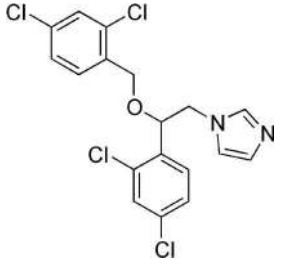
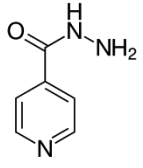
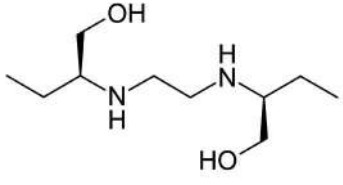
Important Medicinal Agent with its structure, basic ring, IUPAC name, Starting material for synthesis and special properties

Chlordiazepoxide		**Basic Moiety:** 1,4-benzodiazepin-2-imine	7-chloro-4-hydroxy-N-methyl-5-phenyl-3H-1,4-benzodiazepin-2-imine	2-amino-5-chloro-benzophenone + hydroxylamine	**Metabolite:** Nordazepam
Carbamazepine		**Basic Moiety:** Benzazepine Tricyclic Antidepressant.	benzo[b][1]benzazepine-11-carboxamide	5H – dibenzo[b, f] azepine + fremy's salt	Iminostilbene derivative Recently, Oxacarbazepine is used which contains oxo group at 10 position and no aplastic anaemia. Used in Trigeminal Neuralgia and Mania
Imipramine		**Basic Moiety:** Dihydro Benzazepine Tricyclic Antidepressant.	3-(5,6-dihydrobenzo[b][1]benzazepin-11-yl)-N,N-dimethylpropan-1-amine	10,11-dihydro-5H-dibenz[b,f]azepine + 3-dimethylaminopropylchloride + sodium azide	Tertiary amine derivative **Side effect:** 1. Anticholinergic type, 2. Postural hypotension.
Chloramphenicol		D-threo isomer is most active.	2,2-dichloro-N-[(1R,2R)-1,3-dihydroxy-1-(4-nitrophenyl) propan-2-yl]acetamide	p-Nitro acetophenone.	Binds to the bacterial 50S ribosomal subunit and inhibit protein synthesis **Side effect:** Grey baby syndrome Use in Rocky mountain Spotted Fever

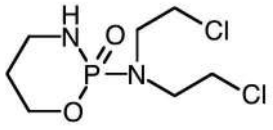
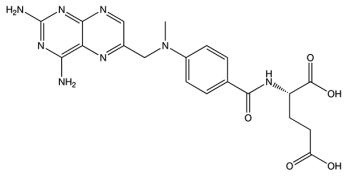
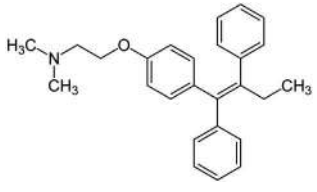
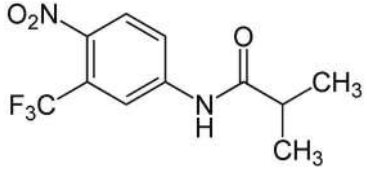
Important Medicinal Agent with its structure, basic ring, IUPAC name, Starting material for synthesis and special properties

Metronidazole		**Basic Moiety:** Nitro-imidazole	2-(2-methyl-5-nitroimid-azol-1-yl)ethanol	Ethane-1,2 diamine + cyanomethane + Zinc	Luminal Tropho-zotocidal Agents and also used in *H. pyroli.* treatment **Side effect:** Metallic taste
Primaquine		**Basic Moiety:** 8-Amino Quinoline	4-N-(6-methoxyquinolin-8-yl)pentane-1,4-diamine	4-methoxy-2-ni-troaniline and glycerol	Primaquin inhibits gametocyte stage, leavo isomer is less active than dextro isomer. Contraindicated in G6PD deficiency
Fluconazole		**Basic Moiety:** Triazole	2-(2,4-difluorophenyl)-1,3-bis(1,2,4-triazol-1-yl) propan-2-ol	2,4 diflourobenzene + chloroacetyl chlo-ride + aluminium hydroxide	It inhibits the fun-gal lanosterol 14 alpha-demethylase which thereby pre-vents the formation of ergosterol which is an essential component in the fungal cell mem-brane.
Ketoconazole		**Basic Moiety:** Piperazin and Dioxolan	1-[4-[4-[[(2S,4R)-2-(2,4-dichlorophenyl)-2-(imidazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy] phenyl]piperazin-1-yl] ethanone	2,4-dichlorophenacyl bromide + glycerol	Inhibits 14-alpha Demethylase **Side effect:** Reduced cortico-steroids synthesis and thereby used in Cushing's Syn-drome

Important Medicinal Agent with its structure, basic ring, IUPAC name, Starting material for synthesis and special properties

Clotrimazole		**Basic Moiety:** Imidazole	1-[(2-chlorophenyl)-diphenylmethyl]imidazole	2-chlorotriphenyl methylchloride + imidazole + triethylamine	Inhibits biosynthesis of the sterol ergostol
Miconazole		**Basic Moiety:** Imidazole	1-[2-(2,4-dichlorophenyl)-2-[(2,4-dichlorophenyl) methoxy]ethyl]imidazole	2,4 dicholoro phenacyl bromide + imidazole	Azole group of antifungal agent binds to fungal cytochrome P-450-dependant 14α-demethylase enzyme that is responsible for the demethylation anosterol to ergosterol.
Isoniazid		**Basic Moiety:** Hydrazide of Nicotinic acid, Basic Moiety: Pyridine	Pyridine-4-carbohydrazide	4-cyanopyridine + water + NaOH	Synthetic derivative of nicotinic acid **Adverse Effect:** 1. Peripheral Neuritis 2. Always advisable with vitamin B6 (Pyridoxine), 3. Hepatotoxicity
Ethambutol		**Basic Moiety:** Diethyl amine derivative (dextro isomer having maximum activity than leavo form)	(2S)-2-[2-[[(2S)-1-hydroxybutan-2-yl]amino]ethylamino]butan-1-ol	Nitropropane + formaldehyde	It inhibits "Arabinosyl transferase enzyme" to prevent polymerization of arabinoglycan in mycobacterial cell wall.

Important Medicinal Agent with its structure, basic ring, IUPAC name, Starting material for synthesis and special properties

Cyclophospha-mide		**Basic Moiety:** 1,3,2-oxaza-phosphinan	N,N-bis(2-chloroethyl)-2-oxo-1,3,2{5}-oxaza-phosphinan-2-amine	Bis(2-chloroethyl) amine + phospho-rous oxychloride	Alkylating agents (**Nitrogen mustard derivative)** **Metabolite:** Phos-phoramide Mustard (Having Antitumor activity) and Acrolein (Toxic to urinary bladder)
Methotraxate		**Basic Moiety:** 2,4-diamino pteridin	(2S)-2-[[4-[(2,4-diaminop-teridin-6-yl)methyl-me-thylamino]benzoyl]amino] pentanedioic acid	*N*-(4-methylamino-benmethylamino-benzoyl) glutaminic acid + 2-amino-4-hydroxyl-6-bromomethylpter-idine	Dihydro folate reduactase(DHFR) inhibitors
Tamoxifen		**Basic Moiety:** Tamoxifen has the same nucleus as diethylstilbestrol but possesses an additional side chain (trans isomer) which accounts for its antiestrogenic activity	2-[4-[(Z)-1,2-diphenylbut-1-enyl]phenoxy]-N,N-di-methylethanamine	Ethyl dezoxy benzoin + 4-methoxyphenyl magnesium bromide	Selective estrogen receptor modula-tors (SERMs), Estrogenic and an-tiestrogenic effects, Used in Osteopo-rosis.
Flutamide		**Basic Moiety:** To-luidine derivative, Non-steroidal anti-androgen	2-methyl-N-[4-nitro-3-(trifluoromethyl)phenyl] propanamide	4-nitro-3-trifluo-romethylaniline + isobutyric acid chloride	Active metabolite 2-hydroxyflutamide competitively block dihydrotestoster-one

MULTIPLE CHOICE QUESTIONS

1. Which of the following is β-halo alkyl amine derivative?
(a) Phenotamine (b) Tolazoline
(c) Phenoxybenzamine (d) None

2. Which of the following is aryl sulfonamide derivative?
(a) Tamsulosin (b) Prazosin
(c) Metaraminol (d) None

3. Which of the following drug is used as mydriatic when cyclopegia is not required?
(a) Phenylephrine
(b) Phenoxybenzamine
(c) Hydroxyamphetamine
(d) None

4. Phenoxybenzmine acts
(a) Directly on alpha receptor
(b) By irreversibly block alpha receptor
(c) By form ethylene iminium ion.
(d) All of the above

5. Which of following imdazoline derivative is selective α_2 agonist?
(a) Naphazoline (b) Tolazoline
(c) Clonidine (d) None

6. Clonidine is used as:
(a) Glucoma
(b) Migraine
(c) Opioid withdrawal syndrome
(d) All

7. Dipivefrin is prodrug of
(a) Adrenaline (b) Noradrenaline
(c) Both (d) None

8. Which of following drug inhibits dopa hydroxylase in noadrenaline synthesis?
(a) Levodopa (b) Carbidopa
(c) Disulfiram (d) Alpha methyl dopa

9. Which of following selective β_2 -agonists contains pyridine ring?
(a) Albuterol (b) Pirbuterol
(c) Terbutaline (d) None

10. Which of following selective β_2–agonists is not metabolized by COMT?
(a) Albuterol (b) Terbutaline
(c) Pibuterol (d) All

11. Which of long acting beta blocker is used for glaucoma?
(a) Timolol (b) Levabunolol
(c) Carteolol (d) Betaxolol

12. Timolol contains which of following basic rings:
(a) 1,2,5-Thiadiazole and morpholine
(b) 1,2,4-Thiadiazole and morpholine
(c) 1,4-Thiazole and morpholine
(d) None

13. The muscarinic receptor contains which of the following amino acids as residue for parasympathetic activity?
(a) Aspargine (b) Aspartic acid
(c) Glutamic acid (d) Glutamine

14. Which of the following is use in the diagnosis of myasthenia gravis?
(a) Physostigmine (b) Neostigmine
(c) Both (d) None

15. Which of following is hydrophilic organophosphate compound?
(a) Parathion (b) Malathion
(c) Ecothiophate (d) None

16. Which of following is selective novel M-3 antagonist?
(a) Drotaverine (b) Pirenzepine
(c) Darcifenacin (d) All

17. The basic ring present in pilocarpine is:
(a) Tetrahydrofuran and Indole
(b) Tetrahydofuran and Imidazole
(c) Tetrahydrofuran and Pyrole
(d) None

18. Which of following synthetic anticholinergic derivative is used in Parkinson disease?
(a) Amino alcohol ester
(b) Amino alcohol ether
(c) Amino amide
(d) None

19. Phenoxybenzmine acts:
(a) By forming aziridinium ion which blocks α receptor
(b) By irreversibly blocking α-receptor
(c) By forming ethylene iminium ion which blocks α-receptor
(d) All of above

20. Which of following is used in Alzheimer disease?
(a) Ambenonium
(b) Demecarium
(c) Oxotremorine
(d) Arecoline

21. What is the starting material for synthesis of salbutamol?
(a) Phenyl acetonitrile
(b) Methyl salicylate
(c) 4-Hydroxy propiophenone
(d) Mesitylene derivatives

22. Oxime is not used as antidote for
(a) Neostagmine (b) Echothiophate
(c) Dyflos (d) Tabun

23. Which of the following has bicyclic structure?
(a) Clidinium bromide
(b) Pyridostigmine
(c) Ecothiophate iodide
(d) Tropicamide

24. Clonidine, metronidazole and tinidazole have which of the group in common?
(a) Quinidine (b) Benzimidazole
(c) Imidazoline (d) None of the above

25. Pseudoepedrine is a
(a) Erythro isomer (b) Threo isomer
(c) Meso isomer (d) Racemic mixture 140.

26. Which isomer of propranolol is more active?
(a) Meso (b) Levo
(c) Dextro (d) Racemic

27. Which one of the following drugs does not act through G protein coupled receptors?
(a) Epinephrine (b) Dopamine
(c) TSH (d) Acetylcholine

28. A steroid nucleus having 19 carbon is _____
(a) Androstane (b) Estrane
(c) Gonane (d) Cholestane

29. Which of the steroids have neuromuscular blocking activity?
(a) Estrogen (b) Pancuronium
(c) Fusidin (d) Digitoxigenin

30. 17-β-hydroxyl androst-4-ene-3-one is IUPAC of
(a) Testosterone (b) Estradiol
(c) Estriol (d) Cortisone

31. Anesaldehyde is a starting material for synthesis of
(a) Diethyl stilbesterol
(b) Dexamethasone
(c) Trans stilbene
(d) Chlortrienisene

32. Which of the following have estrogenic activity?
(a) Gossypol (b) Genistein
(c) Coumesterol (d) Both (b) and (c)

33. Which of the following have anti estrogenic activity?
(a) BOMT (b) Flutamide
(c) Cyproterone (d) All of the above

34. Which of the following is a progesterone antagonist?
(a) Mifepristone (b) Gossypol
(c) Danazol (d) Both (a) and (b)

35. For a molecule to exhibit antihistaminic activity the distance between the aryl and aliphatic N should be?
(a) 5–6 A° (b) 4–5 A°
(c) 2–3 A° (d) 1–2 A°

36. 17 β-Hydroxyandrost-4-en-3-one is
(a) Estriol (b) Prosgesterone
(c) Testosterone (d) Floxymestrenone

37. Hypoglycemic agent with 1-(hexa hydro-1H-azepin-1-yl)-3-(p-tolyl sulphonyl) urea is
(a) GliCiazide (b) Tolazamide
(c) Tolbutamide (d) Gliburide

38. 3-Hydroxy-estra-1,3,5 (10)-trien-17-ones is
(a) Estradiol (b) Estrone
(c) 3-Hydroxyestrone (d) Dienesterol

39. Which is TXA_2 synthesis inhibitor (imidazole analogue)?
(a) Dazoxiben (b) Ridogrel
(c) Moxonidine (d) Aspirin

40. Compounds that have both TXA_2 synthetase inhibition as well as TXA_2 receptor blocking activity is
(a) Dazoxiben (b) Ridogrel
(c) Moxonidine (d) Aspirin

41. Which reagent is used for the conversion of hydrocortisone acetate to cortisone acetate?
(a) CrO_3 (b) $Se0_3$
(c) HOBr (d) m-CPBA

42. Cimetidine is developed from which of the following compounds?
(a) Metiamide (b) Ranitidine
(c) Procainamide (d) None of above

43. Pregnenolone on addition of 3C unit gives _____
(a) Cardenoloids (b) Bufedenoloids
(c) Steroidal moiety (d) All

44. 11-β, 21-dihydroxypregn 4-ene-3,18,20-trione is
(a) Aldosterone (b) Progesterone
(c) Cholesterole (d) Cortisol

45. Which of the following substituent does not increase glucocorticoid activity?
(a) 9-α-fluoro (b) 1-hydroxy
(c) 6-α-methyl (d) 21- hydroxyl

46. Cholesterol contains which of the following?
(a) 1 double bond and 1 OH group
(b) 2 double bond and 1 OH group
(c) 2 double bond and 2 OH groups
(d) 1 double bond and 2 OH groups

47. Which of the following corticosteroids does not have 17-α,21-diol system?
(a) Triamcinolone
(b) Methyl prednisolone
(c) Medrysone
(d) Pregnenolone

48. The starting material used for the synthesis of histamine is
(a) S-Histidine (b) L-Histidine
(c) D-Histamine (d) None

59. Which of following drug causes terfenadine cardiotoxicity?
(a) Erythromycin (b) Azithromycin
(c) Both (d) None

50. Which of following is metabolite of hydroxyzine?
(a) Astemizole (b) Cetrizine
(c) Loratadine (d) Terfenadine

51. The basic ring present in nizatidine is
(a) Imidazole (b) Furan
(c) Thiazole (d) None

52. Which of following is propylamine derivative?
(a) Antazoline (b) Triprolidine
(c) Azotidine (d) None

53. Which of following inhibits ketoconazole absorption?
(a) Ranitidine (b) Nizatidine
(c) Cimetidine (d) Famotidine

54. Which agent is used in Athlet's foot?
(a) Clioquinol (b) Cicloprox
(c) Haloprogin (d) 5-Flucytosin

55. The basic ring present in cicloprox is
(a) 2-Pyridone (b) 2-Piperidone
(c) 2-Pyridine (d) 2-Pyrrolidine

56. Coloroquin act by inhibiting following enzyme
(a) DNA and RNA polymerase
(b) DNA gyrase
(c) Dihydro folate reductase
(d) DNA synthase

57. The anti arrythmatic drug quinidine is a
(a) (+) Stereoisomer of quinine
(b) (–) Stereoisomer of quinine
(c) (+) Racemic mixture of quinine
(d) None of the above

58. The anti- malarial drug quinine contains
(a) Quinoline ring
(b) Quinclidine ring
(c) Isoquinoline ring
(d) Both (a) and (b)

59. Amodiaquine Iminoquinone is _____ product of amodiaquin.
(a) Oxidized (b) Reduced
(c) Alkylating (d) None of the above

60. Following drugs have a asymmetric centre except
(a) Primaquin (b) Pamaquin
(c) Quinocide (d) Pentaquin

61. 4-diethyl amino 1-methyl butyl amino is side chain of following agents
(a) Chloroquin (b) Primaquin
(c) None of the above (d) Both (a) and (b)

62. Which sulphonamide is not used in diuretics?
(a) Tolbutamide (b) Bumetanide
(c) Chlorthalidone (d) Furesemide

63. Which is following is not a prodrug?
(a) Progunil (b) Sulfasalazine
(c) Prontosil red (d) Trimethoprim

64. Sulfonamides are metabolized by humans principally by
(a) Acetylation (b) Deamination
(c) Oxidation (d) Conjugation

65. Which is the major side effect of sulfonamide?
(a) Crystalurea (b) Peripheral neuritis
(c) Kernictus (d) All of the above

66. Mafenide acetateis generally effective against
(a) *Clostridum welchi*
(b) *M. tuberculosis*
(c) *Haemophyllas ducreyi*
(d) None of the above

67. Which is basic ring present in sulfomethoxazole?
(a) Oxazole (b) Isoxazole
(c) Thiazole (d) None of the above

68. Which is the basic ring present in sulfadiazine?
(a) Pyridine (b) Pyrimidine
(c) Pyridazine (d) Piperidine

69. Which sulfonamide after metabolism is converted into sulfapyridine and 5-amino salicylic acid?
(a) Sulfacetamide (b) Sulfamethoxazole
(c) Sulfadiazine (d) Sulfasalazine

70. Which sulfonamides produces "Orange yellow color to urine" under alkaline condition?
(a) Sulfacetamide (b) Sulfamethoxazole
(c) Sulfadiazine (d) Sulfasalazine

71. Which isomer of emetine is clinically useful?
(a) Levo (b) Dextro
(c) D (d) L

72. Which alkaloid is used to treat amoebiasis?
(a) Ipecac (b) Theophylline
(c) Brucine (d) Aconite

73. Glycobiarsol is used in
(a) Antimalarial (b) Anti amoebic
(c) Anticancer (d) Antiashtamatic

74. Which nitroimidazole derivative has morpholino moiety?
(a) Tinidazole (b) Ornidazole
(c) Timorazole (d) Metronidazole

75. Which antibiotic has direct action on trophozoitocidal?
(a) Paramomycin (b) Neomycin
(c) Natamycin (d) Erythromycin

76. Which is not a true for isoniazid?
(a) It is hydrazide of isonicotinic acid
(b) Structurally similar to pyridoxine
(c) It inhibit Mycolase Synthase
(d) It is hydrazide of nicotinic acid

77. Isoniazid is synthesized from
(a) Methyl ester of isonicotinic acid+ hydrazine
(b) Methyl ester of nicotinic acid+ hydrazine
(c) Methyl ester of is nicotinic acid+ Phenyl hydrazine
(d) Methyl ester of is isonicotinic acid+ Methyl hydrazine

78. Which of the following adverse effects is not associated with INH?
(a) Hepatotoxicity (b) Xerostomia
(c) Peripheral neuritis (d) Ototoxicity

79. Match the following

MOA	Drugs
1. Inhibit arabinosyl transfarase	a. Rifampin
2. Inhibits DNA dependent RNA polymerase	b. Thiacetazone
3. Inhibits folic acid synthesis	c. Myambutol
4. Inhibits fatty acid synthase I	d. Pyrizinamida
	e. Ethionamide

(a) 1-c, 2-a, 3-b, 4-d (b) 1-c, 2-a, 3-b, 4-e
(c) 1-c, 2-a, 3-e, 4-d (d) 1-c, 2-a, 3-d, 4-b

80. Which of the following adverse effects is not associated with rifampin?
(a) Flu-like syndrome (b) Xerostomia
(c) Hepatitis (d) Red orange color to urine

81. Which isomer of ethambutol is clinically active?
(a) Dextro (b) Levo
(c) Threo (d) Erythro

82. Monthly eye examination is required with following drug treatment
(a) Ethambutol (b) Pyrazinamide
(c) Ethionamide (d) Streptomycin

83. Lupas like reaction is side effect of
(a) Ethambutol (b) PAS
(c) Ethionamide (d) Streptomycin

84. Cycloserine is analogue of
(a) D-alanine (b) D-serine
(c) L-serine (d) L-alanine

85. Which antibiotic is also known as ansamycin antibiotics?
(a) Polyene (b) Macrolide
(c) Rifampin (d) Tetracycline

86. Orally active phenazine dye is present in
(a) Pyrizinamide (b) Thiacetazone
(c) Clofazimine (d) Prothionamide

87. Which is the principle metabolite of rifampin?
(a) 25-desacetylated RMP
(b) 3-formyl RMP

(c) RMP-quinone
(d) N-demethylated RMP

88. Which is long-acting sulphonamide?
(a) Sulphadoxine (b) Sulphacetamide
(c) Sulphasalazine (d) Sulphadiazine

89. Which is not true point in case of sulphonamide SAR?
(a) N-4 site can be modified to produce prodrug
(b) Benzene ring is necessary for activity
(c) N-1 of sulphonamide must be substituted
(d) Heterocyclic ring on N-1 yielded potent compound

90. The starting material for the synthesis of sulphadiazine is
(a) Guanidine + formyl acetic acid
(b) Propionitrile + ethyl acetate
(c) Guanithidine + formyl acetic acid
(d) Propionitrile + formyl acetic acid

91. Which floro quinolone does not contain cycloprpane ring at N-1 position
(a) Gatifloxacin (b) Ciprofloxacin
(c) Sparfloxacin (d) Ofloxacin

92. Peptidoglacan is made up of _____ amino sugar part.
(a) N-acetyl glucosamine+N-acetyl muramic acid
(b) N-acetyl biosamine+N-acetyl muramic acid
(c) N-acetyl glucosamine+ N-acetyl glucosamine
(d) N-acetyl muramic acid+ N-acetyl muramic acid

93. Which is not true in case of penicillin?
(a) Good oral absorption but relatively acid labile
(b) Ineffective against Gram-negative bacilli
(c) Useful against Gram-positive cocci
(d) Highly stable to acid /base

94. 2,6-Dimethoxy phenyl penicillin is IUPAC of
(a) Methicillin (b) Ampicillin
(c) Amoxicillin (d) Carbencillin

95. Which of the following is broad-spectrum penicillin?
(a) Oxacillin (b) Methicillin
(c) Ampicilline (d) Azlocillin

96. Which of the following is a broad-spectrum ureido penicillin?
(a) Carbenicillin (b) Methicillin
(c) Ticarcillin (d) Azlocillin

97. Which of the following is a anti pseudomonal penicillin?
(a) Carbenicillin (b) Methicillin
(c) Ampicillin (d) Azlocillin

98. Match the following

A. Penicillin-F	1. Phenoxy methyl penicillin
B. Penicillin-G	2. Pent-2-enlypenicillin
C. Penicillin X	3. p-Hydroxy benzylpenicillin
D. Penicillin V	4. Benzly penicillin
E. Penicillin K	5. *n*-Heptyl penicillin

(a) A-2, B-4, C-3, D-1, E-5
(b) A-5, B-4, C-3, D-1, E-2
(c) A-4, B-2, C-3, D-1, E-5
(d) A-3, B-4, C-2, D-1, E-5

99. Which of the following is a β-lactam antibiotic?
(a) Penicillin + cephalosporin
(b) Streptomycin + gentamycin
(c) Minocyclin + doxycycline
(d) Chloramphenicol

100. Which isomer of ampicillin is clinically more active than others?
(a) D-(–) (b) D-(+)
(c) L-(–) (d) L-(+)

101. β-lactamase inhibitor clavunic acid is
(a) 1,1-dioxo penicillanic acid
(b) Carbapenam
(c) Cepham
(d) 1-oxapenam structure, which has no acyl amino side chain

102. Which is an example of penam 1,1-dioxide?
(a) Sulbectam (b) Tazobactam
(c) Clavunic acid (d) Both (a) and (b)

103. Which is an example of monobectam?
(a) Sulfazecin (b) Aztreonam
(c) Tigemonam (d) All

104. Which drug inhibits mycobacterial RNA polymerase and is very useful in treating *Mycobecterium avium complex*?
(a) INH (b) Ethionamide
(c) Capreomycin (d) Rifambutin

105. Clavunic acid has a beta lactam ring fused with
(a) Thienyl system (b) Thiadiazole
(c) Thiazolidone (d) Oxazolidone

106. 4-chloro benzophenone is a starting material of
(a) Mebendazole (b) Albendazole
(c) Thibendazole (d) None of above

107. Which of the following agent has trioxane ring?

(a) Artemether (b) Metronidazole
(c) Halofantrine (d) Prongunil

108. Which of the following is not an alkylating agent?
(a) Cyclophosphamide
(b) 6-Mercaptopurin
(c) Chlorambucil
(d) Thiotepa

109. Which of the following agents has aziridine moiety?
(a) Dacarbazine (b) Busulfan
(c) Altretamine (d) Thiotepa

110. Acreloin toxicity is associated with:
(a) Cyclophosphamide
(b) 6-Mercaptopurin
(c) Melphalan
(d) Dacarbazine

111. Which of the following drug is a phenyl alanine derivative?
(a) Chlorambucil (b) Carmustine
(c) Melphalan (d) Dacarbazine

112. Which of the following drugs is not a derivative of nitrosourea?
(a) Streptozocin (b) Carmustine
(c) Lomustine (d) All of the above

113. Which of the following drugs is a purine base antagonist?
(a) Fludrabin (b) 6-Mercaptopurin
(c) Cladrabin (d) All of the above

114. Which of the following drugs is pyrimidine base antagonist?
(a) Cytrabin (b) Tegafur
(c) Capcitabin (d) All of above

115. All cytotoxic antibiotic have anthracyclin ring, except
(a) Doxorubicin (b) Epirubicin
(c) Iadrubin (d) Dactinomycin

116. Anthracyclinone antibiotics differ from each other by
(a) Location of phenolic –OH group
(b) Location of $-OCH_3$ group
(c) Both (a) and (b)
(d) None

117. Adriamycinol is 13-OH metabolite of:
(a) Doxorubicin (b) Daunorubicin
(c) Iadrubin (d) Dactinomycin

118. Actinomycin having basic ring is
(a) Phenothiazine (b) Phenoxazone
(c) Naphtoquinone (d) None

119. Indoline-containing moiety present in vinca alkaloid is known as
(a) Catranthine (b) Vindoline
(c) Vinleuroside (d) Vinrosidin

120. Which of the following is a semisynthetic derivative of podophyllotoxin?
(a) Etoposide (b) Mithramycin
(c) Paclitaxel (d) Colchicine

121. Which of the following drugs is used as anti androgen in prostate cancer?
(a) Flutamide (b) Aminoglutethimide
(c) Mitotane (d) All

122. Which of the following drug is used as SERM in advance breast cancer?
(a) Flutamide (b) Aminoglutethimide
(c) Mitotane (d) Tamoxifen

123. Which of the following agents is used to cure tumour?
(a) L-aspargin (b) L-asparginase
(c) Pegaspargase (d) Both (b) and (c)

124. Tolcapone is a
(a) Catechol-O-methyltransferase (COMT) inhibitors
(b) Antimuscarinic agents
(c) Inhibitors of MAO-B
(d) Dopa decarboxylase inhibitor

125. Which of the following is an anti fungal antibiotic?
(a) Erthromycin (b) Bleomycin
(c) Cycloserine (d) Cycloheximide

126. Topically used sulphonamide is
(a) Sulphadoxine
(b) Sulphamethoxazole
(c) Silversulphadiazine
(d) Dapsone

127. Rituxumab belongs to which type of monoclonal antibody?
(a) Murine
(b) Chimeric
(c) Humanized
(d) Human monoclonal antibody

128. Sulfasalazine is a prodrug that is activated in the intestine by bacterial enzymes. The enzyme responsible is:
(a) Azoreductase
(b) Choline esterase

(c) Glucuronyltransferase
(d) Amylase

129. In cephalosporins, a higher resistance to hydrolysis by β-Iactamase is shown when _____?
(a) The amino group is acylated
(b) Replacement of sulphur with oxygen
(c) Oxidation of ring sulphur to sulfoxide or sulfone
(d) Introduction of C-7 α-methoxy group

130. Which of the following is not present in macrolide?
(a) A large lactone ring
(b) A glycosidically linked amino sugar
(c) A spiroketal group
(d) A ketone group

131. Which of the following contains diethylamino substituents?
(a) Doxycycline (b) Minocycline
(c) Methacycline (d) Demeclocycline

132. Polyene antibiotics such as amphotericin-B most likely
(a) Inhibits bacterial DNA synthesis
(b) Binds to prokaryotic ribosomes
(c) Acts as anti metabolitis
(d) Reacts with sterols in the membrane

133. β-lactamase inhibitor calvulanic acid is
(a) Carbapenam (b) L-oxopenam
(c) Cepham (d) None of the above

134. Which of the following compounds contains isoxazole group?
(a) Cloxacillin (b) Thiabendazole
(c) Benzimidazole (d) Albendazole

135. What is the chemical name of penicillin V?
(a) Phenoxy methyl penicillin
(b) Benzyl penicillin
(c) D-α-amino-p-hydroxy ethyl penicillin
(d) 2,6-dimethoxyphenyl penicillin

136. Which of the following does not cause hepatitis?
(a) Ethambutol (b) Isoniazid
(c) Rifampin (d) Pyrazinamide

137. Which of the following belongs to class NNRTI?
(a) Ritonavir (b) Abacavir
(c) Nevirapine (d) Lamivudine

138. The following pairs are correct except?
(a) Ivermictin-tonic paralysis
(b) Piperazine-flaccid paralysis
(c) Pyrantel pamoate-spastic paralysis
(d) Levamisole-flaccid paralysis

139. Which of the following is not from an active metabolite?
(a) Cyclophosphamide (b) Thio-tepa
(c) Nitrosoureas (d) Melphalan

140. Whch is the principle alkylator that is formed from cyclophosphamide?
(a) Aldophosphmide
(b) 4-ketocyclophosphamide
(c) 4-hydroxycyclophosphamide
(d) Phosphoramide mustard

141. Which of the antineoplastic agent is metabolized by xanthine oxidase?
(a) 6-Mercaptopurine (b) Cholrambucil
(c) Aminopterine (d) None of the above

142. Diloxanide furoate is a furonyl ester of a phenol and it is synthesized starting from
(a) 0-chlorophenol (b) p-chlorophenol
(c) m-chlorophenol (d) p-aminophenol

143. Which of following is second-generation quinolone antibiotic?
(a) Ciprofloxacin (b) Ofloxacin
(c) Sparfloxacin (d) Nalidixic acid

144. Which of the following is not correct?
(a) Alopecia and cystitis due to acrolein the cyclophosphamide metabolite
(b) Cirtrovorum factor given in methotraxate toxicity
(c) Cytrabine inhibits DNA polymerase
(d) Mitomycin acts as alkylating agent at position 7

145. Which of the statements is correct?
(a) Amino glycoside inhibition is concentration dependent
(b) β-lactam inhibition is time dependent
(c) Macrolide inhibition is concentration dependent
(d) Only (a) and (b) are correct

146. Which of the following acts directly on the cell membrane of microorganism affecting permeability?
(a) Penicillin (b) Nystatin
(c) Tetracycline (d) Erythromycin

147. At which place does penicillin have a carboxylic acid group?
(a) C-3 (b) C-2
(c) C-6 (d) C-7

148. Which of the following is not a synthetic drug?
(a) Isoniazide (b) Rifampin
(c) Pyrazinamide (d) Ethionamide

149. What is the mechanism of PAS?
(a) Inhibits mycolic acid synthesis
(b) Inhibits folic acid synthesis
(c) Inhibits DNA dependent RNA polymerase
(d) Makes the tuberculosis organism susceptible to reactive oxygen

150. Which pair is not matching?
(a) Penicillin Inhibits transpeptidase
(b) Fluoroquinotone Inhibits enzyme topoisomerase
(c) Dapsone Inhibits DHF reductase enzyme
(d) Ethambutol Inhibits arabinosyltranferases

151. Which of the statements is true?
(a) Pyrazinamide is more active in alkaline media
(b) Ethambutol partially crosses BBB
(c) Streptomycin is also used in leprosy
(d) Both (a) and (c)

152. Which of the following paired incorrectly?
(a) Zidovudine Thymadine analogue
(b) Lmivudine Deoxycytidine analogue
(c) Abacavir Guanosine analogue
(d) Stavudine Adenosine analogue

153. Which combination is effective against hepatitis C?
(a) Interferon α + Ribavarin
(b) Zidovudine + Lamivudine
(c) Acylovir + Famciclovir
(d) Both (a) and (d)

154. Which of the following mono clonal antibody is used as anticancer agent?
(a) Rituximab (b) Muromonab
(c) Trastutuzumab (d) (a) and (c)

155. Primaquine is synthesized from?
(a) Toluene (b) Anisole
(c) Phenol (d) p-nitro phenol

156. The active metabolite of anticancer cyclophosphamide is
(a) N-hydroxy cyclophosphamide
(b) N-methyl cyclophosphamide
(c) N-acetyl cyclophosphamide
(d) N-propyl cyclopqosphide

157. Which of the following statement is incorrect?
(a) Resistance to quinolones due to chromosomal mutation producing enzyme DNA gyr
(b) Diuretic + trimethoprime-thrombocytopaenia
(c) Quinolone is more active at acidic pH
(d) Levofloxacin oral bioavailablity-is 100%

158. Which of the following drugs belongs to ansamycin group?
(a) Neomycin (b) Rifampicin
(c) Mithramycin (d) Bleomycin

159. Which of the following is without heterocyclic ring?
(a) Nelfinavir (b) Loviride
(c) Troviridine (d) Zidovudine

160. Which of the following has imidazole nucleus?
(a) Ciclopirox (b) Butaconazole
(c) Griseofulvine (d) Co-trimoxazole

161. Which is the potent inhibitor of tymidylate synthase?
(a) Naftifine (b) 5-fluocytosine
(c) Ciclopirox (d) Ketoconazole

162. Which is an inhibitor of sterol-14-α-demethylase?
(a) Naftifine (b) 5-fluocytosine
(c) Ciclopirox (d) Ketoconazole

163. Which of the following is the antifungal antibiotic?
(a) Naftifine (b) 5-fluocytosine
(c) Nystatine (d) Nafimidone

164. What is the starting material for synthesis of ritonavir?
(a) Pichlorohydrine
(b) Dioxolane
(c) Hydrocinnamyl chloride
(d) Phenylalanine

165. Which of the following is synthesized from 5-chloroantranilic?
(a) Efavirenz (b) Emivjrdine
(c) Loviridine (d) Nevirapine

166. Which of the following is thiazole analogue?
(a) Nelfinavir (b) Ritonavir
(c) Saquinavir (d) Loviride

167. Amodiaquine is a derivative of
(a) 3-Amino quinoline
(b) 4-amino quinoline
(c) 2-amino quinoline
(d) 5-amino quinoline

168. What is the mechanism of action of levamisole?
(a) Nicotine-like action, stimulating and subsequently blocking neuromuscular junction
(b) Reversal inhibition of *S*-adenosyl-L′-methionine-*n*-decarboxylase
(c) Stimulates acetylcholine trasferase
(d) Stereospecific inhibitor of alcohol reductase

169. C-12 position is a part of the keto-enol tautomer in which of the following systems?
(a) Macrolides antibiotics
(b) Penicillins
(c) Tetracyclines
(d) Aminoglycoside antibiotics

170. The cephalosporin antibiotic with a cyanomethyl side chain is _____
(a) Cephalexin (b) Cefadroxil
(c) Cefamandole (d) Cephacetrile

171. The antibiotic with imine functionality is?
(a) Ampicillin (b) Roxithromycin
(c) Doxycyclin (d) Chloramphenicol

172. The naturally occurring tetracyclines contain which of the following?
(a) α-C4 dimethyl amino substituent
(b) α-C3 dimethyl amino substituent
(c) α-C3-C4 keto enol group
(d) α-C3 dihydroxy substituent

173. β-lactum inhibitor clavulanic acid is
(a) Carbapenam (b) 1-Oxopenam
(c) Cepham (d) None of the above

174. An imidazole aromatase inhibitor which is used to reduce estrogen level is?
(a) Mitotane (b) Paramethasone
(c) Emestine (d) Anastrazole

175. Finasteride acts as 5-α-reductase inhibitor because of which property?
(a) It has C-1-2 double bond
(b) It has C-1-5 double bond
(c) It is nonsteroidal
(d) It has 3-keto group

176. Which sulphonamide does not contain free aromatic amino group?
(a) Dapsone (b) Mefenide
(c) Trimethoprim (d) None of the above

177. Which of the following causes inhibition of protein synthesis?
(a) Linezolid (b) Polymyxin
(c) Ciprofloxacin (d) Penicillins

178. Which of the statement is correct?
(a) Sulfonamides resistance due to change in binding site at acetyl transferase
(b) Tetracycline resistance due to efflux protein in cell membrane
(c) Chloramphenicol resistance due to change in porin channel
(d) Both (a) and (c)

179. Which of following is anthranilic acid derivative?
(a) Furosemide (b) Bumetanide
(c) Ethacrynic acid (d) None

180. In AT-II angtagonist, the functional group responsible for AT-1 receptor blocking activity is
(a) Imidazole (b) Tetrazole
(c) Triazole (d) None

181. Which of following is ultra short acting cardioselective beta blocker?
(a) Atenolol (b) Nebivolol
(c) Esmolol (d) None

182. The adverse effect of MG COA-reductase inhibitor is:
(a) Myalgia
(b) Myositis and rhabdomylosis
(c) Angio-oedema
(d) All of the above

183. Cholestyramine is copolymer of:
(a) Divinyl benzene with epichlorohydrin
(b) Tetraethylpentamine with quaternary ammonium salt
(c) Divinyl benzene with quaternary ammonium salt
(d) Tetraethylpentamine with epichlorohydrin

184. Lovastatin is obtained from which of following microorganism?
(a) *Aspergiilus niger* and *Monoscus ruber*
(b) *Aspergiilus terreus* and *Monoscus rubber*
(c) *Penicillium citrinium* and *Monoscus rubber*
(d) *Penicillium citrinium* and *Aspergiilus terreus*

185. Increased risk of arthrosclerosis is associated with decreased serum level of
(a) LDL (b) HDL
(c) Triglyceride (d) VLDL

186. Clofibrate increases toxicity of
(a) Phenytoin (b) Tolbutamide
(c) Coumarin (d) All of the above

187. Which of following drug causes Monday morning sickness?
(a) Isosorbide dinitrate
(b) Glyceryl trinitrate
(c) Isosorbide mononitrate
(d) None

188. For antianginal activity, the nitrate derivative must be metabolized into:
(a) Nitric oxide (b) Nitrous oxide
(c) Both (d) None

189. Which of following diuretics inactivate sulfahydryl (–SH) group of enzyme?
(a) Furosemide (b) Bumetanide
(c) Ethacrynic acid (d) None

190. Diuretics mean _____
(a) Drugs which increases blood pressure
(b) Drugs which increases blood flow
(c) Drugs which increases urine flow
(d) Drugs which decreases urine flow

191. High ceiling diuretics is _____
(a) Ethacrinic acid (b) Bumetanide
(c) Furosemide (d) All of the above

192. Osmotic diuretics are used
(a) To cure higher blood pressure
(b) For treatment of glaucoma.
(c) To cure gout
(d) Both (a) and (b)

193. Metabolite of a spironolactone is _____
(a) Amrinone (b) Milrinone
(c) Canrinone (d) Samzonone

194. Hearing loss is side effect of one of _____
(a) Acetazolamide (b) Aldosterone
(c) Amiloride (d) Hydroclorethiazide

195. Furosemide contains _____ ring
(a) Furan (b) Thiazole
(c) Oxazole (d) Imidazole.

196. Sulphonamide group is present at thiazide diuretic at position
(a) 3 (b) 6
(c) **7** (d) 9

197. Most serious side effect of spironolactone is
(a) Hyperkalemia (b) Hypokalemia
(c) Hypernatremia (d) Hyponatremia

198. Drug used for the treatment of acute attack of gout is _____
(a) Colchicine (b) Probenicide
(c) Sufipyrazone (d) Allopurinol

199. Bumetanide contains _____
(a) Phenoxy group at 4th position
(b) Phenoxy group at 5th position
(c) Phenoxy group at 3rd position
(d) Does not contain any phenoxy group.

200. Increased risk of artheroscerosis is associated with decreased serum level of
(a) LDL (b) HDL
(c) Triglyceride (d) VLDL

201. Intermediate in biosynthesis of cholesterol is
(a) Mevalonic acid and Isopentenyl pyrophosphate
(b) Mevanolic acid and Aldosterone
(c) Isoprenaline and Aldosterone
(d) Isoprenaline and Isopentenyl phosphate

202. Which of the following causes Bartter's syndrome____
(a) Loop diuretics (b) Osmotic diuretics
(c) Thiazide diuretics (d) K^+ sparing diuretics

203. Digoxin absorption is decreased by which of the following drug:
(a) Metoclopramide and sucralfate
(b) Metoclopramide and cholestyramine
(c) Both (a) and (b)
(d) None of above

204. To avoid lithium toxicity patient using lithium carbonate for mood disorder should not be prescribed
(a) Acetazolamide (b) Furosemide
(c) Mannitol (d) Hydrochlorthiazide

205. Patients taking digoxin for CHF are found to have elevated cholesterol level for whom which agent should not be prescribed with it?
(a) Lovastatin (b) Cholestyramine
(c) Clofibrate (d) Niacin

206. One of following diuretics is similar to that of diazoxide:
(a) Acetazolamide (b) Furosemide
(c) Mannitol (d) Chlorthiazide

207. Which of following drugs have 1,3,4 thiadiazole ring?
(a) Amiloride (b) Dichloropenamide
(c) Acetazolamide (d) None

208. Digoxin has the following characteristics _____

(a) Its action is terminated by metabolism
(b) Plasma half-life is 20 hours
(c) Used in atrial fibrillation by increased force of contraction
(d) Both (b) and (c)

209. IUPAC name of amrinone is
(a) 5- amino (3,4'dipyridin)-6-one
(b) 4-amino 3-4'dipyridin)-6-one
(c) 5-amino (3-4'dipyridin)-4-one
(d) 4-amino (3-4'dipyridin)-3-one

210. PDE-III inhibitor
(a) Inhibits Na+-K+ ATPase pump
(b) Inhibits hydrolysis of C-AMP
(c) Both (a) and (b)
(d) None of the above

211. Increased plasma concentration of digoxin occurs due to
(a) Omeprazole (b) Phenylbutazone
(c) Quinidine (d) Both (b) and (c)

212. The plasma half life of digoxin is:
(a) 5–7 days (b) 20 hours
(c) 40 hours (d) 48 hours

213. The sugar present in strophanthin-G is:
(a) Rhamnose (b) Digitoxose
(c) Cymarose (d) None of the above

214. Which of following is not benzimidazole derivative:
(a) Vesverinone (b) Sulmazole
(c) Milrinone (d) Pimabendan

215. In digitalis glycoside 17th position of steroidal ring is substituted by
(a) ά,β unsaturated five-member lactone ring
(b) ά,β unsaturated six-member lactone ring
(c) ά,β unsaturated five-member pyrone ring
(d) ά,β unsaturated five-member lactum ring

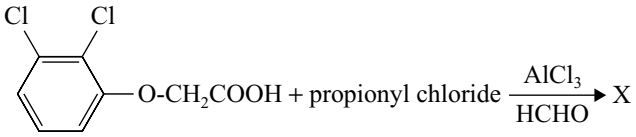
216. The basic ring present in atorvastatin is:
(a) Indole (b) Pyrrole
(c) Napthalene (d) None of the above

217. Predict product obtained by treating 6-chloro-3,5-diamino pyrazine 2-methyl carbonate with guanidine.
(a) Amiloride (b) Hydrochlor thiazide
(c) Triamterene (d) Furosemide

218. To avoid lithium toxicity patient using lithium carbonate for mood disorder should not be prescribed
(a) Acetazolamide (b) Furosemide
(c) Mannitol (d) Hydrochlorthiazide

219. Increase plasma concentration of digoxin occurs by following drug:
(a) Omeprazole (b) Phenylbutazone
(c) Quinidine (d) (b) and (c)

220. The synthesis of following drug is;



(a) X = ethacrynic acid
(b) X = meclofenamic acid
(c) Both
(d) None

221. 3,5-diamino-N-(amino imino methyl)-6-chloropyrazine carboxamide is
(a) Torsemide (b) Amiloride
(c) Furosemide (d) Metiamide

222. In thiazide diuretics electron withdrawing group must be at:
(a) Fifth position (b) Sixth position
(c) Seventh position (d) Eight position

223. The utllity of sulfone group in thiazide diuretics is for:
(a) Increase potency of drug
(b) I.M administration
(c) I.V administration
(d) None

224. Which of following drugs cause digoxin toxicity?
(a) Triamterene (b) Eplerenone
(c) Amiloride (d) Spironolactone

225. Which of following drug conjugate with glucuronic acid?
(a) Bumetanide (b) Ethacrynic acid
(c) Furosemide (d) Calomel

226. Which of following is more potent diuretics?
(a) Amidarone (b) Hydrochlorthiazide
(c) Indapamide (d) None

227. Gitelmann's syndrome is found in which of following diuretics?
(a) Loop diuretics (b) Osmotic
(c) Thiazide (d) Xanthine

228. The site of action of thiazide diuretics is on:
(a) Proximal part (b) Distal part
(c) Loop of Henle (d) All

229. Which of following drugs go 100% into systemic circulation?
(a) Piretanide (b) Furosemide
(c) Bumetanide (d) Ethacrynic acid

230. Which of following is potassium sparing diuretic?
(a) Xipamide
(b) Muzolimin
(c) Dichlorophenamide
(d) Eplerenone

231. In thiazide diuretics position 7 is very important and is occupied by:
(a) Methyl group (b) Chloro group
(c) Sulphamoyl group (d) None

232. Thiazide diuretics cause following toxicity?
(a) Potassium toxicity
(b) Lithium toxicity
(c) Calcium toxicity
(d) Digoxin toxicity

233. Which of the following ACE inhibitor is not bound to plasma or bound 0.1 %?
(a) Captopril (b) Enalpril
(c) Lisinopril (d) Quinapril

234. Which of following causes constipation?
(a) Nifedipine (b) Diltiazem
(c) Nitroglycerine (d) Verapamil

235. Which of following is used in cerebral vasospasm?
(a) Nitredipine (b) Nicardipine
(c) Nimodipine (d) Isradipine

236. Nifedipine blocks _____ calcium channel?
(a) T-type (b) N-type
(c) P-type (d) L-type

237. Plasma half life of renin is
(a) 30 min (b) 15 min
(c) 1min (d) 60 min

238. Bradykinin is
(a) Nonapeptide (b) Heptapeptide
(c) Octapepetide (d) Decapeptide

239. Which of following drug metabolites is more potent than parent?
(a) Valsartan (b) Losartan
(c) Telmisartan (d) Verapamil

240. Which of following contains tertiary amino group in side chain?
(a) Nitredipine (b) Nimodipine
(c) Nicardipine (d) Nifedipine

241. The substrate for ACE is
(a) Dipeptidyl carboxypeptidase
(b) Dipeptidyl oxytripeptidase
(c) Both
(d) None

242. Plasma half life of angiotensin-II is:
(a) 15min (b) 1 min
(c) 1hour (d) None

243. The group responsible for AT-1 receptor blocking activity is
(a) Imidazole (b) Tetrazole
(c) Triazole (d) None

244. Rofecoxib should not be given if patient is already taking
(a) Anxiolytic (b) Antidiabetic
(c) ACE inhibitor (d) All

245. One of following diuretics is similar to that of diazoxide?
(a) Acetazolamide (b) Furosemide
(c) Mannitol (d) Chlorthiazide

246. Which of following drug is used in digitalis-induced arrhythmia?
(a) Lidocaine (b) Amiodarone
(c) Tocainide (d) Phenytoin

247. The basic ring present in amiodarone is
(a) Benzothiazole (b) Benzopyrole
(c) Benzofuran (d) Phenothiazine

248. The antiarrythmic activity of propefenone is given by
(a) R-enantiomer
(b) S-enantiomer
(c) R and S enantiomer
(d) None of the above

249. Which of following drug is used specially in ventricular arrhythmia?
(a) Lidocaine (b) Tocainide
(c) Propafenone (d) All of the above

250. Which of following drugs contraindicates in ventricular arrhythmia?
(a) Verapamil (b) Quinidine
(c) Amiodarone (d) Sotalol

251. Which of following is not methane sulfonamide derivative?
(a) Sotalol (b) Ibutalide
(c) Dofetilide (d) Azimilde

252. Chemical name of hydralazine is
(a) 1-Hydrazinophthalazine
(b) 4-Hydrazinophthalazine
(c) N, N-Diaminothalazine
(d) Phthalic hydrazine

253. Which of following contraindicates with sulfa drug?
(a) Procainamide (b) Disopyramide
(c) Lidocaine (d) Moricizine

254. Which of following is used in digitalis-induced arrhythmia?
(a) Propafenone (b) Amiodarone
(c) Phenytoin (d) All

255. Which of following is insulin secretogogue?
(a) Liraglutide (b) Pramlintide
(c) Exenatide (d) Both (a) and (c)

256. Which of following is not short acting insulin preparation?
(a) Insulin lispro (b) Insulin aspart
(c) Glargine insulin (d) None

257. Which of following phenylalanine derivative is used in type-2 diabetes?
(a) Miglitol (b) Phenformin
(c) Repaglinide (d) Rosiglitazone

258. Which of following sulfonylurea derivatives contains pyrazine ring?
(a) Glibenclamide (b) Glimrpride
(c) Glibonuride (d) Glipzide

259. Which of following derivatives causes lactic acidosis and cynocobalamine deficiency?
(a) Sulfonyl urea (b) Meglinide
(c) Biguanide (d) Thiazolidinedione

260. Metformin have the following property except
(a) It activates GLUT-1 transport and increase glucose uptake
(b) It absorbs vitamin B-12
(c) It causes lactic acidosis
(d) It activates GLUT-4 transport and contraindicates in pregnancy

261. Amiodarone
P. Contain benzfuran ring and benzoyl ring.
Q. Is use in supraventricular tachycardia.
R. Cause slate-gray discoloration of skin.
S. Is potassium channel blocker
(a) P, Q are right but R,S are wrong
(b) P, Q, R are right but S is wrong
(c) All are correct
(d) P,R,S are right but Q is wrong.

262. Following drugs act as an arterials vasodilators except one
(a) Hydralazine (b) Minoxidil
(c) Diazoxide (d) Sodium nitroprusside

263. Minoxidil is synthesized by:
(a) Shaw synthesis (b) Chichibabin synthesis
(c) Pinner synthesis (d) Hantzch pyridine synthesis

264. Verapamil is synthesized by
(a) Shaw synthesis
(b) Chichibabin synthesis
(c) Pinner synthesis
(d) Hantzch pyridine synthesis

265. The starting material used for synthesis of propanolol is:
(a) α-napthol and epichorohydrin
(b) α- napthol and chloropropanol
(c) β-napthol and epicholrohydrin
(d) All

266. In which of following ACE inhibitor ester hydrolysis is not present?
(a) Enalpril (b) Quinapril
(c) Ramipril (d) Lisinopril

267. The amino acid present in lisinpril is:
(a) Proline (b) Lysine
(c) Both (d) None

268. IUPAC name of nifedipine is:
(a) 1,4-dihydro-2,6-dimethyl-4-(3-nitro phenyl)-3,5 pyridine carboxylic acid dimethyl ester
(b) 1,4-dihydro-2,6-dimethyl-4-(2-nitro phenyl)-3,5 pyridine carboxylic acid dimethyl ester
(c) 1,4-dihydro-2,6-dimethyl-4-(2-nitro phenyl)-3,5 pyridine carboxylic acid methyl ethyl ester
(d) 2,4-dihydro-1,6-dimethyl-4-(3-nitro phenyl)-3,5 pyridine carboxylic acid dimethyl ester

269. Which of following α-glucosidase inhibitors is deoxynojirimycin dvt?
(a) Miglitol (b) Acarbose
(c) Varcabose (d) Nateglinide

270. Which of following is newer insulinomimetic agent?
(a) Lisophyllin (b) Aminoguanidine
(c) Vanadium salt (d) All

271. IUPAC name of prazosin is:
(a) 1-(4-amino 6,7 dimethoxy-2-quinzolinyl)-4-(2-furoyl) piperazine
(b) 1-(3-amino 6,7 dimethoxy-2-quinzolinyl)-4-tetrahydro-(2-furoyl) piperazine
(c) 1-(5-amino 6,7 dimethoxy-2-quinzolinyl)-4-(2-furoyl) pyrazine
(d) 1-(4-amino 6,7 dimethoxy-2-isoquinzolinyl)-4-(2-furoyl) piperazine

272. The basic ring present in guanthedine is
(a) Azepine (b) Azocine
(c) Benzepine (d) Aziridine

273. Chemically diltiazem is
(a) 1,4 dihydropyridine derivative
(b) phenyl alkyl amine derivative
(c) benzothiazepine derivative
(d) None

274. Which of following enantiomers of verapamil is calcium channel blocker?
(a) Levo (b) Dextro
(c) Racemic (d) None

275. Chemically nifedipine is
(a) 1,4 dihydropyrimidine derivative
(b) 2,4 dihydropyrimidine derivative
(c) 1,4 dihydropyridine derivative
(d) 2,4 dihydropyridine derivative

276. The utility of thiol group in ACE inhibitor is
(a) To increase binding to caboxylate group of ACE
(b) To increase binding to zinc (co-factor) ion of ACE
(c) To form hydrophobic interaction with peptide linkage
(d) None of this.

277. The antihypertensive drug with a tetrazole nucleus is
(a) Diazoxide (b) Valsartan
(c) Taludipine (d) Fosinopril

278. Antianginal drug useful for the emergency treatment of cyanide poisoning is
(a) Aspirin (b) Glyceryl trinitrate
(c) Amyl nitrate (d) Dipyridamole

279. Amiodarone has _____ basic nucleus.
(a) Benzothiazole (b) Benzophenone
(c) Benzofuran (d) Benzopyrrole

280. The starting material for clonidine synthesis is _____
(a) 2,6-Dichloroaniline + Ammonium thiocynate
(b) 2,5-Dichloroaniline + Ammonium thiocynate
(c) 2,4-Dichloroaniline + Ammonium thiocynate
(d) 3,4-Dichloroaniline + Ammonium thiocynate

281. Prazosin contains _____ as the basic moiety.
(a) Quinoline (b) Isoquinoline
(c) Quinazoline (d) None

282. What is the starting material of captopril?
(b) Acetoacetic acid (b) Methacrylic acid
(c) Alanine (d) Formic acid

283. What is the IUPAC name of ethacrynic acid?
(a) [2,3-dichloro-4-(2-methylenebutyryl)phenoxy] acetic acid
(b) [2,3-dichloro-4-(2-methylenebutyryl)phenoxy] propionic acid
(c) [2-chloro-4-(2-methylenebutyryl)phenoxy] acetic acid
(d) [2,3-dichloro-4-(2-ethylenebutyryl)phenoxy] acetic acid

284. Acetazolamide is synthesized via which of the following intermediate?
(a) 1-amino-2-mercapto-1,3-thiazole
(b) 5-amino-2-mercapto-1,3,4-thiadiazole
(c) 1-amino-2-mercapto-1,3-thiazole
(d) 5-amino-2-mercapto-1,3,4-tetrazole

285. Simvastatin has which of the following rings?
(a) Indole (b) Pyrrole
(c) Naphthyl (d) Pyridine

286. Fluvastatin has which of the following rings?
(a) Indole (b) Imidazole
(c) Naphthyl (d) Pyrrole

287. Naproxen is a derivative of _____
(a) Arylpropionic acid
(b) Arylethanoic acid
(c) Arylpropionic ester
(d) Arylpropionic ether .

288. Ibuprofen contains _____
(a) α-methyl group on acetic acid moiety
(b) β-methyl group on acetic acid moiety
(c) α-methyl group on propionic acid moiety
(d) β-methyl group on propionic acid moiety.

289. One of the following is a pro-drug _____

(a) Ketoprofen (b) Naproxan
(c) Pyroxicam (d) Sulinadac

290. Sulfide metabolites of one of the following is active
(a) Ketoprofen (b) Naproxen
(c) Pyroxicam (d) Sulinadac

291. One of the following is a selective COX-2 inhibiter _____
(a) Paracetamol (b) Nimesulide
(c) Valdecoxib (d) None

292. One of the following is an inflammation-inducing substance used in experimental pharmacology.
(a) Cellulose (b) HPMC
(c) Carrageen (d) Guar gum.

293. Phenylbutazone is a _____
(a) Pyrazolone derivative
(b) Pyrazolidinedione derivative.
(c) N-arylanthranilic acid derivative.
(d) None of the above.

294. One opioid analgesic which does not inhibit PG synthesis is _____
(a) Celecoxib (b) Nafopam
(c) Ketorolac (d) Antipyrine

295. The isoxazole ring is present in which of following drug?
(a) Valdecoxib and paracoxib
(b) Celecoxib and rofecoxib
(c) Celecoxib and valdecoxib
(d) Paracoxib and celecoxib

296. Which of the following drug is given parentrally?
(a) Celecoxib (b) Rofecoxib
(c) Valdecoxib (d) Paracoxib

297. Which of the following drug is a prodrug?
(a) Nimesulide (b) Indomethacine
(c) Diclofenac (d) Nabumetone

298. Pyrazole derivative causes following side effects _____
(a) Bonemarrow depression
(b) Leucopaenia
(c) Agranulocytosis
(d) All

299. Basic ring present in valdecoxib is _____
(a) Pyrazole (b) Furan
(c) Isoxazole (d) None

300. Which of the following gives oil of wintergreen during urine excretion?
(a) Aspirin (b) Salicylamide
(c) Methylsalicylate (d) None

301. Rofecoxib should not be given if the patient is already taking
(a) Anxiolytic (b) Antidiabetic
(c) ACE inhibitor (d) All

302. Toxic metabolite of paracetamol which causes hepatotoxicity is
(a) N-acetyl p-benzoquinone imine
(b) N-acetyl p-benzoquinone amine
(c) O-dealkyl acetaminophen
(d) None

303. Metabolism of paracetamol occurs by
(a) Glucuronide and glycine
(b) Glucuronide and sulphate
(c) Glutathione and sulphate
(d) Glutathione and sulphate

304. Which of following is a natural vasodialator?
(a) Bradykinin (b) Adenosine
(c) Both (d) None

305. Which isomer of ibuprofen is more active?
(a) S (–) isomer (b) R (–) isomer
(c) S (+) isomer (d) R (+) isomer

306. Benorylate is polymeric condensation of
(a) Acetyl salicylate ester of B-napthol
(b) Acetyl salicylate ester of paracetamol
(c) Acetyl salicylate ester of piroxicam
(d) None

307. Starting material for ibuprofen is
(a) Isobutyl benzene
(b) Isopropyl benzene
(c) Isobutyl acetophenone
(d) None

308. Plasma half-life of piroxicam is
(a) 30 hours (b) 2 hours
(c) 45 minutes (d) 45 hours

309. Which of following drug causes anaphylaxis?
(a) Tolmetin (b) Nimesulide
(c) Indomethacin (d) Zomepirac

310. Phenylbutazone is a _____

(a) Pyrazolone derivative
(b) Pyrazolidinedione derivative.
(c) N-arylanthranilic acid derivative
(d) None of the above

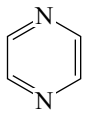
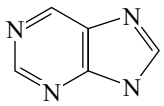
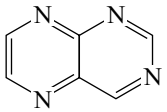
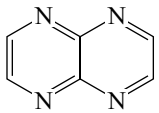
311. One opoid analgesic which does not inhibit PG synthesis is _____
(a) Celecoxib (b) Nafopam
(c) Ketorolac (d) Antipyrine

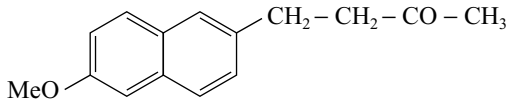
312. Which of following bound 99% to protein?
(a) Ibuprofen (b) Flubiprofen
(c) Naproxen (d) All

313. Metabolism of paracetamol occurs by
(a) Glucuronide and glycine
(b) Glucuronide and sulphate
(c) Glutathione and sulphate
(d) Glutathione and sulphate

314. Which of following is a natural vasodialator?
(a) Bradykinin (b) Adenosine
(c) Both (d) None

315. Which isomer of ibuprofen is more active?
(a) S (–) isomer (b) R (–) isomer
(c) S (+) isomer (d) R (+) isomer

316. Basic ring system in triamterene is
A. 
B. 
C. 
D. 

317. Identify the name of drug of following structure:


(a) Naproxen (b) Nimesulide
(c) Nabumetone (d) None

318. Patient suffering from status epileptics and already takeing folic acid tablet should not be given
(a) Valproic acid (b) Phenytoin
(c) Lamotrigine (d) All

319. Clozapine is
(a) Dibenzoxazepine derivative and D-2 blocker
(b) Dibenzoxazepine derivative and D-4 and 5HT-2a blocker
(c) Dibenzazepine derivative and D-4 and 5HT-2a blocker
(d) Dibenzazepine derivative and D-2 and 5HT-2a blocker

320. The nipecotic acid derivative act by
(a) GABA-α-agonist
(b) Blocking calcium channel
(c) Inhibiting GABA transaminase
(d) Inhibit GABA reuptake

321. Which of the following butyrophenones contains benzimidazolinone side chain?
(a) Haloperidol (b) Droperidol
(c) Penfluridol (d) Trifluperidol

322. Metabolism of phenacetin occurs by
(a) N-dealkylation (b) O-dealkylation
(c) Hydroxylation (d) None of above

323. Which of following drugs gives oil of wintergreen during urinary excretion?
(a) Aspirin (b) Salicylamide
(c) Methyl salicylate (d) All of above

324. Which of following drugs causes lithium and digoxin toxicity?
(a) Nimesulide (b) Diclofenac
(c) Indomethacin (d) Rofecoxib

325. 5,5-Diphenyl hydantoin is prepared by condensing
(a) Benzil and urea
(b) Benzyl cynamide and ethyl carbamate
(c) Phenyl ethyl malonic ester and urea
(d) Ethyl butyl malonic ester and urea

326. Amodiaquine is
(a) 7-Chloro-4-(4-diethylamino methyl 4-hydroxy -phenyl) quinoline
(b) 7-Chloro-4-(3-diethylamino methyl 4-hydroxy -anilino) quinoline
(c) 6 Ethoxy-8-(4-diethylamino methyl 4-hydroxy -phenyl) Isoquinoline
(d) 5-Chloro-4-(4-diethylamino propyl phenyl) quinoline

327. Barbiturates are
(a) Derived from malonic acid
(b) Cyclic ureides
(c) Urea derivatives
(d) All of the above

328. Phenobarbital is classified as a
(a) Short-acting barbiturate
(b) Long acting-barbiturate
(c) Intermediate acting barbiturate
(d) Ultra-short-acting barbiturate

329. Promethazine contains
(a) 2-Dimethyl amoni propyl side chain
(b) 2-Diethyl amoni propyl side chain
(c) Chloro diphenyl methane side chain
(d) None of the above

330. Sedative action of barbiturate is due to substituent at C-5. It is due to
(a) High lipophilicity of group at C-5 position
(b) Electronic withdrawing effect
(c) Sterric effect
(d) Low lipophilicity of group at C-5position

331. Selective serotonin reuptake inhibitors is
(a) Mianserin (b) Doxepin
(c) Fluoxetine (d) Amoxapin

332. Theophylline chemically is a
(a) 1,3,7-Trimethyl xanthine
(b) 1,3,7-Triethyl xanthine
(c) 1,3-Dimethyl xanthine
(d) 3,7-Dimethyl xanthine

333. Morphine undergoes microsomal oxidation by
(a) N-dealkylation
(b) Aromatic hydroxylation
(c) Oxidative deamination
(d) O-dealkylation

334. IUPAC name of diclofenoac is
(a) Sodium 2-[(2,6-dichlorophenyl} amino] phenyl acetate
(b) Sodium 2-[(2-chlorophenyl) amino] phenyl acetate
(c) Sodium 3-[(2,6-Dichlorophenyl) amino] phenyl acetate
(d) Sodium 2-[(6-chlorophenyl} amino] phenyl acetate

335. Paracetamol undergoes metabolism by
(a) N-hydroxylation (b) Deamination
(c) O-dealkylation (d) Oxidative deamination

336. Risperidone belongs to class of
(a) Benzisoxazole (b) Butyrophenone
(c) Benzimidazole (d) DihydroindoJone

337. One of the following is false about benzodiazepines. Identify.
(a) Alkyl substituents at 3-position decreases the activity
(b) N-substituent at 1-position should be small
(c) A phenyl or pyridyl at 5-position decreases the activity
(d) The presence of electron-attracting substituent at position 7 is required for activity

338. Diphenhydramine is synthesized from
(a) Toluene and benzoic acid
(b) Benzene and benzyl chloride
(c) Diphenyl ether and benzyl chloride
(d) Benzene and benzyl chloride

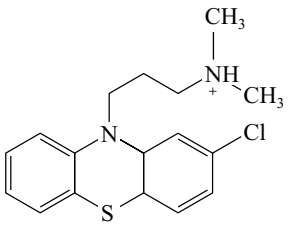
339. Chemical nomenclature of procaine is?
(a) 2-D iethylaminoethyI 4-aminobezoate
(b) N, N-DiethyI4-aminobenzoate
(c) 4-Aminobenzamidoethyl amine
(d) 4-Amino-2-diethylaminoethyl benzoate

340. Dimethyl [3-phenyl-3(2-pyridyl)-propyl]amine is the IUPAC name of _____
(a) Pheniramine (b) Benzocaine
(c) Phenolphthalein (d) Phenformine

341. The IUPAC name of glutethimide is
(a) 3-ethyl, 3'phenyl-2, 6-piperidine dione
(b) p-sulfonamido-chloroimido benzoic acid
(c) 3-(5-nitrofurfurylideneamino) oxazolidin-2-one
(d) 2-(2-fluorobiphenyl-4-yl) propionic acid

342. Morphine and heroine differ from each other by
(a) Methyl group on nitrogen
(b) Acyl group at C3 and C6
(c) Absence of d ring
(d) Acyl group at C4 and C6

343. IUPAC name of below structure is



A.
(a) 3-(3-chlorophenothiazin-10-yl)propyl-*N*, *N*-dimethyl NH_4Cl
(b) 2-(3-chlorophenothiazin-10-yl) propyl-*N*,*N*-dimethyl NH_4CI
(c) 3-(3-chlorophenoth iazin-10-yl)isopropyl-*N*, *N*-dimethyl NH_4CI
(d) 2-(3-chlorophenothiazin-10-yl)propyl-*N*,*N*-dimethyl NH_4Cl

ANSWER KEYS

1. (c)	**2.** (a)	**3.** (a)	**4.** (d)	**5.** (c)	**6.** (d)	**7.** (a)	**8.** (c)	**9.** (b)	**10.** (c)
11. (d)	**12.** (a)	**13.** (b)	**14.** (d)	**15.** (c)	**16.** (c)	**17.** (b)	**18.** (b)	**19.** (d)	**20.** (c)
21. (c)	**22.** (a)	**23.** (c)	**24.** (c)	**25.** (b)	**26.** (b)	**27.** (c)	**28.** (a)	**29.** (b)	**30.** (a)
31. (a)	**32.** (d)	**33.** (d)	**34.** (d)	**35.** (b)	**36.** (c)	**37.** (b)	**38.** (b)	**39.** (a)	**40.** (b)
41. (d)	**42.** (a)	**43.** (b)	**44.** (d)	**45.** (c)	**46.** (a)	**47.** (c)	**48.** (a)	**49.** (a)	**50.** (b)
51. (c)	**52.** (b)	**53.** (c)	**54.** (a)	**55.** (a)	**56.** (a)	**57.** (a)	**58.** (d)	**59.** (a)	**60.** (d)
61. (d)	**62.** (a)	**63.** (d)	**64.** (a)	**65.** (d)	**66.** (a)	**67.** (b)	**68.** (b)	**69.** (d)	**70.** (d)
71. (a)	**72.** (a)	**73.** (b)	**74.** (c)	**75.** (a)	**76.** (d)	**77.** (a)	**78.** (d)	**79.** (a)	**80.** (b)
81. (a)	**82.** (a)	**83.** (b)	**84.** (a)	**85.** (c)	**86.** (c)	**87.** (d)	**88.** (a)	**89.** (c)	**90.** (a)
91. (d)	**92.** (a)	**93.** (d)	**94.** (a)	**95.** (c)	**96.** (d)	**97.** (a)	**98.** (a)	**99.** (a)	**100.** (a)
101. (d)	**102.** (d)	**103.** (d)	**104.** (d)	**105.** (d)	**106.** (a)	**107.** (a)	**108.** (b)	**109.** (d)	**110.** (a)
111. (c)	**112.** (d)	**113.** (d)	**114.** (d)	**115.** (d)	**116.** (a)	**117.** (a)	**118.** (b)	**119.** (b)	**120.** (a)
121. (a)	**122.** (d)	**123.** (d)	**124.** (a)	**125.** (c)	**126.** (c)	**127.** (b)	**128.** (a)	**129.** (b)	**130.** (b)
131. (d)	**132.** (d)	**133.** (c)	**134.** (a)	**135.** (a)	**136.** (a)	**137.** (c)	**138.** (d)	**139.** (b)	**140.** (c)
141. (a)	**142.** (c)	**143.** (a)	**144.** (d)	**145.** (d)	**146.** (b)	**147.** (a)	**148.** (c)	**149.** (b)	**150.** (c)
151. (b)	**152.** (d)	**153.** (a)	**154.** (d)	**155.** (a)	**156.** (a)	**157.** (c)	**158.** (b)	**159.** (a)	**160.** (b)
161. (b)	**162.** (d)	**163.** (b)	**164.** (b)	**165.** (c)	**166.** (d)	**167.** (c)	**168.** (a)	**169.** (b)	**170.** (a)
171. (b)	**172.** (c)	**173.** (b)	**174.** (d)	**175.** (a)	**176.** (d)	**177.** (a)	**178.** (b)	**179.** (a)	**180.** (b)
181. (c)	**182.** (d)	**183.** (c)	**184.** (b)	**185.** (b)	**186.** (d)	**187.** (b)	**188.** (a)	**189.** (c)	**190.** (c)
191. (d)	**192.** (d)	**193.** (c)	**194.** (d)	**195.** (a)	**196.** (c)	**197.** (a)	**198.** (a)	**199.** (a)	**200.** (b)
201. (a)	**202.** (c)	**203.** (c)	**204.** (d)	**205.** (a)	**206.** (d)	**207.** (c)	**208.** (c)	**109.** (a)	**210.** (b)
211. (d)	**212.** (c)	**213.** (a)	**214.** (c)	**215.** (a)	**216.** (b)	**217.** (a)	**218.** (d)	**219.** (d)	**220.** (a)
221. (c)	**222.** (b)	**223.** (b)	**224.** (d)	**225.** (c)	**226.** (b)	**227.** (c)	**228.** (b)	**229.** (c)	**230.** (d)
231. (c)	**232.** (b)	**233.** (c)	**234.** (d)	**235.** (c)	**236.** (d)	**237.** (b)	**238.** (a)	**239.** (b)	**240.** (c)
241. (a)	**242.** (b)	**243.** (b)	**244.** (c)	**245.** (d)	**246.** (d)	**247.** (c)	**248.** (c)	**249.** (d)	**250.** (a)
251. (d)	**252.** (a)	**253.** (a)	**254.** (c)	**255.** (d)	**256.** (c)	**257.** (c)	**258.** (d)	**259.** (c)	**260.** (d)
261. (c)	**262.** (d)	**263.** (b)	**264.** (d)	**265.** (a)	**266.** (d)	**267.** (c)	**268.** (b)	**269.** (b)	**270.** (c)
271. (a)	**272.** (b)	**273.** (c)	**274.** (b)	**275.** (c)	**276.** (b)	**277.** (b)	**278.** (c)	**279.** (c)	**280.** (a)
281. (c)	**282.** (b)	**283.** (a)	**284.** (b)	**285.** (c)	**286.** (a)	**287.** (a)	**288.** (a)	**289.** (d)	**290.** (d)
291. (c)	**292.** (c)	**293.** (b)	**294.** (b)	**295.** (a)	**296.** (d)	**297.** (d)	**298.** (c)	**299.** (c)	**300.** (c)
301. (c)	**302.** (a)	**303.** (b)	**304.** (b)	**305.** (c)	**306.** (b)	**307.** (a)	**308.** (d)	**309.** (d)	**310.** (b)
311. (b)	**312.** (d)	**313.** (b)	**314.** (b)	**315.** (c)	**316.** (c)	**317.** (c)	**318.** (b)	**319.** (c)	**320.** (d)
321. (b)	**322.** (b)	**323.** (c)	**324.** (c)	**325.** (b)	**326.** (b)	**327.** (d)	**328.** (b)	**329.** (d)	**330.** (a)
331. (c)	**332.** (c)	**333.** (a)	**334.** (a)	**335.** (b)	**336.** (a)	**337.** (c)	**338.** (b)	**339.** (a)	**340.** (d)
341. (b)	**342.** (b)	**343.** (a)							

CHAPTER 6

INORGANIC CHEMISTRY

1. TOPICAL PREPARATION

Astringent

It is the substance that tends to shrink or constrict body tissues, usually locally after topical medicinal application and it also precipitates the protein.

Demulcent

It is a medicine or other preparation that has a soothing or emollient influence on an inflamed area of the body.

Emolient

Any preparation or substance that has a softening or soothing effect, especially when applied to the skin.

Adsorbent

Having capacity or tendency to adsorb or cause to accumulate on a surface.

Compounds	Chemical Formula	Category/Use	Analysed by	Charactaristics
Zinc Oxide	ZnO	Astringent and protective	Acidimetric back titration	ZnO Ointment –15% Concentration
Calamine	Chemically, it is ZnO with small amount of Ferric Oxide	Astringent and protective	–	Used as lotion and ointment
Zinc Stearate	$\{CH_3 (CH_3)_{16}COO\}Zn$	Astringent and Antimicrobial agents	Complexometric titration	Used as a Dusting Powder
Alum (Hydrated potassium aluminium sulfate-potassium alum)	$KAl(SO_4)_2.12H_2O$.	Astringent Pharmaceutical aid in stypic pencil which stop the bleeding from small cuts	Gravimetry or precipitation by ammonia	Used in concentration 0.5–5%
Titanium Dioxide	TiO_2	Protective and Pharmaceutical aid	Complexometric titration	–
Hydrogen Peroxide	H_2O_2	Germicides Deodorants	Oxidation reduction titration	
Potassium Permenganate	$KMnO_4$	Anti infective and Antiseptic	Oxidation reduction titration	0.006–2%

Compounds	Chemical Formula	Category/Use	Analysed by	Charactaristics
Mercurous Chloride	HgCl	Anti-infective	Iodometric titration	Used in Eczema
Boric acid or Boracic acid, (Acidum boricum, Hydrogen borate)	H_3BO_3	Anti-infective and germicides	Titrimetric method	4.5% used to wash the eye as a bacteriostatic agent
Selenium Sulphide	SeS_2	Kwashiorkar and Anti dandruff agent	Oxidation reduction titration	Anti oxidant in conjugation with Vitamin E
Iodine Iodophore (Povidon-Iodine)-Complex of I_2 with carrier organic molecule serving as solubilizing agent	I_2	Anti infective and local germicidal	Oxidation reduction titration	5% W/V (Aqueous iodine solution)-Lugol's Solution Iodine Tincture (Weak iodine solution-2%) Strong Iodine Solution-10%
Zinc Sulphate	$ZnSO_4.7H_2O$	Astringent and emetics	Gravimetric	0.6–2 gm dose
Silicone Oil	Chemically, it is Dimethyl silyl ether	Gastric protective and anti flatulent	–	Simethicone (Activated Dimethicone)

2. INORGANIC GASES

Compounds	Formula	Category/Use	Analysed by	Characteristic
Oxygen	O_2	Anti hypoxia and used in artificial respiration	Gasometric titration	O_2 stored in cylinder which are in green colored
Carbon Dioxide	CO_2	Respiratory stimulants	Gasometric titration	CO_2 stored in grey metallic cylinder
Nitrous Oxide	N_2O	Inhalational anasthetics and analgesic	Gasometric titration	N_2O stored in Blue metallic cylinder
Helium (Noble Gas)	He	Carrier gas in gas chromatography cryogenic	Gasometric titration	–
Ammonia	NH_3	Respiratory stimulants	Colorimetry	–

Dental Preparation

- **Cleaning Agent/Dentrifrices**
  $CaCO_3$ (Precipitated Chalk)-Dibasic Calcium Phosphate
  $Ca_3(PO_4)_2$– Tribasic Calcium Phosphate
  Sodium metaphosphate
  Stronium chloride ($SrCl_2.6H_2O$)
  Pumice-It is a complex silicate of Al, P and Na
- **Polishing Agent:** Compound having astringent property can act as a polishing agent.
- **Desensiting Agent:** Strontium chloride and Zinc chloride
- **Oral Antiseptic/Astringent:** H_2O_2, Sodium Perborate, Magnesium peroxide (MgO_2)
- **Mouth Washes:** Zinc sulphate, Zinc chloride, $KMnO_4$, NaCl, $NaHCO_3$
- **Cements and fillers:** Gold and silver, ZnO

Name of Compounds	Chemical Formula	Analyzed by	Category/Use
Sodium Fluoride	NaF	Complexometric Titration	Anti caries agent
Stannous Fluoride	SnF_2	–	Prevent dental dentrifrice

3. GASTRO INTESTINE AGENTS

Name of Compound	Chemical Formula	Assay Method	Use
Aluminium Hydroxide Gel	It is a mixture of Aluminium Oxide, Aluminium Hydroxide and small amount of basic carbonate	Complexometric titration	Antacid
Calclum Carbonate (Synonym: Precipitated Chalk	$CaCO_3$	Complexometric titration	Non Systemic antacid
Calcium Phosphate	$Ca_3 (PO_4)_2$	Complexometric titration	Antacid
Light Magnesium Carbonate	$3MgCO_3$, $Mg (OH)_2.3H_2O$	Complexometric titration	Anatacid and Laxative
Milk of Magnesia (Synonym: Cream of Magnesia)	Magnesium Hydroxide	Back titration	Antacid and Laxative

4. PROTECTIVE AND ADSORBENTS

Name of Inorganic Compound	Chemical Formula	Use
Bismuth Subcarbonate (Bismuth Carbonate)	$(BiO)_2CO_3$	Astringent and adsorbent
Bismuth Subgallete (Bismuth Oxygallete)	$(BiOH)_2.C_7H_2O_5$	Astringent and adsorbent
Light Kaolin	Hydrated aluminium silicate	Adsorbent to neutrilize toxins, gases, As a dignostic agent and in rheumatic arthriritis
Heaby Kaolin (China Clay)	Hydrated aluminium silicate	Pharmaceutical aid in preparation of kaoline paultice along with boric acid and glycerine, dustine powder
Pectin	Purified carbohydrate product obtained from dilute acid extract of inner portion of rind of citrus fruits or from apple pomace	Protective along with kaolin in diarrhoea
Activated Charcoal	Residue from destructive distillation of woods	Antidote in toxins like alkaloids, amines and gases like CO, CO_2, N_2O and NH_3 and heavy metal poisoning

5. SALINE CATHARTICS

Name of Compound	Chemical Formula	Assay Method	Uses
Magnesium Sulphate (Epsom Salt)	$MgSO_4.7H_2O$	–	Laxative and Saline cathartics
Lactulose	Semisynthetic diasaccharides sugar	–	Laxative and Saline cathartics

Name of Compound	Chemical Formula	Assay Method	Uses
Sodium Potassium Tartrate (Rochelle Salt)	KOOC (HO)HC.CH (OH)COONa	Back titration with alkali	Purgative
Heavy Magnesium Carbonate	$3MgCO_3.Mg(OH)_2.4H_20$	Complexometric Titration	Antacid and Laxative
Heavy Magnesium Oxide (Heavy Magnesia)	MgO	Complexometric Titration	Antacid and Laxative
Light Magnesium Oxide (Light Magnesia)	MgO	Complexometric Titration	Antacid and Laxative
Sodium Bicarbonate (Baking Soda)	$NaHCO_3$	Acid-Base titration	Antacid
Sodium Phosphate (Di Sodium Hydrogen Phosphate)	$Na_2HPO_4.12H_2O$	–	Saline laxatice
Potassium Phosphatae	K_2HPO_4	–	Saline laxatice

6. ACID BASE AND BUFFERS

Name of Compound	Chemical Formula	Assay Method	Uses
Boric Acid (Boracic Acid)	H_3BO_3	Titrimetric method	Weak germicidal, local antiinfective and eye and mouth wash
Strong Ammonia Solution (Liquor Ammonia Fortis)	NH_3	Acid-Base titration	Stimulant, counter irritant
Calcium Hydroxide (Slaked Lime)	$Ca(OH)_2$	Complexometrc Titration	Antacids, skin lotion preparation
Sodium Hydroxide (Caustic Soda)	NaOH	Acid-Base titration	Strong alkali, disinfectant for veternary purpose
Potassium Hydroxide	KOH	By Winkder method	Used in preparation of cresol solution
Sodium Carbonate	$Na_2CO_3.10H_2O$	Acid-Base titration	Antacid, pharmaceutical aid, mouth wash and in preparation of vaginal douches
Phosphoric Acid (Orthophospheric Acid)	H_3PO_4	Acid-Base titration	Pharmaceutical aid, lead poisoning and in dental cement
Sodium Carbonate	$Na_2CO_3.10H_2O$	Acid-Base titration	Antacid, pharmaceutical aid, mouth wash and in preparation of vaginal douches
Phosphoric Acid (Orthophospheric Acid)	H_3PO_4	Acid-Base titration	Pharmaceutical aid, lead poisoning and in dental cement

Antidotes

Compound	Poisoning
Activated charcoal	Heavy metal poisoning, alkaloidal, sedative and hypnotic drugs poisoning
Light kaolin	Food and alkaloidal poisoning
Copper sulphate	Phosphorous poisoning
Magnesium sulphate	Heavy metal poisoning
Sodium phosphate	Heavy metal poisoning
D-penicillamine	Cu (copper), Mg (magnesium) and Pb (lead) poisoning
Deferoxamine	Iron (Fe) poisoning
Dimercaprol (-SH group containing drugs)	As, Au (gold) and Hg (mercury) poisoning
Succimer (disulphhydide{-SH} group containing drugs)	As (arsenic), Au (gold) and Hg (mercury) poisoning
Calcium disodium edta Universal antidote	Lead (Pb) posioning
Sodium thiosulphate	Cyanide poisoining
Sodium nitrite	Cyanide poisoining

MISCELLANEOUS AGENT

Compound	Category
Sodium antimony gluconate Antimony potassium tartrate Antimony sodium tartrate	Internal parasiticidal
Cisplatin	Anti neoplastic (cancer) agent
Potassium bromide (kBr)	Sedative/anti convulsant
Lithium carbonate	Anti depressants
Sodium aurothiomalate	Anti rheumatic
Potassium perchlorate	Anti thyroid drugs
Barium sulphate (syn:shadow meal, barium meal)	Diagnostic agent
Plaster of paris ($CaSO_4.1/2H_2O$) Syn:gypsum	Surgical aids
Sulphar dioxide	Disinfectant

Multiple Choice Questions

1. Concentration of fluoride required for use as anticancer agent orally is
(a) 5% (b) 6%
(c) 2% (d) 4%

2. Ammoniacal silver nitrate solution is used in the mouth wash as
(a) Astringent agent
(b) Prevent the hypersensitivity
(c) (a) and (b)
(d) None

3. One of the following is used as dental cement
(a) $ZnCl_2$ (b) NaCl
(c) $KMnO_4$ (d) Zno

4. Concentration of H_2O_2 for use as mouthwash is
(a) 3% W/V (b) 4% W/V
(c) 2% W/V (d) None

5. One of the following is rubifacient
(a) N_2O
(b) Ammonium carbonate
(c) Dilute solution of ammonia
(d) All

6. One of the following is sedative expectorant
(a) NH_4Cl (b) Anise
(c) Lemon (d) Eucylaptus

7. Emetic out through local irritation or gastric mucosa is
(a) Ipecacaunaha (b) Ammonium bicarbonate
(c) Both (d) None

8. Intracellular fluid constituent
(a) 30–50% of body weight
(b) 45–50% of body weight
(c) 12–15% of body weight
(d) 4–5% of body weight

9. The condition in which fluid is accumulated in the intestinal space because of low osmotic pressure is known as
(a) Dehydration (b) Edema
(c) Hypocolemia (d) None

10. ORS (recommended by WHO) contain NaCl in
(a) 3.5 g (b) 1.3 g
(c) 2.5 g (d) 4.5 g

11. Radiopharmaceuticals use in diagnosis of pernicioal anaemia
(a) Ca-45 (b) Cr-51
(c) Co-57 (d) K-42

12. Radiopharmacutical use in study of thyroid uptake
(a) K-42 (b) Cr-51
(c) I-131 (d) S-35

13. Antidotes act by producing the effect oppose to that of poison is known as
(a) Physiological antidotes
(b) Chemical antidotes
(c) Mechanical antidotes
(d) All

14. One of the following is well in cyanide poisoning
(a) Sodium nitrate
(b) Both
(c) Sodium thiosulphate
(d) None

15. Concentration of glycerol recommended as prelenatives
(a) 0.9% (b) 30%
(c) 50% (d) 1.5%

16. The pharmaceutical aid used as astringent and clearing agent is
(a) Agar (b) Alum
(c) Benzyl alcohol (d) All

17. The minimum concentration of colouring agent in Pharmaceutical preparation is
(a) 0.01% w/v (b) 0.0001% w/v
(c) 0.001% w/v (d) 0.1% w/v

18. Unit of radioactivity is
(a) Cane (b) Rad
(c) Rem (d) All

19. 1 Cane = _____
(a) 3.7×10^{10} dps (b) 0.87 rad
(c) 2.58×10^{-4} dps (d) None

20. Ringer lactate solution for injection contain_____ lactic acid

(a) 1.15 g (b) 2.4 ml
(c) 2.5 g (d) None

21. One of the following has a major role in transmission of nerve impulse

(a) Sodium (b) Magnesium
(c) Calcium (d) None

22. The criteria for buffers suitable for use in biological research are as follows except

(a) Permeable to biological membrane
(b) Hydrolytically stable
(c) Posses adaptable buffer capability
(d) All

23. Calculate pH of solution in which the H^+ concentration is 4.2×10^{-4} mol dm^{-3}

(a) 3.39 (b) 3.38
(c) 3.5 (d) 4

24. Concentration of fluorides required to prevent the carries

(a) 1 ppm (b) 2 to 3ppm
(c) 10 ppm (d) < 1 ppm

25. Give the examples of desensitizing agent in dental product

(a) Strontium chloride
(b) Strontium fluoride
(c) Zinc chloride
(d) (a) and (c)

26. Deliquescent materials have tendency to

(a) Absorb moisture (b) Loss water
(c) Both (d) None

27. Which of following use for detection and measurement of radiation?

(a) Photographic plate
(b) Semiconductor detector
(c) Gieger Muller counter
(d) All

28. The unit of measurement of X-ray is

(a) Curie (b) Rontgen
(c) Both (d) All

29. Which of following is used for estimation of reticulo-endothelial activity?

(a) Gold solution (b) Cobalt
(c) Cynocobalamine (d) All

30. In limit test of sulphate which of following is used to prevent supersaturation?

(a) Potassuim sulphate
(b) Barium sulphate
(c) Alcohol
(d) None

31. As per B.P. which of reagent is used for limit test of sulphate?

(a) Sodium sulphtae (b) Magnesium sulphate
(c) Barium sulphate (d) None

32. In limit test for iron interference of other metal cation is removed by

(a) Thioglycolic acid
(b) Citric acid
(c) Both
(d) Ammonia solution

33. The usual limit for heavy metal as I.P. is

(a) 10 ppm (b) 20 ppm
(c) 30 ppm (d) 40 ppm

34. In limit test for lead the reagent used as per I.P. and B.P. is

(a) Dithiazone (b) Lead sulphide
(c) Both (d) Lead nitrate

35. In limit test for arsenic which of following method is used?

(a) Arsine test (b) Gutzeit test
(c) Both (d) None

36. In limit test for arsenic which of following use for convert arsenic into arsine gas?

(a) Potassium iodide
(b) Stannous chloride
(c) Zinc-hydrochloric acid
(d) All

37. The nature of water is

(a) Acid (b) Base
(c) Amphoteric (d) Neutral

38. Zeolite or permutit is

(a) Aluminium hydroxide gel
(b) Aluminium silicate
(c) Magnesium silicate
(d) None

39. As per I.P. the pH of purified water is
(a) 4.5 to 7 (b) 3 to 5
(c) 1 to 3 (d) 7 to 9.5

40. Which of following is tartar emetic?
(a) Potassium bitartrate
(b) Antimony potassium tartrate
(c) Magnesium tartrate
(d) All

41. Mechanism of action like oxidation for antimicrobial activity reacts with
(a) Peptide linkage
(b) Sulfhydryl group of enzyme
(c) Both
(d) None

42. A solution containing one mole of solute per thousand grams of solvent is called
(a) Normal solution
(b) Molal solution
(c) Molar solution
(d) Percent solution

43. Milk of magnesia is
(a) Hydrated magnesium silicate
(b) Hydrated magnesium oxide
(c) Dehydrated magnesium hydroxide
(d) Hydrated magnesium hydroxide

44. Which of following is used in the treatment of syphilis?
(a) Mercury (b) Silver
(c) Zinc (d) Arsenic

45. Which of following is called Rochelle salt?
(a) Sodium potassium tartrate
(b) Potassium bitartrate
(c) Potassium citrate
(d) All

46. Which of following is Cream of Tartar or Argol?
(a) Aluminum hydroxide gel
(b) Sodium potassium tartrate
(c) Potassium bitartrate
(d) Potassium citrate

47. Which of following is Lugol's solution?
(a) Weak iodine solution
(b) Aqueous iodine
(c) Strong iodine
(d) Povidone-iodine

48. Astringents are used as
(a) Styptic action
(b) Anti-inflammatory action
(c) Antiperspiring agent
(d) All of above

49. Which of following is anti-flatulent, anti-spasmodic, sedative and antacid?
(a) Dimethadione (b) Simethicone
(c) Silicondione (d) All

50. Which of following occurs naturally, sulphide called as cinnabar?
(a) Mercury (b) Silver
(c) Zinc (d) Arsenic

51. Which vitamins are necessary for proper tooth formation?
(a) A, C, D (b) B complex
(c) A, D, E (d) C, D, B

52. Color of dithiazone Pb in chloroform
(a) Green (b) Red
(c) Violet (d) None

53. Which one is used as standard substances for limit test of sulphate?
(a) Potassium sulphate
(b) Sodium sulphate
(c) Magnesium sulphate
(d) Iron sulphate

54. In case of limit test of heavy metal which method is used for those substance which do not yield clear specified condition?
(a) Method A (b) Method B
(c) Method C (d) Method D

55. In case of limit test of iron, thioglycolic acid is reacting with _____ form of iron?
(a) Ferric
(b) Ferric anhydride
(c) Ferrous
(d) All of above

56. Which stain paper is used in limit test of arsenic?
(a) pH paper
(b) Cobalt chloride paper

(c) Mercuric chloride paper
(d) None of above

57. As per I.P., limit of sulphate as impurity in the stated compound is
(a) 10 ppm (b) 20 ppm
(c) 25 ppm (d) 15 ppm

58. Oxidation number of free or uncombined element is
(a) 1 (b) 2
(c) 0 (d) < 0

59. What is true about the antacid?
(a) It is an alkaline substance
(b) Used for inhibiting the release of acid
(c) Water soluble in nature
(d) All of the above

60. Give an example of the absorbable antacids
(a) Aluminium hydroxide
(b) Calcium carbonate
(c) Tribasic calcium phosphate
(d) Sodium bicarbonate

61. Antiflatulant compound are used with the antacids for which purpose?
(a) To maintain the pH of GIT
(b) To dispense the foam
(c) To avoid the interaction with absorption of metals
(d) To minimize the effect of evolved CO_2

62. Which compound is used as the protective in GIT?
(a) Bismuth subcarbonate
(b) Caoline
(c) Bentonite
(d) All of above

63. Which one is strong in action?
(a) Laxative (b) Purgative
(c) Cathartics (d) All of above

64. Give an example of the bulk purgative
(a) Methyl cellulose
(b) Sodium CMC
(c) Senna
(d) (a) and (b)

65. What is the true about caustics?
(a) The sub stance which is able to destruct tissue
(b) Having the keratolytic action
(c) KOH and $AgNO_3$
(d) All of above

ANSWER KEYS

1. (c)	**2.** (c)	**3.** (d)	**4.** (a)	**5.** (c)	**6.** (a)	**7.** (c)	**8.** (b)	**9.** (b)	**10.** (a)
11. (c)	**12.** (c)	**13.** (a)	**14.** (b)	**15.** (c)	**16.** (b)	**17.** (c)	**18.** (d)	**19.** (a)	**20.** (b)
21. (a)	**22.** (a)	**23.** (a)	**24.** (d)	**25.** (a)	**26.** (a)	**27.** (d)	**28.** (b)	**29.** (a)	**30.** (c)
31. (c)	**32.** (b)	**33.** (b)	**34.** (a)	**35.** (b)	**36.** (d)	**37.** (c)	**38.** (b)	**39.** (a)	**40.** (b)
41. (b)	**42.** (b)	**43.** (d)	**44.** (a)	**45.** (a)	**46.** (c)	**47.** (b)	**48.** (d)	**49.** (b)	**50.** (a)
51. (a)	**52.** (c)	**53.** (a)	**54.** (a)	**55.** (c)	**56.** (c)	**57.** (a)	**58.** (c)	**59.** (a)	**60.** (d)
61. (d)	**62.** (d)	**63.** (c)	**64.** (d)	**65.** (d)					

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UNIT 4

PHARMACOGNOSY

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CHAPTER 1

INTRODUCTION TO PHARMACOGNOSY

ALKALOIDS

Type of Alkaloids	Meaning	Examples
True Alkaloids	Nitrogen in the Hete-ro cycle and originate from Amino acid	Atropine, Morphine, Nicotine
Pseudo Alkaloids	Which do not originate from Amino acid and nitrogen in side chain	Diterpene and Steroid like Alkaloids, Purine alkaloids (Caffeine, Theobromine, Theophylline)
Proto Alkaloids or Amino Alkaloids	Which contains Nitrogen but not in ring system and originate from Amino acid	Mescaline, Adrenaline, Ephedrine, Colchicine

Properties of Alkaloids

1. Most alkaloids contain oxygen and colorless crystals. Exception-Oxygen-free alkaloids, such as Nicotine or Coniine, are typically volatile, colorless, oily liquids. Some alkaloids have color like Berberin (yellow) and Sanguinarine (Copper Red).
2. Most alkaloids are weak bases.
   Except-Amphoteric (Theobromine and Theophylline).
3. Most alkaloids are poorly soluble in water but readily dissolve in organic solvents.
   Except-Caffeine dissolves well in boiling water.
4. Alkaloidal salts are usually soluble in water and alcohol and poorly soluble in most organic solvents.
   Exception-Scopolamine hydro bromide which is soluble in organic solvents and water-soluble Quinine sulphate.
5. Most alkaloids have a bitter flavor.

Isolation and Extraction of Alkaloids (Stas Otto Process)

Moist drug + Alkali

Free base comes out

Separate it with organic solvent

Biosynthesis of Alkaloidal Drugs

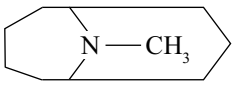
Alkaloidal Class	Synthesis Steps	Examples
Pyrrolidine Derivatives	**Ornithine or Arginine** → Putrescine → N-methylputrescine → N-methyl-Δ^1-pyrroline	Hygrine, Hygroline
Tropane Derivatives	**Ornithine or Arginine** → Putrescine → N- Methylputrescine → N- Methyl-Δ^1-Pyrroline	Atropine, Scopolamine, Hyoscyamine, Cocaine, Ecgonine
Piperidine Derivatives	**Lysine** → Cadaverine → Δ^1-Piperideine **Octanoic Acid** → Coniceine → Coniine	Lobeline, Anaferine, Papaverine, Coniceine, Coniine
Pyridine Derivatives	**Nicotinic acid** → Digidronikotinovaya acid → 1,2-Dihydropyridine	Trigonelline, Recinine, Arecoline, Nicotine, Anabasine

Cont.

Alkaloidal Class	Synthesis Steps	Examples
Isoquinoline Derivatives	Tyrosine or Phenylalanine → Dopamine or Tyramine	Papaverine, Hydrastine, Narcotine (Noscapine), Emetine, Morphine, Codeine, Thebaine
Quinoline Derivatives	**Tryptophan** → Tryptamine → Strictosidine (with Secologanin) → Korinanteal → Cinhoninon	Quinine, Quinidine Cinchonine, Cinhonidine
Indole Derivatives	**Tryptophan** → Tryptamineor 5-Hydroxy Triptophan **Tryptophan** → Chanoclavine → Agroclavine → Elimoclavine → Paspalic acid → Lysergic Acid **Tryptophan** → Tryptamine → Strictosidine (with Secologanin)	Psilocybin, Bufotenin Harman, Harmine, Physostigmine (Eserine), Physovenine Ergotamine, Ergosine Ajmalicine, Sarpagine, Ajmaline, Yohimbine, Reserpine, Strychnine, Brucine
Imidazole Derivatives	Directly from **Histidine**	Pilocarpine, Pilosine
Purine Derivatives	Xantosine → 7-MethylXantone → 7-Methyl Xanthine → Theobromine → Caffeine	Caffeine Theobromine Theophylline
Beta Phenylethyl Amine Derivatives	**Tyrosine or phenylalanine** → Dioxyphenilalanine → Dopamine → Adrenaline and Mescaline, Tyrosine or Phenylalanine → 1-Phenylpropane-1, 2-dione → Cathinone → Ephedrine and Pseudoephedrine	Ephedrine, Pseudoephedrine, Mescaline, Catecholamine's (Adrenaline, Nor adrenaline, Dopamine)
Tropolene Derivatives	**Tyrosine or phenylalanine** → Dopamine → Autumnaline → Colchicine	Colchicine
Diterpene Derivatives	Mevalonic acid → Isopentenyl Pyrophosphate → Geranyl Pyrophosphate	Aconitine
Steroid Derivatives	Cholesterol, Arginine	Solasodine, Solanidine,

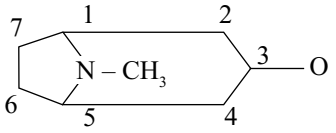
Chemistry of Some Important Alkaloids and Glycosides

Tropane Alkaloids (Solanaceous Alkaloids)

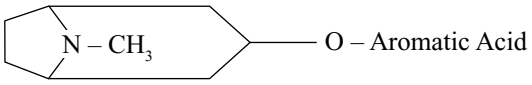


Tropane Nucleus

Bicyclic system made up of a 5-membered ring (1, N, 5, 6, and 7) and a 6-membered ring (1, 2, 3, 4, 5, N). N is common to both. The nucleus always carries oxygen in position 3.



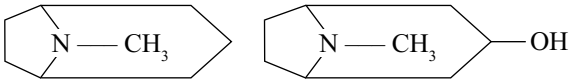
The nitrogen is always methylated. The oxygen is substituted with an aromatic acid, therefore, creating an ester.



- Atropine
- Hyoscyamine
- Hyoscine

Hyoscyamine is the pure optical isomer; (+) Hyoscyamine, (–) Hyoscyamine. Atropine is the racemic of Hyoscyamine.

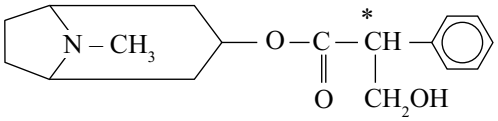
Atropine = (±) Hyoscyamine.



Tropane Tropine

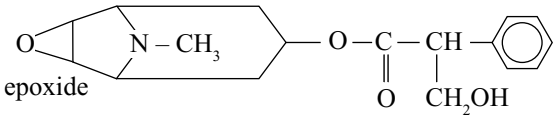
The 3-hydroxy derivative of Tropane is known as TROPINE.

Esterification of tropine with tropic acid yields Hyoscyamine (tropine tropate).



Tropic Acid

* asymmetric center

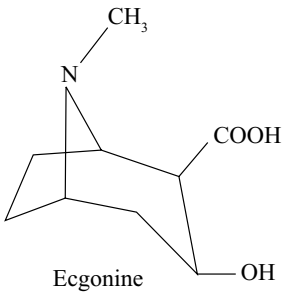


epoxide

Hyoscine

Cocaine

The alkaloids have the same tropane nucleus called ECGONINE.



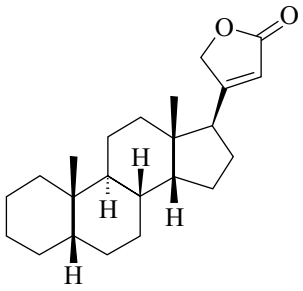
Ecgonine

Chemically all the alkaloids can be extracted and converted to Ecgonine, which is then converted to Cocaine.

Cardiac Glycosides (Steroidal Glycosides)

Aglycone moiety

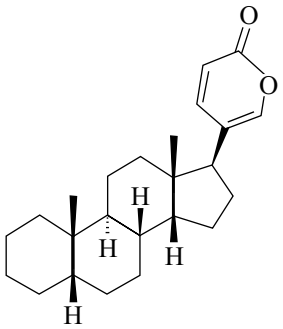
Cardenolide (C-23 Steroidal Nucleus)



Five member α, β unsaturated Gamma lactone ring containing two double bond present at 17 β position.

Example – Digitalis, Strophanthus

Bufadienolide (C-24 Steroidal Nucleus)



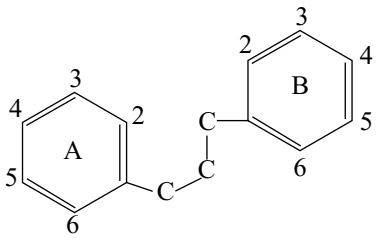
Six member α, β unsaturated Delta lactone ring containing two double bond present at 17 β – position.

Example – Squill

Digitoxigenin	3, 14 dihydroxy Cardenolide
Gitoxigenin	3, 14 dihydroxy Cardenolide + 16-OH
Digoxigenin	3, 14 dihydroxy Cardenolide + 12-OH
Diginatigenin	3, 14 dihydroxy Cardenolide + 12 and 16-OH
Gitaloxigenin	3, 14 dihydroxy Cardenolide + 16-CHO
Strophanthidin	3, 14 dihydroxy Cardenolide + 5-OH and 10-CHO
Ouabagenin (S-strophanthidin)	3, 14 dihydroxy Cardenolide + 5-OH and 10–CH_2 OH + 1,10–OH
Scillaridin A (Scillarenin A)	3, 14 dihydroxy and double bond between C–4 and C–5 Bufadienolide

Flavanoids

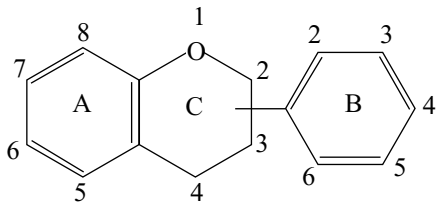
The Flavanoids are polyphenolic compounds possessing 15 carbon atoms; two benzene rings joined by a linear three carbon chain.

