Dr. B R Ambedkar Center for Biomedical Sciences

University of Delhi, Delhi

Ph.D. in Biomedical Sciences

Syllabus for Ph.D. Entrance Examination

I. ORGANIC CHEMISTRY

Reactive Intermediates in Organic Reactions
Carbocations, carbanions, Free Radicals their stability and applications to biological systems, benzynes, carbenes, radical cations and radical anions; their generations and reactions exemplified with suitable case study leading to C-C bond formation.

Stereochemistry of Organic Compounds
The definition of the following terms with suitable examples; Elementary treatment of symmetric elements, Chirality, prochirality; (enantiomer, epimer,diastereomer). Absolute and relative configuration; r and s notation; enantiotopic and diastereotopic faces, endo and exo faces, Regioselective, enantioselective, stereoselective and stereospecific reactions, Confirmation of 2,3 dibromomutane, E & z notations, Cyclohexane diols.

Mechanism and stereochemistry of following reactions
Substitution, elimination and addition reactions; oxidation and reduction, Ester formation and ester hydrolysis, Aromaticity, aromatic and Nucleophilic substitution (with appropriate examples; Woodward Hoffman rules and photocyclization,

Asymmetric synthesis
Cram and Prelog rule, Chiral synthesis (with suitable examples) asymmetric epoxidation.

Heterocyclic Chemistry
Structure, synthesis and reactivity of the following heterocycles and their significance in biology and drugs and materials: furan, pyrrole, thiophene, imidazole, oxazole, thiazole, azepine, thiazine, carbazole, indole pyridine, quinoline and isoquinoline, acridine, phenothiazine, pteridine, purines and pyrimidines.

Bio-organic Chemistry
Aminoacids, peptides and Proteins structure and Functions. Formation of Peptide Bonds. Activation and Protecting groups and peptide bond formation, protein degradation and sequencing of amino acids,DNA and RNA bases, nucleosides and nucleotides, formation of N- and C- glycosides, phosphodiesters, conformation and configuration of 5-carbon

and 6-carbon sugars, maltose, sucrose and lactose, glucosylamine, neuraminic and muramic acids.

Synthetic macromolecules and Polymers in Biology
Building of macromolecules and molecular frameworks and their biomedical applications. Synthetic strategies for artificial systems that mimic biological entities, applications of supramolecular principles to molecular diagnosis, therapeutic applications of supramolecular chemistry. Nanotechnology and its applications in drug delivery and the potential for synthetic peptides to form antibiotic tubes

Mechanisms in Biological Chemistry
Active methylene groups, aldol and retroaldol reactions, schiff bases and enamine reactions, nitrogen, phosphorous and sulfur ylides, Umpolung reaction, Michael addition, Polymer supported organic reactions, phase transfer catalysis, Equivalence of these reactions in biological systems

Enzyme systems
Enzyme classifications, EC number, Inhibitors, Mechanism of Enzymes. Mechanism of coenzyme catalysis: Coenzyme A, NAD^+ and NADPH, FMN and FAD, biotin, pyridoxal, TPP, lipoic acid, tetrahydrofolate, ascorbic acid, cyanocobalamine and cytochrome P-450.

Hammett and Taft Equation
Steric and Solvent effects Role of pH, reaction media on certain reactions.

II. BIOCHEMISTRY

Structure Of Protein
Secondary and tertiary structure of protein: a helix, ß sheets, examples of proteins, Ramachandran plot, factors effecting secondary and tertiary structure (disulphide bonds, heat, organic solvents, detergents). Examples of some common structural motifs in proteins.

Separation techniques for proteins: Ion exchange chromatography, dialysis, molecular sieving, polyacrylamide gel electrophoresis (determination of subunits and molecular weight), electrofocussing affinity chromatography.

Structure and function of hemoglobin: Conformational studies, binding of oxygen and its release, oxygen saturation curves. Methods of protein sequencing. Disorder of Amino Acid and protein metabolism

Enzymology
Introduction: General characteristics of enzymes, definition of coenzyme, holoenzyme, prosthetic groups, classification.
Enzyme Kinetics: Substrate, active site, transition state, activation energy, equilibrium constant Km, Vmax, specificity, Michaelis-Menten equation.

