



SYLLABUS

M.S. (Pharm.) Medicinal Chemistry

**NATIONAL INSTITUTE OF PHARMACEUTICAL
EDUCATION AND RESEARCH (NIPER) GUWAHATI**

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M.S. (Pharm.) Medicinal Chemistry

| Course No. | Course Name | Credits |
|--|--|-----------|
| Semester-I | | |
| MC-510 | Basics of Drug Action | 2 |
| ** MC-511 | Spectral Analysis | 2 |
| MC-520 | Logic in Organic Synthesis-I | 3 |
| * NP-510 | Separation Techniques | 1 |
| ** PE-510 | Pharmaceutical Preformulation-I | 1 |
| PT-510 | Industrial Process and Scale-up Techniques | 1 |
| * GE-510 | Biostatistics | 2 |
| GE-511 | Seminar | 1 |
| LG-510 | General Lab Experience | 3 |
| | TOTAL CREDITS | 16 |
| Semester-II | | |
| MC-610 | Drug Design | 2 |
| MC-620 | Logic in Organic Synthesis-II | 3 |
| MC-630 | Structure and Function of Biomolecules | 2 |
| MC-650 | Stereochemistry and Drug Action | 2 |
| *** PE-660 | Solid State Pharmaceutics | 1 |
| ***PC-610 | Drug Metabolism | 1 |
| GE-611 | Seminar | 1 |
| LS-610 | General Lab Experience in the Area of Specialization | 2 |
| | TOTAL CREDITS | 14 |
| Semester-III | | |
| Project (22 weeks) | | |
| TH-598 | Synopsis | 5 |
| TH-599 | Presentation | 3 |
| | TOTAL CREDITS | 8 |
| Semester-IV | | |
| TH-698 | Thesis | 9 |
| TH-699 | Defence of Thesis | 3 |
| | TOTAL CREDITS | 12 |
| GRAND TOTAL CREDITS (I to IV Semesters) | | 50 |

Note: * Common in all disciplines
 ** Common between Medicinal Chemistry, Pharmaceutics, and Pharmaceutical Analysis
 *** Common between Medicinal Chemistry and Pharmacology & Toxicology

M.S. (Pharm.) Medicinal Chemistry

SEMESTER - I

MC 510 - Basics of Drug Action (2 Credits)

1. **Structure:** Structure of drugs, structure of macro molecules and structures of their complexes. The importance of 3D Structure in Drug Action analysis. Electronic structure of drugs – metformin, omeprazole, Isoniazid, etc.
Electronic structure of ketenes and its importance in the generation of β -lactams. Conservation of orbital symmetry and Diels-Alder reaction. Group theory and Graph theory of drug molecules
2. **Energy concept and its importance in drug action:** Energy of Drugs. Internal energy vs. thermodynamics. Interaction energy and free energy of drug – macromolecule interactions. First, Second and Third laws of thermodynamics and the principles derived from these laws which are of significance to drug action
3. Free energy and Relationship between thermodynamics and statistics. Thermodynamic cycle. Statistical thermodynamics in predicting the structure of biomolecules and their interaction with drug molecules. Macromolecular vs. micromolecular correlation using thermodynamics and statistical thermodynamics.
4. **Inter- and intramolecular interactions.** Weak interactions in drug molecules Covalent, ion-ion, ion-dipole, Hydrogen bonding, C-H hydrogen bonding, dihydrogen bonding, Van der Waals interactions and the associated energies. Charge transfer interactions, salt bridges, homolytic vs. heterolytic cleavage energies
5. **Receptors:** Recognition and amplification components of Drug-receptor interactions, Receptor theories and drug action: Occupancy Theory, Rate Theory, Induced Fit Theory, Macromolecular perturbation theory, Activation-Aggregation theory. Topological and stereo-chemical consideration
6. **Enzyme Action:** Enzyme – substrate interactions. Enzyme catalysis. Enzyme kinetics. Mechanisms of enzyme catalysis, Electrostatic catalysis and desolvation. Covalent catalysis, Acid-base catalysis, Strain / distortion in enzyme catalysis. Coenzyme catalysis
7. **Enzyme inhibition:** Enzyme – Inhibitor interactions, drug action through enzyme inhibition. Varieties of enzyme inhibition – inhibition at substrate binding domain, inhibition at allosteric binding domain, metals as inhibitors. Examples based on PDE4, GSK3, etc. Theories of enzyme inhibition and inactivation. Enzyme activation of drugs prodrugs. Mechanism based Inhibition (MBI) of cytochromes
8. Nucleic Acids (NA) as targets for drug action. Structure of NA, topology of NA. NA as receptors. NA-interactive agents. Classes of drugs that interact with nucleic acids. Intercalation, NA-alkylation, NA-strand breaking and their importance in drug action. Topoisomerase inhibition via NA binding. DNA cleavage
9. **Drug likeness concept:** DruLiTo and drug likeness property evaluation. Organic chemistry of Drug metabolism, drug deactivation and elimination. Organic chemistry of drug toxicity. Enumeration methods, chemical property methods, Lipinski's rules, Weber rules, Ghoshe rules, etc.
10. **Biotransformation and associated drug action:** Phase I and Phase II transformations. Concept of hard and soft drugs. Role of cytochromes in oxidation of drugs. Consequences of drug oxidation reactions

