

## M.S. (Pharm.) Medicinal Chemistry

Course No.	Course Name	Credits
<b>Semester-I</b>		
** 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
*** PC-540	Chemotherapy of Parasitic and Microbial Infections	1
PT-510	Industrial Process and Scale-up Techniques	1
* GE-510	Biostatistics	2
GE-511	Seminar	1
LG-510	General Lab Experience	3
<b>Total Credits</b>		<b>16</b>
<b>Semester-II</b>		
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
* PC-610	Drug Metabolism	1
* PC-611	Pharmacological Screening and Assays	1
GE-611	Seminar	1
LS-610	General Lab Experience in the area of Specialization	2
<b>Total Credits</b>		<b>14</b>
<b>Semester-III</b>		
Project (22 weeks)		
TH-598	Synopsis	5
TH-599	Presentation	3
<b>Total Credits</b>		<b>8</b>
<b>Semester-IV</b>		
TH-698	Thesis	9
TH-699	Defence of Thesis	3
<b>Total Credits</b>		<b>12</b>
<b>Grand Credits (I to IV Semesters)</b>		<b>50</b>

**Note :**

- \* Common in all disciplines
- \*\* Common between Medicinal Chemistry and Pharmaceutics
- \*\*\* Common between Medicinal Chemistry and Pharmacology & Toxicology

# M.S. (Pharm.) Medicinal Chemistry

## SEMESTER - I

### MC 510 - Basics of Drug Action (2 Credits)

1. **Structure:** 2D vs 3D. Structure vs. Electronic structure. Electronic structure of ketenes and its importance in reactivity. Diels-Alder reaction, Symmetry using group theory. Graph theory and 2D structure.
2. **Energy:** Energy concept and its importance in drug action. First, Second and Third laws of thermodynamics and the principles derived from these laws which are of significance to drug action.
3. **Thermodynamics:** Free energy and Relationship between thermodynamics and statistics. Importance of chemical potential in drug action. 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. **Interactions:** Inter- and intramolecular interactions. Weak interactions in drug molecules. Chirality and drug action. Covalent, ion-ion, ion-dipole, Hydrogen bonding, C-H hydrogen bonding, dihydrogen bonding, Van der Waals interactions and the associated energies.
5. **Receptorology:** Drug-receptor interactions, Receptor theories and drug action: Occupancy Theory, Rate Theory, Induced Fit Theory, Macromolecular perturbation theory, Activation-Aggregation theory. Topological and stereochemical consideration.
6. **Enzyme Kinetics:** enzyme kinetics in drug action. Do all molecules of an enzyme have same kinetics? Mechanisms of enzyme catalysis, Electrostatic catalysis and desolvation. Covalent catalysis, Acid-base catalysis, Strain / distortion in enzyme catalysis. Coenzyme catalysis.
7. **Enzyme Inhibition:** Drug action through enzyme inhibition. Examples based on PDE4, GSK3, etc. Theories of enzyme inhibition and inactivation. Enzyme activation of drugs prodrugs.
8. **Nucleic acids:** NA as targets for drug action. NA-interactive agents. Classes of drugs that interact with nucleic acids. Intercalation, NA-alkylation, NA-strand breaking and their importance in drug action.
9. **Drug likeness:** Drug like molecules and theories associated with the recognition of drug like properties. Physical organic chemistry of Drug metabolism, drug deactivation and elimination.
10. **Drug action after Metabolism:** Phase I and Phase II transformations. Concept of hard and soft drugs. Chemistry of ADME and Toxicity properties of drugs.