Reaction Mechanism: Acid -base catalysis and colvalent catalysis (giving examples). Regulation of enzyme activity: Reversible and irreversible inhibition (non-competitive, uncompetitive) and their effects on Km and Vmax, effect of pH, heat, PMSF and other inhibitors.
Allosteric enzymes: Models to explain their kinetic behaviour.
Problems on enzyme kinetics: Determination of active sites and turnover number.

DNA replication and its regulation
Concept of origin of replication, semiconservative hypothesis.

Mechanism of DNA Replication: Structure and function of DNA polymerases. Role of helicase, primase, gyrase, topoisomerase and other proteins in DNA replication in E.coli. replication of viruses and eukaryotes, initiation of replication, elongation and termination of DNA synthesis. DNA Repair

RNA Synthesis
Transcription in prokaryotes using E -coli as an example, Structure & function of RNA polymerases. Transcription initiation, elongation and termination.

Transcription in eukaryotes–Structure of TFIID, and other transcription factors, enhancers, silencers, insulators, general concept of regulation of transcription (in brief). Post-transcritional modifications, Ribozymes–Structure and mechanism of action.

Translation
Translation in Prokaryotes-initiation: activation of amino acid, role of 30s and 50s ribosomal subunits, initiation factors) shine-dalgarno sequences. Elongation factors, peptidyl transferase termination signal, release factors. Inhibition of protein sunthesis - by antibiotics.

Translation in eukaryotes – recent concept in initiation and termination, regulation of protein synthesis, comparison with prokaryotic system. Post translation modification – Methylation, glycosylation, phosphorylation, acetylation, proteolytic processing, addition of prosthatic groups, disulphide bond etc. protein degradation.

III. CELL BIOLOGY

Biomembranes: Basic structure, lipid and protein composition and their basic functions Transport of molecules across membranes. Passive and active transport across membranes. Factors regulating them, ion chanells, ABC pumps of bacteria.

Organelles of eukaryotic cells – Introduction basic structure and function of various organelles, ER, golgi bodies, chloroplasts, mitochondria endosomes, lysosomes etc. separation and visualization methods of various cell organelles.Muscle & Nerve Cells.

Nucleus and Chromosome Structure
Introduction: Prokaryotic and Eukaryotic genome and its organization, eukaryotic

chromosome. Basic structure of DNA; hairpins and cruciform, Z-DNA, triple helix.

DNA Supercoiling: Histones, nonhistone proteins, topoisomerases and telomerase and their functions in chromatin structure. Yeast artificial chromosome.

The Cytoskeleton
Cytoskeleton proteins, Cell motility and shape, protein sorting, Transport of proteins. Microfilaments and actin filaments

ECM Proteins and Cell Adhesion
Cell-cell interaction, Cell junctions, Adhesion proteins, Cell matrix interaction, Integrins, Functional role of adhesion proteins.

Eukaryotic Cell Cycle
Cell cycle and its control: Loss of cell regulation by viral infection, checkpoints in cell cycle regulation.

Cell to Cell Signaling
Cell surface receptors, G-protein mediated signaling, camp, receptors tyrosine kinases, second messengers.

Cell death
Apoptosis, Necrosis, Proapoptotic and Antiapoptotic proteins and mechanism of action Autophagy**,** Senescence, Cell death mechanisms in health and diseases.

Cell Differentiation

Cellular Stress Response
Stress response proteins and pathways, Post translational modifications in stress response, General responses to hyperthermia nutritional deprivation and other stressors.

IV. MEDICAL MICROBIOLOGY

Bacteriology
Introduction, Taxonomy, nomenclature and identification of bacteria, Reproduction and growth, Organization and ultrastructure of micro-organisms and various antibiotics, Antimicrobial used in clinical practical, Normal human flora, Pathogenesis and virulence factors of bacteria, Human diseases caused by bacteria in the following: Respiratory tract infections, Urinary tract infections, Genital tract infections, Gastrointestinal tract infections, Blood stream and CNS infections. Epidemiology of bacterial diseases.

Parasitology
Classification of parasitic protozoa. Cellular organization of parasitic protozoa. Epidemiology of parasitic infections. Immunology and immunopathology of parasitic infections, Control of parasites and parasitic infections. Common parasitic disease: Trypanosomiasis, Leishmaniasis, Malaria, Opportunistic parasitic infections, Helminths.