Recommended Books:

1. The Organic Chemistry of Drug Design and Drug Action by R.B. Silverman

2. Molecular Mechanism of Drug Action by C.J. Coulson, Taylor & Francis
3. A primer of Drug Action by R.M. Julien, Worth Publishers
4. Drug-Receptor Thermodynamics by R.B. Raffa, Wiley
5. Principles of Drug Action by W.B. Pratt, P. Taylor, Churchill Livingstone
6. Medicinal Chemistry How Drugs Act and Why by A. Gringauz
7. Principle of Molecular Recognition A.D. Buckingham, Springer-Science
8. Quantitative Molecular Pharmacology and Informatics by M. Lutz, Wiley
9. Physical Biochemistry by K.E.V Holde. Pearson/Prentice Hall
10. Free Energy calculations in Rational Drug Design by Rami Reddy, Kluwer Academic

MC 511 - Spectral Analysis (2 Credits)

1. Ultraviolet (UV) and visible spectroscopy

- a) **Energy levels and selection rules:** Definitions, molecular orbital approach for energy absorption, various modes of transitions
- b) **Correlation of structural variation with UV absorption:** Factors influencing the position and intensity of absorptions, Inductive and resonance effects, the effect of the ring size, the influence of stereochemical factors
- c) **Predicting UV absorption:** Woodward- Fieser, Fieser-Kuhn and Nelson rules
- d) **Other factors:** Non-conjugative effect, solvent effect, S-Cis band

2. Infrared (IR) spectroscopy

- a) **Characteristic regions of the spectrum:** Various modes of vibrations, Energy levels
- b) **Correlation of structure with IR spectra:** Influence of substituents, ring size, hydrogen bonding, vibrational coupling, and field-effect on frequency
- c) **Applications:** Determination of stereochemistry. Spectral interpretation with examples

3. Nuclear Magnetic Resonance (NMR) Spectroscopy

- a) **Fundamentals:** Physical basis, magnetic nuclei, resonance, relaxation processes, signal-sensitivity
- b) **Instrumentation:** Continuous-Wave (CW) instrument, Pulsed Fourier Transform (FT) instrument, Functions, Relation with sensitivity, Sampling.
- c) **¹H NMR, correlation of structure with spectra:** Chemical environment and shielding, chemical shift and origin of its concept, reference compound, local diamagnetic shielding, and magnetic anisotropy, relation with the chemical shift, chemical and magnetic non-equivalence, spin-spin splitting and its origin, Pascal's triangle, coupling constant, mechanism of coupling, integral, NMR solvents and their residual peaks, protons on heteroatoms, quadrupole broadening and decoupling, the effect of conformations and stereochemistry on the spectrum, Karplus relationship, diastereomeric protons, Heteronuclear coupling to ¹⁹F and ³¹P, virtual coupling, long range coupling-epi, peri, bay effects. Shift reagents-mechanism of action, spin decoupling, and double resonance. Explanation of spectra of some compounds and drugs
- d) **¹³C NMR, correlation of structure with spectra:** Chemical environment, shielding and carbon-13 chemical shift, calculation, proton-coupled C Spectra, Proton decoupled C spectra, Nuclear Overhauser Enhancement (NOE), Problem with integration, Distortionless Enhancement by Polarization Transfer (DEPT), Heteronuclear coupling for carbon to deuterium, carbon to ¹⁹F, carbon to ³¹P. Explanation of spectra of some compounds and drugs

4. Mass spectrometry (MS)

Molecular ion and metastable peak, fragmentation patterns, nitrogen and ring rules, McLafferty rearrangement, electron, and chemical ionization modes, applications