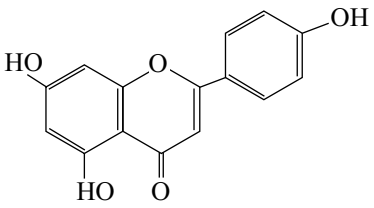
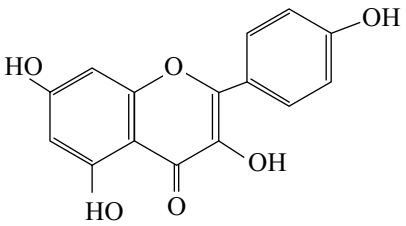
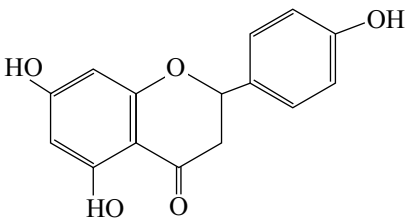
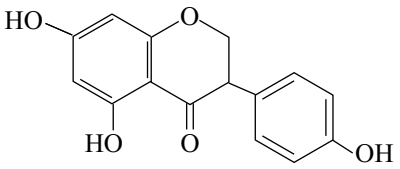
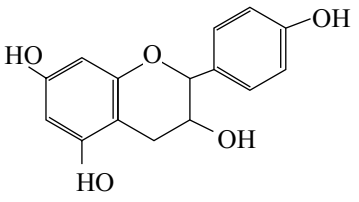


The skeleton above, can be represented as the

$C_6 - C_3 - C_6$ system.

The chemical structure of Flavanoids are based on a C_{15} skeleton with a chromane ring bearing a second aromatic ring B in position 2, 3 or 4.



Type of Flavanoids	Structure	Examples
Flavone		Apigenin (*Apium Graveolens, Petroselinum Crispum*), Luteolin (*Equisetum Arvense*)
Flavonol		Quercitol (*Ruta graveolens, Fagopyrum Esculentum, Sambucus Nigra*), Quarcetin Kaempferol (*Sambucus Nigra, Cassia Senna, Equisetum Arvense, Lamium Album, Polygonum Bistorta*). Myricetin
Flavanone		Eriodictyol, Liquiritigenin, Naringin, Butin
Isoflavonoids or Isoflavones		Soya beans and Red clover, Genistein, Orobol
Anthocyanins		Pomegranate (*Punica Granatum*)

Biosynthesis of Flavanoids

Flavanoids are synthesized by the Phenylpropanoid metabolic pathway in which the amino acid phenylalanine is used to produce 4-coumaroyl-CoA.

This can be combined with malonyl-CoA to yield the true backbone of Flavanoids, a group of compounds called chalcones, which contain two phenyl rings.

Bio–Flavanoids

Flavone

- Luteolin – 5, 7, 3', 4' tetra hydroxy Flavone
- Chrysin – 5, 7 dihydroxy Flavone
- Apigenin – 5, 7, 4' tri hydroxy Flavone

Flavonol

- Quercitin – 5, 7, 3', 4' tetra hydroxy Flavonolor 3, 5, 7, 3', 4' tetra hydroxy Flavone
- Kaempferol – 3, 5, 7, 4' tetra hydroxy Flavonol

Flavonone

- Eriodictyol – 5, 7, 3', 4' tetra hydroxy Flavonone
- Liquiritigenin – 7, 4' di hydroxy Flavonone

GLYCOSIDES

A glycoside is any molecule in which a sugar group is bonded through pure its anomeric carbon to another group via a glycosidic bond. Glycosides can be linked by an O- (an O-glycoside), N- (a glycosylamine), S-(a thioglycoside) or C- (a Cglycoside) glycosidic bond.

The sugar group is then known as the glycone and the non-sugar group as the Aglycone or genin part of the glycoside. The glycone can consist of a single Sugar group (monosaccharide) or several sugar groups (oligosaccharide).

Classification

By glycone/presence of sugar

If the glycone group of a glycoside is glucose, then the molecule is a glucoside; if it is fructose, then the molecule is a fructoside; if it is glucuronic acid, then the molecule is aglucuronide; etc.

By type of glycosidic bond

Depending on whether the glycosidic bond lies "below" or "above" the plane of the cyclic sugar molecule, glycosides are classified as αglycosides or αglycosides.

There are four types of linkages are present between glycone and aglycone:

- C-linkage/glycosidic bond, "non hydrolysable by acids or enzymes" Example-Aloe
- O-linkage/glycosidic bond, Example-Senna, Rhubarb, Frangula
- N-linkage/glycosidic bond, Example-Nucleosides
- S-linkage/glycosidic bond. Example-Black mustard (sinigrin)

By aglycone

1. Alcoholic Glycosides

Salicin which is found in the genus Salix. Salicin is converted in the body into salicylic acid, which is closely related to aspirin and has analgesic, antipyretic and anti-inflammatory effects.

2. Anthraquinone Glycosides

They have a laxative effect. They are mainly found in dicot plants except the Liliaceae family which are monocots. They are present in senna, rhubarb and Aloe species. Antron and anthranol are reduced forms of anthraquinone.

3. Coumarin Glycosides

Apterin which is reported to dilate the coronary arteries as well as block calcium channels. Other coumarin glycosides are obtained from dried leaves of Psoralea Corylifolia.

4. Chromone Glycosides

The aglycone is benzo-gamma-pyrone.

5. Cyanogenic Glycosides

Amygdalin from almonds, Dhurrin, linamarin, lotaustralin, and prunasin

6. Flavonoid Glycosides

- Hesperidin (aglycone: Hesperetin, glycone: Rutinose)
- Naringin (aglycone: Naringenin, glycone: Rutinose)
- Rutin (aglycone: Quercetin, glycone: Rutinose)
- Quercitrin (aglycone: Quercetin, glycone: Rhamnose)

Among the important effects of flavonoids is their antioxidant effect. They are also known to decrease capillary fragility.

7. Phenolic Glycosides

Arbutin found in the Common Bearberry Arctostaphylos Uva-ursi. It has a Urinary antiseptic effect.

8. Saponins Glycosides

These compounds give a permanent froth when shaken with water. They also cause hemolysis of red blood cells. Saponin glycosides are found in liquorice. Their medicinal value is due to their expectorant effect.

9. Steroidal Glycosides or Cardiac Glycosides

Aglycone part is a steroidal nucleus. These glycosides are found in the plant genera Digitalis, Scilla, and Strophanthus. They are used in the treatment of heart diseases e.g. congestive heart failure (historically as nowrecognized does not improve survivability; other agents are now preferred) and arrhythmia.

10. Thioglycosides

These compounds contain sulfur. Examples include sinigrin, found in black mustard, and sinalbin, found in white mustard.

TERPENOIDS

- Terpenes are hydrocarbons resulting from the combination of several isoprene units. Terpenoids can be thought of as modified terpenes, wherein methyl groups have been moved or removed, or oxygen atoms added.
- Mono- and sesquiterpene are the chief constituents of the essential oils while the other terpenes are constituents of balsams, resins, waxes, and rubber.
- Volatile oil is extracted by steam distillation using Clevenger apparatus.

Biosynthesis of Cholesterol and Terpenoids

3-Isopentenyl pyrophosphate or 3, 3-dimethylallyl pyrophosphate (5 Carbon)

↓

Geranyl Pyrophosphate (10 Carbon)

↓

Farnesyl Pyrophosphate (15 C)

↓

Squalene

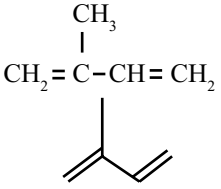
↓

Lanosterol

↓

Zymosterol ⟹ Cholesterol

- Geranyl Pyrophosphate (10 Carbon) = Monoterpenes (10 C)
- Farnesyl Pyrophosphate (15 C) = Sesquiterpene (15 C)
- Squalene = Triperpene and Steroids
- Isoprene: 2-methyl-1,3 butadiene



Isoprene

Terpenoids Type

Type	Number of Isoprene (5C)	Examples
Hemiterpenoids	1	Prenol, Isovaleric acid
Monoterpenoids	2	Eucalyptol, Limonene, Pinene
Sesquiterpenoids	3	Artemisinin, Bisabolol
Diterpenoids	4	Retinol, Retinal, Phytol, Taxol,
Triterpenoids	6	Squalene, Lanosterol
Tetraterpenoids	8	Lycopene, Carotene

PLANT HORMONE

- Plant hormones are signal molecules produced within the plant, and occur inextremely low concentrations. The concentration of hormones required for plant responses are very low (10^{-6} to 10^{-5} mol/L).
- The production of hormones occurs very often at sites of active growth within the meristems, before cells have fully differentiated.
- Plant hormones are not nutrients, but chemicals that in small amounts promote and influence the growth, development, and differentiation of cells and tissues.
- The biosynthesis of plant hormones within plant tissues is often diffuse and not always localized.
- Hormones are transported within the plant by utilizing four types of movements.
  (a) Localized movement
  (b) Cytoplasm streaming within cells

(c) Slow diffusion of ions and molecules between cells are utilized.

(d) Vascular tissues are used to move hormones from one part of the plant to another; these include sieve tubes that move sugars from the leaves to the roots and flowers, and xylem that moves water and mineral solutes from the roots to the foliage.

Abscisic Acid (Dormin) (ABA)

- It found in high concentrations in newly abscissed or freshly fallen leaves.
- It mediates changes within the apical meristems causing bud Dormancy. In plants under water stress, ABA plays a role in closing the stomata.

Auxins

Auxins were the first class of growth regulators discovered. Auxins, especially 1-Naphthaleneacetic acid (NAA) and Indole-3-butyric acid(IBA), are also commonly applied to stimulate root growth when taking cuttings of plants. The most common auxin found in plants is indoleacetic acid or IAA. The correlation of auxins and cytokinins in the plants is a constant (A/C = const.). Synthetic auxin herbicides including 2,4-D and 2,4,5-T have been developed and used for weed control.

- Auxins are compounds that positively influence cell enlargement, bud formation and root initiation. They affect cell elongation by altering cell wall plasticity.
- Auxins decrease in light and increase where it is dark.
- They stimulate cambium cells to divide and in stems cause secondary xylem to differentiate.
- Auxins act to inhibit the growth of buds lower down the stems (apical dominance), and also to promote lateral and adventitious root development and growth.

Cytokinins or Zeatinor Kinetin or Benzyladenine

Cytokinins or CKs are a group of chemicals that influence cell division and shoot formation. The first cytokinins were isolated from yeast cells.

- They also help delay senescence or the aging of tissues, are responsible for mediating auxin transport throughout the plant, and affect internodal length and leaf growth.
- Cytokinins counter the apical dominance induced by auxins; they in conjunction with ethylene promote abscission of leaves, flower parts and fruits.

Ethylene

Ethylene is a gas that forms through the Yang Cycle from the breakdown of methionine, which is in all cells. Ethylene is produced at a faster rate in rapidly growing and dividing cells, especially in darkness. Ethylene affects fruit-ripening.

Gibberellins

They were first discovered when Japanese researchers, including Eiichi Kurosawa, noticed a chemical produced by a fungus called Gibberella fujikuroi that produced abnormal growth in rice plants.

- Gibberellins are important in seed germination, affecting enzyme production that mobilizes food production used for growth of new cells.
- GA produces bolting of rosette-forming plants, increasing internodal length. They promote flowering, cellular division, and in seeds growth after germination. Gibberellins also reverse the inhibition of shoot growth and dormancy induced by ABA.

Tissue Culture

Tissue culture consists of growing plants cells as relatively on organized masses of cells on an agar medium (callus culture) or as a suspension of free cells and small cell masses in a liquid medium (suspension culture).

Tissue culture is used for vegetative multiplication of many species and in some cases for recovery of virus-free plants. It has potential application in production of somatic hybrids, organelles and cytoplasm transfer, genetic transformation and germplasm storage through freeze-preservation.

Plant Tissue Culture

- Tissue culture is the process whereby small pieces of living tissue (explants) are isolated from an organism and grown aseptically for indefinite periods on a nutrient medium.
- The used explants include buds, root tips, nodal segments or germinating seeds and these are placed on suitable culture media where they grow into an undifferentiated mass known as Callus.
- Surface sterilization of explants – disinfectant such as sodium hypochloride, hydrogen peroxide or mercuric chloride.

Protoplasts

- These are cells without their cell walls which form useful material for cell manipulations as under certain conditions, contrasting cell types can be fused to yield

somatic hybrids; a process known as protoplast fusion.
- Protoplasts can be produced from suspension cultures, callus or intact tissues by mechanical disruption or treatment with enzymes.
- Pectinase breaks cell aggregates into individual cells and cellulase removes the cell wall.

Plant Organ Culture

This is the most common type known as Tissue Culture. Here shoot tips are after surface sterilization is placed in growth medium lacking hormones where these develop into single seedling like shoots.

- If instead cytokinin is used in the medium, auxiliary shoots will emerge and produce a shoot culture.

Regeneration of Plants

- The cells capable of developing into intact plants are said to be totipotent; totipotency; being the property of undetermined cells.
- It should be remembered that for callus formation auxin and cytokinin both are required; whereas only a cytokinin is required for shoot culture and only an auxin for root culture.
- The formation of roots or shoots in culture is known as organogenesis.

Note

- Production of pathogen – free plants: The basic method of obtaining virus-free plants is culture of apical meristems.
- Balance between formation of root or shoot is governed by ratio of auxin (A) to cytokinins (c). A to C in 4: 1 cause shoot formation and A to C in 100:1 produce root formation.
- Hairy root culture involves a segment of Ri DNA from Agro bacterium rhizogens. One of the typical growth medium is Murashige and Skoog (MS) Culture medium

Culture Medium

1. Inorganic salts

The concentration of Potassium and Nitrate should be at least 20–25 mM and Concentration of 1–3 mM of phosphate, sulphate, magnesium. Recommended micro nutrients are iodides, boric acid, and salts of zinc, manganese, molybdenum, copper, cobalt and iron.

2. Carbon source

Glucose is the most common at 2–4 % concentration.

3. Vitamins

Thiamine is essential.

4. Antibiotics

Although not required for cell growth, antibiotics are often used to control the growth of bacterial and fungal contaminants.

5. Growth regulator

These substances are needed to induce cell division. The most frequently used are Naphthalene acetic acid (NAA) and 2,4-dichlorophenoxy acetic acid in the molar concentrations of 10^{-7} to 5×10^{-5}.

6. Organic supplement

Protein hydrolyzates, yeast extract, malt extract and coconut milk (liquid endosperm) are used for enhancement in growth rate of the cells in biomass.

Note

- Medium pH - 5.5 to 5.7
- CO_2 Incubators - An atmosphere of 5–10% CO_2.
- Preservation and storage - Liquid N_2 is used to preserve tissue

Culture cells, either in the liquid phase (–196°C) or in the vapor phase (–156°C). Instead of direct freezing, a cryoprotective agent which lowers the freezing point, such as glycerol or DMSO, can added.

Important Tables of Pharmacognosy

Type of Calcium Oxalate Crystals	Examples
Prism/Single Crystal	Quillaia bark, liquorice, Quassia wood, Hyocyamus, Clove stalk, Senna, Cascara, Rauwolfia, Kurchi, Coca
Cluster Crystal/Spheraphides	Senna leaf, Stramonium leaf, Rhubarb, Clove, Wild Cherry Bark
Rosette Crystal	Rhubarb, Umbelliferous Fruits (Fennel, Coriander, Anise, Celery)
Acicular Crystal/Raphides	**Single Acicular**–Gentian root, Cinnamon bark **Bundle of Acicular**–Squill (in Mucilage), Ipecac Root
Micro Crystal/Crystal sand/Micro sphenoid	Cinchona, Belladonna leaf, Datura
Absent	Digitalis and Aloe

Preliminary Phytochemical Screening

Chemical Constituents	Tests	Inferences
Carbohydrates	**Molish's Test – General for Sugars** Aqueous Extract + Alpha Naphthol in alcohol + con. H_2SO_4	Violet ring at the junction of two liquids.
	Test for Reducing Sugars **1. Fehling's test-**Mix equal volume of Fehling's A and B + Add equal volume of test solution then Heat **2. Benedict's test-**Mix equal volume of Benedict's reagent and test sample then heat	First red then brick red colour appears Red colour appears
	Test for Mono Saccharides **Barfoed's Test-**Mix equal volume of Barfoed's reagent and test sample, heat and then cool	Red precipitate
	Test for Pentose Sugars *Bial's Orcinol Test* Bial reagent + test solution and then Boil	Green or purple colour appears
	Test for Hexose Sugars *Seliwanoff's test (For Keto Hexose),* Fructose Seliwanoff's reagent + test solution and then heat	Red colour
	Test for Starch *Iodine Test*	Blue colour disappears on heating and reappears on cooling
	Test for Gum Fehling's test and Benedict's test	Red colour
	Test for Mucilage Ruthenium Red	Red colour

Cont.

Chemical Constituents	Tests	Inferences
Proteins	**Biuret Test (General test)** – NaOH + 1 % $CuSO_4$ **Millon's test (For Proteins)** **Xanthoprotic Test (For tyrosine or tryptophan phenylalanine containing proteins)** Test sample + conc. HNO_3 + strong NH_3 Solution Test for Sulphur Containing Proteins NaOH + Lead Acetate **Precipitation Test** 1. Absolute alcohol 2. Hg_2Cl_2 3. Lead acetate 4. Ammonium sulphate	Violet or pink colour White ppt which turns into red upon heating White ppt which turns into yellow upon heating Black or brownish due to PbS formation Colloidal precipitate
Amino Acids	**Ninhydrin Test (General test)** Test for tyrosine – Millon's reagent Test for Cysteine – NaOH + 10 % lead acetate	Purple or bluish colour Red colour Black precipitate of lead sulphide
Fat and Oil	Sudan red III	Red colour
Steroid/Cholesterol	**Salkowski Reaction** Chloroform + Test sample + con. H_2SO_4 **Lieberman –Burchard Reaction** Chloroform + Test sample + Acetic anhydride + con. H_2SO_4 **Lieberman's Reaction** Test sample + Acetic anhydride + con. H_2SO_4	Chloroform layer appears red and acid layers shows greenish **yellow fluorescence** First red, then blue, finally green colour Blue colour
Glycosides		
Cardiac Glycosides	**Baljet Test**– Sodium Picrate **Legal Test**–For Cardenoloides Pyridine + Sodium Nitroprusside **Keller-Killiani Test – For Deoxy sugars** Glacial Acetic Acid + $FeCl_3$+ con. H_2SO_4 **Libermann's Test – For Bufadienoloides** Same as steroids	**Yellow to orange colour** Pink to red colour Reddish brown colour appears at the junction of two liquid layers and upper layer appears bluish green.
Anthraquinone Glycosides	**Borntrager Test** Dilute H_2SO_4 + Benzene /Chloroform — separate the organic solvent and then add ammonia **Modified Borntrager Test (For C-Glycosides)** $FeCl_3$ + Dil. HCl + Benzene /Chloroform — separate the organic solvent and then add ammonia	Ammonical layer turns pinkish red colour Ammonical layer turns pinkish red colour
Saponin Glycosides	**a. Foam Test (Test Sample + Water)** **b. Heamolytic Test (Dry Powder + Blood)**	Foam Observed Heamolytic zone

Chemical Constituents	Tests	Inferences
Cynogenetic Glycosides	**a. Grignard or Sodium Picrate Test** **b. Mercurous nitrate solution** **c. Copper sulphate and guaiacum resin impregnated filter paper**	Brick red colour Metallic mercury Blue stain
Flavanoids	**Shinoda Test**– 95% ethanol + Con. HCl + Mg	Pink colour
Alkaloids		
Common for Alkaloids	**1. Mayer Test –**Potassium Mercuric iodide **2. Hager Test –** Picric Acid (saturated) **3. Wagner Test-** Iodine in KI solution **4. Dragendorff's Test –** Potassium bismuth iodide solution	Cream coloured ppt Yellow coloured ppt Reddish brown ppt Reddish brown ppt
Specific Test		
Ergot Alkaloids	**Van-urk's Test** **Para dimethyl amino benzaldehyde**	Blue colour
Purine Alkaloids	**Murexide Test** $KClO_3$ + HCl — Heat	Purple colour upon exposure to ammonia solution. This colour disappears upon addition of alkali.
Tropane Alkaloids	**Vitali – Morin Reaction** **Fuming HNO_3** + dry to get residue + add Methanolic potassium hydroxide to an acetone solution of nitrated residue	Violet colour
Opium Alkaloids	**Meconic Acid Test** $FeCl_3$ + Dil. HCl	Reddish purple colour
Cinchona Alkaloids	**Thalleoquin Test** Bromine water + Dil. Ammonia solution	Green colour

Substance	Microscopic reagents
Cellulose	Schultz solution (Chlor-zinc-iodine)
Starch and Hemi-cellulose	Iodine solution
Lignin	Phloroglucinol + con. HCl
Suberin and Cutin	Sudan red
AleuronGrain	Tri nitro Phenol and Ethanol

Pharmacognostic Reagents	Role
Alcohol	Preservative, decolourising agent,
Glycerine	Humectant, mounting agent
Chloral hydrate	Clearing agent (Dissolve Chlorophyll)
Chromic acid solution	Disintegrating and isolating agent
Picric acid	Astringent

Pharmacological Parameter	QC Standard
Bitterness value	Quinine HCl
Haemolytic Activity	Saponin
Astringency	Tannin
Swelling Index	Isapgol
Foaming Index	Saponin

Trichome

Covering /Non-Glandular /Clothing/ Special Type

Unicellular

–Senna (Slightly cured)
–Cannabis
–Nux-Vomica (Lignified)
–Strophanthus Seed

Multi Cellular

–Un-branched
  Uniseriate – Vasaka
  Biseriate – Calendula
  Multi seriate – Male fern
–Branched
  Stellate – Hammalis
  Peltate – Croton
  Candelabra – Verbascum thapsus
  T shape – Pyrethrum

Glandular

Unicellular
  –Vasaka
Multi cellular
  –Digitalis, Belladonna

Hydathode

–Piper betel

Stomata type	Description	Example
Anomocytic/ Ranunculaceous/ Irregular Celled Stomata	Varying number of Subsidiary cells	Digitalis (Foxglove), Clove, Fennel, Buchu, Lobelia, Hemlock
Diacytic/ Caryophyllaceous/ Cross-Celled Stomata	2 Subsidiary cells are right angle to that of guard cell	Vasaka, Peppermint, Spearmint, Mentha
Anisocytic/ Cruciferous/ Unequal Celled Stomata	3 subsidiary cells, one is markedly smaller than others	Belladonna, stramonium, Datura, Henbene, Vinca
Paracytic/ Rubiaceous/ Parallel-Celled Stomata	2 Subsidiary cells are parallel to that of guard cell	SennaLeaves, Coca

Special Points

Aril

- Fleshy covering arising from Hilum and almost completely cover seed or succulent out growth originating from Hilum covering seed. Example – Mace of Nutmeg

Arillode/Arillus/False Aril

- Covering similar to aril but arising from Micropyle. Example – Cardamom

Caruncle

- Localized fleshy out growth arising from micropyle. Example – castor oil, Croton

Strophiole

- Wing like or barrel shaped out growth along with the line of Raphe, due to increase in the amount of Parenchyma tissue. Example – Colchicum (Enlarged Funicle)

Idioblast

- A cell that differ from surrounding in size, cell thickness, form or contents.
- Examples – Stramonium and Henbane (Crystal layer of Idioblast), belladonna, Lignified Idioblast (Lobelia, Hammalis, Tea)

Stone cells

- Thick walled, isodiametric, strengthening cells of sclerenchymatous tissue, occurring singly or in groups also known as Sclerides.

Leaf Constants

1. Palisade Ratio: Average number of palisade cells beneath each upper epidermal cell.
2. Stomatal Number: Average number of stomata per mm^2 of epidermis of leaf
3. Stomatal Index: % proportion of ultimate divisions of epidermis of a leaf which have been converted into stomata.

$I = S / (E + S) \times 100$
S = No. of stomata per unit area
E = No. of epidermal cell in same per unit area

Stomatal number varies considerably with age of leaf but Stomatal index is highly constant for a given species.

4. Vein-Islet Number: Number of Vein-Islet per mm^2 of leaf surface midway between midrib and margin.
5. Vein termination Number: Number of Vein termination per mm^2 of leaf surface midway between midrib and margin.

Stomata Index

Species	Upper surface	Lower surface
Atropa belladonna	3.9	21.7
Cassia senna	12.4	11.8
Cassia angustifolia	19.0	18.3
Digitalis purpurea	2.7	19.2
Digitalis lanata	14.4	16.1
Daturastramonium	18.1	24.9

Quantitative Microscopy (Lycopodium Spore Method)

- Estimation of foreign organic matter in powdered drug
- Lycopodium spore are uniform size (25 micron)
- 1 mg of Lycopodium contains 94,000 spores on an Avg.

$$\% \text{ purity of drug} = N \times W \times 94{,}000 \times 100 / S \times M \times P$$

N = No. of characteristic structure in 25 field
W = weight of Lycopodium in mg taken
M = weight in mg of sample
P = 2, 86, 000 in case of ginger
S = No. of Lycopodium spore in 25 field

Note

Carr Price Reaction

For Vitamin A – Chloroform + Antimony trichloride solution — Blue Colour
For Vitamin D – Chloroform + Antimony trichloride solution — Pinkish-Red colour

Cystolith

- Calcium carbonate forms on outgrowth of cell wall.
- Example Cannabis sativa, Vasaka

Calcium Oxalate Crystal

- Insoluble in Acetic acid /Alkali
- Soluble in dilute HCl and H_2SO_4 without effervescence. With 50% H_2SO_4 gives effervescence.

Note

Clove

1. Hypanthium portion + KOH — Acicular crystal of Potassium eugenolate
2. Clove oil + Alcoholic $Fecl_3$ — Violet colour due to Isoeugenol
3. Clove oil + Aq. $Fecl_3$ — Dark colour due to Tannin content

Cassia and Cassia Cinnamon

- With $FeCl_3$ – Cassia cinnamon gives brown colour due to less content of eugenol, While Cassia Pale – green colour.

  Cinnamaldehyde + $FeCl_3$ = Brown Colour

  Eugenol + $FeCl_3$ = Blue Colour

ENZYMES

Enzymes & proteins	Source	Activity
Papain	Papaya latex	Proteolytic
Diastase	Barley	Amylolytic
Bromelin	Pineapple	Blood clotting
Ficin/Ficain	*Ficus carica* (figs) Latex	Proteolytic, IgG antibody detection
Pepsin	Hog stomach	Proteolytic
Pancreatin	Hog pancreas	Digestive
Hyaluronidase	Human testes	Mucolytic
Urokinase	Human kidney & urine	In pulmonary embolism
Streptokinase	*Streptococci*	Dissolve blood clot
Asparaginase	*E. coli* (r DNA)	Antileukemic
Somatotropin	*E. coli* (r DNA)	In Hypothyroidism
Penicillinase	*Bacillus cereus (staphylococci)*	Treatment in adverse reactions to Penicillin

PAPAIN

Synonyms: Papain, Papayotin

Biological Source: Papain is the dried and purified latex obtained from the milky juice of unripe fruits of Carica papaya Linn, family Caricaceae.

Characteristics: Purified Papain is white or grayish white, slightly hygroscopic powder. It is completely soluble in water and glycerol, and practically insoluble in most organic solvents. The best pH for its activity is 5.0 but it functions also in neutral and alkaline media.

Chemical Constituents: Papain is referred to as vegetable pepsin as it contains enzymes similar to those in pepsin. The Papain molecule consists of one folded polypeptide chain of 212 amino acids with molecular weight up to 23400 Dalton. Papain contains several proteolytic enzymes such as peptidase-I, rennin like milk coagulating enzyme, Amylolytic enzyme and a clotting enzyme similar to pectase. Peptidase - I has the ability to convert proteins into dipeptides and polypeptides.

Uses: Being proteolytic enzyme Papain is used as a digestant for proteins. It shows the proteolytic activity much like pepsin but, unlike pepsin, it can act in acid, neutral or alkaline media. It can be combined with other enzymes such as amylases to produce digestive aids. It is extensively used as a meat-tendering agent in the meat packing industries. Papain (10%) is used in ointment for wound debridement, that is, for the removal of dead tissue. It is also used in the treatment of contact lenses to prolong wearing time in keratoconic patients with papillary conjunctivitis.

BROMELAIN

Synonyms: Bromelin, Bromelain

Biological Source: Bromelin is a mixture of proteolytic enzymes isolated from the juice of Ananas comosus, pineapple, family Bromeliaceae.

Characteristics: Bromelin is incompletely soluble in water. The bromelin obtained from the fruit is acidic in nature while that derived from the stem tissues is a basic protein.

Chemical Constituents: Bromelin is a glycoprotein. It has a molecular weight of about 25000-31000. Other pineapple endopeptidases are ananain and comosain.

Uses: Bromelin has the ability to dissolve fibrin in conditions of inflammatory oedema. It is used for tenderizing meat, chill proofing reagent for beer as a bating reagent for hides and for production of protein hydrolysate.

MALT EXTRACT

Synonym: Diastase, Malt extract

Biological Source: Malt extract is the extract obtained from the dried barley grains of one or more varieties of Hordeum vulgare Linne, family Poaceae.

Characteristics: Malt extract contains enzymes, which are most active in neutral solution. The acidic conditions destroy the activity. It converts starch into disaccharide maltose. The enzyme is destroyed by heat. Many heat sterilized malt extracts do not contain diastase. It is completely soluble in cold water, more readily in warm water. The aqueous solution shows flocculant precipitate on standing.

Chemical Constituents: Malt extract contains dextrin, maltose, traces of glucose and about 8 % of amylolytic enzyme diastase.

Uses: Malt extract and purified diastase, both are used as amylolytic enzymes and as an aid in digesting starch. They are used as bulk producing laxatives.

STREPTOKINASE

Synonym: Estreptokinase, Plasminokinase

Biological Source: Estreptokinase, Plasminokinase is a purified bacterial protein - haemolytic S. griseus?produced from the strains of group C Beta - haemolytic S. griseus.

Characteristics: Streptokinase is a bacterial protein with half-life of 23 minutes. Its anisolylated plasminogen activator complex (APSAC) has a higher half life of 6 hours.

Chemical Constituents: Streptokinase is the purified bacterial protein with about 484 amino acid residues.

Uses: Streptokinase is the first available agent for dissolving blood clots. It binds to plasminogen in a 1:1 ratio and changes molecular conformation. Thus, the complex formed becomes an active enzyme and promotes the activity of fibrinolytic enzyme plasmin. Plasmin breaks fibrin clots. Anistreptase or the anisolylated plasminogen streptokinase activator complex (APSAC) can also be used in a similar way for degrading blood clots. Streptokinase and anistreptase are both used in the treatment of pulmonary embolism, venous and arterial thrombosis and coronary artery thrombosis.

UROKINASE

Synonym: Uroquinase

Biological Source: Urokinase is serine protease enzyme isolated from human urine and from human kidney cells by tissue culture or by recombinant DNA technology.

Characteristics: Urokinase enzyme occurs in two different forms as single and double polypeptide chain forms. It has a half life of 10-16 minutes after intravenous administration. These enzymes act on an endogenous fibrinolytic system.

Chemical Constituents: Urokinase enzymes are serine proteases that occur as a single low molecular weight (33kDa) and double, high molecular weight (54kDa) polypeptide chain forms. They differ in molecular weight considerably. A single chain is produced by recombinant DNA technique and is known as SCUPA.

Uses: Urokinase is used in the treatment of pulmonary embolism, coronary artery thrombosis and for restoring the potency of intravenous catheters.

HYALURONIDASE

Synonym: Spreading factor, Hyalase

Biological Source: Hyaluronidase is an enzyme product prepared from mammalian testes which shows the capability of hydrolysing hyaluronic acid like mucopolysaccharides. Skin is considered as the largest store of hyaluronidase in the body.

Characteristics: Hyaluronidase for injection consists of not more than 0.25 µg of tyrosine for each USP hyaluronidase unit. Due to its action on hyaluronic acid, it promotes diffusion and hastens absorption of subcutaneous infusions. It depolymerises and catalyses hyaluronic acid and similar hexosamine containing polysaccharides.

Chemical Constituents: Hyaluronidases are a group of enzymes such as 4- lycanohydrolase, hyaluronate 3-glycanohydrolase and hyaluronate lyase. They are mucopeptides composed of alternating N-acetylglucosamine and glucuronic acid residues. Hyaluronidases catalyse the breakdown of hyaluronic acid.

Uses: Hyaluronidase for injection is used in the conditions of hypodermoclysis. It is used as a spreading and diffusing agent. It promotes diffusion, absorption and reabsorption.

SERRATIOPEPTIDASE

Synonym: Serrapeptase, Serratiopeptidase

Source: Serratiopeptidase is a proteolytic enzyme isolated from nonpathogenic enterobacteria Serratia E 15. It is also produced by the larval form of the silk moth.

Characteristics: Serratiopeptidase is very much vulnerable to degradation in the acidic pH. When consumed in unprotected tablet or capsule, it is destroyed by acid in stomach. However enteric coated tablets facilitate its absorption through intestine. One unit of the enzyme hydrolyzes casein to produce colour equivalent to 1.0 μ mol of tyrosine per minute at pH 7.5 and 35 Deg C.

Chemical Constituents: Serratiopeptidase is a proteolytic enzyme of protease type XXVI. The preparation contains 7.1 units/mg solid.

Uses: Serratiopeptidase is the most widely prescribed anti-inflammatory enzyme in developed countries and also in India. It eleminates inflammatory oedema and swelling, accelerate liquefaction of pus and sputum, and enhance the action of antibodies. It is also used as a fast wound healing agent.

GELATIN

Synonym: Gelatinum

Biological Source: Gelatin is a protein derivative obtain by evaporating an aqueous extract made from bones, skins and tendons of various domestic animals Some important sources are Ox, Bos taurus, and Sheep, Ovis aries belonging to family Bovidae,

Characteristics: Gelatin occurs in the form of thin sheets or as shredded flakes or powder. It is nearly colourless or pale yellow devoid of odour and taste. It swells in cold water and completely dissolves when heated. It is soluble in acetic acid and glycerin but insoluble in alcohol and organic solvents.

Chemical Constituents: Gelatin consists of a major proportion of protein glutin. Gelatin should be free from protein chondrin which comes from the chondrinogen of connective tissues.

Uses: Gelatin is used as a nutrient and as a styptic. It is largely used for the manufacture of hard and soft gelatin capsules. It is also used for the preparation of suppositories, pesseries, pastilles and pastes. It is a component in the bacteriological culture media. Gelatin is also employed in the micro encapsulation of drugs, in injections and perfumes. It is used for the production of absorbable gelatin sponge and gelatin films.

Multiple Choice Questions

1. Aril is present in
   (a) Nutmeg (b) Cardamom
   (c) Strophanthus (d) Castor
2. Aril is
   (a) Outgrowth from micropyle and covering the seed
   (b) Stiff-bristle like appendages with wavy flowering glume of grasses
   (c) Warty out growth from micropyle
   (d) Succulent growth from hilum covering entire seed
3. What is iodine number of coconut oil?
   (a) 25–28 (b) 45–55
   (c) 7–10 (d) 85–100
4. Which one is also known as extra-nuclear?
   (a) Golgi complex (b) Plastid
   (c) Argon (d) Mitochondria
5. Chemically fixed oils and fats are esters of
   (a) Ketone (b) Glycerol
   (c) Sugar (d) None of the above
6. Fixed oil which is soluble in alcohol is
   (a) Arachis oil (b) Mustard oil
   (c) Castor oil (d) Chaulmoogra oil
7. Which is not one of the parameter of quantitative chemical tests of fixed oils and fat?
   (a) Viscosity (b) Reichert-Meissel value
   (c) Peroxide value (d) Hydroxyl value
8. Palm oil is
   (a) Non-drying oil (b) Drying oil
   (c) Semi-drying oil (d) Fats
9. Olive oil gives fluorescence of colour
   (a) Red white (b) Golden yellow
   (c) Crimson red (d) Whitish blue
10. Halphen's test is used for
    (a) Detection of cotton seed oil as an adulterant
    (b) Detection of artificial invert sugar
    (c) Saponins
    (d) Tannins
11. The most common carbon source for plant tissue culture is
    (a) Dextrose (b) Sucrose
    (c) Charcoal (d) Maltose
12. According to ayurveda PITA (bile) is responsible for:-
    (a) Transmitting sense impression to the mind
    (b) Providing the static energy for holding body tissue together
    (c) All digestive and metabolic activities
    (d) Lubrication of various points of friction
13. Natural cytokinin is
    (a) Kinetin (b) Zeatin
    (c) Adenine (d) None
14. Chrysanthemum is mainly used as
    (a) Pesticide (b) Insecticide
    (c) Rodenticide (d) Larvicide
15. Which of the following causes fruit ripening?
    (a) Auxin (b) Cytokinin
    (c) Gibberellins (d) Ethylene
16. All are plant growth promoters except
    (a) Abscisic acid (b) Auxin
    (c) Gibberellin (d) Cytokinin
17. Lycopodium spore method is used for
    (a) Powdered drugs having well-defined particle size
    (b) Single layered cells or tissues
    (c) The objects of uniform thickness
    (d) All of the above
18. 1 IU of vitamin A represents
    (a) 0.0344 μg of standard preparation
    (b) 0.344 μg of standard preparation
    (c) 0.443 mg of standard preparation
    (d) 0.77g of standard preparation
19. In protoplast culture protoplasm is isolated by using
    (a) Cellulase (b) Macerozyme
    (c) Both (d) None
20. Stellate trichomes are present in
    (a) Humulus (b) Pyrethrum
    (c) Hammaelis (d) Calendula officinalis
21. Keris test is used for
    (a) Caffeine
    (b) Presence of deoxy sugar
    (c) Rancidity of fats and oils
    (d) Aloes

22. The semi solid mass dissolved by boiling a decoction is called
    (a) Asava (b) Aristha
    (c) Lehya (d) None
23. In preparation of Ghrita, if we use mild heating then the paka obtained is known as
    (a) Madhyampaka (b) Kharpaka
    (c) Mrudupaka (d) None
24. Plant tissue culture has potential role in all except
    (a) Secondary metabolite production
    (b) Biotransformation
    (c) Genetic mapping
    (d) Micropropagation
25. Marine fungus is the source for
    (a) Penicillin (b) Cephaelosporin
    (c) Zonarol (d) Avarol
26. Antileukemic compound bryostatin is isolated from marine organism
    (a) Bugula neritina (b) Tethya crypta
    (c) Lissoclinum patella (d) Tridemnum species
27. Centroxylic stands for
    (a) Phloem in the centre surrounded by xylem
    (b) Xylem in the centre surrounded by phloem
    (c) Phloem in the centre surrounded by cambium
    (d) Xylem in the centre surrounded by cambium
28. "Closed-collateral" vascular bundles are the characteristics of
    (a) Dicotyledonous plant
    (b) Monocotyledonous plant
    (c) Weeds
    (d) None of the above
29. For the formation of shoot which ratio of plant growth regulators is required?
    (a) Auxin:cytokinin (1:4)
    (b) Auxin:cytokinin (4:1)
    (c) Auxin:cytokinin (100:1)
    (d) Auxin:cytokinin (1:100)
30. The C_2 of the purine nucleotide comes from
    (a) Aspartare (b) Glycine
    (c) N-10-Formyl THF (d) CO_2
31. Iodine value for oils and fats is measured as
    (a) Iodine present in oils
    (b) Extent of unsaturation
    (c) Extent of saturation
    (d) None of the above
32. Chlorophytum borivillianum is used as
    (a) Anti-fertility (b) Aphrodisiac
    (c) Antipyretic (d) Expectorant
33. The number of milligram of KOH required to combine with fatty acid which are present in glyceride form in 1 gram of sample of oil or fat is called
    (a) Difference between saponification value and acid value
    (b) Ester value
    (c) Acid value
    (d) Both (a) and (b)
34. For Vitamin A,
    (a) 1 IU is, contains 76 mg of standard preparation
    (b) 1 IU is present in 0.344 μg of standard preparation
    (c) 1 IU is contained in 0.025 μg of standard preparation
    (d) 1 IU is present in 7.7 μg of standard preparation
35. Manoalide, a marine drug, is
    (a) Anti-fungal (b) Muscle relaxant
    (c) Anti-inflammatory (d) Anti-pyretic
36. For herbal drugs, optical rotation is determined at ____°C using sodium lamp.
    (a) 25 (b) 110
    (c) 65 (d) 77
37. Biosynthesis of alizarin follows the
    (a) Shikkimic acid pathway
    (b) Mevalonicacid pathway
    (c) Both (a) and (b)
    (d) Acetate pathway
38. In which Ayurvedic formulation preservative is not required?
    (a) Lepa (b) Vatika
    (c) Asava (d) Pisti
39. 'Candelabra' trichomes are present in
    (a) Verbascum thapsus (b) Digitalis purpurea
    (c) Senna angustifolia (d) Helicteris isora
40. Centroxylic vascular bundle is present in
    (a) Malefern (b) Sweat flag
    (c) Maize (b) Sunflower
41. "Open-collateral" vascular bundles are the characteristics of
    (a) Dicotyldenous plant
    (b) Monocotyldenous plant

(c) Weeds
(d) None of the above

42. Which marine drug has a cardiovascular activity?
(a) Spongosine (b) Anthropleurins
(c) Saxitoxin (d) Both (a) and (b)

43. Corm is present in
(a) Saffron (b) Colchicum
(c) Nux-vomica (d) Both (a) and (b)

44. Relation between ester value, saponification value and acid value is
(a) Ester value = Saponification value – Acid value
(b) Ester value = Saponification value + Acid value
(c) Acid value = Ester value – Saponification value
(d) Both (b) and (c)

45. Iodine number of fat is determined to know:
(a) Free fatty acid
(b) Average molecular size
(c) Relative unsaturation
(d) All of the above

46. In plant tissue culture surface sterilization of explant is done by
(a) Sodium hypochloride
(b) Bromine water
(c) Hydrogen peroxide
(d) All of the above

47. Gibberelin obtained from fungus is
(a) Gibberella fujikuroi
(b) Fusarium heterospermum
(c) Aspergillus niger
(d) Both (a) and (b)

48. Adaptogen are substances which
(a) Improve physical endurance
(b) Maintain stamina in adverse and difficult environment
(c) Increase the tolerance to change in environment
(d) All of the above

49. Which one is essential vitamin in culture media?
(a) Thiamine (b) Ascorbic acid
(c) Pantothenic acid (d) Biotin

50. Which one is not an intermediate in shikimik acid pathway?
(a) Erythrose 4 phosphate
(b) Chrosmic acid
(c) Shikimik acid
(d) Prephenic acid

51. As per IP, 1 gram of shark liver oil should contain not less than
(a) 1000 IU of vitamin A
(b) 3000 IU of vitamin A
(c) 6000 IU of vitamin A
(d) 4000 IU of vitamin A

52. The acid hydrolysis of Sterculia gum yields
(a) D-galactose
(b) L-rhamnose
(c) D-galacturonic acid
(d) All of the above

53. Which of the following is not a dicotyledonous type of stomata?
(a) Diacytic (b) Moss
(c) Anisocytic (d) Rubiaceous

54. Palisade ratio is
(a) Total number of palisade cells beneath each upper epidermal cell
(b) Total number of palisade cells beneath mesophyll
(c) Average number of palisade cells beneath each upper epidermal cell
(d) None of the above

55. Which of the following is not a macronutrient?
(a) Carbon (b) Boron
(c) Nitrogen (d) Potassium

56. An essential ingredient in the general preparation of plant tissue culture media is
(a) Auxin
(b) Sucrose or glucose
(c) Gibberlin G1 or gibberlin G2
(d) Pyridoxine HCI

57. Which of the following is not an unorganized drug?
(a) Tragacanth (b) Aloe
(c) Lard (d) Datura

58. Biosynthesis of isothiocyanate aglycone follows
(a) Acetate pathway (b) Mevalonate pathway
(c) Shikkimic pathway (d) None of the above

59. In Lycopodium spore method number of characteristic structure in fields selected is_____.
(a) 26 (b) 43
(c) 25 (d) 56

60. All are true about leaflets, except
    (a) Bud or branch is absent in leaflet
    (b) Leaflets are arranged in pairs
    (c) Leaflets are asymmetric at the bases
    (d) Examples include rose, neem, digitalis and senna etc.
61. Which drug has a cytotoxic activity?
    (a) Anthropleurins (b) Laminine
    (c) Ara c (d) Saxitoxin
62. Caruncle is present in
    (a) Nutmeg (b) Cardamom
    (c) Strophanthus (d) Castor
63. The biological source of cotton fiber is
    (a) Cyamopsis tetragonolobus
    (b) Arachis hypogaea
    (c) Gossypium barbadense
    (d) Saraca indica
64. Silk consists of:
    (a) Keratin (b) Fibroin
    (c) Resins (d) None of the above
65. The callus is
    (a) Differentiated cell mass
    (b) Biomass
    (c) Isolated roots
    (d) Undifferentiated cell mass
66. Which of the following is not a micronutrient?
    (a) Copper (b) Zinc
    (c) Molybdenum (d) Hydrogen
67. Chemodemes refer to
    (a) Chemical race (b) Taxonomic race
    (c) Physical race (d) None of the above
68. Monohybrids describes
    (a) One pair of different characters
    (b) Two pairs of different characters
    (c) More than two pairs of different characters
    (d) None of the above
69. The germination capacity of seeds is tested by
    (a) Rolled towel test
    (b) Germination index
    (c) Locast test
    (d) Testa swelling test
70. Which is not the asexual method of propagation?
    (a) Cutting (b) Grafting
    (c) Budding (d) By seeds

ANSWER KEYS

1. (a)	**2.** (d)	**3.** (c)	**4.** (d)	**5.** (b)	**6.** (c)	**7.** (a)	**8.** (d)	**9.** (b)	**10.** (a)
11. (b)	**12.** (c)	**13.** (b)	**14.** (b)	**15.** (d)	**16.** (a)	**17.** (d)	**18.** (b)	**19.** (d)	**20.** (c)
21. (c)	**22.** (c)	**23.** (c)	**24.** (c)	**25.** (b)	**26.** (a)	**27.** (b)	**28.** (b)	**29.** (b)	**30.** (c)
31. (b)	**32.** (b)	**33.** (d)	**34.** (b)	**35.** (c)	**36.** (a)	**37.** (c)	**38.** (c)	**39.** (a)	**40.** (a)
41. (a)	**42.** (d)	**43.** (d)	**44.** (a)	**45.** (c)	**46.** (d)	**47.** (d)	**48.** (d)	**49.** (a)	**50.** (a)
51. (c)	**52.** (d)	**53.** (b)	**54.** (c)	**55.** (c)	**56.** (b)	**57.** (d)	**58.** (a)	**59.** (c)	**60.** (d)
61. (c)	**62.** (d)	**63.** (c)	**64.** (b)	**65.** (d)	**66.** (c)	**67.** (a)	**68.** (a)	**69.** (a)	**70.** (d)

CHAPTER 2

DRUG CONTAINING ALKALOIDS

ALKALOIDAL DRUGS DESCRIPTION

1. Indole Alkaloids			
Ergot	Sclerotium of fungus *Claviceps Purpurea* (Fam-Hypocreaceae). It is developed in Ovary of Rye plant Secale cereal (Fam-Graminae).	1. Water soluble or Propanolamine Derivatives – Ergometrine (Levo form active) 2. Water insoluble or Peptide derivatives – Ergotamine, Ergosine, Ergotoxine (Ergocrystine, Ergocryptine, Ergocornine)	Ergotamine – used in Migraine Ergometrine – Oxytocic and post partrum haemorrhage
Nux-Vomica (Crow-Fig)	Ripe seed of *Strychnos Nuxvomica* (Fam-Loganiaceae)	Bitter alkaloids – Strychnine and Brucine Glycoside – Loganin	Bitter Stomachic and Tonic
Physostigma (Calabar bean or Ordeal bean)	Ripe seed of *Physostigma Venenosum* (Fam-Leguminosae)	Physostigmine (Eserine) → Eseroline (hydrolysis product) ↓ Rubeserine (Light exposure)	Anti-Cholinesterase Agent
Rauwolfia (Chhotachand, Sarpgandha)	Root of *Rauwolfia Serpentina* (Fam-Apocynaceae)	Reserpine ↓ Methyl alcohol + Reserpic acid + 3,4,5 tri methoxy benzoic acid (Hydrolysis products) Rescinnamine ↓ Methyl alcohol + Reserpic acid + 3,4,5 tri methoxy Cinnamic acid (Hydrolysis products)	Anti Hypertensive drug(depletes the store of catecholamine at nerve endings and inhibit re uptake)
Vinca (Periwinkle)	Whole plant of *Catharanthus Roseus* or *Vinca Rosea* (Fam- Apocyanaceae)	Vincristine and Vinblastine	Anti-Neoplastic agents(Arrest mitosis at metaphase plate)
2. Isoquinoline and Phenanthrene Alkaloids			
Opium	Latex or Exudate of un-ripened fruit(capsule) of *Papaver Somniferum* (Fam-Papaveraceae)	Phenanthrene derivatives – Morphine, Codeine, Thebaine Benzyl iso quinoline derivatives – Narcotine (Noscapine), Narceine, Papaverine	Morphine – Analgesic Codeine – Anti-Tussive Papaverine-Smooth Muscle Relaxant

Curare (South American arrow root poison)	Extract of *Chondrodendron Tomentosum, Strychnos Castelnaea, S.Toxifera* (Fam-Loganiaceae)	D(+)- Tubocurarine	Skeletal Muscle Relaxant
Ipecacuanha	Root and Rhizome of *Cephaelis Ipecacuanha* or *Cephaelis Acuminate* (Fam-Rubiaceae)	Cephaline (Methylated emetine) and Emetine	Expectorant, Emetic Anti protozoal
3. Tropane Alkaloids			
Belladonna (Deadly night shade or European belladonna)	Leaves of *Atropa Belladonna* (European Belladonna) or *Atropa Acuminate* (Indian Belladonna) (Fam-Solanaceae)	Mainly L-hyoscyamine and Atropine Atropine = Tropine (Alcohol) and (±) Tropate Homatropine = Tropine (Alcohol) and (-) Mandelic acid	Anti Cholinergic Agent, Anti Spasmodic Agent
Datura	Leaves and flowering tops of *Datura Metel var. fastuosa* (Fam-Solanaceae)	Mainly Hyoscine Hyoscine = Scopine (Oscine) and (-) Mandelic acid	Anti Cholinergic Agent
Hyoscyamus (Henbane)	Leaves and flowering tops of *Hyoscyamus Niger* (Fam-Solanaceae)	Mainly L-hyoscyamine L-hyoscyamine = Tropine (A Alcohol) and (-) Tropate	Anti Cholinergic Agent
Stramonium (Devil's apple or Thorn apple)	Leaves and flowering tops of *Datura Stramonium* (Fam-Solanaceae)	Mainly L-hyoscyamine and Hyoscine L-hyoscyamine = Tropine (A Alcohol) and (-) Tropate Hyoscine = Scopine (Oscine) and (-) Mandelic acid	Anti Cholinergic Agent
Coca leave	Leaves of *Erythroxylon Coca* (Bolivian or Huanuco coca) or *Erythroxylon Truxillense* (*Peruvian Coca*) (Fam-Erythroxylaceae)	Cocaine – Methyl alcohol + Ecgonine + Benzoic acid Cinnamoyl Cocaine – Methyl alcohol + Ecgonine + Cinnamic acid	Local Anaesthetic Agent
4. Purine Alkaloids			
Coffee	Ripe seed of *Coffea Arabica* or C. *Liberica* (Fam-Rubiaceae)	Caffeine (1,3,7 trimethyl xanthine) Oxidative products – Caffeine = Dimethyl Alloxan + Methyl Urea Theobromine-=Methyl Alloxan + Methyl Urea Theophylline = Dimethyl Alloxan + Urea	CNS Stimulant
Cocoa	Ripe seed of *Theobroma Cocao* (Fam-Sterculiaceae)	Theobromine (3,7 Dimethyl xanthine)	CNS Stimulant
Tea	Leaves and leaf bud of *Thea-Sinensis* (Fam-Theaceae)	Caffeine (1,3,7 trimethyl xanthine) and Theophylline (1,3, Dimethyl xanthine)	CNS Stimulant

5. Quinoline Alkaloids			
Cinchona (Jesuit bark or Peruvian bark)	Bark of *Cinchona Calisaya C. Ledgeriana, C. Officinalis, C. Succirubra* (Fam-Rubiaceae)	Quinine and Qunidine, Cupreine Gylcoside – Quinovin	Quinine-Anti Malarial Drug Qunidine - Cardiac Depressant
Camptotheca (cancer tree)	Stem wood of Camptotheca Acuminate (Fam-Nyssaceae)	Camptothecin	Anti-Neoplastic Agent (Inhibit DNA –Topoisomerase I)
6. Phenylethyl Amine Alkaloids			
Ephedra (Ma-Huang)	Stem of *Ephedra Gerardiana* or *E. Nebrodensis* (Fam-Gnetaceae or Ephedraceae)	Ephedrine (1-phenyl-1-hydroxy -2-methyl amino propane)	As Bronchodilator in Asthma
7. Tropolone (Cylcohepta trien-ol-one ring) Alkaloids/Amino Alkaloids			
Colchicum (Meadow saffron seed or Autumn Crocus)	Ripe seed of *Colchicum Luteum* or *C. Automnale* (Fam-Liliaceae)	Colchicine	Gout and Rheumatism treatment and also induce Polyploidy
8. Imidazole Alkaloids			
Pilocarpine (Jaborandi)	Leaves of *P. Jaborandi or P. Microphyllus* (Fam-Rutaceae)	Pilocarpine → Pilocarpic acid (Hydrolysis product) Pilocarpine → Iso Pilocarpine (Alkali treatment product)	Glaucoma Treatment
9. Other Alkaloids			
Steroidal Alkaloids Kurchi (Holarrhena)	Stem bark of *Holarrhena Antidysenterica* (Fam-Apocyanaceae)	Conessine (Kurchicine), Nor conessine	Amoebic dysentery
Veratrum	Root and Rhizome of *Veratrum Viride* (American or Green hellebore) or Rhizome of *Veratrum Album* (white or European hellebore) Fam-Liliaceae	Proveratrine	Insecticide
Ashwagandha (Withania root)	Root and stem bases of *Withania Somnifera* (Fam-Solanaceae)	Steroidal lactone (Withanolide) - Withanine	Immunomodulatory Drug and Sedative-hypnotic
Lobelia (Indian Tobacco or Asthma weed)	Aerial part (Stem and leaf) of *Lobelia Nicotianaefolia* or *L. Inflata* (Fam-Campanulaceae)	Lobeline – Upon hydrolysis smell of acetophenone comes	Respiratory Stimulant

Areca nut (Betel nut)	Seed of *Areca Catechu* (Fam-Palmae)	Arecoline	Para Sympathomimetic Agent
Aconite (Bachnag or Monkshood) (Diterpene)	Root of *Aconitum Napellus* (Fam- Ranunculaceae)	Aconitine (Di terpene alkaloid) ↓ Benzoyl Aconine + Acetic Acid (Upon Hydrolysis) Benzoyl Aconine ↓ Aconine and Benzoic acid (Hydrolysis)	Treatment of Neuralgia
Vasaka (Adhatoda or adulsa)	Leaves of *Adhatoda Vasica* (Fam-Acanthaceae)	Quinazoline derivatives alkaloids – Vasicine and Vasicinone	Expectorant and Bronco-dilator

Microscopy and Adulteration of Alkaloids

Ergot

Sclerotium

- **outer layer**: flattened polygonal cells, Purple to dark brown colour
- **Inner layer**: dense Pseudo Parenchymatous cells composed of Chitin
- **Central region**-Consists of round/oval high refractive index mycelia cells

Nux-Vomica

- Lignified unicellular covering trichomes
- Collapsed cell layer in seed coat
- Endosperm is made up of polyhedral unlignified cells with plasmodesmata. It also contains Aleurone grain and Oil globules.

Rauwolfia

- **Cork-** Stratified cells in alternating bands of Non lignified cells and lignified cells.
- **Phellogen-**Indistinct
- **Phelloderm-**10–12 rows of parenchymatous cells. Few cells contains starch grains and Prismatic calcium oxalate crystals
- **Secondary phloem (Non lignified)-**Sieve tube, Companion cells, Phloem parenchyma with starch grain and calcium oxalate crystal.
- **Sclerenchymatous cells are absent.**
- **Secondary Xylem-(Lignified)** Xylem fibers, xylem vessel and xylem parenchyma.

Adulteration –

1. **Rauwolfia vomitoria (African Rauwolfia)-**5 discontinued bands of Sclerenchyma and large vessels
2. **R. Tetraphylla-**Uniform cork, Abundant Sclerides, Absence of Rescinnamine
3. **R. Densiflora-**Contains Sclerenchyma

Vinca

- **Lamina-**Dorsiventral
- **Stomata-**Anisocytic or unequalled cells
- **Trichomes-**Unicellular, warty with bulbous base
- **Epidermal cells-**Thin and straight walled Rectangular cells
- **Vessel-** Lignified

Ipecacuanha

- **Cork-**Polygonal cells with granular brown matter.
- **Parenchyma-**Thin walled polyhedral cells with intercellular space and starch grains
- **Calcium oxalate crystals-**Idioblast of acicular Raphides of calcium oxalate crystals.
- **Xylem-**Tracheid with pitted wall. Vessels are absent.

Cinchona Bark

Macroscopic

	C. succirubra	*C. calisaya*	*C. ledgeriana*	*C. officinalis*
Surface	Longitudinal wrinkles but less transverse cracks	Broad longitudinal fissures with transverse cracks	Broad longitudinal fissures with transverse cracks, more in number but less deep	Number of transverse cracks

	Stem Bark	Root Bark
Shape	Curved, Quill or double quill	Curved, twisted or irregularly channelled
Outer surface	Grey colour, rough, Exfoliation in some case	Reddish brown Scaly
Inner surface	Striated and yellowish to deep reddish brown.	Striated and Reddish brown.
Fracture	Short in outer bark and fibrous in inner part	Fibrous

- **Cork –** Flat polygonal cells with reddish brown matter
- **Phloem Fibers –** lignified
- **Calcium Oxalate crystals –** Micro-prism of calcium oxalate crystals
- Starch grains presents
- Stone cell absent

Adulteration

1. Cuprea Bark-(Remijia Penduculata)

Stone cells present, Additional cupreine alkaloids

2. False Cuprea bark (R. purdiena)

Quinine alkaloid is absent, Cusconidine alkaloid is present

Kurchi Bark

- **Cortex -** Lignified stone cells present
- Prismatic calcium oxalate crystals
- Phloem fibers are absent

Vasaka Leaves

- **Stomata –** Cross celled stomata (Caryophyllaceous type)
- **Epidermal cells –** Polygonal thin walled parenchymatous cells with wavy anticlinal walls.
- **Covering Trichome-** 2–4 celled, thich walled, uniseriate
- **Glandular Trichome –** Sessile, with quadracellular heads
- **Cystolith –** Calcium carbonate crystals
- **Calcium oxalate –** Acicular and prismatic type

Ephedra Stem

- **Epidermis –** Unicellular quadrangular cells with thick cuticle, sunken stomata and papillae on the ridge
- **Cortex-** Thin walled cellulosic Parenchyma, Chloroplast present
- Lignified Pericycle fibers, Brownish matter in pith

Coca Leaves

- Lower epidermis shows papillae and numerous Paracytic stomata
- Palisade parenchyma contains prismatic calcium oxalate crystals
- Lignified Idioblast near vein

Belladonna Leaves

Macroscopic

- Ovate-lanceolate to broadly ovate
- Entire margin, acuminate apex

Microscopy

- **Epidermis –** Slightly wavy anticlinal wall and striated cuticle, Anisocytic stomata but also Anomocytic stomata (Less in number)
- **Trichomes –** Covering-Uniseriate, multicellular (2-4 celled)
- **Glandular –** Unicellular stalk, uniseriate, unicellular head
- **Palisade ratio** – 5 to 7
- **Mesophyll –** Sandy crystal of calcium oxalate

Adulteration

1. Phytolacca Americana or P. Decandra

Idioblast present, Needle (Acicular type crystal), Anomocytic stomata

2. Solanum Nigrum

Palisade ratio 2–4

3. Alianthus Glandulosa

Cluster crystal of calcium oxalate, unicellular lignified trichomes, straight walled epidermal cell showing striated cuticle

Belladonna	Sandy crystal of calcium oxalate
Stramonium	Cluster crystal of calcium oxalate
Henbane	Single or twin prism of calcium oxalate

Multiple Choice Questions

1. Libermann–Burchard's reagent is _____
(a) Acetic anhydride + Conc. H_2SO_4
(b) Acetic acid + Conc. H_2SO_4
(c) Acetic anhydride + Conc. HCl
(d) None of the above

2. Which compound undergoes aldol condensation during its biosynthesis?
(a) L-Hyoscyamine
(b) Datura
(c) Tropine
(d) Both (a) and (c)

3. Latex vessels are present in phloem of which drug?
(a) Lobelia (b) Datura
(c) Sarpagandha (d) Gokhru

4. Which of the alkaloids are liquid and volatile in nature?
(a) Nicotine and coniine
(b) Morphine and paparvarine
(c) Atropine and quinine
(d) None of these

5. The degree of basicity of alkaloid mostly depends upon the influence caused due to
(a) Electrostatic status of oxygen atom
(b) Electrostatic status of carbon atom
(c) Electrostatic status of sulphur atom
(d) Electrostatic status of nitrogen atom

6. Heroine is
(a) Methyl morphine (b) Diacetyl morphine
(c) Butyl morphine (d) None of the above

7. Which drug contain quinazoline alkaloid?
(a) Lobelia (b) Vasaka
(c) Coffee (d) Datura

8. Which of the following does not contain steroidal alkaloids?
(a) Ashwagandha (b) Ephedra
(c) Kurchi (d) Veratrum

9. T-shaped trichomes are present in
(a) Varbascum thapsus
(b) Belladonna
(c) Tea
(d) Pyrethrum

10. Wagner reagent contains
(a) Iodine + KI water
(b) KI + bismuth iodide
(c) Iodine
(d) Mercuric chloride + KI in water

11. Mayer's reagent contains
(a) Iodine + KI water
(b) KI + bismuth iodide
(c) Iodine
(d) Mercuric chloride + KI in water

12. Dragendroff's contains
(a) Iodine + KI water
(b) KI + Bismuth iodide
(c) Iodine
(d) Mercuric chloride + KI in water

13. Murexide test is used to detect
(a) Caffeine (b) Datura
(c) Tannins (d) Senna

14. Vitali morin reaction is for
(a) Datura (b) Stramonium
(c) Duboisia (d) All of the above

15. Match the following:

Alkaloids	**Chemical constitutes**
(a) Cinchona	1. Reserpine
(b) Opium	2. Quinine
(c) Ergot	3. Ergometrine
(d) Rauwolfia	4. Morphine
(e) Nux vomica	5. Strychnine
	6. Atropine

(a) a-2, b-4, c-3, d-1, e-5
(b) a-2, b-6, c-3, d-1, e-5
(c) a-2, b-4, c-3, d-6, e-5
(d) a-2, b-4, c-3, d-5, e-1

16. Match the following:

Basic nucleus	**Herbal drugs**
a. Tropane	1. Emetine
b. Quinoline	2. Pilocarpine
c. Isoquinoline	3. Cocaine
d. Imidazole	4. Quinine
e. Purine	5. Caffeine

(a) a-3, b-4, c-2, d-1, e-5
(b) a-3, b-4, c-1, d-2, e-5

(c) a-3, b-1, c-4, d-2, e-5
(d) a-4, b-3, c-1, d-2, e-5

17. Match the following:

a. Cinchona	1. Papaveraceae
b. Opium	2. Graminae
c. Ergot	3. Apocynaceae
d. Rauwolfia	4. Loganiaceae
e. Nux vomica	5. Rubiaceae

(a) a-5, b-1, c-2, d-3, e-4
(b) a-1, b-5, c-2, d-3, e-4
(c) a-5, b-1, c-4, d-3, e-2
(d) a-5, b-1, c-2, d-4, e-3

18. Starting material for biosynthesis of alkaloids

a. Tryptophan	1. Tropane alkaloids
b. Ornithine	2. Indol alkaloids
c. Tyrosine	3. Isoquinoline alkaloids
d. Lysine	4. Piperidine alkaloids
e. Anthranillic acid	5. Quinoline alkaloids

(a) a-2, b-1, c-3, d-4, e-5
(b) a-2, b-1, c-5, d-4, e-3
(c) a-1, b-2, c-3, d-4, e-5
(d) a-2, b-1, c-3, d-5, e-4

19. Match the following:

Alkaloids	**Class**
a. Acointe	1. Diterpene
b. Ephedrine	2. Piperidine
c. Lobeline	3. Amino alkaloids
d. Ergometrine	4. Indole alkaloids
e. Hygrine	5. Pyrrolidine

(a) a-1, b-3, c-2, d-4, e-5
(b) a-1, b-5, c-2, d-4, e-3
(c) a-5, b-3, c-2, d-4, e-1
(d) a-1, b-3, c-3, d-5, e-4

20. Pilocarpine contain _____ basic moiety.
(a) Imidazole (b) Isoxazole
(c) Pyrazole (d) Imidazolidine

21. Which is the example of steroidal alkaloids?
(a) Kurchi (b) Veratrum
(c) Ashwagandha (d) All of the above

22. Vinca comes under
(a) Indole alkaloid
(b) Tropane alkaloid
(c) Quinoline alkaloid
(d) Steroidal alkaloid

23. Which alkaloid is used to treat migraine?
(a) Ergot (b) Physostigma
(c) Rauwolfia (d) Curare

24. Vasaka contains _____ basic moiety.
(a) Quinazoline (b) Quinoline
(c) Isoquinoline (d) Steroidal

25. Which of the following is not tropane alkaloids?
(a) Coca (b) Datura
(c) Duboisia (d) Berberis

26. Which of the following is not indole alkaloids?
(a) Vinca (b) Rauwolfia
(c) Nuxvomica (d) Areca

27. Which is following is known as "protoalkaloid"?
(a) Ephedra (b) Colchicum
(c) Aconite (d) All of the above

28. Stratified cork is characteristic of
(a) Ergot (b) Senna
(c) Cinchona (d) Rauwolfia

29. Pseudoparenchyma is found in
(a) Ergot (b) Nux-vomica
(c) Brahmi (d) Jalap

30. Bundles of acicular crystal of calcium oxalate is identification characteristic of
(a) Datura stramonium
(b) Coca
(c) Urginea maritima
(d) Alianthus glandulosa

31. Atropa belladonna contain _____ type of calcium oxalate crystal
(a) Prism (b) Microsphenoid
(c) Clusters (d) None

32. Rhombohedral crystals are characteristics of
(a) Cinnamon bark (b) Cassia bark
(c) Kurchi bark (d) Cinchona bark

33. All are tyrosine-derived alkaloids, except
(a) Ephedrine (b) Hordenine
(c) Mescaline (d) Hydrastine

34. Anisocytic stomata are present in
(a) Digitalis (b) Senna
(c) Vasaka (d) Belladona

35. Ma Hung is synonym of
(a) Ephedra (b) Ergot
(c) Punarnava (d) Ginseng

36. Diacytic stomata are present in
(a) Digitalis (b) Senna
(c) Vasaka (d) Belladona

37. Opium contains _____ of morphine.
(a) 2.5% (b) 9%
(c) 5% (d) 2.2%

38. Nux vomica is biologically obtained from
(a) Seed of Strychnos Nux Vomica
(b) Leaf of Strychnos Nux Vomica
(c) Fruit of Strychnos Nux Vomica
(d) Root of Strychnos Nux Vomica

39. Which of the following drug is not from Liliaceae?
(a) Colchicum (b) Aloe
(c) Scillia (d) Kurchi

40. Which of the following drug is not from *Apocyanaceae*?
(a) Nux vomica (b) Strophanthus
(c) Vinca (d) Rauwolfia

41. p-dimethyl aminobenzaldehyde is a chemical composition of
(a) Van urk's reagent
(b) Mayer reagent
(c) Hager's reagent
(d) Wagner's reagent

42. Picric acid is a chemical composition of
(a) Van urk's reagent (b) Mayer reagent
(c) Hager's reagent (d) Wagner's reagent

43. Which of the following is a steroidal alkaloid?
(a) Caffine (b) Solanidine
(c) Ephedrine (d) Morphine

44. Which of the following is diterpene class alkaloid?
(a) Aconite (b) Hygrine
(c) Ephedrine (d) Morphine

45. Which of the following is steroidal glycoalkaloids?
(a) Solanum (b) Brahmi
(c) Gingko (d) Chirata

46. Thalleoquin test is used to identify
(a) Cinchona (b) Strychnin
(c) Datura (d) Rhubarb

47. Van Urk's test is used to identify
(a) Ephedra (b) Strychnin
(c) Ergot (d) Rhubarb

48. Indole alkaloids are synthesized from
(a) Tryptophan (b) Tyrosine
(c) Lysine (d) Phenyl alanine

49. Quinoline alkaloids are synthesized from
(a) Tryptophan (b) Tyrosine
(c) Caratenoids (d) Antranillic acid

50. Atropine is biosynthesized from _____ amino acids.
(a) Phenyl alanine, tryptophan, leucine
(b) Phenyl alanine, glycine, ornithine
(c) Ornithine, phenyl alanine, methionine
(d) None of the above

51. Morphine is biogenetically derived from _____
(a) Tryptophan (b) Phenyl alanine
(c) Tyrosine (d) Both (a) and (b)

52. Ephedrine is derived from _____
(a) Ornithine (b) Phenylalanine
(c) Tyrosine (d) Tryptophan

53. Tropane alkaloids are biosynthesized from _____
(a) Ornithine (b) Phenylalanine
(c) Lysine (d) Tryptophan

54. Nicotine is biosynthesized from _____
(a) Lysine (b) Leucine
(c) Methionine (d) Ornithine

55. Papaverine is biogenetically derived from _____
(a) Phenylalanine (b) Ornithine
(c) Tyrosine (d) Lysine

56. Anomocytic or Ranunculaceous type of stomata are present in
(a) Digitalis (b) Buchu
(c) Lobelia (d) All the above

57. Lignified trichomes are identifying characteristic of ____
(a) Strophanthus (b) Lobelia
(c) Nux-vomica (d) Both (a) and (b)

58. Cruciferous stomata are characteristic of _____
(a) Belladonna (b) Speramint
(c) Senna (d) Digitalis

59. Hygrine is biogenetically derived from _____
(a) Phenylalanine (b) Lysine
(c) Isoleucine (d) Ornithine

60. Caryophyllaceous stomata are present in _____
(a) Vinca (b) Datura
(c) Lobelia (d) Vasaka

61. Which of the following shows fibrous fracture?
(a) Cassia (b) Wild cherry
(c) Cinchona (d) Kurchi

62. Which alkaloids give positive murexide test?
(a) Tropane alkaloids
(b) Pyridine alkaloids
(c) Imidazole alkaloids
(d) Purine alkaloids

63. Which of the following possess amino alkaloids?
(a) Tea (b) Datura
(c) Ephedra (d) Opium

64. All are steroidal alkaloid except
(a) Verartrum (b) Aconite
(c) Kurchi (d) Diosgenin

65. Choose the right combination
(a) Quinine, antimalarial, isoquinoline alkaloid
(b) Reserpine, antihypertensive, indole alkaloid
(c) Quantitative microscopy, stomatal number, myrrh
(d) Palmitic acid, salicylic acid, fatty acid

66. In the life cycle of ergot ascospores are
(a) Sexual spores
(b) Asexual spores
(c) Candida spores
(d) All of the above

67. Which of the alkaloid is liquid in nature?
(a) Quinine (b) Catechol
(c) Nicotine (d) Berberine

68. The precursor for the biogenesis of tropane alkaloid is
(a) Ornithine (b) Phenyl alanine
(c) Tryptophan (d) Tyrosine

69. Reserpine and deserpidine differ each other in respect of
(a) Methoxy group at C-3 position
(b) Acetyl group at C-16 position
(c) Methylation at C-10 position
(d) Methylation at C-17 position

70. Idioblasts of crystal layer of calcium oxalate is a diagnostic feature of
(a) Deadly nightshade leaves
(b) Cinchona bark
(c) Senna leaves
(d) Hyoscyamus niger leaves

71. Alkaloids in cinchona bark are determine by
(a) Nessler's reagent (b) Iodine test
(c) Thalloiquine test (d) Wagner's test

72. Strychnine act by
(a) Inhibiting cholinesterase
(b) Depressing inhibitory centre in spinal cord
(c) Stimulating Ach production
(d) None of the above

73. Which of the following alkaloids has steroidal structure?
(a) Connesine (b) Atropine
(c) Caffiene (d) Ephedrine

74. Cinchona alkaloids with Br_2 water and dilute ammonia gives
(a) Violet colour (b) Emerald green colour
(c) Red colour (d) White colour

75. Which one of the following is true for alkaloidal bases?
(a) Water solubility and organic solvent insolubility
(b) Water insolubility and organic solvent insolubility
(c) Water insolubility and organic solvent solubility
(d) Water solubility and organic solvent solubility

76. Plasmodesma is present in
(a) Nux-vomica (b) Ergot
(c) Physostigma (d) Both (a) and (c)

77. Stratified cork and scattered sieve tissues are present in
(a) Datura (b) Coca leaves
(c) Rauwolfia (d) Kurchi

78. Anabasine is biogenetically derived from
(a) Lysine (b) Ornithine
(c) Tryptophan (d) Leucine

79. The best known chemical to cause polyploidy is
(a) Methanol (b) Colchicine
(c) Kerosene (d) Aconite

ANSWER KEYS

1. (a)	**2.** (a)	**3.** (a)	**4.** (a)	**5.** (d)	**6.** (b)	**7.** (a)	**8.** (b)	**9.** (d)	**10.** (a)
11. (d)	**12.** (b)	**13.** (a)	**14.** (d)	**15.** (a)	**16.** (b)	**17.** (a)	**18.** (a)	**19.** (a)	**20.** (a)
21. (d)	**22.** (a)	**23.** (a)	**24.** (a)	**25.** (d)	**26.** (d)	**27.** (d)	**28.** (d)	**29.** (a)	**30.** (c)
31. (b)	**32.** (c)	**33.** (d)	**34.** (d)	**35.** (a)	**36.** (c)	**37.** (b)	**38.** (a)	**39.** (d)	**40.** (a)
41. (a)	**42.** (c)	**43.** (b)	**44.** (a)	**45.** (a)	**46.** (a)	**47.** (c)	**48.** (a)	**49.** (d)	**50.** (c)
51. (c)	**52.** (b)	**53.** (a)	**54.** (d)	**55.** (c)	**56.** (d)	**57.** (d)	**58.** (a)	**59.** (d)	**60.** (d)
61. (c)	**62.** (d)	**63.** (c)	**64.** (d)	**65.** (a)	**66.** (a)	**67.** (c)	**68.** (a)	**69.** (a)	**70.** (b)
71. (c)	**72.** (b)	**73.** (a)	**74.** (b)	**75.** (c)	**76.** (a)	**77.** (c)	**78.** (a)	**79.** (b)	

CHAPTER 3

DRUG CONTAINING GLYCOSIDES

GLYCOSIDES DRUGS DESCRIPTION

1. Cyanogenetic glycosides		
Bitter Almond	Ripe seed of *Prunus Amygdalus* or *Prunus Communis var. amara* (Fam-Rosaceae)	Amygdalin – Upon hydrolysis yields ↓ Benzaldehyde (responsible for odour) + HCN (hydrocyanic acid having poisonous effect) + Gentiobiose Sugar (2 molecules of β-D-Dextrose)
Wild Cherry Bark	Bark of *Prunus Serotina* (Fam-Rosaceae)	Prunasin – Upon hydrolysis yields ↓ Benzaldehyde (responsible for odor) + HCN (hydrocyanic acid having poisonous effect) + β-D-Dextrose)
2. Iso thio cynate/Glucosinolate glycosides		
Mustard (Black or Brown mustard)	Ripe seed of *Brassica Nigra* or *B. Juncea* or *B. Sinapioides* (Fam-Cruciferae)	Sinigrin (Potassium Myronate) Upon hydrolysis ↓ Allyl Isothiocynate (Pungent odor) + $KHSO_4$ + Dextrose
3. Cardiac glycosides (Steroidal Glycosides)		
Digitalis (Fox glove)	Dried leaves of *Digitalis Purpurea* (Fam-Scrophulariceae)	Purpurea Glycoside A (Deacetyl lanatosides A) ↓ Digitoxin + Glucose ↓ Digitoxigenin + 3 Molecules of Digitoxose Purpurea Glycoside B (Deacetyl lanatosides B) Gitoxin + Glucose Gitoxigenin + 3 Molecules of Digitoxose
Peruvoside	Seed of *Thevetia Neriifolia* (Fam-Apocynaceae)	Thevetin A = Peruvoside + 2 mol Glucose units Peruvosides = Cannogenin + L- Thevetose
Strophanthus (Arrow Poison)	Seed of *Strophanthus Kombe* or *S. Hispidus* (Fam-Apocynaceae)	K-Strophanthin (Mixure of Glycosides) 1. K- strophanthoside (Strophoside) = Strophanthidin + Cymarose + 2 Glucose units 2. K-strophanthoside β = Strophanthidin + Cymarose + 1 Glucose units 3. Cymarin = Strophanthidin + Cymarose
Squill	Dried slices of bulb of *Urginea Indica* or *Urginea maritima* (Fam-Liliaceae)	Scillarin A = Proscillaridin A + Glucose ↓ Scillaridin A (Scillarenin A) + Rhamnose Scillarin B = Proscillaridin B + Glucose ↓ Scillaridin B (Scillarenin B)+ Rhamnose (Scillabiose = Rhamnose + Glucose)

4. Anthraquinone glycosides		
Senna	Indian senna (Tinnevelly Senna) Leaflets of *Cassia Angustifolia* (Fam- leguminosae) Alexanderian Senna (*Cassia Senna*)- Leaflets of *Cassia Acutifolia* (Fam-leguminosae)	Sennosides A = 2 mol of Glucose + Sennidin A (Aglycone Portion, Rhein-dianthrone) Sennosides B = 2 mol of Glucose + Sennidin B (AGLYCONE portion , Rhein-dianthrone)
Aloe (Kumari, Musabbar)	Juice of leaves of *Aloe Barbadensis* or *Aloe Perryi* (Fam-Liliaceae)	Aloin is mixture of 3 isomers – Barbaloin, Isobarbaloin and β-Barbaloin.
Rhubarb or Chinese Rhubarb (Revandchini)	Rhizome of *Rheum Emodi* or *R.Palmetum* or *R. Officinalis* or *R.Webbianum* (Fam-Polygonaceae)	1. Rhein and Glucorhein 2. Aloe-emodin, Emodin, Chrysophanol, Physcion 3. Palmidin A = Aloe-Emodin Anthrone + Emodin Anthrone Palmidin B = Aloe-Emodin Anthrone + Chrysophanol Anthrone Palmidin C = Emodin Anthrone + Chrysophanol Anthrone
Cascara (Scared Bark)	Bark of *Rhamnus Purshiana* (Fam-Rhamnaceae)	Both O and C glycosides. Cascarosides A, B are Aloe-Emodin derivatives. Cascarosides C, D are Chrysophanol derivatives.
5. Saponin gylcosides		
Dioscorea (Yam or Rheumatism root)	Tuber of *Dioscorea Deltoida D. Composita* (Fam-Dioscoreaceae)	Dioscin = Diosgenin (Hydrolytic product) 75 % starch
Liquorice (Mulethi)/yasti	Peeled o unpeeled root and stolon of *Glycyrrhiza Glabra* (Fam-Leguminosae)	Tri terpenoid Saponin is Glycyrrhizin (Glycyrrhizic acid) ↓ K and Ca salt of Glycyrrhizinic acid ↓ Glycyrrhetinic acid or Gylcyrrhetic acid Bitter Principle is Glycymarin
Ginseng/Panax	Root of *Panax Ginseng* or *P. Quinquefolium* or *P. Japonica* (Fam-Araliaceae)	1. Ginsenosides = Aglycone portion is Dammarol 2. Panaxosides = Aglycone portion is Oleanolic acid
Brahmi (Jal brahmi)	Leaves and stem of *Bacopa Moniera* or *Herpestis Moniera* (Fam-Scrophulariaceae)	Bacosides A and B ↓ On hydrolysis yield Triterpenoid Aglycone Bacogenin A and B
Brahmi (Mundukparni)	Herb of *Centella Asiatica* or *Hydrocotyl Asiatica* (Fam-Umbelliferrae)	Assiaticosides – Asiatic acid + 2 Glucose + Rhamnose Madecassosides – Madecassic acid + 2 Glucose + Rhamnose
Shatavari	Root and leaves of *Asparagus Racemosus* (Fam-Liliaceae)	4 steroidal Saponin- Shatavarin I – IV Shatavarin I = 3 mol Glucose + 1 mol Rhamnose + Sarsapogenin
Senega	Root of *Polygala Senega Var. Latifolia* (Fam-Polygalaceae)	Triterpenoid Saponin Senegin and Polygalic acid
Quillaia (Panama wood)	Bark of *Quillaja Saponaria* (Fam-Rosaceae)	Quillaia-Saponin (tri terpenoid saponin) ↓ Quillaic Acid (Hydroxy gypsogenin) + Quillia-Sapotoxin

6. Flavonol glycosides		
Silymarin (Marine Thistle)	Seed of *Silybum Marianum* (Fam- Compositae or Asteraceae)	Silybin ,Silycristin and Silydianin
Ginkgo (Maiden Hair tree or kew tree)	Leaves of *Ginkgo Biloba* (Fam-Gingkoaceae)	1. Flavonol – mono, di or tri glycosides of Kaempferol, Quercetin 2. Bi-Flavone – Ginkgetin, Bilobetin 3. Diterpene lactone – Ginkgolides A,B,C
Buck-wheat (Rutin or Vitamin P)	Flower bud of *Fagopyrum Esculentus* (Fam-Polygonaceae) and leaves of Eucalyptus species.	Rutin = Quercitin + Rhamnose + Dextrose Quercitin is 5, 7, 3′, 4′ tetra hydroxy Flavanol or 3, 5, 7, 3′, 4′ penta hydroxy Flavone **Note :** Hesperidin = Hesperetin + Rhamnose + Dextrose Hesperetin is 5, 7, 3′ tri hydroxy 4′ methoxy Flavonones
7. Coumarin glycosides		
Tonka bean	Seed of *Dipteryx Odorata* or *Dipteryx Oppositifolia* (Fam-Leguminosae)	Coumarin = lactone of Cis – O- coumarinic acid
Visnaga (Pick tooth fruit or Khella)	Fruit of *Ammi Visnaga* (Fam-Umbelliferae)	Furano Coumarin derivatives - Visnagin , Khellin
Ammi	Fruit of *Ammi Majus* (Fam-Umbelliferae)	Furano coumarin derivatives –Xanthotoxin, Bergapten
Psoralea Fruit (bavchi)	Fruit of *Psoralea Corylifolia* (Fam-Leguminosae)	Psoralen and Psoralidin
8. Aldehyde gylcosides		
Vanilla	Fruit of *Vanilla Planifolia* or *V. Tahitensis* (Fam-Orchidaceae)	Gluco Vanillin ↓ Vanillin (4-hydroxy-3- methoxy benzaldehyde) + Glucose
9. Phenolic glycosides		
Bearberry (Uva-Ursi)	Leaves of *Arctostaphylous Uva-ursi* (Fam-Ericeae)	Arbutin
10. Bitter glycosides		
Gentian	Fermented Rhizome and Root of *Gentian Lutea* (Fam- Gentianaceae)	Bitter Glycosides – Gentiopicrin (gentio picroside) ↓ Gentiogenin + Glucose • Bitter taste of drug is mainly due to Amarogentin • Gentinin is mixture of Gentiopicrin and • Gentisin (responsible for yellow colour of drug)
Picrorrhiza (Kutki)	Rhizome of *Picrorrhiza Kurroa* (Fam- Scrophulariaceae)	Picrosides and Kutkosides
Quassia wood (Bitter wood)	Stem wood of *Picrasma Excelsa* or *Aeschrion Excelsa* (Fam- Simarubaceae)	Bitter lactone – Quassin and Neo Quassin

MICROSCOPY AND ADULTERATION OF GLYCOSIDES

Senna Leaves

Microscopy

Lamina – Isobilateral Nature

Stomata – Paracytic /Rubiaceous type

Trichome – Conical, Unicellular, covering type

Upper and Lower epidermis – single layered, Polygonal Straight anticlinal walls, covered with cuticle

Mesophyll

- **Upper palisade –** Compactly arranged, Single layer parenchyma
- **Lower palisade –** Loosely arranged

Spongy parenchyma – contains Crystal sheath of calcium oxalate prism and lignified sclerenchymatous sheath

Collenchyma – Multilayered parenchyma present at ventral surface

Adulteration

1. **Dog senna –** leaves of Cassia Obovata. Obovate shape with tapering apex. Papillose cell in lower epidermis. 1% anthraquinone glycosides.
2. **Palthe senna–** leaves of C. Auriculata. Absence of anthraquinone glycosides. When boiled with chloral hydrate solution gives crimson colour.
3. **Leaflets of Mumbai, Mecca and Arabian senna –** Brownish-green in colour, more elongated and narrower in shape.

Alexandrian Senna	Tinnevelley Senna
Ovate-Lanceolate leaf	Lanceolate leaf
Entire and acute margin	Entire but less acute
Surface is greyish-green	Yellowish-green
Stomata has 2 subsidiary cells	2 or 3 subsidiary cells
Stomatal index 11.4 to 13.3	Stomatal index 14 to 20
Vein Islet No: 25-29.5	19.5-22.5

Digitalis Leaves

Microscopy

Lamina – Dorsiventral nature

Stomata – Anomocytic type (Ranunculaceous) stomata greater on lower epidermis compared to upper

Trichome

- Glandular – unicellular stalk and uni or bicellular head
- Covering – Uniseriate, multicellular (3–5–7 celled).Mostly straight and warty with blunt tips. Collapsed trichomes.

Upper and Lower epidermis – single layered, Polygonal Straight anticlinal walls, covered with cuticle

Calcium oxalate crystal is absent.

Adulteration

1. **Mullein leaves** – Leaves of *Verbascum Thapsus* (Fam-Scrophulariaceae) Candelabra trichomes/Woolly hairs
2. **Primrose leaves –** Leaves of *Primula Vulgaris* (Fam-Primulaceae). Uniseriate, multicellular trichomes (8–9 celled)
3. **Comfrey leaves** – Leaves of *Symphytum Officinale* (Fam-Boraginaceae) Multicellular trichomes forming hook at top.

Allied Drugs

1. ***Digitalis Lanata*** **(Woolly fox glove)**
   - Beaded anticlinal wall of epidermal cells
   - 10–14 celled non-glandular Trichome at margin of leaf
   - Glandular – some are bicellular head, Unicellular stalk others are Unicellular head, uniseriate, 3–10 celled
   - Linear lanceolate to oblong lanceolate with entire margin, acuminate apex

Glycosides	Aglycone Portion	Sugar Sequence
Lanatosides A	Digitoxigenin	Glucose-Acetyl digitoxose-(Digitoxose)$_2$
Lanatosides B	Gitoxigenin	Glucose-Acetyl digitoxose-(Digitoxose)$_2$
Lanatosides C	Digoxigenin	Glucose-Acetyl digitoxose-(Digitoxose)$_2$
Lanatosides D	Diginatigenin	Glucose-Acetyl digitoxose-(Digitoxose)$_2$
Lanatosides E	Gitaloxigenin	Glucose-Acetyl digitoxose-(Digitoxose)$_2$

Note

Digoxigenin and Diginatigenin aglycone are specific to *D. Lanata.*

2. ***Digitalis Lutea* (Straws Foxglove)**
   - Oblanceolate with serrate or dentate margin
3. ***Digitalis Thapsi* (Spanich Foxglove)**
   - Lanceolate with crenate margin

- Covering trichomes are absent
- Striated cuticle present
- Prismatic calcium oxalate crystals

Aloe

Curacao Aloe	Cape Aloe	Socotrine Aloe	Zanziber Aloe (Monkey skin aloe)
Yellowish brown to Chocolate brown	Dark brown to greenish brown	Yellowish brown to Blackish brown	Yellowish brown to Blackish brown
Opaque, break with waxy fracture	Glossy mass	Opaque, break with porous fracture	Opaque, break with waxy fracture
In lacto phenol mount-Acicular crystals	In lacto phenol mount-Amorphous	No	No
Needle or slender prism	Angular or Angular fragment	Larger prism	Irregular lumps
Nitrous Acid test- Pink to carmine	Faint pink	Very less change in colour	Very less change in colour
Cupraloin test (klunge's isobarbaloin test) Wine red colour	Faint colouration which rapidly change to yellow	No colour	No colour
Nitric acid test (Brownish-red colour)	Brown changes to green colour	Brownish-yellow	Yellowish-brown

Note

Key points about aloe

- All variety of Aloe gives Greenish fluorescence in Borax.
- Rhapontic Rhubarb gives blue fluorescence in UV but Official Rhubarb gives no colour.
- Ergometrine- give blue fluorescence in water upon exposure to UV light

Wild Cherry Bark

- **Cork –** thick and thin walled Parenchymatous cells with reddish brown colouring matter.
- **Cortex –** Lignified Sclerides
- **Pericycle –** lignified fibers
- **Medullary rays –** Parenchymatous cells contains starch grains and, cluster and prism of calcium oxalate crystals.

Multiple Choice Questions

1. Irridoid containing drug is
(a) Jatamansi (b) Calamus
(c) Nutmeg (d) Valerian

2. The biological source for dioscoria
(a) *Dioscoria deltoid* (b) *Dioscorin floribulda*
(c) *Dioscorin villosa* (d) *Dioscoren compositne*

3. Yam is the synonym of the drug
(a) Stropanthus (b) Dioscoria
(c) Safed musali (d) Liquorice

4. Diosgenin is the hydrolytic product of
(a) α-amyrin (b) β-amyrin
(c) Lupeol (d) Saponin dioscin

5. Liquorice belongs to the family
(a) Liliaceae (b) Apocyanaceae
(c) Loganaceae (d) Leguminosae

6. Which of the following drug is not an alkaloid?
(a) Opium (b) Dioscorea
(c) Tea (d) Vasaka

7. Glycyrrhizinic acid on hydrolysis gives
(a) Glycyrrhetic acid (b) Glycyrrhizin
(c) Liquiritin (d) Isoliquiritin

8. Rhitodoma is characteristic feature of
(a) Cinchona (b) Quillaia
(c) Liquorice (d) Dioscoriea

9. Channeled bark is
(a) Java cinnamon (b) Ashoka
(c) Cassia (d) Cascara

10. The shape of Arjuna bark is
(a) Flat (b) Curved
(c) Recurved (d) Quill

11. Shataverin-IV is the glycoside of
(a) Yamogenin (b) Diosgenin
(c) Sarsapogenin (d) Hederegenin

12. Which of the following barks have flat shape?
(a) Wild cherry (b) Cassia
(c) Quillaia (d) Kurchi

13. Wolfsbain root is
(a) Ipecac (b) Aconite
(c) Liquorice (d) Rhubarb

14. Virginian prune bark is known as
(a) Cinchona (b) Wild cherry
(c) Kurchi (d) Ashoka

15. _____ test is used for identification of deoxy sugar.
(a) Legal (b) Baljet
(c) Killer kiliani (d) Borntrager

16. Madhunashini is
(a) Dioscorea (b) Senna
(c) Gymnema (d) Datura

17. Which of the following is used as precursor for the production of steroidal drugs like corticosteroids and sex hormones?
(a) Reserpine (b) Diosgenin
(c) Thevetin (d) Aloin

18. The diuretic activity of Arjuna is due to the presence of
(a) Tomentosic acid
(b) Arjunolic acid
(c) β sitosterol
(d) None of the above

19. Cochineal contains C-glycosides which are in the form of colouring matter:
(a) Acetic acid (b) Benzoic acid
(c) Cinnamic acid (d) Carminic acid

20. Which drug is under the chemical class of cyanogenic glycoside?
(a) Bitter almond (b) Black mustard
(c) Digitalis (d) Rhubarb

21. Prunasin is biosynthesized from
(a) Ornithine (b) Phenylalanine
(c) Tyrosin (d) All of the above

22. Which drug is not under the class of glycosidal glycoside?
(a) Picrorrhiza (b) Solanum
(c) Henna (d) Gentian

23. Which drug is used as diuretic?
(a) Quillaia (b) Gokhru
(c) Senega (d) Ginseng

24. The family of Gokhru
(a) Liliaceae (b) Cucurbitaceae
(c) Zygophyllaceae (d) Araliaceae

25. In Klung's isobarbaloin test, Curacao aloes show _____ colour.
(a) Yellow (b) Blue
(c) Wine red (d) Green

26. The substitute for aloes is
(a) Cape aloes (b) Socotrine aloes
(c) Curacao aloes (d) Natal aloes

27. Why the aqueous solution of aloes in modified (Borntrager test) is treated with ferric chloride and hydrochloric acid?
(a) To bring out oxidation and hydrolysis of aloe emodin.
(b) To bring out reduction of aloe emodin.
(c) For preservative purpose
(d) To convert into emodin

28. Scillaren A belongs to chemical class:
(a) Cardenolide (b) Bufadienolide
(c) Tropane (d) Protein

29. Scillaroside is used as
(a) Insects poisoning (b) Rabbit poisoning
(c) Rat poisoning (d) Fish poisoning

30. Anthraquinone glycosides of cascara contain
(a) O-glycosides (b) N-glycosides
(c) C-glycosides (d) S-glycosides

31. Tinnevelly senna is obtained from
(a) *Cassia acutifolia* (b) *Cassia angustifolia*
(c) *Cassia auriculata* (d) *Cassia obovata*

32. Rutin is an example of
(a) Triterpene glycoside
(b) Lactone glycoside
(c) Saponin glycoside
(d) Flavanoid glycoside

33. The taste of glycoside of Gentinaceae is
(a) Sweet (b) Salty
(c) Acrid (d) Bitter

34. The most common sugar in glycoside is
(a) α-glucose (b) β-D-glucose
(c) α-L-glucose (d) β-L-glucose

35. In O-glycoside the sugar is combined with a phenolic hydroxyl function as in
(a) Aloin (b) Sennosides
(c) Amygdalin (d) Digitoxin

36. *Digitalis purpurea* is a cardiotonic drug belonging to the family
(a) Apocynaceae (b) Lilliaceae
(c) Polygonaceae (d) Scrophulariaceae

37. Three molecules of digitoxose attached to one molecule of glucose are present in the cardioactive glycoside
(a) Gitaloxin (b) Gitoxin
(c) Digitoxin (d) Purpurea glycoside A

38. The calcium oxalate crystals present in wild cherry possess the shapes of
(a) Acicular (b) Raphides
(c) Microcrystals (d) Prisms

39. Bufadenolides are present in
(a) Squill (b) Strophanthus
(c) Thevetia (d) Arjuna

40. Anomocytic stomata are present in
(a) Digitalis (b) Senna
(c) Vasaka (d) Belladona

41. Covering trichomes are is important characteristic of
(a) Nux vomica (b) Strophanthus
(c) Digitalis (d) Bellodona

42. Paracytic stomata are present in
(a) Digitalis (b) Senna
(c) Vasaka (d) Belladona

43. Which of the following is O-glycoside?
(a) Senna (b) Rhubarb
(c) Both (a) and (b) (d) None

44. The socotrine aloes mounted in lactophenol and observed under microscope will show the following characters
(a) Fragments composed of large number of slender prism
(b) Fragments composed of large prisms grouped irregularly
(c) Transparent brown angular irregular fragments.
(d) None of the above

45. Which is the synonym of aconite?
(a) Monkshood (b) Vachhanag
(c) Both (a) and (b) (d) Yam

46. Sinigrin is an active constitute of
(a) Cascara (b) Mustard
(c) Ginseng (d) Shatavari

47. Which of the following drug is not a glycoside?
(a) Cascara (b) Cocca
(c) Ginseng (d) Aloe

48. Palmidine A has _____ content.
(a) Aloe emodin + chrysophanol
(b) Aloe emodin + emodin
(c) Emodin + chrysophanol
(d) All of the above

49. Which of the following is a flavonol-type glycoside?
(a) Gentian (b) Brahmi
(c) Ginko (d) Psoralea

50. Which of the following is a bitter glycoside?
(a) Gentian (b) Quassia
(c) Chirata (d) All of the above

51. Bundles of acicular crystals of calcium oxalate is present in
(a) Belladonna (b) Stramonium
(c) Squill (d) Senna

52. Cynogenic glycoside present in wild cherry bark is
(a) Amygdalin (b) Isothiocynate
(c) Prunasin (d) Sinigrin

53. Which of the following test is not used to detect glycoside?
(a) Keller killiani (b) Legal test
(c) Kedde test (d) Goldbeater skin test

54. The thick-walled warty trichomes are the identifying character of
(a) Senna (b) Digitalis
(c) Cannabis (d) Datura

55. Cascara bark has _____ shape.
(a) Flat (b) Curved
(c) Recurved (d) Quill

56. Cymerose is the sugar moiety present in
(a) Digitoxin (b) K-strophanthoside
(c) Scillarenin (d) Thevetia

57. Flavanol glycoside are biogenetically derived from
(a) Acetate–mevalonate pathway
(b) Shikimic acid pathway
(c) Both
(d) None.