Medical Mycology

Classification, Cryptococcosis, Candidiasis, Blastomycosis, Histoplasmosis, Coccidiomycosis,
Phycomycosis.

Clinical Virology
The structure, components and classification of viruses. Viral multiplication cycle, effect of virus infection on the host cell, cytopathic effects, inhibition of host cell cytopathic effects, inhibition of host macromolecular biosynthesis, changes in regulation of gene expression. Genetics of animal viruses. History, epidemiology, diagnosis, clinical features, treatment and prevention of small pox, herpes, adenoviruses, arboviruses, picornaviruses, myxoviruses.

V. GENETICS

Introduction to the Science of Genetics
Genetic terminology Impact of Genetics on other disciplines.

Mendelian Genetics
Mendelian Laws of inheritance, its application in animal Genetics, analysis of results of Genetic crosses by various methods.

Chromosomal basis of inheritance and data analysis
Sex chromosomes in grasshopper, maize and co-linearity of genes on chromosomes, Non-disjunction in Drosophila and its role in deciphering chromosomal basis of inheritance. Analysis of patterns of inheritance, Punnett square, statistical methods.

Deviations from Mendelian Genetics I
Codominance, incomplete dominance, RFLP markers, gene interactions, multiple alleles.

Mutation and mutational analysis
Spontaneous occurrence of mutations in bacteria Lederberg and Lederberg experiment, Types of mutations i.e. point mutations, deletions, rearrangements, insertions, dynamic mutations (repeat expansions) with appropriate examples, Chromosomal anomalies. Mutation mapping suing balancers, Clb technique in Drosophila.

Linkage as a deviation from Mendelian Genetics
Recombination, Gene mapping using Drosophila as an example, experiments demonstrating physical basis of recombination, crossing over. Gene mapping using special systems, yeast and Neurospora.

Bacterial genetics
Transformation, Conjugation, genetic map construction in *E.coli*. Phage genetics, fine structure of rII region, work of Seymour Benzer.

Genetic Variation

Transposition and its application in genetic studies. Extra chromosomal inheritance, chloroplast and mitochondrial inheritance, mitochondrial mutations in yeast, human genetic disorders related to mitochondrial inheritance.

Deviations from Mendelian Genetics II
Genomic imprinting in mice, understanding molecular basis of epigenetic inheritance, human disorders related to imprinting, Prader Willi and Angelmen syndrome, Molecular basis of Epigenetic regulation in H19 and Igf2 region, histone modification marks, Position effect variegation.

Genetic control mechanisms and generation of cellular asymmetry
The lambda phage control of lytic and lysogenic phase, molecular basis of regulatory mechanisms in phage lambda. Mating type switching in *Saccharomyces cerevisiae.*

Sex determination in Drosophila and humans
Chromosomal basis to genetic basis, genetics of dosage compensation in Drosophila. X inactivation and its molecular basis in humans.

Introduction to developmental genetics
Early embryonic development in Drosophila. Maternal inheritance, genetic basis of axis determination, regulatory cascade in development in Drosophila, Homeotic genes.

Introduction to human Genetics
Pedigree analysis and basic inheritance patterns in humans.

POPULATION GENETICS

Definition, aim and scope of population genetics, population structure, factors maintaining population boundaries, effective breeding size, gene pool. The Hardy-Weinberg Law and its application, factors affecting the Hardy-Weinberg equilibrium. Human polymorphism (transient and balanced), relationship between sickle cell polymorphism and malaria, other ploymorphisms that may be an adaptation to malaria eg. G6PD deficiency. Duffy blood groups, thalassemia and haptoglobins. X linked polymorphism (G6PD and colour blindness). Incompatibility Selection. Non-random mating, inbreeding and its consequences. Migration and Genetics, types of migration, models to study genetic effects of migration, gene flow, effects of gene flow, admixture and natural selection, calculation of admixture.

VI. MOLECULAR BIOLOGY AND BIOTECHNOLOGY

Regulation of gene expression in Prokaryotes
Coordinated control of clustered genes-operon model, with example of inducible systems like Lac– Operon. Arabinose operon and repressible systems like Trp operon. Role of cyclic AMP.

Role of repressors and activators of transcription in regulation of phage-lytic and lysogeic pathways, lambda repressor.