Recommended Books

1. Spectroscopy by Donald L Pavia, Gary M Lampman, George S Kriz, James A Vyvyan
2. Organic spectroscopy by William Kemp
3. Spectroscopic Methods in Organic Chemistry by Dudley H. Williams & Ian Fleming
4. Spectrometric Identification of Organic Compounds by Robert M. Silverstein, Francis X. Webster & David J. Kiemie
5. Applications of Absorption Spectroscopy of Organic Compounds by Dyer
6. Fundamentals of Molecular Spectroscopy by Colin N. Banwell & Elaine M. McCash
7. Spectroscopy by Pavia, Donald L. Lampman, Gary M. Kriz, George S.

C 520 - Logic in Organic Synthesis-I (3 Credits)**1. Organic reaction mechanism**

- a) Methods of determining reaction mechanisms:** kinetic and non-kinetic methods; Energy profile diagrams, reaction intermediates, crossover experiments, and isotopic labelling; order of reactions; Reversible, consecutive, and parallel reactions; Solvent, ionic strength and salt effects; Acid-base catalysis
- b) Nucleophilic substitution reactions:** Uni- and bimolecular reactions; Attacking and leaving groups; Steric and electronic effects; Neighboring group participation; Formation and hydrolysis of esters, amides, and acyl halides different mechanisms
- c) Electrophilic substitution reactions:** Aromatic electrophilic substitutions including Friedel-Crafts reactions
- d) Addition and elimination reactions:** Addition to C=C and C=O; Mechanism; Dehydrohalogenation, dehydration, etc; E1, E2, and *Syn*-elimination mechanism

2. Principles of synthetic planning: Logic-centered molecular synthesis; Dislocation, synthetic tree, synthons, the logical imposition of boundary conditions, direct associated approach; Structure-functionality relationships, functionality and unsaturation levels; Polar reactivity analysis; Control elements, consonant, and dissonant circuits; Protocol for synthetic design. Nuclear Magnetic Resonance (NMR) Spectroscopy

3. Alkylation:

- a) Enolates:** Regio- and stereo-selective enolate generation, "O" versus "C"-alkylation, effects of solvent, counter cation and electrophiles; Symbiotic effect; Thermodynamically and kinetically controlled enolate formations; Various transition state models for stereoselective enolate formation
- b) Enamines and metalloenamines:** Regioselectivity in the generation, applications in controlling the selectivity of alkylation

4. Reaction of ylides

- a) Phosphorous ylides:** Structure and reactivity, stabilized and Non-stabilized ylides, effects of ligands on reactivity, Wittig reaction, Schlosser modification, WittigHorner, and Horner-Wadsworth-Emmons olefination reactions, Mechanism reactions and synthesis of various scaffolds
- b) Sulphur Ylides:** Stabilized and non-stabilized ylides; thermodynamically and kinetically controlled reactions with carbonyl compounds, regio- and stereoselective reactions

5. **Hydroboration:** Control of chemo-, regio- and stereo-selectivity, rearrangement of alkylboranes; Alkylboranes as organometallic reagents, e.g., 9-BBN, hexylboranes, silylborane, chiral boranes- Ipc_2BH IpcBH_2 , etc.

Recommended Books

1. March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure by Michael B. Smith, and Jerry March
2. Designing Organic Syntheses by Stuart Warren
3. Organic Synthesis: The Disconnection Approach by Stuart Warren
4. Advanced Organic Chemistry: Reactions and Synthesis, Part A: Structure & Mechanism by Francis A. Carey; Richard J. Sundberg
5. Advanced Organic Chemistry: Reactions and Synthesis, Part B: Reaction & Mechanism by Francis A. Carey; Richard J. Sundberg
6. Modern Synthetic Reactions by Herbert O. House
7. Modern Methods of Organic Synthesis by Carruthers, William Coldham, Iain
8. Mechanism and Structure in Organic Chemistry by Gould
9. Advanced Inorganic Chemistry by Cotton, Wilkinson, Murillo and Bochmann
10. Fundamentals of Medicinal Chemistry by Thomas ISBN047084307

NP 510 - Separation Techniques (1 Credit)