#### Recommended Books:

1. The Organic Chemistry of Drug Design and Drug Action by R.B. Silverman
2. C.J. Coulson, Molecular Mechanism of Drug Action by C.J. Coulson
3. A primer of Drug Action by R.M. Julien
4. Drug-Receptor Thermodynamics by R.B. Raffa
5. Principles of Drug Action by W.B. Pratt, P. Taylor
6. Medicinal Chemistry How Drugs Act and Why by A. Gringauz
7. Principles of Molecular recognition by A.D. Buckingham
8. Quantitative molecular pharmacology and Informatics by M. Lutz
9. Physical Biochemistry by K.E.V. Holde
10. Free energy calculations in rational drug design by M. Rami Reddy

## MC 511 - Spectral Analysis (2 Credits)

1. **Ultra Violet (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, effect of ring size, 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)  $^1\text{H}$  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 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, effect of conformations and stereochemistry on the spectrum, Karplus relationship, diastereomeric protons, Heteronuclear coupling to  $^{19}\text{F}$  and  $^{31}\text{P}$ , 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)  $^{13}\text{C}$  NMR, correlation of structure with spectra: Chemical environment, shielding and carbon-13 chemical shift, calculation, proton-coupled  $^{13}\text{C}$  Spectra, Proton-decoupled  $^{13}\text{C}$  spectra, Nuclear Overhauser Enhancement (NOE), Problem with integration, Distortionless Enhancement by Polarization Transfer (DEPT), Heteronuclear coupling for carbon to deuterium, carbon to  $^{19}\text{F}$ , carbon to  $^{31}\text{P}$ . 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.

## MC 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, 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.
- 3. Alkylation:**
  - a) Enolates: Regio- and stereo-selective enolate generation, "O" versus "C"- alkylation, effects of solvent, counter cation and electrophiles; Symbiotic effect; Thermo dynamically and kinetically controlled enolate formations; Various transition-state models for stereoselective enolate formation.
  - b) Enamines and metalloenamines: Regioselectivity in 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, Wittig-Horner and Horner-Wadsworth-Emmons olefination reactions, Mechanism of these reactions and E/Z selectivity; Petersons olefination, Application of Wittig-class of reactions and synthesis of various scaffolds.
  - b) Sulphur Ylides: Stabilized and non-stabilized ylides; thermodynamically and kinetically controlled reactions with carbonyl compounds, regio- and stereo-selective reactions.
- 5. Hydroboration:** Control of chemo-, regio- and stereo-selectivity, rearrangement of alkylboranes; Alkylboranes as organometallic reagents, e.g., 9-BBN, thexylboranes, siamylborane, chiral boranes-  $\text{Ipc}_2\text{BH}$   $\text{IpcBH}_2$  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

## PC 540 - Chemotherapy of Parasitic and Microbial Infections (1 Credit)

1. Introduction to parasitic and infectious diseases.
2. Biology of tuberculosis.
3. Mechanism of action of anti-tuberculosis drugs.
4. Targets for anti-tuberculosis drug development.
5. Mechanism of drug-resistance in tuberculosis.
6. Biology of human amoebiasis
7. Mechanism of action of anti-amoebic drugs
8. Biology of filarial infections

9. Mechanism of action of anti-filarial drugs
10. Targets of anti-filarial drug development.
11. Biology of HIV infection.
12. Mechanism of action of anti-HIV drugs
13. Targets for anti-HIV drug development.
14. Biology of malaria
15. Mechanism of action of anti-malarial drugs.
16. Targets for anti-malarial drug development
17. Mechanism of drug-resistance in malaria.
18. Biology of leishmaniasis.
19. Mechanism of action of anti-leishmanial drugs
20. Targets for anti-leishmanial drug development.
21. Drug-resistance in leishmaniasis.