Regulation of Gene expression in Eukaryotes
Introduction-Organization of genes in eukaryotic DNA; Repetitive DNA sequences, Activators, enhancers. Modular structure of transactivators, repressor complexes, mechanism of their function in gene regulation.

Post transcriptional regulation of transcription regulators by methylation, acetylation, hormones and protein-protein interactions.

Methods used to study protein-protein interactions (yeast two hybrid and co-Immunoprecipitation) and protein-DNA interactions (EMSA and DNA footprinting)

Diseases linked with gene expression.

Chromatin remodeling
Role of various remodeling proteins such as NURF, ACF, CHRAC, SWI-SNF and locus control regions in gene regulation.

Oncogenes
Retroviral and cellular oncogenes, their function and mechanism of action in regulating cell growth and development (using P53 and Ras protein as example).

Recombinant DNA technology and Biotechnology
Types of Restriction endonucleases and how to make restriction maps. Other enzymes used in genetic engineering such as S1 nuclease, polynuceotide kinase, mung bean nuclease etc. Vectors - cloning and expression vectors, prokaryotic and eukaryotic cloning vectors, yeast vectors, shuttle vectors, YAC & BAC. Principles of selection of specific cloned DNA - blue white selection, insertional inactivation, antibiotic markers used in prokaryotic and eukaryotic cloning. Detection and identification of cloned DNA sequences, methods of sequencing of DNA. Application and principles of Polymerase Chain Reaction, RT-PCR, RFLP analysis, real time PCR. Mutagenesis – different methods used to generate mutants (deletion and point mutations). Application of recombinant DNA technology: DNA fingerprinting, gene therapy, diagnostics. Bio-safety and ethics for recombinant DNA technology.

VII. APPLICATION OF STATISTICS AND MATHEMATICS FOR BIOLOGY

Bio-Statistics
Introduction to Mean, mode, median, mean deviation, Standard deviation, coefficient of variation.

Correlation (Karl Passions, Co-efficient of correlation, Rank correlation) and Regression analysis, Regression equations, taking suitable examples from biological data.

Probability: Theorems on probability, Binomial and normal distribution .

Methods of Sampling of biological data and analysis using 't' and 'Z' and 'F' tests of significance for small and large samples.

Bio-Mathematics
Functions, Limits and continuity, differentiation and integration, Maxima & Minima and their use in biological problems.

Differential Equations, separable variables, homogeneous, exact and linear equations of second order, application of differential equations of Biochemistry.

Matrices and determinants, characteristic roots and characteristic equations, Caley Hamilton theorem.

VIII. IMMUNOLOGY

Introduction to Immune System
Innate and acquired Immunity, Active and passive Immunity

Lymphoid System
Lymphoid Tissue: Primary or Secondary, Primary Lymphoid Organs, Secondary Lymphoid organs, Lymphocyte Traffic

Cells involved in the Immune Response
Lymphocytes, Mononuclear Phagocyte, Antigen- presenting cells, Polymorphs and mast cells, Cluster designation Ag specific receptors (comparison of Human and Mouse Lineages)

Antibody Generation, structure and Function
Humoral immunity, Clonal Selection Theory, Immnoglobulins, Antibody Structure and Function, Antibody Effector Mechanism, Antibody Receptors, Antibody Diversity, Immunogolubin Gene Recombination**,** Effect of Somatic Mutations or the Antibody Diversity, Ab Class switching, Antibody Responses in vivo, Enhanced Secondary Responses Isotype switching, Affinity Maturation Development of Memory

Major Histocompatibility Complex
Structure of MHC Class I Molecules, Structure of MHC Class II Molecules, Genomic Organisation of the MHC locus in Mice and Humans, Ontogeny and T-cell Receptors, Genomic Organization of TCR Locus

Antigen Recognition and Presentation
Structure and assembly of MHC molecules/Peptide Complexes. Antigen Processing and

Presentation of T-lymphocytes (CD4+ and CD8+)

Complement System
Nomenclature of classical Complement, Alternative Activation of pathway, Biological Effects of Complement

Cytokines Network
Molecular basis of t- cell activation, Cytokine production from T_H1 and T_H2 CD4+ T-cells, Structure and function of various cytokines, cytokine receptors

Cell Mediated Immune Response
T -Cell independent Defence Mechanisms, T- Cell dependent Defence Mechanisms, Cell Mediated Cytotoxicity, Role of Macrophages in Immune Response

Regulation of Immune Response
Role of Antigen, Antigen Presenting Cell, Antibody, Lymphocytes, Idiotypic Modulation of Response, Neuroendocrine Modulation of Responses, Genetic control of Immune Response.