1. **Separation Techniques:** Need for learning separation techniques, separation techniques in natural product research and drug discovery, extraction techniques
2. **Chromatography:** General principles, classification of chromatographic techniques, normal and reverse phase, bonded phase chromatography, stationary phases, activity of stationary phases, elutropic series, and separation mechanisms.
3. **Column Chromatography and Short column chromatography:** Column packing, sample loading, column development, detection
4. **Flash chromatography and Vacuum liquid chromatography:** Objectives, optimization studies, selecting column and stationary phases, selecting suitable mobile phases, automated flash chromatography, and reverse phase flash chromatography
5. **High performance liquid chromatography:** Principles, instrumentation, peak shapes, capacity factor, selectivity, plate number, plate height, resolution, band broadening, pumps, injector, detectors, columns, column problems, gradient HPLC, HPLC solvents, trouble shooting, sample preparation, method development
6. **Planar Chromatography - TLC/HPTLC/OPLC:** Basic principles, sample application, development of plates, visualization of plates, 2D TLC, densitometry, over pressure layer chromatography
7. **Counter current chromatography:** Basic principles, droplet counter current chromatography, centrifugal partition chromatography, choice of solvents for SP and MP
8. **Gas Chromatography:** Principles, instrumentation, split-splitless injector, head space sampling, columns for GC, detectors, quantification
9. **Biochromatography:** Size exclusion chromatography, ion exchange chromatography, ion pair chromatography, affinity chromatography general principles, stationary phases, and mobile phases
10. **Hyphenated techniques:** Introduction to GC-MS and LC-MS techniques and their applications in natural products

Recommended Books:

1. Methods in Biotechnology, Natural Product Isolation by Sarker, Latif, Gray
2. Methods in Biotechnology, Natural Product Isolation by Richard Canell
3. Various Reviews and Research Papers

PE 510 - Pharmaceutical Preformulation - I (1 Credit)

- 1. Preformulation studies:** Preformulation studies of drug substances, proteins, and peptides. Fundamental and derived properties in preformulation profiling. Preformulation worksheet
- 2. Role of pre-formulation in drug discovery:** material properties in lead selection, 'drugability' of new chemical entities, in silico and high throughput pre-formulation studies
- 3. Role of preformulation in drug development:** Preformulation as support for formulation development, identification of 'developmental challenges' during pharmaceutical development, dosage form specific studies
- 4. Salt selection:** Role of salt selection in drug discovery and development, theoretical concepts for selection of counter ions for salt formation, 'pKa rule' for salt formation, a decision tree for salt selection, appropriate case studies
- 5. Solubilization:** Solubility and solubilization of non-electrolyte, drug solubilization in surfactant systems, use of co-solvents for development of liquid formulations, solidstate manipulations including use of metastable solid forms like amorphous state

PT 510 - Industrial Process and Scale-up Techniques (1 Credit)

- 1. Status of pharmaceutical industry:** Status of the bulk drugs, natural products, and formulations in India vis-a-vis industrialized nations
- 2. Scale-up Techniques:** Scale-up techniques for process optimization, maximization of productivity, in-process control techniques
- 3. Chemical technology of selected drugs:** Case studies with emphasis on rationale for selection of routes, raw materials, process control methods, pollution control procedures, etc.
- 4. Chemical technology of selected drugs:** Data collection during pilot plant trails, preparations of flow diagrams, material balance sheets, and technical data sheets.
- 5. Process technologies for some selected natural products of commercial interest, e.g. 4-hydroxyisoleucine**
- 6. Scale-up techniques for industrial pharmacy, typical standard operating procedures for different dosage forms; In-process control procedures.**
- 7. Pharmaceutical manufacturing equipment:** Equipment used to manufacture bulk drugs
- 8. Pharmaceutical manufacturing equipment:** Equipment used in formulations

Recommended Books:

1. Process Chemistry in Pharmaceutical Industry by Kumar Gadamasetti, Vol I & II
2. Advanced Organic Chemistry by Jerry March
3. Pharmaceutical Process Chemistry for Synthesis: Rethinking the Routes to Scale-Up by Peter J. Harrington, Wiley
4. Practical Process Research and Development by Neal G. Anderson, Academic Press
5. Strategies for Organic Drug Synthesis and Design by Daniel Lednicer

GE 510 - Biostatistics (2 Credits)

- 1. Statistics:** Introduction, its role, and uses. Collection; Organization; Graphics and pictorial representation of data; Measures of central tendencies and dispersion. Coefficient of variation
- 2. Probability:** Basic concepts; Common probability distributions and probability distributions related to the normal distribution