58. Rhubarb contains _____ type of glycoside
(a) C-Glycoside (b) O-Glycoside
(c) S-Glycoside (d) N-Glycoside

59. Alexandrian senna is obtained from biological source
(a) *Cassia angustifolia*
(b) *Cassia alexandria*
(c) *Cassia indiana*
(d) *Cassia acutifolia*

60. Cascara drug belongs to the family
(a) Polygonaceae (b) Rhamnaceae
(c) Scrophulariaceae (d) Leguminoseae

61. Bitter almond is example of
(a) Anthracene glycoside
(b) Cardiac glycoside
(c) Saponin glycoside
(d) Cyanogenetic glycoside

62. Example of isothiocyanate glycoside is
(a) Mustard (b) Ginko
(c) Psoralea (d) Chirata

63. Example of N-type of glycoside is
(a) Rhubarb (b) Black mustard
(c) Cochineal (d) Nucleosides

64. One of the following belongs to Liliaceae family:
(a) Cochineal (b) Aloe
(c) Digitallis (d) Hypericum

65. Spanish flies are known as
(a) Male fern (b) Cantharides
(c) Cochineal (d) Kalmegh

66. Gentian is an example of
(a) Steroidal glycoside
(b) Bitter glycoside
(c) Aldehyde glycoside
(d) Phenol glycoside

67. Kalmegh contains this active chemical constitutent:
(a) Prunasin (b) Andrographolide
(c) Gentiopectin (d) Sinigrin

68. Purgative action is given by one of the following glycosides
(a) Aloe (b) Stropanthus
(c) Brahmi (d) Red squill

69. Gokhru is used as _____
(a) Hypoglycemic agent
(b) Expectorant agent
(c) Diuretic agent
(d) Cardiotonic agen

70. Black mustard is obtained from biological source is
(a) *Cassia indiana* (b) *Stropanthus gratus*
(c) *Prunus amygdalus* (d) *Brassica nigra*

71. Synonym of rutin is
(a) Vitamin H (b) Vitamin A
(c) Vitamin D (d) Vitamin P

72. Psoralea is classified as a
(a) Aldehyde class of glycoside
(b) Coumarine class of glycoside
(c) Flavonol class of glycoside
(d) Saponin class of glycoside

73. Thevetia is derived from biological source is
(a) *Thevetia nerifolia* (b) *Thevetia kombe*
(c) *Urginia nerifolia* (d) *Asparagus racemosus*

74. Which part of quillaia is medicinally important?
(a) Inner bark (b) Seeds
(c) Leaves of bulb (d) Root

75. One of the following is not belonging to Liliaceac family
(a) Aloes (b) Shatavari
(c) Bavachi (d) Indian squill

76. Quassia is belonging to family
(a) Solanaceae (b) Simarubaceae
(c) Rosaceae (d) Scrophulariaceae

77. Primveroside is derived from _____ glycoside drug
(a) Mustard (b) Senega
(c) Salix (d) Ginseng

78. Active chemical constitute of wild cherry bark is
(a) Salicin (b) Senegin
(c) Sinigrin (d) Cymarose

79. Digitalis adulterated with all of the following except
(a) Verbascun thapus (b) Comfrey leaves
(c) Primrose leaves (d) Scilla leaves

80. In microscopical studies of rhubarb _____ shape of calcium oxalate is present
(a) Rhaphides (b) Rosette
(c) Prism (d) None of the above

81. Kalmegh contains
(a) 1.0% of andrographolides
(b) 2.0% of andrographolides
(c) 1.5% of andrographolides
(d) 0.2% of andrographolides

82. Quassia contains _____ of Quassin
(a) 1% (b) 0.6%
(c) 0.2% (d) 1.5%

83. Digitallis contains _____ acid-insoluble ash.
(a) Not more than 5%
(b) Not more than 2%
(c) Not more than 2.5%
(d) Not more than 1%

84. Ginseng contains _____ sulphated ash value.
(a) Not more than 10%
(b) Not more than 12%
(c) Not more than 5%
(d) Not more than 1

85. *Gymnema silvestre* is belonging to _____ family
(a) Asclepiadaceae (b) Acanthaceae
(c) Simarubaceae (d) Asteraceae

86. Hydrolytic product of verdocin is
(a) Digitoxigenin + 3-Digitoxose
(b) Gitoxogenin + 3-Digitoxose
(c) Gitoxogenin + Digitalose
(d) Gitaloxigenin + Digitalose

87. Medicinally important part of *Stropanthus* is
(a) Seeds (b) Roots
(c) Bark (d) Leaves

88. Bearberry is a
(a) Aldehyde class of Glycoside
(b) Coumarine class of Glycoside
(c) Flavonol class of Glycoside
(d) Phenol class of Glycoside

89. Palmidin A is synthesized from
(a) Aloe emodin Anthrone + Chrysophanol
(b) Emodin Anthrone + Chrysophanol
(c) Aloe emodin Anthrone + Emodin Anthrone
(d) Emodin Anthrone + Aloe emodin Anthrone + Chrysophanol

90. Peruvoside contains _____ aglycone portion.
(a) Stropanthidin (b) Digitoxigenin
(c) Digoxigenin (d) Cyanogenin

91. Thevetin A contains _____ aglycone portion.
(a) Digitoxigenin (b) Digoxigenin
(c) Cyanogenin (d) Gitoxigenin

92. Baljet test is used to identify
(a) Aloe (b) Senna
(c) Deoxy sugar (d) Digitallis

93. Kalmegh is used as a
(a) Hepatoprotective agent
(b) Expectorant agent
(c) Diuretic agent
(d) Cardiotonic agent

94. In Digitalis leaf _____ of stomata are present
(a) Anomocytic (b) Paracytic
(c) Diacytic (d) Rubecious

95. One of the following belongs to Ericaceae family:
(a) Dioscorea (b) Gentian
(c) Bearberry (d) Ginseng

96. Peeled liquorice contain _____ of alcohol-soluble extractive.
(a) NLT 25% (b) Less than 25%
(c) Less than 14 % (d) NLT 14 %

97. Medicinally important part of Shatavari is
(a) Root (b) Leaves
(c) Seed (d) Both a and b

98. Example of isothiocynate class of glycoside is
(a) Mustard (b) Ginko
(c) Psoralea (d) Brahmi

99. Standard vein islet number of Alexandrian senna is
(a) 9.5 (b) 25 to 29.5
(c) 11.4 to 13.3 (d) Less than 5

100. Raymond's test is used for identification of
(a) Cardiac glycoside
(b) Alkaloids
(c) Deoxysugar
(d) All of the above

101. Which flavonoid(s) is/are present in mulethi?
(a) Liquiritin (b) Isoliquiritin
(c) Both (a) and (b) (d) None of the above

102. Which of the following is known as 'Ginseng of India'?
(a) *Panax ginseng*
(b) *Withania somnifera*
(c) *Ocimum sanctum*
(d) *Azadirachata indica*

103. The extraction of steroidal saponins on commercial scale is from
(a) Dioscorea (b) Digitalis
(c) Datura (d) Trigonella

104. Chikusetu saponin is present in
(a) Liquorice (b) Ginseng
(c) Senega (d) Quillia

105. Potassium myronate (sinigrin) after hydrolysis in presence of myrosin yields
(a) Allyl isothiocyanate
(b) Allyl thiocyanate
(c) Allyl isocyanate
(d) Amygdalin

106. "Kesar" is obtained from the
(a) Dried stigma of *Crocus sativus*
(b) Dried bark of *Crocus sativus*
(c) Dried cells of *Crocus sativus*
(d) Dried calyx of *Crocus sativus*

107. Which one is a phenol glycoside?
(a) Arbutin (b) Salicin
(c) Vanillin (d) Digoxin

108. The α and β stereo isomers of glycosides are assigned on the basis of
(a) Aglycone component
(b) Glycone component
(c) Glycosidic linkage of glycone and aglycone
(d) None of the above

109. Stropanthus does not respond to
(a) Legal test
(b) Van-urk's reagent test
(c) Keller Killiani test
(d) Baljet test

110. K-strophanthin present in stropanthus is a mixture of
(a) Cymarin and cymarol
(b) K-strophanthoside β
(c) K-strophanthoside
(d) All of the above

111. Does glycoside reduce Fehling's solution directly?
(a) Yes
(b) No
(c) Depends on hydrolysis of glycosides
(d) Never reduces Fehling's solution

112. Stas-Otto method is used for
(a) Isolation of glycoside
(b) Isolation of tannis
(c) Extraction of alkaloid
(d) Extraction of lipid

113. Kedde's test is used for identification of
(a) Isothiocyanide glycoside
(b) Cardiac glycoside
(c) Flavonoid glycoside
(d) Anthraquinone glycoside

114. After hydrolysis of palmidin-B gives
(a) Aloe-emodinanthrone + emodinanthrone
(b) Aloe-emodinanthrone + chrysophanolanthrone
(c) Emodinanthrone + chrysophanolanthrone
(d) Aloe-emodinanthrone + emodinanthrone

115. Encordin is prepared from
(a) Thevetin (b) Nerrifolin
(c) Peruvoside (d) Peruvosidic acid

116. Which of following is known as Indian Gentian?
(a) Picrorrhiza kurroa
(b) Gentianalutea
(c) Swertiachirata
(d) Swertiadensifolia

117. The cyanophoric glycoside present in linseed is
(a) Linamerin (b) Senegin
(c) Vanillin (d) Sinigrin

118. Glycosides on enzymatic or acidic hydrolysis are
(a) One or more sugar moieties (glycone)
(b) Non sugar moieties (aglycone)
(c) Both (a) and (b)
(d) None of the above

119. Cyanogenetic or cyanophoric glycosides on hydrolysis yields
(a) Hydrochloric acid and benzaldehyde
(b) Sulphuric acid and hydrocyanic acid
(c) Hydrocyanic acid and benzaldehyde
(d) Benzaldehyde and nitric acid

120. Socotrine aloe is obtained from
(a) *Aloe barbadensis* (b) *Aloe perryi*
(c) *Aloe ferox* (d) None of the above

121. Chinese rhapontic rhubarb can be distinguished from Indian rhubarb by _____ florescence developed in UV light.
(a) Deep yellow (b) Deep violet
(c) Green (d) Blue

122. *Tribulus terrestrisis* is the botanical name of
(a) Chota gokhru (b) Bada gokhru
(c) Choti harad (d) Bari harad

123. The example of S-glycoside is
(a) Sennoside (b) Sinigrin
(c) Senegin (d) Psoralen

124. Which of the following glycosides produces foam in aqueous solution'?
(a) Anthracene glycosides
(b) Saponin glycosides
(c) Cardiac glycosides
(d) Cyanogenetic glycoside

125. Cardenolides are
(a) C23 glycosides and have five-membered lactone ring
(b) C24 glycosides and have six-membered lactone ring
(c) C2S glycosides and have seven-membered lactone ring
(d) C26 glycosides and have eight-membered lactone ring

126. Rutin is an example of
(a) Triterpenoid glycosides
(b) Tropane alkaloids
(c) Saponin glycosides
(d) Flavonoid glycosides

127. Warty trichomes are present in
(a) Anise (b) Senna
(c) Both a and b (d) Pyrethrum

128. The moisture content in digitalis leaves should not be more than
(a) 10% (b) 5%
(c) 7% (d) 2%

129. Purpurea glycoside A on hydrolysis give
(a) Gitoxin + Glucose
(b) Gitaloxigenin + Digitalose
(c) Digitoxin + Glucose
(d) Digitoxigenin + Glucose

130. Cascaroside is
(a) C-Glycoside (b) N-Glycoside
(c) O-Glycoside (d) Both (a) and (c)

131. Cardenolides contain the following ring system
(a) Unsaturated α-lactones
(b) Unsaturated α,ß-lactones
(c) Unsaturated γ-lactones
(d) Unsaturated δ-lactones

132. Kulnge's test or Cuproin test is for the identification of
(a) Digitoxose (b) Isobarbaloin
(c) Rhein moiety (d) Aloe-emodin

133. The type of stomata in digitalis leaves are
(a) Rubiaceous (b) Caryophylaceae
(c) Cruciferaeae (d) Ranuncolaceous

134. Prism type of calcium oxalate crystals are present in
(a) Quassia (b) Senna
(c) Cascara (d) All

135. Adulterant of Indian senna is
(a) Palthe senna
(b) Casia obovata
(c) Casia angustifolia
(d) Both a and b

136. Mesophyll of European squill contains _____ types of calcium oxalate crystals.
(a) Raphides (b) Acicular
(c) Prism (d) Needles

137. One of the following is also known as Vendayam
(a) Amla (b) Nagod
(c) Methi (d) Satavari

138. Chrysopanic acid is the major constituent of
(a) Nagod (b) Shilajit
(c) Neem (d) Chakramadu

139. Which of the following is C-glycoside?
(a) Barbaloin (b) Sennoside
(c) Diosgenin (d) Amygdalin

140. Shinoda's test is used for identification of
(a) Flavonoids (b) Tannins
(c) Glycosides (d) Alkaloids

141. Plant is used in the treatment of leucoderma
(a) Daru haridra (b) Ipecac
(c) Bavchi (d) Asafoetida

142. The main chemical constituent of senega is
(a) Steroidal glycosides
(b) Triterpenic glycoside
(c) cardiac glycosides
(d) Quassinoids

ANSWER KEYS

1. (d)	**2.** (a)	**3.** (b)	**4.** (d)	**5.** (d)	**6.** (b)	**7.** (a)	**8.** (b)	**9.** (b)	**10.** (a)
11. (c)	**12.** (c)	**13.** (b)	**14.** (b)	**15.** (c)	**16.** (c)	**17.** (b)	**18.** (b)	**19.** (d)	**20.** (a)
21. (b)	**22.** (b)	**23.** (b)	**24.** (c)	**25.** (c)	**26.** (d)	**27.** (a)	**28.** (b)	**29.** (c)	**30.** (c)
31. (b)	**32.** (d)	**33.** (d)	**34.** (b)	**35.** (d)	**36.** (d)	**37.** (d)	**38.** (d)	**39.** (a)	**40.** (a)
41. (c)	**42.** (b)	**43.** (c)	**44.** (b)	**45.** (c)	**46.** (b)	**47.** (b)	**48.** (a)	**49.** (c)	**50.** (d)
51. (c)	**52.** (c)	**53.** (d)	**54.** (a)	**55.** (d)	**56.** (b)	**57.** (c)	**58.** (b)	**59.** (d)	**60.** (b)
61. (d)	**62.** (a)	**63.** (d)	**64.** (b)	**65.** (b)	**66.** (b)	**67.** (b)	**68.** (a)	**69.** (c)	**70.** (d)
71. (d)	**72.** (b)	**73.** (a)	**74.** (a)	**75.** (c)	**76.** (d)	**77.** (b)	**78.** (c)	**79.** (d)	**80.** (b)
81. (a)	**82.** (c)	**83.** (a)	**84.** (b)	**85.** (a)	**86.** (d)	**87.** (a)	**88.** (d)	**89.** (c)	**90.** (c)
91. (c)	**92.** (d)	**93.** (a)	**94.** (a)	**95.** (c)	**96.** (b)	**97.** (d)	**98.** (a)	**99.** (b)	**100.** (a)
101. (c)	**102.** (a)	**103.** (a)	**104.** (b)	**105.** (a)	**106.** (a)	**107.** (a)	**108.** (a)	**109.** (b)	**110.** (d)
111. (c)	**112.** (a)	**113.** (b)	**114.** (b)	**115.** (c)	**116.** (a)	**117.** (a)	**118.** (c)	**119.** (c)	**120.** (b)
121. (d)	**122.** (a)	**123.** (b)	**124.** (b)	**125.** (a)	**126.** (d)	**127.** (c)	**128.** (b)	**129.** (c)	**130.** (d)
131. (b)	**132.** (b)	**133.** (d)	**134.** (c)	**135.** (d)	**136.** (a)	**137.** (c)	**138.** (d)	**139.** (a)	**140.** (a)
141. (c)	**142.** (b)								

CHAPTER 4

DRUG CONTAINING TERPENOIDS

TERPENOID DRUGS DESCRIPTION

Type of Terpenoid	Source	Active Constituents
Camphor Oil	Wood of *Cinnamonuum camphora* (Fam-Lauraceae)	Camphor (Bicyclic mono terpenoid ketone)
Chenopodium Oil (American worm seed oil)	Flowering and fruiting part of *Chenopodium ambrosioides Var. Anthelminticum* (Fam-Chenopodiaceae)	Ascaridole (Unsaturated terpene peroxide) = 70 to 80 % p-Cymene (20 %)
Eucalyptus oil	Leaves of *Eucalyptus globules* (Fam-myrtaceae)	Eucalyptol (Cineole)
Geranium oil	Leaves and stem of *Pelargonium graveolens* (Fam-Geraniaceae)	Alcohol type – Citronellol and Geraniol
Lemon Grass oil	Leaves and aerial parts of *Cymbopogon flexuous* or *C. Citratis* (Fam-Graminae)	Aldehyde type – Citral
Turpentine Oil	Oleo-resin of *Pinus roxburghii* or *Pinus palustris* or Pinus longifolia (family – Pinaceae)	α and β Pinene, Camphere
Peppermint Oil (Mentha oil)	Flowering tops of *Mentha piperita* (Fam-labiatae)	(–) menthol
Lemon oil	Pericarp of fruit of *Citrus limonis* (Fam-Rutaceae)	d-limonene (major) Citral (Minor)
Bitter Orange oil	Pericarp of fruit of *Citrus aurantium* (Fam-Rutaceae)	d-limonene, Hesperidin
Hops (Humulus)	Female flower *of Humulus lupulus* (Fam-Cannabinaceae)	α and β acid as resinous matter
Rasna(Galanga)	Rhizome of *Alpinia officinarum v*(Fam-Zingeberaceae)	Methyl Cinnamate and Cineol Pungent oil – Galangol, Alpinol
Garlic	Bulb of *Allium sativum* (Fam-Liliaceae) Note – Anti diabetic action of garlic is due to s-allyl cysteine sulforidae.	Allyl propyl disulphide, Diallyl disulphide, Alliin and Allicin (Diallyl sulphide oxide)
Tulsi	Leaves of *Ocimum sanctum* (Fam-Labiatae)	Eugenol
Acorus (Vaj or Calamus)	Rhizome of *Acorus calamus* (Fam-Araceae)	Asaraldehyde, Asarone (sesquiterpenoids) Bitter principle – Acorine
Annatto	Seed of *Bix orellana* (Fam-Bixaceae)	Bixin Pigment (Carotenoid Carboxylic Acid) It is responsible for yellow colour.

Type of Terpenoid	Source	Active Constituents
Crocus (Saffron, Kesar)	Stigma and upper part of Style of *Crocus sativus* (Fam-Iridaceae)	Red colouring matter – Crocin and Crocetin Bitter principle – Picrocrosin Odor – Safranol Proto crocin (carotenoid Glycoside) ↙ ↘ 2 mol Picrocrocin 1 mol Crocin ↓ ↓ Saffranol + Glucose Crocetin + 2 mol Gentiobiose
Taxus (Yew)	Stem bark of *Taxus baccata*, *T. Cuspidate, T.brevifolia, T.canadensis* (Fam-Taxaceae)	Taxol (Diterpenoid containing Oxetane ring)
Artemisia (Santonica)	Flower bud of *Artemisia cina, A. Brevifolia, A.maritima* (Fam- Compositae)	Santonin (Sesquiterpene lactone)
Artemisinin	Leaves of *Artemisia annua /Quinghao* (Fam-Compositae)	Artemisinin (Sesquiterpene lactone with internal peroxide linkage)
Black Pipper	Fruit of *Piper nigrum* (Fam-Piperaceae)	Alkaloid – Piperine Volatile Oil – l-Phellandrene and Caryophyllene
Rosemary Oil	Flowering tops of *Rosmarium officinalis* (labiate)	Alcohol type -Borneol
Gaultheria Oil (Oil of Wintergreen or Betula oil)	Leaves of *Gaultheria procumbens* (Fam-Ericaceae)	Glycoside – Gaultherin yields methyl salicylate upon hydrolysis. Characteristic Odor – Enanthic alcohol (n-Heptyl alcohol)
Palmarosa	Leaves and tops of *Cymbopogon maritini* (Fam-Graminae)	Geraniol
Citronella Oil	Leaves of *Cymbopogon nardus* (Fam-Graminae)	Geraniol(Major) and Citronellal (Minor)
Sandal Wood Oil	Heart wood of *Santalum album* (Fam-Santalaceae)	α and β Santalol (Both are isomeric sesquiterpene alcohol)
Thyme	Leaves and flowering tops of *Thymus vulgaris* (Fam-Labiateae)	Thymol
Cardamom (Chhoti-Ilaychi)	Fruit of *Eleteria cardamomum Var. Minuscula* (Fam-Zingiberaceae)	Cineol (2–8 %), Carvone Volatile oil should NLT 4 %
Clove (Lavang)	Flower bud of *Eugenia caryophyllus* or *Syzygium aromaticum* (Fam-Myretaceae)	Volatile oil should NLT 15 % w/v of Clove oil Eugenol (Main) ⟶ Vanillin (upon oxidation)
Nutmeg	Kernel of seed of *Myristica fragrans Houtt* (Fam-Myristicaceae)	Volatile Oil should NLT 5% w/v Myristicin, Saffrole and Elimicin

Type of Terpenoid	Source	Active Constituents
Cassia –Cinnamon (Cassia bark or Chinese cinnamon)	Stem bark of *Cinnamomum cassia* (Fam-Lauraceae)	Volatile Oil should NLT 1% w/v 85 % Cinnamic Aldehyde and small amount of Eugenol
Cinnamom (Cinnamon bark or Ceylon cinnamon or Kalmi-Dalchini)	Inner bark of shoot of coppicied tree of *Cinnamomum zeylanicum* (Fam-Lauraceae)	Volatile oil should NLT 1% w/v 60–70 % Cinnamaldehyde and 5–10 % Eugenol
Fennel (Sauf)	Fruit of *Fructus foeniculum Var. vulgare* (Fam- Umbelliferae)	Volatile oil should NLT 1.4 % w/v Ketone – Fenchone 20 % (Pungent odor) Phenolic ether – Anethole 50 % (Sweet odor and taste)
Coriander (Dhania)	Fruit of *Coriander sativum* (Fam-Umbelliferae)	Volatile oil should NLT 0.3% w/v 90 % D-linalool (Coriandrol)
Dill(European Dill)	Fruit of *Anethum graveolens* (Fam-Umbelliferae)	Volatile oil should NLT 2.5 w/v % 43–63 % Carvone Dill Apiole (Minor)
Caraway	Fruit of *Carum carvi* (Fam-Umbelliferae)	Volatile oil should NLT 3.5 % w/v 45–65 % Carvone Limonene-Terpene
Ajowan	Fruit of *Trychyspermum ammi* (Fam-Umbelliferae)	Volatile oil should NLT 2 % w/v Thymol and p-Cymene
Anise	Fruit of *Pimpinella anisum* (Fam-Umbelliferae)	Anethol 90 %
Cummin(Jira)	Fruit of *Cuminum cyminum* (Fam-Umbelliferae)	Cumin aldehyde
Celery	Fruit of *Apium gravolens* (Fam-Umbelliferae)	d- limonene

MICROSCOPY AND ADULTERATION OF TERPENOIDS

Cardamom Fruit

Macroscopic Feature

- Colour of cardamom without processing is green or pale puff. But change to white upon treatment with SO_2.
- Each capsule of fruit contains three chambers. Each chamber consists two rows of seed, about 5 to 10 in numbers. Seeds are enclosed in membranous Arillus.

Microscopy

Testa – Enclosed in Colourless flattened or collapsed parenchyma called membraneous Arillus.

Inner Integument – Consists of Sclerenchymatous layer (Stone cells)

Perisperm – Thin walled Parenchymatous cells with starch grains and single prismatic Calcium oxalate crystals.

Endosperm – Starch absent, thin walled Parenchymatous cells

Embryo – Oil globules and Aleurone grains present

Adulterants

1. Long wild native Cardamom (*Elettaria Cardamom Var. Major*)
2. *Korarima Cardamom*
3. Loose seeds or Fully Riped seeds
4. *Cardamom Husk*

Clove

Macroscopic Feature

- Crimson to dark brown colour. Hypanthium is surmounted with four thick divergent sepals surrounded by dome shaped corolla. Corolla consists of unexpanded membranous petals with several stamens and single prominent style. Clove is heavier than water.

Microscopy

Epidermis – Single layer, Straight walled cells, Anomocytic stomata, Very thick cuticle

Cortex –

- Outer zone consists of ellipsoidal Schizolysigenous oil glands, Parenchymatous cells containing tannins
- Middle region consists of bicollateral vascular bundle, Xylem consists of lignified vessels, and Lignified pericyclic fibres are presents.

Columella – Cluster of Calcium oxalate crystals

Adulterants

Exhausted cloves – Darken in colour, floats on water

Blown cloves – Expanded flower without corolla

Mother cloves (Anthophylli) – Presence of starch grains

Clove stalk – Stone cells, prismatic Calcium oxalate crystals

Note

As per IP Clove should not contain more than 5 % Clove stalk.

Cassia Cinnamon

Cork – Polygonal tubular cells

Phellogen and Phelloderm are not separable

Cortex – Stone layer cells-Scattered U shape Sclerides, Abundant Starch grains 10 to 20 µ diameter

Pericycle –

- Stone layer cells-scattered U shape Sclerides
- Pericyclic Fibers-Lignified

Secondary Phloem – Abundant Starch grains 10 to 20 µ diameter

Medullary Rays – Multiseriate, Acicular Raphides

Phloem Fibers – Lignified

Mucilage cells – Give pink or red colour with Ruthenium red

Cinnamon bark

Cork and Cortex are Absent

Pericycle –

- Stone layer cells- 3 or 4 layers of Sclerides, U shape
- Pericyclic Fibers-Lignified

Secondary Phloem – Starch grains up to 10 µ diameter

Medullary Rays – Biseriate, Acicular Raphides

Phloem Fibers – Lignified

Mucilage cells – Give pink or red colour with Ruthenium red

Allied drugs –

1. Wild or Jungle Cinnamon: Darker and larger, Less aromatic
2. Java Cinnamon (*C.burmanni*): less aromatic , Medullary rays contains small tabular crystals of calcium oxalate
3. Saigon Cinnamon (*C.loureirii*): Occurs in quills, sweeter than Ceylon cinnamon, outer surface is greyish to greyish-brown.
4. Oliver Bark (*C.oliveri*): Flat strips, fracture is short and fibrous, outer surface is brownish

	Fennel	Coriander	Dill	Caraway
Macroscopic	Cremocarp – consists of 2 equal portions called mericarps, connected by central stalk called carpophores.	Cremocarp	Mericarp separated. Extended portion of mericarp called Wings.	Five primary ridge in each mericarp
Epicarp	Polygonal cells with Smooth cuticle	Polygonal cells with Smooth Cuticle	Striated Cuticle	Striated Cuticle
Mesocarp	Reticulate lignified parenchyma	Absent	Present	Absent
	Sclerides lignified Absent	Present	Absent	Present
	Vittae – Schizogenous oil gland (4 dorsal + 2 Ventral or Commissural surface)	Present	Absent	Present
Endocarp	Parquetry layer arrangement (Group of parallel cells arranged in different directions)	Present	Absent	Absent
Endosperm	Thick walled polygonal cells containing oil globules and Aleurone grains with minute Rosette Calcium oxalate crystals	Same	Same	Same

MULTIPLE CHOICE QUESTIONS

1. Pick tooth fruit has biological source
(a) *Psoralea corylifolia*
(b) *Ammi visnaga*
(c) *Ammi majus*
(d) *Dipteryxodorata*

2. Saffrole is present in
(a) Saffron (b) Nutmeg
(c) Caraway (d) Cinnamon

3. The chief constituents of ammi is
(a) Xanthotoxin (b) Ajmaline
(c) Brucine (d) Senegin

4. Aril is present in
(a) Nutmeg (b) Cardamom
(c) Strophanthus (d) Castor

5. All drugs belong to Labiatae family except
(a) Peppermint oil (b) Spearmint
(c) Tulsi (d) Nutmeg

6. All of the following belongs to Rosaceae family except
(a) Quillia (b) Bitter almond
(c) Wild cherry bark (d) Cochineal

7. Cinnamon consists of the dried inner bark of the shoots of coppiced trees of *Cinnamomum zeylanicum* (Ness) The typical microscopic characters of the bark area
(a) Biseriate medullary rays, secretory cavities containing volatile oil and mucilage and few starch grains in cortical parenchyma and calcium oxalate in parenchymatous cell
(b) 2–5 layers of cork cells containing oil globules. Presence of schizogeneous canal

(c) Modularly rays multiseriate, the pariderm portion cork has both tangentially and radially elongated cells, stone cells are present and no phloem fibers
(d) Ex-foliated cork, non-lignified with 2–4 layers of phelogen, 15–20 rows of pheloderm, prominent vascular tissue

8. Myristicin is active constitute of
(a) Nutmeg (b) Turpentine
(c) Coriander (d) Chenopodium

9. Marijuana is the another name of
(a) Icalodana (b) Jalap
(c) Cannabis (d) Male fern

10. Thymol is the active constituent of
(a) *Coriendrum sativum*
(b) *Myristica fragrance*
(c) *Pelargonium graveolens*
(d) *Tachyspermum ammi*

11. Indian kino tree is
(a) Ashoka (b) Pterocarpus
(c) Aloe (d) Lobelia

12. Centophloic vascular bundles are found in
(a) Fern (b) Papaya
(c) Acorus (d) None

13. Nux-monschata is the synonym of _____
(a) Nux-vomica (b) Jatamansi
(c) Nutmeg (d) Cassia

14. Nutmace gives red colour with iodine solution due to presence of _____
(a) Starch (b) Amylodextrin
(c) Glucose (d) All of the above

15. Which bark shows presence of mucilage?
(a) Arjuna (b) Cascara
(c) Wild cherry (d) Cinnamon

16. Valerian is a
(a) Rhizome (b) Stolon
(c) Root (d) All of the above

17. Rotenone is the insecticidal constituent obtained from _____
(a) Derris root (b) Derris rhizomes
(c) Cube root (d) All of the above

18. Pyrethrum consists of dried flower heads of _____
(a) *Cichorium intibus*
(b) *Coleus forskohlii*
(c) *Cola nitida*
(d) *Chrysanthemum cinerariifolium*

19. The pigment present in tomato is _____
(a) Carotene (b) Lycopene
(c) Malotonin (d) None of the above

20. Natural camphor is distinguished from artificial camphor by _____
(a) Liebermann Buchard test
(b) Colour reaction with vanillin and sulphuric acid
(c) Colour reaction with ferric chloride
(d) All of the above

21. Chenopodium is used as _____
(a) Anti-asthmatic (b) Anti-inflammatory
(c) Anthelmintic (d) Antipyretic

22. Ascaridol is chemically _____
(a) Terpene peroxide (b) Terpene ester
(c) Terpene ether (d) Terpene acid

23. Which fruit shows presence of numerous vittae?
(a) Coriander (b) Caraway
(c) Anise (d) Dill

24. Indian dill contains a poisonous substance _____
(a) Phellandene (b) Anethol
(c) Dill-apiole (d) Carvone

25. Identifying character of Jatamansi is _____
(a) Stone cells
(b) Interxyllary and medullary cork
(c) Crystal sheath
(d) Both (a) and (b)

26. Eculle method is used for extraction of volatile oil from _____
(a) Fresh flower petals
(b) Leaf drugs
(c) Citrus fruits
(d) Air dried subterranean parts

27. Jatamansi is adulterated with rhizomes of
(a) *Selinum vaginatum* (b) *Valeriana officinalis*
(c) *Acorus calamus* (d) None

28. Cassia bark is distinguished from cinnamon bark, chemically it
(a) Does not contain eugenol
(b) Contains eugenol
(c) Contains caryophylline
(d) None

29. Reacting with ferric chloride solution, cinnamon powder shows
(a) Blue colour (b) Pale green colour
(c) Pale violet colour (d) Black precipitates

30. The % of volatile oil present in clove is
(a) 1 (b) 5
(c) 10 (d) 15

31. The main active constituent of *Syzygium aromaticum* is
(a) Cineol (b) Eugenol
(c) Ascaridol (d) Thymol

32. Presence of clove stalks in powdered drug is identified by
(a) Presence of calcium oxalate crystals
(b) Isodiametric sclerieds
(c) Lignified fibres
(d) Both (a) and (b)

33. One of the following is also known as staff tree
(a) Brahmi (b) Amla
(c) Behda (d) Malkangni

34. One of the following is considered as bioavailability enhancer
(a) Amla (b) Arjuna
(c) Piper (d) Garlic

35. Usually volatile oils are mixture of
(a) Mono and sesquiterpenes
(b) Mono and diterpenes
(c) Sesquiterpens and diterpenes
(d) Mono and lower aliphatic compound

36. Thermal decomposition of volatile oils gives
(a) Hydrocarbons (b) Isoprenes
(c) Alcohols (d) Carboxylic acid

37. In the volatile oil of clove, the amount of Eugenol is up to
(a) 50% (b) 60%
(c) 75% (d) 85%

38. *Mentha piperita* is the biological source of peppermint and it belongs to the family
(a) Illiciaceae (b) Umbelliferae
(c) Labiateae (d) Lauraceae

39. Nearly 70% linalool is present in volatile oil of
(a) Fennel (b) Coriander
(c) Cinnamon (d) Eucalyptus

40. Dried stigma and style tops of *Crucus sativus* are known as
(a) Cannabis (b) Cassia
(c) Saffron (d) Camphor

41. The main component of the volatile oil of *Menthe spicata* is
(a) Camphor (b) Safranal
(c) Carvone (d) Phellandrene

42. The part of *Eugenia caryophyllus* used as a drug is known as
(a) Root (b) Rhizome
(c) Leaves (d) Flower buds

43. *Acorus calamus* belongs to the family Araceae and its official part is
(a) Root (b) Rhizome
(c) Leaves (d) Flowers

44. A volatile oil used as mosquito repellant is
(a) Prethrum oil (b) Lemon grass oil
(c) Rosemary oil (d) Citronella oil

45. Colophony is a solid residue of a resin left after removing
(a) Volatile oils (b) Gums
(c) Fixed oils (d) Balsams

46. The red colour of capsicum fruit is due to presence of
(a) Capsanthin (b) Zeaxanthine
(c) Lutein (d) Cryptoxanthin

47. Arillode is present in cardamom is
(a) A succulent growth from hilum
(b) An outgrowth originating from micropyle
(c) A warty outgrowth from micropyle
(d) The point of attachment of seed to stalk

48. Terpenoids are biosynthesized from
(a) Shikimic acid pathway
(b) Acetate-mevalonate pathway
(c) Ornithine cycle
(d) Both (a) and (b)

49. Terpenoids and caratenoids are synthesized from
(a) Mevalonic acid (b) Acetyl-S-CoA
(c) Lysine (d) Phenylalanine

50. The main active chemical constituent of eucalyptus oil is
(a) α-Pinene (b) Phellandrene
(c) Cineol (d) Citral

51. The active constituent of tulsi is
(a) Geraniol (b) Cineol
(c) Citral (d) Eugenol

52. (–) Carvone is the chief constituent of
(a) Caraway (b) Dill
(c) Spearmint (d) All of the above

53. Indian Dill differs from European Dill because
(a) It contains less carvone
(b) It contains Dill-apiole
(c) Both
(d) None

54. The main identifying character of coriander is
(a) Lignified parenchyma of mesocarp
(b) Numerous vittae (25–30)
(c) Lignified fibres
(d) Both (a) and (b)

55. The bitter taste of fennel is due to presence of
(a) Anethole (b) Fenchone
(c) Both (a) and (b) (d) None

56. The % of volatile oil in nutmeg is
(a) 5 (b) 1
(c) 10 (d) 2

57. Linamarin is biogenetically derived from
(a) Tryptophan (b) Phenylalanine
(c) Tyrosine (d) Valine

58. All drugs come under Umbelliferae family except
(a) Caraway (b) Dill
(c) Cummin (d) Lemmon oil

59. Which of the following is heartwood?
(a) Sandal wood (b) Quassia
(c) Both (d) None

60. All drugs come under Lauraceae family except
(a) Camphor (b) Cassia cinnamon
(c) Cinnamon (d) Sandalwood

61. Which of the following drugs comes under Rutaceae family?
(a) Lemmon oil (b) Bitter orange pill
(c) Taxus (d) Both (a) and (b)

62. Which of the following drugs is comes under Zingiberaceae family?
(a) Cardamom (b) Cinnamon
(c) Garlic (d) Clove

63. Garlic comes under _____ family
(a) Rutaceae (b) Zingiberaceae
(c) Liliaceae (d) Labitae

64. *Anethum graveolens* is a biological source of _____
(a) Dill (b) Clove
(c) Cummin (d) Fennel

65. *Ocimum sanctum* is a biological source of _____
(a) Tulsi (b) Thyme
(c) Ajowan (d) None of the above

66. Which parts of clove have medicinal importance?
(a) Dried inner bark (b) Dried ripe fruits
(c) Dried flower buds (d) Dried kernel

67. Which parts of the cummin have medicinal importance?
(a) Dried inner bark (b) Dried ripe fruits
(c) Dried flower buds (d) Dried kernel

68. Which parts of the nutmeg have medicinal importance?
(a) Dried inner bark (b) Dried ripe fruits
(c) Dried flower buds (d) Dried kernel

69. The total volatile oil content present in dill is _____
(a) NLT 2.5% (b) NLT 3.0%
(c) NLT 5.0% (d) NLT 6.5%

70. The total volatile oil content present in fennel is _____
(a) NLT 1.4% (b) NLT 2.5%
(c) NLT 5.0% (d) NLT 6.0%

71. Prismatic calcium oxalate crystal is a characteristic of _____
(a) Cardamom (b) Anise seed
(c) Cinnamon (d) Clove

72. Rosette calcium oxalate crystal is a characteristic of ____
(a) Fennel (b) Anise seed
(c) Both (a) and (b) (d) None

73. Unicellular, thick-walled and warty trichome is a characteristic of _____
(a) Anise seed (b) Cardamom
(c) Peppermint oil (d) Caraway

74. Clove belongs to the family
(a) Myrtaceae (b) Liliaceae
(c) Taxaceae (d) Labiatae

75. One of the following belongs to Umbelliferae family
(a) Cardamom (b) Taxus
(c) Sandal wood oil (d) Dill

76. Characteristic of clove stalks which is a clove adulterant is
(a) It contain only 5% of oil
(b) Oil is removed from clove
(c) Dark brown, ovate and ripened fruits of clove
(d) Expanded flowers of clove trees

77. _____ of fenchone is present in Japanese Fennel.
(a) 22.00% (b) 10.20%
(c) 6.70% (d) Nil

78. Dill is derived from biological sources
(a) *Anethum graveolens*
(b) *Eugenia caryophyllus*
(c) *Carum carvi*
(d) *Allium sativum*

79. Microscopically characteristic of caraway is
(a) Microrosette calcium oxalate
(b) Acicular calcium oxalate crystal
(c) Prismatic calcium oxalate crystal
(d) Absent of calcium oxalate crystal

80. Microscopical characteristic of fennel is all of the following except
(a) Anomocytic stomata are present
(b) Rosette calcium oxalate are present
(c) Aleurone grains are present
(d) Starch grains are present

81. Chenopodium contain
(a) Not less than 65% of ascaridol
(b) Not less than 5% of ascaridol
(c) Not less than 10% of ascaridol
(d) Not less than 6.5% of ascaridol

82. Triterpene class of terpenoid contains _____ number of isoprene units
(a) 9 (b) 6
(c) 3 (d) 1

83. Terpenoid present in eucalyptus is
(a) Eugenol (b) Geraniol
(c) Cineol (d) Zingiberone

84. Alcoholic type of volatile oil is present in
(a) Peppermint (b) Turpentine
(c) Sandalwood oil (d) Clove

85. Chenopodium contains _____ type of volatile oil
(a) Alcoholic (b) Phenolic
(c) Ester (d) Oxide

86. The sedative chemical constituent of calamus is
(a) Asarone (b) Valtrate
(c) Eugenol (d) None

87. Cochineal contains:
(a) Carminic acid (b) Caffeine
(c) Citric acid (d) None of the above

88. Main constituent of wintergreen oil is
(a) Linalool (b) Pinene
(c) Geranial (d) Methyl salicylate

89. Main chemical constituent of chenopodium oil is
(a) CitronellaI (b) Geranial
(c) Ascaridiole (d) Menthol

90. Rugae are present in
(a) Clove (b) Cardamom
(c) Caraway (d) Spearmint

91. Which type of stomata are present on the epidermis of pericarp in fennel?
(a) Anisosytic (b) Anomosytic
(c) Diacytic (d) Paracytic

92. Anethole is present in
(a) *Foeniculam vulgaris*
(b) *Anethum sowa*
(c) *Anethum graveolens*
(d) *Carum carvi*

93. Annato and Crocus can be classified as
(a) Tetraterpenoids (b) Triterpenoids
(c) Monolerpenoids (d) Diterpenoids

94. Sudan-III with volatile oil will give
(a) Red colour (b) Yellow colour
(c) Pink colour (d) Black colour

95. The drug which does not contain ketone volatile oil is
(a) Dill (b) Caraway
(c) Sandalwood oil (d) Cumin

96. Which of the following does not contain chitin?
(a) Lemon oil (b) Yeast
(c) Fungi (d) Annelids

97. Which of the following is not an organized drug?
(a) Fennel (b) Colophony
(c) Ipecac (d) Senna

98. The percentage of abietic acid in colophony is
(a) 90% (b) 60%
(c) 40% (d) 25%

99. Azadirachtin is a strong
(a) Analgesic (b) Antioxidant
(c) Antifeedant (d) Hypnotic

100. Which is the acyclic monoterpenes?
(a) Geranial (b) α-limonine
(c) Zingiberone (d) Santinine

101. Vitamin A is
(a) Acyclic diterpene (b) Monocyclic diterpene
(c) Bicyclic diterpene (d) Tricyclic diterpene

102. Vanillin, the active constituent of vanilla can be synthesized from
(a) Eugenol (b) Carvone
(c) Vincristine (d) Vinblastin

103. Which of the following is not a common use of margosa oil?
(a) Narcotic (b) Insecticide
(c) Spermicide (d) Use in soaps

104. Sesquiterpenes has formula

(a) C_5H_8 (b) $C_{15}H_{24}$
(c) $C_{10}H_{16}$ (d) $C_{30}H_{42}$

105. Caretenoids have _____ number of isoprene units.

(a) 2 (b) 8
(c) 6 (d) 10

106. Chemically isoprene is

(a) 2-methyl-but- 3-ene
(b) 1,3-butadiene
(c) 2-methyl 1,3-butadiene
(d) 1-methyl 1,3-butadiene

107. In the fennel which of tissue is lignified

(a) Parenchyma (b) Mesocarp
(c) Epicarp (d) Endocarp

108. Leiberman-Burchard test is used for the identification of

(a) Sterols (b) Triterpenes
(c) Alkaloids (d) Both (a) and (b)

109. Holy basil is the alternative name for

(a) Tulsi (b) Senna
(c) Mulethi (d) Punarnava

110. Spearmint contains

(a) Carvone (b) Eugenol
(c) Cresol (d) Guiacol

ANSWER KEYS

1. (b)	**2.** (b)	**3.** (a)	**4.** (a)	**5.** (d)	**6.** (d)	**7.** (a)	**8.** (a)	**9.** (c)	**10.** (d)
11. (b)	**12.** (c)	**13.** (c)	**14.** (b)	**15.** (d)	**16.** (d)	**17.** (d)	**18.** (d)	**19.** (b)	**20.** (b)
21. (c)	**22.** (a)	**23.** (c)	**24.** (c)	**25.** (b)	**26.** (c)	**27.** (a)	**28.** (a)	**29.** (b)	**30.** (d)
31. (b)	**32.** (d)	**33.** (d)	**34.** (c)	**35.** (a)	**36.** (b)	**37.** (d)	**38.** (c)	**39.** (b)	**40.** (c)
41. (c)	**42.** (d)	**43.** (b)	**44.** (b)	**45.** (a)	**46.** (a)	**47.** (b)	**48.** (b)	**49.** (a)	**50.** (c)
51. (d)	**52.** (c)	**53.** (c)	**54.** (a)	**55.** (b)	**56.** (a)	**57.** (d)	**58.** (d)	**59.** (a)	**60.** (d)
61. (d)	**62.** (a)	**63.** (c)	**64.** (a)	**65.** (a)	**66.** (c)	**67.** (b)	**68.** (d)	**69.** (a)	**70.** (a)
71. (a)	**72.** (c)	**73.** (a)	**74.** (a)	**75.** (d)	**76.** (b)	**77.** (b)	**78.** (b)	**79.** (a)	**80.** (d)
81. (a)	**82.** (b)	**83.** (c)	**84.** (a)	**85.** (d)	**86.** (a)	**87.** (a)	**88.** (d)	**89.** (c)	**90.** (b)
91. (b)	**92.** (a)	**93.** (a)	**94.** (a)	**95.** (c)	**96.** (a)	**97.** (b)	**98.** (a)	**99.** (c)	**100.** (a)
101. (b)	**102.** (a)	**103.** (a)	**104.** (b)	**105.** (b)	**106.** (c)	**107.** (a)	**108.** (d)	**109.** (a)	**110.** (a)

CHAPTER 5

DRUG CONTAINING CARBOHYDRATE, RESIN AND TANNIN

DRUG CONTAINING CARBOHYDRATE

Name/Synonym	Biological Source/Family	Chemical Constitute	Use	Characteristics
Acacia Gum (Gum Arabic, Indian gum, Kher, Somali gum, yellow thorn	It is dried gummy exudation obtained from stem and branches of *Acacia Senegal* (Leguminosae)	Arabin – complex mixture of Ca, Mg and K salts of Arabic acid. On hydrolysis it is converted into L-Arabinose, D-Galactose, L-Rhamanose and D-Glucronicacid	Demulcent, Binding agent, Pharmaceutical aids for emulsification	Allied drugs-Talka gum, Ghatti gum
Guar Gum (Jagur gum, Gum flour, Decorpa)	It is produced from the powdered endosperm of the seed of *Cyamopsis Tetragonolobus Linn*. (Leguminosae)	Water soluble part of guar gum contain high molecular weight hydro colloidal polysaccharide like Galactomannan is also known as Guaran (linear chain of (1→4)-β-Dmannopyranosyl unit with α-D-Galactopyrasonyl unit)	Disintegrating agent, Emulsifying agent, bulk laxative, appetite depressants, decrease serum LDL level	
Honey (Madhu, Madh, Mel)	It is a viscid and sweet secretion stored in the honey comb by various species of bees such as *Apis Mellifera*, (Apideae)	Dextrose (23–36%).Levulose/ Fructose (30–47%) Sucrose (0.4–6%), Dextrin and Gum 0–7% and in small amount of formic acid, Acetic acid, Succinic acid, Maltose and enzyme like Diastase, Invertase and Inulase	Mild laxative, Sedative, used in ulcer, Honey and onion juice is used in arteriosclerosis in brain	Confirmatory test: Fiehe's Test for Artificial Invert test Adultrant: Canesugar, Artificial invert sugar
Tragacanth (Goat's Thorn, Gum dragon, Hog Gum)	It is air dried gummy exudates, flowering naturally or obtained by incision, from the stems and branches of *Astragalus Gummifer* (Leguminosae)	Tragacanthin -Water soluble fraction (30–40%) & Bassorin-Water insoluble fraction (60–70%), Other three constitutes are Tragacanthic acid on hydrolysis gives galactose, xylose and galactouronic acid and natural polysaccharide and Steroidal glycoside	Demulcent in cough and cold preparation, Emollient in cosmetic, Thickening, suspending and emulsifying agent	Hog tragacanth, Citral gum used as an adulterants

Cont.

Name/Synonym	Biological Source/Family	Chemical Constitute	Use	Characteristics
Karaya Gum (Indian Tragacanth, Sterculia Gum, Bassora tragacanth, Kadaya, Mucara, Kadira Katila and Kullo	It is gummy exudates obtained by incision, from *Sterculia Urens* (Sterculiaceae)	Chemically it is acetylated polysaccharides contain 8% acetyl group and 37% uronic acid. It undergoes hydrolysis under acidic medium in D-galactose, L-rhamanose, D-galactouronic acid and tri-saccharide uronic substance	Bulk laxative, Adsorbents Dental adhesive	Adultrants: Gum Tragacanth
Agar (Japanese Isinglass, Vegetable gelatin)	It is dried gelatinous substance obtained by extraction with water from *Gelidium Amansii* (Gracilariaceae)	It is a complex heterosaccharides & contains agarose and agaro-pectine. Agarose is natural galactose, polymer and responsible for the gel property agar made up of D-galactose and L-galactose Agaro-pectine is made up of sulphonated polysaccharides	Nutrients media for bacterial culture, chronic constipation, laxative, emulsifying agent, gelating agent	Adulterants are gelatin and Danish agar
Xanthan Gum	It is a microbial polysaccharides obtained from *xanthomonus Compestris*	D-glucosyl. D-mannosyl and D-glucosyluronic acid	Stabilizer and suspending agent in emulsion, paints, agriculture and herbicidal spray	Recombinant DNA technology used for commercial production of Xanthan gum
Isapghula (Spongel Seeds) Indian Psyllium Isabgol	It consists of dried seeds of *Plantago Ovate* (Plantaginaceae)	It contains 10% mucilage consists of two complex polysaccharide, pentosan is soluble in cold water and hydrolyzed to xylose, arabinose & Aldobionic acid yields galactouronic acid and rhamanose	Demulcent, Bulk laxative	Microscopy: 1. Pigment layer yellow in colour, 2. Embryo contains three to five vascular bundles Chemical Test: Swelling Factor
Carrageenan (Chondrus extract, Irish moss extract)	It is sulphated polysaccharides obtained from the seaweed called Irish moss, the red algae *Chondrus Crispus Linn*, (Gigartinaceae)	Major constitute is Galactans also known as Carrageenan. Kappa, Iota and Lamda Carrageenan are types of Carrageenan	Emulsifying agent, Stabilizing agent, Solublizing agent, Viscosity builder in food products. It is a popular Phlogistic agent for inducing inflammation in the rat paw oedema model for the study of anti inflammatory activity.	Substitute or adulterant: Gigartinastellata Batt.

DRUG CONTAINING RESIN

- Resin can be defined as the complex amorphous product of more or less solid characteristics which on heating first sets softened and then melt.
- Resin are produced and stored in schizolysigenous glands or cavities.

Name of Drugs/ Synonym	Biological Source/ Family	Chemical constitutes	Use	Characteristic
Asafoetida (Devil's dung, Food of the gods, Asant, Hing, asafoda)	Oleo gum resin obtained from as an exudation by incision of the decapitated rhizome and roots of *Ferula Asafoetida* (Apiceae)	*Volatile oil (4–20%), Resin (40–65%) and gum (25%) *Isobutyl propenyl disulphide (responsible for garlic like order). *Resin consists of ester of asaresinotannol and ferulic acid, pinene, vanillin. *It also contains phellendrene, geranyl acetate, camphene, limonene, eugenol, myrecene, camphene	Carminative, Expectorant, Anti spasmodic	Adultrants: Gumarabica Rosin, gypsum, redclay, chalk, wheat flour
Balsam of Peru (Peruvian balsam, Indian balsam, China oil, Black balsam, Honduras balsam, Surnam balsam,)	It is obtained by incision of the stem of *Myroxylon Balsamum var. pereirae* (Papilionaceae)	Balsamic ester (benzyl cinnamate-cinnamein) Benzyl benzoate and cinnamy lcinnamate (styracin), Alcohol likes farnesol, benzyl alcohol and small amount of vanillin and free cinnamic acid	Miticide, Scabicide, parasiticide, Rubificients flavouring agent	
Balsam of Tolu Thomas balsam, opobalsam, resintolu	It is obtained by incision of the stem of *Myroxylon Balsamum* (L.) Harms. (Papilionaceae)	It contains 80% resins which is a mixture of resin alcohol combined with cinnamic acid and benzoic acid. 30–35% total balsamic acid. Other aromatic acid, benzyl benzoate, banzyl cinnamate, vanillin, styrene, eugenol	Expectorant, Stimulant, Antiseptic, It is an ingredients of cough mixture and compound benzoin tincture flavouring agent	Adulterants: Colophony
Cannabis Indian hemp, hashish, Bhang, Ganja, Charas, Marihuana	Dried flowering plant of *Cannabis Sativa Linn*, (Canabinaceae) (Moraceae)	The major psychoactive chemical compound in cannabis is Δ^9-tetrahydrocannabinol (commonly abbreviated as THC). Canabidiol, canabidolicacid, cannabinol, cannabichromene	Tonic, Sedative, Analgesic, Intoxicants, Stomachic, Antispasmodic, Anti convulsant, Anti tussive, narcotic.	
Capsicum (Cayenne pepper, red pepper, Spanish pepper, mirch)	Dried and ripe fruits of *Capsicum Minimum* and *Capsicum Annum* (Solanaceae)	Oleoresin, caratenoids, capsacutin, capsico (a volatile alkaloids), Thiamine, Ascorbic acid. Pungency of capsicum is due to Capsaicin and capsanthin is a main caratenoids of the red fruits.	Stimulant, Counter irritant, Rubificients, Scarlatina, carminative, stomachic	Allied drugs: Japanese Chillies, Bombay Capsicums

Cont.

Name of Drugs/ Synonym	Biological Source/ Family	Chemical constitutes	Use	Characteristic
Colophony (Rosin, Abiatic anhydride, Yellow resin)	It is solid residue obtained after distillation off the volatile oil from oleoresin obtained from *Pinus Palustris* (Pinaceae)	It contain resin acid (90%), resins 90% isomeric α, β, γ-abietic acid and other 10% Dihydroabietic acid and Dihydroabietic acid Pimeric acid	Stiffening agent in ointment, Adhesive, plaster and cerates. Abietic acid having antimicrobial, anti ulcer and cardiovascular activity	It is collected by Cup and Gutter method
Ginger (Rhizome zingiberis, Zingibere) Sunthi	Dried rhizomes of *Zingiber Officinale Roscoe*, (Zingiberaceae)	1–4% volatile oil responsible for aromatic order (sesquiterpene hydrocarbon like α-zingiberol, α-farnesene), 5–8% pungent resinous mass due to gingerol Gingerone and shogal are less pungent	Anti emetic, Positive ionotropic, spasmolytic, aromatic stimulant, carminative	Adultrants: wormy drug or spent ginger
Guggal (Gumgugul, Salai-gogil)	It is a gum resin obtained by incision of the bark of *Commiphora Mukul* (Burseraceae)	Gum (32%), sterols (guggulsterone I to VI, β-sitosterol, cholesterol, Z & E-guggulsterone), Ellagic acid, sugar and amino acid	Lower serum triglycerides and cholesterol as well as LDL and VLDL and raise HDL level, platelet aggregation inhibitor, Gum is astringent anti-rheumatics	
Myrrh (Myrrha, Arabian or Somali myrrh)	It is oleo gum resin obtained from the stem of *Commiphora Molmol* (Burseraceae)	Resin-25–40% like α, β, γ-commiphoric acid Volatile oil like cumin aldehyde, eugenol, cresol, pinene, limonene, gum containing protein and carbohydrate	Carminative, used in tooth powder and mouth wash	Allied drugs: Four different varieties of bdellium are present
Podophyllum (May apple root, American Mandrake)	Dried roots and rhizomes of *Podophyllum Peltatum Linn* (Berberidaceae)	Resin-Podophyllin, Podophyllotoxin, α and β-peltatin, Flavanoids like quercetin	Cytotoxic activity, Gastrict irritant	Podophyllum is converted into etoposide which is mainly used for lung and testicular cancer
Siam benzoin	It is balsamic resin derived from stem of *Styrax Ton Kinesis Craib* (Styraceae)	It contains coniferyl benzoate, benzoic acid, triterpene siaresinolic acid, vanillin	Expectorant and antioxidants	
Sumatra Benzoin Gum Benjamin, Benzonium, Luban	It obtained from incised stem of *Styrax Benzoin* (Styraceae)	Free Balsamic acid (benzoic acid + cinnamic acid) and triterpenic acid like siaresinolic acid and sumaresinolic acid	Expectorant, Carminative and diuretics	Allied drugs: Palembang benzoin

Name of Drugs/ Synonym	Biological Source/ Family	Chemical constitutes	Use	Characteristic
Turmeric (saffron Indian, haldi, Curcuma)	Dried rhizome of *Curcuma Longa Linn* (Zingiberaceae)	Curcuminoids (5%), coloring matter (Curcumin I–60% in addition to Curcumin-II &III, dihydrocurcumin. Volatile oil-Zingeberene, α-Phellandrene, borneol, cineole	Anti-inflammatory, Stomachic, carminative, blood purifiers, in cough	Adulterants: Acoruscalamus

TANNIN

Tannins are complex organic compound, on nitrogenous plant products, which generally having astringent properties.

Chemically tannins are polyphenolic in nature. It is detected by Goldbeater skin test.

There are two types of tannins –

1. True tannins: It gives Goldbeater skin test positive.
2. Pseudo tannins: It gives Goldbeater skin test negative.

Most of the true tannins are high molecular weight compound and these compounds are complex polyphenolic in nature.

Chemical classification of Tannins

(1) Hydrolysable Tannins:

These tannins are hydrolysable by mineral acids or enzyme such as tannase. It contains certain polyphenolic acid in its structure. It is soluble in water and gives blue colour with ferric chloride.

E.g.: Gallic acid, Ellagic acid and Hexahydroxydiphenic acid etc.

(2) Condensed Tannins or Non-hydrolysable Tannins:

These tannins are not hydrolysable by mineral acids or enzyme. The term pro-anthocynidine is referred as Non hydrolysable tannins. It contains Phenolic nuclei in its structure. It is soluble in water and gives green colour with ferric chloride.

E.g.: Catechin and Leucoanthocyanidin

Biosynthesis of Tannins

Tannins are belongs to the Phenolic class of secondary metabolite. All Phenolic compounds; either primary or secondary are formed through shikimic acid pathway (Phenylpropanoid pathway).

- Gallic acid is derived from quinic acid.
- Ellagotannins are formed from Hexahydroxydiphenic acid ester
- Pro-anthocynidine are biosynthetic precursors are the Leucoanthocyanidin (Flavan 3,4-diols and flavan-4-ol)

Hydrolysable Tannin

Name of Drugs/ Synonym	Biological Source/Family	Chemical constitutes	Use	Characteristic
Myrobalan (Chebulic myrobalam, Harde, Haritaki	Dried fruits of *Terminalia Chebula*, (Combretaceae)	Chebulic acid, Chebulinic acid, D-galloyl glucose, Free tannic acid, ellagic acid and Gallic acid	Purgative, Dental preparation	It is a constitute of Triphala
Bahera (Baleric myrobalam, Baheda, Bibhitak)	Dried ripe fruits of *Terminalia Belerica Linn* (Combretaceae)	Ellagic acid, Gallic acid, Phyllemblin, D-galloyl glucose and Ethyl gallate	Astringent in treatment of Dyspepsia and diarrhoea.	It is a constitute of Triphala. Stone cells and rosettes of Ca-Oxalate crystals are presents in parenchymatous cells.

Arjuna (Arjunbark, Arjun)	Dried stem bark of *Terminalia Arjuna Rob* (Combretaceae)	Tannins are (+) Catechol, Gallocatechol, Epicatechol, Epigallocatechol and Gallic acid Flavanoids are Arjunolone, Arjunone and Baicalein. Tri-terpenoids are Arjunetin, Arjungenin, Arjunglucoside I & II and Terminoic acid	Diuretic due to tri-terpenoids present in bark, Astringent It causes decrease in blood pressure and heart rate.	Adulterants: Terminalia tomentosa Chemical test: By fluorescence, Etheral extract of Arjuna gives pink colour while Terminalia tomentosa gives pale blue colour.
Amla (Emblica, Indian goose berry, Amla)	Dried as well as fresh fruits of *Embilica Officinalis (Phyllanthus Emblica Linn)* (Euphorbiaceae)	Vitamin C (Ascorbic acid), Minerals and Amino acids. Alkaloids are Phyllantine and Phyllantidine	Diuretics, Cooling, Laxative. In diabetes dysentery It has also Anti oxidants, Anti bacterial, Anti fungal and Anti viral properties	It is key ingredient in Triphala Churna, Chyavanpraseh and Jeevan malt.

Condensed Tannins or Non-hydrolysable Tannins

Name of Drugs/ Synonym	Biological Source/Family	Chemical constitutes	Use	Characteristic
Ashoka (Ashoka bark, Ashoka)	Dried stem bark of the plant *Saraca Indica Linn*. (Leguminosae)	It contains 6% tannins and anthocynin derivative such as Leucocynidine, Leucopelargonidine and Leucoanidine Steroidal compounds like 24-Methylcholest-5en-3β-ol and β-Sitosterol	Uterine tonic, Sedative Oxytocic	Adultrants: Polyalthialongifolia Microscopy: It contains prismatic crystals of Ca Oxalate
Pale Catechu (Gambier, Catechu)	Dried aqueous extracts produced from the leaves and young twigs of *Uncaria Gambier Roxburgh* (Rubiaceae)	7–30% Pseudo tannin catechin and 22–55 % pholbatannin catechunic acid It also contains catechu red, Gambier fluorescin and quercetin. Indole alkaloids like gambirtannin	Local astringents Dyeing and tanning industries	It gives positive test with Match stick test, Vanilline HCl acid test and Gambier fluorescin test
Black catechu (Cutch,Kattha)	Dried aqueous extracts produced from the heartwoods *of Acacia Catechu*. (Leguminosae)	Same as pale catechu	Astringents, Appetizers ,cure troubles of mouth, throat and diarrhoea Dyeing and tanning	Microscopy: It contains prismatic crystals of Ca Oxalate

Multiple Choice Questions

1. Chemically gums consist of
(a) Calcium (b) Potassium
(c) Magnesium (d) All of the above

2. Fiehe's test is for
(a) Artificial invert sugar
(c) Glycosides
(b) Alkaloids
(d) Tannins

3. Indian gum is obtained from
(a) *Astragalus gummifer*
(b) *Acacia rabica*
(c) *Gelidium amansi*
(d) *Solanum tuberosum*

4. Carrageen an is a
(a) Sulphated polysaccharide
(b) Glycoside
(c) Alkaloid
(d) Tannin

5. Ferulic acid present in asafoetida on treatment with HCI produces
(a) Oleic acid (b) Umbellic acid
(c) Palmitic acid (d) Stearic acid

6. In which plant trichomes contain resin?
(a) Male fern (b) Colophony
(c) Indian hemp (d) Asafoetida

7. One of the following is also known as Indian gooseberry:
(a) Behda (b) Harde
(c) Amla (d) Neem

8. Behda consist of dried ripe fruits of *Terminalia balerica,* which belongs to family
(a) Compositeae (b) Umbelliferae
(c) Combritaceae (d) Liliaceae

9. Triphlachurna contains
(a) Amla (b) Bahda
(c) Harde (d) All

10. Balsams are resinous substances which contain large proportions of
(a) Resins and volatile oils
(b) Gum, resin and volatile oil
(c) Glycosides and resins
(d) Benzoic acid, cinnamic acid and their esters

11. Galls are vegetable outgrowths formed on the twigs of
(a) Myrobalans (b) Bearberry leaves
(c) Dyer's oak (d) Wild cherry

12. The predominant chemical constituent of galls is
(a) Gallic acid (b) Gallotannic acid
(c) Ellagic acid (d) β-sitosterol

13. The algae *Garcilaria contervoides* is used for the preparation of
(a) Pectin (b) Algin
(c) Agar (d) Isabgol

14. Calcium salt of acidic polysaccharides is present in
(a) Plantago (b) Agar
(c) Bael (d) Guar gum

15. Barium chloride is used for the identification of
(a) Guar gum (b) Agar
(c) Acacia (d) Tragacanth

16. Catechins and gallic acids are the examples of
(a) Hydrolsable tannins
(b) Non-hydrolysable tannins
(c) Condensed tannins
(d) Pseudotannins

17. Gold beater's skin test is used to detect the presence of
(a) Resins (b) Alkaloids
(c) Tannins (d) Glycosides

18. Colophony contains about 90% of
(a) Resins (b) Fatty acid esters
(c) Resins (d) Resin alcohol

19. *Myroxylon balsmum* is the official source of
(a) Peru balsam (b) Tolu balsam
(c) Storax (d) Colophony

20. *Cymopsis tetragonolobus* is a source for
(a) Karay gum (b) Guar gum
(c) Algin (d) Agar

21. Guggulipid obtained from the commiphoramukul belongs to family
(a) Burseracease (b) Solanaceae
(c) Apocynaceae (d) Araliaceae

22. Commercially dextran is known as
(a) Sephadex (b) Sepharose
(c) Bio-gel (d) Both (a) and (b)

23. Black catechu gives _____ colour with $FeCl_3$
(a) Green (b) Blue
(c) Red (d) Violet

24. Synonum of amla is
(a) Arjun (b) Harda
(c) Goose berry (d) Beleric myrobalan

25. Bahera belongs to _____ family.
(a) Leguminpsae (b) Combretaceae
(c) Liliaceae (d) Apocynaceae

26. Example of pseudo tannis type is
(a) Coffee (b) Gallotannis
(c) Cinchona (d) Both (a) and (b)

27. Gallic acid is an active chemical constituent of
(a) Ashoka (b) Arjuna
(c) Pterocarpus (d) Tannic acid

28. *Acacia catechu* belongs to family
(a) Fagaceae (b) Leguminosae
(c) Euphorbiaceae (d) Apocynaceae

29. Condensed tannins
(a) Are non-hydrolysable tannins
(b) Are hydrolysable
(c) Do not show Gold beater skin test
(d) None of the above

30. Ashoka bark contains
(a) 1% of tannins (b) 6% of tannins
(c) 10% of tannins (d) 12% of tannins

31. Gumghatti is classified as a
(a) Glycosides (b) Tannins
(c) Volatile oils (d) Carbohydrates

32. Caramel has _____ as a chemical constituent.
(a) Burnt sugar (b) Glucose
(c) Mannitol (d) Arabin oxidase

33. Arabin oxidase is present in one of the following carbohydrate:
(a) Honey (b) Manna
(c) Caramel (d) Indian gum

34. Trgacanth contains _____ % of moisture content.
(a) 10 (b) 13 to 18
(c) 15 (d) 20

35. _____% of pectin is obtained from carrots.
(a) 10 (b) 10 to 12
(c) 10 to 15 (d) 5

36. Potato starch contains _____ % of ash value.
(a) Not more than 1%
(b) Not more than 8%
(c) Not more than 0.3%
(d) Not more than 4%

37. Wheat is derived from
(a) *Zea mays* (b) *Oryza sativum*
(c) *Triticum sativum* (d) *Solanum tuberosum*

38. All of the following come under Leguminosae except
(a) Acacia (b) Guar gum
(c) Isapgol (d) Tragacanth

39. Iaspgol seeds are adulterated with
(a) *Plantago aristala* (b) *Plantago lanciolata*
(c) *Plantago purshi* (d) *Plantago pysllium*

40. Tannins do not respond to
(a) Goldbeater's skin test
(b) Phenazone test
(c) Match-stick test
(d) Borntrager's test

41. Hydrolysable tannins on hydrolysis by acid yields
(a) Benzoic acid
(b) Gallic acid
(c) Sodium bicarbonate
(d) Stearic acid

42. With ferric chloride hydrolysable tannins produce
(a) Blue colour (b) Red colour
(c) Cream colour (d) Yellow colour

43. The purgative property of myrobalan is due to presence of
(a) Quinoline derivative
(b) Anthracene derivative
(c) Indole derivative
(d) None of the above

44. Gossypol, a compound that has received major attention as male contraceptive
(a) Is a hydroxylated bi naphthalene derivative found in cotton seed oil
(b) Is an aorizanol ester found in rice bran oil

(c) Exhibits toxicity such as hypokalemic-induced paralysis
(d) Acts as an androgen antagonist.

(A) b, c (B) a, d
(C) b, d (D) a, c

45. Myrrh is
(a) Acid resin
(b) Ester resin
(c) Resin alcohols
(d) Resenes

ANSWER KEYS

1. (d)	**2.** (a)	**3.** (b)	**4.** (a)	**5.** (b)	**6.** (c)	**7.** (c)	**8.** (c)	**9.** (d)	**10.** (d)
11. (c)	**12.** (b)	**13.** (c)	**14.** (b)	**15.** (b)	**16.** (d)	**17.** (c)	**18.** (a)	**19.** (b)	**20.** (b)
21. (a)	**22.** (a)	**23.** (b)	**24.** (c)	**25.** (b)	**26.** (c)	**27.** (d)	**28.** (b)	**29.** (a)	**30.** (b)
31. (d)	**32.** (a)	**33.** (d)	**34.** (c)	**35.** (a)	**36.** (c)	**37.** (c)	**38.** (c)	**39.** (b)	**40.** (d)
41. (b)	**42.** (a)	**43.** (b)	**44.** (b)	**45.** (a)					

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UNIT 5

NIPER SPECIAL

NIPER – Seats Matrix

NIPER JEE – Examination Syllabus

NIPER Special

NIPER JEE – Question Paper I

NIPER JEE – Question Paper II

NIPER JEE – Question Paper III

NIPER JEE – Question Paper IV

NIPER JEE – Question Paper V

Some Tips for Preparation of NIPER JEE and GPAT

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NIPER – SEATS MATRIX

MASTER PROGRAMME FOR 2016 – 2017

	NIPER Ahmedabad	
SR. NO.	**Department**	**Total**
1	Medicinal Chemistry	8
2	Pharmaceutics	12
3	Pharmacology & Toxicology	7
4	Biotechnology	7
5	Natural Products	6
6	Pharmaceutical Analysis	8
7	Medical Devices	7
8	Total Seats	55
9	PH Seats	2
10	Total with PH Seats	57
11	Note: One PH Candidate will be adjusted in any discipline	
	NIPER Guwahati	
SR. NO.	**Department**	**Total**
1	Pharmacology & Toxicology	20
2	Pharmacy Practice	10
3	Biotechnology	10
4	Total Seats	40
5	PH Seats	1
6	Total with PH Seats	41
7	Note: One PH Candidate will be adjusted in any discipline	
	NIPER Hajipur	
SR. NO.	**Department**	**Total**
1	Pharmacy Practice	15
2	Biotechnology	15
3	Pharmacoinformatics	15
4	Total Seats	45
5	PH Seats	1
6	Total with PH Seats	46
7	Note: One PH Candidate will be adjusted in any discipline	

	NIPER Hyderabad	
SR. NO.	**Department**	**Total**
1	Medicinal Chemistry	30
2	Pharmaceutics	15
3	Pharmacology & Toxicology	15
4	Pharmaceutical Analysis	15
5	Regulatory Toxicology	8
6	Pharmaceutical Technology (Process Chemistry)	8
7	Total Seats	91
8	PH Seats	3
9	Total with PH Seats	94
10	Note: One PH Candidate will be adjusted in any discipline	
SR. NO.	**Department**	**Total**
1	MBA (Pharm)	20
2	PH Seats	1
3	Total with PH Seats	21
	NIPER Kolkata	
SR. NO.	**Department**	**Total**
1	Medicinal Chemistry	17
2	Natural Products	17
3	Pharmacoinformatics	16
4	Total Seats	50
5	PH Seats	2
6	Total with PH Seats	52
7	Note: One PH Candidate will be adjusted in any discipline	
	NIPER Raebareli	
SR. NO.	**Department**	**Total**
1	Medicinal Chemistry	20
2	Pharmaceutics	15
3	Pharmacology & Toxicology	7
4	Total Seats	42
5	PH Seats	1
6	Total with PH Seats	43
7	Note: One PH Candidate will be adjusted in any discipline	

	NIPER S.A.S Nagar	
SR. NO.	**Department**	**Total**
1	Medicinal Chemistry	43
2	Natural Products	17
3	Traditional Medicine	5
4	Pharmaceutical Analysis	8
5	Pharmacology & Toxicology	22
6	Regulatory Toxicology	9
7	Pharmaceutics	16
8	Pharmaceutical Technology (Formulation)	7
9	Biotechnology	31
10	Pharmacy Practice	8
11	Clinical Research	8
12	Pharmacoinformatics	20
13	Pharmaceutical Technology (Process Chemistry)	16
14	Pharmaceutical Technology (Biotechnology)	10
15	Total Seats	220
16	PH Seats	7
17	Total with PH Seats	227
18	Note: PH Candidates will be adjusted in any discipline	
SR. NO.	**Department**	**Total**
1	MBA (Pharm)	43
2	PH Seats	1
3	Total with PH Seats	44

NIPER JEE – EXAMINATION SYLLABUS

Natural Products:

1. In natural products more stress should be given on Phytochemistry part rather than biological aspects but you should know about biological sources and chemical constituents of important ones.
2. Methods of extraction, isolation and characterization of natural products. Various separation techniques used for isolation of natural products.
3. Biosynthetic pathways.
4. Primary metabolites, their examples.
5. Secondary metabolites, various classes of secondary metabolites - Here most important part is chemistry of these classes. (e.g. Alkaloids, glycosides, tannins, lignans, saponins, lipids, flavonoids, coumarins, anthocyanidines etc.).
6. Important therapeutic classes: antidiabetics, hepatoprotectives, immmunomodulators, neutraceuticals, natural products for gynecological disorders, anti-cancer, anti-viral (mainly anti-HIV), adaptogens etc. dietary antioxidants, marine natural products, plant growth regulators.
7. Standardization of natural products.
8. Stereochemistry and spectroscopy applied to some phytochemical constituents/ pure natural products- NMR, IR. Stereochemistry: Fischer, Sawhorse and Newman projection formulae.

References:

For various therapeutic classes:

- Trease and Evans' Pharmacognosy, 16th Edition., Elsevier

For spectroscopy:

- Spectrometric Identification of Organic Compounds by Robert M. Silverstein, 8th Edition, Willey Publication.
- Organic Spectroscopy by William Kemp, Pelgrave Publication.
- Introduction to Spectroscopy By Donald L. Pavia, 4th Edition, Brooks/Cole Publication.

For stereochemistry:

- Organic Chemistry. Vol. 2 by I.L. Finar., 3rd Edition, Longmans Green & Co. Publication.

Pharmacology and toxicology:

1. Pharmacokinetics, pharmacodynamics, pharmacological effect, desired, undesired, toxic, adverse effects.
2. Bioavailability, bioequivalence, various factors of ADME (From Bramhankar)
3. Drug metabolism: various pathways and other details.
4. Drug interactions, agonist, antagonist, partial agonist, protein binding, drug distribution, distribution volume, excretion pathways etc.
5. Mechanism of drug action, Receptor-theories, types, spare, silent, orphan, pre & post synaptic, drug-receptor interaction- Various adrenergic, cholinergic and other receptors. Detailed study of CNS pharmacology, especially opioid receptors.

6. Diseases: Especially diabetes, malaria, leishmaniasis, TB, hypertension, myocardial ischemia, inflammation, and immunomodulation.
7. Chemotherapy and pathophysiology- knowledge of antibiotics, their mode of action and the microorganisms responsible for various common diseases.
8. Mechanism of Action, toxicity and specific use of every class of drugs.
9. Pharmacological screening: general principles, various screening models, screening methodologies (in vitro and in vivo tests). Detailed study of anti- malarial, anti-tubercular, anti-leishmanial, anti diabetic bioassays. Bioassay methods, various requirements. Brief knowledge of the statistical tests.
10. Concept of CGMP, CAMP, desensitization, tachyphylaxis, drug dependence and drug interaction.
11. Study of basis of threshold areas of work in NIPER in pharmacology dept. mentioned in brochure.

References:

- Rang & Dale's Pharmacology 8th Edition, Elsevier Publication.
- Essentials of Medical Pharmacology By K. D. Tripathi, 7th Edition, Jaypee Brothers Medical Publishers

Practice of Pharmacy:

1. Adverse Drug Reactions.
2. Rational drug use as well as some typical case studies in diabetes and hypertension and some case study regarding Anti-infective therapy, Diabetes, Heart diseases are important.
3. Therapeutic drug monitoring
4. Hospital pharmacy
5. Clinical pharmacy

References:

- Clinical Pharmacy and Therapeutics By Roger Walker, 5th Edition, Churchill Livingstone.
- Remington: The Science and Practice of Pharmacy (Remington the Science and Practice of Pharmacy), 21st Edition, Lippincott Williams & Wilkins (LWW).

Pharmacoinformatics:

1. Terminologies related with new emerging informatics e.g. proteomics, genomics, QSAR (2D, 3D, regression, correlation) and application of every 3D QSAR software.

Biotechnology:

1. General knowledge and understanding of cycles, carbohydrates, mucopolysaccharides, proteins, lipids, amino acid their metabolism.
2. Enzymes- types of enzymes, allosteric inhibition and enzyme kinetics etc.
3. General understanding of Vitamins.
4. Staining.
5. Understanding of HIV, Influenza, Cancer (Role of DNA and Telomerase).
6. Genetic Engg: Gene expression, mutation, replication, transcription, translation, recombination, bacteriophages.
7. Cloning: methods, isolation of nucleic acids, enzymes in cloning (restriction endonucleases, DNA ligase, DNA gyrase, polymerases etc), and functions of these enzymes. Microassays- PCR, Blotting. Pallindromes.

8. Fermentation: fermenters, fermentation process, its regulation, conditions, bioprocessors, various enzymes in fermentation technology. Fermentation of Antibiotics (fermentation of penicillin, cephalosporins, streptomycin- organisms used), vitamins (B12), amino acids, organic acid production- hydroxy acids such as lactic acid etc. Chemical engineering aspects related to fermentation
9. Monoclonal antibodies, insulin, interferons, enkephalins, angiotensin analogues and other peptides.
10. Gene therapy: methods and applications.
11. Vaccines and their storage.
12. Use of microorganisms in pharmaceutical industries.
13. Haematic diseases- anaemia, thalassemia, porpyhyrins.
14. DNA purification, mutation.
15. Electrophoresis.
16. Tests of biochemistry

References:

- Pharmaceutical Biotechnology By S.P. Vyas and V.K. Dixit, CBS Publishers & Distributors Pvt. Ltd.
- Indian Pharmacopoeia 2014, 7th Edition, Appendix Section
- Biochemistry By U.Satyanarayana & U. Chakrapani, 4th Edition, Books and Allied (P) Ltd.

Pharmaceutical analysis:

1. Stability testing of pharmaceuticals, various stability tests, kinetic studies, shelf life determination, thermal stability, formulation stability.
2. Various analytical techniques
3. Tests: physical and chemical tests, limit tests, microbiological tests, biological tests, disintegration and dissolution tests.
4. Spectroscopic methods; UV, NMR, IR, MS, FT-IR, FT-NMR, ATR (Attenuated Total Reflectance), FT-Raman-basics and applications.
5. Thermal techniques: DSC, DTA, TGA, etc. Particle sizing: law of diffraction.
6. Chromatography- detailed.
7. QA and QC: GLP, TQM, ISO system.

Details of every chromatographic method:

General principles, classification, normal & reversed phase, bonded phase, separation mechanisms.

Types:

a) Column chromatography.
b) Flash chromatography.
c) Vacuum liquid chromatography.
d) TLC, HPTLC, OPLC (over pressure layer chromatography)
e) HPLC.
f) Centrifugal chromatography.
g) Counter - current chromatography.
h) Droplet - counter current chromatography.
i) Ion exchange chromatography.

j) Affinity chromatography.
k) Size exclusion & Ion Pair chromatography,
l) Perfusion chromatography.
m) Fast protein liquid chromatography.
n) Supercritical chromatography.
o) GC, GC-MS, LC-MS, LC-MS/MS.

References:

- Spectrometric Identification of Organic Compounds by Robert M. Silverstein, 8th Edition, Willey Publication.
- Organic Spectroscopy by William Kemp, Pelgrave Publication.
- Introduction to Spectroscopy By Donald L. Pavia, 4th Edition, Brooks/Cole Publication.
- Instrumental Methods Of Chemical Analysis by G.R. Chatwal, S.K. Anand, Himalaya Publication House.
- Analytical Chemistry by Gary D. Christian,7th Edition, Willey.

Pharmaceutical Chemistry

1. IUPAC nomenclature, R and S nomenclature, E and Z isomerism, atropiisomerism, Conformations, Hybridization, aromaticity, Huckel's rule reaction mechanisms- Electrophilic, Nucleophilic, SN_1, SN_2, SNi, Elimination E_1 E_2 etc.
2. Ester hydrolysis, Aac1, Aac2 all eight mechanisms (Jerry march) Markovnikoves rule, Bredts rule, Stereoselectivity, stereospecificity, regioselectivity, chemoselectivity, chirality, stereochemistry, conformations, rearrangements, acids and bases.
3. Imine-enamine Tautomerism, keto-enol tautomerism, pericyclic reactions, racemic mixture, resolution methods.
4. Amino acids proteins, various methods for amino acid detection, Ninhydrin test, peptide sequencing, structures of amino acids, essential and nonessential amino acids.
5. Carbohydrates classification, osazone test, mutarotation, etc
6. Various Heterocycles, Heterocycle synthesis and name reactions involve in it.
7. Reaction kinetics, first second third and pseudo first order reactions, radio labeling for determination of mechanism.
8. Common name reactions like Aldol, Claisen, Perkin, Dickmann, Darzen Cannizarro's reaction, Prins reaction, Wolf-kishner and Clemenson reduction.

References:

- March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure, 6th Edition, Willey.
- Organic Chemistry by by Morrison Boyd & Bhattacharjee, 7th Edition, Pearson.
- Organic Chemistry. Vol. 1/ 2 by I.L. Finar., 3rd Edition, Longmans Green & Co. Publication.

Pharmaceutics and Formulation:

1. Drug delivery systems (DDS): NDDS models, osmotic pumps, various release patterns e g. Controlled release, delayed release, sustained release etc., and order of release. Carriers in DDS: polymers and their classification, types, carbohydrates, surfactants, proteins, lipids, prodrugs etc. Oral controlled DDS, factors affecting controlled release. Transdermal drug delivery systems (TDDS): principles, absorption, enhancers, and evaluation of TDDS.
2. Parenterals: requirements, advantages, disadvantages, release pattern, route of drug delivery.
3. Drug targeting: microspheres, nanoparticles, liposomes, monoclonal antibodies, etc. and some idea on polymers used in this field.
4. Preformulation study and application.

5. Complexation, solubilization, polymerization, viscosity measurements.
6. Dosage form development- stages, implications of dosage form.
7. Additives of formulation, types, examples, advantages, disadvantages, drug excipient interaction, incompatibility, various types of incompatibilities.
8. Dosage forms: solid (tablets, capsules, pills etc), liquid (emulsion, suspension etc), sterile (injectables), and aerosols. Principles, advantages, disadvantages and problems.
9. Packaging: materials, labeling etc. Types of containers (eg. Tamper-proof containers)
10. In process controls, Product specification, documentation.
11. Compartmental modeling,Bioavailability, bioequivalence studies, Methods of improvement of oral bioavailability.
12. Evaluation of formulation, principles and methods of release control in oral formulations.

References:

- Remington: The Science and Practice of Pharmacy (Remington the Science and Practice of Pharmacy), 21st Edition, Lippincott Williams & Wilkins (LWW).
- The Theory and Practice of Industrial Pharmacy by Lachman/Liebermans, 4th Edition, CBS Publishers.
- Physical Pharmacy: Physical Chemical Principles in the Pharmaceutical Sciences by Alfred N. Martin. Lippincott Williams & Wilkins.
- Biopharmaceutics and Pharmacokinetics by By Brahmankar DM Jaiswal SB, Vallabh Prakashan.
- Modern Pharmaceutics by Gilbert S. Banker, Juergen Siepmann, Christopher Rhodes, 4th Edition, CRC Press.

Thrust areas of NIPER:

1. Microbial and viral diseases: Tuberculosis, Yeast and Fungi.
2. Parasitic and tropical diseases: Malaria, Leishmaniasis, Amoebiasis.
3. Metabolic Disorders: Diabetes.
4. Strokes, Peptide and carbohydrate chemistry.
5. Genomics and proteomics: Yeast.
6. Fungi, Hormonal disorders: TRH related.

NIPER SPECIAL

ISOSTERES

Isosteres are molecules or ions with the same number of atoms and the same number of valence electrons. As a result, they can exhibit similar pharmacokinetic and pharmacodynamic properties.

Some examples of isoteres are

- fluorine and hydrogen
- carbon dioxide (CO_2) and nitrous oxide (N_2O)

Langmuir

Compounds or groups of atoms having same number of atoms or electrons.

Examples-N_2 and CO, CO_2 and N_2O, N_3– and NCO^-

Grimm (Hydride Displacement Law)

Addition of hydride to an atom gives to the resulting pseudo atom, the properties of the atoms with the next higher atomic numbers.

Hydride Displacement Law

C	N	O	F	Ne	Na^+
	CH	NH	OH	FH	–
		CH_2	NH_2	OH_2	FH_2+
		CH_3	NH_3	OH_2+	
			CH_4	NH_4+	

Erlenmeyer-Atoms, ions or molecules in which peripheral layers of electron can be considered identical.

Examples-Atoms in the same column of periodic table, Cl, CN and SCN.

Bio-Isosterism

Friedmann

Bio-isosteres are atoms or molecules that fit in broadest definition of isosteres and have same biological activity.

Parameters affected with Bio-isosteric replacement

Size	Conformation	Inductive and mesomeric effect	
Solubility	H-bond formation capacity		Polarizibility
Stability	Reactivity	PK_a value	Hydrophobicity

Reason for Bio-isosteric Replacement

Greater selectivity	less side effect	Decreased toxicity
Improved pharmacokinetics	Increased stability	Simplified synthesis
Patented lead compound		

NOTE

1. **OH, NH_2 and SH 2. C=O, C=NH and C=S 3. Methyl and CF_3 4. CN and CF_3**
2. **In sulphonamides, the phenyl group may be replaced by hetero cyclic rings such as sulphathiazole, sulphapyridine, sulphapyrimidine, Sulphapyrazine.**
3. **Carboxylic acid group may be replaced by tetrazole, hydroxyisoxazole, phosphonate, sulphonate, acylcynamide, hydroxamic, sulphonimide, sulphonamide, oxadiazolone.**
4. **Peptide (amide) may be replaced by hydroxyl ethyl or Alpha-difluoroketone.**
5. **Antibacterial sulphonamides are isostere with para amino benzoic acid.**
6. **5-Flurouracil is isostere with uracil and interfere in DNA synthesis.**

2D-NMR (2 Frequency axes and 1 Pseudo intensity axis)

- COSY Spectroscopy-information about Proton-Proton coupling
- NOESY (Nuclear overhauser exchange spectroscopy)-information regarding conformation and 3 dimensional structure of molecule.
- HETCOR (Heteronuclear spectroscopy)-tells about one bond Proton-Carbon coupling.
- HMQC-One bond Proton-Carbon coupling (similar to HETCOR BUT without noise or zero noise level)
- DEPT (Distortion less enhancement by polarization transfer)-information about number of protons attached to the carbon or tells about methyl or methylene or methane protons.
- HMBC-Two or three bond Proton-Carbon coupling
- INADEQUATE (Incredible natural abundance double quantum transfer experiment)-Directly attached (one bond) Carbon-carbon coupling.

Optical Rotary dispersion and Circular Dichronism (ORD-CD)

Optical rotation: The rotation of linearly polarized light by the sample.

- Usually reported as a specific rotation [α], measured at a particular T, concentration and λ (normally 589nm; the Na D line).
- Molar rotation $[\Phi] = [\alpha] \times MW \times 10^{-2}$

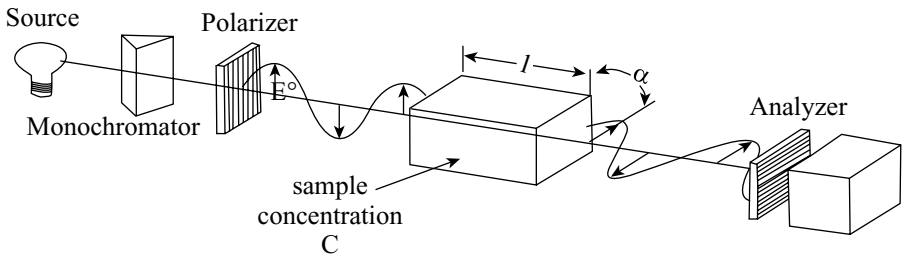
$$[\alpha] = \frac{10^2 \alpha}{lc}$$

l = path length in decimeters

$$c = \frac{g}{100\ mL}$$

$$\text{rotation}\left(\text{rad cm}^{-1}\right) = \phi = \frac{\pi}{\lambda}(n_L - n_R)$$

Where n is refractive index, ι is wavelength, χ is angle of rotation. Note: (1 cm = 10 decimeters)



Optical rotary dispersion: The variation of optical rotation as a function of wavelength. The spectrum of optical rotation.

- If the refractive indices of the sample for the left and right handed polarized light are different, when the components are recombined, the plane-polarized radiation will be rotated through an angle α.
- n_l, n_r are the indices of the refraction for left-handed and right-handed polarized light.
- $\alpha = \frac{n_l - n_r}{\lambda}$ α is in radians per unit length (from λ)

NOTE

- ORD curve is a plot of molar rotation **[α]** or **[*M*]** vs λ.
- Clockwise rotation is plotted positively; counterclockwise rotation is plotted negatively.
- ORD is based solely on the index of refraction.
- So-called plain curve is the ORD for a chiral compound that lacks a chromophore.
- Chiral compounds containing a chromophore can give anomalous or cotton effect curves.

Circular Dichronism: The difference in absorption of left and right circularly light.

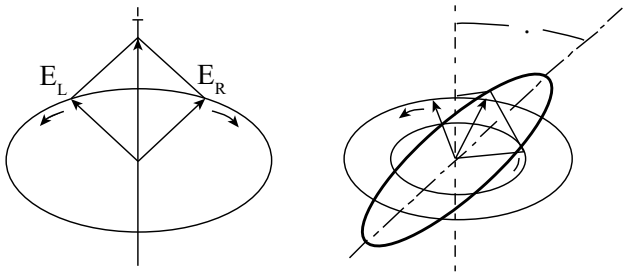
Circular dichronism (CD) spectroscopy measures differences in the absorption of left-handed polarized light versus right-handed polarized light which arise due to structural asymmetry.

- All optically active compounds exhibit CD in the region of the appropriate absorption band.
- CD is plotted as ε_l-ε_r vs λ
- For CD, the resulting transmitted radiation is not plane-polarized but elliptically polarized.

Molar circular dichroism $= \varepsilon_l - \varepsilon_r = \dfrac{k_l - k_r}{c}$ k from $I = I_o 10^{-kd}$

$$q\left(\text{rad cm}^{-1}\right) = \frac{2.303\left(A_L - A_R\right)}{41}$$

$\ominus$ is ellipticity, l is path length and A is absorbance.

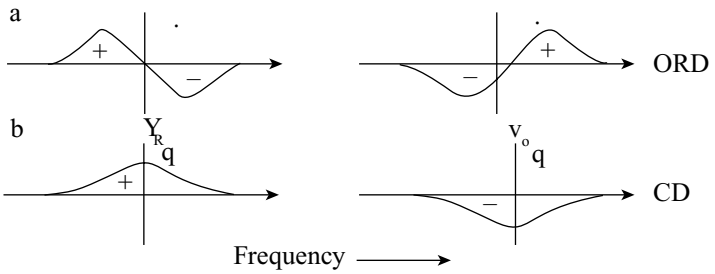


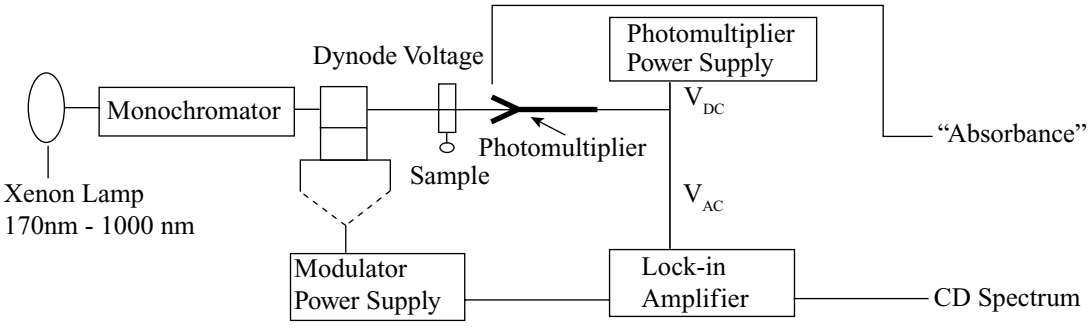
Plain Polarized Light Elliptically Polarized light

The difference between the absorption of left and right handed circularly-polarized light and is measured as a function of wavelength. CD is measured as a quantity called **mean residue ellipticity**, whose units are *degrees-cm²/dmol.*

Comparison of ORD and CD

- CD plots are Gaussian rather than S-shaped.
- Positive or negative deflections depend on the sign of $\Delta\varepsilon$ or $[\theta]$ and correspond to the sign of the Cotton effect.
- ORD spectra are dispersive (called a *Cotton effect* for a single band) whereas circular dichronism spectra are absorptive. The two phenomena are related by the so-called König-Kramers transforms.
- Maximum of the CD occurs at the absorption $\lambda_{max.}$
- Where there is more than one overlapping Cotton effect, the CD may be easier to interpret than the ORD with overlapping S-shaped bands.





The CD spectrometer

Application of CD

Determination of Protein **Secondary structure** (alpha-helix).

THERMA METHOD OF ANALYSIS

(1) Thermogravimetry

PRINCIPLE: TG is a technique in which a change in the weight of a substance is recorded as a function of temperature or time.

Instrument: Instrument used for thermogravimetry is thermobalance. Major components of a thermobalance are:

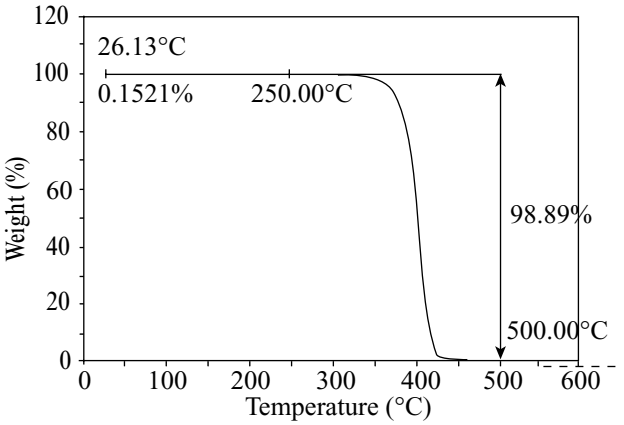
(1) Sample container, usually shallow platinum crucible.
(2) Furnace assembly
(3) Automatic recording balance (Micro balance)

Factors affecting thermogravimetry analysis are:

(1) heating rate
(2) furnace atmosphere
(3) crucible geometry
(4) sample characteristic

Data recorded in form of curve is known as **Thermogram.** Thermograms can be divided into two portions:

(1) Horizontal portion: Indicates region where there is no weight loss.
(2) Curved portion: Indicate regions of weight loss.



(2) Differential Thermal Analysis (DTA)

Principle:

A technique in which the temperature difference between a substance and a reference material is measured as a function of temperature, while the substance and reference are subjected to a controlled temperature programme.

- The difference in temperature called as differential temp (Δt) is plotted against temperature or a function of time.
- Physical changes usually result in endothermic peak, whereas chemical reactions those of an oxidative nature are exothermic.
- Endothermic reaction (absorption of energy) includes vaporization, sublimation, and absorption and gives downward peak.

Exothermic reaction (liberation of energy) includes oxidation, polymerization, and catalytic reaction and gives upward peak.

(3) Differential Scanning Calorimetry

PRINCIPLE: It is a technique in which the energy necessary to establish a zero temperature. Difference between the sample and reference material is measured as a function of temperature.

Here, sample and reference material are heated by separate heaters in such a way that their temp are kept equal while these temp. are increased or decreased linearly.

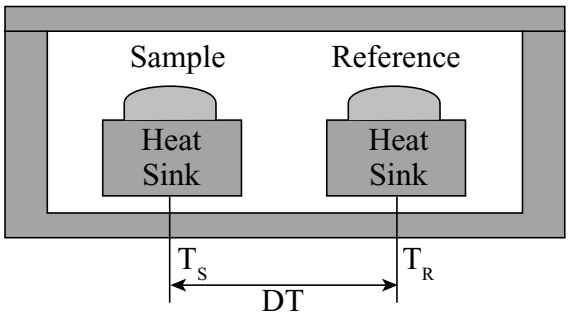
Endothermic reaction: If the sample absorbs some amount of heat during phase transition then reaction is said to be endothermic. In endothermic reaction, more energy is needed to maintain zero temperature difference between sample and reference.

E.g., Melting, boiling, sublimation, vaporization, desolvation.

Exothermic reaction: If the ample releases some amount of heat during phase transition, then reaction is said to be exothermic. In exothermic reaction, less energy needed to maintain zero temp difference between sample and reference.

E.g., crystallization, degradation, polymerization.

INSTRUMENT



Ideal DSC Curve

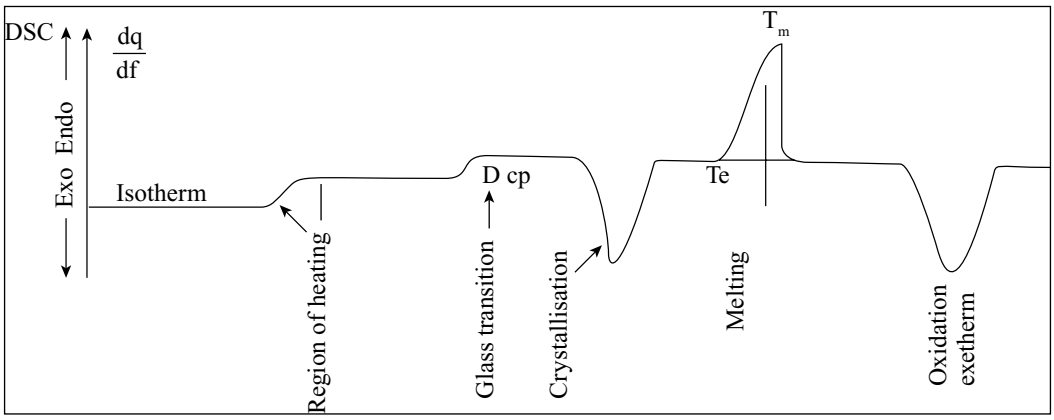


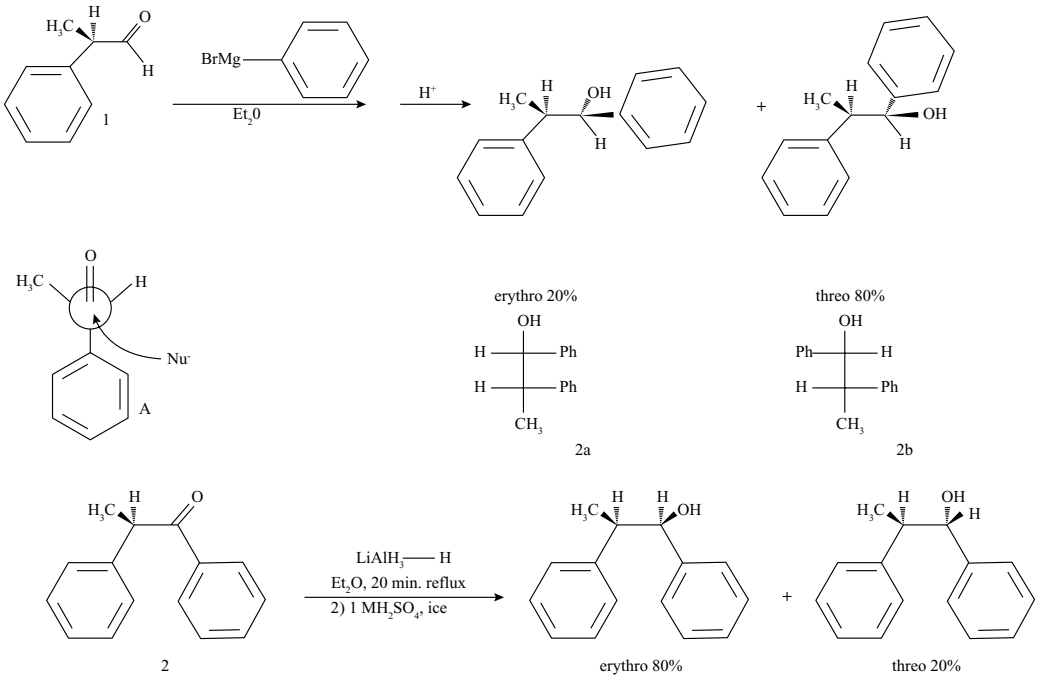
Figure 7.1 Typical transitions observed in DSC: T_s = extrapolated onser. T_m peak maximum.

- DSC is widely used to measure glass transition temperature and characterization of polymer.
- **Glass Transition temp (Tg):** Temperature at which an amorphous polymer or an amorphous part of crystalline polymer goes from hard, brittle state to soft, rubbery state.

Cram's Rule:

The Cram's rule of asymmetric induction developed by Donald J. Cram in 1952 is an early concept relating to the prediction of stereochemistry in certain acyclic systems.

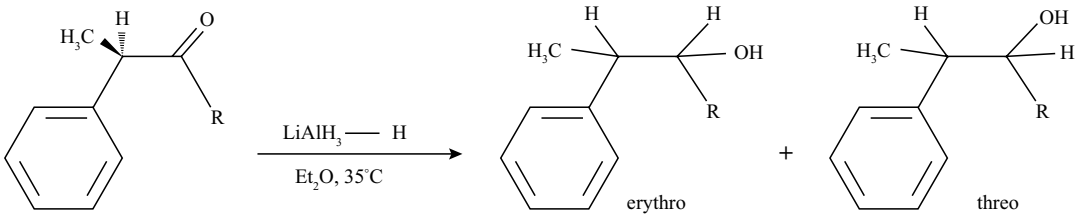
Rule : In certain non-catalytic reactions that diastereomer will predominate, which could be formed by the approach of the entering group from the least hindered side when the rotational conformation of the C-C bond is such that the double bond is flanked by the two least bulky groups attached to the adjacent asymmetric center.



The rule indicates that the presence of an asymmetric center in a molecule induces the formation of an asymmetric center adjacent to it based on steric hindrance.

Felkin model: The **Felkin model** (1968) named after Hugh Felkin also predicts the stereochemistry of nucleophilic addition reactions to carbonyl groups.

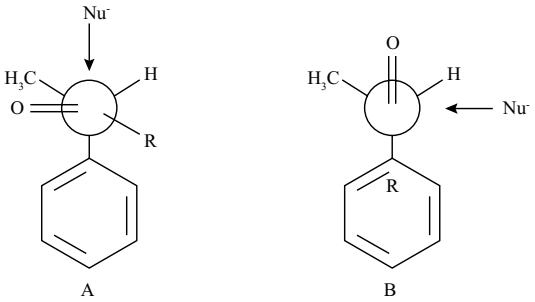
Felkin argued that the Cram model suffered a major drawback: an eclipsed conformation in the transition state between the carbonyl substituent (the hydrogen atom in aldehydes) and the largest α-carbonyl substituent. He demonstrated that by increasing the steric bulk of the carbonyl substituent from methyl to ethyl to isopropyl to isobutyl, the stereoselectivity also increased, which is not predicted by Cram's rule:



R = Me erythro:threo = 74:26
R = Et erythro:threo = 76:24
R = i-Pr erythro:threo = 83:17
R = t-Bu erythro:threo = 98:2

The Felkin rules are:

- The transition states are reactant-like.
- Torsional strain (Pitzer strain) involving partial bonds (in transition states) represents a substantial fraction of the strain between fully formed bonds, even when the degree of bonding is quite low. The conformation in the TS is staggered and not eclipsed with the substituent R skew with respect to two adjacent groups one of them the smallest in TS A.



For comparison TS B is the Cram transition state.

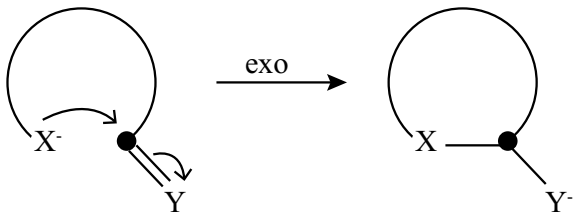
- The main steric interactions involve those around R and the nucleophile but not the carbonyl oxygen atom.
- A polar effect or electronic effect stabilizes a transition state with maximum separation between the nucleophile and an electron-withdrawing group. For instance haloketones do not obey Cram›s rule, and, in the example above, replacing the electron-withdrawing phenyl group by a cyclohexyl group reduces stereoselectivity considerably.

Baldwin Rules for Ring Closure:

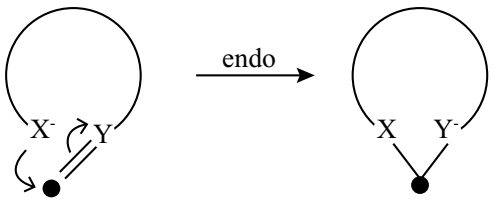
Baldwin's rules discuss the relative rates of ring closures of these various types. These terms are not meant to describe the absolute probability that a reaction will or will not take place, rather they are used in a relative sense. A reaction that is disfavoured (slow) does not have a rate that is able to compete effectively with an alternative reaction that is favoured (fast). However, the disfavoured product may be observed, if no alternate reactions are more favoured.

Terminology Used:

Prefix exo when the breaking bond is exocyclic to the smallest ring formed.



Prefix endo when the breaking bond is endocyclic to the smallest ring formed.



Numerical prefix describe the size of formed ring.

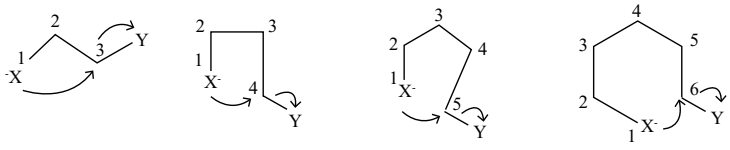
- Sufixes Tet, Trig and Dig indicate the geometry of the carbon undergoing the RC.
- Tetrahedral for sp^3 carbon
- Trigonal for sp^2 carbon
- Digonal for sp carbon

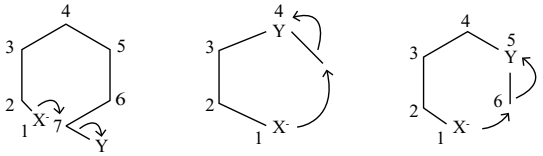
The rules classify ring closures in three ways:

- the number of atoms in the newly formed ring
- into ***exo*** and ***endo*** ring closures, depending whether the bond broken during the ring closure is inside (*endo*) or outside (*exo*) the ring that is being formed
- into ***tet***, ***trig*** and ***dig*** geometry of the atom being attacked, depending on whether this electrophilic carbon is *tet*rahedral (sp^3 hybridised), *trig*onal (sp^2hybridised) or *dig*onal (sp hybridised).

Rule 1: Tetrahedral Systems

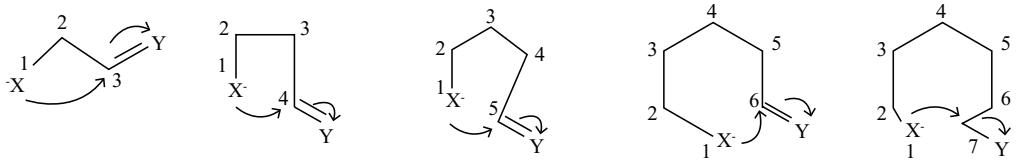
- 3 to 7-exo-Tet are all favoured processes
- 5 to 6-endo-Tet are disfavoured

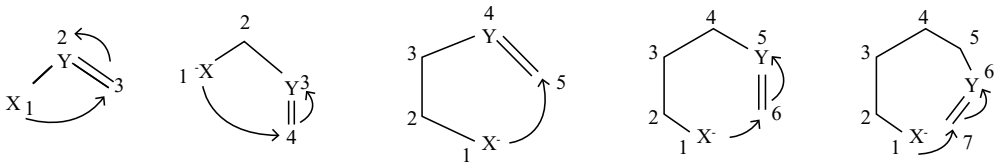




Rule 2: Trigonal systems

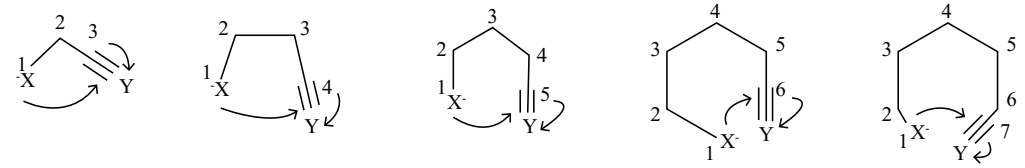
- 3 to 7-exo-Trig are all favoured processes
- 3 to 5-endo-Trig are disfavoured; 6 to 7-endo-Trig are favoured

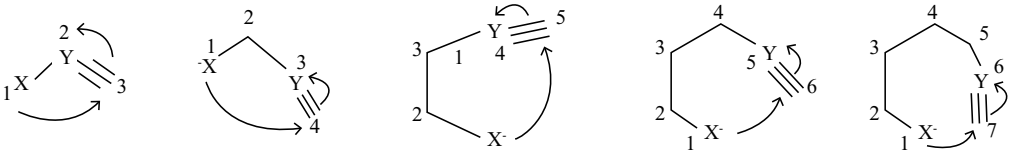




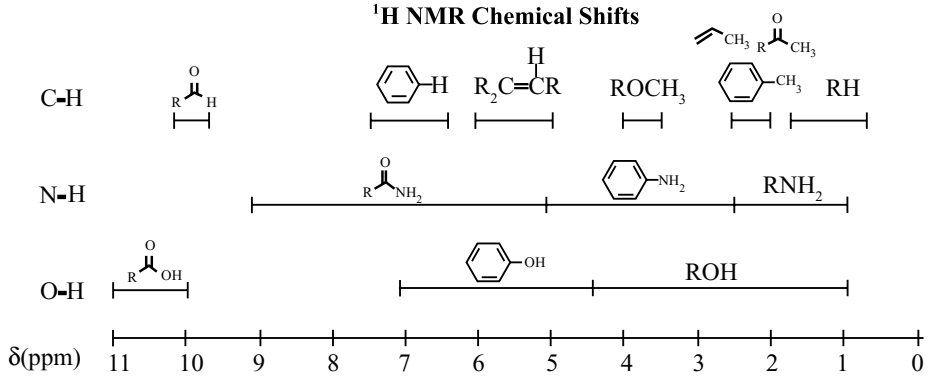
Rule 3: Digonal Systems

- 3 to 4-exo-Dig are disfavoured processes; 5 to 7-exoDig are favoured
- 3 to 7-endo-Dig are favoured

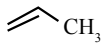
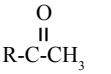




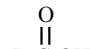
Common δ- Values of ^{1}H NMR Shift



Protons on Carbon

Type of C-H	δ (ppm)	Description of Proton
$R\text{-}CH_3$	0.9	alkyl (methyl)
$R\text{-}CH_2\text{-}R$	1.3	alkyl (methylene)
$R_3\text{-}C\text{-}H$	1.5-2	alkyl (methine)
	1.8	allylic (C is next to a pi bond)
	2-2.3	α to carbonyl (C is next to C=O)
$Ar\text{-}CH_3$	2.3	benzylic (C is next to Ph)
$RC\equiv C\text{-}H$	2.5	alkynyl
$R_2N\text{-}CH_3$	2-3	α to nitrogen (C is attached to N)

Protons on Oxygen/Nitrogen*

Type of H	δ (ppm)	Description
ROH	0.5-5	alcohol
ArOH	4-7	phenol
	10-13	carb. acid
RNH_2	0.5-5	amine
$ArNH_2$	3-5	aniline
	5-9	amide

**Protons on N or O typically have wide ranges of expected chemical shifts; the actual δ value depends on the solvent used, the concentration, temperature, etc.*

$R\text{-}CH_2\text{-}x$	2-4	α to halogen (C is attached to Cl,Br,I)
$RO\text{-}CH_3$	3.8	α to oxygen (C is attached to O)
$R\text{-}CH_2\text{-}F$	4.5	α to fluorine (C is attached to F)
$R_2C{=}C(H)R$	5-5.3	vinylic (H is attached to alkene C)
Ar-H	7.3	aromatic (H is on phenyl ring)
$R\text{-}C(=O)\text{-}H$	9.7	aldehyde (H is on C=O)

Note : aldehyde (-CHO) proton usually does not couple with neighboring H's so appears as a singlet

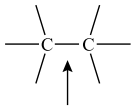
Because these protons are acidic and, therefore, exchangable, they may be broad peaks and usually do not couple with neighboring protons (typically they are broad singlets). If a protic deuterated solvent is used (e.g., D_2O or CD_3OD), then the NH and OH protons will exchange with the deuterium and the peaks will shrink or disappear entirely, since D(^{2}H) does not show up in the ^{1}H NMR spectrum.

R= alkyl group
Ar= aromatic ring, such as phenyl (Ph)

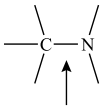
Infrared Tables (short summary of common absorption frequencies):

Bonds to Carbon (stretching wave numbers)

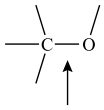
sp^3 C-X single bonds



not used

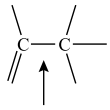


1000-1350
not very useful

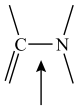


1050-1150
alkoxy C-O

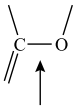
sp^2 C-X single bonds



not very useful

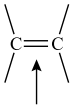


1250

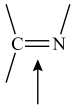


1100-1350
acyl and phenyl C-O

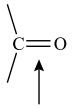
sp^2 C-X double bonds



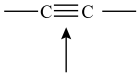
1600- 1680



1640-1690



1640-1810
expanded table
on next page

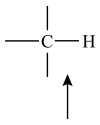


2100-2250

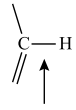
2240-2260

Stronger dipoles produce more intense IR bands and weaker dipoles produce less intense IR bands (sometimes none).