Cell Migration and Adhesion
Patterns of Cell Migration, Structure and function of various adhesion Molecules, Mechanism of Cell Migration and their involvement in disease

Immunopathology
Rh- blood groupings, Autoimmune Diseases, Immuno deficiencies, Genetic disorders congenital and acquired, Hypersensitivity Reactions (type I and type IV), Role of 1gE, Mast cells, Genetic Allergic Response, Tumors

Immune Tolerance
Self Tolerance, Transplantation and Rejection.

Antigen Antibody Interaction

Immunological Techniques
Haemagglutination, Direct/Indirect Immunoflorescence, Isolation of pure antibodies, Hybridoma Technology for Mab Production, Assays for Complement

Gene Targeting: Knock out and Transgenic Animals.

Tumor Immunology, FACS, Vaccines

IX. HUMAN PHYSIOLOGY

Membrane physiology, nerve and muscle
Organization and functional systems of the cell with refers to nerve and muscle cells. Transport of ions and molecules through cell membrane: diffusion and active transport. Membrane potentials and action potentials: Resting membrane potential of nerves. Nerve action potential. Excitation and Contraction of skeletal muscle: Physiologic anatomy of

skeletal muscle. Molecular mechanisms of muscle contraction. Energetics of muscle contraction. Excitation of skeletal muscle. Neuromuscular transmission and excitation-contraction coupling.

Blood physiology

Blood cells, and blood clotting, red blood cells. Blood groups, transfusion, tissue and organ transplantation. Resistance of body to infection. Leukocytes, granulocytes, monocyte-macrophage system and inflammation. Hemostasis and blood coagulation.

Heart and circulation

Physiology of cardiac muscle. Cardiac cycle, Regulation of heart pumping, Rhythmical excitation of heart, Control of excitation and conduction in heart, Characteristics of normal electrocardiogram, Cardiac arrhythmias, Physical characteristics and basic theory of circulation, Vascular distensibility and functions of arterial and venous systems, Microcirculation and lymphatic system, Capillary fluid exchange, interstitial fluid and lymph flow, Local control of blood flow by tissues and humoral regulation, Nervous regulation of circulation, Cardiac output, venous return and their regulation, Heart sounds, dynamics of valvular and congenital heart defects, Cardiac failure and circulatory shock.

Respiration

Pulmonary ventilation: mechanisms of pulmonary ventilation, pulmonary volumes and capacities, alveolar ventilation. Functions of respiratory passageways. Pulmonary circulation, pulmonary edema and pleural fluid. Physical principles of gas exchange, Diffusion of gases through respiratory membrane, Transport of oxygen and carbon dioxide in blood and body fluids. Regulation of respiration: respiratory center, peripheral chemoreceptor system, central chemoreceptor system and their regulatory function.

Gastrointestinal physiology

General principles of gastrointestinal function - motility, nervous control, and blood circulation, Transport and mixing of food in the alimentary tract, Ingestion of food. Motor functions of stomach. Movements of small intestine. Movements of colon. Secretary functions of alimentary tract: Secretion of saliva, Gastric secretion, Pancreatic secretion, Secretion of bile by liver, Secretions of small and large intestine. Digestion and absorption in gastrointestinal tract: Digestion of various foods, Absorption in small intestine.

Kidneys and body fluids

Body fluid compartments: Basic principles of osmosis and osmotic pressure: Extracellular and intracellular fluids. Interstitial fluid and edema. Urine formation by kidneys: Glomerular filtration, renal blood flow and their control, Functions of kidneys in homeostasis, Determinants of glomerular filtration rate, Renal blood flow, Tubular processing of glomerular filtrate, Reabsorption and secretion by renal tubules. Reabsorption and secretion along different parts of nephron, Regulation of tubular reabsorption.