3. **Sampling:** Simple random and other sampling procedures. Distribution of sample mean and proportion
4. **Estimation and Hypothesis Testing:** Point and interval estimation including fiducial limits. Concepts of hypothesis testing and types of errors. Student- t and Chi-square tests. Sample size and power
5. **Experimental design and analysis of variance:** Completely randomized, randomized blocks. Latin square and factorial designs. Post- hoc procedures
6. **Correlation and regression:** Graphical presentation of two continuous variables; Pearson's product moment correlation coefficient, its statistical significance. Multiple and partial correlations. Linear regression; Regression line, coefficient of determination, interval estimation, and hypothesis testing for population slope. Introduction to multiple linear regression models. Probit and logit transformations
7. **Non-parametric tests:** Sign; Mann-Whitney U; Wilcoxon matched pair; Kruskal Wallis and Friedman two-way anova tests. Spearman rank correlation
8. **Statistical techniques in pharmaceuticals:** Experimental design in clinical trials; Parallel and crossover designs. Statistical test for bioequivalence. Dose-response studies; Statistical quality control

Recommended Books:

1. Fundamentals of Biostatistics by Bernard Rosner
2. Pharmaceutical Statistics: Practical and Clinical Applications by Bolton and Bon
3. Statistical Misconceptions by Huck

GE 511 - Seminar (1 Credit)

1. Introduction, information retrieval systems
2. Writing term papers and reports
3. Organization of scientific material, thesis, dissertation, and references
4. Reading research papers
5. Skill in the oral presentation. Each student has to present a seminar before the end of the semester

LG 510 - General Laboratory Experience (3 Credits)

1. **Analytical techniques: (75 hours)**
 - a) Spectral analysis workshop (45 hours)
 - b) Separation Techniques (30 hours)
2. **Computer and application in pharmaceutical sciences (100 hours)**
Introduction to computers, basic unit and functions, H/W and S/W, operating systems, word processing, spread sheet, graphic programs, dbase, windows, statistical S/W programs and packages. Steps involved in S/W development, computer languages with emphasis to FORTRAN language and programming, hands on experience in pharmaceutical software systems. Use of computers in information retrieval systems
3. **Specialization (95 hours)**
Two to three-step synthesis involving witting reaction and glycidic ester condensation, etc. Purification by chromatographic technique and identification by IR, NMR, and MS

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SEMESTER - II

MC 610 - Drug Design (2 Credits)

1. **Wave function of drug molecules.** Hamiltonian of Drugs. Absolute and relative energies of drug conformers. The importance of postulate 4 over postulate 3 in obtaining energy drugs. Energy minimization, comparison between global minimum conformation and bioactive conformation
2. **Conformational search:** Manual and automated conformational search methods, their advantages and disadvantages. Implicit and explicit solvent effects on the structures of drugs. Conformational interconversion, transition-state determination and their role in designing rigid analogs. Molecular graphics. Computer methodologies behind molecular modeling including artificial intelligence methods
3. **Quantum mechanics, and molecular mechanics methods.** Biguanides, nitreons in drugs, rapid racemization in glitazones, metabolism and toxicity of troglitazone, conversion of proguanil to cycloguanil
4. **QSAR:** Steric and electronic effects: Hammett equation, lipophilicity effects. Hanschequation. Experimental and theoretical approaches for the determination of physico-chemical parameters, descriptors from Graph theory. Regression analysis, extrapolation versus interpolation, linearity versus nonlinearity. Descriptor calculation. The importance of biological data in the correct form; 2D QSAR; 3D-QSAR examples of CoMFA and CoMSIA. 4, 5 and 6D QSAR methods
5. **Molecular Docking:** Rigid docking, flexible docking, manual docking, induced fit docking. Algorithms for molecular docking. Advantages and disadvantages of Glide, GOLD, Autodock and Dock software, with successful examples
6. **Pharmacophore Perception:** Unity in diversity; common minimum feature identification. Pharmacophore mapping techniques, methods of conformational search used in pharmacophore mapping. Comparison between the popular pharmacophore methods like Catalyst/HipHop, DiscoTech, GASP with practical examples
7. **Molecular Dynamics:** Trajectories –structural, energy, interaction. Dynamics of drugs, dynamics of biomolecules, dynamics of drug-receptor complexes. Molecular dynamics in estimation of free energy from dynamical methods. Entropy and van der Waals vs. electrostatic component. Residuewise interaction energy estimation using MD simulations. Human vs. PfDHFR interaction energy difference with P218
8. **De novo Design:** Active sites, allosteric sites, sub pockets. Receptor/enzyme cavity size prediction. Predicting the functional components of cavities, designing drugs fitting into cavity. Trypanothione inhibitor Design using De novo design strategies
9. **Virtual Screening:** Protocol development in virtual screening. Qualitative versus quantitative approaches-advantages and disadvantages. Random screening, Non-random screening, drug metabolism studies, clinical observations, rational approaches to lead discovery
10. **Case studies:** Anti-malarial agent design using CADD methods (PfDHFR), Antidiabetic agent design (GSK3), anti-cancer agent design (TopoisomeraseII), Antileishmanial agent design (TR inhibitors)