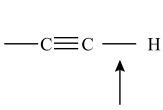
Bonds to Hydrogen (stretching wave numbers)



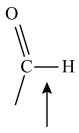
2850-3000
sp^3 C-H



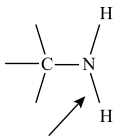
3000-3100
sp^3 C-H
(see sp^2 C-H bend
patterns below)



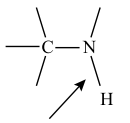
3300
sp^3 C-H
(sp C-H bend ≈ 620)



2700-2760
2800-2860
aldehyde C-H
(two bands)

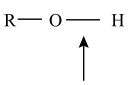


3100-3500
primary NH_2
(two bands)

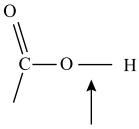


3100-3500
secondary N-H
(one band)

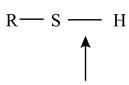
amides = strong, amines = weak



3200-3400
alcohol O-H

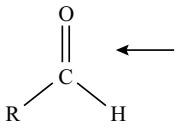
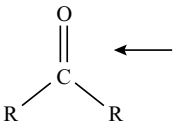
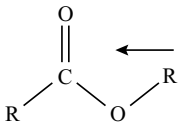
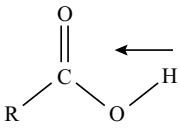


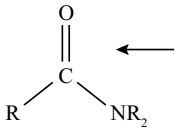
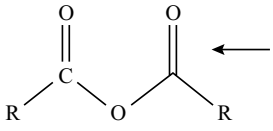
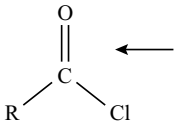
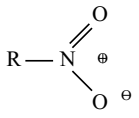
2500-3400
acid O-H



2550-2620
(very weak)
thiol S-H

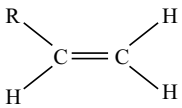
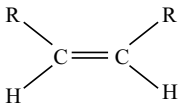
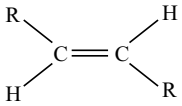
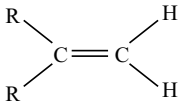
Carbonyl Highlights (stretching wave numbers)

Aldehydes	Ketones	Esters	Acids
			
saturated = 1725 conjugated = 1690 aromatic = 1700	saturated = 1715 conjugated = 1680 aromatic = 1690 6 atom ring = 1715 5 atom ring = 1745 4 atom ring = 1780 3 atom ring = 1850	saturated = 1735 conjugated = 1720 aromatic = 1720 6 atom ring = 1735 5 atom ring = 1775 4 atom ring = 1840	saturated = 1715 conjugated = 1690 aromatic = 1690

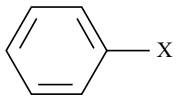
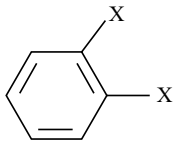
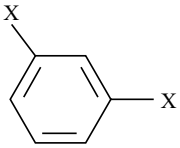
Amides	Anhydrides	Acid Chlorides	nitro
			
saturated = 1650 conjugated = 1660 aromatic = 1660 6 atom ring = 1670 5 atom ring = 1700 4 atom ring = 1745 3 atom ring = 1850	saturated = 1760, 1820 conjugated = 1725, 1785 aromatic = 1725, 1785 6 atom ring = 1750, 1800 5 atom ring = 1785, 1865	saturated = 1800 conjugated = 1770 aromatic = 1770	asymmetric = 1500- 1600 symmetric = 1300- 1390

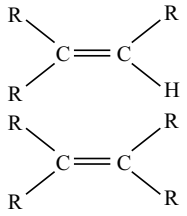
Very often there is a very weak C=O overtone at approximately 2 x $\overline{v}$ (≈3400 cm^{-1}).
Sometimes this is mistaken for an OH or NH peak.

sp^2 C-H bend patterns for alkenes

alkene substitution pattern	descriptive alkene term	absorption frequencies (cm^{-1}) due to sp^2 CH bend
	monosubstituted alkene	985-1000 900-920
	cis disubstituted alkene	675-730 (broad)
	trans disubstituted alkene	960-990
	gemical disubstituted alkene	880-900

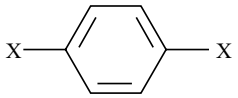
sp^2 C-H bend patterns for aromatics

aromatic substitution pattern	descriptive aromatic term	absorption frequencies (cm^{-1}) due to sp^2 CH bend
	monosubstituted aromatic	690-710 730-770
	ortho disubstituted aromatic	735-770
	meta disubstituted aromatic	680-725 750-810 880-900 (sometimes)



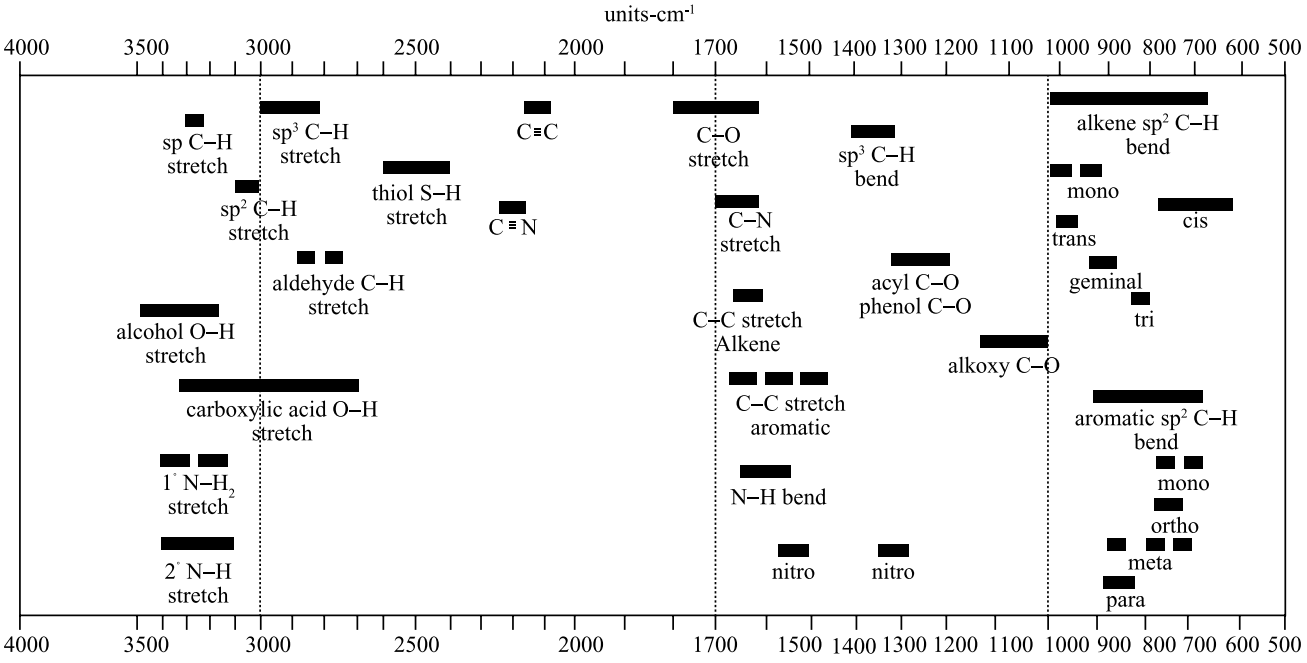
trisubstituted alkene — 790-840

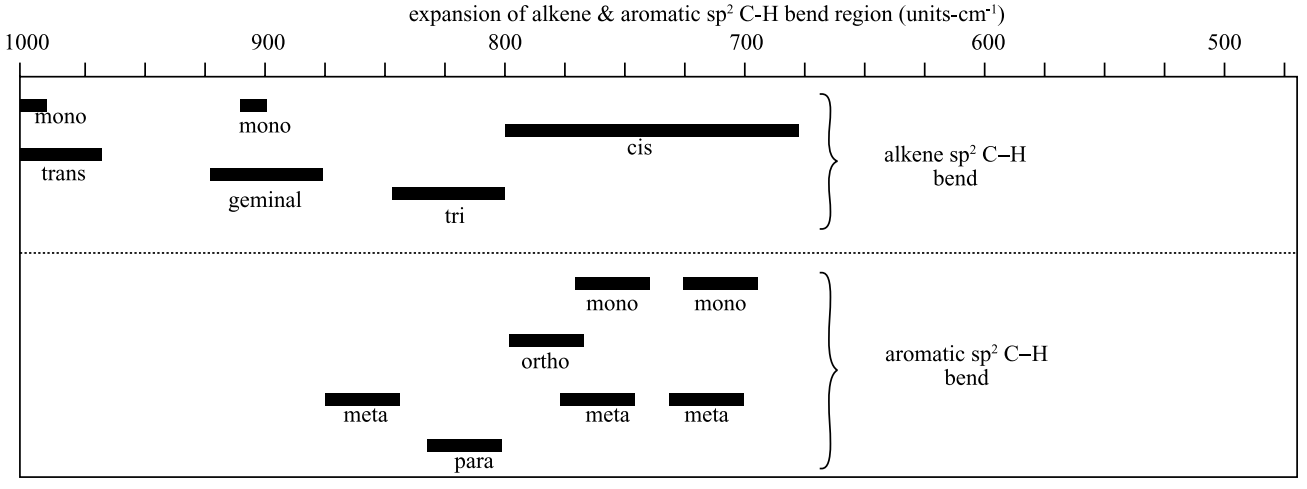
tetrasubstituted alkene — none

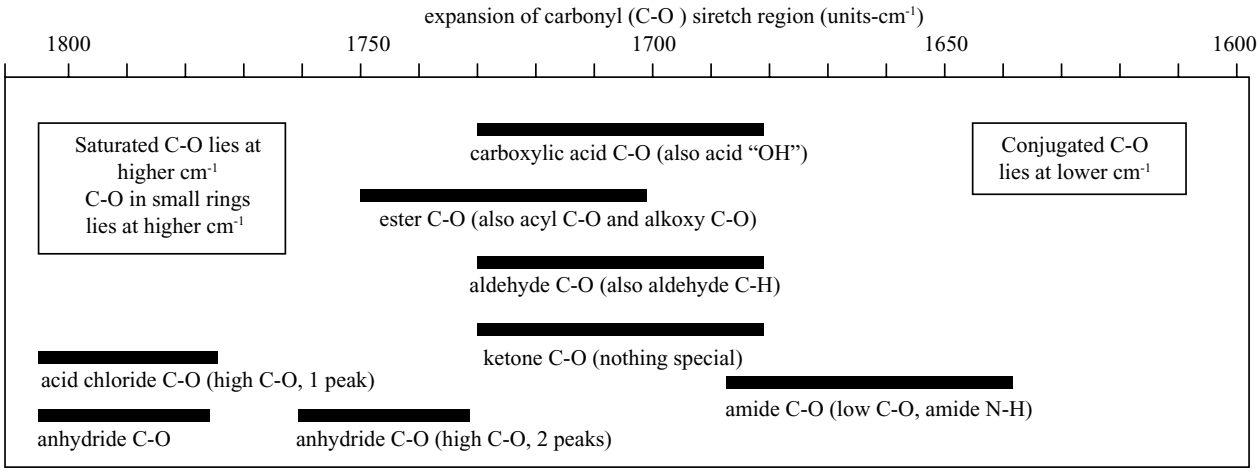


para disubstituted aromatic — 790-840

Aromatic compounds have characteristic weak overtone bands that show up between 1650-2000 cm-¹). Some books provide pictures for comparison (not here). A strong C-O peak will cover up most of this region.







IR Flowchart to determine functional groups in a compound (all values in cm^{-1})

IR Spectrum

has C-O band (1650-1800 cm^{-1}) very strong

$C \equiv C$

$C \equiv N$

does not have C-O band

aldehydes

O ‖ C	1725-1740 (saturated) 1660-1700 (unsaturated)
aldehyde C-H	2860-2800 ← sometimes lost in sp^3 CH peaks 2760-2700 (both weak)

ketones

O ‖ C	1710-1720 (saturated) 1680-1700 (unsaturated) 1715-1810 (rings: higher in small rings)

esters-rule of 3

O ‖ C	1735-1750 (saturated) 1715-1740 (unsaturated) 1735-1820 (higher in small rings)
acyl C—O	1150-1350 (acyl, strong)
alkoxy C—O	(1000-1150 alkoxy, medium)

acids

O ‖ C	1700-1730 (saturated) 1715-1740 (unsaturated) 1680-1700 (higher in small rings)
acyl C—O	1210-1320 (acyl, strong)
acid O—H	2400-3400, very broad (overlaps C-H stretch)

nitriles

$C \equiv N$	≈2250 sharp, stronger than alkynes, a little lower when conjugated

alkynes

$C \equiv C$	2150 (variable intensity) not present or weak when symmetrically substituted, a little lower when conjugated
sp C-H stretch	3300 sharp, strong
sp C-H bend	620

All IR values are approximate and have a range of possibilities depending on the molecular environment in which the functional group resides. Resonance often modifies a peak's position because of electron delocalization (C-O lower, acyl C-O higher etc.). IR peaks are not 100% reliable. Peaks tend to be stronger (more intense) when there is a large dipole associated with a vibration in the functional group and weaker in less polar bonds (to the point of disappearing in some completely symmetrical bonds).

Alkene sp^2 C-H bending patterns

alkanes

sp^3 C-H stretch	2850-3000
sp^3 C-H bend	1460 & 1380
C—C	not useful

alkenes

sp^2 C-H stretch	3000-3100
sp^2 C-H bend	650-1000 (see table for spectral patterns)
C═C	1600-1660 weak or not present

aromatics

sp^2 C-H stretch	3050-3150
sp^2 C-H bend	690-900 (see table), overtone patterns between 1660-2000
C═C	1600 & 1480 can be weak

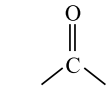
alcohols

alcohol O—H	3600-3500
alkoxy C—O	1000-1260 (3° >2° >1°)

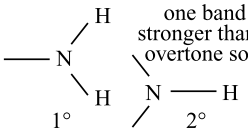
thiols

thiol S—H	≈ 2550 (weak) (easy to overlook)

amides



1630-1680 (saturated)
1745 (in 4 atom ring)
3350 & 3180, two bands for 1° amide,
one band for 2° amides, stronger than in amines, extra overtone sometimes at 3100



N—H N-H bend, 1550-1640, stronger in amides than amines

acid chlorides

1800 (saturated)
1770 (unsaturated)
Inductive pull of Cl increase the electron density between C and O.

anhydrides

1760 & 1820 (saturated)
1725-1785 (unsaturated)
two strong bands
1150-1350 (acyl, strong)

acyl C—O

monosubstituted alkene (985-1000, 900-920)
geminal disubstituted (960-990)
cis disubstituted (675-730)
trans disubstituted (880-900)
trisubstituted (790-840)
tetrasubstituted (none, no sp^2 C-H)

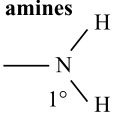
Aromatic sp^2 C-H bending patterns

monosubstituted (730-770, 690-710)
ortho disubstituted (735-770)
meta disubstituted (880-990, sometimes, 750-810,680-725)

para disubstituted (790-840)

There are also weak overtone bands between 1660 and 2000, but are not shown here. You can consult pictures of typical patterns in other reference books. If there is a strong C-O band, they may be partially coverd up.

amines



3300-3500, two bands for 1° amines, one band for 2° amines, weaker than in amides.

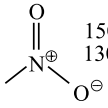
N—H N-H bend, 1550-1640, stronger in amides than amines

N—C 1000-1350 (uncertain)

ethers

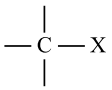
alkoxy C—O 1120 (alphatic) 1040 & 1250 (aromatic)

nitro compounds



1500-1600, asymmetric (strong)
1300-1390, symmetric (medium)

carbon-halogen bonds



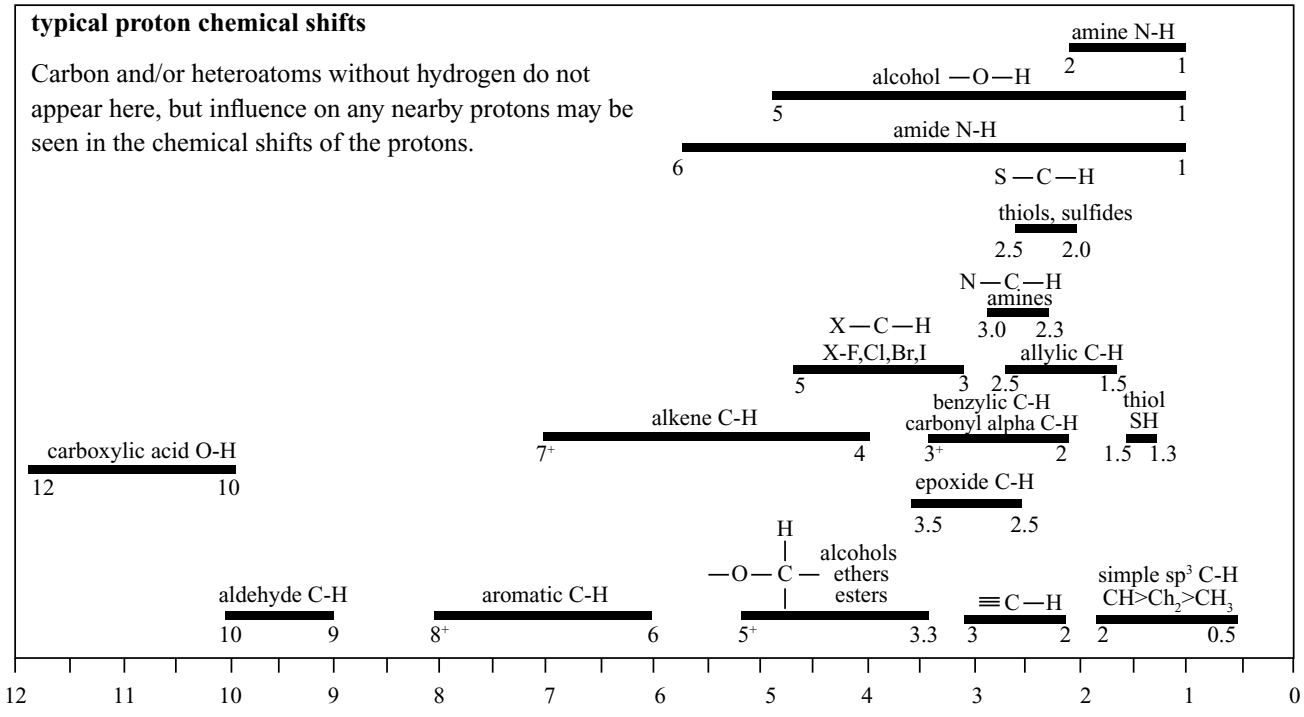
ususlly not very useful

X–F, Cl, Br, I

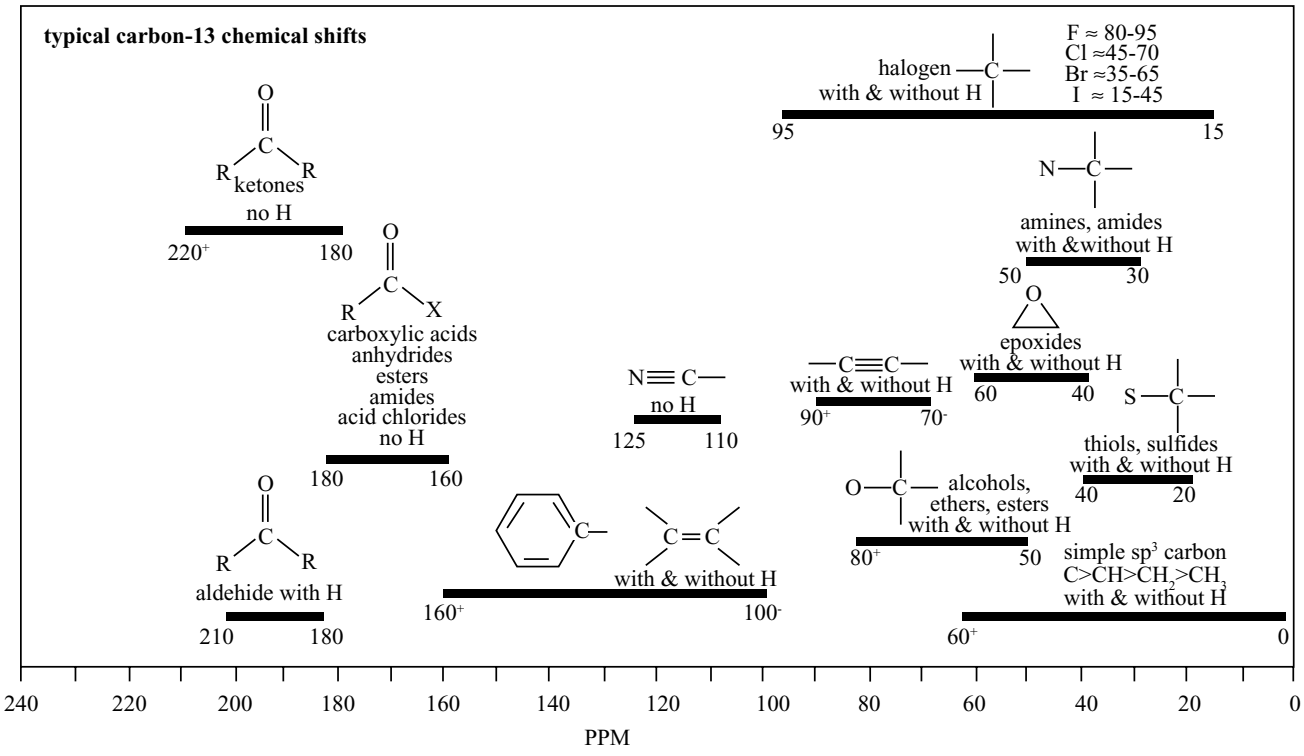
^{1}H NMR Chemical Shift Table:

typical proton chemical shifts

Carbon and/or heteroatoms without hydrogen do not appear here, but influence on any nearby protons may be seen in the chemical shifts of the protons.

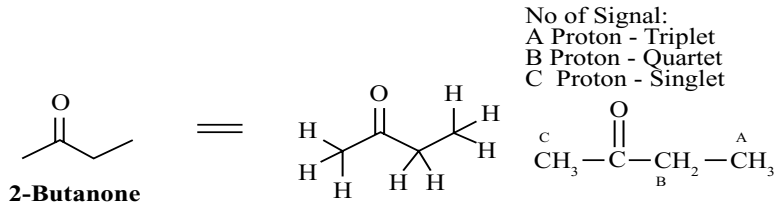


^{13}C NMR Chemical Shift Table:

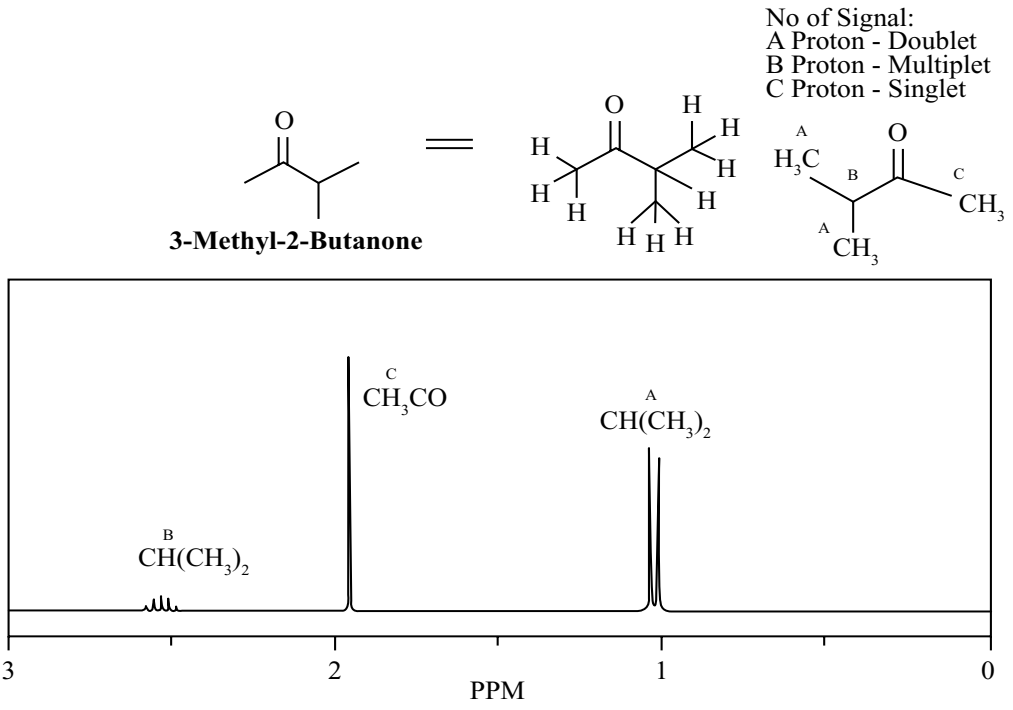


Examples of ^{1}H NMR Spectral Analysis:

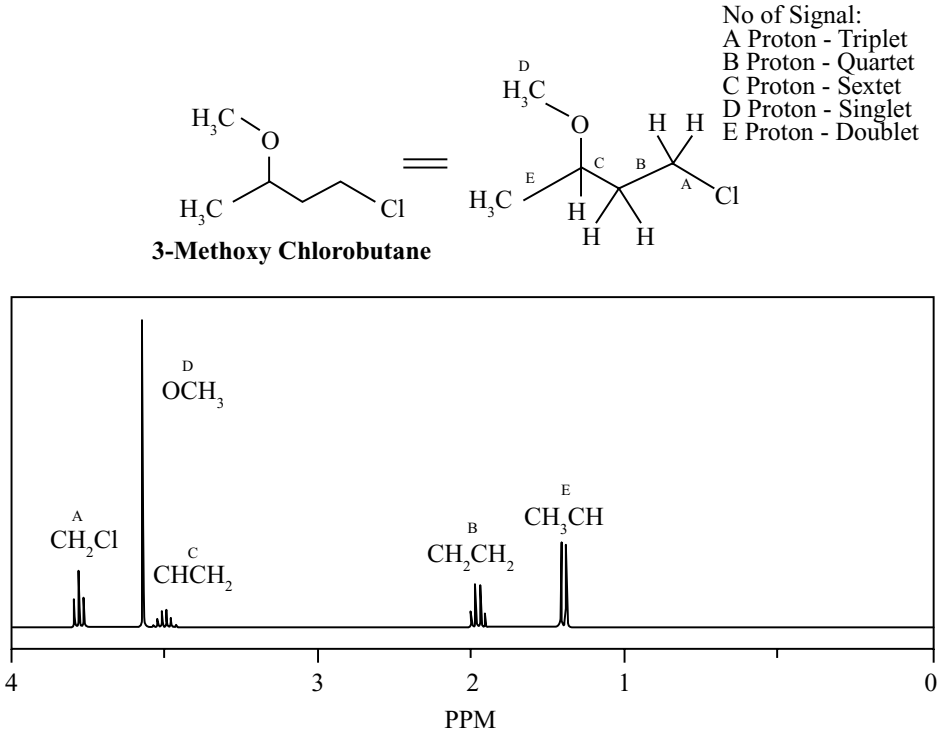
Example 1: 2 Butanone



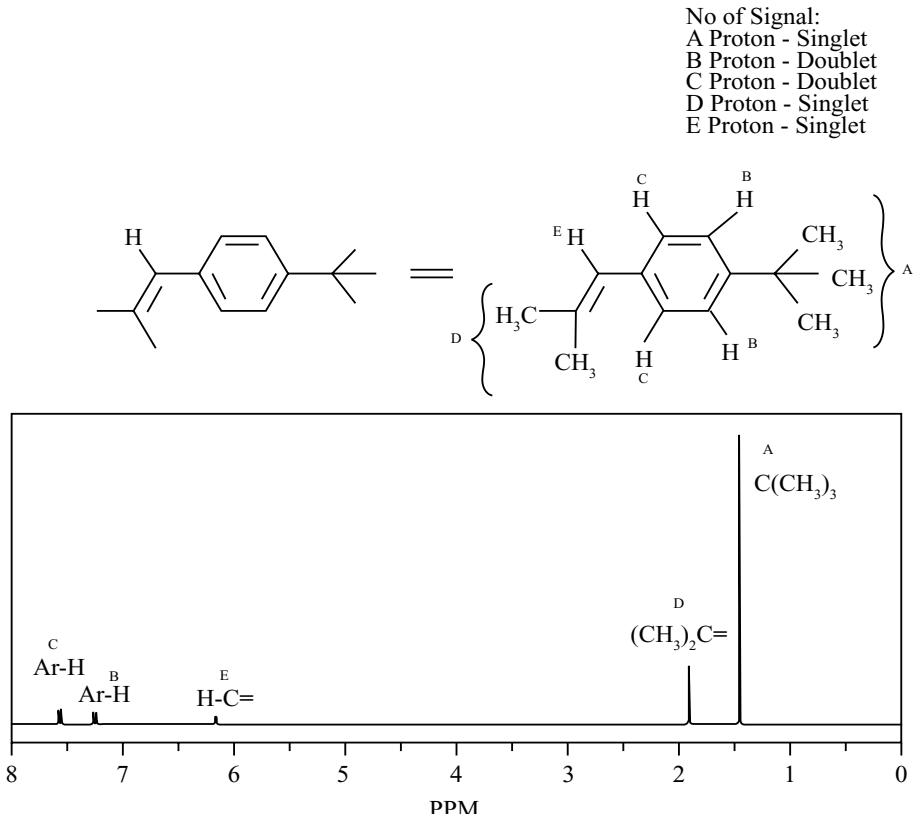
Example 2: 3-Methyl - 2 Butanone



Example 3: 3-Methoxy Chlorobutane



Example 4: 1-*tert*- butyl-4-(2-methylprop-1-enyl) benzene



List of CSIR Approved Laboratories:

1. Biological Sciences

- Centre For Biochemical Technology (CBT), Delhi (*http://www.cbt.res.in)*
- Centre for Cellular and Molecular Biology (CCMB), Hyderabad (*http://www.ccmbindia.org)* Central Drug Research Institute (CDRI), Lucknow – 226001(*http://www.cdriindia.org)*
- Central Food Technological Research Institute (CFTRI), Mysore (*http://www.cftri.org)*
- Central Institute of Medicinal & Aromatic Plants (CIMAP), Lucknow(*http://www.cimap.org*
- Indian Institute of Chemical Biology (IICB), Calcutta
- Institute of Microbial Technology (IMT), Chandigarh (*http://www.imtech.ernet.in)*
- Industrial Toxicology Research Centre (ITRC), Lucknow(*http://www.itrcindia.org)*
- National Botanical Research Institute (NBRI), Lucknow(*http://www.nbri-lko.org)*
- Regional Research Laboratory (RRL,JM), Jammu Tawi
- Institute of Himalayan Bioresource Technolonogy (IHBT),Palampur(*http://www.csir.res.in/ihbt/)*

2. Chemical Sciences

- Central Electrochemical Research (CECRI), Karaikudi(*http://www.cecri-india.org*)
- Central Leather Research Institute (CLRI), Madras
- Central Salt & Marine Chemicals Research Institute (CSMCRI),Bhavnagar
- Indian Institute of Chemical Technology (IICT), Hyderabad(*http://www.iictindia.org*)
- Indian Institute of Petroleum (IIP), Dehradun(*http://www.iip.res.in)*
- National Chemical Laboratory (NCL), Pune(*http://www.ncl-india.org)*
- Regional Research Laboratory (RRL,JOR), P.O. Jorhat

3. Information Sciences

- National Institute of Science Communication & Information Resources (NISCAIR), New Delhi *(http://niscair.res.in)*
- National Institute of Science Technology and Development Studies (NISTADS), New Delhi (*http://nistads.res.in)*

4. Physical Sciences

- Central Electronics Engineering Research Institute (CEERI), Pilani (*http://www.ceeri.ernet.in)*
- Central Scientific Instruments Organisation (CSIO), Chandigarh
- National Geophysical Research Institute (NGRI), Hyderabad(*http://www.ngri.com)*
- National Institute of Oceanography (NIO), Goa (*http://www.nio.org)*
- National Physical Laboratory (NPL), New Delhi

Research Funding Agencies available at National Level which can be approached for Research Work

- Atomic Energy Regulatory Board (AERB)
- Aeronautics Research and Development Board (ARDB)
- Board of Research in Nuclear Sciences (BRNS)
- Council of Scientific & Industrial Research (CSIR)
- Defence Research & Development Organisation (DRDO)
- Department of Atomic Energy
- Department of Biotechnology (DBT)
- Department of Chemicals & Petrochemicals, Ministry of Chemicals & Fertilizers
- Department of Electronics and Information Technology
- European Union
- Indian Council of Agricultural Research (ICAR)
- Indian Council of Medical Research (ICMR)
- Indian Council of Social Science Research (ICSSR)
- Indian National Science Academy (INSA)
- Indian Space Research Organisation (ISRO)
- Ministry of Defence
- Ministry of Earth Science
- Ministry of Environment & Forests (MoEF)
- Ministry of Health & Family Welfare
- Ministry of Petroleum & Natural Gas
- Ministry of Power
- Ministry of Rural Development
- Ministry of Railways
- Ministry of Small Scale Industries
- Ministry of Textiles
- Ministry of Urban Development
- Ministry of Water Resources
- National Board for Higher Mathematics (NBHM)
- Naval Research Board (NRB)
- Petroleum Conservation Research Association (PCRA)
- Science and Engineering Research Board (SERB)
- Tata Institute of Fundamental Research

MAJOR REGULATORY AGENCIES WORLD WIDE

Every country has its own regulatory authority, which is responsible to enforce the rules and regulations and issue guidelines for drug development, licensing, registration, manufacturing, marketing and labelling of pharmaceutical products.

Country	Name of Regulatory Authority
Australia	Therapeutic Goods Administration (TGA)
Brazil	Agencia Nacional de Vigiloncia Sanitaria (ANVISA)
Canada	Health Canada
China	State Food and Drug Administration
Denmark	Danish Medicines Agency
Europe	European Medicines Agency (EMEA)
Germany	Federal Institute for Drugs and Medical Devices
Hong Kong	Department of Health: Pharmaceutical Services

India	Central Drug Standard Control Organization (CDSCO)
Ireland	Irish Medicines Board
Italy	Italian Pharmaceutical Agency
Japan	Ministry of Health, Labour & Welfare(MHLW)
Malaysia	National Pharmaceutical Control Bureau, Ministry of Health
Netherlands	Medicines Evaluation Board
New Zealand	Medsafe - Medicines and Medical Devices Safety Authority
Nigeria	National Agency for Food and Drug Administration and Control (NAFDAC)
Pakistan	Drugs Control Organization, Ministry of Health
Paraguay	Ministry of Health
Singapore	Centre for Pharmaceutical Administration Health Sciences Authority
South Africa	Medicines Control Council
Sri Lanka	SPC, Ministry of Health
Sweden	Medical Products Agency (MPA)
Switzerland	Swissmedic , Swiss Agency for Therapeutic Products
Thailand	Ministry of Public Health
Uganda	Uganda National Council for Science and Technology (UNCST)
UK	Medicines and Healthcare Products Regulatory Agency (MHRA)
Ukraine	Ministry of Health
USA	Food and Drug Administration (FDA)
Australia	Therapeutic Goods Administration (TGA)
INTERNATIONAL ORGANIZATIONS	
World Health Organization (WHO)	
Pan American Health Organization (PAHO)	
World Trade Organization (WTO)	
International Conference on Harmonization (ICH)	
World Intellectual Property Organization (WIPO)	

Nobel Laureates of India

Year	Name of Laureate	Subject	Rationale
1913	Rabindranath Tagore	Literature	Awarded "because of his profoundly sensitive, fresh and beautiful verse, by which, with consummate skill, he has made his poetic thought, expressed in his own English words, a part of the literature of the West."[11]
1930	C. V. Raman	Physics	"For his work on the scattering of light and for the discovery of the effect named after him."[12]
1979	Mother Teresa	Peace	"For work undertaken in the struggle to overcome poverty and distress, which also constitutes a threat to peace."[13]
1998	Amartya Sen	Economic studies	"For his contributions to welfare economics."[14]
2014	Kailash Satyarthi	Peace	Awarded jointly to Kailash Satyarthi and Malala Yousafzai – "for their struggle against the suppression of children and young people and for the right of all children to education."[15]
1913	Rabindranath Tagore	Literature	Awarded "because of his profoundly sensitive, fresh and beautiful verse, by which, with consummate skill, he has made his poetic thought, expressed in his own English words, a part of the literature of the West."[11]

Nobel Laureates: Overseas Citizens of Indian Origin

Year	Name of Laureate	Country	Subject	Rationale
1968	Har Gobind Khorana	United States	Physiology or Medicine	Awarded along with Robert W. Holley and Marshall W. Nirenberg – "for their interpretation of the genetic code and its function in protein synthesis."[16]
1983	Subrahmanyan Chandrasekhar	United States	Physics	"For his theoretical studies of the physical processes of importance to the structure and evolution of the stars."[17]
2009	Venkatraman Ramakrishnan	United Kingdom / United States	Chemistry	"For studies of the structure and function of the ribosome."[18]

Nobel Laureates: Year 2016

Name of Laureate	Subject	Rationale
David J. Thouless, F. Duncan M. Haldane and J. Michael Kosterlitz	Physics	"for theoretical discoveries of topological phase transitions and topological phases of matter"
Jean-Pierre Sauvage, Sir J. Fraser Stoddart and Bernard L. Feringa	Chemistry	"for the design and synthesis of molecular machines"
Yoshinori Ohsumi	Physiology or Medicine	"for his discoveries of mechanisms for autophagy"
Bob Dylan	Literature	"for having created new poetic expressions within the great American song tradition"
Juan Manuel Santos	Peace	"for his resolute efforts to bring the country's more than 50-year-long civil war to an end"
Oliver Hart and Bengt Holmström	Economic	"for their contributions to contract theory"

Nobel Laureates: Year 2015

Name of Laureate	Subject	Rationale
Takaaki Kajita and Arthur B. McDonald	Physics	"for the discovery of neutrino oscillations, which shows that neutrinos have mass"
Tomas Lindahl, Paul Modrich and Aziz Sancar	Chemistry	"for mechanistic studies of DNA repair"
William C. Campbell and Satoshi Ōmura	Physiology or Medicine	"for their discoveries concerning a novel therapy against infections caused by round-worm parasites"
Svetlana Alexievich	Literature	"for her polyphonic writings, a monument to suffering and courage in our time"
National Dialogue Quartet	Peace	"for its decisive contribution to the building of a pluralistic democracy in Tunisia in the wake of the Jasmine Revolution of 2011"
Angus Deaton	Economic	"for his analysis of consumption, poverty, and welfare"

Nobel Laureates: Year 2014

Name of Laureate	Subject	Rationale
Isamu Akasaki, Hiroshi Amano and Shuji Nakamura	Physics	"for the invention of efficient blue light-emitting diodes which has enabled bright and energy-saving white light sources"
Eric Betzig, Stefan W. Hell and William E. Moerner	Chemistry	"for the development of super-resolved fluorescence microscopy"
John O'Keefe, May-Britt Moser and Edvard I. Moser	Physiology or Medicine	"for their discoveries of cells that constitute a positioning system in the brain"
Patrick Modiano	Literature	"for the art of memory with which he has evoked the most ungraspable human destinies and uncovered the life-world of the occupation"
Kailash Satyarthi and Malala Yousafzai	Peace	"for their struggle against the suppression of children and young people and for the right of all children to education"
Jean Tirole	Economic	"for his analysis of market power and regulation"

Nobel Laureates: Year 2013

Name of Laureate	Subject	Rationale
François Englert and Peter W. Higgs	Physics	"for the theoretical discovery of a mechanism that contributes to our understanding of the origin of mass of subatomic particles, and which recently was confirmed through the discovery of the predicted fundamental particle, by the ATLAS and CMS experiments at CERN's Large Hadron Collider"
Martin Karplus, Michael Levitt and Arieh Warshel	Chemistry	"for the development of multiscale models for complex chemical systems"

James E. Rothman, Randy W. Schekman and Thomas C. Südhof	Physiology or Medicine	"for their discoveries of machinery regulating vesicle traffic, a major transport system in our cells"
Alice Munro	Literature	"master of the contemporary short story"
Organisation for the Prohibition of Chemical Weapons (OPCW)	Peace	"for its extensive efforts to eliminate chemical weapons"
Eugene F. Fama, Lars Peter Hansen and Robert J. Shiller	Economic	"for their empirical analysis of asset prices"

Nobel Laureates: Year 2012

Name of Laureate	Subject	Rationale
Serge Haroche and David J. Wineland	Physics	"for ground-breaking experimental methods that enable measuring and manipulation of individual quantum systems"
Robert J. Lefkowitz and Brian K. Kobilka	Chemistry	"for studies of G-protein-coupled receptors"
Sir John B. Gurdon and Shinya Yamanaka	Physiology or Medicine	"for the discovery that mature cells can be reprogrammed to become pluripotent"
Mo Yan	Literature	"who with hallucinatory realism merges folk tales, history and the contemporary"
European Union (EU)	Peace	"for over six decades contributed to the advancement of peace and reconciliation, democracy and human rights in Europe"
Alvin E. Roth and Lloyd S. Shapley	Economic	"for the theory of stable allocations and the practice of market design"

Nobel Laureates: Year 2011

Name of Laureate	Subject	Rationale
Saul Perlmutter, Brian P. Schmidt and Adam G. Riess	Physics	"for the discovery of the accelerating expansion of the Universe through observations of distant supernovae"
Dan Shechtman	Chemistry	"for the discovery of quasicrystals"
Bruce A. Beutler and Jules A. Hoffmann	Physiology or Medicine	"for their discoveries concerning the activation of innate immunity"
Tomas Tranströmer	Literature	"because, through his condensed, translucent images, he gives us fresh access to reality"
Ellen Johnson Sirleaf, Leymah Gbowee and Tawakkol Karman	Peace	"for their non-violent struggle for the safety of women and for women's rights to full participation in peace-building work"
Thomas J. Sargent and Christopher A. Sims	Economic	"for their empirical research on cause and effect in the macroeconomy"

FDA Approved Drugs: 2016

Name	Comment
Ixekizumab	The U.S. Food and Drug Administration approved Taltz (ixekizumab) to treat adults with moderate-to-severe plaque psoriasis. Taltz's active ingredient is an antibody (ixekizumab) that binds to a protein (interleukin (IL)-17A) that causes inflammation. By binding to the protein, ixekizumab is able to inhibit the inflammatory response that plays a role in the development of plaque psoriasis.
Elbasvir and Grazoprevir	The U.S. Food and Drug Administration approved Zepatier (elbasvir and grazoprevir) with or without ribavirin for the treatment of chronic hepatitis C virus (HCV) genotypes 1 and 4 infections in adult patients.
Brivaracetam	The U.S. Food and Drug Administration approved Briviact (brivaracetam) as an add-on treatment to other medications to treat partial onset seizures in patients age 16 years and older with epilepsy. Briviact's effectiveness was studied in three clinical trials involving 1,550 participants. Briviact, taken along with other medications, was shown to be effective in reducing the frequency of seizures.
Obiltoxaximab	The U.S. Food and Drug Administration approved Anthim (obiltoxaximab) injection to treat inhalational anthrax in combination with appropriate antibacterial drugs. Anthim is also approved to prevent inhalational anthrax when alternative therapies are not available or not appropriate. Anthim is a monoclonal antibody that neutralizes toxins produced by B. anthracis. Anthim was approved under the FDA's Animal Rule, which allows efficacy findings from adequate and well-controlled animal studies to support FDA approval when it is not feasible or ethical to conduct efficacy trials in humans.
Reslizumab	The U.S. Food and Drug Administration approved Cinqair (reslizumab) for use with other asthma medicines for the maintenance treatment of severe asthma in patients aged 18 years and older. Cinqair is approved for patients who have a history of severe asthma attacks (exacerbations) despite receiving their current asthma medicines. Cinqair is administered once every four weeks via intravenous infusion by a health care professional in a clinical setting prepared to manage anaphylaxis. Cinqair is a humanized interleukin-5 antagonist monoclonal antibody produced by recombinant DNA technology in murine myeloma non-secreting 0 (NS0) cells. Cinqair reduces severe asthma attacks by reducing the levels of blood eosinophils, a type of white blood cell that contributes to the development of asthma.
Defibrotide sodium	The U.S. Food and Drug Administration approved Defitelio (defibrotide sodium) to treat adults and children who develop hepatic veno-occlusive disease (VOD) with additional kidney or lung abnormalities after they receive a stem cell transplant from blood or bone marrow called hematopoietic stem cell transplantation (HSCT). This is the first FDA-approved therapy for treatment of severe hepatic VOD, a rare and life-threatening liver condition.
Venetoclax	The U.S. Food and Drug Administration approved Venclexta (venetoclax) for the treatment of patients with chronic lymphocytic leukemia (CLL) who have a chromosomal abnormality called 17p deletion and who have been treated with at least one prior therapy. Venclexta is the first FDA-approved treatment that targets the B-cell lymphoma 2 (BCL-2) protein, which supports cancer cell growth and is over expressed in many patients with CLL.Venclexta is indicated for daily use after detection of 17p deletion is confirmed through the use of the FDA-approved companion diagnostic Vysis CLL FISH probe kit.
Pimavanserin	The U.S. Food and Drug Administration approved Nuplazid (pimavanserin) tablets, the first drug approved to treat hallucinations and delusions associated with psychosis experienced by some people with Parkinson's disease. The effectiveness of Nuplazid was shown in a six-week clinical trial of 199 participants. Nuplazid was shown to be superior to placebo in decreasing the frequency and/or severity of hallucinations and delusions without worsening the primary motor symptoms of Parkinson's disease.

Axumin	The U.S. Food and Drug Administration approved Axumin, a radioactive diagnostic agent for injection. Axumin is indicated for positron emission tomography (PET) imaging in men with suspected prostate cancer recurrence based on elevated prostate specific antigen (PSA) levels following prior treatment.
Atezolizumab	The U.S. Food and Drug Administration approved Tecentriq (atezolizumab) to treat the most common type of bladder cancer, called urothelial carcinoma. This is the first product in its class (PD-1/PD-L1 inhibitors) approved to treat this type of cancer. Tecentriq targets the PD-1/PD-L1 pathway (proteins found on the body's immune cells and some cancer cells). By blocking these interactions, Tecentriq may help the body's immune system fight cancer cells. Tecentriq is the first FDA-approved PD-L1 inhibitor and the latest in the broader class of PD-1/PD-L1 targeted biologics approved by the FDA in the last two years. Tecentriq is approved for the treatment of patients with locally advanced or metastatic urothelial carcinoma whose disease has worsened during or following platinum-containing chemotherapy, or within 12 months of receiving platinum-containing chemotherapy, either before (neoadjuvant) or after (adjuvant) surgical treatment.
Daclizumab	The U.S. Food and Drug Administration approved Zinbryta (daclizumab) for the treatment of adults with relapsing forms of multiple sclerosis (MS). Zinbryta is a long-acting injection that is self- administered by the patient monthly. The effectiveness of Zinbryta was shown in two clinical trials. One trial compared Zinbryta and Avonex in 1,841 participants who were studied for 144 weeks. Patients on Zinbryta had fewer clinical relapses than patients taking Avonex. The second trial compared Zinbryta with placebo and included 412 participants who were treated for 52 weeks. In that study, those receiving Zinbryta had fewer relapses compared to those receiving placebo.
Obeticholic acid	The U.S. Food and Drug Administration granted accelerated approval for Ocaliva (obeticholic acid) for the treatment of primary biliary cholangitis (PBC) in combination with ursodeoxycholic acid (UDCA) in adults with an inadequate response to UDCA, or as a single therapy in adults unable to tolerate UDCA.Ocaliva, given orally, binds to the farnesoid X receptor (FXR), a receptor found in the nucleus of cells in the liver and intestine. FXR is a key regulator of bile acid metabolic pathways. Ocaliva increases bile flow from the liver and suppresses bile acid production in the liver, thus reducing the exposure of the liver to toxic levels of bile acids.
Ga 68 dotatate injection	The U.S. Food and Drug Administration approved Netspot, the first kit for the preparation of gallium Ga 68 dotatate injection, a radioactive diagnostic agent for positron emission tomography (PET) imaging. This radioactive probe will help locate tumors in adult and pediatric patients with the rare condition, somatostatin receptor positive neuroendocrine tumors (NETs). Netspot is supplied as a sterile, single-dose kit for preparation of Ga 68 dotatate injection for intravenous use.
Epclusa	The U.S. Food and Drug Administration approved Epclusa to treat adult patients with chronic hepatitis C virus (HCV) both with and without cirrhosis (advanced liver disease). For patients with moderate to severe cirrhosis (decompensated cirrhosis), Epclusa is approved for use in combination with the drug ribavirin. Epclusa is a fixed-dose combination tablet containing sofosbuvir, a drug approved in 2013, and velpatasvir, a new drug, and is the first to treat all six major forms of HCV.
Lifitegrast ophthalmic solution	The U.S. Food and Drug Administration approved Xiidra (lifitegrast ophthalmic solution) for the treatment of signs and symptoms of dry eye disease. Xiidra is the first medication in a new class of drugs, called lymphocyte function-associated antigen 1 (LFA-1) antagonist, approved by the FDA for dry eye disease.

FDA Approved Drugs: 2015

Name	Comment
Edoxaban tablets	The U.S. Food and Drug Administration approved the anti-clotting drug Savaysa (edoxaban tablets) to reduce the risk of stroke and dangerous blood clots (systemic embolism) in patients with atrial fibrillation that is not caused by a heart valve problem. Savaysa also has been approved to treat deep vein thrombosis (DVT) and pulmonary embolism (PE) in patients who have already been treated with an anti-clotting drug administered by injection or infusion (parenterally), for five to ten days.
Secukinumab	The U.S. Food and Drug Administration approved Cosentyx (secukinumab) to treat adults with moderate-to-severe plaque psoriasis. Cosentyx's active ingredient is secukinumab. Secukinumab is an antibody that binds to a protein (interleukin (IL)-17A) which is involved in inflammation. By binding to IL-17A, secukinumab prevents it from binding to its receptor, and inhibits its ability to trigger the inflammatory response that plays a role in the development of plaque psoriasis. Cosentyx is administered as an injection under the skin.
Natpara (parathyroid horomone)	The U.S. Food and Drug Administration approved Natpara (parathyroid horomone) to control hypocalcemia (low blood calcium levels) in patients with hypoparathyroidism, a rare disease that affects approximately 60,000 people in the United States. Natpara, a hormonal injection administered once daily, helps to regulate the body's calcium levels. The FDA granted Natpara orphan drug designation because it is intended to treat a rare disease.
Palbociclib	The U.S. Food and Drug Administration granted accelerated approval to Ibrance (palbociclib) to treat advanced (metastatic) breast cancer. Ibrance works by inhibiting molecules, known as cyclin-dependent kinases (CDKs) 4 and 6, involved in promoting the growth of cancer cells. Ibrance is intended for postmenopausal women with estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative metastatic breast cancer who have not yet received an endocrine-based therapy. It is to be used in combination with letrozole, another FDA-approved product used to treat certain kinds of breast cancer in postmenopausal women.
Lenvatinib	The U.S. Food and Drug Administration today granted approval to Lenvima (lenvatinib) to treat patients with progressive, differentiated thyroid cancer (DTC) whose disease progressed despite receiving radioactive iodine therapy (radioactive iodine refractory disease). Lenvima's efficacy was demonstrated in 392 participants with progressive, radioactive iodine-refractory DTC who were randomly assigned to receive either Lenvima or a placebo. Study results showed Lenvima-treated participants lived a median of 18.3 months without their disease progressing (progression-free survival), compared to a median of 3.6 months for participants who received a placebo. Additionally, 65 percent of participants treated with Lenvima saw a reduction in tumor size, compared to the two percent of participants who received a placebo. A majority of participants randomly assigned to receive the placebo were treated with Lenvima upon disease progression.
Panobinosta	The U.S. Food and Drug Administration approved Farydak (panobinostat) for the treatment of patients with multiple myeloma. Farydak works by inhibiting the activity of enzymes, known as histone deacetylases (HDACs). This process may slow the over-development of plasma cells in multiple myeloma patients or cause these dangerous cells to die. Farydak is the first HDAC inhibitor approved to treat multiple myeloma. It is intended for patients who have received at least two prior standard therapies, including bortezomib and an immunomodulatory agent. Farydak is to be used in combination with bortezomib, a type of chemotherapy, and dexamethasone, an anti-inflammatory medication.

Ceftazidime-Avibactam	The U.S. Food and Drug Administration approved Avycaz (ceftazidime-avibactam), a new antibacterial drug product, to treat adults with complicated intra-abdominal infections (cIAI), in combination with metronidazole, and complicated urinary tract infections (cUTI), including kidney infections (pyelonephritis), who have limited or no alternative treatment options. Avycaz is a fixed-combination drug containing ceftazidime, a previously approved cephalosporin antibacterial drug, and avibactam, a new beta-lactamase inhibitor.Avycaz is the fifth approved antibacterial drug product designated as a Qualified Infectious Disease Product (QIDP). This designation is given to antibacterial products to treat serious or life-threatening infections under the Generating Antibiotic Incentives Now (GAIN) title of the FDA Safety and Innovation Act.
Isavuconazonium Sulfate	The U.S. Food and Drug Administration approved Cresemba (isavuconazonium sulfate), a new antifungal drug product used to treat adults with invasive aspergillosis and invasive mucormycosis, rare but serious infections. Cresemba belongs to a class of drugs called azole antifungal agents, which target the cell membrane of a fungus. Cresemba is available in oral and intravenous formulations. Cresemba is the sixth approved antibacterial or antifungal drug product designated as a Qualified Infectious Disease Product (QIDP). This designation is given to antibacterial or antifungal drug products that treat serious or life-threatening infections under the Generating Antibiotic Incentives Now (GAIN) title of the FDA Safety and Innovation Act.
Dinutuximab	The U.S. Food and Drug Administration approved Unituxin (dinutuximab) as part of first-line therapy for pediatric patients with high-risk neuroblastoma, a type of cancer that most often occurs in young children. Unituxin is an antibody that binds to the surface of neuroblastoma cells. Unituxin is being approved for use as part of a multimodality regimen, including surgery, chemotherapy and radiation therapy for patients who achieved at least a partial response to prior first-line multiagent, multimodality therapy.
Cholic acid	The U.S. Food and Drug Administration approved Cholbam (cholic acid) capsules, the first FDA approved treatment for pediatric and adult patients with bile acid synthesis disorders due to single enzyme defects, and for patients with peroxisomal disorders (including Zellweger spectrum disorders). Patients with these rare, genetic, metabolic conditions exhibit manifestations of liver disease, steatorrhea (presence of fat in the stool) and complications from decreased fat-soluble vitamin absorption.Cholbam is approved as an oral treatment for children aged three weeks and older, and adults. The manufacturer of Cholbam was granted a rare pediatric disease priority review voucher–a provision that encourages development of new drugs and biologics for the prevention and treatment of rare pediatric diseases.
Ivabradine	The U.S. Food and Drug Administration approved Corlanor (ivabradine) to reduce hospitalization from worsening heart failure. Corlanor is approved for use in certain people who have long-lasting (chronic) heart failure caused by the lower-left part of their heart not contracting well. The drug is indicated for patients who have symptoms of heart failure that are stable, a normal heartbeat with a resting heart rate of at least 70 beats per minute and are also taking beta blockers at the highest dose they can tolerate.
Deoxycholic acid	The U.S. Food and Drug Administration approved Kybella (deoxycholic acid), a treatment for adults with moderate-to-severe fat below the chin, known as submental fat. Using Kybella for the treatment of fat outside of the submental area is not approved and is not recommended. Kybella is identical to the deoxycholic acid that is produced in the body. Deoxycholic acid produced in the body helps the body absorb fats. Kybella is a cytolytic drug, which when injected into tissue physically destroys the cell membrane. When properly injected into submental fat, the drug destroys fat cells; however, it can also destroy other types of cells, such as skin cells, if it is inadvertently injected into the skin.

Eluxadoline	The U.S. Food and Drug Administration approved Viberzi (eluxadoline) and Xifaxan (rifaximin), two new treatments, manufactured by two different companies, for irritable bowel syndrome with diarrhea (IBS-D) in adult men and women. Viberzi, which contains a new active ingredient, is taken orally twice daily with food. Viberzi activates receptors in the nervous system that can lessen bowel contractions. Viberzi is intended to treat adults with IBS-D.
Lumacaftor Ivacaftor	The U.S. Food and Drug Administration approved the first drug for cystic fibrosis directed at treating the cause of the disease in people who have two copies of a specific mutation. Orkambi (lumacaftor 200 mg/ivacaftor 125 mg) is approved to treat cystic fibrosis (CF) in patients 12 years and older, who have the F508del mutation, which causes the production of an abnormal protein that disrupts how water and chloride are transported in the body. Having two copies of this mutation (one inherited from each parent) is the leading cause of CF.
Sacubitril/ Valsartan	The U.S. Food and Drug Administration approved Entresto (sacubitril/valsartan) tablets for the treatment of heart failure. The drug has been shown to reduce the rate of cardiovascular death and hospitalization related to heart failure.
Brexpiprazole	The U.S. Food and Drug Administration approved Rexulti (brexpiprazole) tablets to treat adults with schizophrenia and as an add-on treatment to an antidepressant medication to treat adults with major depressive disorder (MDD). The effectiveness of Rexulti in treating schizophrenia was evaluated in 1,310 participants in two 6-week clinical trials. Rexulti was shown to reduce the occurrence of symptoms of schizophrenia compared to placebo (inactive tablet).
Alirocumab	The U.S. Food and Drug Administration approved Praluent (alirocumab) injection, the first cholesterol-lowering treatment approved in a new class of drugs known as proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitors. Praluent is approved for use in addition to diet and maximally tolerated statin therapy in adult patients with heterozygous familial hypercholesterolemia (HeFH) or patients with clinical atherosclerotic cardiovascular disease such as heart attacks or strokes, who require additional lowering of LDL cholesterol.
Sonidegib	The U.S. Food and Drug Administration approved Odomzo (sonidegib) to treat patients with locally advanced basal cell carcinoma that has recurred following surgery or radiation therapy, or who are not candidates for surgery or radiation therapy. Odomzo is a pill taken once a day. It works by inhibiting a molecular pathway, called the Hedgehog pathway, which is active in basal cell cancers. By suppressing this pathway, Odomzo may stop or reduce the growth of cancerous lesions.
Daclatasvir	The U.S. Food and Drug Administration approved Daklinza (daclatasvir) for use with sofosbuvir to treat hepatitis C virus (HCV) genotype 3 infections. Daklinza is the first drug that has demonstrated safety and efficacy to treat genotype 3 HCV infections without the need for co-administration of interferon or ribavirin, two FDA-approved drugs also used to treat HCV infection.
Flibanserin	The U.S. Food and Drug Administration today approved Addyi (flibanserin) to treat acquired, generalized hypoactive sexual desire disorder (HSDD) in premenopausal women. Prior to Addyi's approval, there were no FDA-approved treatments for sexual desire disorders in men or women. Addyi is a serotonin 1A receptor agonist and a serotonin 2A receptor antagonist, but the mechanism by which the drug improves sexual desire and related distress is not known. Addyi is taken once daily. It is dosed at bedtime to help decrease the risk of adverse events occurring due to possible hypotension, syncope and central nervous system depression (such as sleepiness and sedation). Patients should discontinue treatment after eight weeks if they do not report an improvement in sexual desire and associated distress.

Evolocumab	The U.S. Food and Drug Administration today approved Repatha (evolocumab) injection for some patients who are unable to get their low-density lipoprotein (LDL) cholesterol under control with current treatment options. Repatha, the second drug approved in a new class of drugs known as PCSK9 inhibitors, is approved for use in addition to diet and maximally-tolerated statin therapy in adult patients with heterozygous familial hypercholesterolemia (HeFH), homozygous familial hypercholesterolemia (HoFH), or clinical atherosclerotic cardiovascular disease, such as heart attacks or strokes, who require additional lowering of LDL cholesterol.
Rolapitant	The U.S. Food and Drug Administration approved Varubi (rolapitant) to prevent delayed phase chemotherapy-induced nausea and vomiting (emesis). Varubi is approved in adults in combination with other drugs (antiemetic agents) that prevent nausea and vomiting associated with initial and repeat courses of vomit-inducing (emetogenic and highly emetogenic) cancer chemotherapy. Varubi is a substance P/neurokinin-1 (NK-1) receptor antagonist. Activation of NK-1 receptors plays a central role in nausea and vomiting induced by certain cancer chemotherapies, particularly in the delayed phase. Varubi is provided to patients in tablet form.
Cariprazine	The U.S. Food and Drug Administration today approved Vraylar (cariprazine) capsules to treat schizophrenia and bipolar disorder in adults. The efficacy of Vraylar in treating schizophrenia was demonstrated in 1,754 participants in three six-week clinical trials. In each of the trials, Vraylar was shown to reduce the symptoms of schizophrenia compared to placebo.
Trifluridine and Tipiracil	The U.S. Food and Drug Administration approved Lonsurf (a pill that combines two drugs, trifluridine and tipiracil) for patients with an advanced form of colorectal cancer who are no longer responding to other therapies. Lonsurf is an oral medication intended to treat patients with advanced (metastatic) colorectal cancer who have been previously treated with chemotherapy and biological therapy.
Tresiba (insulin degludec injection)	The U.S. Food and Drug Administration approved Tresiba (insulin degludec injection) and Ryzodeg 70/30 (insulin degludec/insulin aspart injection) to improve blood sugar (glucose) control in adults with diabetes mellitus. Tresiba is a long-acting insulin analog indicated to improve glycemic control in adults with type 1 and 2 diabetes mellitus. Dosing of Tresiba should be individualized based on the patient's needs. Tresiba is administered subcutaneously once daily at any time of day.
Aripiprazole lauroxil	The U.S. Food and Drug Administration approved Aristada (aripiprazole lauroxil) extended release injection to treat adults with schizophrenia. Aristada is administered by a health care professional every four to six weeks using an injection in the arm or buttocks. The efficacy of Aristada was demonstrated in part by a 12-week clinical trial in 622 participants. In participants with acute schizophrenia who had been stabilized with oral aripiprazole, Aristada was found to maintain the treatment effect compared to a placebo.
Idarucizumab	The U.S. Food and Drug Administration granted accelerated approval to Praxbind (idarucizumab) for use in patients who are taking the anticoagulant Pradaxa (dabigatran) during emergency situations when there is a need to reverse Pradaxa's blood-thinning effects. The FDA approved Pradaxa in 2010 to prevent stroke and systemic blood clots in patients with atrial fibrillation, as well as for the treatment and prevention of deep venous thrombosis and pulmonary embolism. Praxbind is the first reversal agent approved specifically for Pradaxa and works by binding to the drug compound to neutralize its effect. Praxbind solution is for intravenous injection.
Patiromer for oral suspension	The U.S. Food and Drug Administration today approved Veltassa (patiromer for oral suspension) to treat hyperkalemia, a serious condition in which the amount of potassium in the blood is too high. Veltassa, a powdered medication that patients mix with water and take by mouth, works by binding potassium in the gastrointestinal tract, decreasing its absorption. In clinical trials, Veltassa was effective in lowering potassium levels in hyperkalemic participants with chronic kidney disease on at least one drug that inhibited the renin-angiotensin-aldosterone system.

Trabectedin	The U.S. Food and Drug Administration approved Yondelis (trabectedin), a chemotherapy, for the treatment of specific soft tissue sarcomas (STS) – liposarcoma and leiomyosarcoma – that cannot be removed by surgery (unresectable) or is advanced (metastatic). This treatment is approved for patients who previously received chemotherapy that contained anthracycline.
Asfotase alfa	The U.S. Food and Drug Administration approved Strensiq (asfotase alfa) as the first approved treatment for perinatal, infantile and juvenile-onset hypophosphatasia (HPP). Strensiq is administered via injection three or six times per week. Strensiq works by replacing the enzyme (known as tissue-nonspecific alkaline phosphatase) responsible for formation of an essential mineral in normal bone, which has been shown to improve patient outcomes.
Mepolizumab	The U.S. Food and Drug Administration approved Nucala (mepolizumab) for use with other asthma medicines for the maintenance treatment of asthma in patients age 12 years and older. Nucala is approved for patients who have a history of severe asthma attacks (exacerbations) despite receiving their current asthma medicines. Nucala is administered once every four weeks by subcutaneous injection by a health care professional into the upper arm, thigh, or abdomen. Nucala is a humanized interleukin-5 antagonist monoclonal antibody produced by recombinant DNA technology in Chinese hamster ovary cells. Nucala reduces severe asthma attacks by reducing the levels of blood eosinophils- a type of white blood cell that contributes to the development of asthma.
Genvoyaa (fixed-dose combination tablet containing elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide)	The U.S. Food and Drug Administration approved Genvoya (a fixed-dose combination tablet containing elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide) as a complete regimen for the treatment of HIV-1 infection in adults and pediatric patients 12 years of age and older. Genvoya is approved for use in HIV-infected adults and children ages 12 years and older weighing at least 35 kilograms (77 pounds) who have never taken HIV therapy (treatment-naïve) and HIV-infected adults whose HIV-1 virus is currently suppressed. While Genvoya is not recommended for patients with severe renal impairment, those with moderate renal impairment can take Genvoya.
Cobimetinib	The U.S. Food and Drug Administration today approved Cotellic (cobimetinib) to be used in combination with vemurafenib to treat advanced melanoma that has spread to other parts of the body or can't be removed by surgery, and that has a certain type of abnormal gene (BRAF V600E or V600K mutation). Cotellic works by blocking the activity of an enzyme known as MEK, which is part of a larger signaling pathway. Abnormal activity of signaling pathways can lead to cancer. Cotellic prevents or slows cancer cell growth.
Osimertinib	The U.S. Food and Drug Administration granted accelerated approval for an oral medication to treat patients with advanced non-small cell lung cancer (NSCLC). Tagrisso (osimertinib) is now approved for patients whose tumors have a specific epidermal growth factor receptor (EGFR) mutation (T790M) and whose disease has gotten worse after treatment with other EGFR-blocking therapy.
Daratumumab	The U.S. Food and Drug Administration granted accelerated approval for Darzalex (daratumumab) to treat patients with multiple myeloma who have received at least three prior treatments. Darzalex is the first monoclonal antibody approved for treating multiple myeloma. Darzalex injection, given as an infusion, is a monoclonal antibody that works by helping certain cells in the immune system attack cancer cells.
Ixazomib	The U.S. Food and Drug Administration granted approval for Ninlaro (ixazomib) in combination with two other therapies to treat people with multiple myeloma who have received at least one prior therapy. Ninlaro is a type of cancer drug called a proteasome inhibitor and works by blocking enzymes from multiple myeloma cells, hindering their ability to grow and survive. Ninlaro is the first oral proteasome inhibitor and is approved in combination with another FDA-approved treatment for multiple myeloma called Revlimid (lenalidomide) and dexamethasone (a type of corticosteroid).

Necitumumab	The U.S. Food and Drug Administration approved Portrazza (necitumumab) in combination with two forms of chemotherapy to treat patients with advanced (metastatic) squamous non-small cell lung cancer (NSCLC) who have not previously received medication specifically for treating their advanced lung cancer. Portrazza is a monoclonal antibody that blocks activity of EGFR, a protein commonly found on squamous NSCLC tumors.
Elotuzumab	The U.S. Food and Drug Administration granted approval for Empliciti (elotuzumab) in combination with two other therapies to treat people with multiple myeloma who have received one to three prior medications. Empliciti activates the body's immune system to attack and kill multiple myeloma cells. It is approved in combination with another FDA-approved treatment for multiple myeloma called Revlimid (lenalidomide) and dexamethasone (a type of corticosteroid).
Sugammadex	The U.S. Food and Drug Administration approved Bridion (sugammadex) injection to reverse the effects of neuromuscular blockade induced by rocuronium bromide and vecuronium bromide, which are used during certain types of surgery in adults.
Sebelipase alfa	The U.S. Food and Drug Administration approved Kanuma (sebelipase alfa) as the first treatment for patients with a rare disease known as lysosomal acid lipase (LAL) deficiency. Kanuma is approved for use in patients with LAL deficiency. Treatment is provided via intravenous infusion once weekly in patients with rapidly progressive LAL deficiency presenting in the first six months of life, and once every other week in all other patients.
Alectinib	The U.S. Food and Drug Administration approved Alecensa (alectinib) to treat people with advanced (metastatic) ALK-positive non-small cell lung cancer (NSCLC) whose disease has worsened after, or who could not tolerate treatment with, another therapy called Xalkori (crizotinib). Alecensa is an oral medication that blocks the activity of the ALK protein, which may prevent NSCLC cells from growing and spreading.
Selexipag	The U.S. Food and Drug Administration approved Uptravi (selexipag) tablets to treat adults with pulmonary arterial hypertension (PAH), a chronic, progressive, and debilitating rare lung disease that can lead to death or the need for transplantation. Uptravi belongs to a class of drugs called oral IP prostacyclin receptor agonists. The drug acts by relaxing muscles in the walls of blood vessels to dilate (open) blood vessels and decrease the elevated pressure in the vessels supplying blood to the lungs.
Lesinurad	The U.S. Food and Drug Administration approved Zurampic (lesinurad) to treat high levels of uric acid in the blood (hyperuricemia) associated with gout, when used in combination with a xanthine oxidase inhibitor (XOI), a type of drug approved to reduce the production of uric acid in the body. Zurampic works by helping the kidney excrete uric acid. It does this by inhibiting the function of transporter proteins involved in uric acid reabsorption in the kidney.

NIPER JEE – QUESTION PAPER I

1. Andrographolid is the principle chemical constituent of _____

(a) Quassia (b) Kalmegh–-
(c) Picrorrhiza (d) Visnaga

2. Meaning of P in QSAR equation stands for ____

(a) Permeability (b) Partition coefficient
(c) Porosity (d) Purity

3. What is the side effect of gentamycin?

(a) Hepatotoxicity (b) Ototoxicity
(c) Genotoxicity (d) All

4. Cetyl ether of polyethylene glycol is known as_____

(a) Myrj 56 (b) Brij 56
(c) Cetomacrogol (d) All of the above

5. Colchicines acts by_____

(a) Inhibiting DNA synthesis
(b) Inhibiting RNA synthesis
(c) Superoxides dismutase
(d) (a) and (b)

6. Which of the following is related with of osmotic pressure?

(a) Ficks law
(b) Gibbs-Donnan equation
(c) Pascal law
(d) Jacobus Henricus van't Hoff equation

7. Which of the following is prodrug?

(a) Sulfasalazine (b) Sulindac
(c) Aspirin (d) Siloxane

8. What of the following drug is used in the treatment of schizophrenia, acute psychotic states and delirium?

(a) Methyldopa (b) Carbamazepine
(c) Imipramine (d) Lithium

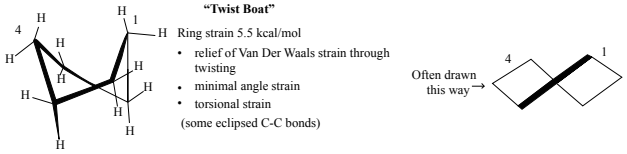
9. Northern blot is used for the separation of

(a) mRNA (b) DNA
(c) Protein (d) Protein DNA interaction

10. Atropioisomerism is shown by _____

(a) Substituted biphenyl system as hindered single bond rotation
(b) Aliphatic ether
(c) Aliphatic aldehyde
(d) Aliphatic acid

11. Identify the structure



(a) Boat (b) Chair
(c) Half chair (d) Twist boat

12. Which of the following is SSRIs used as anti-depressant?

(a) Citalopram (b) Fluoxetine
(c) Sertraline (d) All

13. Molar extinction coefficient is depending upon _____

(a) Path length
(b) Wave length
(c) Concentration of solute
(d) All of the above

14. Erythromycin act by inhibition of_____

(a) Cell wall synthesis
(b) Protein synthesis
(c) Nucleic acid synthesis
(d) Metabolites

15. Specific M1 receptor antagonist is____

(a) Atropine (b) Hyoscine
(c) Ipratropium (d) Pirenzepine

16. What is the biological source of CLOVE?

(a) Syzygium aromaticum
(b) Cinnamomum aromaticum
(c) Cardamom aromaticum
(d) None of these

17. Which amongst the following is used as detector in spectrophotometer?

(a) Golay cell (b) PMT
(c) Faraday cup (d) all

18. National institute of homeopathy is situated at
(a) Mumbai (b) Kolkata
(c) Delhi (d) Jaipur

19. Antibody titration is an important tool to determine_____
(a) Concentration of a specific antibody in the patient's serum
(b) Rate of antigen antibody reaction
(c) Number of sits available on antibody for loading of the drug
(d) Concentration of the drug that can be loaded on antigen

20. _____is the indication of flow property
(a) Bridging (b) Angel of repose
(c) Rat holing (d) All of the above

21. What is the correct sequence in cell cycle?
(a) G_1-G_2-S-M (b) G_1-S-G_2-M
(c) G_1-G_2-M-S (d) G_1-S-M-G_2

22. Rifampicin_____
(a) Inhibits cell wall synthesis
(b) Inhibits DNA-dependent RNA polymerase
(c) Inhibits nucleic acid synthesis
(d) Inhibits mycolic acid synthesis

23. In a class height of 20 students is 120 cm; height of 10 students is 100 cm what is the average height of total class students ?
(a) 115CM (b) 110 CM
(c) 105CM (d) 120CM

24. Acryl amide / dimethyl di-allyl ammonium chloride copolymer is used as
(a) Conditioner
(b) Hair softener
(c) Surfactant in shampoo
(d) Detergent

25. Drave test is used for _____
(a) Wetting agents
(b) Detergent
(c) Emulsifying agent
(d) Surfactant

26. SEC is a widely used for____
(a) Purification and analysis of synthetic and biological polymers
(b) Purification and analysis of synthetic drugs
(c) Purification and analysis of synthetic herbal products
(d) All of the above

27. How many member are required to from a society?
(a) 2 (b) 5
(c) 7 (d) No minimum limit

28. Who is the author of book "SONGS OF BLOOD AND SWORD" is _____
(a) Jhumpa Lahiri (b) Taslima Nasrin
(c) Fatima bhutta (d) Kiran Desai

29. Metformin belongs to which of the chemical class of anti-diabetic drug?
(a) Biguanides
(b) Thiazolidinediones
(c) Sulfonylureas
(d) Alpha-glucosidase inhibitor

30. Glutathione is _____
(a) A tripeptide of cystein and glutamate and a detoxifier
(b) A non essential amino acid, act as antioxidant
(c) Thiol containing vitamin mainly used in antioxidant in formulation
(d) (a) and (b)both

31. Living organisms are detected by ___
(a) Phase contrast microscopy
(b) Hot stage microscopy
(c) Electron microscopy
(d) None

32. _____ is used for litmus of arsenic
(a) Nesseler cylinder
(b) Kipps apparatus
(c) Gutzeit apparatus
(d) None

33. Which of the following is added to avoid crystallization in syrup?
(a) Propylene glycol
(b) Polyhydric alcohol
(c) Glycerol
(d) Ethyl alcohol

34. Clemmensen's reduction is described as_____
(a) Reduction of carboxylic acid to aldehydes using zinc amalgam and hydrochloric acid
(b) Reduction of ketones or aldehydes to alkanes using zinc amalgam and hydrochloric acid

(c) Oxidation of ketones or aldehydes to Carboxylic acid using hydrogen peroxide
(d) Oxidation amine to amide using hydrogen peroxide

35. Family of bael is_____
(a) Scropholariaceae (b) Leguminaceae
(c) Rutaceae (d) Compositae

36. What is the molarity of pure water?
(a) 55.5 (b) 18
(c) 1 (d) None of the above

37. SDS -PAGE is mainly used for_____
(a) Separation of DNA
(b) Separation of proteins
(c) Both
(d) None

38. What is the function of plasmid in r-DNA technology?
(a) Host for DNA multiplication
(b) Vector for transport
(c) Cutting of DNA strands
(d) All

39. Nucleotides are attracted to each other by which kind of bond?
(a) Sulphide (b) Hydrogen
(c) Phosphodiester (d) (b) and (c) both

40. Isoprenoid unit is synthesised from____
(a) Shikimic acid pathway
(b) Acetate pathway
(c) Mevalonic acid pathway
(d) All

41. _____ is the principle chemical constituent of ashwagandha
(a) Withanine (b) Conessine
(c) Germidine (d) Neopelline

42. Polystyrene is synthesized from ____
(a) Glycolic acid (b) PET
(c) Lactic acid (d) Caprolic acid

43. Antiparkinsonian drugs act by ……
(a) Increasing dopamine activity in CNS
(b) Reducing acetylcholine activity in CNS
(c) Increasing blood flow toward brain
(d) All

44. Methotrexate ……..
(a) Competitively inhibits dihydrofolate synthatase (DHFS)
(b) Competitively inhibits dihydrofolate reductase (DHFR)
(c) Competitively inhibits thymidylat reductase (THR)
(d) Competitively inhibits thymidylate synthatase (THS)

45. Melatonin is secreted by which glands?
(a) Pitutary (b) Hypothalamus
(c) Pineal (d) Thyroid

46. Assuming the same molecular weight and carbon content, arrange the following compound classes in the expected order of increasing pKa (lower acidity) : sulphonamide, alkene, alcohol, and amide
(a) (Low pKa) sulfonamide< alcohol< amide< alkene (High pKa)
(b) (Low pKa) alcohol< sulfonamide< amide< alkene (High pKa)
(c) (Low pKa) sulfonamide< amide< alcohol< alkene (High pKa)
(d) (Low pKa) sulfonamide< alcohol< alkene< amide (High pKa)

47. COMSIA is associate with ……..
(a) Virtual screening (b) Molecular docking
(c) QSAR (d) ADME prediction

48. Ionised drugs are concentrated in_____
(a) Brain (b) Liver
(c) Urine (d) Blood

49. Which of the following modification of acetylcholine results in a selective agonist on muscarinic receptor?
(a) Replacement of one N-methyl with N-ethyl
(b) Replacement of the esters with a carbamate
(c) Addition of alpha methyl on ethylene bridge
(d) Increase the ethylene bridge by one atom

50. Anticancer taxol derivatives act by _____
(a) Free radical generation
(b) Inhibitions of tubulin polymerization
(c) Inhibitions topoisomerase
(d) Enhancing tubulin polymerization

51. Enantiomers exhibit ……..
(a) Absolute isomerism
(b) Relative isomerism
(c) Optical isomerism
(d) All

52. Alkaline phosphate test is done for milk to test _____
(a) Liver function test
(b) Enzymatic degradation of the milk
(c) Cheese production
(d) Pasteurization

53. Which of the following HPLC Grade solvent use for peptide and Protein analysis?
(a) Dimethylsulfoxide(DMSO)
(b) Dimethyiformamide(DMF)
(c) Acetonitrile
(d) All

54. The base peak in mass spectrum is given by the_____
(a) Molecular ion (b) Most stable ion
(c) Metastable ion (d) Daughter ion

55. Ramachandran Plot is used for the determination of structure of_____
(a) Amino acid
(b) Protein
(c) Carbohydrates
(d) Enzyme substrate interaction

56. Which type of USP dissolution apparatus are used for oral tablet testing?
(a) Type I and II (b) Type I and III
(c) Type II and III (d) None of the above

57. Macrolide exerts its action by _____
(a) Inhibiting transcription
(b) Altering the genetic code
(c) Terminating protein synthesis prematurely
(d) Post – translational modification

58. pH of blood is _____
(a) 5.6 (b) 6.8
(c) 7.4 (d) 8.2

59. Picrorrhisa plant contains _____
(a) Lignan (b) Flavanoids
(c) Carotenoids (d) Tannins

60. Correct sequence for PCR process is _____
(a) Denaturation,Annealing,Extention
(b) Annealing, Extension,Denaturation
(c) Annealing,Denaturation,Extension
(d) Extension,Denaturation,Annealing

61. Tachyphlaxis refers to which of the following?
(a) Responsiveness increased rapidly after administration of a drug
(b) Responsiveness decreased rapidly after administration of a drug
(c) Responsiveness increased rapidly after maintenance of a drug (hypersensitive)
(d) Responsiveness decreased rapidly after maintenance of a drug (desensitized)

62. Avecil is brand name of_____
(a) Starch (b) MCC
(c) PEG (d) Calcium carbonate

63. Cyanide at 545nm Gives _____ colour
(a) Red (b) Yellow
(c) Green (d) Violet

64. Identify the missing number

5	4
20	9

7	4		9	4
24	11		?	13

(a) 6 (b) 4
(c) 28 (d) 11

65. What is the condition for accelerated stability testing in India?
(a) 30ºC ± 2ºC/ 75% RH ± 5% RH
(b) 40ºC ± 2ºC/ 75% RH ± 5% RH
(c) 40ºC ± 2ºC/ 65% RH ± 5% RH
(d) 30ºC ± 2ºC/ 65% RH ± 5% RH

66. Octadecyl carbon chain (C_{18}) bonded silica column is used in _____ chromatography
(a) Normal phase (b) Reverse phase
(c) Ion pair (d) Size exclusion

67. Which of following is best method to convert crystal from to amorphous from?
(a) Micronization (b) Freeze Drying
(c) Rolling (d) Any of Above

68. Which of the following polymer is used as ion exchange?
(a) Cross-linked polystyrene
(b) Carboxy Methyl Cellulose
(c) Cross-linked polymethacrylate
(d) All of the above

69. Which form of cyclodextrins is more soluble in water?
(a) α (b) β
(c) γ (d) δ

70. The process of change of R- configuration to S is known as
(a) Chirality (b) Walden inversion
(c) Chiral inversion (d) Stearic hindrance

71. Which of the following is INCORRECT and Cocoa butter?

(a) Pale yellow, usually solid at room temperature
(b) Soluble in water
(c) Shows phenomenon of polymorphis
(d) None of the above

72. The largest revenue in India is obtained from?
(a) Sales tax (b) Direct Tax
(c) Excise duties (d) None of These

73. _____is the Ca^{++} channel blocker
(a) Benzodiazepine (b) Verapamil
(c) Phenytoin (d) Minoxidil

74. Serpins are the inhibitors of___
(a) Proteases (b) Integrases
(c) Polymerase (d) Terpene

75. Synonym of AUDACIOUS ___
(a) Dumb (b) Daring
(c) Attractive (d) Dangerous

76. Tetracycline may be inactivated by epimerization
(a) True (b) False
(c) Cannot say (d) Depend upon pH

77. Particle size obtained from a fluid energy mill is _____
(a) 1-30μm (b) 30-60 μm
(c) 60-90 μm (d) 90-120 μm

78. Substituent inductive and field effects
(a) Are proportional to their proximity to the functional group
(b) Are related to the size of the group
(c) Are unrelated to proximity to the functional group
(d) Both (a) and (b)

79. The capsule with smallest size is denoted by number____
(a) 0 (b) 1
(c) 2 (d) 5

80. The largest cotton producer in the world is _____
(a) India (b) China
(c) USA (d) Brazil

81. Synonym of MAGNANIMOUS ___
(a) Attractive (b) Generous
(c) Kind (d) Love

82. Chemically Nujol is____
(a) Geminol diol
(b) Polyhydric alcohol
(c) Liquid paraffin hydrocarbons
(d) Terpene

83. What is the pH of 0.005N HCl?
(a) 2.3 (b) 3.2
(c) 5 (d) 1

84. RBI was established on_____
(a) April 1, 1934 (b) April 1, 1935
(c) April 1, 1937 (d) April 1, 1949

85. Synonym of REBATE ___
(a) Debenture (b) Discount
(c) Dividend (d) Bonus

86. Which of the following is biodegradable polymer?
(a) Chitosan (b) PGA
(c) PCL (d) All of the above

87. Morphine was discovered in ___
(a) 1805 (b) 1892
(c) 1902 (d) 1992

88. Gallic acid is used as _____
(a) Preservatives (b) Emulsifier
(c) Buffer (d) Antioxidant

89. A+B =100 A-B =24, so which is the larger number?
(a) A=62 (b) A=38
(c) B=62 (d) B=38

90. Which of the following is water soluble lubricant?
(a) Lactose (b) Sodium chloride
(c) PEG (d) Sorbitol

91. Stereochemistry of Gossypol is due to ___
(a) Chiral Carbon
(b) Chiral Nitrogen
(c) Restricted Rotation
(d) Null

92. What is the advantage L-Dopa over dopamine?
(a) Less toxic
(b) More soluble
(c) More lipophilic
(d) All

93. Which of the following is carbonic anhydrase inhibitor?
(a) Furosemide (b) Hydrochlorothiazide
(c) Acetazolamide (d) Lithium

94. Cyclohaxanone on reduction gives _____
(a) Cyclohexanol (b) Cyclohexene
(c) Cyclohexadiol (d) None

95. $FeCl_3$+ Catechol gives ___ color

(a) Purple (b) Red
(c) Green (d) Violet

96. Synonym of Infrequently

(a) Isolated (b) Occasional
(c) Scattered (d) All of the above

97. Which functional group is transferred by coenzyme pyridoxal phosphate?

(a) Aldehyde (b) H- atom
(c) Amino (d) Acyl

98. Glutathione is _____

(a) A tripeptide of cysteine and glutamate and a detoxifier
(b) A non-essential amino acid, act as antioxidant
(c) Thiol containing vitamin mainly used as antioxidant in formulation
(d) Both (a) and (b)

99. Phenolphthalein shows colour change at___ pH

(a) 6-8 (b) 8-10
(c) 10-12 (d) 12-14

100. On melting double stranded DNA gives more number of?

(a) C&G (b) C&A
(c) C&T (d) A&T

ANSWER KEYS

1. (b)	**2.** (b)	**3.** (b)	**4.** (c)	**5.** (a)	**6.** (d)	**7.** (a)	**8.** (d)	**9.** (a)	**10.** (a)
11. (d)	**12.** (d)	**13.** (b)	**14.** (a)	**15.** (d)	**16.** (a)	**17.** (b)	**18.** (b)	**19.** (a)	**20.** (b)
21. (b)	**22.** (b)	**23.** (a)	**24.** (a)	**25.** (a)	**26.** (a)	**27.** (b)	**28.** (c)	**29.** (a)	**30.** (a)
31. (a)	**32.** (c)	**33.** (d)	**34.** (b)	**35.** (c)	**36.** (a)	**37.** (c)	**38.** (b)	**39.** (c)	**40.** (c)
41. (a)	**42.** (c)	**43.** (d)	**44.** (b)	**45.** (c)	**46.** (d)	**47.** (c)	**48.** (c)	**49.** (b)	**50.** (d)
51. (d)	**52.** (d)	**53.** (b)	**54.** (d)	**55.** (a)	**56.** (a)	**57.** (c)	**58.** (c)	**59.** (a)	**60.** (a)
61. (b)	**62.** (b)	**63.** (d)	**64.** (c)	**65.** (b)	**66.** (b)	**67.** (d)	**68.** (d)	**69.** (b)	**70.** (b)
71. (b)	**72.** (c)	**73.** (b)	**74.** (a)	**75.** (b)	**76.** (a)	**77.** (a)	**78.** (a)	**79.** (d)	**80.** (b)
81. (b)	**82.** (c)	**83.** (a)	**84.** (b)	**85.** (b)	**86.** (d)	**87.** (a)	**88.** (d)	**89.** (a)	**90.** (c)
91. (c)	**92.** (c)	**93.** (c)	**94.** (a)	**95.** (b)	**96.** (d)	**97.** (c)	**98.** (a)	**99.** (b)	**100.** (a)

NIPER JEE – QUESTION PAPER II

1. Which of the following is directly titrated with acid?
(a) Aminophyllin (b) Phenytoin
(c) Sulphynpyrazone (d) Phenobarbitone

2. Which of the following principle involve in Karl Fischer titration?
(a) Reduction of I_2 by SO_2 in presence of water by removal by pyridine iodate
(b) Reduction of I_2 by SO_2 in presence of water by removal by pyridine sulphate trioxide
(c) Reduction of SO_2 by pyridine in presence of I_2 and water by removal of pyridine iodate
(d) Reduction of I_2 by pyridine in presence of water and SO2 by removal of pyridine sulphate trioxide

3. DLVO therapy is associated with _____
(a) Granulation (b) suspension
(c) Emulsion (d) Compression

4. The anti HIV drug approved by USFDA on 2008 is a non-nucleoside reverse transcriptase inhibitor
(a) Certolizumab (b) Tipranavir
(c) Etravirine (d) Protein DNA interaction

5. Antonym of ONEROUS
(a) Burdensome (b) Arduous
(c) Tedious (d) Easy

6. Amount of blood pumped out from heart in 1min. is called as _____
(a) Cardiac output (b) Stock volume
(c) FEV (d) Minute

7. Phenytoin is used in or as_____
(a) Supraventricular arrhythmias
(b) Ventricular arrhythmias
(c) Bradycardia
(d) Antiepileptic

8. Light year is a unit of_____
(a) Time (b) Distance
(c) Mass (d) Intensity of light

9. Which of the following is protophilic solvent?
(a) Benzene (b) Chloroform
(c) Sulphuric acid (d) None of these

10. Glycolysis occur in _____
(a) Mitochondria (b) Cytosol
(c) Golgi apparatus (d) Ribosome

11. Central dogma of molecular biology is _____
(a) DNA→RNA → Protein
(b) Replication →Transcription →Translation
(c) Information cannot transferred back from protein
(d) All

12. Green bones are used to manufacture _____ gelatin
(a) Type A (b) Type B
(c) Type C (d) Type D

13. HLB of o/w emulsifier is _____
(a) 0-3 (b) 3-6
(c) 7-9 (d) 8-15

14. Platelets are derived from?
(a) Pus cell (b) Lymphoblast
(c) Myoblast (d) Megakaryocytic

15. Which of the following is hydrophobic?
(a) DMSO (b) Ethanol
(c) PEG (d) Stearic acid

16. Identify the photosensitive active pharmaceutical
(a) Ciprofloxacin (b) Nifedipin
(c) Both (a) and (b) (d) Simvastatin

17. Hypertension stage-II falls in the range of _____
(a) Sys = 160 and diastolic = 100
(b) Sys = 140-159 or diastolic = 90-99
(c) Sys = 160 or diastolic = 100
(d) Sys = 140-159 and diastolic = 90-99

18. Which of the following test is detection of caffeine?
(a) Van urk's test (b) Thelloquin test
(c) Murexide test (d) Wagner's test

19. Which of the following reaction occurs faster in H_2O thn D_2O
(a) SN2 (b) SN1
(c) Elimination (d) Hydrolysis

20. India plans a manned mission to the moon by _____
(a) 2020 (b) 2025
(c) 2030 (d) 2012

21. Identity non-ionic surfactant
(a) Sodium lauryl sulfate
(b) Spans
(c) Benzalkonium chloride
(d) Lecithin

22. Meso compounds are optically inactive due to?
(a) Internal compensation
(b) External compensation
(c) Restricted rotation
(d) None

23. Finger print region for IR is _____
(a) 1400-4000 cm^{-1}
(b) 4000-8000cm^{-1}
(c) 400-1400cm^{-1}
(d) None of the above

24. When UV light falls on a molecule it causes_____
(a) Excitation of bonds
(b) Excitation of nuclease
(c) Excitation of molecule
(d) Excitation of electrons

25. % yield =_____
(a) Practical yield/Theoretical yield
(b) Theoretical yield/Practical yield
(c) Practical yield/ Theoretical yield) × 100
(d)(Theoretical yield/ Practical yield) × 100

26. Propranolol is contraindicated in _____
(a)Asthma (b)Angina
(c)Pregnancy (d)All

27. Erythrose and threose are_____
(a) Diastereomers
(b) Enantiomers
(c) Racemic Mixture
(d) Anomers

28. What is the use of UV circular dichroism spectroscopy?
(a) Investigation conformation of 2º structure of proteins
(b) Peptide bond determination
(c) Structure elucidation of synthetic compound
(d) Determination of unsaturation in protein

29. Range of visible light is _____
(a) 0-2 μm (b) 0.2-0.4 μm
(c) 0.4-0.8 μm (d) 200-800 μm

30. The typically used invitation energy for an EI mass spectrometer is: _____
(a) 0.7 eV (b) 70 eV
(c) 700 eV (d) 7000 eV

31. _____ is the example of non-irritating purgative
(a) CMC (b) Anthraquinone
(c) Triphenylmethane (d) Ricinolic acid

32. Material used for packaging during accelerated stability studies is _____
(a) Open containers
(b) Packaging similar to proposed packaging
(c) The containers convenient for sampling
(d) Any of the above

33. Maximum amount of potassium loss is done by _____
(a) Spironolactone (b) Acetazolamide
(c) Chlorthalidone (d) Torasemide

34. Addition of double bond to a chromophore causes _____shifts
(a) Hypsochromic (b) Hypochromic
(c) Bathochromic (d) Hyperchromic

35. Which among the following is an IR source?
(a) Deuterium lamp (b) Nernst glower
(c) Pneumatic cell (d) Tungsten lamp

36. NABARD is _____
(a) Board (b) Bank
(c) Bureau (d) Department

37. Which of the following is not associated with hepatotoxicity?
(a)Rifampicin (b) Pyrazinamide
(c)Ethambutol (d) Streptomycin

38. Podophyllin is used for _____
(a) Ovarian cancer
(b) Constipation
(c) Irritable bowel syndrome(IBS)
(d) Diarrhea

39. Hydrogen bonding is determined by _____ spectroscopic method
(a) Raman (b) NMR
(c) IR (d) UV

40. Most intense peak is obtained is mass spectrum is _____
(a) Molecular ion peak (b) Base peak
(c) Parent ion peak (d) Isotropic peak

41. The range of IR absorption for N-H bond is _____ cm^{-1}

(a) 1700 (b) 3400
(c) 780 (d) 1100

42. Theoretical yield = 1.5gm, practical yield =2gm than percentage yield=?

(a) 15% (b) 20%
(c) 75% (d) 125%

43. If a drug is highly protein bound then it show _____

(a) More efficient diffusion into cell membranes
(b) High potency
(c) Low potency
(d) Low biological half-life

44. Amrinone is _____

(a) PDE-III inhibitor
(b) Na^+/K^+ATPase inhibitor
(c) PDE-IV inhibitor
(d) None of the above

45. Term pharmacognosy was coined by _____

(a) Hypocratus (b) Syndler
(c) Gallon (d) Pasture

46. Dry Solids are sterilised by _____

(a) Dry heat (b) Gaseous
(c) Radiation (d) Steam

47. Streptokinase is obtained from _____

(a) *Streptobacillus* (b) *Streptomyces*
(c) *Streptococci* (d) All of the above

48. Vehicle used in soft gelatin capsule (SGC) is ---------

(a) PEG (b) Sorbitol
(c) Glycerol (d) Propylene glycol

49. Gossypol shows which kind of isomerism?

(a) Optical isomerism
(b) Configurational isomerism
(c) Atropisomers
(d) R and S isomerism

50. The Essar group of companies has been promoted by_____

(a) Ambanis (b) Ruias
(c) Goenkas (d) Kanorias

51. Tween 40 is _____

(a) Polyoxyethylene (20) sorbitan monolaurate
(b) Polyoxyethylene (20) sorbitan monolaurate
(c) Ploy oxyethylene (20) sorbitan monooleate
(d) Polyoxyethylene (20) sorbitan monopalmitate

52. Arrange the following spectroscopic technique in the ascending order of their energies: NMR, IR, UV

(a) NMR>IR>UV (b) NMR<IR<UV
(c) UV<IR<NMR (d) UV>IR>NMR

53. Reference standard used in NMR is _____

(a) $CDCl_3$ (b) D_2O
(c) DPPH (d) TMS

54. Ephedrine exist in how many stereoisomeric forms?

(a) 1 (b) 2
(c) 3 (d) 4

55. Which of the following is true about Cephalin?

(a) Chemistry it is phosphatidylethanolamine
(b) Principal constituent in bacteria
(c) In human physiology it is found in nervous tissue
(d) All of above

56. _____ is used for FT-IR calibration

(a) Water (b) Air
(c) Methanol (d) KMnO4

57. One of the following is associated with discovery of meningitis. Identify

(a) Robert Whytt (b) Robert Koch
(c) Someone Flexner (d) Ian Flemming

58. According to IP, RS means _____

(a) Reducing substance
(b) Reducing standard
(c) Reference standard
(d) Reference substance

59. Chemically Kaolin is _____

(a) Hydrated magnesium slicate
(b) Hydrated aluminium silicate
(c) Calcium carbonate
(d) None

60. Which of the following gum have Anti Diabetic activity?

(a) Acacia (b) Guar
(c) Xanthan (d) Locust bean

61. Heparin is_____

(a) Protein (b) Polysaccharide
(c) Lipid (d) Amino acid

62. Which of the following H2 receptors antagonist has the highest affinity for CYP450?

(a) Nizatidine (b) Ranitidine
(c) Cimetidine (d) Famotidine

63. Which of following element is present in betaine structure?

(a) Sodium (b) Phosphorous
(c) Lithium (d) Chlorine

64. Hepatic toxicity in paracetamol is caused due to an active metabolite.it is _____
(a) N-acyl-p-benzoquinoneimine
(b) N-acetyl-p benzoquinonimine
(c) N-aryl-p benzoquinonimine
(d) N alkyl-p benzoquinonimine

65. Which antihypertensive is relatively safer during pregnancy?
(a) Enalapril (b) Nifedipine
(c) Furosemide (d) None of the above

66. Clonidine is ……
(a) Antiliplda emic (b) Antipsychotic
(c) Antiseizure (d) Antihypertensive

67. Cough is the major side effect of_____
(a) Valsartan (b) Codeine
(c) Enalkiran (d) Captopril

68. During fermentation of penicillin the pH is first adjusted to 2, why?
(a) For maximum growth of *Penicillium chryogenum*
(b) For maximum yield
(c) Penicillin exist as an undissociated acid so it is soluble in organic solvent
(d) To remove the impurity

69. Anthocyanidins possess _____
(a) Flavylium (2-phenylchromenylium)ion skeleton
(b) 2,3-dihydro-2-phenylchromen-4-one
(c) 2-phenylchromen-4-one
(d) Flavan-3,4-diol

70. Asparginase shows _____ activity
(a) Antitumor (b) Antimicrobial
(c) Anti-inflammatory (d) Thrombolytic

71. Gingival hyperplasia is related to _____
(a) Ethosuccimide (b) Gabapentin
(c) Phenytoin (d) Valproic acid

72. Mannitol is an excellent choice for chewable tablets because it has…….
(a) Positive heat of solution
(b) Negative heat of solution
(c) Zero heat of solution
(d) None

73. According to IP, solubility range for sparingly soluble is 1 part of solute-soluble in _____
(a) 0 to 10 (b) 10 to 30
(c) 30 to 100 (d) 100-10000

74. Volume capacity of '000' size capsule is _____ ml
(a) 0.95 (b) 0.85
(c) 0.75 (d) 1.37

75. Chemically Mayer's reagent is …….
(a) Potassium mercuric iodide
(b) Potassium bismuth iodide
(c) I_2 and KI
(d) Picric acid

76. Delta value of Ethylene= 2.3-2.7 ppm, whereas of Acetylene has _____
(a) 2.7-3.2 ppm (b) 6-9 ppm
(c) 4.5-6.5 ppm (d) 1.1-3.0 ppm

77. Right to privacy as a fundamental right is implicit in the
(a) Right to freedom
(b) Right to personal liberty
(c) Right to equality
(d) Right against exploitation

78. Amino acid which describe as an imino acid_____
(a) Proline (b) Lysine
(c) Tyrosine (d) Leucine

79. To detect compound without chormophore _____ is done
(a) Change of solvent
(b) Change of range of UV
(c) Derivitisation
(d) All of the above

80. _____% of Benzyl alcohol is used as preservation
(a) 0.1 (b) 0.5
(c) 1 (d) 0.01

81. Which of the followings is true for circulating RAS system ?
(a) ACE is a dipeptide that acts on carboxyl terminal of A-I to generate A-II
(b) ACE is a dipeptide that acts on amino terminal of A-I to generate A-II
(c) ACE is a tripeptide that acts on carboxyl terminal of A-I to generate A-II
(d) ACE is a dipeptide that acts on angiotensinogen to generate A-I

82. Vulcanizing agent for rubber is…….
(a) Sulphur (b) Sulphur dioxide
(c) Zinc (d) $CaCO_3$

83. Coumarin is_____
(a) 2-phenylchromen-4-one
(b) 3- phenylchromen-4-one
(c) 2H- chormen-2-one
(d) 4-phenylcoumarine

84. Aflotoxins are naturally occurring mycotoxins that are produced by _____
(a) *Bixa orellana* (b) *Aspergillius flavus*
(c) *Cola nitida* (d) *Karenia brevis*

85. When UV light falls on a molecule it causes _____
(a) Excitation of bonds
(b) Excitation of nuclease
(c) Excitation of molecule
(d) Excitation of electrons

86. What is the use of cyclodextrin?
(a) Solubility enhancement
(b) Stability enhancement
(c) Taste masking
(d) All of the above

87. Polypharmacy means_____
(a) Use of multiple medication by a patient
(b) Use of combination of drugs
(c) Medication in geriatric patient
(d) Science polymorphism

88. Which of the following is a sent drug?
(a) Carbidopa (b) Levodopa
(c) Isoniazid (d) Vitamin B

89. Which of the following plastic polymer has higher permeability?
(a) Polyethylene (b) Polypropylene
(c) Nylon (d) Polystyrene

90. Mark-Houwink equation is used to determine molecular weight of colloids from
(a) Viscosity (b) Diffusion
(c) Electronic charge (d) None

91. Which of the following is not associated with hypokalemia?
(a) Hydrochlorothiazide
(b) Furosemide
(c) Triamterene
(d) Amphotericin B

92. MOA of fluorouracil is _____
(a) Inhibition of spindle formation
(b) Inhibition of thymidylate Synthesis
(c) Alkylating DNA
(d) Inhibiting ATP formation

93. Why multi drug treatment given in TB?
(a) To avoid resistance
(b) To minimize side affects
(c) To reduce the duration of therapy
(d) To reduce cost of therapy

94. Amylase consists of _____ glycosidic linkage
(a) α1-4 (b) α1-2
(c) β1-4 (d) β1-2

95. Folate deficiency is caused by_
(a) Methotraxate (b) Cyclofosfamide
(c) Busulfan (d) Etoposide

96. Which of the following vitamins is teratogenic?
(a) Vit. C (b) Vit. E
(c) Vit. D (d) Vit. A

97. Class-III antiarrhythmic agents are _____
(a) Na channel blocker
(b) K channel bloker
(c) Na channel opener
(d) K channel opener

98. Which of following is used to overcome GI irritation caused by NSAIDS?
(a) Mesoprostol (b) PEG
(c) Senna
(d) Bismuth carbonate

99. Which of the following compounds would have the highest boiling point?
(a) $CH_3CH_2CH_2CH_3$ (b) CH_3NH_2
(c) CH_3OH (d) CH_2F_2

100. GABA receptors are _____
(a) Excitatory
(b) Inhibitory
(c) Excitatory followed by inhibition
(d) Inhibition followed by Excitation

ANSWER KEYS

1. (b)	**2.** (b)	**3.** (b)	**4.** (b)	**5.** (d)	**6.** (a)	**7.** (d)	**8.** (a)	**9.** (d)	**10.** (b)
11. (d)	**12.** (b)	**13.** (d)	**14.** (d)	**15.** (d)	**16.** (c)	**17.** (a)	**18.** (c)	**19.** (c)	**20.** (a)
21. (b)	**22.** (a)	**23.** (c)	**24.** (d)	**25.** (c)	**26.** (a)	**27.** (a)	**28.** (a)	**29.** (c)	**30.** (b)
31. (a)	**32.** (b)	**33.** (c)	**34.** (c)	**35.** (b)	**36.** (b)	**37.** (d)	**38.** (b)	**39.** (c)	**40.** (b)
41. (b)	**42.** (c)	**43.** (c)	**44.** (a)	**45.** (b)	**46.** (a)	**47.** (c)	**48.** (a)	**49.** (c)	**50.** (b)
51. (d)	**52.** (d)	**53.** (d)	**54.** (d)	**55.** (d)	**56.** (b)	**57.** (a)	**58.** (c)	**59.** (b)	**60.** (b)
61. (b)	**62.** (c)	**63.** (b)	**64.** (b)	**65.** (b)	**66.** (d)	**67.** (d)	**68.** (c)	**69.** (a)	**70.** (a)
71. (c)	**72.** (b)	**73.** (c)	**74.** (d)	**75.** (a)	**76.** (c)	**77.** (b)	**78.** (a)	**79.** (d)	**80.** (c)
81. (a)	**82.** (a)	**83.** (c)	**84.** (b)	**85.** (d)	**86.** (d)	**87.** (a)	**88.** (a)	**89.** (d)	**90.** (a)
91. (c)	**92.** (b)	**93.** (a)	**94.** (a)	**95.** (a)	**96.** (b)	**97.** (b)	**98.** (a)	**99.** (d)	**100.** (b)

NIPER JEE – QUESTION PAPER III

1. Calculate the area of rectangle width=5cm, height=1/2 width

(a) 2.5 cm^2 (b) 12.5cm^2

(c) 1.25 cm^2 (d) 125 cm^2

2. Isoelectric point of insulin is 5. How one can make its long acting formulation?

(a) Decrease pH formulation above isoelectric point

(b) Increase pH of formulation above isoelectric point

(c) Both of the above

(d) None of above

3. What is the additional value of α-methyl group for α, β-unsaturated carbonyl compounds according to Woodward- Fischer rule?

