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, benzenes, 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, azipine, thazine, carbazole, indole pyridine, quinoline and isoquinoline, acridine, phenothiazone, 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**

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 covalent 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.


**Translation**

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

**Cellular 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**

**Parasitology**

**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 using 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**

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

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

POPULATION GENETICS

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 lysogenic pathways, lambda repressor.

**Regulation of Gene expression in Eukaryotes**
Introduction-O rganization 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, polynucleotide 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

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 IgE, 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**

**Blood physiology**

**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**

**Gastrointestinal physiology**

**Kidneys and body fluids**

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

**Sensory Physiology**


**Nervous system: motor and integrative neurophysiology**


**Metabolism and Temperature Regulation**


**Endocrine glands & 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, Dioxygenases 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**

**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**

**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 surveillance 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 Interactions in Development of cancer**
Cell-cell interaction, integrins, invasions, invasions by cancerous cells. Angiogenesis, Neoangiogenesis, 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, coagulants and anticoagulants.

**Principles of Toxicology**

**Definition, scope and different branches of toxicology.**

**A brief review of toxic substances:**


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**
mechanisms of cardiovascular toxicity and cardiotoxic agents- subcellular and biochemical mechanisms.