Regulation of extracellular fluid osmolarity and sodium concentration. Role of thirst in

controlling extracellular fluid osmolarity and sodium concentration. Integration of renal mechanisms for control of blood volume and extracellular fluid volume. Renal regulation of potassium, calcium, phosphate and magnesium. Regulation of acid-base balance.

Sensory Physiology

Central nervous system synapses. Some special characteristics of synaptic transmission, Sensory receptors. Neuronal circuits for processing information. Somatic sensations: Tactile and position senses. Sensory pathways for transmission of somatic signals into the central nervous system. Transmission in dorsal column – medial lemniscal system. Pain, headache, and thermal sensations: Pain receptors and their stimulation, Dual transmission of pain signals into the central nervous system. Referred and visceral pain. Eye: Optics of vision, Receptor and neural function of retina, Photochemistry of vision, Color vision, Neural function of retina. Central neurophysiology of vision, Organization and function of visual cortex. Hearing: Tympanic membrane and ossicular system, Cochlea, Central auditory mechanisms, Vestibular sensations and maintenance of equilibrium. The chemical senses - taste and smell.

Nervous system: motor and integrative neurophysiology

Motor functions of spinal cord. Spinal cord reflexes. Muscle sensory receptors - muscle spindles and Golgi tendon organs and their roles in muscle control, Flexor reflexes and withdrawal reflexes, Reflexes of posture and locomotion. Cortical and brain stem control of motor function: Motor cortex and corticospinal tract, Role of brain stem in controlling motor function. Cerebellum, basal ganglia and motor control. Integration of all parts of total motor control system. Cerebral Cortex: intellectual functions of brain, learning and memory. Physiologic anatomy of cerebral cortex. Functions of specific cortical areas, Association areas. Function of brain in communication - language input and output. Function of corpus callosum and anterior commissure. Thoughts, consciousness and memory. Behavioral and motivational mechanisms of brain. Limbic system and hypothalamus. Activating-driving systems of brain. Functional anatomy and functions of limbic system and hypothalamus. States of brain activity. Sleep. Slow-wave sleep. REM sleep. Basic theories of sleep. Brain waves. Origin in brain of brain waves (EEG). Epilepsy, Psychotic behavior and dementia - roles of specific neurotransmitter systems.

Metabolism and Temperature Regulation

Metabolism of carbohydrates and formation of adenosine triphosphate. Lipid metabolism. Dietary balances, regulation of feeding, obesity and starvation. Vitamins and minerals. Energetics and metabolic rate. Body temperature, temperature regulation and fever.

Endocrine glands & Hormones

Endocrine glands & Hormones, Pituitary: Structure and function, Hypothalamic control of pituitary glands. Thyroid structure, function of parathyroid hormones. Adernal Cortex, Structure and function of its hormones; Adrenal Medullar; function of its hormones. Pancreas: Function of its hormones.

Environmental Physiology

High altitude, space and Deep Sea Diving Physiology: Effect of low oxygen pressure on

the body, Effects of Acceleratory forces on the body in aviation and space physiology, Effect of High partial pressure of gases on the body.

X. MEDICINAL CHEMISTRY

Role of Medicinal Chemistry in discovery of drugs

Drug Design
Discovery of lead compound, lead modification, conventional drug screening, structural modification, bioisosteres, structure activity relationship, Quantitative structure activity relationships, introduction to molecular modeling and molecular graphics, pharmacophore descriptors

Receptors
Chemical nature of receptors, Neurotransmitters and their receptors, Receptor modulation and mimics, Receptor sites, Drug receptor interactions, active transport, affinity and efficacy, antagonism, partial antagonism, inverse agonism, allosteric binding sites Chirality and receptor binding, Signal transduction and second messenger systems, classification of receptors and receptor subtypes.

Introduction of various classes of drugs based on their interaction with target site. Drugs interacting with receptors, enzymes, DNA, carbohydrates etc with suitable examples.

Structure activity relationship illustrated with examples from Sulphonamides, β-lactams, Quinolones, Nucleosides and Alkaloids.

Drug Metabolism
Biotransformations and their mechanisms, Phase I and Phase II metabolism, Oxidation, Reduction, Hydrolysis, Deamination and Conjugation (GSH, Sulfate, Glucuronide and Amino acids), Role of non-specific enzymes: Oxidases, Mono-oxygenases, Di-oxygenases and Peroxidases: Biotransformations illustrated by suitable examples of commonly used drugs, Chirality and drug metabolism.