#### **Recommended Books:**

1. Chemotherapy by Frank Hawking
2. Parasitic Protozoa by Julius P. Kreier and Ristic
3. Maraia by Julius P. Kreier
4. Chemotherapy and Drug Resistance in Malaria by Wallace Peter
5. Atlas of Tropical Medicine and Parasitology by Wallace Peter and Geoffrey Pasvol
6. Manson's Tropical Diseases: Expert Consult Basic by Gordon C. Cook
7. Tropical Infectious Diseases: Principles, Pathogens and Practice by Richard L. Guerrant, David H. Walker and Peter F. Weller
8. Essentials of Tropical Infectious Disease by Richard L. Guerrant, David H. Walker, Peter F. Weller
9. History of Human Parasitology by F. E. G. Cox
10. Malaria Parasites and other Haemosporidia by P. C. C. Garnham
11. Diagnostic Microbiology by Bailey & Scott
12. Medical Microbiology by Samuel Baron
13. Textbook of Microbiology by P. C. Baveja
14. Human Parasitic Infections of Pharmaceutical & National Importance edited by Prati Pal Singh and V. P. Sharma
15. Quantitative Real-time PCR in Applied Microbiology edited by Martin Filion

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

1. Status of pharmaceutical industry: Status of 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 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 model. 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 oral presentation.

## LG 510 - General Laboratory Experience -15 hours / week (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, dDbase, windows, statistical S/W programs and packages. Steps involved in S/W development, computer lan guages 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 estr condensation etc. Purification by chromatographic technique and identification by IR, NMR, and MS.



# M.S. (Pharm.) Medicinal Chemistry

## SEMESTER - II

### MC 610 - Drug Design (2 Credits)

1. **Electronic Structure methods:** Quantum chemical methods semi-empirical and ab initio methods. Conformational analysis, energy minimization, comparison between global minimum conformation and bioactive conformation. Predicting the mechanism of organic reactions using electronic structure methods. Complete and constrained conformational search methods, their advantages and disadvantages. Theoretical aqueous solvation calculations for design of ligands. Conformational interconversion, transition-state determination and their role in designing rigid analogs.
2. **Quantum chemical methods of analyzing drugs:** Metformin, its comparison to carbonates, rapid racemization in glitazones, metabolism and toxicity of troglitazone, conversion of proguanil to cycloguanil.
3. **Molecular modeling:** Energy minimization, geometry optimization, conformational analysis, global conformational minima determination; approaches and problems. Bioactive vs. global minimum conformations. Automated methods of conformational search. Advantages and limitations of available software. Molecular graphics. Computer methodologies behind molecular modeling including artificial intelligence methods.
4. **Structure Activity Relationships in drug design:** Qualitative versus quantitative approaches-advantages and disadvantages. Random screening, Non-random screening, drug metabolism studies, clinical observations, rational approaches to lead discovery. Homologation, chain branching, ring-chain transformations, bioisosterism. Insights into molecular recognition phenomenon. Structure based drug design, ligand based drug design.
5. **QSAR:** Electronic effects: Hammett equation, lipophilicity effects. Hansch equation, steric effects. Taft equation. Experimental and theoretical approaches for the determination of physico-chemical parameters, parameter inter-dependence; case studies. Regression analysis, extrapolation versus interpolation, linearity versus non-linearity. Descriptor calculation. The importance of biological data in the correct form; 2D QSAR; 3D-QSAR examples of CoMFA and CoMSIA.
6. **Molecular docking:** Rigid docking, flexible docking, manual docking. Advantages and disadvantages of Flex-X, Flex-S, Autodock and Dock softwares, with successful examples.
7. **Molecular dynamics:** Dynamics of drugs, biomolecules, drug-receptor complexes, Monte Carlo simulations and Molecular dynamics in performing conformational search and docking. Estimation of free energy from dynamical methods.
8. **Pharmacophore concept:** Pharmacophore mapping, methods of conformational search used in pharmacophore mapping. Comparison between the popular pharmacophore methods like Catalyst/HipHop, DiscoTech, GASP with practical examples.
9. **De Novo drug design techniques:** Receptor/enzyme cavity size prediction. Predicting the functional components of cavities, designing drugs fitting into cavity.
10. **Informatics methods in drug design:** Brief introduction to bioinformatics, chemoinformatics. Their relation to drug design as per the topics discussed in items 1-9 above.