Recommended Books:

1. Molecular Modelling, by A. R. Leach
2. Organic Chemistry of Drug Design and Drug Action, by R.B. Silverman

3. Practical Applications of computer aided drug design, by P.S. Charifson
4. Molecular modeling in Drug Design, by C. Cohen
5. Chemical Applications of Molecular modeling, by J. Goodman
6. Pharmacophore perception, by O.F. Guner

MC 620 - Logic in Organic Synthesis-II (3 Credits)

1. **Metal/ammonia reduction:** Reduction of mono-, bi- and tri-cyclic aromatic systems and various functional groups, reductive alkylation, regio- and stereoselectivity; Reduction of alkynes; Complex metal hydrides and selectrides
2. **Reaction of electron-deficient intermediates:** Carbene, nitrene and free radical, their stabilities and modes of generation; Addition and insertion reactions of carbenoids and nitrenoids - regio- and stereoselectivity, the role of the metal catalysts in the transition-metal catalyzed reactions, other types of the reaction of carbenoids, e.g., ylide generation, 1,3- dipolar addition, rearrangement, etc.; Intra-molecular radical trapping process leading to ring annulation - Baldwin's rule
3. **Organometallics:** Applications of organo-lithium, cadmium and cerium reagents, heteroatom directed lithiation; Oxy- and amido-mercurations; Gilman reagent, mixed and higher-order cuprates, uses in nucleophilic substitution, cleavage of epoxides and conjugate addition reactions; Mechanism of action; Spiro-annulation; Wacker oxidation, Wilkinson's catalyst, carbonylation/hydroformylation reactions; Heck arylation; Role of metal- ligands in controlling regio- and stereo-selectivity; Catalytic and stoichiometric oxidation reactions; Homogeneous and heterogeneous processes; Chemo-selective reactions; Bio-mimicking processes
4. **Umpolung and unpoled sythons:** Concept, acyl, and glycine cation/anion, homoenolate anion, vicinyl dicarbonian, carbonyl dication equivalence, etc.
5. **Asymmetric synthesis:** Chiral induction-factors controlling facial selectivity; Chiral reagents/catalysts, auxiliaries, enzymes, and antibodies; Kinetic resolution, double asymmetric induction, acyclic diastereoselection, asymmetric amplification; Asymmetric synthesis of amino acids and beta-lactams
6. **Concerted reactions and photochemistry:** Molecular orbital symmetry, frontier orbitals of 1,3-butadiene, 1,3,5- hexatrienes, allyl system, classification of pericyclic reactions; FMO approach, Woodward-Hoffman correlation diagram method and PMO approach to pericyclic reactions; Electrocyclic-reactions-conrotatory and disrotatory motions, [4n], [4n+2] and allyl systems, secondary orbital interaction; Cycloaddition- antarafacial and the suprafacial additions, [4n] and [4n+2] systems with stereo chemical effects, 1,3 -dipolar cycloadditions, chelotropic reactions; Sigmatropic rearrangements-supra and antarafacial shifts of H, sigmatropic shifts of carbon moiety, retention and inversion of configuration, [3,3] and [3,5] sigmatropic rearrangements, fluxional tautomerism, ene reactions; Franck-Condon principle, Jablonski diagram, singlet and triplet states, photosensitization, quantum efficiency; Photochemistry of carbonyl compounds, norish type-I and type-II cleavages, Paterno-Buchi reaction, photoreduction, photochemistry of enones and para-benzoquinones
7. **Synthesis of complex molecules:** Various approaches for the synthesis of Taxol, Forskolin, FK-506, Gibberellines, Prostaglandins, Spatol, Aphidicolin, etc. on the basis of disconnection and direct associative approaches

Recommended Books:

