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, 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. Purification by chromatographic technique and identification by IR, NMR, and MS.

II Semester

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 carbones, 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 nonlinearity. 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: 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 transitionmetalcatalyzed reactions, other types of reactions 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-mimicking processes.
4. Umpolung and umpoled sythons: Concept, acyl and glycine cation/anion, homoenolate anion, vicinyl dicarbanion, 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 rearangements-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 parabenzoquinones.
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; A techniques 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 thearapeutic 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, fluoresent 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, gauche 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)

(Refer to Page No. 29)

PC-611 Pharmacological Screening and Assays (1credit)

(Refer to Page No. 30)

GE-611 Seminar (1 credit)

(Refer to Page No. 23)

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 modeling.