(a) 5 (b) 10

(c) 12 (d) 18

4. Which of the following cardigan toxicity?

(a) Doxorubicin (b) Cisplatin

(c) Nifedipine (d) All of the above

5. Stereoisomers of cyclic carbohydrates is known as_____

(a) Epimer (b) Anomer

(c) Enantiomer (d) Diasterioisomer

6. Cycloserine acts by _____

(a) Competitive inhibition 2 terminal alanines to initial tripeptide side chain on N-AMA

(b) Prevent addition to the growing end of the peptidoglycan

(c) Interferes with regeneration of lipid carries by blocking dephosphrylation

(d) Inhibit transpeptidation cross linking by blocking binding to PBPs

7. Synonym of solicitor is _____

(a) Attorney-at-law (b) Barrister

(c) Counselor (d) All of the above

8. _____ is longer acting penicillin

(a) Procaine penicillin (b) Benzathin penicillin

(c) Penicillin V (d) Ampicillin

9. What is m/z ratio for butyrophenone according to Mac-lafferty arrangement?

(a) 120 (b) 106

(c) 110 (d) Both (a) and (b)

10. DOT in the treatment of tuberculosis stands for _____

(a) Directly observed therapy

(b) Department of TB treatment recommendation

(c) Daily observation of TB patient

(d) Department of TB irradication program

11. What is the synonym of machine?

(a) Cadaverous (b) Ghastly

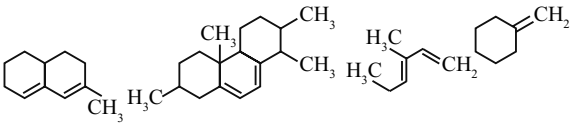
(c) Deathly (d) All of the above

12. Which of the following is used as a sorbent in tablet bottles?

(a) MCC (b) Silica

(c) Both (a) and (b) (d) None

13. Which of the following is not a heteroannular diene?



(a) (b) (c) (d)

14. Which of the following is induced in allergic reaction?

(a) IgG (b) IgM

(c) IgE (d) IgA

15. Earth day is observed on _____

(a) April 22 (b) April 17

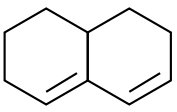
(c) April 30 (d) April 24

16. ANVISA is a regulatory body of _____

(a) U.S.A. (b) Japan

(c) Brazil (d) Portugal

17. Why does the diene shown below fail to undergo a diels-alder reaction with even the most reactive dienophiles?



(a) The diene cannot achieve the necessary s-cis conformation
(b) This is not diene
(c) It is not monocyclic
(d) It is planar molecule

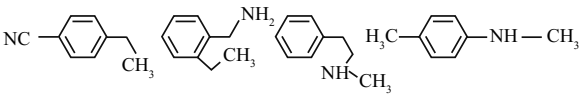
18. Site for phase-II reaction is _____
(a) Cytosole (b) ER
(c) Mitochondria (d) Golgi apparatus

19. _____ is the principle of gas chromatography
(a) Adsorption (b) Partition
(c) (a) and (b) both (d) None

20. Benzopyaran-2-one is_____
(a) Warfarin
(b) Sitosterol
(c) Coumarin
(d) Benzoquinone

21. 5, 7-Dihydroxyflavone is_____
(a) Chrysin (b) Rutin
(c) Chalcone (d) Quercetin

22. Provide a structure that is consistent with the data below. C_9H_9N
IR (cm^{-1}): 3050, 2950, 2240, 1630
1H NMR (δ): 7.5(2H, d), 7.1 (2H, d), 2.3 (2H, q), 0.9 (3H, t)



(a) (b) (c) (d)

23. Since when the product patent came in the existence in India?
(a) 2000 (b) 2002
(c) 2005 (d) 2007

24. Contact angle for complete wetting is _____
(a) 180 (b) 90
(c) 0 (d) 60

25. Find out the missing number 24:15::63:?
(a) 56 (b) 38
(c) 48 (d) 28

26. 1:9:17:33:49:73:?
(a) 105 (b) 8
(c) 97 (d) 16

27. Rheum rhizome is used as_
(a) Laxative (b) Carminative
(c) Anti diarrhea (d) Purgative

28. Which of the following is cardio toxic?
(a) Vancomycin (b) Adriamycin
(c) Amphotericin (d) Penicillin

29. Paclitaxel acts by_____
(a) Free radical generation
(b) Inhibition of tubulin polymerization
(c) Inhibiting topoisomerase
(d) Enhancing tubulin polymerization

30. Share premium is _____
(a) Capital receipt
(b) Revenue receipt
(c) Both (a) and (b)
(d) None of above

31. _____ is the anticholinergic agent used in peptic ulcer treatment
(a) Dicyclomine (b) Pirenzepine
(c) Rolxatidine (d) Rebeprazole

32. Calcium channels in heart are of which type?
(a) Ligand gated (b) Voltage gated
(c) Enzyme gated (d) Ion gated

33. Selective α-1 blocker is_____
(a) Prazosin (b) Atenolol
(c) Salbutamol (d) Losartan

34. A, B, C, D represent 2,5,3,4 and I, N, O, X represent 1, 6, 9, 0 than I, B, C, X represent what?
(a) 1,2,3,4 (b) 2,4,5,6
(c) 1,5,3,0 (d) 1,0,2,6

35. Therapeutical index denotes_____
(a) Margin of safety
(b) Margin of efficacy
(c) Margin of therapy
(d) All

36. Which of the following formulation technique is used for targeting drug to liver?
(a) Liposome
(b) Niosome
(c) Microencapsulation
(d) Resealed erythrocyte

37. Receptors are made up of_____
(a) Carbohydrate (b) Proteins
(c) Lipids (d) Amino acid

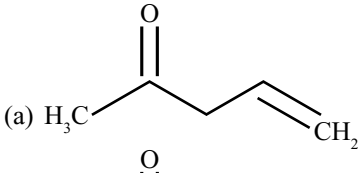
38. Which of the following is the principal component if cell membrane?

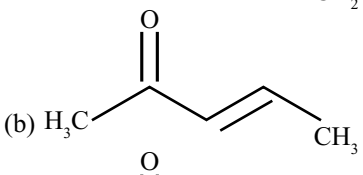
(a) Phospholipids (b) Glycolipid
(c) Lipoprotein (d) All of the above

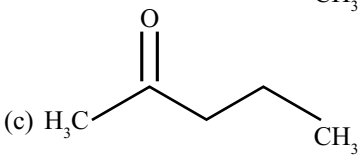
39. MALDI is related with _____
(a) Mass spectroscopy
(b) Soft ionization technique
(c) Protein and peptide study
(d) All of above

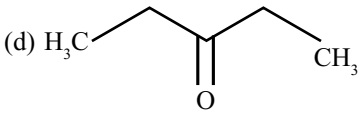
40. A non-animals gelatin capsule has been developed with_____
(a) Pullalan
(b) Hydroxypropyl methyl cellulose
(c) Both (a) and (b)
(d) None

41. Which of the following compounds will have its carbonyl absorbance (c=o) appear at the lowest frequency?

(a) 

(b) 

(c) 

(d) 

42. Serotonin is _____
(a) Monoamine
(b) Chemical mediators
(c) Neurotransmitter
(d) All of these

43. Actin and myosin are _____
(a) Contractile protein
(b) Motor protein
(c) Transport protein
(d) Structural protein

44. In which of following registration is legally compulsory?
(a) Sole proprietorship
(b) Partnership
(c) Joint stock committee
(d) Co-operative undertaking

45. Nitric oxide is _____
(a) Vasodilator
(b) Vasoconstrictor
(c) Bronchodilator
(d) Broncho constrictor

46. Which of the following is/are second messenger system?
(a) Calcium (b) cAMP
(c) cGMP (d) All the above

47. Cytokinins are _____
(a) Plant hormone regulators
(b) Cytotoxic mediators
(c) Inflammatory mediators
(d) Enzymes

48. Which of the following is used in pre-anesthetic medication?
(a) Atropine (b) Midazolam
(c) Morphine (d) All of the above

49. Promius pharma is owened by _____
(a) Piramal health care
(b) Reddy's Laboratory
(c) Cipla
(d) Wockhardt

50. Which of the following is centrally acting skeleton muscle relaxant?
(a) Nitric oxide (b) Propranalol
(c) Mivacurium (d) Mephenesin

51. _____% of shares should be held by a company in another company so as to become subsidiary
(a) More than 50 (b) More than 40
(c) More than 30 (d) More than 20

52. Which of the following alkaloid is present in cough syrup?
(a) Phenytoin epinephrine
(b) Codeine
(c) Morphine
(d) Glycyrrhizin

53. Morphine shows its action by acting on _____ receptor
(a) μ (b) μ and δ
(c) κ and δ (d) γ and μ

54. Bloch and Purcell won Nobel prize of 1952 for their contribution in _____

(a) IR (b) NMR
(c) DSC (d) Fourier transmission

55. Which statement is false about aspirin?
(a) It inhibitor COX and thromboxane A2
(b) It is safer in asthmatics
(c) It is drug of choice for Reye's syndrome
(d) G-6-PD deficiency may enhance aspirin toxicity

56. Nicotinic receptor is _____
(a) Ligand gated ion channel
(b) Tyrosine Kinase
(c) GPCR
(d) Acid type

57. Ethyl-acetoacetate is prepared from ethyl acetate by the _____
(a) Benzoin condensation
(b) Aldol condensation
(c) Claisen condensation
(d) Dieckmann condensation

58. In QSAR studies the biological activity is expressed in terms of concentration C. The expression used is
(a) C (b) log C
(c) log 1/c (d) Any of the above

59. Which of the following is neurodegenerative disorder?
(a) Steven Johnson's syndrome
(b) Brain tumor
(c) Raynaud's syndrome
(d) Alzheimer's disease

60. What ^{13}C NMR decoupling technique provides information about the number of hydrogens attached to each carbon?
(a) Off-resonance
(b) Broadband
(c) Chemical shift
(d) J –value

61. Indian Ginseng is the synonym of _____
(a) *Withania somnifera*
(b) *Ginkgo biloba*
(c) *Andographis peniculata*
(d) None

62. Low solubility of general anesthetic in body fluid means____
(a) Prolonged action
(b) Enhancement of potency
(c) Decrease MAC
(d) All of the above

63. Bosentan is _____
(a) Serotonin uptake inhibitor
(b) Endothelin receptor
(c) Leukotrine modifier
(d) Calcium sensitizer

64. What is the meaning of welfare state?
(a) State plays a key role in protection, promotion of economics, social well-being of citizens
(b) Cater to state based societies
(c) Providing subsidies to the needed operations
(d)Protects, govern, or control particular aspects of society

65. Which of the following causes Hyperpyrexia?
(a) Suxamethonium
(b)Drug interaction of MAO inhibitor with pethidine
(c) Halothane
(d) All of the above

66. Who is the known as the father of chemotherapy?
(a) Robert Koch
(b) Gallan
(c) Paul Ehrlich
(d) Alexander Flaming

67. Which of the following is used for the treatment of alopecia?
(a) Finasteride (b) Minoxidil
(c) Cortisone (d) All of the above

68. Bohr's effect is related to _____
(a) Lipids (b) Plasma proteins
(c) Heamoglobin (d) Vitamins

69. Ginseng is obtained from _____
(a) *P. ginseng*
(b) *P. iaponica*
(c) *P. notoginseng*
(d) All of the above

70. Bacteria are absent in____
(a) Soil (b) Ice
(c) Dust (d) Blood

71. Peripheral & central emesis is caused by _____
(a) Apomorphine (b) $CuSO_4$
(c) Digitalis (d) Ergot

72. Which of the following is not a photogenic solving?
(a) Water (b) Acetic acid
(c) Sulphuric acid (d) CCl4

73. Which among the following act as secondary messenger for nicotinic receptor?
(a) IP3 (b) cAMP
(c) Ions (d) All

74. Placket-Bumman design is _____
(a) Computer aided design
(b) Drug design tool
(c) Type of experimental design
(d) Type of HPLC column design

75. _____ are cholesterol reducing agents
(a) Statins (b) Dipins
(c) Triptans (d) Sartans

76. _____ contains diacytic stomata
(a) Senna (b) Digitalis
(c) Vasaca (d) Coca

77. Which of the following drug interaction is hazardous?
(a) Terfinadine + Erythromycin
(b) Diazepam + Clarithromycin
(c) Cimetidine + Penicillin
(d) All of the above

78. Enalapril act by _____
(a) ACE inhibition
(b) Renin inhibition
(c) Renin antagonism
(d) Aldesteron antagonism

79. Which of the following causes cardiac arrhythmia?
(a) Amlodipine (b)Terfinadine
(c) Phenytoin (d) Amphotericin B

80. Corex a cough formulation is a product of _____
(a) Pfizer (b) Novartis
(c) GSK (d) Cipla

81. Protein synthesis is started by _____
(a) Entronic DNA (b) Exonic DNA
(c) mRNA (d) None of the above

82. Biochemical target in pharmaceutical lead discovery can be _____
(a) Enzymes (b) Receptor
(c) Ion channels **(d) All of these**

83. Phase-IV clinical trials deal with ___
(a) Post marketing survey
(b) Safety and efficacy
(c) Micro dosing
(d) Bioequivalence study

84. What is the function of RNA primer?
(a) Initiation of new DNA synthesis replication
(b) Separate the 2 stand (zip opener)
(c) DNA synthesis from 5`-3` direction
(d) it produces Okazaki fragments

85. Levodopa and Carbidopa are used as _____
(a) Anti conclusion (b) Anti Parkinson's
(c) Anti Alzheimer's (d) Anti histamine

86. β-2 selective agonist is _____
(a) Salbutamol (b)Propranolol
(c)Atenolol (d) Timolol

87. In which phase micro dosing is directly given to patient without pre-clinical testing?
(a) 0 phase (b) I phase
(c) II phase (d) III phase

88. _____ is used in case of cerebral malaria
(a) Primaquine (b) Chloroquine
(c) Quinine (d) Quinidine

89. Which malaria is deadly?
(a) *P. vivax* (b) *P. falciperum*
(c) *P. Malaria* (d) All

90. Tryptophan is coded by _____
(a) GGU (b) GUG
(c) UGG (d) GUU

91. In Michalis-Menten equation V_{max} is measure of _____
(a) Substrate affinity (b) Coenzyme activity
(c) Catalytic efficiency (d) Cofactor affinity

92. Principle of nephelometry and turbidymetary is _____
(a) Absorption of light (b) Reflection of light
(c) Scattering of light (d) Emission of light

93. Which of the following route is used for BCG vaccine administration?
(a) Subcutaneous (b) Intradermal
(c) Transdermal (d) Oral

94. Where the Indian institute of toxicological research is located?
(a) Kanpur (b) Izzatnagar
(c) Allahabad (d) Lucknow

95. Primaquine is used in _____
(a) Choloroquine resistant P.falciperum
(b) Malaria in pregnancy

(c) African malaria
(d) American malaria

96. Followings are stop codons except
(a) UAA (b) UGG
(c) UAG (d) UGA

97. Tamoxifen acts as _____
(a) Aromatase inhibitor
(b) Estrogen agonist
(c) Estrogen antagonist
(d) Progesterone antagonist

98. Anstrazole acts as _____
(a) Aromatase inhibitor
(b) Estrogen agonist
(c) Estrogen antagonist
(d) Progesterone antagonist

99. A+B > C+D, B+E = 2C, C+D > B+E which of the following is correct?
(a) B+E > A+B (b) C+D =2C
(c) A+B < C+D (d) A+B > 2C

100. Metallic elements are detected by _____
(a) ESR (b) IR
(c) AAS (d) Fluorescence

ANSWER KEYS

1. (b)	**2.** (b)	**3.** (b)	**4.** (d)	**5.** (b)	**6.** (a)	**7.** (d)	**8.** (b)	**9.** (d)	**10.** (a)
11. (d)	**12.** (b)	**13.** (b)	**14.** (c)	**15.** (a)	**16.** (c)	**17.** (a)	**18.** (a)	**19.** (c)	**20.** (c)
21. (a)	**22.** (a)	**23.** (c)	**24.** (a)	**25.** (c)	**26.** (c)	**27.** (d)	**28.** (b)	**29.** (d)	**30.** (b)
31. (b)	**32.** (b)	**33.** (a)	**34.** (c)	**35.** (a)	**36.** (d)	**37.** (b)	**38.** (a)	**39.** (d)	**40.** (c)
41. (b)	**42.** (d)	**43.** (a)	**44.** (c)	**45.** (a)	**46.** (d)	**47.** (a)	**48.** (d)	**49.** (b)	**50.** (c)
51. (a)	**52.** (b)	**53.** (a)	**54.** (b)	**55.** (c)	**56.** (a)	**57.** (c)	**58.** (c)	**59.** (d)	**60.** (a)
61. (a)	**62.** (d)	**63.** (b)	**64.** (a)	**65.** (d)	**66.** (c)	**67.** (d)	**68.** (c)	**69.** (d)	**70.** (d)
71. (a)	**72.** (d)	**73.** (c)	**74.** (c)	**75.** (a)	**76.** (c)	**77.** (a)	**78.** (a)	**79.** (b)	**80.** (a)
81. (c)	**82.** (d)	**83.** (a)	**84.** (a)	**85.** (b)	**86.** (a)	**87.** (b)	**88.** (c)	**89.** (b)	**90.** (c)
91. (c)	**92.** (c)	**93.** (c)	**94.** (d)	**95.** (a)	**96.** (b)	**97.** (c)	**98.** (a)	**99.** (d)	**100.** (c)

NIPER JEE – QUESTION PAPER IV

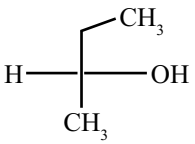
1. What is H5N1 in the news in recent times?
(a) A new multi-purpose helicopter of India Amy
(b) The nearest galaxy to own milky way
(c) A virus causing bird flu
(d) A virus causing swine flu

2. Persistent raspy cough is the side effect of _____
(a) ACE inhibitors
(b) Renin inhibitors
(c) Ramon antagonists
(d) Aldosterone antagonist

3. Enthalpy is used to measure_____
(a)Viscosity
(b) Flow property
(c) Heat transfer
(d) Temperature of solid

4. The amino acid alanine in our body has _____configuration
(a) S (b) R
(c) Both (a) and (b) (d) None of these

5. This projection formula is called as _____



(a) Newmann (b) Fisher
(c) Sawhorse (d) Gauche

6. Rifampicin is used not only in TB but in ____ also
(a) Steven Jonson syndrome
(b) Leishmaniasis
(c) Whipping cough
(d) Leprosy

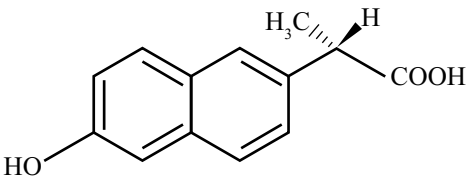
7. Luminescence, fluorescence and phosphorescence are the types of _____
(a) Absorption spectroscopy
(b) Emission spectroscopy
(c) Both (a) and (b)
(d) Transmittance

8. Rate kinetics deals with
(a) Order of reaction
(b) Molecularity of reaction
(c) Concentration of reactant
(d) All of the above

9. Which of the following cytotoxic product obtained from Marin source?
(a) Polymeric 3-alkylpyridibum
(b) Tentacles
(c) Bryostatin
(d) Paclitaxel

10. Which one of the following fatty acid is biosynthesized by human body?
(a) Lauric acid (b) Oleic acid
(c) Linoleic acid (d) All

11. Give the conformation of asymmetric carbon in structure below



(a) R (b) S
(c) E (d) Z

12. What do the letters XP stand for in the product Window XP?
(a) Extended product
(b) Extra pampering
(c) Experience
(d) Entry level product

13. Rault's law is related with
(a) Osmotic pressure
(b) Vapor pressure
(c) Atmospheric pressure
(d) All

14. Betaine is an intermediate of the ____ reaction
(a) Witting (b) Favorskii
(c) Claisen (d) Hoffman

15. _____ is the dominant antibody produced in primary immune response
(a) IgM (b) IgE
(c) IgG (d) IgA

16. Tyandalization is _____
(a) Heating the medium at 115°C for 30 min
(b) Heating the medium at 72°C for 15s
(c) Heating the medium at 80°C for 1hr on three successive days
(d) Heating the medium at 68.2°C for 30 min

17. Which is a novel histone deacetylase inhibitor used for cancer treatment?
(a) Romidepsin (b) Rituximab
(c) Rotigaptide (d) Ritanserin

18. Ring analogues of sugar are called as _____
(a) Enantiomers (b) Epimers
(c) Anomers (d) Diasterioisomers

19. Increased level of creatinine kinase is the indication for _____
(a) Acute hepatitis (b) Myasthenia gravis
(c) Cirrhosis (d) Myocardial infraction

20. Which microscopic technique is used for identification of cellular structure?
(a) Electron microscopy
(b) Dark field microscopy
(c) Phase contrast microscopy
(d) None

21. DOPP and PAO tests are used for the evaluation of efficiency of ____
(a) Membrane filter (b) Seitz filter
(c) G 3 filter (d) HEPA filter

22. The range of IR absorption for acid chloride is ____ cm^{-1}
(a) 1810 (b) 1720
(c) 1770 (d) 1680

23. Preparative HPLC is used for
(a) Separation of protein and peptide
(b) Separation of enantiomer compound
(c) Troubleshooting tool
(d) All of the above

24. Which of the following is added to avoid crystallization of syrup?
(a) Propylene glycol (b) Polycystic alcohol
(c) Glycerol (d) Lemon juice

25. The size of droplet in emulsion is _____
(a) 0.5-50μm (b) 5-50μm
(c) 0.1-1μm (d) 1-100μm

26. Ropinirole is used as _____
(a) Anti convulsions (b) Anti Parkinson
(c) Antialzheimers (d) Anti histaminics

27. Methotrexate exerts its action by _____
(a) Interfering with purine synthetase
(b) Intracellular formation of an amine adducts
(c) Forming conjugate with nucleic acid
(d) Inhibiting the synthesis of folic acid

28. Kurchi bark belongs to _____ family
(a) Rubiaceae (b) Apocynaceae
(c) Loganiaceace (d) Leguminoceae

29. The range of IR absorption for lactam rings is _____ cm^{-1}
(a) 1810 (b) 1720
(c) 1770 (d) 1680

30. Eye drops differ from parenteral preparation by
(a) Sterility (b) Particulate matter
(c) Pyrogenicity (d) Isotonicity

31. For IR region lies in the range of _____
(a) 0.8-2.5 μm (b) 2.5-15 μm
(c) 15-200 μm (d) 200 – 400 μm

32. Isocratic technique is the technique of elution that includes_____
(a) Changing adsorbent for different substances
(b) Changing solvent composition
(c) Keeping solvent system same throughout the process
(d) Rising evaporating temperature

33. The reversible cholinesterase inhibitor indicated in the treatment of alzheimer's disease is _____
(a) Tacrine
(b) Edrophonium
(c) Neostigmine
(d) Pyridostigmine

34. Reaction at chiral Carbon through SN2 mechanism causes _____
(a) Retention of configuration
(b) Inversion of configuration
(c) Racemization
(d) No change

35. N-allyl derivative of dihydrohydroxymorphine is _____

(a) Naloxone (b) Thebain
(c) Nalorphine (d) Naltrexone

36. Tolvaptan is___

(a) Competitive arginine vasopressin receptor 2 agonist
(b) Competitive arginine vasopressin receptor 2 antagonist
(c) Noncompetitive arginine vasopressin receptor 2 agonist
(d) Noncompetitive arginine vasopressin receptor 2 antagonist

37. Allosteric binding means_____

(a) Binding of the substrate at the active site of the enzyme
(b) Binding to site other than active binding site on the same enzyme
(c) Binding to the enzyme substrate complex
(d) Binding to endogenous substrate

38. GC is 50% stronger base pair as compared to AT Why?

(a) Electro negativity difference GC is more than AT
(b) Stearic hindrance in AT is more than GC
(c) GC forms 3 hydrogen bond but AT forms 2
(d) None of the above

39. Which software used in 3D-QSAR _____

(a) Linux (c) Chemic
(b) Chemdraw (d) coMFA

40. Who has authority to print one rupee currency note?

(a) Government of India
(b) RBI
(c) Indian bank
(d) Swiss bank

41. First pass metabolism is the problem associated with _____

(a) Vaginal (b) Nasal
(c) I.V (d) Oral

42. Morphine does not cause _____

(a) Constriction of pupil
(b) CNS depression
(c) Respiratory depression
(d) Diarrhoea

43. Biologically active from of Vit.D in humans is _____

(a) Cholecalciferol (b) Calcifediol
(c) Calciferol (d) Calcitriol

44. Nitrilase enzymes catalyze the hydrolysis of _____

(a) Nitriles to carboxylic acid and ammonia
(b) Nitriles to amides
(c) Nitriles to amine
(d) Nitriles to nitrates

45. Which of the following is soft ionisation source in mass spectrometer?

(a) Chemical ionisation
(b) Electrostatic spray ionisation
(c) MALDI
(d) All of the above

46. Which of the following is false about glycolysis?

(a) It occurs in both aerobic and anaerobic condition
(b) It is the major pathway for ATP production in tissue lacking mitochondria
(c) Lactate is the end product of aerobic condition
(d) It is essential for brain

47. Homatropine is _____

(a) Tropine ester of amino acetic acid
(b) Tropine ester of mendelic acid
(c) Tropine methyl bromide ester of mendelic acid
(d)Tropine ester of amino formic acid

48. Q is symbol for which amino acid?

(a) Glutamic acid (b) Glutamine
(c) Aspartic acid (d) Asparagine

49. The anti-markownikov addition of HBr to styrene gives

(a) β-bromoethyl benzene
(b) 1-bromoethyl benzene
(c) Bromobenzene
(d) Ethylbenzene

50. The function of Alcohol dehydrogenase is_____

(a) Conversion of toxic alcohols to aldehydes
(b) Conversion of toxic alcohols to dehydrates
(c) Conversion of toxic alcohols to water
(d) Conversion of toxic alcohols to amide

51. If hour hand of a clock at 12 noon is at north east, then at 1pm where will be the hour hand of the clock?

(a) South (b) East
(c) North (d) West

52. Chemical shift in NMR is expressed as _____

(a) δ (b) λ
(c) Hz (d) Tesla

53. Alkaloid used in the treatment of gout is _____
(a) Topotecan (b) Colchicin
(c) Vincristine (d) Etoposide

54. When was RBI nationalised?
(a) 1 January 1938 (b) 1 January 1949
(c) 15 August 1949 (d) 26 January1949

55. Major product obtained from purine metabolism is_____
(a) Urea (b) Uric acid
(c) Ammonia (d) Nucleic acid

56. Which of the following is directly compressible polymer?
(a) PVP (b) Avicel
(c) DI-Tab (d) HPMC

57. Nobel prize for HIV virus detection was awarded to____
(a) Harald Zur hauser (b) Francose barre-Sinoussi
(c) Luc montagnier (d) All of them

58. Which of the following compounds will show two spikes at the N-H stretching?
(a) A primary amine (b) A tertiary amine
(c) A secondary amine (d) All

59. Serotonin is_____
(a) Monoamine (b) Chemical mediator
(c) Neurotransmitter (d) All

60. Which of the following is used for enteric coating?
(a) PVP (b) HPMC
(c) CAP (d) HPC

61. Antibody consists of
(a) 4-polypeptides – two heavy chains and two light chains joined to from a "Y" shaped molecule
(b) 3-polypeptides – one heavy chain and two light chains joined to from a "Y" shaped molecule
(c) 4-polypeptides – two heavy chains and two light chains joined to from an "X" shaped molecule
(d) 3-polypeptides – two heavy chains and one light chain joined to from a "Y" shaped molecule

62. Endotheline is_____
(a) Vasoconstricting peptide
(b) Endothelial cells of blood vessels
(c) Neurotransmitter
(d) Protein

63. In many of the neurodegenerative disease, there is a repeat of ____
(a) GAC nucleotide triplet which encoded for aspartic acid
(b) ACG nucleotide triplet which encoded for threonine
(c) GCA nucleotide triplet which encoded for alanine
(d) CAG nucleotide triplet which encoded for the amino acid glutamine

64. Which anti-TB drug can cross BBB?
(a) Ethambutol (b) Rifampin
(c) Cycoserine (d) None of the above

65. If the drug is susceptible to hydrolysis then which of the following is suitable?
(a) Direct compression
(b) Film Coating by Organic solvent
(c) Inject able emulsion
(d) None of the above

66. Phenytoin is used in_____
(a) Supraventricular arrhythmias
(b) Ventricular arrhythmias
(c) Brady arrhythmias
(d) Digitalis induced an arrhythmia

67 First planning commission of India set up on?
(a) 15 March 1938 (b) 15 March 1950
(c) 26 January 1949 (d) 15 August 1950

68. One of the following methods is not used the determination of pka
(a) Sirius potentiometer method
(b) Yeseuda shedlovsky experiment
(c) Shake flask method
(d) UV spectrophotometer

69. Primaquine is used in _____ phase of malarial cycle
(a) Pre-erythrocytic (b) Post erythrocytic
(c) Both (a) & (b) (d) None

70. Which of the following is dopamine agonist?
(a) Ropinirole (b) Rotigotine
(c) Pramipexole (d) All

71. Dissolution of partnership is done for a firm based on
(a) Aggrement (b) Compulsion
(c) Notice or Order (d) Aspirin

72. What does the Bredt's rule state?
(a) SN_2 reaction always produce inversion of configuration
(b) 30 carbocation is more stable than 20

(c) Symmetry compound doesn't have dipole movement
(d) Double bond cannot be placed at the bridgehead of a bridged ring system

73. Proteomics is study of _____
(a) DNA (b) RNA
(c) Genomes (d) Proteins

74. Persistent deafness is a side effect of
(a) Penicillin (b) Streptomycin
(c) Quinine (d) Aspirin

75. Statins are used as _____
(a) Hyperlipidemic agent
(b) Hypolipidemic agent
(c) Ant diabetics
(d) Antiparkinson

76. is the 15 carbon intermediate in Mavalonic acid pathway
(a) Geranyl pyrophosphate
(b) Femesyl pyrophosphate
(c) 3,3-dimethyl allyl pyrophosphate
(d) Squalene pyrophosphate

77. Aliskeren is_____
(a) ACE inhibitor (b) Renin inhibitor
(c) Renin antagonist (d) Aldosterone Antagonist

78. $GABA_B$ agonist is _____
(a) Baclofen (b) Baclofen
(c) Bicuculine (d) Benzodiazepine

79. Which type of chromatography is also called as 'Planer chromatography'?
(a) Thin Layer Chromatography
(b) Paper Chromatography
(c) Open bed chromatography
(d) All of these

80. Aspirin is_____
(a) Irreversible and non-competitive COX inhibitor
(b) Reversible COX inhibitor
(c) Reversible and non-competitive COX inhibitor
(d) Irreversible COX inhibitor

81. Catalepsy means.....
(a) Loss of consciousness with rigidity of muscles that keeps limbs in fixed condition
(b) Chronic attach of seizers due to electrical imbalance in brain
(c) Loss of consciousness after tonic clonic seizers
(d) None of the above

82. Tonifier is the important agent in _____
(a) Parenterals (b) Vaginal
(c) Buccal (d)Transdermal

83. Metoclopramide, an antiemetic, acts as_____
(a) $5\text{-}HT_4$, $5\text{-}HT_3$ agonist and D_2 antagonists
(b) D_2, $5\text{-}HT_3$ agonist and $5\text{-}HT_4$ antagonist
(c) $5\text{-}HT_4$, $5\text{-}HT_3$ antagonist and D_2 agonist
(d) D_2, $5\text{-}HT_3$ antagonist and $5\text{-}HT_4$ agonist

84. Which of the following is keto sugar?
(a) Xylose (b) Talose
(c) Ribulose (d) Allose

85. GHOST peak in chromatography is due to.....
(a) Solve
(b) Column packing
(c) Temperature variation
(d) Impurity

86. The following drug only acts as arterial vasodilator _____
(a) Hydralazine
(b) Sodium nitroprusside
(c) Diazoxide
(d) Minoxidil

87. Ondansetron is used for _____
(a) Schizophrenia
(b) Parkinson's disease
(c) Anticancer agent induced emesis
(d) All of the above

88. PG is synthesized by_____
(a) COX I (b) COX II
(c) COX III (d) All of the above

89. Normality of conc. HCl is approximately.....
(a) 11.7N (b)17N
(c) 35N (d) 71N

90. Cis and Trans stilbenes are called as ___
(a) Epimer (b) Enantiomers
(c) Anomers (d) Diastereomers

91. Ostwald ripening is an important parameter in the formulation of _____
(a) Emulsion (b) SMEDDS
(c) Suspension (d) Liposome

92. Osmotic pressure of the human blood is _____
(a) 7.65 atm (b) 0.9 atm
(c) 5 atm (d) 76.5 atm

93. SMON syndrome is related to.....
(a) Metronidazole
(b) Diloxinide
(c) Quiniodochlor
(d) Tetracycline

94. Most stable confirmation in mono substituted cyclohexane is _____
(a) Equatorial (b) Axial
(c) Both (d) Cis

95. Which of the following species contain highest amount of quinine?
(a) *C.calisaya* (b) *C.officinalis*
(c) *C.ledgeriana* (d) *C.succirubra*

96. Which of the following is not a primary packaging material in injectables except?
(a) Glass (b) PVC
(c) Elastomers (d) Aluminum foils

97. Which of the following is a free trade port in India?
(a) Kandla (b) Tutikotin
(c) Cochin (d) Madras

98. Insulin acts on _____
(a) Liver and muscles (b) Alpha cells
(c) Beta cells (d) Neurons

99. Trehalose is.....
(a) Lyoprotectant (b) Disintegrate
(c) Swelling agent (d) Diluents

100. Onset of action for nasal delivery system is _____
(a) Less than 1 min (b) 3-5 min
(c) 1 hr (d) 6-8 hr

ANSWER KEYS

1. (c)	**2.** (a)	**3.** (c)	**4.** (a)	**5.** (b)	**6.** (d)	**7.** (b)	**8.** (d)	**9.** (c)	**10.** (b)
11. (b)	**12.** (c)	**13.** (b)	**14.** (a)	**15.** (a)	**16.** (c)	**17.** (a)	**18.** (c)	**19.** (a)	**20.** (c)
21. (d)	**22.** (a)	**23.** (b)	**24.** (b)	**25.** (a)	**26.** (b)	**27.** (a)	**28.** (b)	**29.** (c)	**30.** (c)
31. (c)	**32.** (c)	**33.** (b)	**34.** (b)	**35.** (c)	**36.** (b)	**37.** (b)	**38.** (c)	**39.** (d)	**40.** (a)
41. (d)	**42.** (d)	**43.** (d)	**44.** (b)	**45.** (d)	**46.** (c)	**47.** (b)	**48.** (b)	**49.** (a)	**50.** (a)
51. (b)	**52.** (a)	**53.** (b)	**54.** (b)	**55.** (b)	**56.** (b)	**57.** (a)	**58.** (a)	**59.** (d)	**60.** (c)
61. (a)	**62.** (a)	**63.** (d)	**64.** (b)	**65.** (a)	**66.** (d)	**67.** (b)	**68.** (c)	**69.** (c)	**70.** (d)
71. (d)	**72.** (d)	**73.** (d)	**74.** (b)	**75.** (b)	**76.** (b)	**77.** (b)	**78.** (a)	**79.** (d)	**80.** (a)
81. (a)	**82.** (a)	**83.** (d)	**84.** (c)	**85.** (d)	**86.** (a)	**87.** (c)	**88.** (d)	**89.** (a)	**90.** (d)
91. (c)	**92.** (a)	**93.** (c)	**94.** (a)	**95.** (a)	**96.** (d)	**97.** (a)	**98.** (a)	**99.** (a)	**100.** (b)

NIPER JEE – QUESTION PAPER V

1. Which of the following is the chemical composition of Saliwanoff's reagent?
(a) Copper sulphate pentahydrate
(b) Copper acetate and copper oxide in 1%acetic acid
(c) Resorcinol in HCl
(d) Anhydrous sodium carbonate and sodium citrate

2. N-acetyl glucosamine and N- acetyl muramic acid are major cell wall components of ____
(a) Gram positive bacteria
(b) Gram negative bacteria
(c) Mycobacteria
(d) Spirochetes

3. Cycloaddition occur in .....reaction
(a) Diels alder (b) Favorskii
(c) Claison (d) Hoffman

4. Which of the following is correct equation for relative centrifugal force (RCF)?
(a) $r(2\varpi N)^2 / g$ (b) $r(2\varpi N)/ g$
(c) $r^2\varpi N/g$ (d) $(2\varpi N)/r^2g$

5. For the formation of one molecule of hexose sugar, how many turns of Calvin cycle are needed?
(a) One-sixth (b) One
(c) Six (d)Thirty-six

6. The primary requirement for the drug molecule to cross BBB is
(a) Hydrophilicity (b) Lipophilicity
(c) Optimum HLB (d) Biocompatibility

7. Which of following shows QT interval prolongation in ECG?
(a) Amlodipine (b) Terfinadine
(c) Phenytoin (d) Amphotericin B

8. Biphenyl shows which kind of isomerism?
(a) Optical isomerism
(b) Configurational isomerism
(c) Atropisomers
(d) R and S isomerism

9. Redness is tomato is due to _____
(a) Canthaxanthin (b) Lycopene
(c) Lawson (d) Tomopene

10. Following are the air pollutants except _
(a)VOC (b) Toxic metals
(c)Ozone (d) UV radiation

11. Solubility of gelatin capsule is decreased by _____
(a) Fumaric acid (b) Formalin
(c) Titanium oxide (d) All of the above

12. Which of the following drug assay involves back titration method?
(a) Paracetamol (b) Acetazolamide
(c) Nifidipine (d) N-acetyl salicylic acid

13. Which of the following nutraceutical reduce risk of coronary heart disease?
(a) Psyllium seed husk
(b) Broccoli
(c) Fiddleheads
(d) Berries

14. In Roche friabilator, plastic chamber revolves at speed_____
(a) 25 rpm (b) 50 rpm
(c) 15 rpm (d) 30 rpm

15. Isoabsorptive point means……..
(a) A point at which 2 bond give same peak
(b) A point at which 2 compound absorb UV light
(c) A point at which 2 atom have same precissional frequency
(d) None of the above

16. Largest saffron cultivating Indian state is
(a) Gujarat (b) Bengal
(c) Kerala (d) Jammu and Kashmir

17. DSC belongs to which kind of analytical method?
(a) Spectroscopy (b) Thermal
(c) Hyphenated (d) Chromatography

18. Q-fever is caused by……
(a) *Coxiella burentii*
(b) *Clostridium botulinum*
(c) *Bacillus quilli*
(d) *E. fisheleoni*

19. In NMR _____ peaks will be observed for 1, 4-dioxane

(a) 1 (b) 2
(c) 3 (d) 4

20. Diffusivity of a solute is affected by _____

(a) Temperature (b) Pressure
(c) Chemical nature (d) All

21. Thyroid and steroid receptor are type of_____ receptors

(a) Voltage gated (b) Ligand gated
(c) Nuclear type (d) GPCR

22. Two amide bonds are present in _____

(a) Monopeptide (b) Dipeptide
(c) Tripeptide (d) Butapeptide

23. Onset of action for mucoadhesive delivery system is _____

(a) Less than 1 min (b) 3-5 min
(c) 1 hr (d) 6-8 hr

24. _____has the highest number of U.S.FDA approved manufacturing facilities outside the united states

(a) Brazil (b) China
(c) India (d) Philippines

25. Which of the following is true regarding immunoglobulin?

(a) It contain 2 light chains
(b) It contains 2 heavy chains
(c) It contain disulphide bonds
(d) All

26. Which of these is not a standards institution?

(a) BIS (b) ISO
(c) ASTM (d) IDMA

27. What is Action of digitalis?

(a) Anti-emetic
(b) Analgesic
(c) Increase force of contraction of heart
(d) Negative ionotropic effect

28. Un-saturation in an organic compound is determined by____

(a) Bromination (b) Hydrogenation
(c) Ozonolysis (d) All of the above

29. A+B=102, A-B=24, then A=?

(a) A=63 (b) A=38
(c) A=62 (d) A=38

30. The first stereo-active compound observed and isolated was by……

(a) Kekul (b) Lacobus henricus
(c) Louis Pasteur (d) Robert Koch

31. Capping in tablets mainly due to

(a) Less upper punch pressure
(b) Poor flowability of granules
(c) Proper formulation design
(d) Entrapment of air in tablet during compression

32. Detector used in IR spectroscopy is

(a) Thermocouples (b) Ginger Muller counter
(c) PMT (d) Flame Ionisation detector

33. Who is the inventor of ager as solidifying medium?

(a) Robert Koch (b) Walther Hesse
(c) Fannie Hesse (d) Losephle Bel

34. DAEWOO of South Korea has collaboration with which Indian company?

(a) Hindustan (b) DCM
(c) Maruti (d) TATA

35. Podophyllotoxin is _____

(a) Lignin derivative (b) Lignan derivative
(c) Diterpenoid (d) Marine toxin

36. Drug with high affinity but no efficacy is also called as……

(a) Agonist (b) Partial agonist
(c) Antagonist (d) Partial antagonist

37. Antonym of ABSTRUSE

(a) Enigmatic (b) Subtle
(c) Concrete (d) Transcendental

38. Which of the following is non-reducing sugar?

(a) Lactose (b) Maltose
(c) Sucrose (d) Starch

39. Formula for angle of repose is.....

(a) $\tan \theta = r/h$ (b) $\tan \theta = h/r$
(c) $\tan^{-1} \theta = r/h$ (d) $\tan^{-1} \theta = h/r$

40. Which of the following shows highest first pass metabolism?

(a) Propranolol (b) Digoxin
(c) Phenobarbital (d) Phenytoin

41. Abscisic acid is _____

(a) Monoterpenoid (b) Sesquiterpenoids
(c) Diterpenoid (d) Triterpenoid

42. A condition that is characterised by loss of consciousness with rigidity of muscles that keeps limbs in fixed
(a) Schizophrenia (b) Parkinsonism
(c) Sedation (d) Catalepsy

43. The largest cotton producer in the world is
(a) India (b) China
(c) USA (d) Brazil

44. Steroidal receptor is.....
(a) Ligand gated ion channel
(b) Tyrosine kinase
(c) GPCR
(d) Nuclear type

45. Causative organism of amoebiasis is
(a) *G. Lambia* (b) *Plasmodium falciparum*
(c) *E. Histolytic* (d) *Trypanosoma brucei*

46. Psychometric chart is related to _____
(a) Osmotic pressure (b) Humidity
(c) Solubility (d) Evaporation

47. Which of the following is the mechanism of competitive inhibition?
(a) Binding of the inhibitor to the active site of the enzyme
(b) Binding of the inhibitor to site other then active binding site on the same enzyme
(c) Binding of the inhibitor to the enzyme substrate complex
(d) Binding of the inhibitor to endogenous substrate

48. Which of the following used for vascular disorders?
(a) Ginko biloba (b) Silymarin
(c) Cantharides (d) Ammi

49. Alanine exhibits which type of isomerism?
(a) Optical isomerism (b) Absolute isomerism
(c) Relative isomerism (d) All

50. α and β form of cyclic glucose are known as…….
(a) Epimer (b) Anomer
(c) Enantiomer (d) Diasterioisomer

51. D-Erythrose and D-Threose are_____
(a) Epimers (b) Enantiomers
(c) Diastereomers (d) Anomers

52. Which of the following herbs is considered as valuable 'Nutraceutical'?
(a) Senna (b) Spirulina
(c) Vasaka (d) Bael

53. Iodine value is used for.....
(a) To determine no. of double bond present in unsaturated fatty acid
(b) To determine no. of double bond present in saturated fatty acid
(c) To determine no. of acidic group present in unsaturated fatty acid
(d) To determine no. of acidic group present in saturated fatty acid

54. Chemical yasbestos is _____
(a) Silica (b) Cellulose
(c) Alumino silicate (d) Silica tungstate

55. Oral pharmaceutical aerosol involves the use of all propellants except _____
(a) Trichloromonofluoromethane
(b) Dichlorodifuoromethane
(c) Dichlorotetrafluoromethane
(d) Isobutane

56. In microbiology term COMPETENCE stand for?
(a) Ability of microbes to generate resistance to antibiotic
(b) Ability of host cell destruction
(c) Genetically transformable
(d) None of the above

57. In exothermic process, increase in temperature indicates _____
(a) Reactant concentration is more
(b) Product yield is more
(c) Reaction has stopped
(d) Equilibrium has been achieved

58. One of the figure is different. Identify

[a]

	O		
X		X	
	O		O
	O		

[b]

			O
O	O	X	
			O
X			

[c]

	O		O
		X	
	O		O
X			

[d]

	O	X	O
X	O		
	X	O	O

59. Indole alkaloids are derived from _____
(a) Tyrosine (b) Phenylalanine
(c) Omithine (d) Tryptophan

60. Bloom strength of gelatin capsule is directly proportional to _____
(a) Molecular weight
(b) Molecular chain length
(c) Solubility of gelatin
(d) Weak forces

61. Shortening the carbon chain of aldoses is known as……
(a) Ruff degradation
(b) Kiliani-fisher synthesis
(c) Oxidative degradation
(d) Amdt-Eistert synthesis

62. Terpenoid is synthesized by _____
(a) Mevalonic acid pathway
(b) MEP/DOXP pathway
(c) Both (a) & (b)
(d) Can't say

63. Digitalis act by.....
(a) Inhibits GABA reuptake in to nerve endings
(b) Ach reuptake inhibition
(c) Inhibits H-K ATPase pump
(d) Inhibits Na-K ATPase

64. What is the use of UV circular dichroism spectroscopy?
(a) Investigation confirmation of secondary structure of proteins
(b) Peptide bond determination
(c) Structure elucidation of synthetic compound
(d) Determination of unsaturation in protein

65. Ghost peak in chromatography generally arises due to _____
(a) Septum leaching effect
(b) Mobile phase
(c) Gradient system
(d) Pump system

66. During Fermentation of penicillin the pH is first adjusted to 2. Why?
(a) For maximum growth of Penicillium chrysogenum
(b) For maximum yield
(c) Penicillin exists as an undissociated acid so it is Soluble in organic Solvents
(d) To remove the impurity

67. Recommended velocity for laminar air flow unit is_____
(a) 0.36 m/s-0.45m/s (b) 0.46m/s-0.55m/s
(c) 0.56m/s-0.60m/s (d) None of the above

68. Diosgenin contain _____ skeleton
(a) Steroidal (b) Torpedoed
(c) Phenanthrine (d) Pentacyclic

69. Causative organism for syphilis is.....
(a) *G.lamblia*
(b) *Plasmodium*
(c) *Trepnonema pallidium*
(d) *Trypanosoma brucei*

70. Microbes are present in all of the following except _____
(a) Ice (b) Sea
(c) Water (d) Distilled water

71. Lipinski's "rule of five" predicts _____
(a) Drug like character
(b) Oral bioavailability
(c) Ability to cross BBB
(d) All

72. Ethyl acetate gives ……peaks in ^{1}H-NMR
(a) 4 (b) 2
(c) 3 (d) 5

73. Zafirlukast acts as antagonist of _____
(a) Prostaglandin (b) Leukotriene
(c) Interleukin (d) COX II

74. Mulethi is _____
(a) *Glycyrrhiza echinata*
(b) *Glycyrrhiza lepidota*
(c) *Glycyrrhiza glabra*
(d) *Glycyrrhiza uralensis*

75. What is the hybridization state of carbanion?
(a) SP^3 (b) SP^2
(c) SP (d) Non-hybridized

76. Squeezing of WBCs through the pores of blood capillaries is called as _____
(a) Passive diffusion (b) Diapedesis
(c) Chemotaxis (d) Pinocytosis

77. Schedule 'S' as per the drugs and cosmetics act deals with _____
(a) Standards for cosmetics
(b) Biological and special product
(c) Life period of drugs
(d) GMP requirement

78. Which of the following is not true about low of thermodynamics?

(a) The zeroth low of thermodynamics allows the assignment of a unique temperature to system
(b) The 1st low expresses the existence of a quantity called the internal energy of a system
(c) The 2nd low expresses the existence of a quantity called the entropy of a system
(d) The 3rd low concerns the internal energy of perfect crystal at elevated Temperature

79. Sigma blade mixers are commonly used in _____
(a) Crude fiber mixing (b) Powder mixing
(c) Dry granulation (d) Wet granulation

80. Material exhibiting plastic flow is known as.....
(a) Shear thinner (b) Shear thickener
(c) Bingham body (d) Thixotropic

81. One of the following dominantly contain mucilage identity
(a) Isapghol (b) Cascara
(c) Liquorice (d) Ajwan

82. C-peptide assay in hyperglycemic patient is done to determine……..
(a) Elevated blood sugar level
(b) To determine type of diabetes
(c) To check safety of insulin therapy
(d) None of the above

83. The number of isoprene units in triterpenoid are _____
(a) 3 (b) 4
(c) 6 (d) 5

84. Synonym of STRAFE is _____
(a) To punish (b) To strengthen
(c) To run away (d) To work very hard

85. Ziegler- Natta catalyst is formed from.....
(a) Titanium oxide and diethyl aluminum
(b) Platinum oxide and try ethyl aluminum
(c) Titanium chloride and diethyl aluminum
(d) Titanium chloride and try ethyl aluminum

86. Craig plot is used in _____
(a) Drug designing
(b) Protein structure determination
(c) Nucleic acid structure determination
(d) Carbohydrate structure determination

87. P watch goes back to 1 min. day and Q watch goes back to ½ min. day ,after how many days P watch will be 5min. back then Q watch?
(a) 5 days (b) 10 days
(c) 2.5 days (d) 2 days

88. Ca^{++} channel blocker is used in which of the following conditions
(a) Cerebral ischemia
(b) Myocardial infraction
(c) Angina
(d) All

89. Thiomers are thiolated polymers. These have which of the following action?
(a) Mucoadhesion
(b) Permeation enhancement
(c) Efflux pump, enzyme inhibition
(d) All of the above

90. Totipotency is_____
(a) Ability of a single cell to divide and produce all the differentiated cells in an organism
(b) Ability of a single cell to differentiate into any of the 3 germ layers: endoderm, mesoderm, ectoderm
(c) Potential to give rise to cell from multiple, but a limited number of lineages
(d) All of the above

91. What is antonym of obstrude?
(a) Obstinate (b) Rigid
(c) Soft (d) Pardon

92. In maltose two glucose units are linked as _____
(a) 1α - 4α (b) 1α -1α
(c) 1α - 2β (d) 1α - 4β

93. Which of the following is false about secondary structure of protein?
(a) Twisting and folding of polypeptide produces secondary structure
(b) Extensive hydrogen bonding stabilizes the secondary structure
(c) All peptide bond does not participate in hydrogen bonding
(d) α-helix is unstable conformation because it formed spontaneously with highest energy

94. Which of the following contains chromosome or DNA?
(a) Mitochondria (b) ER
(c) Golgi body (d) Cytoplasm

95. Autoimmune disorder myasthenia gravis is caused by _____
(a) Destruction of articular cartilage and ankylosis of the joints
(b) Circulating antibodies that block Ach receptors at the postsynaptic neuromuscular junction

(c) Antigen antibody reaction which destruct the neuromuscular junction
(d) Deficiency of Ach at neuronal junction

96. What is the function of t-RNA?
(a) Carries instructions on how to connect several amino acids into a peptide chain
(b) Translate the language of RNA into language of protein
(c) Translate the language of DNA into language of RNA
(d) Translate the language of RNA into language of DNA

97. What is the relationship of fexofenidine and terfenidine?
(a) Metabolite (b) Bioisoster
(c) Higher homolog (d) Lower homolog

98. Which of the following is correct NMR data for CH_3-COO-C_2H_5?
(a) δ =1.56m (3H), δ=3.69s (2H), δ=1.02t (3H)
(b) δ =2.66s (3H), δ=2.89m (5H),
(c) δ =3.66s (3H), δ=2.32q (2H), δ=1.1t (3H)
(d) None of the above

99. Which one is not used in Perkin reaction?
(a) Benzaldehyde
(b) Acetic anhydride
(c) Cinnamaldehyde
(d) Benzene

100. _____ can be used in colon specific drug delivery system
(a) Glucose (b) Mannose
(c) Lactulose (d) Xylulose

ANSWER KEYS

1. (c)	**2.** (a)	**3.** (a)	**4.** (a)	**5.** (c)	**6.** (b)	**7.** (b)	**8.** (c)	**9.** (b)	**10.** (d)
11. (b)	**12.** (d)	**13.** (a)	**14.** (a)	**15.** (b)	**16.** (d)	**17.** (b)	**18.** (a)	**19.** (a)	**20.** (d)
21. (c)	**22.** (c)	**23.** (d)	**24.** (c)	**25.** (d)	**26.** (a)	**27.** (c)	**28.** (a)	**29.** (a)	**30.** (b)
31. (d)	**32.** (a)	**33.** (c)	**34.** (b)	**35.** (b)	**36.** (c)	**37.** (c)	**38.** (c)	**39.** (b)	**40.** (a)
41. (b)	**42.** (d)	**43.** (b)	**44.** (d)	**45.** (c)	**46.** (b)	**47.** (a)	**48.** (a)	**49.** (d)	**50.** (b)
51. (c)	**52.** (b)	**53.** (a)	**54.** (c)	**55.** (d)	**56.** (c)	**57.** (b)	**58.** (c)	**59.** (d)	**60.** (a)
61. (a)	**62.** (c)	**63.** (d)	**64.** (a)	**65.** (a)	66. (c)	67. (a)	68. (c)	69. (c)	**70.** (d)
71. (a)	**72.** (c)	**73.** (b)	**74.** (d)	**75.** (a)	**76.** (b)	**77.** (a)	**78.** (d)	**79.** (d)	**80.** (c)
81. (a)	**82.** (b)	**83.** (c)	**84.** (a)	**85.** (d)	**86.** (a)	**87.** (b)	**88.** (c)	**89.** (d)	**90.** (a)
91. (c)	**92.** (d)	**93.** (b)	**94.** (a)	**95.** (b)	**96.** (b)	**97.** (b)	**98.** (c)	**99.** (d)	**100.** (d)

SOME TIPS FOR PREPARATION OF NIPER JEE AND GPAT

1. Clear your basic concepts from your B Pharm text books before you use additional study material.
2. Study ALL topics given in detailed syllabus apart from important topics
3. Revise all charts, flow diagram & tables and kept it in mind all time.
4. Pay attention to details as most often questions are based on specific points.
5. Always Read Pharmacology and Medicinal Chemistry simultaneously.
6. Practice sketching molecular structures, it will help you remember them easily
7. Group study is helpful for GPAT preparation; you can quiz each other with Multiple Choice Questions
8. Although the GPAT examination is based on Multiple Choice Questions practice writing answers in your own words. This will help you check your understanding of the topic
9. Practice numerical, although there are not many numerical problems in exam paper, regular practice will score you easy marks on the 3-4 numerical questions that do come in the question paper
10. The most effective way to prepare is by practicing sample papers/previous year papers
11. Attempt all the questions when you practice sample papers/previous year papers and correct them after you complete the entire paper. This will help you identify your weak areas and you can study those areas thoroughly
12. During the exam skip any question you are not sure of to avoid negative marking.

UNIT 6

SOLVED PAPERS

L. M. College of Pharmacy, Gujarat (Government of Gujarat) Assistant Professor Recruitment Examination Question Paper 2016

ESIC Pharmacist (Employees State Insurance Corporation-Allopathic) Recruitment Question Paper 2016

UPSC Drug Inspector Examination Paper 2011

Gujarat Government Lecturer Examination in Degree/ Diploma Pharmacy College-GPSC 2010

Gujarat Drug Inspector Exam Paper—GPSC 2010

GPAT Paper 2012

GPAT Paper 2011

GPAT Paper 2010

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L. M. COLLEGE OF PHARMACY, GUJARAT (GOVERNMENT OF GUJARAT) ASSISTANT PROFESSOR RECRUITMENT EXAMINATION QUESTION PAPER 2016

1. Hausner's ratio refers to
(a) Adhesion property of the material
(b) Relative lubrication ability
(c) Ratio of two polymorphs in API
(d) Compressibility

2. Pareto ratio represents
(a) Ratio of good to defective tablets in a batch
(b) Relative population of defective ampules in a batch
(c) Sorted effect of variables during experiments
(d) Failure analysis

3. The ability of human eye using illuminated area to detect a particle is limited to
(a) 0.4 micron
(b) 25 micron
(c) 50 micron
(d) 10 micron

4. Technetium 99 m is used because of the following reason
(a) It is excellent anticancer isotopes
(b) Thyroid treatment is faster
(c) It gives gamma photons for better image
(d) It gives beta particles

5. The role of borax in cold cream is
(a) Anti-microbial agent
(b) To provide fine particles to polish skin
(c) In-situ emulsifier
(d) Micelle forming agent to dissolve skin lipids

6. Thioglycolic acid like compounds have application in cosmetic in
(a) Depilatory preparation
(b) Epilitory preparation
(c) Fragrance
(d) Polymorph inhibitor

7. The role of glycine as tablet excipient is as
(a) Amino acid supplement
(b) Fungal growth inhibitor
(c) Lubricant
(d) Sweetener

8. What quantities of 95% v/v and 45% v/v alcohol are to be mixed to make 800 ml of 65% v/v alcohol?
(a) 480 ml of 95% and 320 ml of 45% alcohol
(b) 320 ml of 95% and 480 ml of 45% alcohol
(c) 440 ml of 95% and 360 ml of 45% alcohol
(d) 360 ml of 95% and 440 ml of 45% alcohol

9. In the preparation of tablets lubricating agents are used to
(a) Break the tablet
(b) Improve strength and hardness
(c) Prevent sticking
(d) Increase the bulk

10. What is the HLB range for w/o emulsifying agents?
(a) 8-18 (b) 3-6
(c) 7-9 (d) 13-15

11. Name the super disintegrant from the followings
(a) Starch
(b) Magnesium stearate
(c) Sodium starch gylcolate
(d) Talc

12. The other name for cold cream is
(a) Day cream (b) Cleansing cream
(c) Foundation cream (d) Hand cream

13. The purpose of conditioning agent on shampoo is
(a) To bring moisture to hair
(b) To keep the hair away from moisture
(c) To keep hair oily texture
(d) To cause brittleness to hair

14. The particle size of the abrasives used in the tooth paste should be in the range of
(a) 1-6 microns (b) 7-15 microns
(c) 15-20 microns (d) Above 25 microns

15. Short duration of action of the drug is due to
(a) Less biological half life
(b) Ability to get distributed in peripheral and shallow compartments
(c) High lipid solubility
(d) All of the above

16. Pyrogen test is usually done in which of the following species?
(a) Rabbits (b) Humans
(c) Mice (d) Rat

17. Bloom strength is used to check the quality of
(a) Gelatin (b) Binder in tablets
(c) Hardness of tablets (d) Suspensions

18. Which of the following is water soluble ointment base?
(a) Bees wax (b) Soft paraffin
(c) Macrogols (d) Lanolin

19. In the mixing of thymol and menthol the following type of incompatibility occurs
(a) Physical incompatibility
(b) Chemical incompatibility
(c) Therapeutic incompatibility
(d) Tolerated incompatibility

20. Angle of repose is a measure of
(a) Surface tension
(b) Viscosity
(c) Flow property of powders
(d) Density

21. Which of the following is a flocculating agent for a negatively charged drug?
(a) Aluminium chloride
(b) Acacia
(c) Tragacanth
(d) Sodium biphosphate

22. The healing agent used in hand cream is
(a) Soft paraffin (b) Bees wax
(c) Urea (d) Stearyl alcohol

23. The application of noyes- whitney equation is to describe
(a) First order kinetics
(b) Zero order kinetics
(c) Mixed order kinetics
(d) Dissolution rate

24. What is the pH of tears?
(a) 6.8 (b) 7.0
(c) 7.4 (d) 6.3

25. The in vivo sink condition according to fick's first law of diffusion is
(a) Concentration at the absorbing membrane C_b> concentration at the serosal site Cs
(b) $C_s > C_b$
(c) $C_s = C_b$ (d) $C_s >> C_b$

26. Adult dose of ibuprofen is 400 mg, calculate the dose for 6 years old child according to dilling's rule
(a) 150 mg (b) 120 mg
(c) 160 mg (d) 100 mg

27. Measurement of inulin renal clearance is a measure of
(a) Effective renal blood flow
(b) Renal drug excretion rate
(c) Active renal excretion
(d) Glomerular filtration rate

28. According to drug and cosmetic act and rules phenobarbital is a
(a) Schedule X drug (b) Schedule G drug
(c) Schedule H drug (d) Schedule C drug

29. In the drugs and cosmetic act and rules the schedule related to GMP is
(a) Schedule M (b) Schedule C
(c) Schedule Y (d) Schedule H

30. Biopharmaceutical classification system is based on
(a) Molecular weight, partition coefficient and dipole moment
(b) Solubility parameter, dissolution and partition coefficient
(c) Solubility, dissolution and permeability
(d) Crystal structure, partition coefficient and dielectric constant

31. What does R for in R/S configuration nomenclature?
(a) Rectos (b) Rectgegen
(c) Rectus (d) Rusamenn

32. Which of the following drug has minimum anti-inflammatory activity?
(a) Acetaminophen (b) Aspirin
(c) Ibuprofen (d) Diclofenac sodium

33. Insect can walk on surface of water due to
(a) Viscosity (b) Surface tension
(c) Refractivity (d) Optical activity

34. Which of the following antibiotic is macrolide
(a) Chloramphenicol (b) Doxycycline
(c) Oleandomycin (d) Streptomycin

35. Stoke's shift is the term associated with-
(a) IR spectroscopy
(b) Fluorescence spectroscopy
(c) NMR spectroscopy
(d) UV-visible spectroscopy

36. Which of the following aqueous solution will have the highest pH?
(a) Sodium acetate
(b) Sodium chloride
(c) Ammonium phosphate
(d) Calcium chloride

37. H2O2 act as oxidizing agent in
(a) Neutral medium
(b) Acidic medium
(c) Alkaline and neutral medium
(d) Alkaline and acidic medium

38. Which of the following electromagnetic radiation has maximum energy?
(a) Gamma rays (b) X-rays
(c) IR radiation (d) Radio waves

39. A drug is reported to have a biological half-life of 2 hours. At the end of 8 hours, what percentage of the drug's original activity will remain?
(a) 2.5% (b) 12.5%
(c) 25% (d) 6.25%

40. Hansch analysis is used in
(a) Drug design (b) Enzyme kinetics
(c) Drug transport (d) Receptor binding studies

41. Nitrazepam can be synthesized from
(a) 2-bromo-5-aminobenzophenone
(b) 2-nitro-5-chloro acetophenone
(c) 2-amino-5- nitro cyclohexanone
(d) 2-amino-5- nitro benzophenone

42. Which of the following opioid agonist is only administered by parenteral route?
(a) Morphine (b) Codeine
(c) Fentanyl (d) Methadone

43. 19- carbon basic steroidal skeleton is called as
(a) Androstane (b) Gonane
(c) Estrane (d) Pregnane

44. Karl- fischer titration is commonly used for determination of –
(a) Water
(b) Nitrogen
(c) Mg containing compounds
(d) Protein

45. Standard calomel electrode contains-
(a) 0.1 M KCl
(b) 1.0 M KCl
(c) Saturated solution of KCl
(d) None of the above

46. Which of the following local anesthetics is useful for topical administration only?
(a) Procaine (b) Bupivacaine
(c) Etidocaine (d) Benzocaine

47. Hypnotic drug should
(a) Reduce anxiety and exert a calming effect
(b) Induce absence of sensation
(c) Produce drowsiness, encourage the onset and maintenance of sleep
(d) Prevent mood swing in patient with polar effective disorder

48. Indomethacin belongs to which class
(a) N-arylanthranilic acid derivatives
(b) Aryl acetic acid derivatives
(c) Salicylic acid derivative
(d) None of the above

49. The vitamin which deodorant property is –
(a) Vitamin A (b) Vitamin E
(c) Vitamin D (d) Vitamin C

50. For normal phase HPLC, which of the following statement is true?
(a) Both stationary and mobile phase are equally polar
(b) Stationary phase is more polar than mobile phase
(c) Mobile phase is more polar than stationary phase
(d) None of above

51. How many lines do you expect in NMR spectra of isopropyl bromide?
(a) One (b) Two
(c) Three (d) Four

52. Benzene trear=ted with chlorine in the presence of sunlight gives rise to –
(a) O-dichlorobenzene
(b) O and p-dichlorobenzene
(c) Benzene hexachloride
(d) 2, 4, 6-trichlorobenzene

53. The hofmann rearrangement has an intermediate that is electronically similar to that in a
(a) Pinacol rearrangement
(b) Claisen rearrangement
(c) Cope rearrangement
(d) Beckmann rearrangement

54. Which of the following can exhibit geometric isomerism?
(a) 1- pentene (b) 2- pentene
(c) 2-methyl pentene (d) 1- butane

55. Atropine on hydrolysis with barium hydroxide gives-
(a) Tropanol and tropicacid
(b) Scopine and tropic acid
(c) Ecogenine and benzoic acid
(d) Benzyl ecogenine and methanol

56. What are two main targets currently used in anti HIV therapy?
(a) Reverse transcriptase and protease
(b) Reverse transcriptase and integrase
(c) Protease and integrase
(d) The viral glycoprotein gp120 and gp41

57. Major product for penicillin degradation under weakly acid and alkaline hydrolytic condition is –
(a) Penilic acid (b) Penilloic acid
(c) Penicillenic acid (d) Penicilloic acid

58. What is the name given to the non-super impossible mirror image forms of chiral compound
(a) Cis trans (b) Enantiomers
(c) Functional isomers (d) Diasteriomers

59. DNA gyrase inhibitor is –
(a) Tetracycline (b) Quinolones
(c) Monobactum (d) Erythromycin

60. How many isoprene units are there in tri terpenoids
(a) Four (b) Three
(c) Two (d) Six

61. Following is not a substrate for CYPIAQ isoenzyme
(a) Caffeine (b) Methadone
(c) Paracetamol (d) Tacrine

62. Catecholamine are mainly metabolized by _____ enzyme
(a) MAO-A (b) MAO-B
(c) COMT (d) All of the above

63. Clinical use of vasoactive agents is/ are in the treatment of –
(a) Systematic hypertension
(b) Shock
(c) Raynaud's diseases
(d) All the above

64. Which of the following is the prodrug
(a) Cortisone (b) Prednisolone
(c) Dexamethasone (d) Aldosterone

65. No tears is approach to –
(a) Medication review
(b) Improve prescribing
(c) Risk prevention and reduction
(d) Cognitive strategy

66. Change in plasma concentration δc immediately after a single dose can be determined using the formula
(a) δc = lnC1- lnC2/t
(b) δc =SxFx dose/Vd
(c) δc= exVd/ SxF
(d) δc = Div xAUCiv/Dp.o. x AUCp.o.

67. which of the following drug show toxicity due to saturable hepatic metabolism
(a) digoxin (b) verapamil
(c) theophylline (d) oral contraceptives

68. following drug/s is/ are known to cause hyperkalaemia
(a) cyclosporine (b) aspirin
(c) terbutaline (d) all the above

69. for the therapeutic purpose a child is
(a) a small adult
(b) 4 weeks to 12 months of age
(c) 3 to 16 years of age
(d) 1 to 12 years of age

70. Following is not a part of liver function test
(a) Transaminase
(b) Electrolytes
(c) Alkaline phosphatase
(d) Prothrombine time

71. Following are the symptoms of schizophrenia
(a) Awkward social behavior
(b) Auditory illusions
(c) Delusions
(d) All the above

72. Accurate diagnosis of thyroid status can be arrived by measurement of-
(a) Free T4 and TSH
(b) Free T4 and free T3
(c) Free and combined T4
(d) All the above

73. In humans nuclear hormone receptors comprise a superfamily of _____ receptors that respond to diverse set of ligands
(a) 36 (b) 48
(c) 03 (d) 29

74. Transporters localized in the brain and involved in the receptake of neurotransmitter into presynaptic neurons are known as_____
(a) SLC1 (b) URAT1
(c) SLC6 (d) GAT2

75. Any measurable or discrenable trait associated with a drug is known as _____
(a) Pharmacogenetic trait
(b) Genotyping trait
(c) Criggler-nijjar trait
(d) SNP trait

76. Hemicholium acts by _____
(a) Interference with synthesis of transmitter
(b) Blockade of transport system at nerve-terminal membrane
(c) Blockade of transport system of storage vesicles
(d) Inhibition of enzymatic breakdown of transmitter

77. Pathogenesis of migraine headache involves_____
(a) Neural elements (b) Vascular elements
(c) MAO inhibitors (d) (a) and (b)

78. Which of the following antidepressant has highest potency at muscarinic receptors?
(a) Nefazodone (b) Fluoxamine
(c) Bupropion (d) Imipramine

79. Tricyclic antidepressant are antagonist of _____
(a) Alpha 1 adrenergic receptors
(b) Muscarinic receptors
(c) Cholinergic receptors
(d) H1 receptors

80. Following drug is a nonselective inhibitor of phospho diesterase
(a) Theophylline (b) Methimanole
(c) Pyrantel pamoate (d) Bevacezumale

81. Asafetida is obtained from the species of –
(a) Styrax (b) Ferula
(c) Myroxylon (d) Andrographis

82. Shellac is a resin secreted by the female lac bug
(a) Laccifer lacca (b) Cleviceps purpurea
(c) Culex migde (d) Crane flies

83. Gums and mucilage are commonly tested by
(a) Wagner's test (b) Molisch test
(c) Biuret test (d) Millon's test

84. An example of alkaloid which is in liquid state
(a) Nicotine (b) Papaverine
(c) Hesperidine (d) Emetine

85. Which gives pink colouration on treatment with phluroglucinol and HCl?
(a) Starch (b) Calcium oxalate
(c) Tannins (d) Lignins

86. The type of stomata present in digitalis leaf is-
(a) Anomocytic (b) Anisocytic
(c) Diacytic (d) Paracytic

87. Meyer's reagent is used for detection of alkaloids. Chemically Meyers reagent is –
(a) Potassium bismuth iodide
(b) Potassium mercuric iodide
(c) Potassium cadmium iodide
(d) Potassium iodide

88. Powder ginger can be analyzed with the help of-
(a) Fibre
(b) Trichomes
(c) Lycopodium spore method
(d) Scheibler's reagent

89. Salicin is-
(a) Coumarin glycoside
(b) Flavonoid glycoside
(c) Phenol glycoside
(d) Cyanogenetic glycoside

90. Stratified cork is a characteristic microscopic identification of the following crude drug
(a) Ipecae (b) Kurchi
(c) Rauwolfia (d) Quillia

91. Which of the following compounds are source of pseudoalkaloid ?
(a) Steroidal alkaloid (b) Terpenoid alkaloid
(c) Purine alkaloid (d) All of the above

92. Cantharanthus roseus is the main source for the extraction of following alkaloids
(a) Vincristine and vinblastine
(b) Ecogenine and cocaine
(c) Atropn and homatropin
(d) Quinine and cinchonine

93. Optimum temperature for cultivation of cinchona is –
(a) 55-70ºC (b) 60-70ºC
(c) 70-90ºC (d) 50-100ºC

94. Artemisin, a rapidly acting antimalarial agent, is being produced commercialy from
(a) Artemisia peltatum (b) Artemisia ovale
(c) Artemisia annua (d) Artemisia mukul

95. The following is intensively sweet plant metabolite
(a) Artemisin (b) Glycyrrhizin
(c) Forskolin (d) Guggulipid

96. Turmeric, ginger, valerian and podophyllum can be morphologically grouped as –
(a) Roots (b) Rhizomes
(c) Tubers (d) Fruits

97. The key intermediate in biogenesis of carbohydrate and related plant product is –
(a) Perphenic acid (b) Chorismic acid
(c) Shikimic acid (d) Phenylalanine

98. The commercial supply of tropane alkaloid, scopolamine is from different species of-
(a) Datura (b) Dubosiq
(c) Atropa (d) Hyoscimus

99. The seed of following plant contain a complex secondary metabolites known as azadirachtin
(a) Neem (b) Palm
(c) Dioscorea (d) Cassia

100. Which of the following is not an isoquinoline alkaloid?
(a) Emetine (b) Cephaline
(c) Psychotrine (d) Thebaine

ANSWER KEYS

1. (d)	**2.** (c)	**3.** (b)	**4.** (c)	**5.** (c)	**6.** (a)	**7.** (d)	**8.** (b)	**9.** (c)	**10.** (b)
11. (c)	**12.** (b)	**13.** (a)	**14.** (a)	**15.** **(x)**	**16.** (a)	**17.** (a)	**18.** (c)	**19.** (a)	**20.** (c)
21. (a)	**22.** (c)	**23.** (d)	**24.** (c)	**25.** **(x)**	**26.** (b)	**27.** (d)	**28.** (a)	**29.** (a)	**30.** (c)
31. (c)	**32.** (a)	**33.** (b)	**34.** (c)	**35.** (b)	**36.** (a)	**37.** (d)	**38.** (a)	**39.** (d)	**40.** (a)
41. (d)	**42.** (c)	**43.** (a)	**44.** (a)	**45.** (b)	**46.** (d)	**47.** (c)	**48.** (b)	**49.** (b)	**50.** (b)
51. (b)	**52.** (c)	**53.** (d)	**54.** (b)	**55.** (a)	**56.** (a)	**57.** (d)	**58.** (b)	**59.** (b)	**60.** (d)
61. (b)	**62.** (d)	**63.** (d)	**64.** (a)	**65.** (a)	**66.** (b)	**67.** (c)	**68.** (a)	**69.** (d)	**70.** (b)
71. (d)	**72.** (a)	**73.** (b)	**74.** (c)	**75.** (a)	**76.** (b)	**77.** (d)	**78.** (c)	**79.** (d)	**80.** (a)
81. (b)	**82.** (a)	**83.** (b)	**84.** (a)	**85.** (d)	**86.** (a)	**87.** (b)	**88.** (c)	**89.** (c)	**90.** (c)
91. (d)	**92.** (a)	**93.** (b)	**94.** (c)	**95.** (b)	**96.** (b)	**97.** (c)	**98.** (b)	**99.** (a)	**100.** (d)

Note: (x) denotes that questions were cancelled by examining authoroties.

ESIC PHARMACIST (EMPLOYEES STATE INSURANCE CORPORATION - ALLOPATHIC) RECRUITMENT QUESTION PAPER 2016

1. Crystalluria is the side effect associated with
(a) Quinolones (b) Azoles
(c) Sulphonamides (d) Taxol

2. The Drugs and Cosmetic Act was passed in
(a) 1940 (b) 1945
(c) 1947 (d) 1946

3. Which of the following is a female sex hormone?
(a) Stilbesterol (b) Testosterone
(c) Estrogen (d) Benzesterol

4. Chloroquine is a
(a) 4-Amino Quinoline (b) Acridine
(c) Biguanide (d) Pyrimidine

5. In the pediatric dose calculation, children in the first twenty days of birth comes under the class of
(a) Infant (b) Child
(c) Neonatal (d) Just born

6. A naturally occurring carminative is
(a) Asafoetida (b) Asoka
(c) Arjuna (d) Agar

7. The meaning of Latin term Rx
(a) Take thou (b) when necessary
(c) send (d) write

8. The DPO (Drug Price Control Order) was exercised by central government in
(a) 1985 (b) 1995
(c) 1987 (d) 1997

9. Myocardium is a special muscle tissue found only in the
(a) Brain (b) Heart
(c) Stomach (d) Lungs

10. Ths schedule to which 'List of drugs to be sold on prescription only' belong to
(a) Schedule L (b) Schedule W
(c) Schedule X (d) Schedule M

11. Mannitol is
(a) Loop diuretic
(b) Osmotic diuretic
(c) Potassium sparing diuretic
(d) Carbonic anhydrase diuretic

12. The formulations used for dental hygiene are known as
(a) Insufflation (b) Snuffs
(c) Cachets (d) Dentifrices

13. Erythroblastosis foetalis arises due to the incompatibility in the
(a) Lymph (b) Blood
(c) Synovial fluid (d) Bile

14. A parenteral anticoagulant drug is
(a) Penicillin (b) Phfenindione
(c) Warfarin (d) Heparin

15. Drugs and Magic Remedies act was passed in
(a) 1956 (b) 1954
(c) 1952 (d) 1953

16. A non-drug part added to formulation to aid dilution, stability maintaining, taste masking et(c) is known as
(a) Presensitive (b) Active ingredient
(c) Additive (d) Binding agent

17. Tropaue alkaloids can be identified by
(a) Thalloquin test (b) Vitali test
(c) Biuret test (d) Millon's test

18. The powerhouse of the cell is
(a) Golgi bodies (b) Mitochondria
(c) Ribosomes (d) Nucleus

19. Which of the following is not a benzodiazepine?
(a) Diazepam (b) Nitrazepam
(c) Zolpidem (d) Triazolam

20. Which of the following is a natural emulsifying agent obtained from vegetable source?
(a) Starch (b) Gelatin
(c) Egg yolk (d) Wool fat

21. A chelating agent used in the case of poisoning is
(a) Sodium phosphate (b) Dimercaprol
(c) Ferroin (d) Bismuth subnitrate

22. Filter sheets made of cellulose are
(a) Seitz filter (b) Membrane filter
(c) Glass fiber filter (d) Sintered glass filter

23. One fluid ounce is
(a) 60 ml (b) 15 ml
(c) 30 ml (d) 10 ml

24. The plant drug which is oxytoxic
(a) Ergot (b) Kurchi
(c) Vinca (d) Cocaine

25. The diagnostic agent used for the functioning of thyroid gland
(a) Fe-59 (b) I-131
(c) Co-60 (d) P-32

26. The constituent of cholesterol termed as bad cholesterol is
(a) HDL (b) LDL
(c) VLDL (d) Triglycerides

27. Sterols belong to the class of
(a) Lipids (b) Waxes
(c) Carbohydrates (d) Proteins

28. Hepatitis is a
(a) Bacterial infection (b) Protozoal infection
(c) Fungal infection (d) Viral infection

29. A leukotriene receptor antagonist used in allergic cough is
(a) Rofecoxib (b) Theophylline
(c) Losartsn (d) Montelukast

30. The sulphonamide used for bum Therapy is
(a) Sulfadiazine (b) Sulfadoxine
(c) Sulfacetamide (d) Sulfapyridine

31. A hypotonic solution can be made isotonic by The addition of
(a) Sodium chloride (b) Potassium chloride
(c) Calcium chloride (d) Magnesium chloride

32. The pathogenic organism in milk is killed by
(a) Tyndalization (b) Pasteurization
(c) Autoclaving (d) Dry heat sterilization

33. Agents promoting easy bowel evacuation is termed as
(a) Protective (b) Antacids
(c) Adsorbents (d) Laxatives

34. Morphine, codeine and thebaine is contained in
(a) Quassia (b) Kurchi
(c) Gelatin (d) Opium

35. Amantadine is the drug used as
(a) Antibacterial (b) Antiviral
(c) Antifungal (d) Antiprotozoal

36. The antifungal drug, fluconazole belongs to the class of
(a) Pyridine (b) Azoles
(c) Pyrimidines (d) Acridines

37. The first Indian Pharmacopoeia was published in
(a) 1948 (b) 1960
(c) 1955 (d) 1966

38. Ranitidine is a
(a) H2 antagonist
(b) HI antagonist
(c) Beta adrenergic antagonist
(d) Alpha adrenergic antagonist

39. Creams are
(a) Emulsions (b) Suspensions
(c) Ointments (d) Pastes

40. Ocuserts are
(a) Ear preparations (b) Nasal preparations
(c) Oral preparations (d) Eye preparations

41. Eugenol is contained in
(a) Clove (b) Capsicum
(c) Cardamom (d) Coriander

42. Tuberculosis is diagnosed by
(a) Widal test (b) Elisa test
(c) Mantoux test (d) Alerts method

43. One among the following is a communicable disease
(a) Cancer (b) Diabetes
(c) Hypertension (d) Filariasis

44. An example of sulfonyl urea is
(a) Metformin (b) Tolbutamide
(c) Rosiglitazone (d) Repaglinide

45. Blood plasma and blood serum preparations are dried by
(a) Freeze dryer (b) Vacuum dryer
(c) Spray dryer (d) Fluidized bed dryer

46. The medicinal agents used for the increase in mine output is known as
(a) Urinary antiseptics (b) Diuretics
(c) Stimulants (d) Antiseptics

47. Phenobarbitone is a
(a) Sedative (b) Antitussive
(c) Antipsychotic (d) Anxiolytic

48. An analgesic containing para amino phenol group is
(a) Paracetamol (b) Ibuprofen
(c) Aspirin (d) Indomethacin

49. Acetyl salicylic acid is
(a) Sulindac (b) Aspirin
(c) Mefenamic acid (d) Nalidixic acid

50. Chlorpromazine is an antipsychotic drug possessing
(a) Butyrophenone (b) Thioxanthine
(c) Phenothiazine (d) Acridine

51. Which among the following is a tricyclic antidepressant drug?
(a) Amitryptiline (b) Trazodone
(c) Phenelezine (d) Fluoxetine

52. Salbutamol is a
(a) Mast cell stabilizer
(b) Bronchodilator
(c) Immunosuppressant
(d) Antitussive

53. Which among the following is an anti-dandruff drug?
(a) Zinc sulphate (b) Selenium sulfide
(c) Zinc carbonate (d) Sodium fluoride

54. The component of tablet machine which controls the shape and size of the tablet is
(a) Hopper (b) Punches
(c) Cam track (d) Dies

55. Calamine is
(a) Basic zinc oxide
(b) Basic zinc sulfide
(c) Basic zinc carbonate
(d) Basic zinc hydroxide

56. Vitamin tablets are generally formulated as;
(a) Hypodermic tablets
(b) Sublingual tablets
(c) Effervescent tablets
(d) Chewable tablets

57. Ciprofloxacin is a
(a) Quinoline ding
(b) Quinolone drug
(c) Isoquinoline drug
(d) Quinuclidine drug

58. The crude drug with the Latin name Withania somnifera is
(a) Brahmi (b) Hyoscyamus
(c) Aswagandha (d) ipecac

59. One among the following is a volatile oil containing crude drug
(a) Chirata (b) Cardamom
(c) Linseed (d) Myrobalan

60. A crude drug used as cardiotonic
(a) Dhatura (b) Cinchona
(c) Ephedra (d) Ergot

61. Belladona belongs to the family of
(a) Solanaceae (b) Piperaceae
(c) Papavaraceae (d) Rutaceae

62. The active ingredient that forms froth when shaken with water
(a) Alkaloid (b) Tannin
(c) Gum (d) Saponin

63. Emetine is the main ingredient of
(a) Ipecac (b) Isapgol
(c) Pyrethrum (d) Rhubarb

64. The rod shaped bacteria are
(a) Coccus (b) Spirilla
(c) Bacillus (d) Vibrios

65. Widal test is used for the diagnosis of
(a) Typhoid (b) AIDS
(c) Jaundice (d) Meningitis

66. The disease caused by Entamoeba histolytica;
(a) Malaria (b) Trypanosomiasis
(c) Filariasis (d) Amoebiasis

67. Hospital acquired infectious are called
(a) Primary infection
(b) Secondary infection
(c) Nosocomial infection
(d) Latent infection

68. EEG is utilized to diagnose the diseases associated with the
(a) Heart (b) Kidney
(c) Abdomen (d) Brain

69. Which of the following is an antidiuretic hormone?
(a) Oxytocin
(b) Follicle stimulating hormone
(c) Vasopressin
(d) Luteinizing hormone

70. The hormone involved in the secretion and regulation of milk
(a) TSH (b) FSH
(c) Prolactin (d) Thyroxine

71. An antimalaria1 obtained from natural source is
(a) Strychnine (b) Brucine
(c) Reserpine (d) Quinine

72. Ascaris lumbricoides is a
(a) Helminth (b) Protozoa
(c) Amoeba (d) Virus

73. Kala Azar is a type of
(a) Giardiasis (b) Leishmaniasis
(c) Helminthiasis (d) Schistosomiasis

74. The presence of pathogenic bacteria hi blood is called
(a) Toxemia (b) Septicemia
(c) Bacteremia (d) Anemia

75. Dettol is used as
(a) Antiseptic (b) Disinfectant
(c) Antimicrobial (d) Antibiotic

76. An antibiotic possessing the beta lactam ring is
(a) Penicillin (b) Erythromycin
(c) Streptomycin (d) Chloramphenicol

77. Which of the following is a catecholamine?
(a) Thyroxine (b) Melanine
(c) Tyramine (d) Dopamine

78. Passive immunity is obtained by injecting
(a) Antiserum (b) Antigens
(c) Vaccines (d) Antibodies

79. An acid contained in bacterial cell wall is
(a) Muramic acid (b) Formic acid
(c) Stearic acid (d) Palmitic acid

80. Which among the following is an antihistaminic drug?
(a) Diphenhydramine (b) Chlordiazepoxide
(c) Pilocarpine (d) Amphetainine

81. A narcotic analgesic
(a) Reserpine (b) Papaverine
(c) Quinine (d) Morphine

82. Which of the following is not an eicosanoid?
(a) Interleukin (b) Leukotriene
(c) Thromboxane (d) Prostaglandin

83. Which of the following is a NS AID drag?
(a) Morphine (b) Heroin
(c) Codeine (d) Diclofenac

84. The extraction process where powdered crude ding is kept in contact with suitable solvent for suitable time
(a) Percolation (b) Decoction
(c) Maceration (d) Reserved percolation

85. Which of the following is used as a binder?
(a) Talc (b) Starch
(c) Cellulose (d) Kaolin

86. Which of the following is an analeptic drag?
(a) Caffeine (b) Nikethamide
(c) Cocaine (d) Amphetamine

87. Which among the following is an anti-filarial drug?
(a) DEC (b) FNH
(c) PAS (d) DDS

88. The schedule for Good manufacturing practices and requirements of factoiy premises for the manufacture of belongs to
(a) Schedule X (b) Schedule W
(c) Schedule L (d) Schedule M

89. A preparation containing killed or attenuated viruses is termed as
(a) Vaccine (b) Antiserum
(c) Toxin (d) Toxoid

90. Dapsone is used for the therapy of
(a) Tuberculosis (b) Amoebicide
(c) Leprosy (d) Helminthiasis

91. Curcmninoids are present in
(a) Squill (b) Turmeric
(c) Honey (d) Acacia

92. The cardiovascular disease associated with the disorder of heart rate or rhythm is called
(a) Arrhythmia (b) Myocardial infarction
(c) Angina pectoris (d) Ischemia

93. Yeasts come under a group of
(a) Bacteria (b) Fungi
(c) Protozoa (d) Virus

94. Drugs suppressing nausea and vomiting are
(a) Anti-emetic (b) Anti-diarrheal
(c) Anti-ulcer (d) Antiseptic

95. Which of the following drugs is used as a neuromuscular blocking agent?
(a) Methocarbamol (b) Succinyl choline
(c) Tizanidine (d) Baclofen

96. Which of the following is beta adrenergic blocker?
(a) Ramipril (b) Valsartan
(c) Verapamil (d) Propranolol

97. Agents used for reducing acidity in stomach is termed as
(a) Acidifier (b) Protective
(c) Adsorbent (d) Antacid

98. The complete separation of two phases in emulsion is called
(a) Creaming (b) Sedimenting
(c) Cracking (d) Leaching

99. Lachrymal glands produces
(a) Tear (b) Wax
(c) Sweat (d) Sebum

100. One among the following is an alkylating anticancer ding
(a) Chloramphenicol (b) Chlorambucil
(c) Chlorhexidine (d) Clotrimazole

101. The Reserve Bank of India (RBI) was formerly called as
(a) National Rank Of India
(b) Union Bank Of India
(c) Central Bank Of India
(d) Imperial Bank Of India

102. Normally (b)(c)G. vaccine is used for
(a) Rabies (b) Tuberculosis
(c) Cancer (d) Polio

103. For producing sound , a CD audio player uses
(a) Quartz Crystal (b) Laser Beam
(c) Titanium Crystal (d) Barium Titanium Ceramic

104. Manav Seva Award has been instituted in the memory of
(a) Rajiv Gandhi (b) Dr. Rajendra Prasad
(c) Indira Gandhi (d) Jawaharlal Nehru

105. Aryabhata - The first Indian satellite was launched horn
(a) Palamor (U.K.) (b) Cape Kennedy (U.S.A)
(c) Sriharikotta (India) (d) Bears Lake (U.S.S.R)

106. The capital of Puducherry is
(a) Karaikal (b) Mahie
(c) Puducherry (d) Yanam

107. Which one of the following is nor matched correctly?
(a) PTMNNXTPOA = PTMNNXTPOA
(b) 5678766817= 5678766317
(c) CA6S2XP190 = CA6S2X919G
(d) 768X176891 = 768X176891

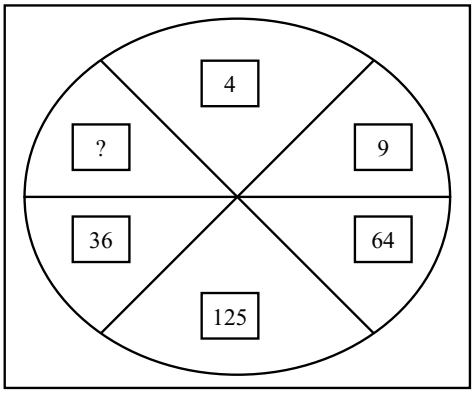
108. 1/2 of 4/7 of 5/7 of number is 50. What is the number?
(a) 254 (b) 245
(c) 300 (d) 250

109. On 10th February 1995 it was Friday. The day of the week on 10th February 1994 was
(a) Saturday (b) Sunday
(c) Thursday (d) Friday

110. I.BOOK II. PAPER III. PEN IV.LIBRARY V. AUTHOR
(a) V, II, III, I, IV
(b) IV, V, III, II, I
(c) III, I, II, V, IV
(d) V III. II. I. IV

111. Find the odd one out
(a) And (b) If
(c) Now (d) By

112. Insert the missing number



(a) 49 (b) 64
(c) 25 (d) 27

113. 729Z. 512Y, 343X, 216W,..... ?
(a) 136R (b) 182T
(c) 125V (d) 64P

114. Calculate the avenge of the cubes of first seven natural numbers

(a) 121 (b) 122
(c) 120 (d) 112

115. Two numbers are in the ratio of 3 4. If 5 is added to both the numbers, the ratio becomes 4 5. Find the greater number
(a) 20 (b) 10
(c) 15 (d) 25

116. The present age of father is three times the sum of the ages of his two daughters. After 5 years hence, his age will be double the sum of their ages. The present age of the father is
(a) 54 years (b) 35 years
(c) 45 years (d) 53 years

117. The equivalent discount to consecutive discounts of 15% and 20% will be
(a) 35% (b) 36%
(c) 32% (d) 30%

118. Rajesh invested an amount ofRsl2050 at simple interest. He got an amount of Rs 13496 at the end of 2 years. At what rate of interest did lie invest?
(a) 6,5% per annum (b) 6% per annum
(c) 8% per annum (d) 8.5% per annum

119. In a hostel having 60 students, an addition of 5 members increases the gross monthly expenditure by Rs 45 but diminishes the average cost per head by Rs 5. What did the total monthly expenses (in Rs) originally amount to?
(a) 4500 (b) 4440
(c) 4700 (d) 4044

120. If A is the brother of X B is X's brother and A is brother of Y. then which of the following statements is definitely true?
(a) X is B's brother (b) X is Y's brother
(c) A is B's brother (d) Y is A's brother

121. If ACTION is coded as ZXGRLM, then how will you write'BOOKING'?
(a) YLLRPMT (b) YRLLPMT
(c) YLILPRMT (d) YPLLRMT

122. P. Q. R. S and T are sitting on a bench in a park. P is sitting next to Q. R is sitting next to S, S is not sitting with T who is on the left end of the bench. R is on the second position from the right. P is on the right of Q and T. P and R are sitting together. In which position is P sitting?
(a) between R and T (b) between Q and S
(c) between Q and R (d) between T and S

123. Origami Paper Ikebana ?
(a) Flower (b) Thermacoal
(c) Glass (d) Paper

124. Mithran earns more than Sharma and less than Dinesh. Vishnu earns more than Mithran and Dinesh, Sibi earns more than only Shann(a) Who earns the least among the five?
(a) Vishnu (b) Shanna
(c) Mithran (d) Sibi

125. How many times in a day do the minute and hour hands of a clock point in the same direction?
(a) 32 (b) 22
(c) 24 (d) 44

ANSWER KEYS

1. (c)	**2.** (a)	**3.** (c)	**4.** (a)	**5.** (c)	**6.** (a)	**7.** (a)	**8.** (b)	**9.** (b)	**10.** (a)
11. (b)	**12.** (d)	**13.** (b)	**14.** (d)	**15.** (b)	**16.** (c)	**17.** (b)	**18.** (b)	**19.** (c)	**20.** (a)
21. (b)	**22.** (b)	**23.** (c)	**24.** (a)	**25.** (b)	**26.** (b)	**27.** (a)	**28.** (d)	**29.** (d)	**30.** (a)
31. (a)	**32.** (b)	**33.** (d)	**34.** (d)	**35.** (b)	**36.** (b)	**37.** (c)	**38.** (a)	**39.** (a)	**40.** (d)
41. (a)	**42.** (c)	**43.** (d)	**44.** (b)	**45.** (a)	**46.** (b)	**47.** (a)	**48.** (a)	**49.** (b)	**50.** (c)
51. (a)	**52.** (b)	**53.** (b)	**54.** (d)	**55.** (a)	**56.** (d)	**57.** (b)	**58.** (c)	**59.** (b)	**60.** (a)
61. (a)	**62.** (d)	**63.** (a)	**64.** (c)	**65.** (a)	**66.** (d)	**67.** (c)	**68.** (d)	**69.** (c)	**70.** (c)
71. (d)	**72.** (a)	**73.** (b)	**74.** (b)	**75.** (a)	**76.** (a)	**77.** (d)	**78.** (d)	**79.** (a)	**80.** (a)
81. (d)	**82.** (a)	**83.** (d)	**84.** (c)	**85.** (b)	**86.** (b)	**87.** (a)	**88.** (d)	**89.** (a)	**90.** (c)
91. (b)	**92.** (a)	**93.** (b)	**94.** (a)	**95.** (b)	**96.** (d)	**97.** (d)	**98.** (c)	**99.** (a)	**100.** (b)
101. (c)	**102.** (b)	**103.** (b)	**104.** (a)	**105.** (a)	**106.** (c)	**107.** (c)	**108.** (b)	**109.** (c)	**110.** (a)
111. (c)	**112.** (a)	**113.** (c)	**114.** (d)	**115.** (a)	**116.** (c)	**117.** (c)	**118.** (b)	**119.** (b)	**120.** (c)
121. (c)	**122.** (c)	**123.** (a)	**124.** (b)	**125.** (b)					

UPSC DRUG INSPECTOR EXAMINATION PAPER 2011

1. Assume that for a digoxin, the therapeutic range is cited as Cavg 5.5 = 0.8 –2mg/ml. If the patient is assumed to have an estimated digoxin t1/2 of 48 hours, how long would you wait to take serum digoxin concentration measurement and when during the dosing interval would you schedule it?

(a) 28 days then 3–4 hours after the dose is administered
(b) 14 days then 6–8 hours after the dose is administered
(c) 7 days then 10–14 hours after the dose is administered
(d) 3 days then 1–2 hours after the dose is administered

2. Which drug is used to prevent embolism in lungs and also during myocardial infarction?

(a) Human growth hormone
(b) Alteplase
(c) Epogen (EPO)
(d) Granulocyte-macrophage colony stimulating factor (GM-CSF)

3. Which enzyme is used by the human immunodeficiency virus (HIV) to form deoxyribonucleic acid (DNa) in the host cell?

(a) Restriction endonuclease
(b) DNA-directed polymerase only
(c) Reverse transcriptase only
(d) Both (b) and (c)

4. For two drug products, generic and brand to be considered bio-equivalent, the 90% confidence intervals about the ratio of the means of the Cmax and AUC values for generic/brand product must be within

(a) 80%–120% of the brand product
(b) 80%–100% of the brand product
(c) 80%–85% of the brand product
(d) 80%–90% of the brand product

5. The renal clearance of inulin is used as a measurement of

(a) Effective renal blood flow
(b) Active renal secretion
(c) Glomerular filtration rate
(d) Intrinsic enzyme activity

6. Which condition usually increases the rate of drug dissolution from a tablet?

(a) Increases in the particle size of the drug
(b) Use of the ionized or salt form of the drug
(c) Decreases in the surface area of the drug
(d) Use of the free acid or free base form of the drug

7. The amount of nitroglycerine that a transdermal patch delivers within a 24 hour period will not depend on

(a) Occlusive backing on the patch
(b) Diffusion rate of nitroglycerine from the patch
(c) Surface area of the patch
(d) Dissolution rate of nitroglycerine from the patch

8. A very fine powdered chemical/drug is defined as one that

(a) Completely passes through a sieve #240
(b) Completely passes through a sieve #120
(c) Completely passes through a sieve #60
(d) Passes through a sieve # 60 and not more than 40% through a sieve # 120

9. Which equation is used to predict the stability of a drug product at room temperature from experiment at accelerated temperature?

(a) The stokes equation
(b) The Arrhenius equation
(c) The mickaelis-menten equation
(d) The Hixson-Crowell equation

10. In 25 ml of a solution for injection, there are 4 mg of the drug. If the dose to be administered to a patient is 200 μg, what quantity of this solution should be used?

(a) 1.25 ml (b) 0.125 ml
(c) 12 ml (d) 1.2 ml

11. The rate of drug administration that gives the most rapid onset of the pharmacologic effect is

(a) Per oral administration
(b) Intradermal injection
(c) Intravenous injection
(d) Subcutaneous injection

12. Dose dumping is a problem in the formulation of
(a) Soft gelatin capsules
(b) Compressed tablets
(c) Hard gelatin capsules
(d) Modified release drug products

13. The extent of ionization of a weak electrolyte drug is dependent on the
(a) Particle size and surface area of the drug
(b) Noyes-Whitney equation for the drug
(c) Polymorphic form of the drug
(d) pH of the media and pKa of the drug

14. The characteristic of an active transport process includes all of the following except:
(a) Active transport moves drug molecules against concentration gradient
(b) Active transport follows Kick's law of diffusion
(c) Active transport require energy
(d) Active transport of drug molecules may be saturated at high drug concentration

15. In order to determine the absolute bioavailability of a drug given as an oral extended-release tablet, the bioavailability of the drug must be compared to bioavailability of the drug from,
(a) An immediate-release oral tablet containing the same amount of the active ingredient
(b) A reference (brand) extended-release that is a pharmaceutical equivalent
(c) A parenteral solution of the drug given by IV bolus or IV infusion
(d) An oral solution of the drug in the same dose

16. A single dose four-way cross over fasting, comparative bioavailability study was performed in 24 healthy, adult male subjects. Plasma drug concentration was obtained for each subject and following result was obtained:

Product	Dose (mg)	C_{max} (µg/ml)	T_{max} (h)	AUC $_{0\rightarrow\infty}$ (µghr/ml)
IV injection	100			1714
Oral emulsion	200	21.3	1.2	3143
Capsule	200	17	2.1	2822
Reference tablet	200	16.5	1.9	2715

The relative bioavailability of the drug from the capsule compared to the reference tablet is
(a) 82.3% (b) 91.7%
(c) 96.2% (d) 103.9%

17. How many grams of aspirin should be used to prepare 1.250 kg of the given powder?
Powder formula:

ASA	6 parts
Phenacetin	3 parts
Caffeine	1 part

(a) 125 (b) 750
(c) 186 (d) 366

18. Which technique is typically used to mill Camphor?
(a) Levigation
(b) Pulverization by Intervention
(c) Geometric dilution
(d) Attrition

19. Content uniformity test for tablets is used to ensure which quality?
(a) Bioeuivalency (b) Potency
(c) Purity (d) Toxicity

20. The route of drug administration that provides complete (100%) bioavailability is
(a) Intramuscular Injection
(b) Intravenous Injection
(c) Intradermal Injection
(d) Subcutaneous Injection

21. The rate of drug bioavailability is most rapid when the drug is formulated as
(a) Controlled release product
(b) Hard gelatin Capsule
(c) Solution
(d) Compressed tablet

22. The sedimentation of particles in a suspension can be minimized by which of the following?
1. Adding Sodium Benzoate
2. Increasing the viscosity of the suspension
3. Reducing the particle size of the active ingredient
4. Adding a suspending agent

Select the correct answer using the code given below:
(a) 1 and 2 only (b) 2, 3 and 4
(c) 1, 3, and 4 (d) 2 and 4 only

23. Which one among the following statements is not correct?

(a) Vaccines stimulate active immunity
(b) Vaccines are used for long term prophylaxis
(c) Patient receives antibodies in active immunization
(d) Patient produces antibodies in active immunization

24. Which one of the following is not correct?
(a) Vaccines are antigen containing preparations
(b) Toxoids are bacterial toxins modified to destroy or reduce their toxicity
(c) Antibody containing preparations are known as Anti sera
(d) Vaccines are used for passive immunization

25. Class 100 clean room is defined as a room in which the particle count in the air is
(a) Not more than 100 per cubic foot of 0.5µm and larger in size
(b) Not more than 120 per cubic foot of 0.5µm and larger in size
(c) Not more than 100 per cubic foot of 0.5µm and larger in size
(d) Not more than 99 per cubic foot of 0.3µm in size

26. Which of the following is not used as enteric coating material?
(a) Cellulose acetate phthalate
(b) Pectin
(c) Acrylase Polymers
(d) Polyvinyl acetate phthalate

27. Which of the following cannot be used for buffering of injections?
(a) Phosphate buffers (b) Citrate buffers
(c) Borate buffers (d) Acetate buffers

28. Which one of the following chemical/pharmacological classes of agents is incorrectly matched with its nature?
(a) Adrenergic agonist: Basic
(b) Prostaglandin: Acidic
(c) 4-Quinolones: Basic
(d) Meglitinides: Acidic

29. Which one of the following acids has the highest degree of ionization in an aqueous solution?
(a) Aspirin (pKa = 3.5)
(b) Indomethacin (pKa = 4.5)
(c) Ibuprofen (pKa = 5.2)
(d) Phenobarbital (pKa = 7.4)

30. All of the following statement about first order degradation are true, except
(a) Its rate is dependent on the concentration
(b) Its half life is a changing parameter
(c) A plot of the log of concentration versus time yields a straight line
(d) Its $t_{90\%}$ is dependent of the concentration

31. Vanishing cream is an ointment that may be classified as
(a) A water soluble base
(b) An oleaginous base
(c) An absoption base
(d) An emulsion base

32. Rofecoxib
(a) Has a similar effect to diclofenac
(b) Provides protection against ischemic cardiovascular events
(c) Is indicated for long term use in osteoarthritis
(d) Can be given to patients with active peptic ulceration

33. Schedule 'R' of drugs and cosmetics act would apply to
(a) Requirement of factory premises and hygienic conditions for ayurvedic (including sidhha) drugs
(b) Standards for mechanical contraceptives
(c) Standard for medical devices
(d) None of these

34. An alcoholic solution contains 57.77% u/v alcohol. The strength will be labelled as
(a) Over proof (b) Under proof
(c) Proof spirit (d) Prof gallons

35. Probenecid increases serum levels and prolongs activity of penicillin derivatives by
(a) Plasma protein binding
(b) Blocking their glomerular filtration
(c) Blocking their tubular secretion
(d) Blocking their reabsorption

36. In the preparation of calamine lotion, sodium citrate is used as
(a) Suspending agent (b) Solubilizer
(c) Buffering agent (d) Bacteriostatic

37. Water which is free from volatile and non-volatile impurities, microorganism and pyrogens is called
(a) Purified Water IP
(b) Water for injection IP
(c) Sterile water for injection IP
(d) Potable water

38. A new drug has completed phase-I clinical trial in USA, the pharmaceutical company wants to do the multicentric, multinational trial including in India.

The firm will apply in India to conduct

(a) Phase-I trial
(b) Phase-II trial
(c) Pre-clinical trial
(d) Pharmacolimetric data trial

39. Match the following:

1. Schedule V	I. Particulars to be shown in the various records of manufacture of drugs
2. Schedule T	II. List of drugs which can be marketed under generic names only
3. Schedule U	III. Life period of Drugs
4. Schedule W	IV. Standards of patent of proprietory medicines
5. Schedule P	V. Requirements of factory premises and conditions for ayurvedic and Unani drugs

Which is the correct match?