Enzyme Inhibition
Reversible and irreversible, Adverse drug reactions, Drugs acting on cell wall, Fungal membrane and Nuclear membrane, Drugs inhibiting protein synthesis.

XI. ANALYTICAL & BIOMEDICAL TECHNIQUES AND INSTRUMENTATION

Introduction
Principles of Instrumental Analysis, Types of Instrumental Methods to be covered in the course. Selecting an analytical method and developing a new Analytical Technique.

Separation Methods

An introduction to chromatographic separation, Gas Chromatography, High Pressure Liquid Chromatography and FPLC, Supercritical fluid chromatography

Mass Spectrometry
Explanation of mass Spectrometry. Forming charged particles: Electron impact (EI) and Chemical Ionization(CI), Fast Atom Bombardment (FAB), Field Desorption (FD), Electrospray Ionization, Matrix Assisted Laser Desorption Ionization (MALDI). Mass Analyzers: Magnetic sector mass spectrometers, Double focusing mass spectrometers, Quadrupole pole mass spectrometers, ion cyclotron resonance, Time of Flight mass analyzers. Combine the mass spectrometer with Gas Chromatography (GC/MS) and with liquid chromatography (LC/MS). Applications of mass spectrometry in Biomedical field.

Nuclear Magnetic Resonance Spectroscopy
Theory of NMR: Quantum description, Classical description – Processional motion, Larmour frequency, Relaxation processes, T1 and T2 and their measurement. Fourier Transform NMR: Pulsed excitation, FID, Types of NMR Spectra – Wild line and high resolution spectra. NMR Spectrometers: Instrumentation. Environmental Effects: Types, Chemical shift theory, Magnetic anisotropy, Spin–spin splitting, first order and second order spectra, Double Resonance Techniques, Proton on heteroatom. Application of proton NMR: Identification of compounds. 13C NMR: Proton decoupling: Broad band, off-resonance, Pulsed decoupling, NOE, application to structure determination. Magnetic Resonance Imaging: The concept of MRI, Application in Muscle Physiology, functional mapping of brain. Other nuclei : 31P, 19F, 23Na, 15N

Optical Methods and their applications in Biomedical Sciences
Ultraviolet / Visible molecular absorption spectroscopy, Fluorescence and Phosphorescence, Infrared, CD and ORD

Miscellaneous
Confocal Microscopy: Applications in Cell Biology, Electron Microscopy, Tracer Techniques in Biology: tumor diagnosis and imaging, infectious diseases such as tuberculosis, Flow Cytometry, Mangetic Assisted Cell Sorting

XII. MOLECULAR ONCOLOGY

The Cancer Problem
Epidemiology, Environmental carcinogens and risk factors, life style, changing patterns, the Indian scenario.

Mechanisms of Carcinogenesis
Various theories, multi-step and multistage processes, Initiation, Promotion and Progression. Role of DNA damage, repair and mutations by physicochemical agents and viruses, interaction of various agents. Differentiation: hyperplasia and precancerous lesions. Strategies of chemoprevention.

Tumor types and leukemia
Benign and malignant tumors, localized and metastatic disease, Schemes of

classification, WHO classification, staging and grading, degree of malignancy. Classification of leukemia, types of chromosomal translocations.

Tumor Immunology
Immune suppression and role of immune survelliance in growth of tumors. Tumor specific antigens and immune response. Modulation of immune response and immunotherapy, cancer vaccines.

Modulation of the Eukaryotic Cell Cycle and cell death in cancer
Cell cycle and its control: Mechanism of deregulation of cell cycle during cancer. Apoptosis, Necrosis, Proapoptotic and Antiapoptotic proteins and mechanism of action.

Cell Interactions in Development of cancer
Cell-cell interaction, integrins, invasions, invasions by cancerous cells. Angiogenesis, Neoarrgiogenesis, Stem Cell Differentiation, Morphogens

Experimental Model Systems in Cancer Research
Microbial Models, Primary Cell Cultures, Established Cell Lines, Organ Cell Cultures, Spheroids.

Tumor suppressor genes and Viral oncogenes
Mechanisms of P53, Rb, Ras action in normal and transformed cells and viral oncogenes, Role of oncogenes in gene regulation using examples erb, rel, jun-fos, large Tantigen etc.