#### 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, role of the metal catalysts in the transition metal catalyzed reactions, other types of 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 heterogenous processes; Chemo-selective reactions; Bio-mimicing processes.
4. **Umpolung and umpoled 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; Electrocycli-creactions-conrotatory and disrotatory motions, [4n], [4n+2] and allyl systems, secondary orbiatl interaction; Cycloaddition- antarafacial and the suprafacial additions, [4n] and [4n+2] sytems 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 effeciency; 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 systhesis 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 lectures

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

1. **Methods for the determination of structure of biomolecules:** Biological crystallography-crystallisation data collection, refinement, identification of active site, phase determination heavy atom derivatives, electron density maps; Differences in the small molecule and biomolecules crystallography; Spectrofluorimetry- basic principles of fluorescence, intensity of fluorescence, fluorescent group, sensitivity of fluorescence to environment and biological applications; Optical activity measurements, ORD/CD applications to nucleic acids and proteins; Differential scanning calorimetry (DSC) and thermogravimetric analysis (TA) of biomolecules and other thermodynamics based instrumental methods estimating the structural features of biomolecules.
2. **Properties of amino acids and peptide bond:** End group determination of peptides, sequencing of peptides using various chemical and analytical techniques; Aptechiniques with case studies like LHRH and TRH peptides.
3. **Protein structure building block to quaternary structure of proteins:** Ramachandran plots; Peptidomimetics; Protein-ligand interactions; Multiple binding modes.
4. Structure of lipoproteins and glycoproteins in relation to their function.
5. **Structure of lipids, polysaccharides and carbohydrates:** Relation-ship between their physico-chemical properties and their biological function.
6. **Detailed structure of nucleic acids and protein-nucleic acid interactions:** Nucleic acid and small molecule interactions; DNA damage and repair.
7. **Structure and function of biomolecules pertaining to different therapeutic areas:** Cancer- tubuline-role in cell proliferation, various binding sites, the chemistry and biology of tubuline inhibitors; farnesyl transferase- X-ray structure, ras protein and its role; Inflammation- COX-1 and COX-2 their structures and physiological role; Hyperlipidimia-HMG-CoA its structure and role in cholesterol manipulation.
8. **Biological crystallography:** Crystallisation data collection, refinement, identification of active site, phase determination heavy atom derivatives, electron density maps. Differences in the small molecule and biomolecule crystallography.
9. **Spectrofluorimetry and Optical methods:** Basic principles of fluorescence, intensity, fluorescent group, sensitivity of fluorescence to environment, biological applications. Optical activity measurements, ORD/CD applications to Nucleic acids and proteins.
10. **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 Neucleic 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 tri-cyclic compounds.
  - c) Conformational analysis of acyclic compounds: potential energy diagrams of various acyclic systems, gauch effect, generalized anomeric effect.
5. **Assignment of configuration**: Various projectional formulae, molecular with chiral center, 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 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 class room teaching.

## 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 effecting drug metabolism.
5. Drug metabolism in fetus and new born.
6. Models to study drug metabolism.
7. Dose-effect relationships.

8. Excretion of drugs, biliary and fecal 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.

### **PC 611 - Pharmacological Screening and Assays (1 Credit)**

1. General principles of screening, correlations between various animal models and human situations, animal ethics.
2. Pharmacological screening models for therapeutic areas such as hypertension, cerebral ischaemia, pain, epilepsy, depression, Parkinson's disease, Alzheimer's disease, diabetic, leishmania etc.
3. Correlation between *in-vitro* and *in-vivo* screens; Special emphasis on cell-based assay, biochemical assay, radioligand binding assay, high through put screening, high through put pharmacokinetic analysis, specific use of reference drugs and interpretation of results.

**Recommended Books:**

1. Drug Discovery and Evaluation: Pharmacological Assays by Vogel
2. CPCSEA guidelines.

### **GE 611 - Seminar (1 Credit)**

Students are required to submit 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 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 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.