(a) 1-I, 2-III, 3-IV, 4-V, 5-II
(b) 1-V, 2-IV, 3-I, 4-II, 5-III
(c) 1-IV, 2-V, 3-I, 4-II, 5-III
(d) 1-IV, 2-V, 3-II, 4-I, 5-III

40. 0.9% w/v sodium chloride has a freezing point depression of

(a) –0.50ºC (b) –0.52ºC
(c) –0.56ºC (d) –0.58ºC

41. Subcoating is given to the tablets to

(a) Prevent dissolution in acidic medium
(b) Round the edges and build up the tablet size
(c) Prevent moisture penetration in to the tablet
(d) Avoid Deterioration due to microbial attack

42. Which one among the following is observed in first order kinetic?

(a) Clearance is constant
(b) Dose dependent elimination occurs
(c) Rate of elimination decreases with increases in plasma concentration
(d) Rate of elimination does not depend on plasma concentration

43. Which one of the following drug is not metabolized by liver?

(a) Phenytoin (b) Erythromycin
(c) Penicillin-G (d) Cefotaxime

44. Which one among the following is not an oral third generation cephalosporin?

(a) Cefditoren (b) Cefdinir
(c) Cefaclor (d) Ceftibuten

45. Which one among the following statements regarding Placebo is correct?

(a) Placebo does not produce any effect
(b) Placebo is a dummy medication
(c) All patients respond to placebo
(d) Placebo is the inert material added to drug for making tablets

46. Pharmacovigilance is used to monitor

(a) Unauthorized drug manufacturing
(b) Drug toxicity
(c) Pharmacokinetics
(d) Cost of drugs and pharmaceuticals

47. Clonidine is

(a) Alpha one selective agonist
(b) Alpha two selective agonist
(c) Alpha one selective antagonist
(d) Alpha two selective antagonist

48. Mala-N contains

(a) Ethinyl Estradiol (b) Norethisterone
(c) D-norgestrel (d) Norepinephrine

49. Prolonged use of steroids may cause

(a) Hypoglycemia
(b) Hypotension
(c) Decrease in bone matrix protein
(d) Early healing of wound

50. Anti-inflammatory action of glucocorticoids is due to blocking of

(a) Prostaglandin synthase
(b) Thromboxane synthase
(c) 15-lipoxygenase
(d) Breakdown of phospholipids

51. Good Laboratory Practice (GLP) certification in India is

(a) Mandatory for all pharmaceutical industries
(b) Compulsory for industries which involve in manufacturing of biologicals
(c) Compulsory for industries which involve in manufacturing of non-biologicals
(d) Optional for pharmaceutical industries

52. Good Laboratory Practice (GLP) certification is issued in India by

(a) Controller, Weights and measure, Government of India
(b) Bureau of Indian Standard (BIS), Government of India
(c) Department of science and Technology, Government of India
(d) Drug controller General of India (DCGI), Government of India

53. Which one of the following is second generation H_1-Anti histamine?
(a) Cetrizine (b) Cinnarizine
(c) Pheneramine (d) Promethazine

54. Prostaglandins have effect on a variety of tissues in human body. The different Prostaglandins may have different effects. Which one of the following statement is not correct?
(a) PGE2 is bronchodilator where as PGF2 alpha is a broncho constrictor
(b) PGE2 has marked oxytoxic action while PGF2 alpha has tocolytic action
(c) PGE1 and PGE2 inhibit platelet aggregation, whereas TXA2 facilitate aggregation
(d) The human arteriolar smooth muscle is relaxed by PGE2 AND PGI2, whereas TXA2 and PGF2 alpha cause vasoconstriction

55. Which one of the following statements is true regarding NSAID's?
(a) They cause release of histamine
(b) They cause relaxation of bronchial smooth muscle
(c) They indirectly increase leukotriene production
(d) They cause airway irritation

56. Which of the following statement is not correct?
(a) Rate of killing of bacteria by antibiotic follows the first order kinetics
(b) The bactericidal effects of Penicillin depends upon its attained C max
(c) The antibiotics having time dependent bactericidal effects are given in a large single dose rather than multiple daily doses
(d) Aminoglycosides produce bactericidal effect in a concentration dependent manner

57. Which of the following is not a correct combination of drug and its important adverse effect?
(a) Rifampicin: Hepatotoxicity
(b) Isoniazide: Pepripheral neuropathy
(c) Ethambutol: Increased uric acid
(d) Streptomycin: Ototoxicity

58. Chemotherapeutic agent, which does not inhibit the microtubule formation is
(a) Paclitaxel (b) Colchicine
(c) Vincristine (d) Vinblastine

59. Following antibiotics have been correctly paired to their mechanism of action, except:
(a) Vancomycin-Inhibits synthesis of phospholipids and peptidoglycan polymerization
(b) Tetracyline-Binds to 30s ribosome and inhibits protein synthesis
(c) Erythromycin-Binds to bacterial 70s ribosome and inhibits protein synthesis
(d) Ciprofloxacin-Interferes with the action of bacterial topoisomerase II

60. The pharmacokinetics 'half-life' of which one of the following resembles to its pharmacodynamic 'half-life'?
(a) Morphine (b) Terfenadine
(c) Isoprenaline (d) Suxamethonium

61. The following properties of a drug encourage its accumulation in breast milk, except:
(a) High lipid solubility
(b) Unionized state
(c) Low molecular weight
(d) Weak acid

62. As per the schedule 'Y' of the Drugs and Cosmetics Act, the animal toxicity study requirement for marketing of a drug depends upon tentative route and duration of administration in humans. In this context, which one of the following statements is incorrect?
(a) Single dose human use–animal toxicity for 2 weeks in 2 species
(b) Oral use for 2 weeks in human-animal toxicity for 4 weeks in 2 species
(c) Aerosol use by repeated use in humans-animal toxicity in 2 species for 24 weeks
(d) Multiple daily ocular application for short duration-irrigation test in 1 species for 3 weeks

63. In one of the clinical trails of vaccine, there were 6 deaths reported by the media. You have been deputed by authority to investigate the causality of incidence. Inspection of the following documents will be helpful except:
(a) Source data
(b) Standard operating procedures
(c) Data safety monitoring records
(d) Informed consent forms

64. Which one among the following is an antimalarial drug having a metabolite with triazine moiety?
(a) Quinine (b) Proguanil
(c) Pyrimethamine (d) Primaquine

65. Which one among the following is an antitubercular drug with hydrazine moiety?
(a) Ethionamide (b) Isoniazide
(c) Pyrazinamide (d) Thiacetazone

66. Codeine differ from morphine structurally in
(a) Methaylation of phenolic hydroxyl group
(b) Methaylation of alcholic group
(c) Methaylation of nitrogen group
(d) Oxidation of phenolic hydroxyl group

67. Tropane system is fusion of
(a) Pyrrolidine and piperdine
(b) Pyrrolidine and Pyrimidine
(c) Prrole and pyrazine
(d) Thiophene and Piperdine

68. The local anesthetics exert their action by blocking of the following types of ion channels:
(a) Ligand gated sodium channel
(b) Voltage gated sodium channel
(c) Ligand gated calcium channel
(d) Voltage gated calcium channel

69. Which one of the following statements with regard to the SAARC summit held in Bhutan in April, 2010 is not correct?
(a) The summit has held in Bhutan for the first time
(b) It was the silver jubilee summit of SAARC
(c) The summit recommended to declare 2010–2020 as the 'Decade of intra-regional connectivity in SAARC'
(d) The summit-central theme was 'Cross Border Terrorism'

70. Which one of the following statements with regard to the Right to Education Act, 2010 is not correct?
(a) All children in 6–14 year age group must get free and compulsory education.
(b) No children shall be held back, expelled or required to pass a board examination till Class VIII.
(c) There must be 25% reservation for poor children even in private schools.
(d) Gram Panchayats and Municipal Councils are responsible to look into violations of Right to Education laws.

The next three items are based on the following passage:
The detritus food chain (DFc) begins with dead organic matter. It is made up of decomposers which are heterotrophic organisms, mainly fungi and bacteria. They meet their energy and nutrient requirements by degrading dead organic matter or detritus. These are the saprotrophs which secrete digestive enzymes to break down the dead and waste matter into simple inorganic materials,which are subsequently absorved by them. DFC may be connected with the grazing food chain at some levels—some of the organisms of DFC are prey to the grazing food chain animals. Some animals like cockroaches, crows etc., are omnivores. These interconnections create a food web.

Organisms occupy a place in their natural surroundings according to their feeding relationship with others. The source of their nutrition of food dictates its tropic level. Autotrophs belong to the first tropic level and in turn feed the next tropic level of herbivores. Primary and secondary carnivores constitute the third and fourth levels. Only about 10% energy gets transferred from the lower to the next higher tropic level which eventually restricts the number of levels in a food chain.

71. Which trophic level in the grazing food chain do lions belong to?
(a) Trophic level 1 (b) Trophic level 2
(c) Trophic level 3 (d) Trophic level 4

72. The number of trophic levels in grazing food chain is restricted because
(a) the higher levels like to restrict their number to improve availability
(b) of loss of avalibility of food from consumption in the lower levels
(c) of an incremental number of organisms in the next higher level
(d) of sequential transfer loss of energy

73. The trophic level of a given species depends on it
(a) functionality (b) strength
(c) number (d) size

74. The president of India has no power to grant pardon under Article 72 of the Constitution of India where sentence
(a) is given by court martial
(b) of death has been awarded
(c) is for an offence relating to a matter to which the executive power to the Union extends
(d) is for an offence relating to a matter to which the executive power to the State extends

75. Who among the following won the Australian Open Tennis Cup (Men's Singles) 2011?

(a) Andy Murray (b) Novak Djokovic
(c) Rafael Nadal (d) Roger Federer

The next three items are based on the following passage:
Before performing an operation in the hospital, a doctor administes a drug or a gas to make the patient unconscious of pain. This state of unconsciousness is known as 'Anaesthesia' from greek word meaning 'loss of feeling'. The substance causing loss of feeling is called an anaesthetic. The discovery of anaesthetic in the 19th century was one of the greatest achievement in the field of medicine. Before anaesthetics, operations were done in very rare cases. Patients needing surgery were given alcohol or various drugs extracted from plant juices to reduce the pain. Even then, operations were always very painful and were undertaken only in extreme emergency. Today, with anaesthetics, it is possible to produce many hours of pain free unconsciousness and this enables surgeons to perform complex life saving operations.

76. Before performing an operation, how does a doctor lessen the pain of the patient?

(a) Gives alcohol
(b) Gives a drug or gas to make patient unconscious
(c) Give juice extract of plants
(d) Use extreme methods to dull the pain

77. Before 19th century, operations were done in very rare cases because

(a) Patient could not be given anything except alcohol to lessen pain
(b) There was absence of one of the greatest achievement in the field of science and medicine
(c) Anesthetics were discovered only in the 19th century
(d) Drug extracted from plant juice could not dull pain sufficiently

78. Today, surgeons can perform complex life saving operations due to

(a) There being emergency facilities
(b) The fact that patient can be kept pain free for many hours with anaesthetics
(d) Powerful plant extract are available today
(d) The fact that operations are done in rare cases

79. The Chairman of the Investigational New Drug (INd) committee in India is

(a) Drugs Controller General of India, Government of India
(b) Secretary, Department of Health Research, Government of India
(c) Directorate General of Health Sciences, Government of India
(d) Secretory Department of Biotechnology, Government of India

80. In India, the Drug Controller General of India (DCGI) can issue an order to ban a drug on the recommendation of

(a) Indian Council of Medical Research
(b) Pharmacy council of India
(c) Drug Technical Advisory Board
(d) National Pharmaceutical Advisory Board

81. Pregnancy test kits are designed to detect which substance?

(a) Leutinizing Hormone
(b) Progesterone
(c) Human Chorionic Gonadotropin
(d) Estrogen

82. Which one among the following is neither an input nor output device?

(a) CD-ROM (b) Floppy disk
(c) Hard disk (d) Pen drive

83. Which among the following is/are units of RAM?

1. Giga byte and Mega byte
2. RPM
3. GBPS and MBPS

Select the correct answer the using the code given below:

(a) 1, 2 and 3 (b) 1 and 2 only
(c) 2 and 3 only (d) 1 only

84. If you mix four parts of 40% with 1 part of 90% alcohol you will get

(a) 45.7% alcohol (b) 40% alcohol
(c) 50% alcohol (d) 57% alcohol

85. The loading dose (DL) of a drug is usually based on the

(a) Total body clearance of the drug
(b) Fraction of drug excreted unchanged in the urine
(c) Apparent volume of distribution (Vd) and desired drug concentration in plasma
(d) Area under the plasma drug concentration versus time curve(AUC)

86. The activity of which one of the following drugs is dependent on a p-phenyl-N-alklypiperidine moiety?

(a) Phenobarbital (b) Chlorpromazine
(c) Imipramine (d) Meperidine

87. Flurazepam has pKa of 8.2. What percentage of flurazepam will be ionized at a urine pH of 5.2?
(a) 0.1% (b) 1%
(c) 99% (d) 99.9%

88. Recrudescene of malaria refers to the
(a) Re-infection of patient my mosquito bite
(b) Re-infection by exoerythocytic hypozoites
(c) Incomplete clearance of sporozoites from blood
(d) Incomplete clearance of schizonts from blood

89. Which one of the following drugs should not be prepared in a horizontal laminar flow hood?
(a) Ampicillin (b) Dopamine
(c) Cisplatin (d) Niteoglycerine

90. Prostaglandin plays a major role in the biological activity of proton pump inhibitor such as omeprazole and Esomeprazole. The protonation takes place on the
(a) Aromatic Methyl chain
(b) Bemzimidzole ring
(c) Methoxy side chain
(d) The ring that has dimethyl groups

91. The carboxyl group aspirin after esterification with N-acety-P-aminophenol gives
(a) 3-acetamidophenyl-O-acety salicylate
(b) 4-acetamidophenyl-O-acety salicyate
(c) O-(2-hydroxybenzoyl) salicyclic acid
(d) 2-acetamidophenyl-O-acetyl salicylaye

92. A prescription order calls for 500 ml 2.0% aminosyn, but the pharmacy has 8.0% solution in stock. How much of the aminosyn 8.0% solution is required to prepare 500 ml of above solution?
(a) 120 ml (b) 147 ml
(c) 125 ml (d) 250 ml

93. Which of the following is/are the symptoms of venous thrombosis?
1. Oedema
2. Lower leg becoming bluish in colour
3. Dry skin

Select the correct answer using the code given below:
(a) 1, 2 and 3 (b) 1 and 2 only
(c) 2 and 3 only (d) 1 only

94. Interferon beta
1. Can be administered orally.
2. May cause myalgia
3. Is used in multiple sclerosis

Which of the above statement is/are correct?
(a) 1, 2 and 3 (b) 1 and 2 only
(c) 2 and 3 only (d) 1 only

95. Which of the following is/are the side effects associated with testosterone?
1. Headache
2. Hirustism
3. Gynaecomastia

Select the correct answer using the code given below:
(a) 1, 2 and 3 (b) 1 and 2 only
(c) 2 and 3 only (d) 1 only

96. Rosiglitazone
1. Should be used with caution in patients with cardiovascular disease.
2. Should not be used with glicazide.
3. Is a biguanide.

Which of the above statement is/are correct?
(a) 1, 2 and 3 (b) 1 and 2 only
(c) 2 and 3 only (d) 1 only

97. Iron salts
1. Should always be taken on empty stomach.
2. Should be given by mouth unless there are good reasons for using another route.
3. In the form of ferric salts are better absorbed than the ferrous salts.

Which of the above statement is/are correct?
(a) 1, 2 and 3 (b) 1 and 2 only
(c) 2 and 3 only (d) 1 only

98. Doxycycline
1. Is bacteriostatic
2. Is a broad spectrum antibacterial drug.
3. May be administered in renal impairment.

Which of the above statement is/are correct?
(a) 1, 2 and 3 (b) 1 and 2 only
(c) 2 and 3 only (d) 1 only

99. Testosterone may be used
1. To treat breast and endometrial cancer is females.
2. To treat hypogonadism in males.
3. To suppress postpartum breast enlargement.

Which of the above statement is/are correct?

(a) 1, 2 and 3 (b) 1 and 2 only

(c) 2 and 3 only (d) 1 only

100. Following adverse effects are rightly paired with a causative anti-malarial drug except:

(a) Lichenoid skin eruptions : Chloroquine

(b) Steven-Johnson Syndrome : Quinine

(c) Hallucinations : Mefloquine

(d) Prolongation of QT interval : Halofantrine

ANSWER KEYS

1. (b)	**2.** (b)	**3.** (c)	**4.** (c)	**5.** (c)	**6.** (b)	**7.** (a)	**8.** (d)	**9.** (b)	**10.** (a)
11. (c)	**12.** (d)	**13.** (d)	**14.** (b)	**15.** (a)	**16.** (d)	**17.** (b)	**18.** (a)	**19.** (b)	**20.** (b)
21. (c)	**22.** (b)	**23.** (c)	**24.** (d)	**25.** (a)	**26.** (b)	**27.** (c)	**28.** (a)	**29.** (a)	**30.** (b)
31. (d)	**32.** (c)	**33.** (b)	**34.** (c)	**35.** (d)	**36.** (c)	**37.** (b)	**38.** (d)	**39.** (c)	**40.** (b)
41. (b)	**42.** (c)	**43.** (c)	**44.** (d)	**45.** (b)	**46.** (b)	**47.** (b)	**48.** (a)	**49.** (c)	**50.** (a)
51. (d)	**52.** (d)	**53.** (a)	**54.** (c)	**55.** (c)	**56.** (b)	**57.** (c)	**58.** (a)	**59.** (a)	**60.** (a)
61. (d)	**62.** (d)	**63.** (c)	**64.** (b)	**65.** (b)	**66.** (a)	**67.** (a)	**68.** (b)	**69.** (d)	**70.** (c)
71. (c)	**72.** (d)	**73.** (d)	**74.** (b)	**75.** (c)	**76.** (b)	**77.** (d)	**78.** (b)	**79.** (a)	**80.** (c)
81. (c)	**82.** (c)	**83.** (d)	**84.** (c)	**85.** (c)	**86.** (d)	**87.** (d)	**88.** (c)	**89.** (d)	**90.** (b)
91. (b)	**92.** (c)	**93.** (b)	**94.** (c)	**95.** (b)	**96.** (b)	**97.** (b)	**98.** (a)	**99.** (c)	**100.** (c)

GUJARAT GOVERNMENT LECTURER EXAMINATION IN DEGREE/DIPLOMA PHARMACY COLLEGE-GPSC 2010

1. Which one of the following drugs is metabolized to a cytotoxic product?
(a) Vincristine (b) Dactinomycin
(c) 5-Fluoroucil (d) Lomustine

2. Which one of the following agent shows cytotoxicity that is cell-cylce specific?
(a) Methotrexate (b) Dactinomycin
(c) Cisplastin (d) Mechlorethamine

3. Which one of the following antiviral agent exhibits the greatest selective toxicity for the invading virus?
(a) Interferon (b) Amantadine
(c) Acyclovir (d) Zidovudine

4. In which one of the following conditions would aspirin be contraindicated?
(a) Myalgia (b) Fever
(c) Peptic ulcer (d) Rheumatoid arthritis

5. A water soluble substance used as coating material in microencapsulation process is
(a) Polyethylene
(b) Silicone
(c) Hydroxy ethyl cellulose
(d) Paraffin

6. How many parts of 10% ointment be mixed with 2 parts of 15% ointment to get 12% ointment?
(a) 2 (b) 3
(c) 5 (d) 6

7. A retardant material that forms a hydrophilic matrix in the formulation of matrix tablets is
(a) H.P.M.C. (b) C.A.P.
(c) Polyethylene (d) Carnauba wax

8. Measurement of particle size in pharmaceutical aerosols is by
(p) Cascade Impactor
(q) Light Scatter Decay
(r) Karl Fichser Method
(s) IR spectroscopy
(a) (p),(q) (b) (q),(r)
(c) (r),(s) (d) (p),(s)

9. Which test organism is used for microbiological assay of ampicillin?
(a) Micrococcus luteus
(b) Staphylococcus aureus
(c) Bacillus subtillis
(d) E.Coli

10. Staphylococcus aureus produces a pigment during their growth having
(a) Red colour (b) Green colour
(c) Yellow colour (d) Black colour

11. The particle size of the dispersed solid in a suspension is usually greater than
(a) 0.5 μm (b) 0.4 μm
(c) 0.2 μm (d) μm

12. The purpose of seal coating in sugar coating process for tablets is
(a) To prevent moisture penetration into the tablet core
(b) To round the edges and build up the tablet weight
(c) To impart the desired colour to the tablet
(d) To give lusture to the tablet

13. Lactose is the most widely used diluent in the tablet formulation. However, it is not used in the formulation of which one of the following?
(a) Pyrazinamide (b) Ibuprofen
(c) Sulfacetamide (d) Isoniazide

14. One thousand nanogram equals to one
(a) Centigram (b) Gram
(c) Kilogram (d) Microgram

15. Aglcone of the steroidal saponins commonly referred to as a "Spirostane" due to spiro character of
(a) C22 (b) C19
(c) C13 (d) C18

16. Ephedra sinica and Ephedra equisentia can be distinguished by type of
(a) Branching (b) Stomata
(c) Scaly leaves (d) Alkaloids

17. Tetraterpenoids include which of the following?
(a) Carotenes (b) Xanthophylls
(c) Carotenoidic acid (d) All of the above

18. Vincristine and Vinblastine act by
(a) Interfering with synthesis of t-RNA
(b) Inhibiting the fragmentation of DNA
(c) Binding of Protein
(d) Incorporating into folic acid metabolism

19. Lycopodium spore method can be used to find out the percentage purity of crude drug which contains
(a) Multi-layered cells or tissues
(b) Well defined particles can be counted
(c) Oil globules
(d) Characteristics particles of irregular thickness, the length of which can be measured

20. Single cells in tissue culture can be isolated by all of the following except:
(a) Mechanical method
(b) Filter paper method
(c) Enzymatic method
(d) Suspension culture

21. In Liberman-Burchard test for steroids, the compound is dissolved in
(a) Methanol (b) Chloroform
(c) Benzene (d) Ethanol

22. Rutin is extracted from all of the following, except:
(a) Sophora Japonica
(b) Fagopyrum esculentum
(c) Eucalyptus macrorrhyncha
(d) Ginko biloba

23. Cinchona robusta is a hybrid of
(a) C.calisaya and C.micrantha
(b) C.Succirubra and C.Officinalis
(c) C.Calisaya and C.Officinalis
(d) C.Calisaya and C.Succirubra

24. Microscopical character of flower buds of Eugenia Caryophullus is
(a) Collenchymatous parenchyma containing in its outer part numerous ellipsoidal schizolysigenous oil glands
(b) Small transulent endosperm containing aleurone grains
(c) Wide parenchymatous starchy cortex, the endosperm containing volatile oils
(d) Outer surface consisting of external perisperm, rough, dark brown with reticulate furrows

25. The Schedule in D and C Act that deals with the standards for disinfection fluids is
(a) Schedule O (b) Schedule F
(c) Schedule B (d) Schedule M

26. The Schedule in drug and cosmetics act that deals with the requirement and guidelines of clinical trials, import and manufacture of new drug is
(a) Schedule O (b) Schedule M
(c) Schedule F (d) Schedule Y

27. State pharmacy council should have the following number of elected members
(a) Six (b) Nine
(c) Five (d) Seven

28. Schedule D as per D and C Act is concerned with
(a) List of drugs exempted from the provision of import of drugs
(b) Diseases or aliments which a drug may not purport to prevent or cure
(c) Requirement of factory premises
(d) List of prescription drugs

29. One of the following Ex-Officio member of state pharmacy council
(a) Chief pharmacist of government hospital
(b) Chief administrative medical officer of the state
(c) Registered pharmacist
(d) Assistant drug controller

30. The education regulation is published in official gazette by
(a) Ministry of Education
(b) Central government
(c) Drug Controller
(d) President, Pharmacy council of India

31. The total area required for the manufacture of cosmetics aerosol as per the Schedule M of drug and Cosmetics act is
(a) 15 m^2 (b) 25 m^2
(c) 30 m^2 (d) 35 m^2

32. VRDL antigen is to be tested and analysed by the
(a) Drug inspector
(b) Excise commissioner
(c) Serologist and chemical examiner
(d) Drug controller of India

33. Chloramphenicol comes under schedule
(a) G (b) H
(c) W (d) P

34. The general formula of monosaccharides is
(a) $C_nH_{2n}O_n$ (b) $C_{2n}H_2O_n$
(c) $C_nH_2O_{2n}$ (d) $C_nH_{2n}O_{2n}$

35. The general formula of polysaccharides is
(a) $(C_6H_{10}O_5)n$ (b) $(C_6H_{12}O_5)n$
(c) $(C_6H_{10}O_6)n$ (d) $(C_6H_{10}O_6)n$

36. The aldose sugar is
(a) Glycerose (b) Ribulose
(c) Erythrulose (d) Dihydroxyacetone

37. A triose sugar is
(a) Glycerose (b) Ribulose
(c) Erythrulose (d) Fructose

38. A pentose sugar is
(a) Dihydroxyacetone (b) Ribulose
(c) Erythrulose (d) Glucose

39. A pentose sugar present mainly in the heart muscle is
(a) Lyxose (b) Ribose
(c) Arabinose (d) Xylose

40. Polysaccharides are
(a) Polymers (b) Acids
(c) Proteins (d) Oils

41. The number of isomers of glucose is
(a) 2 (b) 4
(c) 8 (d) 16

42. Two sugars which differ from one another only in configuration around a single carbon atom are termed as
(a) Epimers (b) Anomers
(c) Optical isomers (d) Stereoisomers

43. Pilocarpine is an
(a) Isomer of pillocarpic acid
(b) Lactone derivative of pillocarpic acid
(c) Anomers of pillocarpic acid
(d) Ketone of pillocarpic acid

44. The most important epimer of glucose is
(a) Galactose (b) Fructose
(c) Arabinose (d) Xylose

45. Isomers differing as a result of variations in configuration of the –OH and –H on carbon atoms 2,3 and 4 of glucose are known as
(a) Epimers (b) Anomers
(c) Optical isomers (d) Stereoisomers

46. Which type of stomata is present in Vasaka leaf?
(a) Dicytic (b) Anisocytic
(c) Anomocytic (d) Paracytic

47. Lumirhodopsin is stable only at temperature below
(a) –10°C (b) –20°C
(c) –40°C (a) –50°C

48. Vitamins are
(a) Accessory food factors
(b) Generally synthesized in the body
(c) Produced in endocrine glands
(d) Proteins in nature

49. Vitamin A or Retinal is a
(a) Steroid
(b) Polyisoprenoid compound containing a cyclohexenyl ring
(c) Benzoquinone derivative
(d) 6-Hydroxychromane

50. Carotene precursor of Vitamin A is oxidatively cleaved by
(a) Carotene dioxygenase
(b) Oxygenase
(c) Hydroxylase
(d) Transferase

51. Fat soluble vitamins are
(a) Soluble in alcohol (b) One or more propene units
(c) Stored in liver (d) All of these

52. Preformed Vitamin A is supplied by
(a) Milk, Fat and Liver
(b) All yellow vegetables
(c) All yellow fruits
(d) Leafy green vegetables

53. Retinol and Retinal are interconverted requiring dehydrogenase or reductase in the presence of
(a) NAD or NADP (b) NADPH
(c) FAD (d) NADH+H+

54. Retinal is reduced to retinol in intestinal mucosa by a specific retinaldehyde reductase utilizing
(a) NADPH+H+ (b) FAD
(c) NAD (d) NADH+H+

55. The international unit of Vitamin A is equivalent to the activity caused by
(a) 0.3 μg of Vitamin A alcohol
(b) 0.344 μg of Vitamin A alcohol
(c) 0.6 μg of Vitamin A alcohol
(d) μg of Vitamin A alcohol

56. Compounds having the same structural formula but differing in spatial configuration are known as
(b) Epimers (c) Anomers
(d) Optical isomers (d) Stereoisomers

57. Retinol is transported in blood bound to
(a) Aporetinol binding protein
(b) 2-Globulin
(c) βGlobulin
(d) Albumin

58. Among the following preparations, which one will be the most irritating to the eye?
(a) Purified water
(b) 0.7% NaCl solution
(c) 0.9% NaCl solution
(d) 1% NaCl solution

59. One of the following mills works on both the principles of attrition and impact:
(a) Cutter mill (b) Hammer mill
(c) Roller mill (d) Fluid energy mill

60. Choose the correct excipients for enhancing solubility in tablet manufacture.
(a) PEG (b) Microcrystalline cellulose
(c) Talc (d) Lactose

61. The area under the serum concentration time curve of a drug represents
(a) The biological half-life of the drug
(b) The amount of drug in the original dosage form
(c) The amount of drug absorbed
(d) The amount of drug excreted in the urine

62. The 'Unna parte' contains
(a) Zinc oxide
(b) Zinc oxide and Sulphur
(c) Zinc oxide and Gelatin
(d) Zinc oxide and Boric acid

63. "Capping" in a tablets occur due to
(a) Entrapment of Air
(b) Excessive moisture
(c) Increased rate of evaporation
(d) None of the above

64. The dip tube in an aerosol container is made from which one of the following?
(a) Polypropylene (b) Glass
(c) Staineless steel (d) Aluminium

65. The diameter of the mesh aperture in the IP disintegration test apparatus is given below:
(a) 2.00 mm (b) 4.00 mm
(c) 3.00 mm (d) 1.50 mm

66. Which one of the following device is useful to increase the efficiency of drug delivery via aerosols
(a) Tube spacers (b) Metered valve
(c) Actuator (d) Pressure valve

67. The most common causative agent of bacterial pneumonia
(a) Staphylococcus aureus
(b) Escherichia coli
(c) Sterptococcus pneumonia
(d) Mycopalsma pneumonia

68. Codeine differs in structure from morphine by
(a) N-methyl group (b) Acetyl group at C_1 and C_6
(c) $-OC_2H_5$ group (d) $-OCH_3$ group

69. Sanguiamarine belongs to the subgroup of
(a) Morphinans
(b) Benzyl isoquinolines
(c) Phthalide isoquinolines
(d) Benzophenantherenes

70. Dovers powder used as a diaphoretic contains
(a) Ipecac and Opium
(b) Senna and Cinchona
(c) Opium and Cinchona
(d) All of the above

71. _____ is the dimmer of flavones and flavonones.
(a) Chalcones (b) Aurones
(c) Biflavanoids (d) Dihydrofalvones

72. Isoquinoline alkaloids are biosynthesized via _____ pathway.
(a) Shikimic acid-tyrosine
(b) Shikimic acid-tryphtophan
(c) Shikimic acid-cathinone
(d) None of the Above

73. _____ is a precursor for indole alkaloids.
(a) Strictosidine (b) Diosgenine
(c) Ornithine (d) Hygrine

74. Catharanthine is an alkaloids of _____ type.
(a) Coryname (b) Ibogane
(c) Aspidospermane (d) All of the above

75. Different kinds of currents that contributes to the polarographic waves are
(a) Residual current (b) Migration current
(c) Diffusion current (d) All of the above

76. Which of the following radiation has the greatest penetrating power?
(a) Alpha radiation (b) Beta radiation
(c) Gamma radiation (d) UV radiation

77. Energy produced in the UV region produces changes in the
(a) The rotation energy of the molecule
(b) The vibrational energy of the molecule
(c) The electronic energy of the molecule
(d) All of the above

78. The wavelength of a radiation is 5μ wave number corresponding to that is
(a) 4000 cm^{-1} (b) 3000 cm^{-1}
(c) 2000 cm^{-1} (d) 1000 cm^{-1}

79. The important example of liquid-liquid partition chromatography is
(a) Thin layer (b) Column
(c) Paper (d) Ion exchange

80. In amperometric titrationsm, one of the following is kept constant:
(a) Current (b) Resistance
(c) Voltage applied (d) Conductance

81. In any colorimeter
(a) Unabsorbed radiation is measured
(b) Absorbed radiation is measured
(c) Absorbed radiation intensity is measured
(d) None of the above

82. Super critical fluid chromatography is specifically used for analysis of
(a) Thermolabile compounds
(b) Thermolabile macromolecules
(c) Thermostable macromolecules
(d) None of the above

83. An interferone filter consists of
(a) An iron plate coated with selenium
(b) A layer of silver on both sides of MgF_2 deposited on glass
(c) A tungson plate coated with AgO
(d) A solid sheet of glass coloured by pigment

84. Tetrabutyl ammonium phosphate is used in HPLC
(a) For adjusting pH of the mobile phase
(b) As stationary phase
(c) As chelating agent
(d) As ion pairing agent for anions

85. Desipramine is metabolized in liver mainly by
(a) N-Oxidation (b) Hydroxylation
(c) Both A and B (d) Alkylating agent

86. 2-Amino pyridine and 2-dimethyl amino ethyl chloride are starting material for the synthesis of
(a) Mepyramine (b) Diphenylhydramine
(c) Chlorpheniramine (d) Pheniramine

87. One of the following antihypertensive has a similar structure as that of diuretic agent chlothiazide:
(a) Minoxidil (b) Diazoxide
(c) Guanethedine (d) Propranolol

88. Condensation of N-m-hydroxy phenyl 1-N-p-tolyl glycine with ethylene diamine gives
(a) Tolazoline (b) Phentolamine
(c) Prazocin (d) Phenoxy benzamine

89. The IUPAC name of stilbesterol is
(a) (E) α, β Diethyl stilbene-4,4' diol
(b) (R) α, α Diethyl stilbene-4,4' diol
(c) (E) α, β Dimethyl stilbene-4,4' diol
(d) (E) β, β Diethyl stilbene-4,4' diol

90. Dienosterol is synthesized starting from
(a) p-Hydroxy acetophenone
(b) p-Chloro-propiophenone
(c) p-Hydroxy propiophenone
(d) p-Chloro acetophenone

91. Ethacrynic acid belongs to the class of
(a) Loop Diuretic
(b) ACE inhibitor
(c) Aldostrerone antagonist
(d) Thiazide derivative

92. In cephalosporins, lactam ring is fused with
(a) Thiazolidine system
(b) 1,3 dihyrothiazine system
(c) Thiazine system
(d) Dehydro thiazolidine system

93. Which of the following is a β–Lactamse inhibitor?
(a) Chloram phenicol
(b) Cefadroxil
(c) Clavunilic acid
(d) Ampicillin

94. Penicilline on hydrolysis with alkali gives
(a) Penicilloic acid (b) Penaldic acid
(c) Penicillic acid (d) Penicillamine

95. The therapeutic effect of theophylline is achieved at plasma conc. of
(a) 5-15 μg/mL (b) 10-20 μg/mL
(c) 15-25 μg/mL (d) 20-30 μg/mL

96. Phase I oxidative processes frequently involves all of the following, except:
(a) Cytochrome P-450
(b) NADPH and NADP cofactors
(c) Liver endoplasmic reticulum
(d) Esterases

97. All of the following drugs are useful in treating complex partial seizures, except:
(a) Ethozuximide
(b) Phenobarbital
(c) Carbamazepine
(d) Phenytoin

98. A 50-year old male farm worker is brought to the emergency room. He was found confused in the orchard and since then lost consciousness. His heart rate is 45 and his blood pressuer is 80/40 mmHg. He is sweating and salivating profusely. Which of the treatment is indicated?
(a) Physostigmine (b) Norepinephirne
(c) Trimethaphan (d) Atropine

99. A 45-year old man who has been injured in a car accident is brought into the emergency room. His blood alcohol level on admission is 275 mg/dL. Hospital records show a prior hospitalization for alcohol related seizures. His wife confirms that he has been drinking heavily for 3 weeks. What treatment should be provided to the patient if he goes into withdrawal?
(a) Pentobarbital (b) Lorazepam
(c) Benzodiazepine (d) Phenytoin

100. Which one of the following drugs act as central α_2 presynaptic receptor?
(a) Minoxidil (b) Verapamil
(c) Clonidine (d) Enalapril

ANSWER KEYS

1. (c)	**2.** (a)	**3.** (c)	**4.** (c)	**5.** (c)	**6.** (b)	**7.** (a)	**8.** (a)	**9.** (c)	**10.** (a)
11. (a)	**12.** (a)	**13.** (d)	**14.** (d)	**15.** (a)	**16.** (a)	**17.** (d)	**18.** (c)	**19.** (b)	**20.** (b)
21. (b)	**22.** (d)	**23.** (b)	**24.** (a)	**25.** (a)	**26.** (d)	**27.** (a)	**28.** (a)	**29.** (b)	**30.** (b)
31. (c)	**32.** (d)	**33.** (b)	**34.** (a)	**35.** (a)	**36.** (a)	**37.** (a)	**38.** (b)	**39.** (a)	**40.** (a)
41. (d)	**42.** (a)	**43.** (b)	**44.** (a)	**45.** (a)	**46.** (a)	**47.** (a)	**48.** (a)	**49.** (b)	**50.** (a)
51. (d)	**52.** (a)	**53.** (d)	**54.** (d)	**55.** (d)	**56.** (d)	**57.** (a)	**58.** (a)	**59.** (d)	**60.** (a)
61. (c)	**62.** (d)	**63.** (a)	**64.** (a)	**65.** (a)	**66.** (b)	**67.** (c)	**68.** (d)	**69.** (b)	**70.** (a)
71. (b)	**72.** (b)	**73.** (a)	**74.** (b)	**75.** (d)	**76.** (c)	**77.** (c)	**78.** (c)	**79.** (c)	**80.** (c)
81. (c)	**82.** (b)	**83.** (d)	**84.** (b)	**85.** (a)	**86.** (a)	**87.** (b)	**88.** (b)	**89.** (a)	**90.** (c)
91. (a)	**92.** (a)	**93.** (c)	**94.** (a)	**95.** (b)	**96.** (d)	**97.** (a)	**98.** (d)	**99.** (d)	**100.** (c)

GUJARAT DRUG INSPECTOR EXAM PAPER—GPSC 2010

1. Patients suffering from multidrug resistant tuberculosis can be treated with all of the following drugs except:
(a) Tobramycin (b) Amikacin
(c) Ciprofloxacin (d) Clarithromycin

2. Which of the following anti malarial drug is safe during pregnancy?
(a) Amodiaquine (b) Proguanil
(c) Primaquine (d) Chloroquine

3. Mechanism of action of Ketoconazole is
(a) Inhibits ergosterol synthesis
(b) Inhibits DNA gyrase
(c) Inhibits dihydropteroate synthetase
(d) Induces translation misreadings

4. Monitoring plasma drug concentration is useful while using
(a) Antihypertensive drugs
(b) Levodopa
(c) Lithium carbonate
(d) MAO inhibitors

5. Codeine differs in structure from morphine by
(a) N-methyl group (b) Acetyl group at C_1 and C_6
(c) $-OC_2H_5$ group (d) $-OCH_3$ group

6. Sanguiamarine belongs to the subgroup of
(a) Morphinans
(b) Benzyl isoquinolines
(c) Phthalide isoquinolines
(d) Benzophenanthrenes

7. Dovers powder used as a diaphoretic contains
(a) Ipecac and Opium
(b) Senna and Cinchona
(c) Opium and cinchona
(d) All of the above

8. _____ is the dimmer of flavones and flavonones.
(a) Chalcones (b) Aurones
(c) Biflavanoids (d) Dihydroflavones

9. The wavelength source in NMR spectrometer is
(a) Goniometer
(b) Radiofrequency oscillator
(c) High voltage generator
(d) Klystron oscillator

10. Morphine does not cause
(a) Constriction of the pupil
(b) CNS depression
(c) Respiratory depression
(d) Diarrhoea

11. o,m,p-isomers can be differentiated on the basis of
(a) Chemical Shift
(b) Coupling constant
(c) Extinction coefficient
(d) Dipole moment

12. Isotopes differ in
(a) The number of protons
(b) The valency number
(c) The chemical activity
(d) The number of neutrons

13. Purity of water for injection is checked by
(a) Potential testing (b) Pyrogen testing
(c) Conductivity testing (d) pH Testing

14. The phosphate of a metal has the formula $MHPO_4$. The formula of its Bromide would be
(a) MBr (b) MBr_2
(c) MBr_3 (d) MBr_4

15. Geometrical isomerism is possible in case of
(a) 2-Pentene (b) Pentane
(c) Propene (d) Ethene

16. The IUPAC name of the compound having the formula $(CH_3)_2CHCH_2Cl$
(a) 2-methyl-3-chloropropane
(b) 1-chloro-3-methyl butane
(c) 1-chloropentane
(d) 2-methyl-4-chlorobutane

17. In mammals, the major fat in adipose tissue is
(a) Triglyceride (b) Cholesterol
(c) Sphingolipids (d) Phospholipids

18. Ferritin is
(a) Co enzyme
(b) The stored form of iron
(c) Non-protein moiety
(d) Isoenzyme

19. Active form of Vitamin D in man is
(a) Cholecalciferol (b) Calcifediol
(c) Calciferol (d) Calcitriol

20. Many drugs are chiral. In a synthesis of chiral drug molecules in symmetric environment,
(a) Always one enantiomer is obtained
(b) Always both enantiomers are in equal amounts
(c) Always both enantiomers are in unequal amounts
(d) None of the above

21. Homatropine is a
(a) Tropine ester of amino acetic acid
(b) Tropine ester of mendelic acid
(c) Tropine methyl bromide ester of mendelic acid
(d) Tropine ester of amino formic acid

22. List of the drugs whose import, manufacture and sale, labelling and packaging are governed by special provisions are included in schedule
(a) X (b) K
(c) H (d) G

23. Dose dumping may be a general problem in the formulation of
(a) Soft gelatin capsules
(b) Suppositories
(c) Modified release drug products
(d) None of the above

24. Which of the following is useful as diluent, binder, disintegrating agent as well as lubricant in tablet formulations?
(a) Starch (b) Tragacanth
(c) Sucrose (d) None of the above

25. Capping in tablets mainly occurs due to
(a) Less upper punch pressure
(b) Poor flowability of granules
(c) Proper formulation design
(d) Entrapmernt of air in tablet during compression

26. The franz diffusion cell which is used for the evaluation of transdermal drug delivery systems consists of
(a) 1 chamber (b) 2 chamber
(c) 3 chamber (d) None of the above

27. Quick breaking aerosols are applicable
(a) Orally (b) Parenterally
(c) Topical (d) Ophthalmically

28. In an osmotic drug delivery system, the drug is released through
(a) Polymeric matrix (b) Delivery orifice
(c) Plastic matrix (d) None of the above

29. Parenteral product must be
(a) Packed in bottle
(b) Sterilized
(c) Free from viable/living organism
(d) Pyrogenic

30. Water attack test is generally performed for
(a) USP type I glass
(b) USP type II glass
(c) USP type III glass
(d) All of above

31. Silicone based adhesives used in transdermal drug delivery possess
(a) Excellent chemical stability
(b) Low toxicity
(c) Skin compatibility
(d) All of the above

32. The plasma drug concentration in mcg/ml data obtained after the oral administration of 50 mg of a drug are 5.5 in 1 h, 9.2 in 2 h, 14.9 in 3 h,10.3 in 4 h, 7.1 nin 5 h, and 2.2 in 6 h. The AUC for the blood data will be
(a) 45.35 mcg/ml. h (b) 55.35 mcg/ml. h
(c) 50.35 mcg/ml. h (d) 46.35 mcg/ml. h

33. Schleuniger tester is used for the tablets to measure
(a) Roughness (b) Hardness
(c) Dissolution (d) Friability

34. Creatinine clearance is used as a measurement of
(a) Passive renal absorption
(b) Glomerular filtration rate
(c) Drug metabolism rate
(d) Renal excretion rate

35. The drug of choice in prolonged febrile convulsions is
(a) Carbamazepine (b) Diazepam
(c) Phenytoin (d) Paracetamol

36. Which one of the following antihistamines is least to cause sedation?

(a) Diphenhydramine (b) Desloratadine
(c) Chlorphenamine (d) Alimemazine

37. The following electrolyte disturbance causes digitalis toxicity
(a) Hypocalcemia (b) Hypernatremia
(c) Hypokalemia (d) Hyperkalemia

38. Which of the following antifungal drug causes drug-drug interaction as it has a greater propensity to inhibit mammalian cytochrome P 450 enzymes?
(a) Itraconazole (b) Fluconazole
(c) Ketoconazole (d) Miconazole

39. Select the incorrect statement from the following:
(a) Half life of atropine is 4 hours
(b) Acetylcholine and atropine show irreversible antagonism
(c) Atropine is a central nervous system stimulant
(d) Atropine produces cycloplegia

40. The anti-inflammatory agent which selectively inhibits COX-II gene expression is
(a) Rofecoxib (b) Dexamethasone
(c) Ibuprofen (d) Nimesulide

41. Vascular endothelial growth factor and Fibroblast growth factor are similar in all respects except:
(a) Both are potent endothelial cell mitogens
(b) Both are localized on cells and extracellular matrix, particularly in the lungs
(c) Both stimulate endothelial cell synthesis of proteases including plasminogen activator and metalloptreinases
(d) Both lack a Secretory signal sequence

42. Ma-Huang is the synonym of which drug?
(a) Belladonna (b) Opium
(c) Ephedra (d) Ipecac

43. Coffee Arabica contains _____ caffeine.
(a) 10% (b) 1–2%
(c) 20% (d) 0.5%

44. Anaferine and Anahygrine alkaloids are present in
(a) Hyocyomus (b) Ashwagandha
(c) Vinca (d) Vasaka

45. Constituents which exhibit steroidal type of action are found in
(a) Dioscorea (b) Senega
(c) Ashwagandha (d) Ajuga parviflora

46. Select the synonyms of aconite root.
(a) Vachang (b) Mouckshood
(c) All of the above (d) None of the above

47. Diosgenine is
(a) An alkaloid obtained from dioscorea
(b) A carbohydrate from dioscorea
(c) A glycoside from dioscorea
(d) None of the above

48. Glandular hair having a unicellular or occasionally a short unicellular padiel with a unicellular or bicellular terminal gland is characteristic of
(a) Senna leaves
(b) Belladona Leaves
(c) Datura Stramonium leaves
(d) Digitalis purpurea leaves

49. The drug which is bacterial to all three pools extracellular, intracellular, and necrotic caseum of turbercle bacilli is
(a) Isoniazide (b) Ethambutol
(c) Pyrazinamide (d) Rifampin

50. The most useful class of drugs in the long term treatment of hypertension is
(a) Thiazide diuretics (b) Osmotic diuretics
(c) Mercurial diuretics (d) Pentazocine

51. Which of the following drug is not acting on opioid β (Kappa) receptor?
(a) Buprenorphine (b) Butorphanol
(c) Nalbuphine (d) Pentazocine

52. Which of the following crosses the blood-brain barrier?
(a) GABA (b) Propranolol
(c) Suxamethonium (d) Dopamine

53. Most of the drugs are absorbed in the body by means of
(a) Active transport (b) Passive transport
(c) Ion-pair transport (d) Facilitated diffusion

54. Insulin stimulates glucose transport by promoting the translocation of
(a) GLUT 4
(b) GLUT 2 and GLUT 4
(c) GLUT 1 and GLUT 4
(d) GLUT 2

55. Ptylin is secreted by
(a) Pancreas (b) Lachrymeal gland
(c) Parotid gland (d) None of the above

56. Which of the following is COX-2 inhibitor?
(a) Aspirin
(b) Ibuprofen
(c) Diclofenac sodium
(d) Celecoxib

57. Which following adrenergic agonist does not contain 3,4-dihydroxy nucleus?
(a) Ephedrine
(b) Albuterol
(c) Phenylpropanolamine
(d) Terbutaline

58. _____ is selective ACE inhibitor.
(a) Atenolol (b) Ramipril
(c) Losartan (d) Nifedipine

59. Which of the following is third generation fluoroquinolone?
(a) Lomefloxacin (b) Ciprofloxacin
(c) Gemifloxacin (d) Gatifloxacin

60. QSAR stands for
(a) Qualitative structure activity relationship
(b) Quantitative structure action relationship
(c) Quantitative structure activity relationship
(d) Qualitative structure activity relativity

61. Which of the following is a cholesterol absorption inhibitor?
(a) Atorvastatin (b) Ezetimibe
(c) Fenofibrate (d) Nicotinic acid

62. One of the following is HIV NNRT inhibitor:
(a) Lopinavir (b) Efavirenz
(c) Zidovudine (d) Acyclovir

63. Which of the following is not a sulpha drug?
(a) Captopril (b) Enalapril
(c) Fosinopril (d) Losartan

64. _____ is potassium sparing diuretic.
(a) Furosemide (b) Eplerenone
(c) Ethacrynic acid (d) Hydrochlorthiazide

65. Which of the following beta blocker produces nitric oxide?
(a) Atenolol (b) Pindolol
(c) Metoprolol (d) Betaxolol

66. As per ICH guideline, lower limit of quantification is S/N ratio.
(a) 2 (b) 3
(c) 5 (d) 10

67. 0.9%w/v NaCl solution is equal to
(a) 2 meq per 10ml
(b) 1.53 meq per 10 ml
(c) 20 meq per 10 ml
(d) None of the above

68. RP-HPLC involves
(a) Less polar mobile phase less than stationary phase
(b) Less polar stationary phase less than mobile phase
(c) Reverse osmosis
(d) Forward osmosis

69. The statement "Store in cool place" as per IP means
(a) Store at room temperature
(b) Store between 2ºC to 8ºC
(c) Store at any temperature between 8ºC to 25ºC
(d) Store at 8ºC

70. A retardant material that forms a hydrophilic matrix in the formulation of matrix tablet is
(a) H.P.M.C. (b) C.A.P.
(c) Polyethylene (d) Carnuba wax

71. Tetrabromofluorecin produces _____ stain during the application on the lips.
(a) Bluish Red (b) Reddish blue
(c) Orange Yellowish (d) Yellowish blue

72. If the expiry date of tablet is not mentioned on the tablet, means that expiry time in years is
(a) 2 years (b) 3 years
(c) 4 years (d) 5 years

73. Which order of the reaction is followed by photo decomposition of the drug?
(a) First (b) Pseudo first
(c) Second (d) Zero

74. Glass used for the preparation of vials ampoules and transfusion bottles is
(a) Type-II sodalime glass
(b) Type-III sodalime glass
(c) Borosilicate glass
(d) Neutral glass

75. Which tissue has the greatest capacity of biotransformation of drugs?
(a) Brain (b) Kidney
(c) Liver (d) Lung

76. Clinical trials are performed on
(a) Animals (b) Humans
(c) Both (d) None of the above

77. The loading dose (D_L) of a drug is usually based on the
(a) Total body clearance (Cl_T) of the drug
(b) Percentage of drug bound to plasma proteins
(c) Fraction of drug excreted unchanged in the urine
(d) Apparent volume of distribution (V_d) and desired drug concentration in plasma

78. License for wholesale of drug specified in Schedule C and C_1 are issued in the forms
(a) 20 A (b) 20 B
(c) 21 B (d) 22 A

79. On cancellation of manufacturing license, the loan license is
(a) Cancelled
(b) Suspended
(c) Temporary suspended
(d) None of the above

80. Drug retail sale licenses are issued by
(a) Drug controller of India
(b) Union health minister
(c) Drug controller authority of the states
(d) Director of Health services

81. The record for the drugs having date of expiry should be preserved for a period of at least
(a) 5 years (b) 2 years
(c) 1 year (d) 3 years

82. Which type of trichome is present in ashwagandha?
(a) Branched (b) Lignified
(c) Glandular (d) None of the above

83. Chotta chand is synonym for
(a) Rauwolfia Serpentina
(b) Rauwolfia Densiflora
(c) Rauwolfia Perakensis
(d) Rauwolfia Tetraphylla

84. How can we detect the rhizomes from the root of the Rauwolfia?
(a) By the presence of small central pith
(b) By the absence of small central pith
(c) By the presence of vascular bundle
(d) None of the above

85. Ergotoxine group of alkaloid is/are mixture of
1. Ergocristine 2. Ergocornine
3. Ergocryptine 4. Ergometine
(a) 1, 2 and 3 (b) 2, 3 and 4
(c) 1, 2 and 4 (d) None of the above

86. A disease called 'stripe canker' is connected with which of the following drug?
(a) Nux vomica (b) Rauwolfia
(c) Ashwagandha (d) Cinchona

87. If cyanocobalamine is imported under the name of tetracycline, it will be called adulterated drug
(a) Spurious drug (b) Misbranded drug
(c) Substitute drug (d) None of the above

88. Ergot powder gives blue colour with
(a) p-dimethylamino benzaldehyde
(b) o-dimethylamino benzaldehyde
(c) All of the above
(d) None of the above

89. Neomycin is obtained from
(a) E.Coli (b) B.Subtilis
(c) S.aeruginosa (d) S.fradiae

90. Biological and biotechnological products are listed in Schedule
(a) A (b) B
(c) C and C_1 (d) X

91. Carbopols are polymerized from
(a) Methacrylate esters
(b) Acrylic acid
(c) Ethylene glycols
(d) Bis-phenol + phosgene

92. Hard gelatin capsule of size 3 will accommodate approximately _____ volume in ml.
(a) 0.1 (b) 0.2
(c) 0.3 (d) 0.75

93. The international name for small box vaccine is
(a) BCG (b) DTP
(c) Viriola (d) Vibrio

94. Blood flow through a capillary is described by the equation known as
(a) Lengmuir (b) Noyes Whitney
(c) Stokes (d) Hilderbrand

95. Compact size and low weight mass instrument is
(a) EI-TOF (b) Maldi-Quadrupole
(c) Maldi-TOF (d) Lon trap

96. In polarography _____current must be blocked.
(a) Residual (b) Migration
(c) Diffusion (d) None

97. IP 2007 and USP 2006 use nitrite titration for those drugs having
(a) Phenolic structure (b) 1º Aromatic amine
(c) Unsaturation (d) 3º Nitrogen

98. A non-hazardous substitute for RIA is
(a) Flame Photometry (b) HPLC
(c) Fluorometry (d) GCMS

99. LCMS is widely used in
(a) Multielectrolyte assay
(b) Drug metabolite study
(c) Complex mixture assay
(d) Palnt biosynthesis

100. Pantothenic acid is a part of
(a) Renin
(b) Carboxypeptidase
(c) Co-enzyme A
(d) NAD

ANSWER KEYS

1. (c)	**2.** (d)	**3.** (a)	**4.** (c)	**5.** (d)	**6.** (b)	**7.** (a)	**8.** (c)	**9.** (b)	**10.** (d)
11. (b)	**12.** (d)	**13.** (c)	**14.** (b)	**15.** (a)	**16.** (a)	**17.** (a)	**18.** (b)	**19.** (d)	**20.** (b)
21. (b)	**22.** (a)	**23.** (c)	**24.** (a)	**25.** (d)	**26.** (b)	**27.** (c)	**28.** (b)	**29.** (b)	**30.** (b)
31. (d)	**32.** (a)	**33.** (b)	**34.** (b)	**35.** (b)	**36.** (b)	**37.** (c)	**38.** (c)	**39.** (b)	**40.** (b)
41. (b)	**42.** (c)	**43.** (b)	**44.** (b)	**45.** (c)	**46.** (c)	**47.** (c)	**48.** (d)	**49.** (d)	**50.** (a)
51. (a)	**52.** (b)	**53.** (b)	**54.** (c)	**55.** (c)	**56.** (d)	**57.** (b)	**58.** (b)	**59.** (d)	**60.** (c)
61. (b)	**62.** (b)	**63.** (a)	**64.** (b)	**65.** (d)	**66.** (d)	**67.** (b)	**68.** (b)	**69.** (c)	**70.** (d)
71. (a)	**72.** (b)	**73.** (a)	**74.** (a)	**75.** (c)	**76.** (b)	**77.** (d)	**78.** (c)	**79.** (d)	**80.** (a)
81. (a)	**82.** (a)	**83.** (a)	**84.** (a)	**85.** (a)	**86.** (d)	**87.** (b)	**88.** (a)	**89.** (d)	**90.** (c)
91. (b)	**92.** (c)	**93.** (c)	**94.** (d)	**95.** (d)	**96.** (d)	**97.** (b)	**98.** (c)	**99.** (b)	**100.** (c)

GPAT PAPER 2012

1. Which of the following respective Phase-I and Phase-II reactions are the most common drug in biotransformation reactions?

(a) Oxidation and glucuronidation
(b) Reduction and acetylation
(c) Hydrolysis and glucuronidation
(d) Oxidation and glutathion conjugation

2. Which one of the following drugs has positive inotropic and negative chronotropic action?

(a) Dopamine (b) Epinephrine
(c) Digoxin (d) Isoprenaline

3. Which one of the following therapeutic classes has been proved clinically as a first line therapy for heart failure and has shown decreased hospitalization, improved symptoms and delayed disease progression?

(a) Cardiac glycosides
(b) ACE inhibitors (ACEIs)
(c) Renin antagonists
(d) Nitrites

4. Which one of the following glucose transporters is the new drug target for the management of type-2 diabetes mellitus?

(a) Sodium glucose linked transporter-2 (SGLT2)
(b) Glucose transporter-1 (GLUT1)
(c) Sodium glucose linked transporter-1 (SGLT1)
(d) Glucose transporter-2 (GLUT2)

5. Which one of the following modes of HIV transmission carries highest relative risk of infection with single exposure?

(a) Transfusion of blood and blood products
(b) Perinatal – from mother to child
(c) Sexual contacts with infected partners
(d) Syringe sharing with drug addicts

6. Which of the following are the critical neurotransmitters playing major role in depression?

(a) Acetylcholine, norepinephrine and dopamine
(b) Dopamine, norepinephrine and serotonin
(c) Serotonin, dopamine and y-amino butyric acid
(d) Acetylcholine, serotonin and y-amino butyric acid

7. A 55 years old man is under DOTS treatment for pulmonary tuberculosis for the last four months. Now, he has developed symptoms of peripheral neuritis. Which one of the following is the right addition to his therapy to manage peripheral neuritis?

(a) Cyanocobalamin (b) α-Lipoic acid
(c) Pyridoxine (d) Prednisolone

8. What is the primary mechanism of action of local anaesthetics?

(a) Activation of ligand-gated potassium channels
(b) Blockade of voltage-gated sodium channels
(c) Stimulation of voltage-gated N-type calcium channels
(d) Blockade of GABA-gated chloride channels

9. Which one of the following anti-asthmatic drugs can cause convulsions and arrhythmia?

(a) Prednisolone (b) Salmeterol
(c) Zafirlukast (d) Theophylline

10. Which one of the following anti-arrhythmic drugs acts by inhibiting potassium, sodium and calcium channels?

(a) Quinidine (b) Lignocaine
(c) Amiodarone (d) Flecainide

11. A 48 years old woman is having the symptoms of weight gain, cold intolerance, constipation, bradycardia, puffy face, lethargy and dry skin. These symptoms are suggestive of which of the following?

(a) Over use of corticosteroid
(b) Hypothyroidism
(c) Estrogen deficiency
(d) Over use of thyroxin sodium

12. Increased risk of hypoglycemia and weight gain is the common side effect of drugs used in the management of Type-2 diabetes mellitus. Following are some commonly used drugs, alone or in combination, for the management of Type-2 diabetes mellitus:

[P]: Metformin [Q]: Pioglitazone
[R]: Glipizide [S]: Sitagliptin

Choose the correct combination which is weight neutral and without risk of hypoglycemia.

(a) P and Q (b) Q and R
(c) R and S (d) P and S

13. Which one of the following receptors is *not* a ligand-gated ion channel receptor?
(a) Nicotinic receptor
(b) 5HT3 – receptor
(c) GABAA – receptor
(d) H2 – receptor

14. Which one of the following classes of drugs causes side effects like dryness of mouth, tachycardia, urinary retention, constipation, blurring of vision, precipitation of glaucoma, drowsiness and impairment of cognition?
(a) Anti-adrenergic (b) Anti-cholinergic
(c) Anti-serotonergic (d) Anti-dopaminergic

15. Which of the following cytokines are the most important regulators in inflammation and are the targets for anti-inflammatory agents used in rheumatoid arthritis?
(a) Tumour necrosis factor-α and interleukin-1
(b) Acetylcholine esterase and eicosanoids
(c) Leucotrienes and isoprostanes
(d) Adhesion factor and monoamine oxidase A

16. Which one of the following is a *false* statement for competitive antagonists?
(a) They have an affinity for the agonist binding site on receptor
(b) They have no intrinsic activity
(c) They cause parallel rightward shift of the control dose response curve
(d) Maximum response of the agonist cannot be achieved in their presence by increasing the concentration of the agonist.

17. Atypical antipsychotics differ from the typical antipsychotics in various ways that define them as atypical. Which one of the following is *not* a defining property of the atypical antipsychotics?
(a) Sustained hyperprolactinemia
(b) Improved efficacy in treating the negative symptoms
(c) Lower risk for extrapyramidal side effects (EPSs)
(d) Greater serotonin receptor blockade than dopamine blockade

18. Which one of the following drugs produces significant relaxation of both venules and arterioles?
(a) Hydralazine (b) Minoxidil
(c) Diazoxide (d) Sodium nitroprusside

19. Antiviral action of purine analogues is primarily related to the followings.
[P]: Inhibition of RNA synthesis
[Q]: Inhibition of DNA polymerase
[R]: Immunomodulation
[S]: Inhibition of viral penetration
Choose the correct option:
(a) R is correct and Q is incorrect
(b) Q is correct and S is incorrect
(c) P is correct and R is incorrect
(d) S is correct and P is incorrect

20. All of the given four drugs are sympathomimetics:
[P]: Adrenaline [Q]: Isoprenaline
[R]: Phenylephrine [S]: Noradrenaline
Choose the correct statement related to their effects on blood pressure.
(a) P and Q increase systolic and diastolic blood pressure
(b) Q and R increase systolic and diastolic blood pressure
(c) R and S increase systolic blood pressure
(d) P and S increase systolic and diastolic blood pressure

21. All of the given four drugs are neuromuscular blocking agents.
[P]: Gallamine [Q]: Succinylcholine
[R]: Vecuronium [S]: d-Tubocurarine
Choose the correct statement about them.
(a) P and Q are competitive neuromuscular blocking agents
(b) Q and R are competitive neuromuscular blocking agents
(c) R and S are non-competitive neuromuscular blocking agents
(d) P and S are competitive neuromuscular blocking agents

22. Which one of the followings is a tyrosine kinase inhibitor indicated for a variety of malignancies?
(a) Imatinib (b) Paclitaxel
(c) Ezetimibe (d) Mitomycin

23. Which one of the following is the most likely positive sign of pregnancy when detected in urine?
(a) Estrogens
(b) Progesterone
(c) Human chorionic gonadotropin (HCG)
(d) Corticotropic hormone

24. Following are some opioid analgesics:
[P]: Morphine [Q]: Pethidine
[R]: Pentazocine [S]: Fentanyl

Choose the correct order of respiratory depressant propensity of these agents.

(a) P>Q>R>S (b) Q>P>R>S
(c) R>P>Q>S (d) S>P>Q>R

25. Corticosteroids are administered to treat some of the given disease states:

[P]: Peptic ulcer [Q]: Bronchial asthma
[R]: Nephrotic syndrome [S]: Myasthenia gravis

Choose the correct statement about the use of corticosteroids for the treatment of these diseases.

(a) P, Q and S are treated while R is *not*
(b) P, R and S are treated while Q is *not*
(c) Q, R and S are treated while P is *not*
(d) P, Q and R are treated while S is *not*

26. Which one of the following statements is *false* for fluoroquinolones?

(a) These are highly effective by oral and parenteral routes
(b) These are relatively more susceptible to development of resistance
(c) These are effective against those bacteria that are resistant to β-lactam and aminoglycoside antibiotics
(d) These are bactericidal with broad spectrum of activity

27. Increased serum levels of which one of the following may be associated with decreased risk of atherosclerosis?

(a) VLDL (b) LDL
(c) HDL (d) Total Cholesterol

28. Metformin causes the following actions *except* for the one. Identify that.

(a) Reduces hepatic neoglucogenesis
(b) Increases glucose uptake in skeletal muscles
(c) Enhances sensitivity to insulin
(d) Increases HbA1c by 1% to 2%

29. Misoprostol has a cytoprotective action on gastrointestinal mucosa because of one of the following actions. Identify that.

(a) It enhances secretion of mucus and bicarbonate ion
(b) It neutralizes hydrochloric acid in stomach
(c) It antagonizes nonsteroidal anti-inflammatory drugs
(d) It is bactericidal to H. pylori

30. Which of the following drugs can precipitate bronchial asthma?

[P]: Indomethacin [Q]: Codeine phosphate
[R]: Rabeprazole [S]: Theophylline

Choose the correct option.

(a) P and R
(b) P and Q
(c) R and S
(d) S and Q

31. Which one of the following alkaloids is derived from lysine?

(a) Emetine (b) Chelidonine
(c) Lobeline (d) Stachydrine

32. Histologically the barks of *Cinnamomum cassia* and *Cinnamomumzeylanicum differ* in one of the following features. Identify that.

(a) Sclerieds (b) Phloem fibers
(c) Pericyclic fibres (d) Cortex

33. The following characteristic properties are given in the context of saponins:

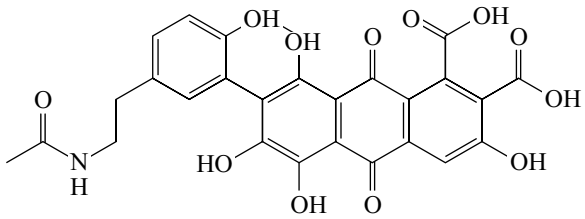
[P]: Saponins give precipitate by shaking with water.
[Q]: Saponins are diterpenes and give foam on shaking with water.
[R]: Saponins are triterpenoidal compounds and cause haemolysis of erythrocytes.
[S]: They are steroidal or triterpenoidal compounds with tendency to reduce surface tension of water.

Choose the correct option.

(a) P is true; Q is true; R is true; S is true
(b) P is false; Q is true; R is false; S is true
(c) P is false; Q is true; R is true; S is true
(d) P is false; Q is false; R is true; S is true

34. Read the given statements about the constituents of Shellac:

[P]: Shellolic acid, a major component of alicyclic fraction is responsible for colour.
[Q]: Shellolic acid, a major component of aromatic fraction is responsible for colour.
[R]: Shellolic acid is a major component of aliphatic fraction and laccaic acid is a component of aromatic fraction.
[S]: Aliphatic components are shellolic acid which is alicyclic and aleuratic acid which is acyclic, while laccaic acid is an aromatic colouring principle.



What is the correct combination of options?

(a) P is true; Q is true; R is true; S is true
(b) P is false; Q is false; R is false; S is true
(c) P is false; Q is false; R is true; S is true
(d) P is true; Q is false; R is false; S is true

35. Major component of *Cymbopogon citratus* is citral which is utilized commercially for the synthesis od vitamin A from the following:

[P]: Directly from citral
[Q]: By first converting to T-ionone
[R]: By first converting to T-ionone followed by conversion to a-ionone which is very important intermediate for carotenoid synthesis
[S]: By first conversion of citral to T-ionone followed by conversion to P-ionone which is an important intermediate for carotenoid synthesis

Which is the correct combination of options?

(a) P is true; Q is true; R is true; S is true
(b) P is false; Q is true; R is false; S is true
(c) P is false; Q is false; R is true; S is true
(d) P is false; Q is false; R is false; S is false

36. Which one of the following constituents is reported to have anti-hepatotoxic activity?

(a) Podophyllotoxin (b) Andrographoloid
(c) Linalool (d) Safranal

37. Geranial and Neral are the monoterpene aldehyde constituents of volatile oil. Read the following statements about them:

[P]: Geranial and Neral are both optical isomers
[Q]: Geranial and Neral are both geometric isomers
[R]: Geranial has Z configuration and Neral has E configuration
[S]: Geranial has E configuration and Neral has Z configuration

Choose the correct combination of answers for them.

(a) P is true; Q is true; R is false; S is true
(b) P is false; Q is true; R is true; S is false
(c) P is true; Q is false; R is true; S is true
(d) P is false; Q is true; R is false; S is false

38. Identify the *incorrect* statement applicable to lignans.

(a) Lignans are formed by the dimerization of the phenylpropane moiety
(b) Podophyllotoxin can be termed phytochemically as a lignan
(c) Lignans can be formed by cyclization of phenylpropane nucleus
(d) Lignans are the secondary metabolites formed from the shikimic acid pathway

39. Naringin, obtained from orange peel, can be named as one of the following. Identify the correct name.

(a) 5,4'-Dihydroxy-7-rhamnoglucoside of flavanone
(b) 5,4'-Dihydroxy-7-glucoside of flavanone
(c) 5,3',4'-Trihydroxy-7-rhamnoglucoside of flavone
(d) 5,3',4'-Trihydroxy-7-glucoside of flavone

40. Rhizomes of Zingiberofficinale contain some sesquiterpene hydrocarbons. Some hydrocarbons are given below:

[P]: β-Bisabolene [Q]: Gingerone A
[R]: Gingerol [S]: Zingiberene

Identify the correct pair of constituents present in the rhizomes.

(a) P and S (b) P and Q
(c) Q and S (d) Q and R

41. Listed below are the chemical tests used to identify some groups of phytoconstituents. Identify the test for the detection of the purine alkaloids.

(a) Keller-Killani test (b) Murexide test
(c) Shinoda test (d) Vitali-Morin test

42. Given below are four statements in context of hecogenin:

[P]: It is a saponin
[Q]: It is useful for the semi-synthesis of steroidal drugs
[R]: It is not a glycoalkaloid
[S]: It is obtained from Dioscorea tubers

Choose the correct combination of statements.

(a) P, Q and R are correct while S is incorrect
(b) P, Q and S are correct while R is incorrect
(c) Q, R are correct while P, S are incorrect
(d) All are correct statements

43. Atropine biosynthesis involves a pair of precursors. Identify the correct pair.

(a) Ornithine and phenylalanine
(b) Tyrosine and tryptophan
(c) Tryptophan and dopamine
(d) Tyrosine and dopamine

44. Study the following statements:

[P]: Lutein and zeaxanthin are flavonoids
[Q]: Lutein and zeaxanthin are xanthophylls

[R]: Lutein and zeaxanthin are required to control age-related macular degeneration

[S]: Lutein is a flavonoid while zeaxanthin is its glycoside Choose the correct answer.

(a) P is correct while Q, R and S are incorrect
(b) Q and R are correct while P and S are incorrect
(c) Statement P is the only correct statement
(d) Statement S is the only correct statement

45. Listed below are some phytoconstituents.

[P]: Galactomannan
[Q]: Glucomannan
[R]: Barbaloin
[S]: Phyllanthin

Identify the constituent(s) present in Aloe vera.

(a) Only P (b) Q and R
(c) Only S (d) P and S

46. Choose the correct answer for the binomial nomenclature of fruits of star-anise.

(a) *Pimpinellaanisum* (b) *Illiciumverum*
(c) *Illiciumanisatum* (d) *Illiciumreligiosum*

47. Given herewith are two statements:

[P]: Digitoxin is a secondary glycoside from *Digitalis purpurea*

[Q]: Digitoxin is a partially hydrolysed glycoside of purpurea glycoside A

Determine the correctness of the above statements.

(a) Both P and Q are true
(b) P is true but Q is false
(c) Both P and Q are false
(d) P is false but Q is true

48. Peruvoside is naturally obtained from one of the following plants. Identify the correct name.

(a) *Dioscorea* (b) *Ginseng*
(c) *Liquorice* (d) *Thevetia*

49. One of the following is *not* required for the initiation and maintenance of plant tissue culture. Identify that.

(a) Sucrose (b) Kinetin
(c) Auxin (d) Absicic acid

50. Study the relationship between the given two statements:

[P]: Capsanthin is a red coloured principle from Capscicum annum

[Q]: Capsanthin is a vanillylamide of isodecenoic acid Choose the correct answer.

(a) Both P and Q are correct
(b) Both P and Q are incorrect
(c) P is correct but Q is incorrect
(d) P is incorrect but Q is correct

51. For the equation PV = nRT to hold true for a gas, all of the following conditions are necessary except for one. Identify that.

(a) The molecules of the gas must be of negligible volume
(b) Collisions between molecules must be perfectly elastic
(c) The velocities of all molecules must be equal
(d) The gas must not be decomposing

52. Atracuriumbesylate, a neuromuscular blocking agent, is metabolized through one of the following reactions. Identify that.

(a) Hoffman elimination
(b) Hoffman rearrangement
(c) Michael addition
(d) Claisen condensation

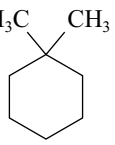
53. Identify the metabolite of prontosil responsible for its antibacterial activity.

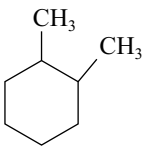
(a) Sulphacetamide
(b) Sulphanilamide
(c) p-Amino benzoic acid
(d) Probenecid

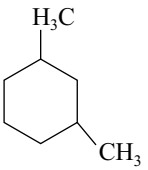
54. The central bicyclic ring in penicillin is named as one of the following. Find the correct name.

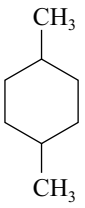
(a) 1-Thia-4-azabicyclo[3.2.1]heptane
(b) 4-Thia-1-azabicyclo[3.2.0]heptane
(c) 4-Thia-l-azabicyclo[3.2]heptane
(d) 1-Thia-4-azabicyclo[1.2.3]heptane

55. Both of the CMR and PMR spectra of an unknown compound show four absorption peaks each. Identify the unknown compound.

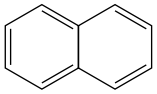
(a) 

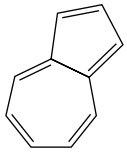
(b) 

(c) 

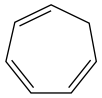
(d) 

56. Out of the four given compounds choose the one which is aromatic?

(a) 

(b) 

(c) 

(d) 

57. Quantification of minute quantity of a drug from a complex matrix, without prior separation can be done using one of the following techniques. Identify that.

(a) Coulometry
(b) Potentiometry
(c) Fluorescence spectroscopy
(d) Radioimmunoassay

58. Which one of the following fragmentation pathways involves a double bond and a y- hydrogen in mass spectrometry?

(a) α-Fission
(b) p1- Fission
(c) Mc-Lafferty rearrangement
(d) Retro-Diel's Alder rearrangement

59. Read the following statements carefully about non-aqueous titrations:

[P]: Acetate ion is the strongest base capable of existence in acetic acid.
[Q]: Mixtures of bases of different strengths can be analyzed by selecting a differentiating solvent for the bases.
[R]: Acetic acid acts as a leveling solvent for various acids like perchloric and hydrochloric acids.
[S]: Mixtures of bases of different strengths can be analyzed by selecting a leveling solvent for the bases.

Choose the correct answer.

(a) P and Q are true and R and S are false
(b) P and S are true and R and Q are false
(c) R and Q are true and P and S are false
(d) R and S are true and P and Q are false

60. Read the following statements carefully about Volhard's method:

[P]: In Volhard's titration, silver ions are titrated with thiocyanates in acidic solution.
[Q]: Ferric ions act as indicator in Volhard's method, yielding reddish brown ferric thiocyanate.
[R]: Volhard's method is used to determine halides.
[S]: Volhard's method is a direct titration.

Choose the correct set of answers.

(a) P, Q and R are true and S is false
(b) Q, R and S are true and P is false
(c) R. S and P true and Q is false
(d) P, Q, R and S all are true

61. Identify the group of enzymes that utilizes NADP or NAD as coenzymes and catalyses biochemical reactions by the transfer of electrons from one molecule to another.

(a) Isomerases (b) Oxidoreductases
(c) Transferases (d) Ligases

62. Glucose is the only source of energy for one of the following. Identify that.

(a) Cardiac cells (b) Nephrons
(c) RBCs (d) Thrombocytes

63. Determine the correctness or otherwise of the following assertion [a] and reason [r]:

Assertion [a]: Halogens are unusual in their effect on electrophilic aromatic substitution; they are deactivating yet ortho-, para – directing.

Reason [r]: In electrophilic aromatic substitution reactions, reactivity is controlled by stronger inductive effect while orientation is controlled by the stronger hyperconjugation effect.

Choose the correct statement.

(a) [a] is true but [r] is false
(b) Both [a] and [r] are true and [r] is the correct reason for [a]
(c) Both [a] and [r] are false
(d) Both [a] and [r] are true but [r] is *not* the correct reason for [a]

64. Given are the four statements about dehydration of alcohols to give alkenes:

[P]: Ease of dehydration of alcohols takes place in the order 3°> 2°>1°
[Q]: Dehydration is acid catalyzed.
[R]: Orientation of the alkene formed is strongly Saytzeff.
[S]: Dehydration is irreversible.

Choose the correct combination of statements.

(a) P and Q are correct while R and S are not
(b) P, Q and R all three are correct but S is not

(c) P, Q, R and S all are correct
(d) P, Q and S all three are correct but R is not

65. Choose the correct statement regarding the synthesis of phenyl n-propyl ether.
(a) Phenyl n-propyl ether is prepared from n-propyl bromide and sodium phenoxide
(b) Phenyl n-propyl ether is prepared from bromobenzene and sodium n-propoxide
(c) Phenyl n-propyl ether can be prepared by either of the two methods
(d) Both (A) and (B) are not the correct methods for the synthesis of phenyl n-propyl ether

66. Read the following statements about SN1 reactions:
[P]: They proceed with complete inversion (Walden inversion).
[Q]: They proceed with racemization plus some net inversion.
[R]: They are characterized by rearrangements.
[S]: They are characterized by the reactivity sequence, CH3>1°>2°>3° Choose the correct combination.
(a) P and Q are true while R and S are false
(b) P and R are true while S and Q are false
(c) Q and R are true while P and S are false
(d) R and S are true while P and Q are false

67. Read the following statements carefully:
[P]: Pyrrole and thiophene undergo electrophilic aromatic substitution reactions much faster than benzene
[Q]: Pyrrole and thiophene undergo Diels Alder addition reaction very fast
[R]: Pyrrole and thiophene undergo nucleophilic aromatic substitution reaction faster than benzene
[S]: Pyrrole is a pie excessive system while thiophene is a pie deficient system

Choose the correct combination of statements.
(a) Q only is true while P, R and S are false
(b) R and S are true while P and Q are false
(c) P and R are true while Q and S are false
(d) P only is true while Q, R and S are false

68. Among the following which one is not only a non-reducing sugar but also does not exhibit mutarotation?
(a) Glucose (b) Maltose
(c) Lactose (d) Sucrose

69. Choose the most basic heterocyclic compound among the following.
(a) Pyridine (b) Imidazole
(c) Pyrrole (d) Pyrrolidine

70. Following are some drug derivatives used to increase/decrease the water solubility of the parent drugs:
[P]: Rolitetracycline
[Q]: Erythromycin lactobionate
[R]: Chloramphenicol succinate
[S]: Erythromycin stearate

Choose the correct combination of statements.
(a) Q and R are used to increase water solubility while P and S are used to decrease it
(b) P, Q and R are used to increase water solubility while S is used to decrease it
(c) Q, S and R are used to increase water solubility while P is used to decrease it
(d) Q and S are used to increase water solubility while P and Q are used to decrease it

71. Study the following statements on prevention of crystalluria. Identify the approach by which this can be prevented.
[P]: By co-administration of sulfadiazine, sulfamerazine and sulfamethazine
[Q]: By increasing the pH of urine
[R]: By co-administration of sulphanilamide, sulphamethoxazole and folic acid
[S]: By administration of co-trimoxazole

Choose the correct combination of statements.
(a) P and Q are correct (b) R and S are correct
(c) P and R are correct (d) Q and R are correct

72. Progesterone is obtained from diosgenin through the following sequence of chemical reactions:
[P]: Acetylation, CrO_3 (oxidation), acetolysis, H_2/Pd, hydrolysis and Oppenauer oxidation
[Q]: Oppenauer oxidation, acetylation, CrO_3 (oxidation), acetolysis, H_2/Pd and hydrolysis
[R]: CrO_3 (oxidation), acetolysis, acetylation, Oppenauer oxidation, hydrolysis and H_2/Pd
[S]: Acetylation, H_2/Pd, hydrolysis, CrO_3 (oxidation), Oppenauer oxidation and acetolysis

Choose the correct sequence of reactions.
(a) P (b) Q
(c) R (d) S

73. Following statements are given for local anaesthetic drug lidocaine:
[P]: It contains a xylidine moiety.
[Q]: It can be used as an antiarrhythmic agent on oral administration.

[R]: When administered along with adrenaline its toxicity is reduced and its effect is prolonged.

[S]: Chemically it is 2-diethylamino-2',6'-dimethyl-phenyl acetamide Choose the correct combination of statements.

(a) P, Q and S (b) P, Q and R
(c) P, R and S (d) Q, R and S

74. One of the following ring systems can be used as the bio-isosteric replacement for benzene ring in drug design:

[IP]: Thiophene
[Q]: Cyclohexa-1,3-diene
[R]: Pyrrolidine
[S]: Imidazoline

Identify the correct answer.

(a) P (b) Q
(c) R (d) S

75. Some of the following statements describe the properties of dropping mercury electrode (DME) correctly:

[P] Constant renewal of electrode surface eliminates poisoning effects.
[Q] Mercury makes many metal ions easily reducible.
[R] Mercury has large hydrogen over-voltage.
[S] The electrode can get oxidised with ease.

Identify the correct combination of statements.

(a) P, Q, R and S (b) P, Q and R
(c) P, R and S (d) P, Q and S

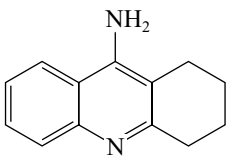
76. Penicillin ring system is derived from two of the following amino acids:

[P]: Alanine and methionine
[Q]: Cysteine and valine
[R]: Glycine and cysteine
[S]: Methionine and leucine

Choose the correct pair.

(a) P (b) Q
(c) R (d) S

77. For the management of which disease the given drug tacrine is used? Identify.



(a) Glaucoma
(b) Antidote for acticholinesterase poisoning
(c) As an insecticide
(d) Alzheimers disease

78. Low dose aspirin acts as an anti-platelet aggregating agent by which one of the following mechanisms? Find the correct answer.

(a) It acts as a suicide substrate for COX-1 enzyme present in platelets
(b) It acts as a transition state analog for COX-2 enzyme present in the platelets
(c) It acts as a reversible inhibitor of lipoxigenase present in the platelets
(d) It acts as an affinity label of oxidoreductases present in the platelets

79. Some statements are given for clavulanic acid, sulbactam and tazobactam:

[P]: All three lack the 6-acylamino side chain
[Q]: All are potent inhibitors of the enzyme β-lactamase
[R]: All are prodrugs of penicillin
[S]: All have weak antibacterial activity

Choose the correct combination of statements.

(a) P, Q and R are true while S is false
(b) Q, R and S are true while P is false
(c) P, R and S are true while Q is false
(d) P, Q and S are true while R is false

80. Electrophilic aromatic substitution reactions in indole give one of the following products preferably. Identify that.

(a) 3-Substituted indole
(b) 2-Substituted indole
(c) 5-Substituted indole
(d) 6-Substituted indole

81. Which one of the following species is an intermediate in the reaction shown below?

$$2CH_3CH_2CHO \xrightarrow{NaOH} CH_3CH_2CH(OH).CH(CH_3).CHO$$

(a) $+CH_2.CH_2.CHO$ (b) $-CH_2.CH_2.CHO$
(c) $CH_3.+CH.CHO$ (d) $CH_3.-CH.CHO$

82. Which detector is used in gas chromatography for halogen containing compounds specifically?

(a) Katharometer
(b) Electron capture detector
(c) Flame ionization detector
(d) Thermal conductivity detector

83. Precessional frequency of a nucleus depends on the following:

[P]: Quantum of externally applied magnetic field
[Q]: Quantum of electron density present around the nucleus
[R]: Frequency of applied electromagnetic radiations
[S]: Electronegativity of the element

Choose the correct combination of statements.
(a) P and Q are true (b) P and R are true
(c) Q and R are true (d) P and S are true

84. Some statements are given about disodium edetate:
[P]: Disodium edetate is a bidentate ligand
[Q]: Disodium edetate is a complexing agent but not a chelating agent
[R]: Disodium edetate can be used for the assay of lithium carbonate
[S]: Disodium edetate can be used for the assay of zinc sulphate

Choose the correct answer.
(a) Q, R and S are true (b) Q and S are true
(c) S only is true (d) P, Q, R and S all are true

85. Which one of the following amino acids is the most effective contributor of protein buffer?
(a) Alanine (b) Glycine
(c) Histidine (d) Arginine

86. Given are some statements about cycloalkanes:
[P]: Bayer's theory does not apply to four membered rings.
[Q]: Cyclohexane and cyclodecane rings are not flat but are puckered.
[R]: Chair form of cyclohexane experiences van der Waals strain due to flagpole interactions.
[S]: Boat form of cyclohexane experiences both torsional and van der Waals strain. Choose the correct combination of statements.

(a) P, Q and R are true and S is false
(b) Q and S are true and P and R are false
(c) P, Q and S are true and R is false
(d) Q, R and S are true and P is false

87. Phenols are more acidic than alcohols. Identify the reason.
(a) Alkoxide ions are better stabilized by the electron releasing alkyl groups
(b) Resonance stabilizes both phenols and phenoxide ions to the same extent
(c) Phenols are better stabilized than the phenoxide ions while reverse is true for alcohols and alkoxides
(d) Phenoxide ions are much better stabilized than the alkoxide ions

88. Study the following statements on alkylating agents as antineoplastics:
[P]: They get converted to aziridinium ions and bind to 7th position -N atom of guanine of DNA base pairs
[Q]: Nitrogen mustards and sulphur mustards belong to this class of drugs
[R]: They inhibit dihydrofolatereductase enzyme thereby inhibiting DNA synthesis
[S]: They chelate electropositive atoms present in the DNA thereby inhibiting DNA uncoiling

Choose the correct combination of statements.
(a) P and Q are correct
(b) R and S are correct
(c) P and S are correct
(d) Q and R are correct

89. Study the following statements about the stereochemistry of steroidal aglycones in cardiac glycosides:
[P]: Rings A-B and C-D are cis fused while B-C is trans fused.
[Q]: Rings A-B and C-D are trans fused while B-C is cis fused.
[R]: Rings A-B are trans fused while B-C and C-D are els fused.
[S]: Rings A-B are cis fused while B-C and C-D are trans fused.

Choose the correct statement.
(a) P is true while Q, R and S are false
(b) Q is true while P, R and S are false
(c) R is true while P, Q and S are false
(d) S is true while P, R and Q are false

90. Following are some statements about Captopril:
[P]: It is a prototype molecule in the design of ACE inhibitors
[Q]: It contains a sulphonyl group in its structure
[R]: It has a proline moiety in its structure
[S]: It has an ester linkage

Choose the correct combination of statements.
(a) P and Q are true while R and S are false
(b) Q and R are true while P and S are false
(c) P and R are true while Q and S are false
(d) R and S are true while P and Q are false

91. Cetirizine as an antihistaminic agent has a low sedative potential due to one of the following reasons. Identify that.

(a) It has a chiral center
(b) It has high log P value
(c) It has high polarity
(d) It has low molecular weight

92. There are some criteria which an ideal antacid should fulfill. Some of the criteria are given below:

[P]: The antacid should be absorbable orally and should buffer in the pH range of 4–6.

[Q]: The antacid should exert its effect rapidly and should not cause a large evolution of gas.

[R]: The antacid should not be a laxative or should not cause constipation.

[S]: The antacid should react with the gastric acid and should inhibit pepsin.

Choose the correct combination of criteria for an ideal antacid.

(a) P, Q and R (b) Q, R and S
(c) Q and R (d) R and S

93. Titanium dioxide is used in sun screen products as a topical protective. The topical protective effect of titanium dioxide is arising due to one of the following properties. Identify that.

(a) It has a high bulk density
(b) It has a high LTV absorptivity
(c) It has low water solubility
(d) It has a high refractive index

94. Deferoxamine is used for the treatment of toxicity caused by one of the following ions. Identify that.

(a) Arsenic (b) Cyanide
(c) Iron (d) Lead

95. Parachor and Molar refraction can be categorized under one of the following properties. Identify that.

(a) Additive properties
(b) Constitutive properties
(c) Colligative properties
(d) Additive and constitutive property

96. East's camphor method is used for determination of molecular weight of solutes which are soluble in molten camphor. The basic principle of the method is dependent on one of the following properties. Identify that.

(a) Elevation of freezing point of camphor by the solute
(b) Lowering of vapour pressure of camphor by the solute
(c) Lowering of freezing point of camphor by the solute
(d) Elevation of boiling point of camphor by the solute

97. In polarography, when the limiting current is achieved, which one of the following processes takes place?

(a) The rate of electron transfer just matches the rate of mass transfer
(b) The rate of electron transfer is slower than the rate of mass transfer
(c) The rate of electron transfer becomes independent of the rate of mass transfer
(d) The rate of electron transfer far exceeds the rate of mass transfer

98. Starch-iodide paste/paper is used as an external indicator in which one of the following titrations?

(a) lodometric titration of copper sulphate using sodium thiosulphate as titrant
(b) Iodimetric titration of ascorbic acid using iodine solution as titrant
(c) Diazotisation titration of sulphadiazine using sodium nitrite as titrant
(d) Potassium dichromate titration using sodium thiosulphate as titrant

99. For a dye to be used as metal indicator in complexometric titrations, some of the dye properties are listed below:

[P]: The dye should have distinct colour than the dye-metal complex

[Q]: The dye-metal complex should have a higher stability than the metal-chelate (titrant) complex

[R]: The dye should be capable of complexing with the metal ions

Choose the correct combination of statements for the dye to be used as an indicator in complexometric titrations.

(a) P and Q are correct while R is not
(b) Q and R are correct while P is not
(c) P and R are correct while Q is not
(d) P, Q and R all are correct

100. In amperometry, rotating platinum electrode (RPE) is used as indicating electrode. It has certain advantages as well as disadvantages. Read the following statements about the use of rotating platinum electrode in amperometry:

[P]: It causes large diffusion current due to rotation resulting in greater mass transfer

[Q]: It causes greatly reduced residual current due to lack of condenser effect

[R]: It has a low hydrogen over potential

Choose the correct combination of statements.

(a) P, Q and R are all advantages of using RPE in amperometry

(b) P and R are advantages of RPE while Q is a disadvantage
(c) Q and R are advantages of RPE while P is a disadvantage
(d) P and Q are advantages of RPE while R is a disadvantage

101. What will be the approximate T_{max} of a drug exhibiting K_a of 2 hr^{-1} and K of 0.2 hr^{-1}?
(a) 1.2 hr (b) 2.4 hr
(c) 4.8 hr (d) 2.0 hr,

102. There are some statements related to the protein binding of drugs as given below:
[P]: Protein binding decreases the free drug concentration in the system.
[Q]: Protein binding to plasma albumin is an irreversible process.
[R]: Drugs with a low lipophilicity have a high degree of protein binding.
[S]: Protein binding of one drug can be affected by the presence of other drug.
Choose the correct combination of statements.
(a) P and Q are true while R and S are false
(b) Q and R are true while P and S are false
(c) R and S are true while P and Q are false
(d) P and S are true while Q and R are false

103. Based on Henderson-Hasselbalch equation, at what pH value a weak acid would be 99.9% ionized?
(a) At pH equivalent to p*K*a + 3
(b) At pH equivalent to p*K*a – 3
(c) At pH equivalent to p*K*a – 1
(d) At pH equivalent to p*K*a + 1

104. Some statements about crystals are given below:
[P]: The crystal lattice is constructed from repeating units called unit cells.
[Q]: The external appearance of a crystal is described by crystal habits, such as needles, prisms, rosettes etc.
[R]: Polymorphism is the ability of a compound to crystallize as more than one distinct crystalline species with different internal lattice.
[S]: Hydrates are always more soluble than anhydrous form of the same drug.

Choose the corrected combination of statements about crystals.
(a) P, Q and S are correct but R is wrong
(b) P, Q and R are correct but S is wrong
(c) Q, R and S are correct but P is wrong
(d) R, S and P are correct but Q is wrong

105. Which one of the followings is *not* used in preparation of baby powders?
(a) Stearic acid (b) Boric acid
(c) Kaolin (d) Calcium carbonate

106. According to Kozeny Carmen equation a 10% change in porosity can produce:
(a) Two fold change in viscosity
(b) Five-fold change in viscosity
(c) Three-fold change in viscosity
(d) None of the above

107. Speed disk atomizer rotates at a speed of:
(a) 3000–5000 revolutions per min
(b) 3000–50000 revolutions per min
(c) 300–50000 revolutions per min
(d) 300–5000 revolutions per min

108. The thickness of gold coating USP dissolution apparatus – I basket is
(a) Not more than 2.5 μm in thickness
(b) Not more than 0.001 mm in thickness
(c) Not more than 0.025μ in thickness
(d) Not more than 0.1 mm in thickness

109. Containers used for aerosols should withstand a pressure of:
(a) 130–150 Psig at 130°F
(b) 140–180 Psig at 130°F
(c) 140–170 Psig at 120°F
(d) 120–140 Psig at 120°F

110. Study the following two statements:
[X]: If the gas is cooled below its critical temperature, less pressure is required to liquefy it.
[Y]: At critical temperature and critical pressure, the liquid will have highest vapor pressure.

Choose the correct combination of statements.
(a) Both X and Y are correct
(b) X is incorrect and Y is correct
(c) X is correct and Y is incorrect
(d) Both X and Y are incorrect

111. Determine the correctness or otherwise of the following Assertion [a] and the Reason [r]:

Assertion [a]: For an API of approximately same particle size, the angle of repose will increase with departure from spherical shape.

Reason [r]: Angle of repose is a function of surface roughness and particle size.

With constant particle size, increase in roughness increases angle of repose.

(a) Although [a] is true but [r] is false
(b) Both [a] and [r] are false
(c) Bothfa] and [r] are true and [r] is the correct reason for [a]
(d) Both [a] and [r] are true but [r] is *not* the correct reason for [a]

112. Study the following two statements:

[X]: When used as granulating agent PEG 6000 improves dissolution rate of the dosage form as it forms a complex with a better solubility.

[Y]: Sodium CMC when used as a binder affects dissolution rate of the dosage form as it is converted to less soluble acid form at low pH of the gastric fluid.

Choose the correct answer.

(a) Both X and Y are correct
(b) X is incorrect and Y is correct
(c) X is correct and Y is incorrect
(d) Both X and Y are incorrect .

113. Study the following statements about Gram staining:

[P]: Gram positive bacteria are stained deep violet and Gram negative bacteria are stained red.

[Q]: Gram positive bacteria are stained red and Gram negative bacteria are stained deep violet.

[R]: The sequence of addition of staining reagents is crystal violet, iodine solution, alcohol and safranin.

[S]: In Gram positive bacteria the purple color developed during staining is lost during alcohol treatment. The cells later take up the safranin and stain red.

Choose the correct combination of statements.

(a) P, Q, R and S all are false
(b) P and Q are false and R and S are true
(c) P and S are false and Q and R are true
(d) P and R are false and Q and S are true

114. Choose the correct formula for the calculation of the retail price of a formulation, given by the Government of India.

(a) R.P. = (M.C. + E.D. + P.M. + P.C.) × (1 + MAPE/100) + C.C.
(b) R.P. = (M.C. + C.C. + P.M. + P.C.) × (1 + MAPE/100) + E.D.
(c) R.P. = (M.C. + C.C. + E.D. + P.C.) × (1 + MAPE/100) + P.M.
(d) R.P. = (M.C, + C.C. + P.M.+ E.D.) × (1 + MAPE/100) + P.C,

115. Determine the correctness or otherwise of the following assertion [a] and the reason [r]:

Assertion [a]: In arsenic poisoning, dimercaprol, injected intramuscularly, acts as antidote by metal complexation.

Reason [r]: EDTA acts as an antidote in lead poisoning, by solubilizing the toxic metal ions from the tissues.

(a) Although [a] is true but [r] is false
(b) Both [a] and [r] are false
(c) Both [a] and [r] are true and [r] is the correct reason for [a]
(d) Both [a] and [r] are true but [r] is *not* the correct reason for [a]

116. Determine the correctness or otherwise of the following Assertion [a] and the Reasons [r and s]:

Assertion [a]: Butylatedhydroxytoluene is added as one of the ingredients in the lipstick formulation.

Reason [r]: It is a good solvent for the wax – oil mixtures and coloring pigments present in the lipstick.

Reason [s]: It is an antioxidant and prevents rancidity on storage.

(a) [a] is true, and [r] and [s] are true and correct reasons for [a]
(b) [a], [r] and [s] are all false
(c) [a] is true, [s] is false, and [r] is the correct reason for [a]
(d) [a] is true, [r] is false, and [s] is the correct reason for [a]

117. Which one of the following statements is *false* about Interferons?

(a) Interferons are cellular glycoproteins produced by virus infected cell
(b) Interferons have no effects on extracellular virus
(c) Interferons are virus specific agents that can interfere either with DNA or RNA virus
(d) They are produced as potent broad spectrum antiviral agents

118. In relation to sodium chloride and water mixture, read the following statements:

[P]: Mixture is eutectic in nature

[Q]: It has eutectic point –21.2°C

[R]: The composition of eutectic is 25.3% by Mass

[S]: The mixture is a true eutectoid and may exist as peritectic also.

Which of the set of statements is correct?

(a) P and Q (b) Q, R and S
(c) P, Q and S (d) P, R and S

119. In relation to sterilization, what is the meaning of D300F – 2 minutes?

(a) Death of all microorganisms in 2 minutes
(b) Death of 300 microorganisms in 2 minutes
(c) Death of all microorganisms in 2 minutes at 300°F
(d) Death of 90% microorganisms in 2 minutes at 300°F

120. Choose the correct combination:

(i) Rod mill
(ii) Hammer mill
(iii) Fluid energy mill

(p) Dried plant drug
(q) Thermolabile drug
(r) Paint

(a) i and q, ii and p, iii and r
(b) i and r, ii and p, iii and q
(c) I and q, ii and r, iii and p
(d) I and p, ii and q, iii and r

121. Which one of the following statements is *not* true for stainless steel 316?

(a) It is also called inox steel
(b) It contains 10.5–11% chromium
(c) Due to the presence of chromium it exhibits passivation phenomenon
(d) It is not affected by acids

122. Precise control of flow is obtained by which one of the following?

(a) Needle valve (b) Butterfly valve
(c) Gate valve (d) Globe valve

123. Heat sensitive materials like fruit juice are evaporated in which one of the following?

(a) Long tube vertical evaporator
(b) Calandria type evaporator
(c) Falling film type evaporator
(d) Forced circulation type evaporator

124. Which of the following conditions favor formation of large crystals?

(a) High degree of supersaturation
(b) Low nucleation rate
(c) High magma density
(d) Rapid cooling of magma

125. If M, L, T, Q and θ are dimensional representations of mass, length, time, heat and temperature respectively, then what is the dimension of fluid thermal conductivity?

(a) Q/Mθ (b) Q/TL2θ
(c) Q/TLθ (d) M/LT

126. Which one of the following properties is characteristic of microemulsions?

(a) These are transparent systems with droplet size less than 1 μm
(b) These are transparent systems with droplet size less than 10 μm
(c) These are non-transparent systems with droplet size less than 1 μm
(d) These are transparent systems with droplet size less than 1 nm

127. Which one of the followings would be an offence in accordance with the provisions of the Drugs and Cosmetics Act, 1940?

(a) Packing of paediatric oral drops in 30 ml pack
(b) Packing of oxytocin injection in a single unit blister pack
(c) Packing of schedule X drugs in 5 ml injection pack
(d) Packing of aspirin tablets (75 mg) in 14 tablet strip pack

128. Which one of the following colours is *not* permitted to be used in drugs by the Drugs and Cosmetics Act, 1940?

(a) Chlorophyll (b) Riboflavin
(c) Tartrazine (d) Amaranth

129. At equal concentrations which one of the following mucilages will possess maximum viscosity?

(a) Maize starch (b) Rice starch
(c) Wheat starch (d) Potato starch

130. By which mechanism the microorganisms are killed by autoclaving?

(a) Coagulation of the cellular proteins of the microorganisms
(b) Alkylation of essential cellular metabolites of microorganisms
(c) Stopping reproduction of microorganism cells as a result of lethal mutations
(d) Oxidation of RNA of microorganisms

131. Manufacture and sale of some of the following drugs is prohibited in India:

[P]: Fixed dose combination of atropine and antidiarrhoeals
[Q]: Penicillin eye ointment
[R]: Nimesulidepaediatric drops
[S]: Gatifloxacin tablets

Choose the drugs which are prohibited.

(a) P, Q and R (b) Q, S and R
(c) R, S and P (d) P, Q, R and S

132. Following are the phases of clinical trials:

[P]: Human pharmacology
[Q]: Therapeutic confirmatory trials
[R]: Post marketing trials
[S]: Therapeutic exploratory trials

Choose the correct order of phases of clinical trial.

(a) P, Q, R, S (b) P, R, Q, S
(c) P, Q, S, R (d) P, S, Q, R

133. The integrity of seals in case of vials and bottles is determined by some tests. Some of them are given below:

[P]: Leaker's test
[Q]: Water hammer test
[R]: Spark tester probe

Choose the correct answer.

(a) P and Q (b) Q and R
(c) P and R (d) P, Q and R

134. Study the following four statements:

[P]: Gram negative bacteria produce potent pyrogenic substances called endotoxins
[Q]: Ethylene oxide mixed with carbon dioxide or fluorinated hydrocarbons is used in gas sterilization
[R]: D value is the time (for heat or chemical exposure) or the dose (for radiation exposure) required for the microbial population to decline by one logarithmic unit
[S]: Spores of *Geobacillus stearothermophilus* (*Bacillus stearothermophilus*) are used for sterility testing of moist heat sterilization process

Choose the correct answer.

(a) P, Q and R are correct but S is incorrect
(b) Q, R and S are correct but P is incorrect
(c) R, S and P are correct but Q is incorrect
(d) P, Q, R and S all are correct

135. Read the following statements:

[P]: The surface area measurement using BET approach utilizes argon gas for adsorption
[Q]: Full form of BET is Brunauer, Emmett and Teller

Choose the correct answer.

(a) P and Q both are correct
(b) P is correct but Q is incorrect
(c) Q is correct but P is incorrect
(d) Both P and Q are incorrect

136. Based on the DLVO theory of force of interaction between colloidal particles, which one of the following lead to attractive interaction between two particles?

(a) Solvation forces
(b) Electrostatic forces
(c) van der Waals forces
(d) Steric forces

137. Read the following statements with regard to viscosity of a polymer solution:

[P]: Specific viscosity of a polymer solution is obtained as relative viscosity + 1
[Q]: Relative viscosity is the ratio of the viscosity of the solution to the viscosity of pure solvent
[R]: Kinematic viscosity is defined as the viscosity of the liquid at a definite temperature
[S]: The unit for kinematic viscosity is poise or dyne sec cm"2 Indicate the correct combination of statements.

(a) P and S are correct but Q and R are wrong
(b) Q and R are correct but P and S are wrong
(c) P and Q are correct but R and S are wrong
(d) R and S are correct but P and Q are wrong

138. Determine the correctness or otherwise of the following assertion [a] and the reason [r]

Assertion [a]: Salts having no ions in common with the slightly soluble electrolyte increase its solubility

Reason [r]: Such salts lower the activity coefficient of the slightly soluble electrolyte

(a) Both [a] and [r] are true and fr] is the correct reason for [a]
(b) Both [a] and [r] are false
(c) Although [a] is true but [r] is false
(d) Both [a] and [r] are true but [r] is *not* the correct reason for [a]

139. What negative adsorption would do?

(a) Decrease the surface free energy as well as the surface tension
(b) Increase the surface free energy as well as the surface tension
(c) Decrease the surface free energy but increase the surface tension
(d) Increase the surface free energy but decrease the surface tension

140. Read the following statements:

[P]: At temperature below Kraft point, micelles will, not form

[Q]: At Kraft point, solubility of surfactant equals CMC

[R]: Kraft point increases with increasing chain length of hydrocarbon

[S]: Kraft point is normally exhibited by non-ionic surfactants

Choose the correct combination of answers.

(a) P is correct but Q, R and S are wrong
(b) R and S are correct but P and Q are wrong
(c) P, Q and R are correct but S is wrong
(d) P, Q, R and S all are correct

141. Two statements are given regarding the uniformity of dispersion test (LP):

[P]: It is evaluated using 6 tablets and 500 mL water

[Q]: It involves measuring the dispersion time of each tablet

Choose the correct set of statements.

(a) P is correct while Q is incorrect
(b) P and Q both are correct
(c) P is incorrect while Q is correct
(d) Both P and Q are incorrect

142. Read the following statements:

[P]: Caramelization occurs in acidic conditions

[Q]: Caramel is optically inactive glucose

[R]: Caramel is obtained by burning of glucose

[S]: Caramel is obtained by degradation of fructose

Choose the right combination of statements.

(a) P and Q are true but R and S are false
(b) P and S are true but Q and R are false
(c) Q and R are true but P and S are false
(d) R and S are true but P and Q are false

143. Read the following statements regarding value added tax (VAT):

[P]: It is an indirect tax

[Q]: It is charged at the rate of 8%

[R]: It is tax at source

[S]: It is effective since April 2010

Choose the correct option.

(a) P and Q are true R and S are false
(b) R and S are true P and Q are false
(c) P and R are true Q and S are false
(d) Q and S are true P and R are false

144. Find the process by which the conversion of sulfasalazine to sulphapyidine and 5-amino salicylic acid takes place in the colon?

(a) Hydrolysis (b) Deamination
(c) Acetylation (d) Azoreduction

145. How much quantity (in grams) of sodium chloride is needed to make 30 ml of a 2% isotonic drug (sodium chloride equivalent 0.20) solution?