1. March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure by Michael B. Smith, and Jerry March

2. Advanced Organic Chemistry: Reactions and Synthesis, Part A: Structure & Mechanism by Francis A. Carey; Richard J. Sundberg
3. Advanced Organic Chemistry: Reactions and Synthesis, Part B: Reaction & Mechanism by Francis A. Carey; Richard J. Sundberg
4. Modern Synthetic Reactions by Herbert O. House
5. Modern Methods for Organic Synthesis, W. Carruthers and Iain Coldham
6. Asymmetric Synthesis, Vol 3, Editor: J. D. Morrison Advanced Organic Chemistry by March
7. Mechanism and Structure in Organic Chemistry by Gould
8. Advanced Inorganic Chemistry by Cotton, Wilkinson, Murillo and Bochmann
9. Fundamentals of Medicinal Chemistry by Thomas
10. Web resources

In each case the treatment of the topic starts from the entry level discussion from the above text/reference books followed by relevant research articles from the original research work as well as review articles published in peer reviewed journals of international repute. Such suggested readings are provided along with the progress of the lecture

MC 630 - Structure and Function of Biomolecules (2 Credits)

1. **Properties of amino acids and peptide bond:** End group determination of peptides, sequencing of peptides using various chemical and analytical techniques; A techniques with case studies like LHRH and TRH peptides
2. **Protein structure building block to quaternary structure of proteins:** Ramachandran plots; Peptidomimetics; Protein-ligand interactions; multiple binding modes
3. Structure of lipoproteins and glycoproteins in relation to their function
4. **Structure of lipids, polysaccharides, and carbohydrates:** Relationship between their physicochemical properties and their biological function
5. **Detailed structure of nucleic acids and protein-nucleic acid interactions:** Nucleic acid and small molecule interactions; DNA damage and repair
6. **Structure and function of biomolecules pertaining to different therapeutic areas:** Cancer- tubulin-role in cell proliferation, various binding sites, the chemistry and biology of tubulin inhibitors; farnesyl transferase- X-ray structure, ras protein, and its role; Inflammation- COX-1 and COX-2 their structures and physiological role; Hyperlipidaemia-HMG-CoAits structure and role in cholesterol manipulation
7. **Biological crystallography:** Crystallisation data collection, refinement, identification of the active site, phase determination heavy-atom derivatives, electron density maps. Differences in the small molecule and biomolecule crystallography
8. **Spectrofluorimetry and Optical methods:** Basic principles of fluorescence, intensity, fluorescent group, the sensitivity of fluorescence to the environment, biological applications. Optical activity measurements, ORD/CD applications to nucleic acids and proteins
9. **Thermodynamical methods:** Differential Scanning Calorimetry (DSC) and Thermogravimetric analysis (TA) of biomolecules, Isothermal Titration Calorimetry (ITC). Various thermodynamics based instrumental methods for estimation of structural features of biomolecules, enthalpy vs entropy contribution to free energy

Recommended Books:

1. Physical Biochemistry: Applications to Biochemistry and Molecular Biology by David Freifelder
2. Methods in Modern biophysics, by B. Nolting
3. Introduction to Biophysical methods in Protein and Neucleic Acid research, by J.A. Glasel
4. Monosaccharides. Their Chemistry and Their Roles in Natural Products
5. Essentials of Glycobiology by Varki
6. Carbohydrates by Osborn
7. Modern Methods in Carbohydrate Synthesis by Khan and O'Neill
8. Organic Synthesis with Carbohydrates by Boons and Hale

9. Enzymes in Synthetic Organic Chemistry by Wong and Whitesides
10. Methods in Modern Biophysics by B. Nolting
11. Introduction to Biophysical Methods in Protein and Nucleic Acid Research by J.A. Glasel.

MC 650 - Stereochemistry and Drug Action (2 Credits)

1. **Molecular isomerism:** Molecular motion, time scales, and energy, Conformation of open chain and saturated cyclic systems
2. **Chirality and molecular symmetry:** Nomenclature and representations, Macromolecular stereochemistry, Dynamic stereochemistry
3. **Group theoretical interpretation of chirality group:** Laws of group theory, symmetry elements and operations, classification of symmetry operation into groups, chiral and achiral point groups, determination of molecular structures into symmetry point groups platonic solids, disymmetrisation
4. **Conformational analysis:**
 - a) Definitions: Internal coordinates distinction between conformation and configuration
 - b) Conformational analysis of cyclic compounds: carbocycles and heterocycles, bi- and tricyclic compounds
 - c) Conformational analysis of acyclic compounds: potential energy diagrams of various acyclic systems, gauche effect, generalized anomeric effect
5. **Assignment of configuration:** Various projectional formulae, molecular with the chiral centre, axis, and plane.
6. **Front on projectional formula of conformers and configurational isomers:** Rational with specific examples.
7. **Resolution procedures:** Biological and chemical; Analytical chiral integrity determinations; Pfeiffer rule and its violations; Recent attempts to develop a continuous scale for chirality; Chiral ligands
8. **Chirality and drug action:** Realization that stereoselectivity is a pre-requisite for evolution; Role of chirality in selective and specific therapeutic agents; Case studies; Enantioselectivity in drug absorption, metabolism, distribution, and elimination