Growth factor-signalling pathways in cancer
Relationship between oncogene products and growth factors, using example of Src, Wnt, Abl, GAP and growth factors. Effect of viral infection on signal transduction.

Cancer genetics, familial cancers.

Emerging Cancer Therapy
Cellular, tissue and molecular markers, potential targets for Cancer Therapy, Drug Discovery Strategy.

XIII. TOXICOLOGY & PHARMACOLOGY

Introduction to pharmacology, scope of pharmacology.
Routes of administration of drugs, their advantages and disadvantages. Various processes of absorption of drugs and the factors affecting them;
Adsoption, metabolism, distribution and excretion of drugs.
Pharmacodynamics: General mechanism of drug action and the factors, which modify drug action.

Pharmacological classification of drugs; the discussion of drugs should emphasize the following aspects:

Drugs acting on the central nervous system: Anesthetics, pshychopharmacological agents

Drugs acting on the autonomic nervous system: Cholinergic drugs, anticholinergic drugs, anticholinesterase drugs, Adrenergic drugs and adrenergic receptor blockers, Neuron blockers and ganglion blockers, Neuromuscular blockers, drugs used in myasthenia gravis.

Hormones and hormone antagonists, Drugs acting on the respiratory system-bronchodilators, expectorants and antitussive agents, Drugs acting on the digestive system, Cardiovascular drugs, cardiotonics, antianginal agents, antihypertensive agents, peripheral vasodilators and drugs used in atherosclerosis, coaogulants and anticoaogulants.

Principles of Toxicology

Definition, scope and different branches of toxicology.

A brief review of toxic substances:
Synthetic organic compounds: Chemical additives in food, Chemicals in the work place, Solvents, Pesticides, Cosmetics, Drugs of abuse. Inorganic chemicals: Industrial and chemical environmental inorganic toxicants polluting air/ water/ food. Naturally occurring poisons: Mycotoxins, Bacterial toxins, Plant toxins and Animal toxins.

Types of toxicity and its measurement: Acute, Sub-acute or Chronic and its manifestations. Acute toxicity: Mode of application/ administration/ exposure, in-vitro tests, Dose response relationship, Measurement of TD 50/ TC 50 and LD 50/ LC 50. Subacute and chronic toxicity. Risk and safety analysis: Margin of safety, Therapeutic index, Ideal therapeutic index. Inter-species extrapolation of dose-response data, NOEL, ADI, TLV, WHO standards. Special toxicity studies: Carcinogenecity, teratogenicity, in-vitro mutagenicity tests.

Epidemiology of toxicity: Cohort study, Retrospect study, Case-control study,
Cross-sectional study, Confounding.

Pharmacokinetic aspects of toxicants:
Absorption, Distribution, Metabolism and Excretion (ADME) of drugs and chemicals. A general study only. Site of metabolism, Metabolizing enzymes of liver, kidney, lung, GI tract, skin and their role in activation and detoxification of drugs and chemicals. Physiological (route of exposure, species, sex and age), Nutritional and environmental (temperature, altitude and circadian rhythms related) factors affecting metabolism, detoxification and toxic responses of drugs and chemicals.

Organ toxicities
Hepatotoxicity: A brief description of morphological and functional aspects of liver with special reference to hepatotoxicity, various hepatotoxic agents, types of liver injuries-Fatty liver formation, Necrosis, Cholastosis, Hepatitis, Fibrosis, Cirrhosis, Carcinogenesis. Nephrotoxicity: A brief description of morphological and functional aspects of kidney in relation of nephrotoxicity, nephrotoxic agents, Detailed mechanisms of chemical induced nephrotoxicity. Cardiovascular toxicity: A brief description of

mechanisms of cardiovascular toxicity and cardiotioxic agents- subcellular and biochemical mechanisms.

Neurotoxicity: A brief description neurotoxic agents and types of neurotoxic effects- Axanopathy, Neropathy, Neuronopathy, Mylenopathy. Broncho-pulmonary (inhalation) toxicity. Gastro-intestinal toxicity. Skin toxicity/ photosensitivity. Tests for evaluation of toxicities in different organs. Therapeutic aspects: General measures and treatment of poisoning cases, Specific antidotes, Agents of first choice, Contraindication.