(a) 0.60 (b) 0.27
(c) 0.15 (d) 0.12

146. Read the following statements about lyophilisation:

[P]: Lyophilisation cannot be done in final containers like multiple dose containers.

[Q]: Lyophilised product needs special methods for reconstitution.

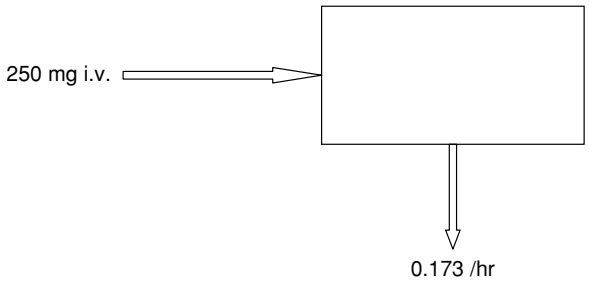
[R]: Lyophilisation causes protein denaturation in tissues.

[S]: Lyophilisation is suitable for drying the thermolabile products.

Choose the correct combination of statements.

(a) P is true and Q, R and S are false
(b) Q is true and P, R and S are false
(c) R is true and P, Q and S are false
(d) S is true and P, Q and R are false

147. In a pharmacokinetic model depicted in the following scheme, what is the half-life of the drug if the apparent volume of distribution of the drug is 25 L?



(a) 1.7 hr (b) 2hr
(c) 4 hr (d) 3 hr

148. A sample of paracetamol tablets claims to contain 500 mg of paracetamol. But, on analysis by government analyst, it was found to contain 200 mg. As per Drugs and Cosmetics Act, 1940, this product would be categorised as what?

(a) Misbranded drug (b) Adulterated drug
(c) Spurious drug (d) Unethical drug

149. Use of which of the following artificial sweeteners is permitted in various dosage forms of Ayurveda, Siddha and Unani proprietary medicines?

(a) Sucralose (b) Aspartame
(c) Saccharin (d) All of them

150. What will be the maintenance dose of a sustained release 12 hour formulation of drug X exhibiting one compartment kinetics with a half-life of 6 hours, plasma concentration (steady state) 6 μg/ml, volume of distribution 30 L, and an oral bioavailability of 80%?

(a) 249.48 mg (b) 225.48 mg
(c) 311.85 mg (d) 281.85 mg

ANSWER KEYS

1. (a)	**2.** (c)	**3.** (b)	**4.** (a)	**5.** (a)	**6.** (b)	**7.** (c)	**8.** (b)	**9.** (d)	**10.** (c)
11. (b)	**12.** (d)	**13.** (d)	**14.** (b)	**15.** (a)	**16.** (d)	**17.** (a)	**18.** (d)	**19.** (b)	**20.** (c)
21. (d)	**22.** (a)	**23.** (c)	**24.** (d)	**25.** (c)	**26.** (b)	**27.** (c)	**28.** (d)	**29.** (a)	**30.** (b)
31. (c)	**32.** (d)	**33.** (d)	**34.** (c)	**35.** (b)	**36.** (b)	**37.** (b)	**38.** (d)	**39.** (a)	**40.** (a)
41. (b)	**42.** (a)	**43.** (a)	**44.** (b)	**45.** (b)	**46.** (b)	**47.** (a)	**48.** (d)	**49.** (d)	**50.** (c)
51. (c)	**52.** (a)	**53.** (b)	**54.** (b)	**55.** (b)	**56.** (b)	**57.** (d)	**58.** (c)	**59.** (a)	**60.** (a)
61. (b)	**62.** (b)	**63.** (a)	**64.** (b)	**65.** (a)	**66.** (c)	**67.** (d)	**68.** (d)	**69.** (d)	**70.** (b)
71. (a)	**72.** (a)	**73.** (c)	**74.** (a)	**75.** (a)	**76.** (b)	**77.** (d)	**78.** (a)	**79.** (d)	**80.** (a)
81. (d)	**82.** (b)	**83.** (a)	**84.** (c)	**85.** (c)	**86.** (b)	**87.** (d)	**88.** (a)	**89.** (a)	**90.** (c)
91. (c)	**92.** (c)	**93.** (d)	**94.** (c)	**95.** (d)	**96.** (c)	**97.** (d)	**98.** (c)	**99.** (c)	**100.** (d)
101. (a)	**102.** (d)	**103.** (a)	**104.** (a)	**105.** (b)	**106.** (b)	**107.** (c)	**108.** (b)	**109.** (b)	**110.** (a)
111. (c)	**112.** (b)	**113.** (c)	**114.** (b)	**115.** (d)	**116.** (d)	**117.** (c)	**118.** (a)	**119.** (d)	**120.** (b)
121. (d)	**122.** (a)	**123.** (c)	**124.** (b)	**125.** (d)	**126.** (a)	**127.** (a)	**128.** (d)	**129.** (d)	**130.** (a)
131. (d)	**132.** (d)	**133.** (b)	**134.** (d)	**135.** (c)	**136.** (c)	**137.** (b)	**138.** (a)	**139.** (b)	**140.** (c)
141. (d)	**142.** (b)	**143.** (c)	**144.** (d)	**145.** (c)	**146.** (d)	**147.** (c)	**148.** (a)	**149.** (d)	**150.** (c)

GPAT PAPER 2011

1. Quinoline alkaloids are biosynthesized via which one of the following pathways?
(a) Shikimic acid-tyrosine
(b) Shikimic acid-tryptophan
(c) Shikimic acid-cathinone
(d) Shikimic acid-phenylalanine

2. Khellin is an active constituent of which one of the following plants?
(a) Prunus serona (b) Tribulus terrestis
(c) Ammi visnaga (d) Vanilla planifolia

3. Which one of the following compounds is useful for the stimulation of cell division and release of lateral bud dormancy?
(a) Zeatin
(b) 2,4-Dichlorophenoxyacetic acid
(c) Indoleacetic acid
(d) Picloram

4. A powdered drug has the following microscopic characters: Anther cells, arenchyma, pollen grains, phloem fibers, volatile oil cells and stone cells. The powder is obtained from which of the following?
(a) Clove bud powder
(b) Clove bud powder with stalk
(c) Mother clove
(d) None of the above

5. Which of the following ergot alkaloids is water soluble and shows blue fluorescence?
(a) Ergosine (b) Ergotamine
(c) Ergocristine (d) Ergometrine

6. Goldbeater's skin test is used to detect the presence of which one of the following classes of compounds?
(a) Tannins (b) Steroids
(c) Glycerides (d) Resins

7. Phenylethylisoquinoline is the precursor of which of the following alkaloids?
(a) Colchicine (b) Papaverine
(c) Emetine (d) Cephaline

8. Arrange the following fatty acids in decreasing order of their unsaturation (highest to lowest):
(P) Stearic (Q) Oleic acid
(R) Linolenic acid (S) Linoleic acid
(a) P>Q>R>S (b) S>R>P>Q
(c) R>S>Q>P (d) Q>P>R>S

9. Each of the following option lists a phytoconstituent, its phytochemical grouping, pharmacological activity and corresponding semisynthetic analogue. Find a mismatching option.
(a) Podophyllotoxin, lignan, anticancer, etoposide
(b) Sennoside, anthraquinone, laxative, sinigrin
(c) Atropine, alkaloid, anticholinergic, homatropine
(d) THC. terpenophenolic, psychoactive, nabilone

10. Which of the following mechanisms is not related to platelet aggregation inhibitory action?
(a) ADP receptor antagonism
(b) Glycoprotein IIb/IIIa receptor antagonism
(c) Phosphodiesterase inhibition
(d) Prostacvclin inhibition

11. Which of the following species is being inactivated by the enzyme Dipeptidyl peptidase-4?
(a) Oxytocin (b) Vasopressin
(c) Incretin (d) Glucagon

12. Two genetic types of Cannabis i.e., drug type and Hemp type are cultivated.
(P) Drug type cannabis is rich in (-)A-trans-tetrahydrocannabinol.
(Q) Hemp type cannabis is rich in cannabidiol
(R) Drug type cannabis is rich in cannabidiol
(S) Hemp type cannabis contains elongated bast fibres
Which one of the given statements is correct?
(a) P is true, Q is true, R is true, S is true
(b) P is true, Q is false, R is false, S is true
(c) P is true, Q is true, R is false, S is true
(d) P is false, Q is false, R is true, S is false

13. Inhibition/induction of which of the following Cytochrome P450 enzyme system is most likely to be involved in important drug-drug interactions?
(a) CYP3A4 (b) CYP2D6
(c) CYP2C9 (d) CYP1A2

14. Choose the correct statement about the given four diseases:

(P) Cardiomyopathy (Q) Rheumatoid arthritis
(R) Myasthenia gravis (S) Ulcerative colitis

(a) Q and S are autoimmune disorders
(b) P and Q are autoimmune disorders
(c) P and R are not autoimmune disorders
(d) R and S are not autoimmune disorders

15. Most of the emergency contraceptives have one of the following active ingredients?

(a) Estradiol (b) Norethindron
(c) Misoprostol (d) Levonorgesterel

16. Antiretroviral Raltegravir is unique because of which of the following actions?

(a) Integrase inhibition
(b) CCR5 Co-receptor antagonism
(c) Fusion inhibition
(d) Reverse transcriptase inhibition

17. Which one of the followings is not an example of G-protein coupled receptor?

(a) Muscarinic cholinergic receptor
(b) Alpha adrenoceptor
(c) Nicotinic cholinergic receptor
(d) Beta adrenoceptor

18. Which of the following statements is false for artemisinin?

(a) It is a sesquiterpene lactone endoperoxide
(b) It is a drug of choice in prophylaxis of malaria
(c) It does not cure relapsing malaria
(d) It is useful in treatment of cerebral falciparum malaria

19. Which of the following antibiotics produces concentration dependent bactericidal action and also possesses post-antibiotic effect?

(a) Ceftazidime (b) Azithromycin
(c) Amikacin (d) Piperacillin

20. What is chemotaxis?

(a) Toxicity of chemicals
(b) Taxonomy of chemicals
(c) Inhibition of Inflammation
(d) Movement of leucocytes in inflammation

21. Which of the following used in the treatment of rheumatoid arthritis is not a biologic response modifier?

(a) Anakinra (b) Leflunomide
(c) Etanercept (d) Infliximab

22. Which of the following is a non-competitive inhibitor of the enzyme reverse transcriptase in HIV?

(a) Lamivudine (b) Nevirapine
(c) Abacavir (d) Tenofovir

23. Which one of the following is a beta lactamase inhibitor?

(a) Penicillanic acid
(b) Embonic acid
(c) Cephalosporanic acid
(d) Clavulanic acid

24. Neural tube defects may occur by which one of the following anti-seizure drugs?

(a) Ethosuximide (b) Vigabatrin
(c) Valproic acid (d) Primidone

25. Which one of the following drying methods is commonly used in pharma industry for drying of soft shell capsules?

(a) Truck drying (b) Fluid bed drying
(c) Vacuum drying (d) Microwave drying

26. If C is the concentration of dissolved drug and Cs is the saturation concentration. In which case, the sink conditions are said to be maintained?

(a) C < 20% of Cs (b) C > 20% of Cs
(c) C < 10% of Cs (d) C >10% of Cs

27. All of the following are indications for the use of ACE inhibitors except one. Identify that.

(a) Hypertension
(b) Myocardial infarction
(c) Left ventricular dysfunction
(d) Pheochromocytoma

28. Which water is used for hand washing in a change room of pharmaceutical manufacturing plant?

(a) Potable water
(b) Purified water
(c) Disinfectant water
(d) Soap water

29. Which one of the following does not afford a macromolecular inclusion compound?

(a) Zeolites (b) Dextrins
(c) Silica gels (d) Cyclodextrins

30. Which condition does not apply as per Indian law while conducting single dose bioavailability study of an immediate release product?

(a) Sampling period should be atleast three t½ ei
(b) Sampling should represent pre-exposure, peak exposure and post-exposure phases

(c) There should be at least four sampling points during elimination phase
(d) Sampling should be continued till measured AUC is atleast equal to 80% of AUC

31. Which of the following isothems are produced when the heat of condensation of successive layers is more than the heat of adsorption of first layer?
(a) Type III and IV (b) Type II and V
(c) Type I and III (d) Type III and V

32. The minimal effective flow rate of air in Luminar Flow Hood should be not less than how many cubic feet per minute?
(a) 10 (b) 50
(c) 100 (d) 1000

33. Which of the following pumps is used in handling of corrosive liquids?
(a) Turbine pump (b) Volute Pump
(c) Air binding pump (d) Baltic pump

34. Convert 90% v/v alcohol to Proof strength. Choose the correct answer.
(a) 57.77° under proof
(b) 57.77° over proof
(c) 47.41° over proof
(d) 47.41° under proof

35. What is the heat of vaporization of water at 1000?
(a) 2790 cal/mole (b) 7290 cal/mole
(c) 7920 cal/mole (d) 9720 cal/mole

36. Which of the following acts as a non-ionic emulsifying agent?
(a) Triethanolamine oleate
(b) Polyoxyethylene sorbitan monooleate
(c) N-Cetyl-N-ethylmorpholinium ethosulfate
(d) Dioctyl sulphosuccinate

37. Which of the following Schedules include shelf-life of drugs?
(a) Schedule F (b) Schedule M
(c) Schedule G (d) Schedule P

38. By addition of which of the following, the shells of soft gelatin capsules may be made elastic?
(a) Polyethylene glycol
(b) Sorbitol
(c) Propylene glycol
(d) Dibutyl phthalate

39. Department of Transport Test (DOT) is performed for which of the following?
(a) Strip packing (b) Aerosols
(c) Injection packing (d) Glass containers

40. How many mL of 50% (w/v) dextrose solution and how many mL of 5% (w/v) dextrose solution is required to prepare 4500 mL of a 10% (w/v) solution?
(a) 500 mL of 50% and 4000 mL of 5%
(b) 1000 mL of 50% and 3500 mL of 5%
(c) 4000 mL of 50% and 500 mL of 5%
(d) 1500 mL of 50% and 3000 mL of 5%

41. P-Glycoprotein pump is responsible for which one of the following?
(a) Transporting the drugs from the enterocytes into the gut lumen
(b) Transporting the drugs from gut lumen into enterocytes
(c) Transporting the drugs from oral mucosa into blood capillaries
(d) Transporting the drugs from Peyer's patches into the gut lumen

42. The first stage of wetting on addition of a granulating agent to the powders is characterized by which one of the following?
(a) Capillary state (b) Pendular state
(c) Funicular state (d) Droplet state

43. The degree of flocculation of a suspension is 1.5 and the sedimentation volume is 0.75. What will be the ultimate volume of deflocculated suspension?
(a) 2.0 (b) 1.5
(c) 0.75 (d) 0.5

44. A drug is administered to a 65 kg patient as 500 mg tablets every 4 hours. Half-life of the drug is 3 h, volume of distribution is 2 litre/kg and oral bioavailability of the drug is 0.85. Calculate the steady state concentration of the drug.
(a) 5.05mcg/ml (b) 4.50 mcg/ml
(c) 3.53 mcg/ml (d) 3.00 mcg/ml

45. Statement [X]: Hofmeister series grades coagulating power of electrolytes as per their ionic size.
Statement [Y]: The relative coagulating power is given by:
(P) $Al^{+++} > Ba^{++}$
(Q) $Li^- > F^-$ (R) $NH_4^+ > Na^+$ Choose the correct statement:
(a) Statement X is true but P, Q and R are false in Statement Y
(b) Statement X is false and P, Q and R are false in Statement Y

(c) Statement X is true and Q and R are false in Statement Y
(d) Statement X is false and P is false in Statement Y

46. Larger values of Ky in the Heckel Plot indicate formation of what quality of tablets?
(a) Harder tablets (b) Softer tablets
(c) Fluffy tablets (d) Brittle tablets

47. Which is not applicable to protein binding?
(a) Klotz reciprocal plot
(b) Sandberg modified equation
(c) Blanchard equation
(d) Detli plot

48. According to USP, the speed regulating device of the dissolution apparatus should be capable of maintaining the speed within limits of what% of the selected speed?
(a) 1% (b) 2%
(c) 4% (d) 5%

49. Which statement is not true for steam distillation?
(a) It is also called differential distillation.
(b) It can be used for separation of immiscible liquids.
(c) It can be applied for volatile substances.
(d) It can be used for separation of miscible liquids.

50. What is Primogel?
(a) Substituted HPMC for direct compression
(b) Modified microcrystalline cellulose for direct compression
(c) Hydro gelling polymer for gel formation
(d) Modified starch for disintegration

51. Statement (P): Soft gelatin capsules contain 12–15% moisture.
Statement (Q): Hard gelatin capsule shells contain 6–10% moisture.

Choose the correct statement.
(a) Both of the above statements P and Q are true
(b) Both of the above statements P and Q are false
(c) Statement P is true and Q is false
(d) Statement P is false and Q is true

52. A drug whose solubility is 1 g/L in water, when given orally at a dose of 500 mg is absorbed upto 95% of the administered dose. The drug belongs to which class according to the BCS classification?
(a) Class I (b) Class II
(c) Class III (d) Class IV

53. The area of clear opening of any two successive sieves according to Tyler standard is in the ratio of
(a) 1: 4 (b) 1: 6
(c) 1: $\sqrt{2}$ (d) 1: $\sqrt{3}$

54. Iodine-131 as sodium iodide solution is used as a radiopharmaceutical for diagnostic and therapeutic purposes. Its usage is dependent on the release of the following emissions:
(P) Alpha particles (Q) Positrons
(R) Beta emission (S) Gamma radiation

Choose the correct combination of statements:
(a) R and S (b) Q and S
(c) P and R (d) P and S

55. Alkenes show typical electrophilic addition reactions. If an electronwithdrawing group is attached to one of the carbons bearing the double bond, what will happen to the mechanism of the addition reaction?
(a) It remains electrophilic
(b) It becomes free radical addition
(c) It becomes pericyclic reaction
(d) It becomes nucleophilic

56. Five-membered heteroaromatic compounds show a much higher rate of electrophilic aromatic substitution reactions than the six-membered ones. This is due to which one of the following reasons?
(a) Five-membered heteroaromatic compounds have higher circulating electrondensity in the ring than the six-membered ones.
(b) Five-membered heteroaromatic compounds have lower circulating electron density in the ring than the six-membered ones.
(c) Five-membered rings are smaller in size than the six membered ones which affects their reaction rates.
(d) Six membered heteroaromatic rings are flat while the five-membered ones are puckered.

57. Arrange the following Lowry-Bronsted acids into their decreasing order of acidity (highest to lowest)?
(P) C_2H_5OH (Q) H_3C-CsCH
(R) H_2O (S) CH_3NH_2
(a) R>P>Q>S (b) P>R>Q>S
(c) P>Q>R>S (d) R>Q>P>S

58. Aprotic polar solvents increase the rate of SN2 reactions manifold. Enhancement in the rate of such reactions is due to which one of the following effects?
(a) Solvation of the anion by the solvent leaving the cation unaffected
(b) Solvation of both of the ionic species

(c) Desolvation of the cation and solvation of the anion
(d) Solvation of the cation by the solvent leaving the anion unaffected

59. In context of complexometry (complexometric titrations), the two terms labile and inert complexes, are used frequently. Choose the correct statement about them.
(a) Labile complexes are formed instantly while inert complexes take hours or days in their formation
(b) Labile complexes take much longer time in formation than inert complexes
(c) Labile complexes get hydrolyzed in water immediately while inert complexes are stable in water
(d) Labile complexes get decomposed on mild heating in aqueous solutions while inert complexes do not decompose

60. In colorimetric estimation of a drug, the following sequence of reactions is carried out: treatment of the aqueous solution of the drug with sodium nitrite solution in acidic medium followed by addition of sulphamic acid and then treatment with N-(lnaphthyl) ethylene-diamine in slightly basic medium to obtain a pink colour; which is measured at a fixed wavelength to correlate the quantity of the drug with the optical density. Identify the drug under estimation.
(a) Streptomycin sulphate
(b) Thiamine hydrochloride
(c) Dexamethasone
(d) Sulphamethoxazole

61. In the electrochemical series, the standard reduction potentials of copper and zinc are + 0.337 V and – 0.763 V, respectively. If the half cells of both of these metals are connected externally to each other through an external circuit and a salt bridge, which one of the following processes will take place?
(a) Zinc metal electrode will start cussohing.in solution while copper ions will start depositing on the copper electrode.
(b) Copper metal electrode will start dissolving in solution while zinc ions will start depositing on the zinc electrode
(c) Both of the metal electrodes will start dissolving in the solution
(d) Both types of ions will start depositing on their respective electrodes

62. Indicators used in complexometric titrations are chelating agents. Choose the correct statement about them.
(a) Indicator-metal ion complex should have higher stability than EDTA-Metal ion complex
(b) Indicator-metal ion complex should have lower stability than EDTA-Metal ion complex
(c) Indicator-metal ion complex should have equal stability as EDTA-Metal ion complex
(d) Stability of the indicator-metal ion complex is not an important criterion in complexometric titrations

63. Name the compound used for standardization of Karl-Fisher reagent in aquametry.
(a) Sodium tartrate dihydrate
(b) Copper sulphate pentahydrate
(c) Sodium iodide
(d) Sodium thiosulphate

64. The following statements are given:
(P) Conformational isomers are interconvertible by rotation around a single bond while configurational isomers cannot be interconverted without breaking a bond.
(Q) Configurational isomers could be optically active or optically inactive while conformational isomers are optically inactive.
(R) Geometric isomers must have a double bond in their structures.
(S) Geometric and optical isomers are the two distinct categories of configurational isomers.

Choose the correct combination of statements.
(a) P, Q and S are true while R is false
(b) P, R and S are true while Q is false
(c) Q, R and S are true while P is false
(d) P, Q and R are true while S is false

65. Determine the correctness or otherwise of the following Assertion (A) and the Reason (R):

Assertion (A): Formaldehyde and benzaldehyde both undergo Cannizaro reaction while acetaldehyde and phenyacetaldehyde undergo Aldol condensation.

Reason (R): Aldehydes can undergo both Cannizaro as well as Aldol condensation while ketones undergo only Cannizaro reaction.
(a) Both (A) and (R) are false
(b) (A) is true but (R) is false
(c) (A) is false but (R) is true
(d) Both (A) and (R) are true

66. Choose the correct statement for writing the sequence of amino acids in a polypeptide.
(a) Amino terminal is to be written on the left hand side while the carboxyl terminal is to be written on the right hand side.
(b) Carboxyl terminal is to be written on the left hand side while the amino terminal is to be written on the right hand side

(c) Any of the amino acid terminals can be written on any sides but it is to be mentioned by specifying the amino terminal and the carboxyl terminal in abbreviations.
(d) It varies from author to author how the sequence of amino acids in a polypeptide is to be written.

67. A carbocation will not show one of the following properties. Choose that.
(a) Accept an electron to give a carbene
(b) Eliminate a proton to afford an alkene
(c) Combine with a negative ion
(d) Abstract a hydride ion to form an alkane

68. Choose the false statement for E2 mechanism in elimination reactions.
(a) These reactions are accompanied by rearrangements.
(b) These reactions show a large hydrogen isotope effect.
(c) These reactions show a large element effect
(d) These reactions are not accompanied by hydrogen exchange.

69. Polyamine polystyrene resins belong to which category of ion-exchange resins?
(a) Strongly Acidic Cation Exchange Resins
(b) Strongly Basic Anion Exchange Resins
(c) Weakly Acidic Cation Exchange Resins
(d) Weakly Basic Anion Exchange Resins

70. Which amongst the following auxochromes produces a shift towards higher energy wavelength?
(a) $-CH_3$ (b) $-NHCH_3$
(c) –Cl (d) $-C=0$

71. Chloroform is stored in dark coloured bottles because it is oxidized in presence of light and air to a toxic compound. Identify that.
(a) CH_2Cl_2 (b) $COCl_2$
(c) CO (d) CCl_4

72. Given are the four statements about NMB:
(P) 13CMR is a less sensitive technique than PMR
(Q) Both 13C and: H have 1=1/2
(R) Precessional frequency of the nucleus is directly proportional to the applied magnetic field.
(S) Deuterium exchange studies can be performed to ascertain protons attached to heteroatoms.
Choose the correct combination of statements.
(a) P, Q and R are true while S is false
(b) R, S and Q are true while P is false
(c) S, P and Q are true while R is false
(d) All are true

73. Discrepancies in potential measurements involving factors like 'alkaline error' and 'asymmetry potential' are associated with which of the following electrodes?
(a) Hydrogen electrode
(b) Quinhydrone electrode
(c) Saturated calomel electrode
(d) Glass Electrode

74. What is the wavenumber equivalent of 400 nm wavelength?
(a) 0.0025 cm^{-1} (b) 0.25 cm^{-1}
(c) 2500 cm^{-1} (d) 25000 cm^{-1}

75. All of the given compounds show n —> sigma* transition. Identify which one will have the highest βmax.
(a) Methanol (b) Methylamine
(c) Methyl iodide (d) Methyl bromide

76. Which of the following statements are true for ginseng root?
(P) It is among the most traded plant material of Brazil.
(Q) It is obtained from Panax ginseng and Panax quinquefolium.
(R) It is obtained from young plants of six months to one year age.
(S) It contains derivatives of protopanaxadiol.
(a) P and Q (b) R and S
(c) Q and R (d) Q and S

77. Which of the following alkaloids is derived from tyrosine?
(a) Quinine (b) Morphine
(c) Atropine (d) Ephedrine

78. Anomocytic stomata, trichomes with collapsed cell and absence of calcium oxalate crystals are some of the microscopic features of which plant?
(a) Digitalis (b) Hyoscyamus
(c) Mentha (d) Senna

79. A glycoalkaloid,
(P) Contains sulphur in addition to nitrogen in its molecule.
(Q) Is glycosidic in nature.
(R) Can be hydrolysed to an alkaloid.
(S) Always contains endocyclic nitrogen in its molecule.
Choose the correct option.
(a) P and R (b) Q and S
(c) Q and R (d) P and Q

80. Which of the following drugs is a triterpenoid containing root?

(a) Valerian (b) Brahmi
(c) Satavari (d) Adusa

81. The following options carry the name of the plant, part used and its family. Find a wrong combination.

(a) Aegle marmelos, fruit and Rutaceae
(b) Conium maculatum, fruit and Umbelliferae
(c) Glycyrrhiza glabra, root and stolon and Leguminosae
(d) Strophanthus gratus, seed and Scrophulariaceae

82. Each of the following options lists the name of the drug, its class, pharmacological action and plant source. Choose an option showing a wrong combination.

(a) Asafoetida, oleo-gum-resin, anti-flatulence, Ferula foetida
(b) Benzoin, balsam, antiseptic, Styrax benzoin
(c) Myrrh, gum-resin, antiseptic, Commiphora wightii
(d) Papaine, enzyme, proteolytic, Carica papaya

83. Determine the correctness or otherwise of the following Assertion (A) and the Reason (R).

Assertion (A): Tannins are polyphenohc substances occurring in plant cell sap. Hydrolysable and condensed tannins are differentiated by match stick test.

Reason (R): The condensed tannin are resistant to acid hydrolysis, therefore stain the lignin present in match stick.

(a) Both (A) and (R) are true, and (R) is not the correct reason for (a)
(b) Both (A) and (R) are true, but (R) is not the correct reason for (A)
(c) (A) is true but (R) is not the correct reason for (A)
(d) Both (A) and (R) are false

84. In acetate mevalonate pathway, geranyl pyrophosphate leads to formation of monoterpenes, the major constituents of volatile oils.

(P) Geranyl pyrophosphate contains two isoprene units
(Q) Monoterpenes have 15 carbon atoms
(R) The two isoprene units condense in head to tail fashion to give monoterpenes
(S) Isoprene unit has molecular formula of $C_5 H_8$.

Which one of the given statements is correct?

(a) P is true, Q is false, R is true, S is false
(b) P is false, Q is true, R is true, S is false
(c) P is true, Q is true, R is false, S is true
(d) P is true, Q is false, R is true, S is true

85. Determine the correctness or otherwise of the following Assertion (A) and the Reason (R):

Assertion (A): Castor oil is soluble in alcohol and is used as purgative.

Reason (R): The oil contains ricinoleic acid having a hydroxyl group at C-12 position which is responsible for its solubility in alcohol and its purgative action.

(a) Both (A) and (R) are true but (R) is not the correct reason for (A)
(b) (R) is true but (R) is not the correct reason for (A)
(c) Both (A) and (R) are true and (R) is the correct reason for (R)
(d) Both (A) and (R) are false

86. Which of the following drug does not induce mydriasis?

(a) Atropine (b) Ephedrine
(c) Phentolamine (d) Cocaine

87. Which of the following beta blockers has been shown clinically to reduce mortality in patients of symptomatic heart failure?

(a) Atenolol (b) Carvedilol
(c) Propranolol (d) Esmolol

88. Rhabdomyolysis is the side effect associated with which of the following classes of drugs?

(a) ACE inhibitors
(b) Statins
(c) Calcium channel blockers
(d) Sodium channel blockers

89. Patients taking isosorbide mononitrate or nitroglycerine should be advised not to take sildenafil. This drug-drug interaction causes which of the following actions?

(a) Respiratory failure
(b) Severe hypotension
(c) Prolongation of QT interval
(d) Myocardial ischemia

90. Which of the following statements is true for angiotensin-II?

(a) Causes myocyte hypertrophy
(b) Decreases the action of sympathetic nervous system
(c) Increases force of myocardial contraction
(d) Decreases the synthesis and release of aldosterone

91. All of the given four drugs cause vasodilatation. Choose the correct statement about them.

(P) Bradykinin (Q) Minoxidil
(R) Acetylcholine (S) Hydralazine

(a) P and Q cause release of nitric oxide
(b) Q and R do not cause release of nitric oxide
(c) R and S cause release of nitric oxide
(d) P and S do not cause release of nitric oxide

92. Blood level monitoring of HbAlc is important in which of the given diseased states?
(a) Hypercholesterolemia
(b) Diabetes mellitus
(c) Myocardial infarction
(d) Congestive heart failure

93. Which of the following is the most effective monotherapy for raising HDL cholesterol?
(a) Statins (b) Niacin
(c) Ezetimibe (d) w-3-Fatty acids

94. Which of the following pairs has high binding affinity for Sa-reductase?
(a) Letrozole and androstenedione
(b) Finasteride and testolactone
(c) Finasteride and 5-DHT
(d) Finasteride and testosterone

95. Which is the molecular target for the vinca alkaloids as anti-cancer agent?
(a) Tyrosine kinase (b) DNA
(c) Ribosomes (d) Tubulin

96. A 64 year old woman with a history of Type II diabetes is diagnosed with heart failure. Which of the following would be a poor choice in controlling her diabetes?
(a) Metformin (b) Pioglitazone
(c) Glipizide (d) Exenatide

97. Which of the following parameters from plasma concentration time profile study gives indication of the rate of drug absorption?
(a) Cmax (b) Tmax
(c) AUC (d) tl/2

98. Which of the following skeletal muscle relaxants acts directly on the contractile mechanism of the muscle fibers?
(a) Pancuronium (b) Baclofen
(c) Dantrolene (d) Chlorzoxazone

99. Choose the correct pair of the neurodegenerative disorders from those given below.
(a) Parkinson's disease and Alzheimer's disease
(b) Schizophrenia and Mania
(c) Alzheimer's disease and Schizophrenia
(d) Parkinson's disease and Autism

100. Mifepristone and gemeprost combination is used for medical termination of pregnancy. The action is caused due to which of the following mechanisms?
(a) Mifepristone is an antiestrogen while gemeprost is a prostaglandin E receptor agonist.
(b) Mifepristone is an antiprogestin while gemeprost is a prostaglandin E receptor agonist.
(c) Mifepristone is an antiandrogen while gemeprost is a prostaglandin E receptor agonist.
(d) Mifepristone is an antiprogestin while gemeprost is a prostaglandin E receptor antagonist.

101. Upon standing, sometimes gel system shrinks a bit and little liquid is pressed out. What is this phenomenon known as?
(a) Oozing (b) Syneresis
(c) Shrinking (d) Desolvation

102. Study the following two statements and choose the correct answer:
(P) Antibodies are serum proteins providing immunity.
(Q) IgG provides immunity to new born babies while IgM is the first generated antibody.
(a) P is correct and Q is incorrect
(b) P is incorrect and Q is correct
(c) Both P and Q are correct
(d) Both P and Q are incorrect

103. Non-linear pharmacokinetics can be expected due to
(P) Enzyme induction
(Q) Active secretion
Choose the correct answer.
(a) Both P and Q are true
(b) P is true, Q is false
(c) Q is true, P is false
(d) Both P and Q are false

104. Which of the following statements is incorrect?
(a) Chick Martin test uses organic matter in media
(b) The organism in Rideal-Walker test is S. typhi
(c) Rideal-Walker test uses organic matter in media
(b) The organism in Chick Martin test is S. typhi

105. Which of the following routes of administration of drugs is associated with Phlebitis?
(a) Subcuteneous (b) Intravenous
(c) Intraspinal (d) Intradural

106. Which microbe is used for validation of sterilization by filtration process?
(a) Bacillus stearothermophilus
(b) Pseudomonas diminuta

(c) Bacillus subtilis
(d) Pseudomonas aeruginosa

107. Which wavelength of the UV light provides maximum germicidal action?
(a) 253.7 nm (b) 275.5 nm
(c) 283.5 nm (d) 240.0 nm

108. Which of the following forces contribute to stability of charge-transfer complexes?
(a) Resonance forces
(b) Resonance and London dispersion forces
(c) Dipole-dipole interactions and London dispersion forces
(d) Resonance forces and dipole-dipole interactions

109. Determine the correctness or otherwise of the following statements:
(P) Rheopexy is the phenomenon when a sol forms gel more readily when sheared gently.
(Q) In a rheopectic system, sol is the equilibrium form.
(R) Rheopexy is a phenomenon when a sol forms gel when the material is kept at rest.
(a) (R) is true but (P) and (Q) are false
(b) (P) is true but (Q) and (R) are false
(c) (P), (Q) and (R), all are false
(d) (P), (Q) and (R), all are true

110. Molecules in the smectic liquid crystals are characterized by which one of the following?
(a) Mobility in three directions and rotation in one axis
(b) Mobility in two directions and rotation in one axis
(c) Mobility in two directions and no rotation
(d) Mobility in three directions and no rotation

111. Determine the correctness or otherwise of the following Assertion (A) and the Reason (R):
Assertion (A): For a pharmaceutical powder, true density is greater than the granule density.
Reason (R): Mercury displacement used for determining granule density, allows penetration of liquid into internal pores of the particles.
(a) (A) is true but (R) is false
(b) Both (A) and (R) are false
(c) Both (A) and (R) are true and (R) is the correct reason for (A)
(d) Both (A) and (R) are true but (R) is not the correct reason for (A)

112. Define Plasmapheresis. Choose the correct answer.
(a) The process of collecting plasma and returning the red blood cells concentrate to the donor.
(b) The process of collecting red blood cells concentrate and returning the plasma to the donor.
(c) The process of separating white blood cells from blood.
(d) The process of generating artificial blood plasma expanders.

113. Choose the correct sequence of Moisture Vapour Transmission Rate in packaging materials.
(a) Paper > Aluminium foil > PVC > PVdC
(b) Aluminium foil > PVC > PVdC > Paper
(c) Aluminium foil > PVdC > PVC > Paper
(d) Paper > PVC > PVdC > Aluminium foil

114. What will be the dose required to maintain therapeutic concentration of 20 microgram/ml for 24 h of a drug exhibiting total clearance of 2 L/h?
(a) 96 mg (b) 480 mg
(c) 960 mg (d) 48 mg

115. The Reynolds number widely used to classify flow behaviour of fluids is the ratio of which one of the following?
(a) Inertial forces to gravitational forces
(b) Inertial forces' to viscous forces
(c) Viscous forces to inertial forces
(d) Viscous forces to gravitational forces

116. What for the baffles are provided in a shell and tube heat exchanger?
(a) To increase turbulence
(b) To decrease turbulence
(c) To prevent corrosion
(d) To increase shell side passes

117. Which statement is false for Association Colloids?
(a) They are also called amphiphiles
(b) They contain aggregated molecules
(c) They show partial solvation
(d) They are also called micelles

118. What will be the time required for a drug exhibiting first order rate constant of 4.6/h to be degraded from initial concentration of 100 mg/ml to 10 mg/ml?
(a) 2 h (b) 4 h
(c) 9 h (d) 0.5 h

119. What will be the urine to plasma ratio of a weakly acidic drug having pKa of 5? [Urine (pH = 5) Plasma (pH = 7)]
(a) 1: 101 (b) 1: 201
(c) 2: 101 (d) 1: 202

120. If the distillation graph using McCabe Thiele method is parallel to X-axis, then the feed is which one of the following?

(a) Saturated liquid (b) Saturated vapour
(c) Superheated liquid (d) Superheated vapour

121. SOS means which one of the following?

(a) Take occasionally
(b) Take immediately
(c) Take when necessary
(d) Take as directed

122. Which of the following is not a reciprocating pump?

(a) Plunger pump (b) Diaphragm pump
(c) Gear pump (d) Piston pump

123. Hydrogen peroxide solution (20 volumes) is used topically as a mild antiseptic. It is mainly used for cleaning of wounds which could be due to some of the following actions of hydrogen peroxide.

(P) Astringent action
(Q) Nascent hydrogen releasing action
(R) Oxidizing action
(S) Mechanical cleansing action

Choose the correct statements for the use of hydrogen peroxide as cleaning agent for the wounds.

(a) P and R (b) P and Q
(c) R and Q (d) R and S

124. Boric acid is a weak acid (pKa 9.19) which cannot be titrated with a standard solution of sodium hydroxide using phenolphthalein as indicator. This titration becomes possible on addition of glycerol due to one of the following reactions. Choose the correct reaction.

(a) Boric acid becomes boronic acid on reaction with glycerol.
(b) Boric acid gives a monoprotic tetravalent boron ester with glycerol.
(c) Boric acid gives a tribasic acid on reaction with glycerol.
(d) Two boric acid molecules combine to give an anhydride in presence of glycerol.

125. A tooth paste contains stannous fluoride and calcium pyrophosphate along with other formulation constituents. Choose the correct statement out of the following.

(a) Stannous fluoride is an anticaries agent while calcium pyrophosphate is a dentifrice agent.
(b) Stannous fluoride is a dentifrice while calcium pyrophosphate is a desensitizing agent.
(c) Stannous fluoride is a desensitizing agent while calcium pyrophosphate is an anticaries agent.
(d) Both are dentifrices while calcium pyrophosphate is additionally a desensitizing agent.

126. Magnesium trisilicate is considered to be a better antacid than aluminium hydroxide due to its following additional properties:

(P) It has a fixed chemical composition.
(Q) It forms colloidal silicone dioxide.
(R) Magnesium ions overcome constipation.
(S) Magnesium ions cause higher inhibition of pepsin than aluminium ions.

Choose the correct combination of statements.

(a) Q and S (b) R and S
(c) P and Q (d) Q and R

127. An iron compound used as heamatinic agent must meet two requirements i.e., it should be biologically available and be non-irritating. Which one of the following compounds meet the above two requirements most closely?

(a) Ferric chloride
(b) Ferric ammonium sulphate
(c) Ferric ammonium citrate
(d) Ferrous thioglycollate

128. Diels-Alder reaction can be earned out in which of the following heterocyclic compounds most readily?

(a) Pyrrole (b) Thiophene
(c) Furan (d) Pyridine

129. Determine the correctness or otherwise of the following Assertion (A) and the Reason (R):

Assertion (A): Quaternary ammonium phase transfer catalysts can enhance the rate of nucleophilic aliphatic substitution reactions in biphasic systems with water soluble nucleophiles.

Reason (R): Quaternary ammonium compounds are highly polar, positively charged water soluble compounds.

(a) Both (A) and (R) are true but (R) is not the correct reason for (A)
(b) Both (A) and (R) are true and (R) is the correct reason for (A)
(c) (A) is true (R) is false
(d) Both (A) and (R) are false

130. Pyridine is more basic than pyrrole. This is due to which of the following facts?

(a) Lone pair of electrons on N in pyrrole is localized
(b) Lone pair of electrons on N in pyridine is localized
(c) Nitrogen of pyrrole has one hydrogen atom attached to it while pyridine does not have any
(d) Pyridine has three double bonds while pyrrole has only two

131. In nucleophilic aliphatic substitution reactions arrange the following leaving groups in decreasing order of their leaving capacity.

(P) Brosyl (Q) Hydroxyl
(R) Chloro (S) Mesyl

(a) S>R>P>Q (b) P>S>R>Q
(c) R>Q>S>P (d) R>S>Q>P

132. Which one of the given compounds can be used as primary standard for standardization of perchloric acid solution in non-aqueous titrations?

(a) Potassium hydrogen phthalate
(b) Sodium bicarbonate
(c) Potassium dihydrogen phosphate
(d) Sodium methoxide

133. Following are the desirable properties of the liquid phase used in GLC except for one of the followings. Identify that.

(a) It should be inert to the analyse.
(b) It should have high viscosity at operating temperature
(c) It should have low vapour pressure at the operating temperature
(d) It should have a high resolving power

134. To synthesize sulphonylurea antidiabetics, which of the following reactions can be used?

(a) Reacting a suitably substituted sulphonyl chloride with a desired urea derivative under basic conditions.
(b) Reacting a suitably substituted sulphonamide with a desired isocyanate derivative.
(c) Reacting a suitably substituted sulphonic acid with a desired isocyanate derivative.
(d) Reacting a suitably substituted sulphoxide with a desired urea derivative.

135. In polarography, DME has a number of advantages. One of the advantages is that mercury has large hydrogen overpotential. It means which one of the following?

(a) Hydrogen ions get easily reduced on the DIME
(b) Hydrogen gas gets easily reduced on the DME
(c) Hydrogen ions require high potential to be reduced at DME
(d) Water is difficult to get oxidized at DME

136. In HPLC analysis, what type of column would you prefer?

(a) A column with high HETP and high number of plates
(b) A column with low HETP and low number of plates
(c) A column with high HETP and low number of plates
(d) A column with low HETP and high number of plates

137. In an optically active organic compound, a chiral carbon has the following attached groups:

(P) –CO—CH_3 (Q) –C—OH
(R) –CH = CH_2 (S) –C=CH

Using 'Sequence Rules', choose the correct order of priority of the groups.

(a) Q > P > S > R (b) P > Q > R > S
(c) Q > P > R > S (d) P > Q > S > R

138. Which one is an example of a bulk property detector used in HPLC?

(a) Fluorescence detector
(b) Photo diode array detector
(c) Refractive index detector
(d) UV detector

139. A 250 jig/ml solution of a drug gave an absorbance of 0.500 at 250 nm at a path length of 10 mm. What is the specific absorbance of the drug at 250 nm?

(a) 0.002 cm-1gm-1 litre
(b) 0.002 cm-1gm-1 dl
(c) 20 cm-1gm-1 litre
(d) 20 cm1gm-1dl

140. Following statements are given for a chemical reaction:

Change in Gibb's free energy of the reaction has a negative value.

Change in enthalpy of the reaction has a negative value.

Change in entropy of the reaction has a positive value.

Based on the above statements, choose the correct answer.

(a) The reaction is spontaneous.
(b) The reaction is non-spontaneous.
(c) The reaction could either be spontaneous or non-spontaneous.
(d) The reaction can never be spontaneous.

141. Which of the following statements is wrong?
(a) The energy required for removing an electron from a molecule varies in the given order: Lone pair < Conjugated n < Non conjugated n < a
(b) Isotopic ratio is particularly useful for the detection and estimation of number of S, CI and Br atoms in the compound in MS
(c) Neutral fragments and molecules do not get detected in the detector in MS
(d) The most intense peak in the MS is called the molecular ion peak

142. The protons ortho to the nitro group in p-nitrotoluene are examples of which one of the following types?
(a) Chemically equivalent but magnetically non-equivalent protons
(b) Chemically and magnetically equivalent protons
(c) Chemically and magnetically non-equivalent protons.
(d) Chemically non-equivalent but magnetically equivalent protons

143. The peak at m/z 91 in the mass spectrum for alkylbenzenes is due to which one of the following?
(a) Alpha fission
(b) Mc-Laffartey rearrangement
(c) Retro Diels-Alder rearrangement
(d) Tropylium ion formation

144. Which one of the following is not a bioisostearic pair?
(a) Divalent ether (-0-) and amine (–N-H)
(b) Hydroxyl (-OH) and thiol (-SH)
(c) Carboxylate (C02-) and sulfone (SO2)
(d) Hydrogen (-H) and fluorine (-F)

145. The catalytic triad in acetylcholineesterase is composed of which of the following amino acid residues?
(a) Serine, Histidine and Glutamate
(b) Serine, Arginine and Glutamate
(c) Threonine, Histidine and Aspartate
(d) Threonine, Arginine and Glutamate

146. Which of the following statement is true?
(a) Aliphatic protons have chemical shifts > 7 ppm
(b) Spin quantum number of proton is 1
(c) Chemical shift describes electronic environment of a proton
(d) Vicinal coupling constant is always higher than geminal coupling constant

147. Beta-Carboline ring system is present in
(a) Emetine (b) Riboflavine
(c) Deserpidine (d) d-Tubocurarine

148. Of the four stereoisomers of chloramphenicol, which one is the biologically active isomer?
(a) L-Erythro (b) L-Threo
(c) D-Erythro (d) D-Threo

149. Fajan's method of titrimetric analysis involves detection of the end point on the basis of which one the following?
(a) Colour change
(b) Appearance of a precipitate
(c) Neutralization reaction
(d) Adsorption phenomenon

150. In FT-IR instruments. Michaelson interferometer is used in place of grating. The function of the interferometer is to act as a modulator'. What do you understand by this statement?
(a) The function of the interferometer is to act as a monochromator
(b) The function of the interferometer is to convert high frequency radiations into low ones
(c) The function of the interferometer is to convert low frequency radiations into high ones
(d) The function of the interferometer is to convert frequency domain spectra into time domain spectra

ANSWER KEYS

1. (b)	**2.** (c)	**3.** (a)	**4.** (b)	**5.** (d)	**6.** (a)	**7.** (a)	**8.** (c)	**9.** (b)	**10.** (c)
11. (d)	**12.** (c)	**13.** (a)	**14.** (a)	**15.** (d)	**16.** (a)	**17.** (c)	**18.** (b)	**19.** (c)	**20.** (d)
21. (b)	**22.** (b)	**23.** (d)	**24.** (c)	**25.** (c)	**26.** (c)	**27.** (d)	**28.** (a)	**29.** (c)	**30.** (c)
31. (d)	**32.** (c)	**33.** (d)	**34.** (b)	**35.** (d)	**36.** (b)	**37.** (d)	**38.** (b)	**39.** (b)	**40.** (a)
41. (a)	**42.** (a)	**43.** (a)	**44.** (d)	**45.** (d)	**46.** (a)	**47.** (d)	**48.** (c)	**49.** (d)	**50.** (d)
51. (b)	**52.** (b)	**53.** (c)	**54.** (c)	**55.** (a)	**56.** (a)	**57.** (a)	**58.** (d)	**59.** (c)	**60.** (d)
61. (a)	**62.** (b)	**63.** (a)	**64.** (b)	**65.** (b)	**66.** (a)	**67.** (a)	**68.** (a)	**69.** (d)	**70.** (b)
71. (b)	**72.** (d)	**73.** (a)	**74.** (d)	**75.** (d)	**76.** (d)	**77.** (b)	**78.** (a)	**79.** (b)	**80.** (a)
81. (d)	**82.** (c)	**83.** (b)	**84.** (d)	**85.** (c)	**86.** (c)	**87.** (b)	**88.** (b)	**89.** (b)	**90.** (a)
91. (a)	**92.** (b)	**93.** (b)	**94.** (c)	**95.** (d)	**96.** (b)	**97.** (b)	**98.** (c)	**99.** (a)	**100.** (b)
101. (b)	**102.** (c)	**103.** (a)	**104.** (c)	**105.** (b)	**106.** (a)	**107.** (a)	**108.** (d)	**109.** (b)	**110.** (b)
111. (a)	**112.** (a)	**113.** (c)	**114.** (c)	**115.** (b)	**116.** (a)	**117.** (c)	**118.** (d)	**119.** (b)	**120.** (a)
121. (c)	**122.** (c)	**123.** (a)	**124.** (b)	**125.** (a)	**126.** (d)	**127.** (b)	**128.** (c)	**129.** (b)	**130.** (b)
131. (b)	**132.** (a)	**133.** (b)	**134.** (b)	**135.** (a)	**136.** (d)	**137.** (a)	**138.** (c)	**139.** (d)	**140.** (a)
141. (d)	**142.** (a)	**143.** (d)	**144.** (a)	**145.** (a)	**146.** (c)	**147.** (c)	**148.** (d)	**149.** (a)	**150.** (a)

GPAT PAPER 2010

1. The vitamin essential in tissue culture medium is
(a) Pyridoxine (b) Thiamine
(c) Nicotinic acid (d) Inositol

2. Gingkgo biloba is used for its
(a) Expectorant activity
(b) Lipid lowering activity
(c) PAF antagonistic activity
(d) Antidepressant activity

3. The amount of barbaloin present in Aloe vera is
(a) 1% (b) 3.5–4%
(c) 1–1.5% (d) 2–2.5%

4. Sildenafil is used for treatment of one of the following disorders:
(a) Systolic hypertension
(b) Unstable angina
(c) Pulmonary hypertension
(d) Hypertension due to eclampsia

5. Cardiac glycosides have the following configuration in the Aglycone part of the steroid nucleus:
(a) 5a, 1 4 a– (b) 5a, 14β–
(c) 5β 1 4 a– (d) 5β 14β–

6. Quassia wood is adulterated with
(a) Brucea antidysentrica
(b) Cassia angustifoila
(c) Cinnamomum zeylanicum
(d) Cephaelis ipecacuanaha

7. Eugenol is present in
(a) Fennel (b) Tulsi
(c) Cardamom (d) Coriander

8. Which one of the following drugs is prescribed for the treatment of Philadelphia chromosome positive patients with chronic myeloid Leukemia?
(a) Pentostatin (b) Methotrexate
(c) Imatinib (d) L-Asparaginase

9. Which of the following monoclonal antibodies is prescribed for patients with non-Hodgkin's Lymphoma?
(a) Infliximab (b) Abciximab
(c) Gemtuzumab (d) Rituximab

10. Identify the drug which is not used in the treatment of malaria caused by Plasmodium falciparum.
(a) Artemisinin (b) Primaquine
(c) Quinine (d) Mefloquine

11. Which one of the following drugs does not act through G-Protein coupled receptors?
(a) Epinephrine (b) Insulin
(c) Dopamine (d) TSH

12. Which one of the following drugs is most effective in preventing transmission of HIV virus from the mother to the foetus?
(a) Lamivudine (b) Zidovudine
(c) Indinavir (d) Ribavirin

13. Improvement of memory in Alzheimer's disease is brought about by drugs which increase transmission in
(a) Cholinergic receptors
(b) Dopaminergic receptors
(c) GABAergic receptors
(d) Adrenergic receptors

14. Which of the following non-opioid analgesics is a prodrug?
(a) Piroxicam (b) Celecoxib
(c) Nabumetone (d) Ketorolac

15. Which one of the following drugs is not a typical anti-psychotic agent?
(a) Chlorpromazine (b) Haloperidol
(c) Risperidone (d) Flupentixol

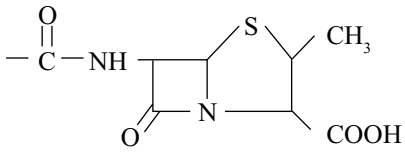
16. Which one of the following is a plasminogen activator?
(a) Tranexamic acid
(b) Streptokinase
(c) Aminocaproic acid
(d) None of the above

17. Myasthenia gravis is diagnosed with improved neuro-muscular function by using
(a) Donepezil (b) Edrophonium
(c) Atropine (d) Pancuronium

18. Which one of the following drugs specifically inhibits calcineurin in the activated T lymphocytes?
(a) Daclizumab (b) Prednisone
(c) Sirolimus (d) Tacrolimus

19. The chemical behaviour of morphine alkaloid is
(a) Acidic (b) Basic
(c) Neutral (d) Amphoteric

20. At physiological pH, the following compound would be mostly in the



(a) Cationic form (b) Unionized form
(c) Zwitterionic form (d) Anionic form

21. Which one of the following is used as a mood stabilizer for bipolar disorder and also in certain epileptic convulsions?
(a) Phenytoin (b) Lithium
(c) Sodium valproate (d) Fluoxetine

22. An isosteric replacement for carboxylic acid group is
(a) Pyrrole (b) Isoxazole
(c) Phenol (d) Tetrazole

23. The given antibiotic is an example of ansamycins:
(a) Roxythromycin (b) Adriamycin
(c) Aureomycin (d) Rifamycin

24. For glyburide, all of the following metabolic reactions are logical except:
(a) O-demethylation
(b) Aromatic oxidation
(c) Benzylic hydroxylation
(d) Amide hydrolysis

25. The effects observed following systemic administration of levodopa in the treatment of Parkinsonism have been attributed to its catabolism to dopamine. Carbidopa can markedly increase the proportion of levodopa that crosses the blood-brain barrier by
(a) Increasing penetration of levodopa through BBB by complexation with it
(b) Decreasing peripheral metabolism of levodopa
(c) Decreasing metabolism of levodopa in the CNS
(d) Decreasing clearance of levodopa from the CNS

26. Ethambutol molecule has
(a) two chiral centers and 3 stereoisomers
(b) two chiral centers and 4 stereoisomers
(c) two chiral centers and 2 stereoisomers
(d) one chiral center and 2 stereoisomers

27. A compound will be sensitive towards IR radiation only when one of the following properties undergo transition on
(a) Polarizability (b) Dielectric constant
(c) Dipole moment (d) Refractivity

28. X-ray crystallographic analysis of an optically active compound determines its
(a) Optical rotatory dispersive power
(b) Absolute configuration
(c) Relative configuration
(d) Optical purity

29. Which one of the following statements is wrong?
(a) A singlet or triplet state may result when one of the electrons from the HOMO is excited to higher energy levels.
(b) In an excited singlet state, the spin of the electron in the higher energy orbital is paired with the electron in the ground state orbital.
(c) Triplet excited state is more stable than the singlet excited state.
(d) When the electron from the singlet excited state returns to ground state, the molecule always shows fluorescence phenomenon.

30. Aminotransferases usually requires the following for their activity:
(a) Niacinamide
(b) Vitamin B12
(c) Pyridoxal phosphate
(d) Thiamine

31. Purity of water can be assessed by determining one of its following properties instrumentally:
(a) pH (b) Refractivity
(c) Viscosity (d) Conductivity

32. Which one of the following statements is wrong?
(a) Carbon NMR is less sensitive than proton NMR
(b) 12C nucleus is not magnetically active
(c) Both 13C and *H have same spin quantum numbers
(d) The gyromagnetic ratio of *H is lesser than that of 1C

33. In the TCA cycle, at which of the following enzyme-catalysed steps, incorporation of elements of water into an intermediate of the cycle takes place?
(a) Citrate synthase
(b) Aconitase
(c) Maleate dehydrogenase
(d) Succinyl Co-A synthase

34. Humectants added in cosmetic preparations generally act by
(a) hydrogen bond formation
(b) covalent bond formation
(c) complex formation
(d) the action of London forces

35. In the mixing of thymol and menthol, the following type of incompatibility occurs:
(a) Chemical incompatibility
(b) Therapeutic incompatibility
(c) Physical incompatibility
(d) Tolerance incompatibility

36. Bloom strength is used to check the quality of
(a) Lactose (b) Ampoules
(c) Hardness of tablets (d) Gelatin

37. The characteristic of non-linear pharmacokinetics includes:
(a) Area under the curve is proportional to the dose
(b) Elimination half-life remains constant
(c) Area under the curve is not proportional to the dose
(d) Amount of drug excreated through remains constant

38. In the Drugs and Cosmetics Act and Rules, the Schedule relating to GMP is
(a) Schedule M (b) Schedule C
(c) Schedule Y (d) Schedule H

39. Thioglycolic acid-like compounds have applications in following type of cosmetic formulations:
(a) Depilatory preparations
(b) Epilatory preparations
(c) Vanishing creams
(d) Skin tan preparations

40. Which one of the following is a flocculating agent for a negatively charged drug?
(a) Aluminium chloride
(b) Bentonite
(c) Tragacanth
(d) Sodium biphosphate

41. The healing agent used in hand creams is
(a) soft paraffin (b) urea
(c) bees wax (d) stearyl alcohol

42. Measurement of inulin renal clearance is a measure for
(a) Effective renal blood flow
(b) Renal drug excretion rate
(c) Active renal secretion
(d) Glomerular filtration rate

43. Highly branched three dimensional macromolecules with controlled structures with all bonds originating from a central core are known as
(a) Cyclodextrins (b) Dextrans
(c) Dendrimers (d) Liposomes

44. Which one of the following is the commonly used bulking agent in the formulation of freeze dried low dose drug products?
(a) Sodium chloride (b) Mannitol
(c) Starch (d) HPMC

45. The applicability of Noyes-Whitney equation is to describe
(a) First order kinetics
(b) Zero order kinetics
(c) Mixed order kinetics
(d) Dissolution rate

46. Which filler can not be used for the preparation of tablets for amine containing basic drugs to avoid discolouration of the tablets?
(a) Dicalcium phosphate
(b) Microcrystalline cellulose
(c) Starch
(d) Lactose

47. The ability of human eye using illuminated area to detect a particle is limited to
(a) 0.4 micron (b) 25 micron
(c) 50 micron (d) 10 micron

48. What quantities of 95% v/v and 45% v/v alcohols are to be mixed to make 800 mL of 65% v/v alcohol?
(a) 480 mL of 95% and 320 mL of 45% alcohol
(b) 320 mL of 95% and 480 mL of 45% alcohol
(c) 440 mL of 95% and 360 mL of 45% alcohol
(d) 360 mL of 95% and 440 mL of 45% alcohol

49. The role of borax in cold creams is
(a) anti-microbial agent
(b) to provide fine particles to polish skin
(c) in-situ emulsifier
(d) antioxidant

50. Choose the right combination:
(a) Quinine, antimalarial, isoquinoline alkaloid
(b) Reserpine, antihypertensive, indole alkaloid
(c) Quantitative microscopy, stomatal number, myrrh
(d) Palmitic acid, salicylic acid, fatty acids

51. Triterpenoids are active constituents of
(a) Jaborandi (b) Rhubarb
(c) Stramonium (d) Brahmi

52. Alkaloids are not precipitated by
(a) Mayer's reagent (b) Dragendroff Reagent
(c) Picric acid (d) Millon's reagent

53. Anisocytic stomata are present in
(a) Senna (b) Digitalis
(c) Belladonna (d) Coca

54. Bacopa monnieri plant belongs to the family
(a) Scrophulariacea (b) Leguminosae
(c) Polygalaceae (d) Rubiaceae

55. Tropane alkaloids are not present in
(a) Datura stramonium
(b) Erythroxylum coca
(c) Duboisia myoporoides
(d) Lobelia inflata

56. Guggul lipids are obtained from
(a) Commiphora molmol
(b) Boswellia serrata
(c) Commiphora wightii
(d) Commiphora abyssinica

57. An example of N-glycoside is
(a) Adenosine (b) Sinigrin
(c) Rhein-8-glucoside (d) Aloin

58. One mg of Lycopodium spores used in quantitative microscopy contains an average of
(a) 94,000 spores (b) 92,000 spores
(c) 90,000 spores (d) 91,000 spores

59. Select the correct combination of drugs for the treatment of patients suffering from Hepatitis C.
(a) Interferon with Ribavirin
(b) Interferon with Zidovudine
(c) Interferon with Stavudine
(d) Interferon with Lamivudine

60. Aliskiren acts by
(a) inhibiting the conversion of Angiotensin I to II
(b) inhibiting the release of rennin
(c) inhibiting the binding of Angiotensin II to the receptor
(d) inhibiting the action of aldosterone

61. Digitalis toxicity is enhanced by co-administration of
(a) Potassium (b) Quinidine
(c) Diuretics (d) Antacids

62. The rate limiting step in cholesterol biosynthesis is one of the following:
(a) LDL-receptor concentration
(b) VLDL secretion
(c) Mevalonic acid formation
(d) Co-enzyme A formation

63. Which one of the following drugs is withdrawn from the market due to torsade de pointes?
(a) Chlorpromazine (b) Astemizole
(c) Haloperidol (d) Domperidone

64. Ganciclovir is mainly used for the treatment of infection caused by
(a) Cytomegalovirus (b) Candida albicans
(c) Herpes zoster virus (d) Hepatitis B virus

65. Identify the one rational combination which has clinical benefit:
(a) Norfloxacin-Metronidazole
(b) Alprazolam-Paracetamol
(c) Cisapride-Omeprazole
(d) Amoxycillin-Clavulanic acid

66. Stevens Johnson syndrome is the most common adverse effect associated with one of the following category of drugs:
(a) Sulphonamides (b) Macrolides
(c) Penicillins (d) Tetracyclines

67. Amitryptyline is synthesized from the following starting material:
(a) Phthalic anhydride
(b) Terephthalic acid
(c) Phthalamic acid
(d) Phthalimide

68. The common structural feature amongst the three categories of anti-convulsant drugs barbiturates, succinimides and hydantoins is
(a) ureide (b) imidazolidinone
(c) dihydropyrimidine (d) tetrahydropyrimidine

69. Nicotinic action of acetylcholine is blocked by the drug
(a) Atropine (b) Carvedilol
(c) Neostigmine (d) d-Tubocurarine

70. Chemical nomenclature of procaine is
(a) 2-Diethylaminoethyl 4-aminobenzoate
(b) N,N-Diethyl 4-aminobenzoate
(c) 4-Aminobenzamidoethyl amine
(d) 4-Amino-2-diethylaminoethyl benzoate

71. Barbiturates with substitution at the following position possess acceptable hypnotic activity:

(a) 1,3-Disubstitution (b) 5,5-Disubstitution
(c) 1,5-Disubstitution (d) 3,3-Disubstitution

72. Selective serotonin reuptake inhibitor is
(a) Imipramine (b) Iproniazide
(c) Fluoxetin (d) Naphazoline

73. Proton pump inhibitors like omeprazole and lansoprazole contain the following ring system:
(a) Pyrimidine (b) Benzimidazole
(c) Benzothiazole (d) Oxindole

74. A metabolite obtained from Aspergillus terreus that can bind very tightly to HMG CoA reductase enzyme is
(a) Fluvastatin (b) Cerivastatin
(c) Lovastatin (d) Somatostatin

75. Cyclophosphamide as anticancer agent acts as
(a) alkylating agent before metabolism
(b)alkylating agent after metabolism
(c) phosphorylating agent after metabolism
(d) DNA intercalating agent

76. Artemisinin contains the following group in its structure:
(a) an endoperoxide (b) an exoperoxide
(c) an epoxide (d) an acid hydrazide

77. Indicate the HPLC detector that is most sensitive to change in temperature:
(a) PDA detector
(b) Refractive Index detector
(c) Electrochemical detector
(d) Fluorescence detector

78. One of the following statements is not true:
(a) Accuracy expresses the correctness of measurement
(b) Precision represents reproducibility of measurement
(c) High degree of precision implies high degree of accuracy also
(d) High degree of accuracy implies high degree of precesion also

79. In thiazides, following substituent is essential for diuretic activity:
(a) Chloro group at position 6
(b) Methyl group at position 2
(c) Sulphamoyl group at position 7
(d) Hydrophobic group at position 3

80. Streptomycin cannot be given orally for treatment of tuberculosis because
(a) it gets degraded in the GIT
(b) it causes severe diarrhoea
(c) it causes metallic taste in the mouth
(d) it is not absorbed from the GIT

81. In organic molecules, fluorescence seldom results from absorption of UV radiation of wavelengths lower than
(a) 350 nm (b) 200 nm
(c) 300 nm (d) 250 nm

82. Glass transition temperature is detected through
(a) X-Ray diffractometery
(b) Solution calorimetery
(c) Differential scanning calorimetery
(d) Thermogravimetric analysis

83. In Gas-Liquid Chromatography, some of the samples need to be derivatized in order to increase their
(a) volatility
(b) solubility
(c) thermal conductivity
(d) polarizability

84. Oxidative phosphorylation involves
(a) Electron transport system
(b) Substrate level phosphorylation
(c) Reaction catalysed by succinic thiokinase in TCA cycle
(d) None of the above

85. Coulter counter is used in determination of
(a) particle surface area
(b) particle size
(c) particle volume
(d) all of the above

86. Drugs following one compartment open model pharmacokinetics eliminate
(a) bi-exponentially (b) tri-exponentially
(c) non-exponentially (d) mono-exponentially

87. The temperature condition for storage of drug products under cold temperature is given as
(a) temperature between 8°C and 25°C
(b) temperature below 20C
(c) temperature at 0°C
(d) temperature between 2cC and S:C

88. Many xenobiotics are oxidized by cytochrome P450 in order to
(a) increase their biological activity
(b) increase their disposition in lipophilic compartments of the body
(c) increase their aqueous solubility
(d) all of the above

89. The following protein/polypeptide has a quaternary structure:
(a) cc-Chymotrypsin (b) Hemoglobin
(c) Insulin (d) Myoglobin

90. Drugs in suspensions and semi-solid formulations always degrade by
(a) first order kinetics (b) second order kinetics
(c) zero order kinetics (d) non-linear kinetics

91. In nail polish, the following polymer is used as a film-former:
(a) Nitrocellulose
(b) Polylactic acid
(c) Hydroxypropyl methylcellulose
(d) Cellulose acetate phthalate

92. Rabies vaccine (living) is prepared using
(a) Sheep blood (b) Mice lymph
(c) Horse plasma (d) Fertile eggs

93. A drug (200 mg dose) administered in tablet form and as intravenous injection (50 mg dose) showed AUG of 100 and 200 microgram h/mL, respectively. The absolute availability of the drug through oral administration is
(a) 125% (b) 250%
(c) 12.5% (d) 1.25%

94. Geriatric population should be included in the following phase of clinical trials:
(a) Phase I (b) Phase II
(c) Phase III (d) Phase IV

95. Class 100 area is referred to
(a) Manufacturing area (b) Aseptic area
(c) Clean room (d) Ware house

96. How many mL of a 1:500 w/v stock solution should be used to make 5 litres of 1:2000 w/v solution?
(a) 750 mL (b) 1000 mL
(c) 1250 mL (d) 1500 mL

97. The volume of distribution of a drug administered at a dose of 300 mg and exhibiting 30 microgram/mL instantaneous concentration in plasma shall be
(a) 10 L (b) 100 L
(c) 1.0 L (d) 0.10 L

98. It is required to maintain a therapeutic concentration of 10 microgram/mL for 12 hours of a drug having half life of 1.386 h and Vd of 5 L. The dose required in a sustained release product will be
(a) 600 mg (b) 300 mg
(c) 30 mg (d) 60 mg

99. Which one of the following is not an ex-officio member of Pharmacy Council of India?
(a) The Director General of Health Services
(b) The Director of Central Drugs Laboratory
(c) The Drugs Controller General of India
(d) The Director of Pharmacopoeia Laboratory

100. In which of the following techniques, the sample is kept below triple point?
(a) Lyophilization (b) Spray drying
(c) Spray congealing (d) Centrifugation

ANSWER KEYS

1. (b)	**2.** (c)	**3.** (b)	**4.** (c)	**5.** (d)	**6.** (b)	**7.** (b)	**8.** (c)	**9.** (d)	**10.** (b)
11. (b)	**12.** (b)	**13.** (a)	**14.** (c)	**15.** (c)	**16.** (b)	**17.** (b)	**18.** (d)	**19.** (b)	**20.** (d)
21. (b)	**22.** (d)	**23.** (d)	**24.** (b)	**25.** (b)	**26.** (b)	**27.** (c)	**28.** (b)	**29.** (c)	**30.** (c)
31. (d)	**32.** (d)	**33.** (c)	**34.** (a)	**35.** (c)	**36.** (d)	**37.** (c)	**38.** (a)	**39.** (a)	**40.** (a)
41. (a)	**42.** (d)	**43.** (c)	**44.** (b)	**45.** (d)	**46.** (d)	**47.** (d)	**48.** (b)	**49.** (a)	**50.** (b)
51. (d)	**52.** (d)	**53.** (c)	**54.** (a)	**55.** (d)	**56.** (c)	**57.** (a)	**58.** (a)	**59.** (b)	**60.** (b)
61. (b)	**62.** (c)	**63.** (b)	**64.** (a)	**65.** (d)	**66.** (a)	**67.** (b)	**68.** (a)	**69.** (d)	**70.** (a)
71. (b)	**72.** (c)	**73.** (b)	**74.** (c)	**75.** (b)	**76.** (a)	**77.** (b)	**78.** (c)	**79.** (c)	**80.** (d)
81. (a)	**82.** (c)	**83.** (d)	**84.** (a)	**85.** (d)	**86.** (d)	**87.** (d)	**88.** (d)	**89.** (b)	**90.** (c)
91. (a)	**92.** (d)	**93.** (c)	**94.** (c)	**95.** (b)	**96.** (c)	**97.** (a)	**98.** (a)	**99.** (d)	**100.** (a)

MOCK TEST - I

1. Colchicine is biogenetically derived from one of the following
(a) Tyrosine and Phenylalanine
(b) Tryptophan and phenylalanine
(c) Ornithine and Tryptophan
(d) Ornithine and phenylalanine

2. The diagnostic character for the microscopically identification of Kurchi bark is
(a) Fibers with Y-shaped pits
(b) Horse shoe shaped stone cells
(c) steroids containing calcium oxalate crystals
(d) Stratified cork

3. It is possible to initiate the development of complete plants from callus cell Cultures by suitable manipulation of the medium with respect to
(a) Minerals (b) Vitamins
(c) Carbohydrates (d) Hormones

4. Polyploidy is defined as
(a) Addition of one chromosome
(b) Multification of entire chromosome set
(c) Submicroscopic change in DNA material
(d) Gross structural change

5. The starting material for the synthesis of ALPRAZOLAM is
(a) 3-amino-5-bromoactophenone
(b) 2-amino-5-chloroactophenone
(c) 2-amino-5-chlorobenzophenone
(d) 3-amino-5-chlorobenzophenone

6. Simplification of Morphinan system gave one BENZOMORPHAN derivative
(a) Pentazocin (b) Pethidine
(c) Levorphanol (d) Buprenorphine

7. A metabolite of SPIRONOLACTONE is
(a) Aldosterone (b) Canrenone
(c) Corticosterone (d) Pregnenolone

8. The IUPAC name for NAPROXEN is
(a) (S)-2-(6-ethoxy-2-naphthyl)-acetic acid
(b) (S)-2-(6-methoxy-2-naphthyl)-acetic acid
(c) (S)-2-(6-ethoxy-2-naphthyl)-propionic acid
(d) (S)-2-(6-methoxy-2-naphthyl)-propionic acid

9. The metabolic function of Riboflavin involves the following
(a) FMN and FAD (b) NADP and NADPH
(c) AMP and ATP (d) Retin and Retinine

10. X-ray spectral lines Kα doublet arises from transition of electrons from
(a) M shell to K shell (b) L shell to K shell
(c) L shell to M shell (d) M shell to K shell

11. The method of expressing magnetic field strength
(a) Cycles/sec (b) Pulses/sec
(c) Debye units (d) Gauss

12. A solvent used in NMR
(a) Chloroform
(b) Acetone
(c) Carbon tetrachloride
(d) Methanol

13. A widely accepted detector electrode for pH measurement is
(a) Platinum wire (b) Glass electrode
(c) Ag-AgCl electrode (d) Lanthanum fluoride

14. Commercial production of citric acid is carried out by the microbial culture of
(a) Fusarium moniliformi
(b) Rhizopus nigrican
(c) Aspergillus Niger
(d) Candida utilis

15. For thermophilic micro-organisms, the minimum growth temperature required is
(a) 20°C (b) 37°C
(c) 45°C (d) 65°C

16. Obligatory anaerobes
(a) Can tolerate oxygen and grow better in its presence
(b) Do not tolerate oxygen and die in its presence
(c) Can grow in oxygen levels below normal
(d) Can grow in presence of atmospheric oxygen

17. Plasmid is a
(a) Macromolecule involved in the protein synthesis
(b) Circular piece of duplex DNA
(c) A hybrid DNA that is formed by joining pieces of DNA
(d) Endogenous substance secreted by one type of cell

18. Lactose intolerance is because of the lack of
(a) Acid phosphates
(b) Lactate dehydrogenase
(c) Galactose-1-phosphate-uridyl transferase
(d) Amylase

19. Synthesis of UREA takes place exclusive in
(a) Kidney (b) Liver
(c) Gall bladder (d) Urinary bladder

20. A term which describes a cofactor that is finally bound to an enzyme
(a) Holoenzyme (b) Prosthetic
(c) Coenzyme (d) Transferase

21. How many parts of 10 % ointment be mixed with 2 parts of 15 % ointment to get 12% ointment
(a) 2 (b) 3
(c) 5 (d) 6

22. The correct non-ionic surfactant used as a penetration enhancer in the preparation of mucoadhasives
(a) Oleic acid (b) Tween-80
(c) Glycerol (d) Propylene glycol

23. One of the ex-officio member of the Pharmacy Council of India is
(a) Director General of Health Services
(b) Government Analyst
(c) Registrar of the State Pharmacy Council
(d) Director General of veterinary Research Institute

24. The Schedule in Drugs and Cosmetics Act that deals with the requirements and guidelines for clinical trials, import and manufacture of new drugs is
(a) Schedule 'O' (b) Schedule 'M'
(c) Schedule 'F' (d) Schedule 'Y'

25. A retardant material that forms a hydrophilic matrix in the formulation of matrix tablets is
(a) H.P.M.C (b) C.A.P
(c) Polyethylene (d) Carnauba wax

26. A drug which causes pink to brownish skin pigmentation within a weeks of the initiation of the therapy is
(a) Itraconazole (b) Clofazimine
(c) Lomefloxacin (d) Neomycin

27. The risk of Digitalis toxicity is significantly increased by concomitant administration of
(a) Triamterene (b) Lidocaine
(c) Captopril (d) Hydrochlorothiazide

28. An agent used in Prinzmetal angina has spasmolytic action which increases coronary blood supply is
(a) Nitroglycerine (b) Nifedipine
(c) Timolol (d) Isosorbide mononitrate

29. An organism which has been implicated as a possible cause of chronic gastritis and peptic ulcer is
(a) *Campylobacter Jejuni*
(b) *Escherichia Coli*
(c) *Helicobacter pylori*
(d) *Giardia lambia*

30. A 5HT1D receptor agonist useful in migraine is
(a) Sumatriptan (b) Ketanserin
(c) Ergotamine (d) Methysergide

31. At present, different species of Papaver such as P. orientale are being cultivated instead of *P. somniferum* because they contain
(a) More of morphine (b) Less of morphine
(c) Only codeine (d) Only thebaine

32. Guggulipid, a resin is
(a) A hypolipidemic agent obtained from cotton plants containing multifunctional compound (±) Gossypol
(b) A lipid obtained from Arctium lappa, Asteracese traditionally used for the treatment of dermatoses
(c) Cathartic glucoresin obtained from Ipmoea orizabensis and used since ancient time
(d) A hypolipidemic agent obtained from Commiphora mukul consisting of mixture of sterols including Z-pregna-(20)-diene-3, 16-diene

33. In nitrofuantion synthesis, 5-nitrifurfuraldehyde diacetate is treated with one of the following intermediate in presence of $CH_2COOH+H_2SO_4+C_2H_2OH$
(a) Hydantoin
(b) 1-5-diamino hydantoin
(c) 1-3-diamino hydantoin
(d) 1-amino-hydantoin

34. 4-hydroxy-3-hydroxymethyl benzaldehyde is treated with acetic anhydride and then kept with other solvent, t-butyl cyanide and acetic acid for ten days. Resulting compound is reduced with LiAIH4 in tetra hydrofuran. The final product is

(a) Isoprenaline (b) Dobutamine
(c) Salbutamol (d) Orciprenaline

35. 2-iminothiazolidine is treated with phenyl oxirane to get a drug used in roundworm infection

(a) Piperazine (b) Tetramisole
(c) Thiabendazole (d) Levamisole

36. Thiamine hydrochloride on treatment with alkaline potassium ferricyanide gives

(a) Thymochrome with fluorescence
(b) Oxythiamine with golden yellow color
(c) Neopyrithiamine with orange yellow color
(d) Thiochrome with blue fluorescence

37. A new drug delivery system which is composed of phospholipids that spontaneously form a multiamellar, concentric bilayer vesicles with layers of aqueous media separating the lipid layers is

(a) Prodrugs (b) Liposomes
(c) Osmotic pumps (d) Nanoparticles

38. Unless otherwise stated in the individual monograph of the pharmacopeia, in the disintegration test for enteric coated tablets, first the dissolution is carried out in

(a) 0.1 MHCI (b) Phosphate buffer
(c) Water (d) 0.1 MH_2SO_4

39. What us the proportion of NaCl required to render a 1.5% solution of drug isotonic with blood plasma? The freezing point of 1% w/v solution of drug is -0.122^{0}C and that of NaCl is -0.576^{0}C

(a) 0.65% (b) 0.585%
(c) 0.9% (d) 0.5%

40. IR Spectra appear as dips in the curve rather than maxima as in UV-Visible spectra because it is a plot of

(a) % Absorbance against wave no.
(b) % Transmittance against concentration
(c) % Absorbance against Concentration
(d) % Transmittance against wave no

41. ESR is applied to only those substances showing para magnetism which is due to the magnetic moments of

(a) Neutrons (b) Protons
(c) Paired electrons (d) Unpaired electron

42. Rotation of electrons about the proton generates a secondary magnetic field which may oppose the applied magnetic field. The proton is then said to be

(a) Shielded (b) Shifted
(c) Hydrogen (d) Deshielded

43. The analyte is used in the form of a solution flame photometry because it should undergo

(a) Evaporation (b) Condensation
(c) Nebulization (d) Precipitation

44. Isoniazid is a primary anti-tubercular agent that

(a) Requires pyridoxine supplementation
(b) Causes ocular complication that are reversible if the drug is discontinued
(c) Is ototoxic and nephrotoxic
(d) Should never be used due to its hepatotoxicity

46. Decreased risk of Atherosclerosis is associated with increase in

(a) Very-low-density lipoproteins
(b) Low-density
(c) Cholesterol
(d) High-density

47. The mechanism of action of Paclitaxel is

(a) Bing to DNA through intercalation between specific bases and block the synthesis of new RNA or DNA, cause DNA strand scission
(b) Mitotic spindle poison through the enhancement of tubulin polymerization
(c) Competitive partial agonist-inhibitor of estrogen and binds to estrogen receptors
(d) S-Phase specific antimetabolite that is converted by deoxy kinase to the 5'-monoucleotide

48. Lycopodium spore method can be used to find out percentage purity of crude drug which contain

(a) Multi-layered tissues or cells
(b) Well defined particles which can be counted
(c) Oil globules
(d) Characteristic particles of irregular thickness the length of which can measured

49. The microscopical character flower buds of *Eugenia caryophyllus* is

(a) Collenchymatous parenchyma containing in its outer part numerous ellipsoidal schizolysigenous oil glands
(b) Small translucent endosperm containing aleurone grains

(c) Wide parenchymatous starchy cortex, the endosperm containing volatile oil
(d) Outer surface consisting of external perisperm, rough, dark brown with reticulate furrows

50. In protein blosynthesis, each amino acid
(a) Recognises its own codon by a direct interaction with the m-RNA template
(b) Is added in its proper place to a growing peptide chain through "adaptor" function of t-RNA
(c) Is first attached to an anti codon specific for the amino acid
(d) Undergoes fidelity translation which is assured by the presence of traces of DNA on the ribosome

51. Starting material for the synthesis of L-Thyroxine is
(a) 2-amino-5-chloro-acetophenone
(b) Phenylalanine
(c) 5-amino-2-chloro-acetophenone
(d) L-tyrosine

52. One of the following antianxiety agent is an azaspirodecanedione derivative.
(b) Lorazepam (b) Cycloheptadiene
(c) Meprobamate (d) Buspirone

53. Include the following drug under proper classification. NIFEDIFINE
(a) Quinoline derivative
(b) Aryl piperidine
(c) Isoquinoline derivative
(d) Pyridine derivative

54. Acetazolamide can be synthesized from on of the following intermediates.
(a) 5-amino-2-mercapto-1,3-thiazole
(b) 5-amino-2-mercapto-1,3,4-thiadiazole
(c) 5-amino-2-mercapto-1,2,3-thiadiazole
(d) 5-amino-2-mercapto-1,3,4-tetrazole

55. Choose the correct trichomes of *Digitalis purpurea*
(a) Numerous covering trichomes and a few glandular trichomes
(b) Few covering trichomes
(c) Few glandular trichomes and few covering trichomes
(d) Few glandular trichomes

56. PANAXADIOL is a constituent of
(a) Ginger (b) Jatamansi
(c) Ginseng (d) Pepper

57. The plant hormone which shows specific effect on the cell division is
(a) Auxins (b) Abscisic Acid
(c) Cytokinins (d) Ethylene

58. One of the following condition is maintained in programmed temperature gas chromatography
(a) Temperature of the whole column is raised during analysis
(b) Temperature at the Sample injection system is raised
(c) Temperature at the detector is gradually raised
(d) Temperature at the recorder alone is raised

59. A BOLOMETER consist of
(a) Two metals welded together
(b) A thin blackened platinum strip in an evacuated vessel
(c) Deuterated triglycine sulphate
(d) Tungsten

60. Choose the correct excepient for enhancing solubility in tablet manufacture.
(a) PEG (b) Microcrystalline cellulose
(c) Talc (d) Lactose

61. Two or more ions present together can be determined successfully by polarograph even if their half wave potentials overlap or interfere by
(a) Titration (b) Complexation
(c) Filtration (d) Heating

62. One of the following is selective. SEROTONIN reuptake inhibitor
(a) Despramine (b) Fluoxetine
(c) Buspropion (d) Maprotiline

63. Plasmodial resistance of CHLOROQUINE is due to
(a) Induction of inactivating enzymes
(b) Change in receptor structure
(c) Increase in the activity of DNA repair mechanism
(d) Decreased carrier-mediated drug transport

64. One of the following actions of opioid analgesic is mediated via kappa receptors
(a) Cerebral vascular dilation
(b) Euphoria
(c) Spinal analgesia
(d) Physical dependence

65. One of the following drugs has activity against Herpes simplex virus type I and is used topically. Systematic administration of the same results in bone marrow depression, hepatic dysfunction and nephrotoxity.
(a) Acyclovir (b) Amantadine
(c) Vidarabine (d) Idoxuridine

66. A woman has to be treated for upper respiratory tract infection. Six years back she was found hypersensitive to penicillin V. The cultures now reveal a strain of Streptococcus pneumonia that is sensitive to all of the following drugs. Which one would be the best choice for the patient

(a) Amoxicillin (b) Erythromycin
(c) Cefaclor (d) Cyclacillin

67. The units of measurement for conductance is

(a) Ohms (b) Amperes
(c) mhos (d) Mili volts

68. The shells of soft gelatin capsules made elastic or plastic like, by addition of

(a) Sorbitol (b) Povidone
(c) PEG (d) HPMC

69. The rate of drug bioavailability is most rapid when the drug is formulated as a

(a) Controlled release product
(b) Hard gelatin capsule
(c) Tablet
(d) Solution

70. The loading dose of a drug is usually based on

(a) Total body clearance of the drug
(b) Percentage of the drug bound to plasma proteins
(c) Fraction of drug excreted unchanged in urine
(d) Apparent volume of distribution and desired drug concentration in plasma

71. Browne's tubes are most commonly used chemical indicator for

(a) Ethylene oxide sterilization
(b) Radiation sterilization
(c) Heat process sterilization
(d) Filtration sterilization

72. A specimen obtained from a patient's cerebrospinal fluid, cultured in specialized media for about five weeks showed the presence of bent rods and tested positive with Ziehl-Neelsen reagent. Identify the organism

(a) Nesseria meningitides
(b) Mycobacterium tuberculosis
(c) Bacteroides fragilis
(d) Leptospira interrogans

73. Staphylococcus aureus is used for the I.P. assay of

(a) Doxycycline (b) Bleomycin
(c) Kanamycin (d) Carbenicillin

74. State pharmacy council should have the following number of elected members

(a)Six (b) Nine
(c) Five (d) Seven

75. Drug combination WARFARIN/VITAMIN-K results in a specific interaction. Identify.

(a) Antagonistic
(b) Increased sedation
(c) No known interaction
(d) Harmful only in the presence of oxidizing agent

76. In the glucuronidation reaction of OXAZEPAM-the functional group responsible is

(a) OH (b) COOH
(c) SH (d) NH2

77. Benzhydryl bromide when treated with 2-dimethyl amino ethanol in presence of K_2CO_3 gives one of the following

(a) 2-diphenyl ethoxy-N,N-dimethylethylamine
(b) 2-diphenyl methoxy-N,N-diethylethylamine
(c) 2- diphenyl methoxy-N,N-dimethylethylamine
(d) 2-diphenyl methoxy-N,N-diethylethylamine

78. Demeclocycline differs from Chlortetracycline only by

(a) Absence of methyl group on C_6
(b) Absence of OH group on C_6
(c) Absence of dimethylamino group on C_4
(d) Absence of OH group on C_3

79. Choose the IUPAC name for Carbamazepine

(a) 5[3-(dimethylamino)ethyl] 10-11 dihydro-5Hdibenz [b, f]azepine
(b) 5H dibenz[b, f] azepine-5-carboxamide
(c) 5H dibenz[b, f] azenpine-5-acid chloride
(d) 5[3-(dimethylamino)propyl]10-11 dihydro-5Hdibenz[b,f]azenpine

80. Reserpine is derived from

(a) Squalene
(b) Homoserine
(c) Tryptophan and tryptamine
(d) Asparazine

81. An alkaloid from Atropa belladone having the molecular formula $C_{17}H_{23}O_3N$ having α-$D22^0$ when warmed with ethanolic alkaline solution is converted into

(a) (-) Hyoscyamine (b) (±) Hyomoserine
(c) (+) Hyoscyamine (d) (±) Hyoscine

82. Choose the appropriate description for Ergot
(a) Loosely arranged or in small more or less agglutinated angular mass
(b) A pseudoparenchyma formed by the interwooving closely appressed compact septate hyphae
(c) The crystocarps have fallen out leaving corresponding oval perforations in the ramuli
(d) Colourless septate hyphae about one quarter the width of the cotton trichome and they become twisted together

83. Characteristic bands observed in the IR spectra of alcohol result from
(a) OH and CO stretching
(b) OH stretching
(c) CO stretching only
(d) CH bending only

84. Bulking agent used for parenteral preparation is
(a) Sodium metabisulphide
(b) Benzyl alcohol
(c) Carbolic acid
(d) Sorbitol

85. Identify the correct non-flammable propellant
(a) Trichloromonofluoromethane
(b) Dichloromonofluoromethane
(c) Dimethylether
(d) Difluoromethane

86. Elastomer used in rubber stopper formulation is
(a) Polybutadiene (b) Butyl Stearate
(c) Titanium Dioxide (d) Butylated hydroxyl toluene

87. Schedule D as per D & C Act is concerned with
(a) List of drugs exempted from the provision of import of drugs
(b) Diseases or ailments which a drug may not purport to prevent or cure
(c) Requirements of factory premises
(d) List of prescription drugs

88. Official method for the analysis of Ciprofloxacin is by
(a) Potentiometry
(b) HPLC
(c) Gas Chromatography
(d) Non-aq. Titration

89. The radiofrequency radiation is associated with
(a) Light consisting of one colour only
(b) Nuclear Magnetic Resonance
(c) Mass Spectrometry
(d) ESR

90. How many grams of drug should be used in preparing 500 ml of a 1:2500 solution
(a) 0.2 (b) 0.02
(c) 0.4 (d) 1.25

91. The pyroelectric detector converts electromagnetic radiation into
(a) Electrical Signal (b) Fluoroscence
(c) Electrons (d) Visible light

92. The mechanism of Digitalis is
(a) Decreases intracellular Na concentration
(b) Inhibits Na-K ATPase
(c) Activated adenyl cyclase which produces c-AMP
(d) Decreased Release of Calcium from Sarcoplasmic reticulum

93. The mechanism of action for Dactinomycin is
(a) Inhibits Topoisomerase II
(b) Cross links DNA
(c) Inhibits functions of microtubules
(d) Inhibits DNA Polymerase

94. One of the drugs when coadministered with Terfenadine may lead to life threatening Cardiac dysarrythmia
(a) Lomafloxacine (b) Clofazimine
(c) Itraconazole (d) Neomycin

95. Adverse effects of one of the drug include amenorrhea, bone marrow depression gastrointestinal distress and haemorrhagic distress. Identify?
(a) Cyclizine (b) Piroxicam
(c) Cyclophosphamide (d) Cimetidine

96. Varicella zoster is the causative organism for
(a) Small Pox (b) Dermatophytosis
(c) Herpes (d) Infectious mononucleosis

97. One of the following is confirmed by diagnosis test
(a) Hyperuricemia (b) Cystic fibrosis
(c) Acute pancreatitis (d) Hyperlipidemia

98. The conversion of fructose 1,6-biphosphate to Glyceraldehyde-3-phosphate is catalysed by
(a) Phosphoglycerate kinase
(b) Enolase
(c) Aldolase
(d) Triosephosphate isomerase

99. Morphine undergoes microsomal oxidation by
(a) N-dealkylation
(b) Aromatic hydroxylation
(c) Oxidative deamination
(d) O-dealkylation

100. SULFASALAZINE is a prodrug that is activated in the intestine by bacterial enzymes
(a) Azoreductase
(b) Choline esterase
(c) Glucuronyl transferase
(d) Amylase

101. Which of the following metals has no therapeutic use?
(a) Lead (b) Lithium
(c) Gold (d) Platinum

102. Anti-asthamatic agent which is not a mast cell stabillizer
(a) Ketotifen (b) Terbutaline Sulftate
(c) Nedocromil (d) Sodium Chromoglycate

103. The drug which was used as 'LIE DETECTOR' during the Second world war is
(a) Nitrous Oxide (b) Chloroquine
(c) Carbamazepine (d) Hyoscyine

104. Choose the "Cholineesterase reactivator"
(a) Atropine (b) Pralidoxime
(c) Pirenzepine (d) Ipratropium

105. Which one of the following is used in treatment of Ulceratice Colitis?
(a) Sulfasalazine (b) Mesalazine
(c) Olsalazine (d) All of the above

106. A source of anitcarcinogenic drug is
(a) Belladona (b) Nux vomica
(c) Vinca rosea (d) Cascara

107. Organic nitrates are not very useful in acute angina attacks because they
(a) are insoluble
(b) can only be given orally
(c) cause very severe side effects
(d) must be biconverted before being active

108. Which one of the following interacts with vasopressin
(a) Chloramphenicol (b) Diphenylhydantoin
(c) Chlorpropamide (d) Dicumarol

109. Choose the correct statement
(a) Quinine and Quindine are dextrorotatory, cinchonine and cinchonidine are levorotatory
(b) Quinine and Quindine are levorotatory, cinchonine and cinchonidine are Dextrorotatory
(c) Quinine and cinchonidine are levorotatory, Quindine and cinchonine are dextrorotatory
(d) Quinine and cinchonine are dextrorotatory, Quindine and cinchonidine are Levorotatory

110. Ergotoxine is a mixture of
(a) 2 alkaloids (b) 3 alkaloids
(c) 4 alkaloids (d) 6 alkaloids

111. The active constituents of cassia bark consists of all of the following EXCEPT
(a) Cinnamic acid (b) Caryophylline
(c) Eugenol (d) Coumarin

112. Tropane is
(a) 6, 7 epoxy tropane
(b) 3 α - hydroxy tropine
(c) 3 β - hydroxy tropine
(d) 3 apatropine

113. Cyanogenetic glycosides are
(a) S – Glycosides (b) O – Glycosides
(c) C – Glycosides (d) N – Glycosides

114. Which of following test is for Deoxy sugar contain cardiac glycoside?
(a) Baljest test
(b) Legal test
(c) Libermann's Sterol Test
(d) Killer-killani test

115. One of the following is used in preparing grating:
(a) Iron (b) Teflon
(c) Aluminium (d) Glass

116. Fellgett advantage is due to:
(a) FTIR (b) UV
(c) Mass spectroscopy (d) IR

117. The region of electromagnetic spectrum below 200 nm is:
(a) Vaccum UV (b) Far UV
(c) Low UV (d) Microwave region

118. The role of borax in cold creams is
(a) Anti-microbial agent
(b) To provide fine particle to polish skin
(c) in-situ emulsifier
(d) Antioxidant

119. Geiger Muller counter is filled with
(a) Helium (b) Argon
(c) Krypton (d) Xenon

120. Radiation source in Atomic absorption spectroscopy is:
(a) Deuterium lamp
(b) Lasers
(c) Hollow cathode lamp
(d) Mercury lamp

121. Which of the following drugs is NOT a typical antipsychotic agent?
(a) Chlorpromazine (b) Haloperidol
(c) Resperidone (d) Flupentixol

122. Myasthenia gravis is diagnosed with improved neuromuscular function by using
(a) Donepezil (b) Edrophonium
(c) Atropine (d) Pancuronium

123. Which one of the following drugs specially inhibits calcineurin in the activated T Lymphocytes?
(a) Daclizumab (b) Prednisone
(c) Sirolimus (d) Tacrolimus

124. The chemical behaviour of morphine alkaloid is
(a) Acidic (b) Basic
(c) Neutral (d) Amphoteric

125. Which one of the followingis used as a mood stabilizer for bipolar disorders and also in certain epilieptic convulsions?
(a) Phenytoin (b) Lithium
(c) Sodium valproate (d) Fluoxetine

ANSWER KEYS

1. (a)	**2.** (b)	**3.** (d)	**4.** (b)	**5.** (c)	**6.** (a)	**7.** (b)	**8.** (d)	**9.** (a)	**10.** (b)
11. (d)	**12.** (c)	**13.** (b)	**14.** (c)	**15.** (c)	**16.** (b)	**17.** (b)	**18.** (c)	**19.** (b)	**20.** (b)
21. (b)	**22.** (b)	**23.** (a)	**24.** (d)	**25.** (a)	**26.** (b)	**27.** (d)	**28.** (b)	**29.** (c)	**30.** (a)
31. (a)	**32.** (d)	**33.** (d)	**34.** (c)	**35.** (c)	**36.** (d)	**37.** (b)	**38.** (a)	**39.** (b)	**40.** (d)
41. (d)	**42.** (a)	**43.** (c)	**44.** (c)	**45.** (a)	**46.** (d)	**47.** (b)	**48.** (b)	**49.** (a)	**50.** (b)
51. (b)	**52.** (d)	**53.** (b)	**54.** (b)	**55.** (d)	**56.** (c)	**57.** (a)	**58.** (a)	**59.** (b)	**60.** (a)
61. (a)	**62.** (b)	**63.** (d)	**64.** (c)	**65.** (d)	**66.** (c)	**67.** (c)	**68.** (a)	**69.** (d)	**70.** (d)
71. (c)	**72.** (a)	**73.** (a)	**74.** (a)	**75.** (a)	**76.** (a)	**77.** (c)	**78.** (a)	**79.** (b)	**80.** (c)
81. (a)	**82.** (b)	**83.** (b)	**84.** (d)	**85.** (b)	**86.** (b)	**87.** (a)	**88.** (b)	**89.** (b)	**90.** (a)
91. (a)	**92.** (b)	**93.** (a)	**94.** (c)	**95.** (c)	**96.** (a)	**97.** (b)	**98.** (a)	**99.** (a)	**100.** (a)
101. (a)	**102.** (b)	**103.** (b)	**104.** (b)	**105.** (a)	**106.** (c)	**107.** (c)	**108.** (c)	**109.** (c)	**110.** (b)
111. (d)	**112.** (a)	**113.** (d)	**114.** (d)	**115.** (c)	**116.** (a)	**117.** (a)	**118.** (c)	**119.** (b)	**120.** (c)
121. (c)	**122.** (b)	**123.** (d)	**124.** (d)	**125.** (b)					

MOCK TEST - II

1. The entropy of a pure crystal is zero at absolute zero. This is a statement of
(a) First law of thermodynamics
(b) Second law of thermodynamics
(c) Third law of thermodynamics
(d) None of these

2. Parachor is having properties of
(a) Additive (b) Constitutive
(c) Both a & b (d) None of the above

3. Hofmann elimination is observe in
(a) Quaternary ammonium hydroxide
(b) Phosphonium hydroxide
(c) Haloalkane
(d) Both a and b.

4. Which drug block coupling of Acetyl Choline and large electrochemical gradient?
(a) Hemicholinium (b) Vesamicol
(c) Botulinum (d) Neostigmine

5. Which of following drug is used to terminate Paroxymal superventricular tachycardia?
(a) Methacholine (b) Bathanechol
(c) Triptamine (d) All of the above

6. Which of following drug is used in post operative non obstructive urinary retention?
(a) Methacholine (b) Bathanechol
(c) Triptamine (d) All of the above

7. Only organophosphate, which is not lipid soluble is
(a) Echothiophate (b) Tabun
(c) Tacrine (d) Soman

8. pH of Buffer system is calculated using
(a) pH Partition theory
(b) Michaelis Menton equation
(c) Handerson Hasselbalch equation
(d) Noyes whitney equation

9. Range of particle size for colloidal dispersion is
(a) Less than 1 nm (b) 0.5µm-1 nm
(c) 1-5 µm (d) > 5 µm

10. Molecular weight of colloid can be calculated using
(a) Faraday Tyndall Effect
(b) Light scattering effect
(c) Brownian motion
(d) All of the above

11. Method for determining Surface Area is
(a) Karl fisher Method
(b) Air permibility Method
(c) Carr's index
(d) All of the above

12. Water soluble Qinghaosu Alkaloid
(a) Artemether (b) Artesunnate
(c) Artemisinin (d) All of the above

13. Malignant tertian Malaria caused by
(a) Plasmodium Vivax
(b) PlasmodiumFalciparum
(c) Plasmodium Ovale
(d) Plasmodium malariae

14. ß lactamase resistant penicillin is
(a) Cloxacillin (b) Clavulanic acid
(c) Sulbactam (d) Tolbactam

15. Monobactam antibiotic is
(a) Aztreonam (b) Imipenam
(c) Meripenam (d) All of above

16. Which Vitamin is known as "anti-egg White injury factor"
(a) B_1 (b) B_2
(c) B_7 (d) B_{12}

17. Simethicone is component of several antacid formulation, chemically it is
(a) Wax (b) Fat
(c) Silicon (d) Alginates

18. All of the following physiochemical constants are used in predicting solubility of drug except
(a) pka of drug (b) Ionization
(c) Valency (d) Dielectric constant

19. D-Fructose on simple reduction gives
(a) L-Fructose (b) Sorbitol
(c) Mannitol (d) Both b and c

20. Ethylene oxide acts as sterilizing agent by
(a) Oxidation (b) Alkylation
(c) Coagulation (d) All of above

21. Glucose have _____ total isomers
(a) 4 (b) 8
(c) 16 (d) 32

22. The order of stability of carbanion is
(a) Tertiary> Secondary > Primary
(b) Secondary > Tertiary > Primary
(c) Primary > Secondary > Tertiary
(d) Primary > Tertiary > Secondary

23. Tag open cup apparatus is used for measurement of
(a) Flame projection (b) Flame point
(c) Flash light (d) Flame intensity

24. p53 is called as
(a) Guardian of the cell
(b) Guardian of the genome
(c) Both
(d) Destructor of the cell

25. Orange Peel Effect is due to
(a) High viscosity of coating solution
(b) Overwetting of tablet
(c) Rapid escape of solvent
(d) Rapid migration of color.

26. Ratio of dry glycerine to dry gelatine for hard capsule should be
(a) 0.4 (b) 0.6
(c) 0.8 (d) 1.0

27. What is the proportion of NaCl required to render a 1.5% solution of drug isotonic with blood plasma?
(a) 0.65% (b) 0.585%
(c) 0.9% (d) 0.5%

28. Schedule P states
(a) Packaging requirement
(b) Life period of drug
(c) Patent or Proprietary medicines
(d) List of Pigments

29. Vaccines and Sera are covered under which schedule
(a) Schedule X (b) Schedule C
(c) Schedule G (d) Schedule H

30. Drug Technical Advisory Board (DTAB) is constituted by_____ and consist of _____members.
(a) Central Govt and 18 members
(b) Central Govt. And 16 members
(c) State Govt. And 18 members
(d) State Govt. And 16 members

31. Schedule "k" states
(a) Minimum equipment required for running pharmacy
(b) Drugs exempted from certain provision relating to manufacture of drugs
(c) Disease or ailment which a drug may not purport to prevent or cure
(d) List of drugs exempted from the provision of import.