Recommended Books:

1. StereoChemistry of Organic Compounds by Ernest L. Eliel, Samuek H. Wilen, Lewis N. Mander
2. StereoChemistry of Carbon Compounds by Ernest L. Eliel
3. Chemical Application of Group Theory by F. Albert Cotton
4. Relevant research articles as suggested time to time during the progress of classroom teaching.

PE 660 - Solid State Pharmaceutics (1 Credit)

1. **Levels of solid-state properties:** Molecular/particle/bulk level properties, the interdependence of various levels on each other, role of different levels during pharmaceutical development and process development
2. **Molecular level:** Crystalline form, definition, concept of long-range order, supramolecular arrangements, building blocks of crystals, unit cell, basic types of unit cells, demonstration of unit cells using crystal visualization software.
3. **Polymorphism:** Definition, the significance of polymorphism in drug product performance, packing/conformational polymorphism, thermodynamics of polymorphs, enantiotropy/monotropy, the concept of the transition temperature, Burger and Ramberger rule
4. **Crystallization process:** Molecular aggregation events in crystallization, energetic of crystallization, enthalpy entropy balance, types of nucleation, Ostwald's step rule, experimental protocols for polymorph screening

5. **Implications of polymorphism in pharmaceutical development:** Regulatory concerns related to polymorphism, introduction to the latest regulatory position on polymorphism
6. **Amorphous state:** Definition, long-range order versus short-range order, the disorder in the amorphous state, the concept of glass transition temperature (T_g), the thermodynamic necessity for T_g, entropy crisis
7. **Role of amorphous state in drug delivery:** Solubility advantage, spring parachute effect during solubility studies, physical instability of the amorphous form, techniques for stabilization of amorphous form, amorphous solid dispersions
8. **Co-crystals:** Introduction, synthons used for the formation of co-crystals and applications in drug delivery
9. **Particulate level properties:** Crystal habit, generation of different crystal habits, implications of crystal habit on product performance and processing
10. **Bulk level:** Bulk density, compressibility, flow properties, cohesivity, electrostatics, aggregation, agglomeration, role in formulation development, and processing

Recommended Books:

1. Polymorphism in Pharmaceutical Solids Edited by Harry Brittain
2. Solid State Characterization of Pharmaceuticals Edited by Angeline and Mark Zarkzewski
3. Crystal Engineering: A textbook, Edited by G. R. Desiraju, J. J. Vittal and A. Ramanan

PC 610 - Drug Metabolism (1 Credit)

1. Biotransformation of drugs
2. Enzymes responsible for bio-transformations, microsomal and non-microsomal mechanisms.
3. Factors influencing enzyme induction and inhibition.
4. Factors affecting drug metabolism.
5. Drug metabolism in foetus and new-born.
6. Models to study drug metabolism.
7. Dose-effect relationships.
8. Excretion of drugs, biliary, and faecal excretion.
9. Adverse drug reactions and drug interactions; Toxic reactions, allergic reactions, idiosyncrasy.
10. Acute poisoning and its treatment

Recommended Books:

1. Introduction to Drug Metabolism, by G. Gordon Gibson and Paul Skett
2. Drug Metabolism Handbook Concepts and Applications Edited by Ala F. Nassar, Wiley

GE 611 - Seminar (1 Credit)

Students are required to submit the written record and present details of the project to be pursued in semester-III & IV This should include the purpose and basis of the project, stating aims, objectives, and probable outcomes, be able to supplement these with the necessary information, literature review towards it and process for the project itself

LS 610 - General Laboratory Experience 10 hours/week (2 Credits)

Synthesis of a drug that includes 4 to 5 reaction steps; Isolation of each product by chromatographic and other techniques; Identification of the structure of products by spectral and other analytical techniques; Report of yield; Understanding the correlation between theoretical and practical aspects of chemistry. Study of theoretical organic chemistry using computation methods for the same reactions and learning the techniques of molecular modelling