32. Mulling agent used in sample preparation of IR is____
(a) Nujol (b) KBr
(c) Perfluorokerosene (d) Both a and c

33. Which of the following will exhibit λmax at larger wavelength?
(a) $CH_3CH_2CH_2CH=CH_2$
(b) $CH_2=CHCH_2CH_2CH=CH_2$
(c) $CH_2=CHCH=CH_2$
(d) $CH_2=CHCH=CHCH=CH_2$

34. Which of the following cannot be used as a source of UV radiations?
(a) Tungsten lamp (b) Hydrogen lamp
(c) Deuterium lamp (d) Nernst glower

35. Which of the following drugs is not estimated by non aqueous titration officially?
(a) Atropine
(b) Adrenaline
(c) Sulphamethoxazole
(d) Ethambutol

36. Karl – Fisher reagent is standardized with:
(a) Total molecular weight of resin
(b) Methyl alcohol
(c) Solubility of ion exchange resin
(d) Glacial acetic acid

37. Following laws are used to predict energy requirements for comminution process.
(a) Rittinger's law (b) Kick's law
(c) Bond's law (d) All

38. Following is/are dimentionless number(s)
(a) Reynold's number
(b) Power number
(c) Mass transfer number
(d) All

39. Kjedahl titration method is used for the detection of:
(a) Water (b) Organic compound
(c) S (d) N_2

40. Iupac name of Nifedipine is:
(a) 1,4-dihydro-2,6-dimethyl-4-(3-nitro phenyl)-3,5 pyridine carboxylic acid dimethyl ester
(b) 1,4-dihydro-2,6-dimethyl-4-(2-nitro phenyl)-3,5 pyridine carboxylic acid dimethyl ester
(c) 1,4-dihydro-2,6-dimethyl-4-(2-nitro phenyl)-3,5 pyridine carboxylic acid methyl ethyl ester
(d) 2,4-dihydro-1,6-dimethyl-4-(3-nitro phenyl)-3,5 pyridine carboxylic acid dimethyl ester

41. Which of following drug produce occulomucotaneous syndrome?
(a) Timolol (b) Atenolol
(c) Practolol (d) Metoprolol

42. Which of following antiulcer agent obtain from liquorice root?
(a) Sucralfate (b) Carbinoxolone
(c) Misopristol (d) None

43. Chemically Diltiazem is
(a) 1,4 dihydropyridine dvt
(b) Phenyl alkyl amine dvt
(c) Benzothiazepine dvt
(d) None

44. The starting material for clonidine synthesis is _____
(a) 2,6-Dichloroaniline + Ammonium thiocynate
(b) 2,5-Dichloroaniline + Ammonium thiocynate
(c) 2,4-Dichloroaniline + Ammonium thiocynate
(d) 3,4-Dichloroaniline + Ammonium thiocynate

45. The basic moiety present in Prazosin is
(a) Quinoline (b) Isoquinoline
(c) Quinazoline (d) None

46. Chemically proton pump inhibitor is
(a) Pyridyl methyl sulfinyl benzindole dvt
(b) Pyridyl methyl sulfinyl benzimidazole dvt
(c) Pyimidyl methyl sulfinyl benzindole dvt
(d) Pyrimidyl methyl sulfinyl benzimidazole dvt

47. Predict the product obtained by treating 6-chloro-3,5-diaminopyrazine-2-methyl carboxylate with guanidine
(a) Amiloride (b) Hydrochlorthiazide
(c) Triamterene (d) Furosemide

48. Which of following drug use in cohn's syndrome ?
(a) Triamterene (b) Amiloride
(c) Spironolactone (d) All

49. Which of following synthesized by Fischer-indole synthesis?
(a) Sulindac (b) Indoprofen
(c) Indomethacin (d) All

50. Chemically Nimesulide is:
(a) Napthayl acetic acid dvt
(b) Aryl acetic acid dvt
(c) Methane sulfonamide dvt
(d) All

51. Which of following neurotoxin inhibit Ach release and use in blepherospasm?
(a) Botulinium toxin (b) beta-bungarotoxin
(c) Vesamicol (d) Hemicholinium

52. One of the following is not a triazolobenzodiazepine derivative:
(a) Alprazolam (b) Triazolam
(c) Midazolam (d) Estazolam

53. One of the following is false about benzodiazepines:
(a) Alkyl substituents at 3-position decreases the activity
(b) The N-substituent at I-position should be small
(c) A phenyl or pyridyl at the 5-position decreases activity
(d) The presence of electron-attracting substituents (CI, F, Br, NO_2) at position 7 is required for activity

54. One of the following belongs to imidazolidine-2,4-dione class:
(a) Phenytoin (b) Trimethadione
(c) Phensuximide (d) Paramethadione

55. In limit test for iron interference of other metal cation is removed by
(a) Thioglycolic acid (b) Citric acid
(c) Both (d) Ammonia solution

56. The usual limit for Heavy metal as I.P is
(a) 10 ppm (b) 20 ppm
(c) 30 ppm (d) 40 ppm

57. Electron is filled in lowest energy orbital then higher energy orbital is given by
(a) Pauli-principle (b) Hund rule
(c) Auf-bau rule (d) Heisenberg principle

58. Chhotachand is the common name of
(a) Ashwagandha (b) Nuxvomica
(c) Rauwolfia (d) Colchicum

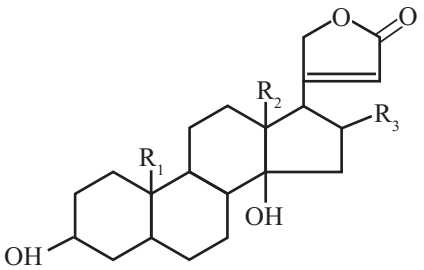
59. Quinine is identified by
(a) Thalloquine test (b) Vitali- morine test
(c) Borntrager test (d) Libberman Buchard test

60. The botanical source of chitrak is
(a) Tinospora cordifolia
(b) Vitex nigundo
(c) Plumbago zylanicum
(d) Cassia tora

61. One of the following is also known as staff tree
(a) Brahmi (b) Amla
(c) Behda (d) Malkangni

62. Karunjin, Pongapin, Pinnatin are the constituent of
(a) Palash (b) Karanj
(c) Nagod (d) Neem

63. In the following structural formula, select the functional groups for Digitoxigenin



(a) $R_1 = CH_3$, $R_2 = R_3 = H$
(b) $R_1 = CH_3$, $R_2 = H$, $R_3 = OH$
(c) $R_1 = CH_3$, $R_2 = OH$, $R_3 = H$
(d) R1 = CHO, $R_2 = R_3 = H$

64. Triphla churna contain
(a) Amla (b) Bahda
(c) Harde (d) All

65. The calcium oxalate crystals present in wild cherry possess shapes of
(a) Acicular (b) Raphides
(c) Microcrystals (d) Prisms

66. Three molecules of Digitoxose attached to one molecule of glucose are present in the cardioactive glycoside
(a) Gitaloxin (b) Gitoxin
(c) Digitoxin (d) Purpurea glycoside A

67. Chitral gum obtained from Astragulus strobiliferus is one of the adulterant of
(a) Acacia (b) Algin
(c) Agar (d) Tragacanth

68. Cochlospermum gossypium of the family bixaceae is one of the source of
(a) Starch (b) Algin
(c) Sterculia gum (d) Gattigum

69. Smaller granules are present in starch of
(a) Maize (b) Wheat
(c) Rice (d) Potato

70. Catechins and gallic acids are the examples of
(a) Hydrolsable tannins
(b) Non-hydrolysable tannins
(c) Condensed tannins
(d) Pseudotannins

71. Goldbeater's skin test is used to detect the presence of
(a) Resins (b) Alkaloids
(c) Tannins (d) Glycosides

72. Green bones are used for the preparation of gelatin of the type
(a) A (b) B
(c) C (d) A and B

73. Bufadenolides are present in
(a) Squill (b) Strophanthus
(c) Thevetia (d) Arjuna

74. All micronutrients required for plant tissue culture are
(a) Organic compounds
(b) Combined organic and inorganic material
(c) Inorganic elements
(d) None

75. The most common carbon source for PTC is
(a) Dextrose (b) Sucrose
(c) Charcoal (d) Maltose

76. In protoplast culture protoplasm is isolated by using
(a) Cellulase (b) Macerozyme
(c) Both (d) None

77. Plant tissue culture has potential role in all except
(a) Secondary metabolite production
(b) Biotranformation
(c) Genetic mapping
(d) Micropropogation

78. Marine fungus is the source for
(a) Penicillin (b) Cephaelosporin
(c) Zonarol (d) Avarol

79. Coloroquine act by inhibiting following enzyme
(a) DNA & RNA polymerase
(b) DNA gyrase
(c) Dihydro folate reductase
(d) DNA synthase

80. Which sulphonamide is not used in diuretics?
(a) Tolbutamide (b) Bumetanide
(c) Chlorthalidone (d) Furesemide

81. Which is following is not a prodrug
(a) Progunil (b) Sulfasalazine
(c) Prontosil red (d)Trimethoprim

82. Which alkaloid is used to treat amoebiasis?
(a) Ipecac (b) Theophylline
(c) Brucine (d) Aconite

83. Glycobiarsol used in
(a) Anti malarial (b) Anti amoebic
(c) Anti cancer (d) Anti ashtamatic

84. Which Nitroimidazole derivative having Morpholine moiety?
(a) Tinidazole (b) Ornidazole
(c) Timorazole (d) Metronidazole

85. Which antibiotic having direct action on trophozoitocidal?
(a) Paramomycin (b) Neomycin
(c) Natamycin (d) Erythromycin

86. Which is not a true for Isoniazid?
(a) It is Hydrazide of isonicotinic acid
(b) Structurally similer to Pyridoxine
(c) It inhibit Mycolase Synthase
(d) It is Hydrazide of nicotinic acid

87. Isoniazid is synthesized from
(a) Methyl ester of isonicotinic acid+ Hydrazine
(b) Methyl ester of nicotinic acid+ Hydrazine
(c) Methyl ester of is nicotinic acid+ Phenyl Hydrazine
(d) Methyl ester of is isonicotinic acid+ Methyl Hydrazine

88. Normalisation in GC is used to detect _____ by using area under curves.
(a) Steroids (b) Volatile compounds
(c) Terpenes (d) Sugars

89. Highest column loadings in GC are observed with:
(a) Packed columns (b) WCOT
(c) SCOT (d) PLCOT

90. In flocculation occurring in suspension, the particles in floccules are held by _____?
(a) Repulsive forces (b) Gravitational force
(c) Vanderwaal forces (d) None

91. Pseudoplastic flow is typically exhibited by
(a) Emulsion (b) Polymer solution
(c) Suspension (d) Ointment

92. In polarography ____ is used for qualitative analysis.
(a) Halfwave potential (b) Migration current
(c) Diffusion current (d) Limiting current

93. In polarography ____ is used for quantitative analysis.
(a) Halfwave potential (b) Migration current
(c) Diffusion current (d) Limiting current

94. Catherometer is an alternative name for:
(a) Thermal conductivity detector
(b) Electron capture detector
(c) Flame ionization detector
(d) Thermionic detector

95. Anode and cathode are not used in:
(a) Photo ionisation detector
(b) Electron capture detector
(c) Flame photometer detector
(d) Thermionic detector

96. The Carbocation is reactive intermediate have following characteristic
(P) It is positively charge reactive intermediate
(Q) The Tertiary carbocation is more stable than Secondary and Primary carbocation
(R) The electron donating group increase stability of carbocation
(S) The electron withdrawing group decrease stablility of carbocation
(a) P, R is correct but Q,S is incorrect
(b) P, Q, R is correct but S is incorrect
(c) P, Q, is correct but R,S is incorrect
(d) All statement is correct

97. Which one of the following is not evaluation parameter in suspension?
(a) Zeta potential (b) Sedimentation ratio
(c) Phase inversion (d) Particle size

98. Film former used in nail liquor is
(a) Ethyl acetate
(b) Nitro cellulose
(c) Cellulose acetate phthalate
(d) Poly ethylene glycol

99. Humectants used in tooth paste is
(a) Glycerine (b) Zinc carbonate
(c) Titanium dioxide (d) Calcium fluoride

100. An isoelectric point for type A gelatin capsule is at pH
(a) 2 (b) 6
(c) 9 (d) 12

101. Which of following tablet is composed of readily water soluble ingredient and intended to be added to a sterile water for parentral administration?
(a) Effervescent tablet (b) Dispensing tablet
(c) Hypodermic tablet (d) Tablet triturates

102. Which chemical indicator is used for validation of gaseous sterilization method.
(a) Brownes tube
(b) Bowie dick heat sensitive tapes
(c) Royce sachet
(d) Chemical dosimeter

103. In parenterals, Water attack test is used for which type of glass?
(a) Type-1 (b) Type -2
(c) Type-3 (d) Non-parentral

104. Test organism for Bacitracin Assay is
(a) Bacillus subtilis (b) Bacillus pumilus
(c) Micrococcus luteus (d) Staphylococcus aureus

105. Test organism for Amikacin Assay is
(a) Bacillus subtilis (b) Bacillus pumilus
(c) Micrococcus luteus (d) Staphylococcus aureus

106. Optimum value of BLOOM STRENGTH should be
(a) 50-100 g (b) 100-150 g
(c) 150-250 g (d) More than 250 g

107. Tyndallisation require following condition
(a) 80 C for 3days(20 min)
(b) 60 c for 3 days(20 min)
(c) 120 C for 3 days(20 min)
(d) None

108. Validation of moist heat sterilisation is done using
(a) Bacillus subtilis (b) Bacillus cogulans
(c) Bacillus niger (d) Clostridium sporogens

109. Schedule "k" states
(a) Minimum equipment required for running pharmacy
(b) Drugs exempted from certain provision relating to manufacture of drugs
(c) Disease or ailment which a drug may not purport to prevent or cure
(d) List of drugs exempted from the provision of import

110. Active form of chloramphenicol is
(a) D-Erythro (b) D-Threo
(c) L-Erythro (d) L-Threo

111. Z value in sterilization is
(a) Bio burden
(b) Resistance value
(c) Sterilization process eq. time
(d) Probability of nonsterility

112. Efficiency of HEPA filter to remove particles upto 0.3 micron is
(a) 99.99% (b) 98.97%
(c) 99.89% (d) 99.97%

113. Bingham bodies is the term used to represent following rheologic system
(a) Plastic system (b) Newtonion liquids
(c) Dilatant systems (d) Thixotropic systems

114. To avod lithium toxicity patient using lithium carbonate for mood disorder should not prescribed
(a) Acetazolamide (b) Furosemide
(c) Mannitol (d) Hydrochlorthiazide

115. Patient take digoxin for CHF is found to have elevated cholesterol level which agent not prescribed with it?
(a) Lovastatin (b) Cholestyramine
(c) Clofibrate (d) Niacin

116. Rofecoxib not given if patient is already taking
(a) Anxiolytic (b) Antidiabetic
(c) ACE inhibitor (d) all

117. The usual limit for Heavy metal as I.P is
(a) 10 ppm (b) 20 ppm
(c) .30 ppm (d) 40 ppm

118. In Limit test for lead the reagent use as Per I.P and B.P is
(a) Dithiazone (b) Lead sulphide
(c) Both (d) Lead nitrate

119. In limit test for arsenic which of following method used ?

(a) Arsine test (b) Gutzeit test
(c) Both (d) None

120. Bretylium tosylate is

(a) Sec. amine (b) Ter. Amine
(c) Quat. Amine (d) Quat. Amide

121. Benzofuran ring containg drugs

(a) Amiodarone (b) Griseofulvin
(c) Frusemide (d) a & b

122. Due to five membered lactone ring present at C-17 the digitalis glycosides respond positively to

(a) Borntragers test (b) Keller killani test
(c) Libermanns test (d) Zimmermann test

123. Hal- phen's test is used for

(a) Detection of cotton seed oil as an adulterant
(b) Detection of artificial invert sugar
(c) Saponins
(d) Tannins

124. Stratified cork is characteristic of

(a) Ergot (b) Senna
(c) Cinchona (d) Rauwolfia

125. Precursor for Ethacrynic Acid is

(a) 2,4-dichloro phenoxyacetic acid
(b) 2,3- dichloro phenoxyacetic acid
(c) 3,4-dichloro phenoxyacetic acid
(d) 2,5- dichloro phenoxyacetic acid

ANSWER KEYS

1. (c)	**2.** (c)	**3.** (d)	**4.** (b)	**5.** (a)	**6.** (b)	**7.** (a)	**8.** (c)	**9.** (c)	**10.** (b)
11. (b)	**12.** (b)	**13.** (b)	**14.** (a)	**15.** (a)	**16.** (c)	**17.** (c)	**18.** (c)	**19.** (b)	**20.** (b)
21. (c)	**22.** (c)	**23.** (b)	**24.** (b)	**25.** (a)	**26.** (a)	**27.** (b)	**28.** (c)	**29.** (b)	**30.** (a)
31. (b)	**32.** (d)	**33.** (d)	**34.** (d)	**35.** (c)	**36.** (b)	**37.** (d)	**38.** (d)	**39.** (d)	**40.** (b)
41. (c)	**42.** (b)	**43.** (c)	**44.** (a)	**45.** (c)	**46.** (b)	**47.** (a)	**48.** (c)	**49.** (d)	**50.** (c)
51. (a)	**52.** (c)	**53.** (c)	**54.** (a)	**55.** (b)	**56.** (b)	**57.** (c)	**58.** (c)	**59.** (a)	**60.** (c)
61. (d)	**62.** (b)	**63.** (c)	**64.** (d)	**65.** (d)	**66.** (d)	**67.** (d)	**68.** (c)	**69.** (c)	**70.** (d)
71. (c)	**72.** (b)	**73.** (a)	**74.** (c)	**75.** (b)	**76.** (d)	**77.** (c)	**78.** (b)	**79.** (a)	**80.** (a)
81. (d)	**82.** (a)	**83.** (b)	**84.** (c)	**85.** (a)	**86.** (d)	**87.** (a)	**88.** (b)	**89.** (a)	**90.** (c)
91. (b)	**92.** (a)	**93.** (c)	**94.** (a)	**95.** (c)	**96.** (d)	**97.** (c)	**98.** (b)	**99.** (a)	**100.** (c)
101. (c)	**102.** (c)	**103.** (b)	**104.** (c)	**105.** (d)	**106.** (c)	**107.** (a)	**108.** (d)	**109.** (b)	**110.** (b)
111. (b)	**112.** (d)	**113.** (a)	**114.** (d)	**115.** (a)	**116.** (c)	**117.** (b)	**118.** (a)	**119.** (b)	**120.** (c)
121. (d)	**122.** (b)	**123.** (a)	**124.** (d)	**125.** (b)					

MOCK TEST - III

1. Which one of the following is NOT an ex-officio member of Pharmacy Council of India?
(a) The direactor general of Health services
(b) The direactor of Central Drugs Laboratory
(c) The Drugs Controller General of India
(d) The Director of Pharamacopoeia Laboratory

2. Phototubes are used as detectors in:
(a) UV (b) IR
(c) NMR (d) Mass

3. A titration in which potential applied across the two electrodes is maintained at a constant value and the current is measured and plotted against volume of titrant is:
(a) Potentiometric titration
(b) Amperometric titration
(c) Displacement titration
(d) Conductometric

4. To avod lithium toxicity patient using lithium carbonate for mood disorder should not prescribed
(a)Acetazolamide (b) Furosemide
(c) mannitol (d) Hydrochlorthiazide

5. Patient take digoxin for CHF is found to have elevated cholesterol level which agent not prescribed with it?
(a) Lovastatin (b) cholestyramine
(c) clofibrate (d) niacin

6. Rofecoxib not given if patient is already taking
(a) Anxiolytic (b) Antidiabetic
(c) ACE inhibitor (d) all

7. Toxic metabolite of paracetamol which cause hepatotoxicity is
(a) N-acetyl p-benzoquinone imine
(b) N-acetyl p-benzoquinone amine
(c) 0-dealkyl acetaminophen
(d) all

8. At therapeutic dose metabolism of paracetamol occur by
(a) Glucuronide and Glycine
(b) Glucuronide and sulphate
(c) Glutathione and sulphate
(d) none

9. Which of following is Natural vasodialator?
(a) Bradykinin (b) adenosine
(c) both (d) none

10. which isomer of ibuprofen is more active?
(a) S (-) isomer (b) R (-) isomer
(c) S (+) isomer (d) R (+) isomer

11. Benorylate is polymeric condensation of
(a) Acetyl salicylate ester of B-napthol
(b) Acetyl salicylate ester of paracetamol
(c) Acetyl salicylate ester of piroxicam
(d) none

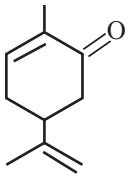
12. Starting material for ibuprofen is
(a) Isobutyl benzene
(b) isopropyl benzene
(c) isobutyl acetophenone
(d) none

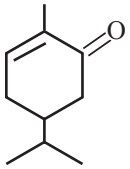
13. Which of following drug have 1,3,4 thiadiazole ring ?
(a) amiloride
(b) dichloropenamide
(c) acetazolamide
(d) none

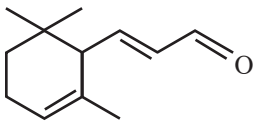
14. The Pyrazine is having dipole moment is
(a) 4.7 (b) 2.4
(c) zero (d) 1.0

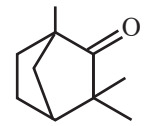
15. In the volatile oil of clove, the amount of Eugenol is up to
(a) 50% (b) 60 %
(c) 75 % (d) 85 %

16. The structure of bicyclic monoterpenic ketone known as Fenchone is

(a) 

(b) 

(c) 

(d) 

17. The principle constituent of the volatile oil Pimpenella anisum present upto 90 % is

(a) α-Terpene (b) Carione
(c) Anethole (d) Cymene

18. One of the following is also known as Indian gooseberry

(a) Behda (b) Harde
(c) Amla (d) Neem

19. Behda consist of dried ripe fruits of Terminalia balerica belongs to family

(a) Compositeae (b) Umbelliferae
(c) Combritaceae (d) Liliaceae

20. One of the following is having activity against Mycobacterium Laprae

(a) Nagod (b) Brahmi
(c) Piper (d) Garlic

21. Aleurone grains when treated with Iodine/ ethanol, they will give

(a) Blue color (b) Brown color
(c) Red color (d) white

22. Acid insoluble ash indicates

(a) extraneous matter
(b) amount of silica present in soil
(c) Amount of foreign matter
(d) All

23. Foaming index F.I =

(a) 1000 * a (b) a / 1000
(c) 1000 / a (d) none

24. Kreis test is used for

(a) Caffeine
(b) presence of deoxy sugar
(c) Rancidity of fats and oils
(d) Aloes

25. Hal- phen's test is used for

(a) detection of cotton seed oil as an adulterant
(b) Detection of artificial invert sugar
(c) Saponins
(d) Tannins

26. Stratified cork is characteristic of

(a) ergot (b) Senna
(c) Cinchona (d) Rauwolfia

27. Pseudoparenchyma found in

(a) Ergot (b) Nux-vomica
(c) Brahmi (d) Jalap

28. All micronutrients required for plant tissue culture are

(a) Organic compounds
(b) Combined organic and inorganic material
(c) Inorganic elements
(d) None

29. The most common carbon source for PTC is

(a) Dextrose (b) Sucrose
(c) Charcoal (d) Maltose

30. In protoplast culture protoplasm is isolated by using

(a) Cellulase (b) Macerozyme
(c) Both (d) None

31. Plant tissue culture has potential role in all except

(a) Secondary metabolite production
(b) Biotranformation
(c) Genetic mapping
(d) Micropropogation

32. Gas chromatography is mainly used for:

(a) Quantitative analysis
(b) Qualitative analysis

(c) Both (a) and (b)
(d) none

33. In gel permeation chromatography, the molecules are separated on the basis of:
(a) chemical nature (b) partition coefficient
(c) size and shape (d) adsorptive properties

34. An essential requirement for mobile phase in HPLC is:
(a) It must have constant flow rate with pulses
(b) It must be freshly distilled
(c) It must run at 20^0C only
(d) It must flow with pulses

35. Ion exchange chromatography is the method of choice for separation of:
(a) Metals (b) Sugars
(c) Fatty acids (d) Sterols

36. Correct order of eluent power is
(a) Benzene < Ether < Chloroform < ethyl acetate
(b) Ether<chloroform<Ethyl acetate< benzene
(c) Ethyl acetate< ether< benzene<chloroform
(d) chloroform<benzene<ethyl acetate<ether

37. The detector used in gas chromatography is:
(a) Bolometer
(b) Thermal conductivity detector
(c) Golay counter
(d) Geiger conter

Thermal conductivity detector is best indicator in gas chromatography.

38. In adsorption chromatography, a polar solute tends to be sorbed in:
(a) polar phases (b) non polar phases
(c) neutral phases (d) amphoteric phases

39. The most common detector used in liquid chromatography is:
(a) Refractive index detector
(b) Polarography detector
(c) UV detector
(d) Electrical conductivity detector

40. Normalisation in GC is used to detect _____ by using area under curves.
(a) steroids (b) volatile compounds
(c) terpenes (d) sugars

41. Removal of single electron from a molecule results in the formation of:
(a) Metastable ion (b) Fragment ion
(c) Molecular ion (d) Rearrangement ion

42. NMR is not shown by
(a) C13 (b) O16
(c) H1 (d) N15

43. In which of the following vibration the bond angle does not change?
(a) Assymetric stretching
(b) Wagging
(c) Scissoring
(d) Twisting

44. The absorption maximum for polar compounds is usually shifted with the change in polarity of solvent due to:
(a) Hydrogen bonding
(b) Chemical reaction
(c) Ionisation of compound
(d) Change in chromophore

45. Which of the following cannot be used as a source of UV radiations?
(a) Tungsten lamp (b) Hydrogen lamp
(c) Deuterium lamp (d) Nernst glower

46. Which of the following is not a step of MS?
(a) Acceleration of ions
(b) Ionisation
(c) Absorption of visible radiation
(d) Dispersion of ions by their m/z ratios

47. An electron undergoes a transition from excited singlet state to triplet state and then returns back to the ground state. This phenomenon is called:
(a) Fluorescence
(b) Phosphorescence
(c) Photodecomposition
(d) Quenching

48. On dilution the molar conductance of a solution of a weak electrolyte ____ and strong electrolyte
(a) Increases, Increases
(b) Increases, Decreases
(c) Increases, Decreases
(d) Decreases, Decreases

49. Polarogram is a plot of current v/s. _____
(a) Voltage
(b) emf
(c) Volume of titrant added
(d) pH

50. The electrode most commonly used in Amperometry is:
(a) Calomel electrode (b) Glass electrode
(c) Mercury electrode (d) All

51. The conductivity cell is calibrated using
(a) KOH (b) NaOH
(c) KCl (d) HCl

52. Which one of the following is not evaluation parameter in suspension?
(a) zeta potential (b) sedimentation ratio
(c) phase inversion (d) particle size

53. Film former used in nail liquor is
(a) Ethyl acetate
(b) Nitro cellulose
(c) Cellulose acetate phthalate
(d) Poly ethylene glycol

54. Humectants used in tooth paste is
(a) Glycerine (b) Zinc carbonate
(c) Titanium dioxide (d) Calcium fluoride

55. An isoelectric point for type A gelatin capsule is at pH
(a) 2 (b) 6
(c) 9 (d) 12

56. Which of following tablet is composed of readily water soluble ingredient and intended to be added to a sterile water for parentral administration?
(a) Effervescent tablet (b) Dispensing tablet (c) Hypodermic tablet (d) Tablet triturates

57. Which chemical indicator is used for validation of gaseous sterilization method.
(a) Brownes tube
(b) bowie dick heat sensitive tapes
(c) Royce sachet
(d) chemical dosimeter.

58. In parenterals, Water attack test is used for which type of glass?
(a) Type-1 (b) Type – 2
(c) Type-3 (d) Non-parentral

59. Multi dose injections are packed in
(a) Vials (b) Ampoules
(c) Infusion bottles (d) Disposable sets

60. The Hausners ratio <1.25 indicates which type of flow?
(a) excellent (b) very poor
(c) extreme poor (d) good

61. Which of the following preservatives is used in Eye Drops ?
(a) Vinyl Alcohol (b) Phenyl Mercuric Acetate
(c) Benzoic acid (d) Para hydorxy Benzoate

62. The Leaker test is use for
(a) Vials (b) Ampoules
(c) Infusion bottles (d) Disposable sets

63. Which of the following sweetening agent is 200 times more sweet than sucrose ?
(a) Sucralose (b) Saccharine
(c) Aspartame (d) Cellulase

64. Moisture content of propellant is determined by
(a) Karl Fischer Method
(c) Both a and b
(b) Gas Chromatography
(d) None

65. Ac-di-sol is bramd name of
(a) Sodium CMC (b) Crosslinked Sodium CMC
(c) PVP (d) Crosslinked PVP

66. The temperature at which the given mixture of air and water vapor must be cooled to become saturated is
(a) Yield Point (c) Kraft point
(b) Cloud point (d) dew point

67. All of the following are oil soluble antioxidant except
(a) Propyl Gallate (b) BHT
(c) α - tocopherol (d) Ascorbic acid

68. Which of following use for detection and measurement of radiation ?
(a) Photographic plate
(b) Semiconductor detector
(c) Gieger mullar counter
(d) all

69. The unit of measurement of X-ray is
(a) Curie (b) Rontgen
(c) Both (d) all

70. Which of following use for estimation of reticuloendothelial activity?
(a) Gold solution (b) Cobalt
(c) Cynocobalamine (d) all

71. As per B.P which of reagent use for limit test of sulphate?
(a) Sodium sulphtae (b) Magnesium Sulphate
(c) Barium Sulphate (d) none

72. In limit test for iron interference of other metal cation is removed by
(a) Thioglycolic acid (b) Citric acid
(c) both (d) Ammonia solution

73. The usual limit for Heavy metal as I.P is
(a) 10 ppm (b) 20 ppm
(c) 30 ppm (d) .40 ppm

74. In Limit test for lead the reagent use as Per I.P and B.P is
(a) Dithiazone (b) Lead sulphide
(c) both (d) Lead nitrate

75. In limit test for arsenic which of following method used ?
(a) Arsine test (b) Gutzeit test
(c) both (d) none

76. Which one of the following drugs is 'Topoisomerase I inhibitor' ?
(a) Doxorubicin (b) Irinotecan
(c) Etoposide (d) Vincristine

77. bretylium tosylate is
(a) sec. amine (b) ter. Amine
(c) Quat. Amine (d) Quat. Amide

78. Benzofuran ring containg drugs
(a) amiodarone (b) Griseofulvin
(c) Frusemide (d) a&b

79. Valeronitrile deri. Act as calcium channel bloker is
(a) nifedipine (b) Verapamil
(c) Diltiazem (d) Bretylium

80. Diazoxide has
(a) 1,2,4-benzothiazine
(b) 1,2,3-benzothiazine
(c) 2,3,4-benzothiazine
(d) 1,3,4-benzothiazine

81. Dipyridamol+Adenosine
(a) increase adenosine activity
(b) decrease adenosine activity
(c) no interaction
(d) antagonise adenosine

82. This drug is a Class IA antiarrhythmic drug:
(a) Sotalol (b) Propranolol
(c) Verapamil (d) Quinidine

83. The Convection based heat transfer is having property except
(a) It occur by force or naturally.
(b) Natural convection is concentrate on film coefficient
(c) Force convection is affected by geometry of system
(d) It also based on emission process.

84. Mier's supersaturation theory is based on following condition
[P] The solute and solvent must be pure
[Q] The solution must be free from solid solute particle
[R] Soft or weak crystal must not form during process
[S] There should be no fluctuation in temperature
(a) P is incorrect but Q,R,S is correct
(b) P,Q,R is correct but S is incorrect
(c) P,Q,S is correct but R is incorrect
(d) All statement is correct.

85. Which of following interaction is possible between non-polar molecule
(a) Hydoen bonding
(b) Ion-Dipole interaction
(c) Dipole-Dipole interaction
(d) London force

86. Hyperconjugation is modified resonance effect which involve
(a) Delocalization of sigma electron
(b) Delocalization Pi-electron
(c) both
(d) none

87. The Tautomer is type of structural isomer contain following property:
[P] It is isomer in which isomer is dynamic equilibrium with each other
[Q] It involve movement of double bond
[R] It is one type of functional isomer also
[S] It has independent existence
(a) P, R is correct but Q, S is incorrect
(b) P, Q, R is correct but S is incorrect
(c) P, Q is correct but R, S is incorrect
(d) All statement is correct

88. Which of following formulation not require addition of preservative?
(a) Elixirs (b) Linctus
(c) Enema (d) Syrup

89. Simple syrup IP contains following concentration of sugar.

(a) 85 % w/w sugar (b) 85 % w/v sugar
(c) 66.67 % w/w sugar (d) 66.67 % w/v sugar

90. The E-2 is elimination reactions have following property
[P] Follow first order kinetic
[Q] Reactivity order is 3°>2°>1°
[R] Always β-Hydrogen abstracted
[S] Single step reaction
(a) P, R is correct but Q, S is incorrect
(b) Q, R, S is correct but P is incorrect
(c) P, Q is correct but R, S is incorrect
(d) All statement is correct

91. Which of following indicator is use in detection of end's point by Mohr's method?
(a) Crystal violet
(b) Xylenol orange
(c) Potassium chromate
(d) Methylene blue

92. Tropane alkaloid can synthesized by
(a) Acetate mevanolate pathway
(b) Shikimic acid pathway
(c) Ornithine pathway
(d) None

93. The cinchona and ergot alkaloid can synthesized from following amino acid
(a) Tyrosine (b) Phenyl alanine
(c) Tryptophan (d) Lysine

94. The order of stability of carbocation is
(a) Tertiary> Secondary > Primary
(b) Secondary > Tertiary > Primary
(c) Primary > Secondary > Tertiary
(d) Primary > Tertiary > Secondary

95. Which of following intermediate is neutral particle
(a) Carbocation (b) Carbanion
(c) Carbene (d) Free radical

96. α-D-glucose and β-D-glucose both are
(a) Keto-aldo pairs (b) Anomer
(c) Epimers (d) Stereoisomers

97. Perchloric acid prepared in glacial acetic acid is used as titrant in non aqueous titrations. It is standardised by:
(a) Standard alcoholic KOH solution
(b) KHP solution in glacial acetic acid
(c) 0.1 N KMnO4
(d) None

98. According to pH partition theory, a weakly acidic drug will be most likely absorbed from the stomach because the drug exists in:
(a) Ionised form (b) unionised form
(c) weak acid (d) weak base

99. The hydrogen ion concentration does not migrate under influence of electrical field is called as
(a) Isobestic point (b) Isoelectric point
(c) Isoosmotic point (d) None

100. Test organism for Bacitracin Assay is
(a) Bacillus subtilis (b) Bacillus pumilus
(c) Micrococcus luteus (d) Staphylococcus aureus

101. Test organism for Amikacin Assay is
(a) Bacillus subtilis
(b) Bacillus pumilus
(c) Micrococcus luteus
(d) Staphylococcus aureus

102. Optimum value of BLOOM STRENGTH should be
(a) 50-100 g (b) 100-150 g
(c) 150-250 g (d) more than 250 g

103. Tyndallisation require following condition
(a) 80 C for 3days(20 min)
(b) 60 c for 3 days(20 min)
(c) 120 C for 3 days(20 min)
(d) None

104. Validation of moist heat sterilisation is done using
(a) Bacillus subtilis (b) Bacillus cogulans
(c) Bacillus niger (d) Clostridium sporogens

105. Schedule "k" states
(a) Minimum equipment required for running pharmacy
(b) Drugs exempted from certain provision relating to manufacture of drugs
(c) Disease or ailment which a drug may not purport to prevent or cure
(d) List of drugs exempted from the provision of import

106. Active form of chloramphenicol is
(a) D-Erythro (b) D-Threo
(c) L-Erythro (d) L-Threo

107. Only organophosphate which is not lipid soluble is
(a) Echothiophate (b) Tabun
(c) Tacrine (d) Soman

108. Non-steroidal anti-androgens useful as anticancer agent is?

(a) Tamoxifen (b) Flutamide
(c) Etoposide (d) Aminoglutethimide

109. Which of the following a free radical alkylatine drug ?
(a) Carmustine (b) Thiotepa
(c) Procarbazine (d) Altretamine

110. Which is not true in case of penicillin?
(a) Good oral absorption but relatively acid labile
(b) Ineffective against Gm –ve bacilli
(c) Useful against Gm+ve cocci
(d) Highly stable to acid /base

111. 2, 6-Dimethoxy phenyl penicillin is IUPAC of
(a) Methicillin (b) Ampicillin
(c) Amoxicillin (d) Carbencillin

112. In cephalosporin's a higher resistance to hydrolysis by β-Iactamase is shown when ... ?
(a) The amino group is acylated
(b) Replacement of sulphur with oxygen
(c) Oxidation of ring sulphur to sulfoxide or sulfone
(d) Introduction of C-7 α-Methoxy group

113. Which of the following statement is incorrect?
(a) Resistance to quinolones due to chromosomal mutation producing enzyme DNA gyrase
(b) Diuretic+ Trimethoprime-thrombocytopenia
(c) Quinolone more active at acidic pH
(d) Levofloxacin oral bioavailablity-100%

114. Which of following is insulin secretogogue?
(a) Liraglutide (b) Pramlintide
(c) Exenatide (d) a and c

115. Which of following is long acting insulin preparation?
(a) Insulin lispro (b) Insulin aspart
(c) Glargine insulin (d) None

116. Which of following is alkyl ester of PABA
(a) Amethocaine (b)Dibucaine
(c) Xylocaine (d) Benzocaine

117. Which of following is selective MAO-B inhibitor?
(a) Sellegiline
(b) Meclobemide
(c) Isocarboxazide
(d) Iproniazid

118. Which of following is M-4 antagonist?
(a) Tropicamide (b) Isopropamide
(c) Glycopyrrolate (d) Darcifenacin

119. The unequal distribution of color on tablet is
(a) Capping (b) Mottling
(c) Double impression (d) Chipping

120. Most intense peak in mass spectra
(a) base peak
(b) metastable peak
(c) molecular ion peak
(d) fragment ion peak

121. Which principle is involved in i.rabsorbtion?
(a) Neuclearoverhauser effect
(b) Hookes law
(c) Maxwell law
(d) Woodward fisher rule

122. MALDI source use which laser?
(a) Nitrogen laser 390 nm
(b) nitrogen laser 337 nm
(c) argon laser 320 nm
(d) nitrogen laser 357 nm

123. Z value in sterilization is
(a) Bio burden
(c) Resistance value
(b) Sterilization process eq. time
(d) Probability of nonsterility

124. Efficiency of HEPA filter to remove particles upto 0.3 micron is
(a) 99.99% (b) 98.97%
(c) 99.89% (d) 99.97%

125. Bingham bodies is the term used to represent following rheologic system
(a) Plastic system (b) Newtonion liquids
(c) Dilatant systems (d) Thixotropic systems

ANSWER KEYS

1. (d)	**2.** (a)	**3.** (b)	**4.** (d)	**5.** (a)	**6.** (c)	**7.** (a)	**8.** (b)	**9.** (b)	**10.** (c)
11. (b)	**12.** (a)	**13.** (c)	**14.** (c)	**15.** (d)	**16.** (d)	**17.** (c)	**18.** (c)	**19.** (c)	**20.** (b)
21. (b)	**22.** (b)	**23.** (c)	**24.** (c)	**25.** (a)	**26.** (b)	**27.** (a)	**28.** (c)	**29.** (b)	**30.** (d)
31. (c)	**32.** (a)	**33.** (c)	**34.** (a)	**35.** (a)	**36.** (a)	**37.** (b)	**38.** (b)	**39.** (c)	**40.** (b)
41. (c)	**42.** (b)	**43.** (a)	**44.** (a)	**45.** (d)	**46.** (c)	**47.** (b)	**48.** (a)	**49.** (a)	**50.** (a)
51. (c)	**52.** (c)	**53.** (b)	**54.** (a)	**55.** (c)	**56.** (c)	**57.** (c)	**58.** (b)	**59.** (a)	**60.** (a)
61. (b)	**62.** (b)	**63.** (c)	**64.** (b)	**65.** (b)	**66.** (d)	**67.** (d)	**68.** (d)	**69.** (b)	**70.** (a)
71. (c)	**72.** (b)	**73.** (b)	**74.** (a)	**75.** (b)	**76.** (b)	**77.** (c)	**78.** (a)	**79.** (b)	**80.** (a)
81. (a)	**82.** (d)	**83.** (d)	**84.** (d)	**85.** (d)	**86.** (a)	**87.** (b)	**88.** (d)	**89.** (c)	**90.** (b)
91. (c)	**92.** (c)	**93.** (c)	**94.** (a)	**95.** (d)	**96.** (b)	**97.** (b)	**98.** (b)	**99.** (b)	**100.** (c)
101. (d)	**102.** (c)	**103.** (a)	**104.** (d)	**105.** (b)	**106.** (b)	**107.** (a)	**108.** (d)	**109.** (b)	**110.** (d)
111. (a)	**112.** (b)	**113.** (b)	**114.** (d)	**115.** (c)	**116.** (d)	**117.** (a)	**118.** (a)	**119.** (b)	**120.** (a)
121. (b)	**122.** (b)	**123.** (c)	**124.** (d)	**125.** (a)					

MOCK TEST - IV

1. One of the substances is listed is used as muco adhesive

(a) Acacia (b) S.C.M.C
(c) Burnt sugar (d) Saccharin

2. In the preparation of multilayer tablets one of the substances listed is used to Hydrophilic matrix coating

(a) C.M.C (b) Shellac
(c) Stearyl alcohol (d) Bees wax

3. Choose the correct pH of the lachrymal fluid

(a) 8.0 (b) 6.2
(c) 7.4 (d) 9.0

4. The dip tube in an aerosol container is made from one of the following. Choose the correct one

(a) Polypropylene (b) Glass
(c) Stainless steel (d) Aluminium

5. The diameter of the mesh aperture in the I.P disintegration test apparatus is given below. Choose the correct size.

(a) 2.00 mm (b) 4.00 mm
(c) 1.00 mm (d) 1.50 mm

6. Choose the correct source of radiation for N.M.R from the listed ones

(a) Klystron oscillator
(b) Globar source
(c) Radio frequency oscillator
(d) Deuterium lamp

7. Choose the correct semi-rigid gel used for exculsion chromatography

(a) Sephadex (b) Gelatin
(c) Cellulose (d) Alumina

8. One the following is measured in amperometric titration

(a) Resistance (b) Conductance
(c) Voltage (d) Current

9. The oil obtained from *Cymbopogan flexuousus* contains one of the following

(a) Citral (b) α-terpeniol
(c) α-pinene (d) Neral

10. Choose the correct key intermediate for the biosynthesis of C6-C3 units, which serves as a precursor for the biosynthesis of amino acid

(a) Shikimic acid
(b) Pyruvic acid
(c) Dehydro quinic acid
(d) Mevalonic acid

11. β-phenyl-N-alkyl piperidine moiety is largely responsible for activity in one of the following.
Choose the correct one

(a) Buprenorphine (b) Pethidine
(c) Cycloserine (d) Amitryptiline

12. Which one of the following is a Histamine H^1 receptor antagonist?

(a) 4-(5-H di benzo [a, d] cyclohepten-5-Ylidene)-1-methyl pyridine hydrochloride
(b) 4-(5-H di benzo [a, d] cyclohepten-5-Ylidene)-1-methyl pyrimidine hydrochloride
(c) 4-(5-H di benzo [a, d] cyclohepten-5-Ylidene)-1-methyl piperidine hydrochloride
(d) 4-(5-H di benzo [a, d] cyclopentane-5-Ylidene)-1-methyl piperidine hydrochloride

13. Dienoestrol is synthesised from

(a) 4-Hydroxy propiophenone
(b) 4-amino acetophenone
(c) 4-Chloro butyrophenone
(d) 4-Bromo propiophenone

14. One of the following diuretics has a similar structure as that of antihypertensive agent diazoxide

(a) Acetozolamide (b) Chlorothiazide
(c) Spironolactone (d) Furosemide

15. Which one of the following is an antifungal polyene macrolide antibiotics with seven conjugated double bond, an internal ester, a free carboxyl group and a glycoside side chain with primary amino group

(a) Streptomycin (b) Echinocandins
(c) Rifamycin (d) Amphotericin-B

16. Choose the correct class IV anti-arrhythmic that is primarily indicated for the treatment of supra ventricular tachyarrhythmias

(a) Mexiletine (b) Diltiazem
(c) Nifedipine (d) Propranolol

17. One of the following antiviral agents exhibits the greatest selective toxicity for the invading virus

(a) Amantadine (b) Zidovudine
(c) Idoxuridine (d) Acyclovir

18. Choose the drug that often causes tachycardia when given in regular doses

(a) Verapamil (b) Guanethidine
(c) Propranolol (d) Isosorbide dinitrate

19. Choose one appropriate therapeutic use for Imipramine

(a) Insomnia
(b) Epilepsy
(c) Bed wetting in children
(d) Mania

20. The following prescription is given to the pharmacist by the physician to dispense

Rx
Calciferol solution 0.3
Water to Q.S 5.0 ml send 25 ml
Final dosage of this prescription will be

(a) Solution (b) Elixir
(c) Emulsion (d) Suspension

21. Purpose of a combined drug regimen in tuberculosis is to

(a) Delay the emergence of drug resistance
(b) Reduce the duration of active therapy
(c) Schedule the onset of therapy
(d) Promote a placebo effect on the patient

22. The R-W coefficient test is used to evaluate

(a) Antibiotic activity
(b) Sterility of packaging material
(c) Nature of organism in bacterial infection
(d) Bactericidal activity

23. Diclofenac tablet coated with cellulose acetate phthalate has been administered to a patient. Where do you except the drug to be released?

(a) Stomach (b) Oral cavity
(c) Small intestine (d) Liver

24. A microscopic examination of a culture isolate revealed spherical bodies with a smooth outline growing in long chains. Identify the micro organism

(a) Staphylococcus aureus
(b) Streptococcus pyogenes
(c) Rhizopus stolonifer
(d) Bacillus subtilis

25. An original license or renewed license to sell drugs remains valid upto

(a) 31st March next year in which it is granted
(b) 30th June of the following year in which it is granted or renewed
(c) 31st January of the same year in which it is granted
(d) 31st December of the year following the year in which it is granted or renewed

26. A highly ionized drug ?

(a) Is excreted mainly by the kidney
(b) Can cross the placental barrier easily
(c) Is well absorbed from the intestine
(d) Accumulates in the cellular lipids

27. Nevirapine is a ?

(a) Protease inhibitor
(b) Nucleoside reverse transcriptase inhibitor
(c) Non-nucleoside reverese transcriptase inhibitor
(d) Fusion inhibitor

28. Which one of the following drugs is 'Topoisomerase I inhibitor' ?

(a) Doxorubicin (b) Irinotecan
(c) Etoposide (d) Vincristine

29. The following drugs have significant drug interaction with digoxin, except ?

(a) Cholestyramine (b) Thiazide diuretics
(c) Quinidine (d) Amlodipine

30. One of the following is not true about nesiritide ?

(a) It is a brain natriuretic peptide analogue
(b) It is used in acutely decompensated heart failure
(c) It has significant oral absorption
(d) It has a short half-life

31. The following statements regarding finasteride are true except ?

(a) It is used in the medical treatment of benign prostatic hypertrophy (BPH)
(b) Impotence is well documented after its use
(c) It blocks the conversion of dihydrotestosterone to testosterone
(d) It is a 5-α-reductase inhibitor.

32. Oculogyric crisis is known to be produced by all of the following drugs except ?
(a) Trifluoperazine (b) Atropine
(c) Perchlorperazine (d) Perphenazine

33. inverse agonist of benzodiazepine receptor is ?
(a) Phenobarbitone (b) Flumazenil
(c) Beta-carboline (d) Gabapentin

34. The group of antibiotics which possess additional anti-inflammatory and
immunomodulatory activities is ?
(a) Tetracyclines (b) Polypeptide antibiotics
(c) Fluoroquinolones (d) Macrolides

35. With which of the following theophylline has an antagonistic interaction ?
(a) Histamine receptors
(b) Bradykinin receptors
(c) Adenosine receptors
(d) Imidazoline receptors

36. One of the following is not penicillinase susceptible ?
(a) Amoxicillin (b) Penicillin G
(c) Piperacillin (d) Cloxacillin

37. Which one of the following is best associated with Lumefantrine ?
(a) Antimycobacterial (b) Antifungal
(c) Antimalarial (d) Antiamoebic

38. Which one of the following drugs increases gastrointestinal motility ?
(a) Glycopyrrolate (b) Atropine
(c) Neostigmine (d) Fentanyl

39. Which one of the following is the fastest acting inhalational agent ?
(a) Halothane (b) Isoflurane
(c) Ether (d) Sevoflurane

40. Which one of the following drugs has been shown to offer protection from gastric aspiration
syndrome in a patient with symptoms of reflux ?
(a) Ondansetron (b) Metoclopramide
(c) Sodium citrate (d) Atropine

41. Which one of the following is true of adrenal suppression due to steroid therapy ?
(a) It is not associated with atrophy of the adrenal glands
(b) It does not occur in patients receiving inhaled steroids
(c) It should be expected in anyone receiving > 5mg, Prednisolone daily
(d) Following cessation, the stress response normalises after 8 weeks

42. Hofmann rearrangement is
(1) Reaction of amide into one carbon less amine
(2) It form Nitrene intermediate
(3) It require bromine and base
(4) It form isocyanate intermediate.
(a) 1 and 2 statement is right but 3 and 4 is wrong
(b) 1 and 3,4 is right but 2 is wrong..
(c) 1,4 is right but 2 and 3 is wrong.
(d) 1,2,4 is right but 3 is wrong
(e) all statement is right.

43. Meso compound is
(1) Having plane of symmetry
(2) Identical mirror image
(3) Achiral molecule
(4) optially inactive.
(a) 1 and 2 statement is right but 3 and 4 is wrong
(b) 1 and 3,4 is right but 2 is wrong.
(c) 1,4 is right but 2 and 3 is wrong.
(d) 1,2,4 is right but 3 is wrong
(e) all statement is right.

44. IR spectra appear as dips in curves because:
(a) Wave no. is plotted against %T
(b) Wave no is plotted against concentration
(c) Wave no is plotted against absorbance
(d) Absorbance is plotted against concentration

45. The hydrogen deficiency index is a measure of:
(a) Number of C atoms
(b) number of hydrogen fragments formed
(c) Sites of unsaturation
(d) Reactivity of functional group

46. Haloperidol is classified structurally as a;
(a) benzodiazepine (b) phenothiazine
(c) butyrophenone (d) diphenylbutylpiperidine

47. Which local anaesthetic is also given intravenously to treat arrhythmias?

(a) Tetracaine (b) Mepivacaine
(c) Lignocaine (d) Bupivacaine

48. Which laxative acts by a detergent-like effect?

(a) Psyllium (b) Polycarbophil
(c) Phenolphthalein (d) Docusate sodium

49. Which of the following metals has no therapeutic use?

(a) Lead (b) Lithium
(c) Gold (d) Platinum

50. Anti-asthamatic agent which is not a mast cell stabillizer

(a) Ketotifen (b) Terbutaline Sulfte
(c) Nedocromil (d) Sodium Chromoglycate

51. The drug which was used as 'LIE DETECTOR' during the Second world war is

(a) Nitrous Oxide (b) Chloroquine
(c) Carbamazepine (d) Hyoscyine

52. Taste sensation of some liquid oral formulation are given. Match the compatible flavour used in the formulation

(1) Salt (a) Wild cherry
(2) Sour (b) Vanilla
(c) Citrus
(d) Chocolate

53. Excipients used in parentral products are given. Match them

(1) Chelating agents (a) Benzyl alcohol
(2) Local anaesthetic (b) Phenol
(c) Gelatin
(d) Disodium edetate

54. HLB values are given. Match them with correct surfactant

(1) 0 – 3 (a) Solubilizing agent
(2) 4 – 6 (b) Detergent
(c) Antifoaming agent
(d) W/O emulgents

55. Given below are the type of excipients. Match them with the examples

(1) Disintegrant (a) Talc
(2) Glidant (b) P.V.P
(c) Lactose
(d) Acacia

56. Listed below are the Schedules to the Drugs and Cosmetics Act. Match them

(1) Schedule 'M' (a) Standard for disinfectant fluids
(2) Schedule 'O' (b) Standard for ophthalmic preparation
(c) Requirement of factory premises
(d) Standard for cosmetics

57. Match the following drug with their receptor sub types

(1) Methadone (a) Agonist of μ & δ receptor
(2) Enkephanlins (b) Antagonist of μ, δ & κ receptor
(c) Agonist of μ receptor
(d) Agonist of μ, δ & κ receptor

58. Match the drug with their mechanism of action

(1) Mebendazole (a) Unkown mechanism
(2) Ivermectin (b) Neuromuscular blockade by interaction with nicotinic receptor
(c) Intensifies GABA mediated neurotransmission in nematode and cause immobilization of parasite
(d) Selectively inhibits microtubule synthesis in nematodes

59. Match the following drugs for their mechanism of action

(1) Procainamide (a) Blocks Ca^{++} channel
(2) Verapamil (b) Blocks K^{+} channel
(c) Blocks Na^{+} channel
(d) Block β adrenoceptors

60. The metabolic reactions of drugs mentioned in a to d are given. Match them

(1) Nitro reduction (a) Oxprenolol
(2) Deamidation (b) Isoniazid
(c) Chloramphenicol
(d) Lidocaine

61. Drugs given below have the characteristics mentioned in a to d. Match them

(1) Ibuprofen (a) An aryl acetic acid
(2) Acetaminophen (b) A salicyclic acid derivative
(c) An active metabolite of

another drug
(d) Hydrolysed in the blood stream

62. The systematic names of the following drugs are given. Match them

(1) Tinidazole	(a) 2-[4-3-2-trifluoro-methyl pheno selenazine-10-yl propyl piperazine-1-yl] ethanol
(2) Fluphenazine decanoate	(b) 1[2-(ethyl sulphonyl) ethyl]-2-methyl-5-nitro imidazole
	(c) 1-[2-ethyl sulphonyl)-propyl]-2-methyl-5-nitro imidazole
	(d) 2-[4-3-(2-trifluoro-methyl phenothiazin-10-yl) propyl piperazin- 1-yl] ethanol

63. Match the heterocyclic system with the drug

(1) Aziridine	(a) Thiotepa
(2) Pteridine	(b) Azathioprine
	(c) Atropine
	(d) Methotrexate

64. Techniques mentioned in A to D used for the analysis of the following drugs

(1) Sulphamethoxazole I.P	(a) Conductometry
(2) Piroxicam I.P	(b) H.P.L.C
	(c) Non-aqueous titration
	(d) Dead stop end point

65. Digitalis cardenolides mentioned below are different hydroxy derivatives. Match them

(1) Gitoxigenin	(a) 3β, 12β, 14β trihydroxy cardenolide
(2) Digoxigenin	(b) 3β, 14β dihydroxy cardenolide
	(c) 3β, 14β, 16β trihydroxy cardenolide
	(d) 3β, 12β, 6β trihydroxy cardenolide

66. Match the following Vitamins with their biochemical roles

(1) Riboflavin	(a) Free radical scavenger
(2) Pyridoxal	(b) As a coenzyme in redox reactions
	(c) Essential in the synthesis of rhodopsin
	(d) As a coenzyme for amino acid decarboxylases

67. Match the diseases with their clinical tests

(1) Diabetes mellitus	(a) Decrease in Haemoglobin levels
(2) Cystic fibrosis	(b) Increase in blood sugar levels
	(c) D.N.A diagnosis
	(d) Decreased levels of TSH

68. Match the correct pathways of the following

(1) Glyceraldehyde-3-Phosphate	(a) Cholesterol synthesis pathway
(2) Arachidonic acid	(b) Citric acid cycle
	(c) Glycolysis
	(d) Prostaglandin synthesis pathway

69. Given below are two vaccines. Their compositions are mentioned. Match them

(1) B.C.G	(a) Living attenuated Mycobacterium tuberculosis
(2) Whooping cough	(b) Experimentally killed and freeze dried polio virus
	(c) Antibodies obtained from the sera of tuberculosis patients
	(d) Killed bordetella pertussis bacteria

70. Match the following diseases with their causative organisms

(1) Helminthiasis	(a) Plasmodium flaciparus
(2) Jaundice	(b) Taenia sodium
	(c) Hepatitis-A-Virus
	(d) Toxoplasma gondii

71. Given below are the Schedules as per D and C act 1940. Match them with information to be given in the label

(1) Schedule H	(a) For external use only
(2) Schedule G	(b) For therapeutic use only
	(c) Caution-It is dangerous to take this preparation except under medical supervision
	(d) To be sold by retail on the prescription of a R.M.P. only

72. Identify the metabolite of prontosil responsible for its antibacterial activity.
(a) Sulphacetamide (b) Sulphanilamide
(c) p-Amino benzoic acid (d) Probenecid

73. The central bicyclic ring in penicillin is named as one of the followings. Find the correct name.
(a) l-Thia-4-azabicyclo[3.2.1]heptane
(b) 4-Thia-l-azabicyclo[3.2.0]heptane
(c) 4-Thia-l-azabicyclo[3.2]heptane
(d) l-Thia-4-azabicyclo[1.2.3]heptanes

74. Quantification of minute quantity of a drug from a complex matrix, without prior separation can be done using one of the following techniques. Identify that.
(a) Coulometry
(b) Potentiometry
(c) Fluorescence spectroscopy
(d) Radioimmunoassay

75. Which one of the following fragmentation pathways involves a double bond and a y- hydrogen in mass spectrometry?
(a) a-Fission
(b) p1- Fission
(c) Mc-Lafferty rearrangement
(d) Retro-Diel's Alder rearrangement

76. Identify the group of enzymes that utilizes NADP or NAD as coenzymes and catalyzes biochemical reactions by the transfer of electrons from one molecule to another.
(a) Isomerases (b) Oxidoreductases
(c) Transferases (d) Ligases

77. Glucose is the only source of energy for one of the followings. Identify that.
(a) Cardiac cells (b) Nephrons
(c) RBCs (d) Thrombocytes

78. Read the following statements carefully:
[P] Pyrrole and thiophene undergo electrophilic aromatic substitution reactions much faster than benzene
[Q] Pyrrole and thiophene undergo Diels Alder addition reaction very fast
[R] Pyrrole and thiophene undergo nucleophilic aromatic substitution reaction faster than benzene
[S] Pyrrole is a pie excessive system while thiophene is a pie deficient system Choose the correct combination of statements.
(a) Q only is true while P, R and S are false
(b) R and S are true while P and Q are false
(c) P and R are true while Q and S are false
(d) P only is true while Q, R and S are false

79. Among the followings which one is not only a non-reducing sugar but also does not exhibit mutarotation?
(a) Glucose (b) Maltose
(c) Lactose (d) Sucrose

80. Choose the most basic heterocyclic compound among the followings.
(a) Pyridine (b) Imidazole
(c) Pyrrole (d) Pyrrolidine

81. Followings are some drug derivatives used to increase/decrease the water solubility of the parent drugs:
[P] Rolitetracycline
[Q] Erythromycin lactobionate
[R] Chloramphenicol succinate
[S] Erythromycin stearate
Choose the correct combination of statements.
(a) Q and R are used to increase water solubility while P and S are used to decrease it
(b) P, Q and R are used to increase water solubility while S is used to decrease it
(c) Q, S and R are used to increase water solubility while P is used to decrease it
(d) Q and S are used to increase water solubility while P and R are used to decrease it

82. Use of which of the following artificial sweeteners is permitted in various dosage forms of Ayurveda, Siddha and Unani proprietary medicines?
(a) Sucralose (b) Aspartame
(c) Saccharin (d) All of them

83. Progesterone is obtained from diosgenin through the following sequence of chemical reactions:
[P] Acetylation, Cr03 (oxidation), Acetolysis, H2/Pd, Hydrolysis and Oppenauer oxidation
[Q] Oppenauer oxidation, Acetylation, Cr03 (oxidation), Acetolysis, H2/Pd and Hydrolysis
[R] Cr03 (oxidation), Acetolysis, Acetylation, Oppenauer oxidation, Hydrolysis and H2/Pd
[S] Acetylation, H2/Pd, Hydrolysis, Cr03 (oxidation), Oppenauer oxidation and Acetolysis Choose the correct sequence of reactions.
(a) P (b) Q
(c) R (d) S

84. Following statements are given for local anaesthetic drug lidocaine:

[P] It contains a xylidine moiety

[Q] It can be used as antiarrhythmic agent on oral administration.

[R] When administered along with adrenaline its toxicity is reduced and its effect is prolonged.

[S] Chemically it is 2-diethylamino-2',6'-dimethylphenyl acetamide Choose the correct combination of statements.

(a) P, Q and S (b) P, Q and R
(c) P, R and S (d) Q, R and S

85. For the management of which disease the given drug tacrine is used? Identify.

(a) Glaucoma
(b) Antidote for acticholinesterase poisoning
(c) As an insecticide
(d) Alzheimers disease

86. Low dose aspirin acts as anti-platelet aggregating agent by which one of the following mechanisms? Find the correct answer.

(a) It acts as a suicide substrate for COX-1 enzyme present in platelets
(b) It acts as a transition state analog for COX-2 enzyme present in the platelets
(c) It acts as a reversible inhibitor of lipoxigenase present in the platelets
(d) It acts as an affinity label of oxidoreductases present in the platelets

87. Some statements are given for clavulanic acid, sulbactam and tazobactam:

[P] All three lack the 6-acylamino side chain

[Q] All are potent inhibitors of the enzyme P-lactamase

[R] All are prodrugs of penicillin

[S] All have weak antibacterial activity

Choose the correct combination of statements.

(a) P, Q and R are true while S is false
(b) Q, R and S are true while P is false
(c) P, R and S are true while Q is false
(d) P, Q and S are true while R is false

88. Electrophilic aromatic substitution reactions in indole give one of the following products preferably. Identify that.

(a) 3-Substituted indole
(b) 2-Substituted indole
(c) 5-Substituted indole
(d) 6-Substituted indole

89. Which detector is used in gas chromatography for halogen containing compounds specifically?

(a) Katharometer
(b) Electron capture detector
(c) Flame ionization detector
(d) Thermal conductivity detector

90. Precessional frequency of a nucleus depends on the followings:

[P] Quantum of externally applied magnetic field

[Q] Quantum of electron density present around the nucleus

[R] Frequency of applied electromagnetic radiations

[S] Electronegativity of the element

Choose the correct combination of statements.

(a) P & Q are true (b) P & R are true
(c) Q & R are true (d) P & S are true

91. Some statements are given about disodium edetate:

[P] Disodium edetate is a bidentate ligand

[Q] Disodium edetate is a complexing agent but not a chelating agent

[R] Disodium edetate can be used for the assay of lithium carbonate

[S] Disodium edetate can be used for the assay of zinc sulphate Choose the correct answer.

(a) Q, R & S are true (b) Q & S are true
(c) S only is true (d) P, Q, R & S all are true

92. Which one of the following amino acids is the most effective contributor of protein buffer?

(a) Alanine (b) Glycine
(c) Histidine (d) Arginine

93. Given are some statements about cycloalkanes:

[P] Bayer's theory does not apply to four membered rings.

[Q] Cyclohexane and cyclodecane rings are not flat but are puckered.

[R] Chair form of cyclohexane experiences van der Waals strain due to flagpole interactions.

[S] Boat form of cyclohexane experiences both torsional and van der Waals strain. Choose the correct combination of statements.

(a) P, Q & R are true and S is false
(b) Q & S are true and P & R are false
(c) P, Q & S are true and R is false
(d) Q, R & S are true and P is false

94. Phenols are more acidic than alcohols. This is due to one the following reasons. Identify that.

(a) Alkoxide ions are better stabilized by the electron releasing alkyl groups
(b) Resonance stabilizes both phenols and phenoxide ions to the same extent
(c) Phenols are better stabilized than the phenoxide ions while reverse is true for alcohols and alkoxides
(d) Phenoxide ions are much better stabilized than the alkoxide ions

95. Study the following statements on alkylating agents as antineoplastics:

[P] They get converted to aziridinium ions and bind to 7th position -N atom of guanine of DNA base pairs

[Q] Nitrogen mustards and Sulfur mustards belong to this class of drugs

[R] They inhibit dihydrofolate reductase enzyme thereby inhibiting DNA synthesis

[S] They chelate electropositive atoms present in tHE DNA thereby inhibiting DNA uncoiling

Choose the correct combination of statements.

(a) P and Q are correct
(b) R and S are correct
(c) P and S are correct
(d) Q and R are correct

96. Study the following statements about the stereochemistry of steroidal aglycones in cardiac glycosides:

[P] Rings A-B and C-D are cis fused while B-C is trans fused.

[Q] Rings A-B and C-D are trans fused while B-C is cis fused.

[R] Rings A-B are trans fused while B-C and C-D are els fused.

[S] Rings A-B are cis fused while B-C and C-D are trans fused. Choose the correct statement.

(a) P is true while Q, R and S are false
(b) Q is true while P, R and S are false
(c) R is true while P, Q and S are false
(d) S is true while P, R and Q are false

97. Following are some statements about Captopril:

[P] It is a prototype molecule in the design of ACE inhibitors

[Q] It contains a sulphonyl group in its structure

[R] It has a proline moiety in its structure

[S] It has an ester linkage

Choose the correct combination of statements.

(a) P & Q are true while R & S are false
(b) Q & R are true while P & S are false
(c) P & R are true while Q & S are false
(d) R & S are true while P & Q are false

98. Cetirizine as an antihistaminic agent has a low sedative potential due to one of the following reasons. Identify that.

(a) It has a chiral center
(b) It has high log P value
(c) It has high polarity
(d) It has low molecular weight

99. There are some criteria which an ideal antacid should fulfill. Some of the criteria are given below:

[P] The antacid should be absorbable orally and should buffer in the pH range of 4 - 6

[Q] The antacid should exert its effect rapidly and should not cause a large evolution of gas

[R] The antacid should not be a laxative or should not cause constipation

[S] The antacid should react with the gastric acid and should inhibit pepsin Choose the correct combination of criteria for an ideal antacid.

(a) P, Q&R (b) Q, R&S
(c) Q&R (d) R & S

100. Titanium dioxide is used in sun screen products as a topical protective. The topical protective effect of titanium dioxide is arising due to one of the following properties. Identify that.

(a) It has a high bulk density
(b) It has a high LTV absorptivity
(c) It has a low water solubility
(d) It has a high refractive index

101. Deferoxamine is used for the treatment of toxicity caused by one of the following ions. Identify that.

(a) Arsenic (b) Cyanide
(c) Iron (d) Lead

102. Parachor and Molar refraction can be categorized under one of the following properties. Identify that.

(a) Additive properties
(b) Constitutive properties
(c) Colligative properties
(d) Additive and constitutive property

103. Rast's camphor method is used for determination of molecular weight of solutes which are soluble in molten camphor. The basic principle of the method is dependent on one of the following properties. Identify that.

(a) Elevation of freezing point of camphor by the solute
(b) Lowering of vapour pressure of camphor by the solute
(c) Lowering of freezing point of camphor by the solute
(d) Elevation of boiling point of camphor by the solute

104. In polarography, when the limiting current is achieved, one of the following processes takes place. Choose that.
(a) The rate of electron transfer just matches the rate of mass transfer
(b) The rate of electron transfer is slower than the rate of mass transfer
(c) The rate of electron transfer becomes independent of the rate of mass transfer
(d) The rate of electron transfer far exceeds the rate of mass transfer

105. Starch-iodide paste/paper is used as an external indicator in one of the following titrations. Identify that.
(a) Iodometric titration of copper sulphate using sodium thiosulphate as titrant
(b) Iodimetric titration of ascorbic acid using iodine solution as titrant
(c) Diazotisation titration of sulphadiazine using sodium nitrite as titrant
(d) Potassium dichromate titration using sodium thiosulphate as titrant

106. For a dye to be used as metal indicator in complexometric titrations, some of the dye properties are listed below:

[P] The dye should have distinct colour than the dye-metal complex

[Q] The dye-metal complex should have a higher stability than the metal-chelate (titrant) complex

[R] The dye should be capable of complexing with the metal ions

Choose the correct combination of statements for the dye to be used as an indicator in complexometric titrations.
(a) P & Q are correct while R is not
(b) Q & R are correct while P is not
(c) P & R are correct while Q is not
(d) P, Q & R all are correct

107. In amperometry, rotating platinum electrode (RPE) is used as indicating electrode. It has certain advantages as well as disadvantages. Read the following statements about the use of rotating platinum electrode in amperometry:

[P] It causes large diffusion current due to rotation resulting in greater mass transfer

[Q] It causes greatly reduced residual current due to lack of condenser effect

[R] It has a low hydrogen over potential Choose the correct combination of statements.
(a) P, Q & R are all advantages of using RPE in amperometry
(b) P & R are advantages of RPE while Q is a disadvantage
(c) Q & R are advantages of RPE while P is a disadvantage
(d) P & Q are advantages of RPE while R is a disadvantage

108. What will be the approximate Tmax of a drug exhibiting Ka of 2 hr"1 and K of 0.2 hr-1?
(a) 1.2 hr (b) 2.4 hr
(c) 4.8 hr (d) 2.0 hr

109. Based on Henderson-Hasselbalch equation, at what pH value a weak acid would be 99.9% ionized?
(a) At pH equivalent to pka + 3
(b) At pH equivalent to pka — 3
(c) At pH equivalent to pka - 1
(d) At pH equivalent to pka + 1

110. Some statements about crystals are given below:

[P] The crystal lattice is constructed from repeating units called unit cells.

[Q] The external appearance of a crystal is described by crystal habits, such as needles, prisms, rosettes etc.

[R] Polymorphism is the ability of a compound to crystallize as more than one distinct crystalline species with different internal lattice.

[S] Hydrates are always more soluble than anhydrous form of the same drug Choose the corrected combination of statements about crystals.
(a) Statement P, Q and S are correct but R is wrong
(b) Statement P, Q and R are correct but S is wrong
(c) Statement Q, R and S are correct but P is wrong
(d) Statement R, S and P are correct but Q is wrong

111. Which one of the followings is NOT used in preparation of baby powders?
(a) Stearic acid (b) Boric acid
(c) Kaolin (d) Calcium carbonate

112. According to Kozeny Carmen equation a 10% change in porosity can produce:
(a) Two fold change in viscosity
(b) Five fold change in viscosity
(c) Three fold change in viscosity
(d) None of the above

113. Speed disk atomizer rotates at a speed of:
(a) 3000 - 5000 revolutions per min
(b) 3000 - 50000 revolutions per min
(c) 300 - 50000 revolutions per min
(d) 300 - 5000 revolutions per min

114. Containers used for aerosols should withstand a pressure of:
(a) 130-150 Psig at 130 °F
(b) 140-180 Psig at 130 °F
(c) 140-170 Psig at 120 °F
(d) 120-140Psigat120°F

115. Which one of the following statements is FALSE about Interferons?
(a) Interferons are cellular glycoproteins produced by virus infected cell
(b) Interferons have no effects on extracellular virus
(c) Interferons are virus specific agents that can interfere either with DNA or RNA virus
(d) They are produced as potent broad spectrum antiviral agents

116. In relation to sodium chloride and water mixture, read the following statements:
[P] Mixture is eutectic in nature
[Q] It has eutectic point -21.2°C
[R] The composition of eutectic is 25.3% by Mass
[S] The mixture is a true eutectoid and may exist as peritectic also. Which of the set of statements is correct?
(a) P&Q (b) Q, R&S
(c) P, Q&S (d) , P, R & S

117. In relation to sterilization, what is the meaning of D300F - 2 minutes?
(a) Death of all microorganisms in 2 minutes
(b) Death of 300 microorganism in 2 minutes
(c) Death of all microorganism in 2 minutes at 300°F
(d) Death of 90% microorganism in 2 minutes at 300°F

118. Choose the correct combination:
(i) Rod mill (p)Dried plant drug
(ii) Hammer mill (q)Thermolabile drug
(iii) Fluid energy mill (r) Paint
(a) i & q, ii & p, iii & r
(b) i&r, ii&p, iii & q
(c) i & q, ii & r, iii & p
(d) i&p, ii&q, iii & r

119. Precise control of flow is obtained by which one of the followings?
(a) Needle valve (b) Butterfly valve
(c) Gate valve (d) Globe valve

120. Heat sensitive materials like fruit juice are evaporated in which one of the followings?
(a) Long tube vertical evaporator
(b) Calandria type evaporator
(c) Falling film type evaporator
(d) Forced circulation type evaporator

121. Which one of the following properties is characteristic of microemulsions?
(a) These are transparent systems with droplet size less than 1 MICRO METER
(b) These are transparent systems with droplet size less than 10 MICRO METER
(c) These are non-transparent systems with droplet size less than 1 MICRO METER
(d) These are transparent systems with droplet size less than MICRO METER

122. Which one of the following colours is NOT permitted to be used in drugs by the Drugs and Cosmetics Act, 1940?
(a) Chlorophyll (b) Riboflavin
(c) Tartrazine (d) Amaranth

123. At equal concentrations which one of the following mucilages will possess maximum viscosity?
(a) Maize starch (b) Rice starch
(c) Wheat starch (d) Potato

124. Find the process by which the conversion of sulfasalazine to sulfapyidine and 5-amino salicylic acid takes place in the colon?
(a) Hydrolysis (b) Deamination
(c) Acetylation (d) Azoreduction

125. How much quantity (in grams) of sodium chloride is needed to make 30 ml of a 2% isotonic drug (sodium chloride equivalent 0.20) solution?
(a) 0.60 (b) 0.15
(c) 0.27 (d) 0.12

ANSWER KEYS

1. (b)	**2.** (a)	**3.** (c)	**4.** (a)	**5.** (a)	**6.** (c)	**7.** (a)	**8.** (d)	**9.** (a)	**10.** (a)
11. (b)	**12.** (c)	**13.** (a)	**14.** (b)	**15.** (d)	**16.** (b)	**17.** (d)	**18.** (b)	**19.** (c)	**20.** (c)
21. (b)	**22.** (d)	**23.** (c)	**24.** (a)	**25.** (d)	**26.** (a)	**27.** (b)	**28.** (b)	**29.** (c)	**30.** (c)
31. (c)	**32.** (b)	**33.** (c)	**34.** (d)	**35.** (c)	**36.** (d)	**37.** (c)	**38.** (c)	**39.** (d)	**40.** (b)
41. (c)	**42.** (e)	**43.** (a)	**44.** (a)	**45.** (c)	**46.** (c)	**47.** (c)	**48.** (d)	**49.** (a)	**50.** (b)
51. (a)		**52.** (b)&(c)		**53.** (d)&(a)		**54.** (c)&(d)		**55.** (d)&(a)	
56. (c)&(a)		**57.** (d)&(a)		**58.** (d)&(c)		**59.** (d)&(c)		**60.** (c)&(a)	
61. (a)&(c)		**62.** (b)&(d)		**63.** (a)&(d)		**64.** (d)&(b)		**65.** (c)&(a)	
66. (b)&(d)		**67.** (b)&(c)		**68.** (c)&(d)		**69.** (a)&(d)		**70.** (b)&(c)	
71. (d)&(c)	**72.** (b)	**73.** (b)	**74.** (d)	**75.** (c)	**76.** (b)	**77.** (c)	**78.** (d)	**79.** (d)	**80.** (d)
81. (b)	**82.** (d)	**83.** (a)	**84.** (c)	**85.** (d)	**86.** (a)	**87.** (d)	**88.** (a)	**89.** (b)	**90.** (a)
91. (c)	**92.** (c)	**93.** (b)	**94.** (d)	**95.** (a)	**96.** (a)	**97.** (c)	**98.** (c)	**99.** (c)	**100.** (d)
101. (c)	**102.** (d)	**103.** (c)	**104.** (d)	**105.** (c)	**106.** (c)	**107.** (d)	**108.** (a)	**109.** (a)	**110.** (b)
111. (a)	**112.** (c)	**113.** (b)	**114.** (b)	**115.** (c)	**116.** (a)	**117.** (d)	**118.** (b)		
119. (a)	**120.** (c)	**121.** (a)	**122.** (d)	**123.** (d)	**124.** (d)	**125.** (b)			

MOCK TEST - V

1. A glycoalkaloid,

[P] Contains sulphur in addition to nitrogen in its molecule

[Q] is glycosidic in nature.

[R] Can be hydrolysed to an alkaloid.

[S] Always contains endocyclic nitrogen in its molecule.

Choose the correct option.

(a) P & R (b) Q & S

(c) Q & R (d) P & R

2. Which of the following statements are true for ginsengroot?

[P] It is among the most traded plant material of Brazil.

[Q] It is obtained from *Panax ginseng* and *Panax quinquefolium.*

[R] It is obtained from young plants of six months to one year age.

[S] It contains derivatives of protopanaxadiol.

(a) P & Q (b) R & S

(c) Q & R (d) Q & S

3. Which of the following drugs is a triterpenoid containing root?

(a) Valerian (b) Brahmi

(c) Satavari (d) Adusa

4. Which of the following alkaloids is derived from tyrosine?

(a) Quinine (b) Morphine

(c) Atropine (d) Ephedrine

5. The following options carry the name of the plant, part used and its family. Find a WRONG combination.

(a) *Aegle marmelos,* fruit & Rutaceae

(b) *Conium maculatum,* fruit & Umbelliferae

(c) *Glycyrrhiza glabra,* root and stolon & Leguminosae

(d) *Strophanthus gratus,* seed & Scrophulariaceae

6. Anomocytic stomata, trichomes with collapsed cell and absence of calcium oxalate crystals are some of the microscopic features of which plant?

(a) Digitalis (b) Hyoscyamus

(c) Mentha (d) Senna

7. Each of the following options lists the name of the drug, its class, pharmacological action and plant source. Choose an option showing a WRONG combination.

(a) Asafoetida, oleo-gum-resin, anti-flatulence, *Ferula foetida*

(b) Benzoin, balsam, antiseptic, *Styrax benzoin*

(c) Myrrh, gum-resin, antiseptic, *Commiphora wightii*

(d) Papaine, enzyme, proteolytic, *Carica papaya*

8. Quinoline alkaloids are biosynthesized via which one of the following pathways?

(a) Shikimic acid - tyrosine

(b) Shikimic acid - tryptophan

(c) Shikimic acid - cathinone

(d) Shikimic acid - phenylalanine

9. Which of the following ergot alkaloids is water soluble and shows blue fluorescence?

(a) Ergosine (b) Ergotamine

(c) Ergocristme (d) Ergometrine

10. Khellin is an active constituent of which one of the following plants?

(a) *Prunus serona* (b) *Tribulus terrestis*

(c) *Ammi visnaga* (d) *Vanilla plamfoli*

11. Goldbeater's skin test is used to detect the presence of which one of the following classes of compounds?

(a) Tannins (b) Steroids

(c) Glycerides (d) Resins

12. Which one of the following compounds is useful for the stimulation of cell division and release of lateral bud dormancy?

(a) Zeatin
(b) 2, 4-Dichlorophenoxyacetic acid
(c) Indoleacetic acid
(d) Picloram

13. Phenylethylisoquinoline is the precursor of which of the following alkaloids?
(a) Colchicine (b) Papaverine
(c) Emetine (d) Cephaline

14. A powdered drug has the following microscopic characters:

Anther cells, arenchyma, pollen grains, phloem fibers, volatile oil cells and stone cells.

The powder is obtained from which of the followings?
(a) Clove bud powder
(b) Clove bud powder with stalk
(c) Mother Clove
(d) None

15. Arrange the following fatty acids in decreasing order of their unsaturation (highest to lowest):
[P] Stearic
[Q] Oleic acid
[R] Lmolenic acid
[S] Linoleic acid
(a) P > Q > R > S (b) S > R > P > Q
(c) R > S > Q > P (d) Q > P > R > S

16. Inhibition/induction of which of the following Cytochrome P450 enzyme system is in important drug-drug interactions?
(a) CYP3A4 (b) CYP2D6
(c) CYP2C9 (d) CYP2D1

17. Which of the following mechanisms is NOT related to platelet aggregation inhibitory action?
(a) ADP receptor antagonism
(b) Glycoprotein Ilb/IIIa receptor antagonism
(c) Phosphodiesterase inhibition
(d) Prostacyclin inhibition

18. Choose the correct statement about the given four diseases?
[P] Cardiomyopathy
[Q] Rheumatoid arthritis
[R] Myasthenia gravis
[S] Ulcerative colitis
(a) Q & S are autoimmune disorders
(b) P & Q are autoimmune disorders
(c) P & R are not autoimmune disorders
(d) R & S are not autoimmune disorders

19. Which of the following species is being inactivated by the enzyme Dipeptidyl peptidase-4?
(a) Oxytocin (b) Vasopressin
(c) Incretins (d) Glucagon

20. Patients taking isosorbide mononitrate or nitroglycerine should be advised not to take Sildenafil. This drug- drug interaction causes which of the following actions?
(a) Respiratory failure
(b) Severe hypotension
(c) Prolongation of QT interval
(d) Myocardial ischemia

21. Which of the following drugs does NOT induce mydriasis?
(a) Atropine (b) Ephedrine
(c) Phentolamine (d) Cocaine

22. Which of the following statements is TRUE for angiotensm-II?
(a) Causes myocyte hypertrophy
(b) Decreases the action of sympathetic nervous system
(c) Increases force of myocardial contraction
(d) Decreases the synthesis and release of aldosterone

23. Which of the following beta blockers has been shown clinically to reduce mortality in patients of symptomatic heart failure?
(a) Atenolol (b) Carvedilol
(c) Propranolol (d) Esmolol

24. Rhabdomyolysis is the side effect associated with which of the following classes of drugs?
(a) ACE inhibitors
(b) Statins
(c) Calcium channel blockers
(d) Sodium channel blockers

25. Blood level monitoring of HbAlc is important in which of the given diseased states?
(a) Hypercholesterolemia
(b) Diabetes mellitus
(c) Myocardial infarction
(d) Congestive heart failure

26. Most of the emergency contraceptives have which one of the following active ingredients?
(a) Estradiol (b) Norethindron
(c) Misoprostol (d) Levonorgesterel

27. Which of the following antibiotics produces concen-

tration dependent bactericidal action and also possesses post-antibiotic effect?

(a) Ceftazidime (b) Azithromycin
(c) Amikacin (d) Piperacillin

28. Antiretroviral Raltegravir is unique, because of which of its following actions?

(a) Integrase inhibition
(b) CCR5 Co-receptor antagonism
(c) Fusion inhibition
(d) Reverse transcriptase inhibition

29. Which one of the followings is NOT an example of G-protein coupled receptor?

(a) Muscarinic cholinergic receptor
(b) Alpha adrenoceptor
(c) Nicotinic cholinergic receptor
(d) Beta adrenoceptor

30. Which of the followings used in the treatment of rheumatoid arthritis is NOT a biologic response modifier?

(a) Anakinra (b) Leflunomide
(c) Etanercept (d) Infliximab

31. Which of the following statements is FALSE for artemisinin?

(a) It is a sesquiterpene lactone endoperoxide
(b) It is a drug of choice in prophylaxis of malaria
(c) It does not cure relapsing malaria
(d) It is useful in treatment of cerebral falciparum malaria

32. Which of the followings is a noncompetitive inhibitor of the enzyme reverse transcriptase m HIV?

(a) Lamivudine (b) Nevirapine
(c) Abacavir (d) Tenofovir

33. Which of the followings is the most effective monotherapy for raising HDL cholesterol?

(a) Statins (b) Niacin
(c) Ezetimibe (d) to-3-Fatty acids

34. Which of the following parameters from plasma concentration time profile study gives indication of the rate of drug absorption?

(a) Cmax (b) Tmax
(c) AUC (d) t l/2

35. Which of the following pairs has high binding affinity for 5α-reductase?

(a) Letrozole and androstenedione
(b) Finasteride and testolactone
(c) Finasteride and 5-DHT
(d) Finasteride and testosterone

36. Which of the following skeletal muscle relaxants acts directly on the contractile mechanism of the muscle fibers?

(a) Pancuronium (b) Baclofen
(c) Dantrolene (d) Chlorzoxazone

37. Which is the molecular target for the vinca alkaloids as anticancer agents?

(a) Tyrosine kinase (b) DNA
(c) Ribosomes (d) Tubulin

38. A 64 year old woman with a history of Type II diabetes is diagnosed with heart failure. Which of the followings would be a POOR choice in controlling her diabetes?

(a) Metformin (b) Pioghtazone
(c) Glipizide (d) Exenatide

39. Mifepristone and gemeprost combination is used for medical termination of pregnancy. The action is caused due to which of the following mechanisms?

(a) Mifepristone is an antiestrogen while gemeprost is a prostaglandin E receptor agonist.
(b) Mifepristone is an antiprogestin while gemeprost is a prostaglandin E receptor agonist.
(c) Mifepristone is an antiandrogen while gemeprost is a prostaglandin E receptor agonist.
(d) Mifepristone is an antiprogestin while gemeprost is a prostaglandin E receptor antagonist

40. Which one of the followings is a beta lactamase inhibitor?

(a) Penicillanic acid
(b) Embonic acid
(c) Cephalosporanic acid
(d) Clavulanic acid

41. All of the followings are indications for use of ACE inhibitors EXCEPT for one. Identify that.

(a) Hypertension
(b) Myocardial infarction
(c) Left ventricular dysfunction
(d) Pheochromocytoma

42. Neural tube defects may occur by which one of the following anti-seizure drugs?

(a) Ethosuximide (b) Vigabatnn
(c) Valproic acid (d) Primidone

43. Which water is used for hand washing in a change room of pharmaceutical manufacturing plant?

(a) Potable water (b) Purified water
(c) Disinfectant water (d) Soap water

44. Which one of the following drying methods is commonly used in Pharma industry for drying of soft shell capsules?

(a) Truck drying. (b) Fluid bed drying
(c) Vacuum drying (d) Microwave drying

45. Which one of the followings does NOT afford a macromolecular inclusion compound?

(a) Zeolites (b) Dextrins
(c) Silica gels (d) Cyclodextrins

46. Which one of the following alkaloids is derived from Lysine?

(a) Emetine (b) Chelidonine
(c) Lobeline (d) Stachydrine

47. Histologically the barks of Cinnamomum cassia and Cinnamomum zeylanicum differ in one of the following features. Identify that.

(a) Sclerieds (b) Phloem Fibers
(c) Pericyclic Fibres (d) Cortex

48. Which one of the following constituents is reported to have anti-hepatotoxic activity?

(a) Podophyllotoxin (b) Andrographoloid
(c) Linalool (d) Safranal

49. Naringin, obtained from orange peel, can be named as one of the followings. Identify the correct name.

(a) 5,4'-Dihydroxy-7-rhamnoglucoside of flavanone
(b) 5,4'-Dihydroxy-7-glucoside of flavanone
(c) 5,3',4'-Trihydroxy-7-rhamnoglucoside of flavone
(d) 5,3',4'-Trihydroxy-7-glucoside of flavones

50. Rhizomes of Zingiber officinale contain some sesquiterpene hydrocarbons. Some hydrocarbons are given below:

[P] 3-Bisabolene

[Q] Gingerone A

[R] Gingerol

[S] Zingiberene Identify the correct pair of constituents present in the rhizomes.

(a) P and S (b) P and Q
(c) Q and S (d) Q and R

51. Listed below are the chemical tests used to identify some groups of phytoconstituents. Identify the test for the detection of the purine alkaloids.

(a) Keller-Killani Test (b) Murexide Test
(c) Shinoda Test (d) Vitali-Morin Test

52. Peruvoside is naturally obtained from one of the following plants. Identify the correct name.

(a) Dioscorea (b) Ginseng
(c) Liquorice (d) Thevetia

53. One of the followings is NOT required for the initiation and maintenance of plant tissue culture. Identify that.

(a) Sucrose (b) Kinetin
(c) Auxin (d) Absicic acid

54. If C is the concentration of dissolved drug and Cs is the saturation concentration. In which case the sink conditions are said to be maintained?

(a) C < 20% of Cs (b) C > 20% of Cs
(c) C < 10% of Cs (d) C > 10% of Cs

55. Which condition does not apply as per Indian law while conducting single dose bioavailability study of an immediate release product?

(a) Sampling period should be at least three *t1/2* el
(b) Sampling should represent pre-exposure, peak exposure and post-exposure phases
(c) There should be at least four sampling points during elimination phase
(d) Sampling should be continued till measured AUC is at least equal to 80% of AUC

56. Upon standing sometimes gel system shrinks a bit and little liquid is pressed out. What is this phenomenon known as?

(a) Oozing (b) Syneresis
(c) Shrinking (d) Desolvation

57. Which of the following routes of administration of drugs is associated with Phlebitis?

(a) Subcutaneous (b) Intravenous
(c) Intraspinal (d) Intradural

58. Study the following two statements and choose the correct answer:

[P] Antibodies are serum proteins providing immunity.
[Q] IgG provides immunity to new born babies while IgM is the first generated antibody.

(a) P is correct and Q is incorrect
(b) P is incorrect and Q is correct
(c) Both P and Q are correct
(d) Both P and Q are incorrect

59. Which microbe is used for validation of sterilization by filtration process?

(a) *Bacillus stearothermophilus*
(b) *Pseudomonas diminuta*
(c) *Bacillus subtilis*
(d) *Pseudomonas aeruginosa*

60. Which wavelength of the UV light provides maximum germicidal action?
(a) 253.7 nm (b) 275.5 nm
(c) 283.5 nm (d) 240.0 nm

61. Which of the following statements is INCORRECT?
(a) Chick Martin test uses organic matter in media
(b) The organism in Rideal-Walker test is *S. typhi*
(c) Rideal-Walker test uses organic matter in media
(d) The organism in Chick Martin test is *S. typhi*

62. Which of the following forces contribute to stability of charge-transfer complexes?
(a) Resonance forces
(b) Resonance and London dispersion forces
(c) Dipole-dipole interactions and London dispersion forces
(d) Resonance forces and dipole-dipole interactions

63. Which of the following isotherms are produced when the heat of condensation of successive layers is more than the heat of adsorption of first layer?
(a) Type III and IV (b) Type II and V
(c) Type I and III (d) Type III and V

64. Which of the followings act as a non-ionic emulsifying agent?
(a) Triethanolamine oleate
(b) Polyoxyethylene sorbitan monooleate
(c) N-Cetyl-N-ethylmorpholinium ethosulfate
(d) Dioctyl sulphosuccinate

65. The minimal effective flow rate of air in laminar flow hood should be not less than how many cubic feet per minute?
(a) 10 (b) 50
(c) 100 (d) 1000

66. Which of the following Schedules include shelf life of drugs?
(a) Schedule F (b) Schedule M
(c) Schedule G (d) Schedule P

67. Which of the following pumps is used in handling of corrosive liquids?
(a) Turbine pump (b) Volute pump
(c) Air binding pump (d) Peristaltic pump

68. By addition of which of the followings the shells of soft gelatin capsules may be made elastic?
(a) Polyethylene glycol (b) Sorbitol
(c) Propylene glycol (d) Dibutyl phthalate

69. Convert 90% v/v alcohol to Proof strength. Choose the correct answer.
(a) 57.77° under proof (b) 57.77° over proof
(c) 47.41° over proof (d) 47.41° under proof

70. Department of Transport Test (DOT) is performed for which of the followings?
(a) Strip packing (b) Aerosols
(c) Injection packing (d) Glass containers

71. What is the Heat of vaporization of water at 100°C?
(a) 2790 cal/mole (b) 7290 cal / mole
(c) 7920 cal/mole (d) 9720 cal / mole

72. Molecules in the smectic liquid crystals are characterized by which one of the followings?
(a) Mobility in three directions and rotation in one axis
(b) Mobility in two directions and rotation in one axis
(c) Mobility in two directions and no rotation
(d) Mobility in three directions and no rotation

73. Choose the correct sequence of Moisture Vapor Transmission Rate in packaging materials?
(a) Paper > Aluminium foil > PVC > PVdC
(b) Aluminium foil > PVC > PVdC > Paper
(c) Aluminium foil > PVdC > PVC > Paper
(d) Paper > PVC > PVdC > Aluminium foil

74. How many mL of 50% (w/v) dextrose solution and how many mL of 5% (w/v) dextrose solution are required to prepare 4500 mL of a 10% (w/v) solution?
(a) 500 mL of 50% and 4000 mL of 5%
(b) 1000 mL of 50% and 3500 mL of 5%
(c) 4000 mL of 50% and 500 mL of 5%
(d) 1500 mL of 50% and 3000 mL of 5%

75. A drug is administered to a 65 Kg patient as 500 mg tablets every 4 hours. Half- life of the drug is 3 h, volume of distribution is 2 liter/Kg and oral bioavailability of the drug is 0.85. Calculate the steady state concentration of the drug?
(a) 5.05mcg/ml (b) 4.50 mcg/ml
(c) 3.53 mcg/ml (d) 3.00 mcg/ml

76. P-Glycoprotein pump is responsible for which one of the followings?
(a) Transporting the drugs from the enterocytes into the gut lumen
(b) Transporting the drugs from gut lumen into enterocytes
(c) Transporting the drugs from oral mucosa into

blood capillaries
(d) Transporting the drugs from Peyer's patches into the gut lumen

77. The first stage of wetting on addition of a granulating agent to the powders is characterized by which one of the followings?
(a) Capillary state (b) Pendular state
(c) Funicular state (d) Droplet state

78. Larger values of Ky in the Heckel Plot indicate formation of what quality of tablets?
(a) Harder tablets (b) Softer tablets
(c) Fluffy tablets (d) Brittle tablets

79. What will be the time required for a drug exhibiting first order rate constant of 4.6/hr to be degraded from initial concentration of 100 mg/ml to 10 mg/ml?
(a) 2 hr (b) 4hr
(c) 9 hr (d) 0.5 hr

80. What will be the dose required maintaining therapeutic concentration of 20 microgram/ml for 24 hr of a drug exhibiting total clearance of 2 L/hr?
(a) 96 mg (b) 480 mg
(c) 960 mg (d) 48 mg

81. The Reynolds number widely used to classify flow behavior of fluids is the ratio of which one of the followings:'
(a) Inertial forces to gravitational forces
(b) Inertial forces to viscous forces
(c) Viscous forces to inertial forces
(d) Viscous forces to gravitational forces

82. What for the baffles are provided in a shell and tube heat exchanger?
(a) To increase turbulence
(b) To decrease turbulence
(c) To prevent corrosion
(d) To increase shell side passes

83. Which statement is FALSE for Association Colloids?
(a) They are also called amphiphiles
(b) They contain aggregated molecules
(c) They show partial solvation
(d) They are also called micelles

84. Which of the followings is NOT a reciprocating pump?
(a) Plunger pump (b) Diaphragm pump
(c) Gear pump (d) Piston pump

85. According to USP, the speed regulating device of the dissolution apparatus should be capable of maintaining the speed within limits of what % of the selected speed?
(a) 1 % (b) 2 %
(c) 4 % (d) 5 %

86. A drug whose solubility is 1 g/L in water, when given orally at a dose of 500 mg is absorbed up to 95% of the administered dose.
The drug belongs to which class according to the BCS classification?
(a) Class I (b) Class II
(c) Class III (d)Class IV

87. Which statement is NOT true for steam distillation?
(a) It is also called differential distillation
(b) It can be used for separation of immiscible liquids
(c) It can be applied for volatile substances
(d) It can be used for separation of miscible liquids

88. What is Primogel?
(a) Substituted HPMC for direct compression
(b) Modified microcrystalline cellulose for direct compression
(c) Hydro gelling polymer for gel formation
(d) Modified starch for disintegration

89. A tooth paste contains stannous fluoride and calcium pyrophosphate along with other formulation constituents. Choose the correct statement out of the followings?
(a) Stannous fluoride is an anticaries agent while calcium pyrophosphate is a dentifrice
(b) Stannous fluoride is a dentifrice while calcium pyrophosphate is a desensitizing agent
(c) Stannous fluoride is a desensitizing agent while calcium pyrophosphate is an anticaries agent
(d) Both are dentifrices while calcium pyrophosphate is additionally a desensitizing agent

90. Hydrogen peroxide solution (20 volumes) is used topically as a mild antiseptic. It is mainly used for cleaning of wounds which could be due to some of the following actions of hydrogen peroxide.
[P] Astringent action
[Q] Nascent hydrogen releasing action
[R] Oxidizing action
[S] Mechanical cleansing action
Choose the correct statements for the use of hydrogen peroxide as cleaning agent for wounds?
(a) P & R (b) P & Q
(c) R & Q (d) R & S

91. Magnesium trisilicate is considered to be a better ant-

acid than aluminium hydroxide due to its following additional properties:

[P] It has a fixed chemical composition

[Q] It forms colloidal silicone dioxide

[R] Magnesium ions overcome constipation

[S] Magnesium ions cause higher inhibition of pepsin than aluminium ions Choose the correct combination of statements?

(a) Q & S (b) R & S

(c) P & Q (d) Q & R

92. Iodine-131 as sodium iodide solution is used as a radiopharmaceutical for diagnostic and therapeutic purposes. Its usage is dependent on the release of the following emissions:

[P] Alpha particles

[Q] Positrons

[R] Beta emission

[S] Gamma radiation Choose the correct combination of statements?

(a) R & S (b) Q & S

(c) P & R (d) P & S

93. Arrange the following Lowry-Bronsted acids into their decreasing order of acidity (highest to lowest)?

[P] C_2H_5OH

[Q] $H_3C\text{-}C\equiv CH$

[R] H_20

[S] CH_3NH_2

(a) R > P > Q > S (b) P > R > Q > S

(c) P > Q > R > S (d) R > Q > P > S

94. Alkenes show typical electrophilic addition reactions. If an electron withdrawing group is attached to one of the carbons bearing the double bond, what will happen to the mechanism of the addition reaction?

(a) It remains electrophilic

(b) It becomes free radical addition

(c) It becomes pericyclic reaction

(d) It becomes nucleophilic

95. Aprotic polar solvents increase the rate of SN_2 reactions manifold. Enhancement in the rate of such reactions is due to which one of the following effects?

(a) Solvation of the anion by the solvent leaving the cation unaffected

(b) Solvation of both of the ionic species

(c) Desolvation of the cation and solvation of the anion

(d) Solvation of the cation by the solvent leaving the anion unaffected

96. Five-membered heteroaromatic compounds show a much higher rate of electrophilic aromatic substitution reactions than the six-membered ones. This is due to which one of the following reasons?

(a) Five-membered heteroaromatic compounds have higher circulating electron density in the ring than the six-membered ones

(b) Five-membered heteroaromatic compounds have lower circulating electron density in the ring than the six-membered ones

(c) Five-membered rings are smaller in size than the six membered ones which affects their reaction rates

(d) Six membered heteroaromatic rings are flat while the five-membered ones arc puckered

97. Pyridine is more basic than pyrrole. This is due to which of the following facts?

(a) Lone pair of electrons on N in pyrrole is localized

(b) Lone pair of electrons on N in pyridine is localized

(c) Nitrogen of pyrrole has one hydrogen atom attached to it while pyridine does not have any

(d) Pyridine has three double bonds while pyrrole has only two

Diels-Alder reaction can be carried out in which of the following heterocyclic compounds most readily?

(a) Pyrrole (b) Thiophene

(c) Furan (d) Pyridine

98. In nucleophilic aliphatic substitution reactions arrange the following leaving groups in decreasing order of their leaving capacity?

[P] Brosyl

[Q] Hydroxyl

[R] Chloro

[S] Mesyl

(a) S > R > P > Q (b) P > S > R > Q

(c) R > Q > S > P (d) R > S > Q > P

99. Determine the correctness or otherwise of the following Assertion [a] and the Reason [r]:

Assertion (a) : Quaternary ammonium phase transfer catalysts can enhance the rate of nucleophilic aliphatic substitutionreactions in biphasic systems with water soluble nucleophiles.

Reason (r): Quaternary ammonium compounds are highly polar, positively charged water soluble compounds.

(a) Both (a) and (r) are true but (r) is not the correct reason for (a)

(b) Both (a) and (r) are true and (r) is the correct reason for (a)

(c) (a) is true (r) is false
(d) Both (a) and (r) are false

100. Which one of the given compounds can be used as primary standard for standardization of perchloric acid solution in non-aqueous titrations?
(a) Potassium hydrogen phthalate
(b) Sodium bicarbonate
(c) Potassium dihydrogen phosphate
(d) Sodium methoxide

101. Indicators used in complexometric titrations are chelating agents. Choose the correct statement about them?
(a) Indicator-metal ion complex should have higher stability than EDTA-Metal ion complex
(b) Indicator-metal ion complex should have lower stability than EDTA-Metal ion complex
(c) Indicator-metal ion complex should have equal stability as EDTA-Metal ion complex
(d) Stability of the indicator-metal ion complex is not an important criterion in complexometric titrations

102. Name the compound used for standardization of Karl-Fisher reagent in aquametry?
(a) Sodium tartrate dihydrate
(b) Copper sulphate pentahydrate
(c) Sodium iodide
(d) Sodium thiosulphate

103. In polarography. DME has a number of advantages. One of the advantages is that mercury has large hydrogen over potential. It means which one of the followings?
(a) Hydrogen ions get easily reduced on the DME
(b) Hydrogen gas gets easily reduced on the DME
(c) Hydrogen ions require high potential to be reduced at DME
(d) Water is difficult to get oxidized at DME

104. Following are the desirable properties of the liquid phase used in GLC EXCEPT for one of the followings. Identify that.
(a) It should be inert to the analytes
(b) It should have high viscosity at operating temperature
(c) It should have low vapour pressure at the operating temperature
(d) It should have a high resolving power

105. In HPLC analysis what type of column would you prefer?
(a) A column with high HETP and high number of plates
(b) A column with low HETP and low number of plates
(c) A column with high HETP and low number of plates
(d) A column with low HETP and high number of plates

106. To synthesize sulphonyl urea antidiabetic, which of the following reactions can be used?
(a) Reacting a suitably substituted sulphonyl chloride with a desired urea derivative under basic conditions
(b) Reacting a suitably substituted sulphonamide with a desired isocyanate derivative
(c) Reacting a suitably substituted sulphonic acid with a desired isocyanate derivative
(d) Reacting a suitably substituted sulphoxide with a desired urea derivative

107. The following statements are given:
[P] Conformational isomers are interconvertible by rotation around a single bond while configurational isomers cannot be interconverted without breaking a bond.
[Q] Configurational isomers could be optically active or optically inactive while conformational isomers are optically inactive
[R] Geometric isomers must have a double bond in their structures
[S] Geometric and optical isomers are the two distinct categories of configurational isomers. Choose the correct combination of statements.
(a) P, Q & S are true while R is false
(b) P, R & S are true while Q is false
(c) Q, R & S are true while P is false
(d) P, Q & R are true while S is false

108. A carbocation will NOT show one of the following properties. Choose that.
(a) Accept an electron to give a carbene
(b) Eliminate a proton to afford an alkene
(c) Combine with a negative ion
(d) Abstract a hydride ion to form an alkane

109. Choose the FALSE statement for E2 mechanism in elimination reactions?
(a) These reactions are accompanied by rearrangements
(b) These reactions show a large hydrogen isotope effect.
(c) These reactions show a large element effect
(d) These reactions are not accompanied by hydrogen exchange

110. BETA-Carboline ring system is present in
(a) Emetine (b) Riboflavine
(c) Deserpidine (d) d-Tubocurarine

111. Which one of the followings is NOT a bioisosteric pair?
(a) Divalent ether (-0-) and amine (-NH)
(b) Hydroxyl (-OH) and thiol (-SH)
(c) Carboxylate (C02-) and sulfone (S02)

(d) Hydrogen (-H) and fluorine (-F)

112. Of the four stereoisomers of chloramphenicol which one is the biologically active isomer?

(a) L-Erythro (b) L-Threo
(c) D-Erythro (d) D-Threo

113. The catalytic triad in acetyl cholinesterase is composed of which of the following amino acid residues?

(a) Serine, Histidine and Glutamate
(b) Serine, Arginine and Glutamate
(c) Threonine, Histidine and Aspartate
(d) Threonine, Arginine and Glutamate

114. Fajan's method of titrimetric analysis involves detection of the end point on the basis of which one the followings?

(a) Colour change
(b) Appearance of a precipitate
(c) Neutralization reaction
(d) Adsorption phenomenon

115. Which of the following statements is true?

(a) Aliphatic protons have chemical shifts > 7 ppm
(b) Spin quantum number of proton is 1
(c) Chemical shift describes electronic environment of a proton
(d) Vicinal coupling constant is always higher than geminal coupling constant

116. In FT-IR instruments Michaelson interferometer is used in place of grating. The function of the interferometer is to act as a modulator'. What do you understand by this statement?

(a) The function of the interferometer is to act as a monochromator
(b) The function of the interferometer is to convert high frequency radiations into low ones
(c) The function of the interferometer is to convert low frequency radiations into high ones
(d) The function of the interferometer is to convert frequency domain spectra into time domain spectra

117. Which amongst the following auxochromes produces a shift towards higher energy wave length?

(a) -CH3 (b) -NHCH3
(c) -Cl (d) -C=0

118. What is the wave number equivalent of 400 nm wavelength?

(a) 0.0025 cm-1 (b) 0.25 cm-1
(c) 2500 cm-1 (d) 25000 cm-1

119. Given are the four statements about NMR:

[P] 13CMR is a less sensitive technique than PMR

[Q] Both 13C and :H have I=1/2

[R] Precessional frequency of the nucleus is directly proportional to the applied magnetic field

[S] Deuterium exchange studies can be performed to ascertain protons attached to heteroatoms.

Choose the correct combination of statements.

(a) P, Q & R are true while S is false
(b) R, S & Q are true while P is false
(c) S, P & Q are true while R is false
(d) All are true

120. The protons *ortho* to the nitro group in p-nitrotoluene are examples of which one of the Following types ?

(a) Chemically equivalent but magnetically non-equivalent protons
(b) Chemically and magnetically equivalent protons
(c) Chemically and magnetically nonequivalent protons
(d) Chemically nonequivalent but magnetically equivalent protons

121. A 250 μg/ml solution of a drug gave an absorbance of 0.500 at 250 nm at a path length of 10 mm.
What is the specific absorbance of the drug at 250 nm?

(a) 0.002 cm-1 gm-1 litre
(b) 0.002 cm-1 gm-1 dl
(c) 20 cm-1gm-1 litre
(d) 20 cm-1 gm-1 dl

122. The peak at m/z 91 in the mass spectrum for alkyl benzenes is due to which one of the followings?

(a) Alpha fission
(b) Retro Diels-Alder rearrangement
(c) Mc-Laffartey rearrangement
(d) Tropylium ion formation

123. Increased serum levels of which one of the followings may be associated with decreased risk of atherosclerosis?

(a) VLDL (b) LDL
(c) HDL (d) Total Cholesterol

124. Metformin causes the following actions EXCEPT for the one. Identify that.

(a) Reduces hepatic neoglucogenesis
(b) Increases glucose uptake in skeletal muscles
(c) Enhances sensitivity to insulin
(d) Increases HbAlc by 1% to 2%

125. Misoprostol has a cytoprotective action on gastrointestinal mucosa because of one of the following actions. Identify that.

(a) It enhances secretion of mucus and bicarbonate ion
(b) It neutralizes hydrochloric acid in stomach
(c) It antagonizes nonsteroidal anti-inflammatory drugs
(d) It is bactericidal to H. pylori

ANSWER KEYS

1. (b)	**2.** (d)	**3.** (a)	**4.** (b)	**5.** (d)	**6.** (a)	**7.** (c)	**8.** (b)	**9.** (d)	**10.** (c)
11. (a)	**12.** (a)	**13.** (a)	**14.** (b)	**15.** (c)	**16.** (a)	**17.** (d)	**18.** (a)	**19.** (c)	**20.** (b)
21. (c)	**22.** (a)	**23.** (b)	**24.** (b)	**25.** (b)	**26.** (d)	**27.** (c)	**28.** (a)	**29.** (c)	**30.** (b)
31. (b)	**32.** (b)	**33.** (b)	**34.** (b)	**35.** (c)	**36.** (c)	**37.** (d)	**38.** (b)	**39.** (b)	**40.** (d)
41. (d)	**42.** (c)	**43.** (d)	**44.** (c)	**45.** (d)	**46.** (c)	**47.** (d)	**48.** (c)	**49.** (a)	**50.** (a)
51. (b)	**52.** (d)	**53.** (d)	**54.** (c)	**55.** (c)	**56.** (b)	**57.** (b)	**58.** (c)	**59.** (a)	**60.** (a)
61. (c)	**62.** (d)	**63.** (d)	**64.** (b)	**65.** (c)	**66.** (d)	**67.** (d)	**68.** (b)	**69.** (b)	**70.** (b)
71. (d)	**72.** (b)	**73.** (d)	**74.** (a)	**75.** (d)	**76.** (a)	**77.** (b)	**78.** (a)	**79.** (d)	**80.** (c)
81. (b)	**82.** (a)	**83.** (c)	**84.** (c)	**85.** (c)	**86.** (a)	**87.** (d)	**88.** (d)	**89.** (a)	**90.** (c)
91. (d)	**92.** (a)	**93.** (c)	**94.** (d)	**95.** (d)	**96.** (a)	**97.** (b)	**98.** (b)	**99.** (b)	**100.** (a)
101. (b)	**102.** (a)	**103.** (a)	**104.** (b)	**105.** (d)	**106.** (b)	**107.** (b)	**108.** (a)	**109.** (a)	**110.** (c)
111. (a)	**112.** (d)	**113.** (a)	**114.** (b)	**115.** (c)	**116.** (a)	**117.** (b)	**118.** (d)	**119.** (d)	**120.** (a)
121. (d)	**122.** (d)	**123.** (c)	**124.** (d)	**125.** (a)					