SYLLABUS

M.S. (Pharm.) Medicinal Chemistry

NATIONAL INSTITUTE OF PHARMACEUTICAL EDUCATION AND RESEARCH 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
MC-530	Natural Products Chemistry	1
MC-540	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-640	Synthetic Aspects of Process Chemistry	2
MC-650	Stereochemistry and Drug Action	2
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

M.S. (Pharm.) Medicinal Chemistry SEMESTER - I

MC 510 - Basics of Drug Action (2 Credits)

1. **Structure:** Structure of drugs, the structure of macromolecules, 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 the 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 the substrate-binding domain, inhibition at the allosteric binding domain, metals as inhibitors. Examples based on PDE4, GSK3, etc. Theories of enzyme inhibition and inactivation. Enzyme activation of drugs prodrugs. Mechanism-basedinhibition (MBI) of cytochromes
8. Nucleic Acids (NA) as targets for drug action. Structure of NA, the 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. The organic chemistry of drug metabolism, drug deactivation, and elimination. The 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 the

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) **^{1}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 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 ^{19}F and ^{31}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}C 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 (DEFT), Heteronuclear coupling for carbon to deuterium, carbon to ^{19}F, carbon to ^{31}P. Explanation of spectra of some compounds and drugs

4. **Mass spectrometry (MS)**

a) Basic principles of Mass Spectrometry
b) Instrumentation: Ionization techniques: Electron ionization, Chemical ionization, Atmospheric pressure ionization (Electrospray ionization, APCI, and APPI), other sources: MALDI, ICP, etc.
c) Mass Analyzers: Quadrupole, Time of flight, Ion traps, LIT, FTICR, Orbitrap, High-Resolution Mass Spectrometry
d) Hyphenated Mass Spectrometry: GC/MS, HPLC/UPLC-MS and Tandem Mass Spectrometry (Product ion scan, Precursor ion scan, neutral loss scan, SIM and MRM)
e) Interpretation of mass spectra: Isotopes and ion abundances, the fragmentation pattern of organic molecules with different functional groups, qualitative analysis, Quantitative analysis
f) Applications: Application of mass spectrometry in Pharmacology/Toxicology, Environmental Monitoring/Analysis and Organic chemistry (Structure elucidation of organic molecules, A brief outline of metabolomics study including the scope of biomarkers study.

Recommended Books

1. Donald L Pavia, Gary M Lampman, George S Kriz, James A Vyvyan; Introduction to Spectroscopy, 5th Edition, Cengage Learning, USA, 2013
2. William Kemp; Organic spectroscopy, 3rd Edition; Palgrave Publishers Ltd (formerly Macmillan Press Ltd). 2002
3. Spectroscopic Methods in Organic Chemistry by Dudley H. Williams & Ian Fleming
4. Robert M. Silverstein, Francis X. Webster & David J. Kiemie, Spectrometric Identification of Organic Compounds, 7th edition, John Wiley and Sons, Inc. 2005
5. Applications of Absorption Spectroscopy of Organic Compounds by Dyer
6. Colin N. Banwell& Elaine M. McCash; Fundamentals of Molecular Spectroscopy, 4th Edition, McGraw Hill Education, 1994.

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 labeling; 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, thexylboranes, siamylborane, chiral boranes- Ipc2BH IpcBH2, etc.

Recommended Books

1. Michael B. Smith, and Jerry March; March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure, 6th Edition, WILEY-INTERSCIENCE A JOHN WILEY & SONS, INC., PUBLICATION 2007
2. Stuart Warren, Designing Organic Syntheses: A Programmed Introduction to the Synthon Approach; JOHN WILEY & SONS, 1978
3. Stuart Warren and Paul Wyatt; Workbook for organic synthesis: the disconnection approach; 2nd edition, John Wiley & Sons Ltd 2009
4. Francis A. Carey; Richard J. Sundberg; Advanced Organic Chemistry: Reactions and Synthesis, Part A: Structure & Mechanism, 5th edition, Springer 2008
5. Francis A. Carey; Richard J. Sundberg; Advanced Organic Chemistry: Reactions and Synthesis, Part B: Reaction & Mechanism; 5th edition, Springer 2008
6. Modern Synthetic Reactions by Herbert O. House
7. William Carruthers, Iain Coldham, Modern Methods of Organic Synthesis, 4th edition, Cambridge University Press 2004
8. Jonathan Clayden, Nick Greeves and Stuart Warren; Organic Chemistry; 2nd edition, Oxford 2012
9. Morrison and Boyd; Organic Chemistry; 6th edition; Prentice-Hall of India Private Limited 2002

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, the 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 the 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, troubleshooting, sample preparation, method development
6. **Planar Chromatography - TLC/HPTLC/OPLC:** Basic principles, sample application, development of plates, visualization of plates, 2D TLC, densitometry, overpressure layer chromatography
7. **Counter currentChromatography:** Basic principles, droplet counter-current chromatography, centrifugal partition chromatography, choice of solvents for SP and MP
8. **Gas Chromatography:** Principles, instrumentation, split-splitless injector, headspace 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

MC-530 -Natural Products (1 Credit)

1. Approaches available for drug development, the role of natural products in new drug development.
2. Plant-derived drugs, novel drug templates, and chemical diversity.Chemistry and biology of marine natural products.
3. **Bioactive compounds from microorganisms:** Antibiotics, non-antibiotic drugs from fungal and other microbial sources, microbial phytotoxins.
4. Methods for extraction, isolation, molecular separation, and purification of biomolecules from natural sources.
5. Disease pattern where the use of natural products is preferred, recent developments onadaptogens, immunomodulators, memory enhancers, anti-inflammatory agents, anti-parasitic along with screening methods for isolation guidance.
6. Genetically engineered natural products, naturally occurring proteins, biotechnology-derived products.

Recommended Books:

1. Chemistry of Alkaloids by S. W. Pelletier
2. Alkaloids by Manske.
3. Plant Physiology by Dieter Hess.
4. Steroids by Fieser and Fieser.
5. Organic Chemistry by I. L. Finar Vol. II.
6. Chemistry of Natural Products by K. W. Bentley.
7. Biosynthesis of Aromatic Compounds by Ulrich Weiss & J. Michael Edwards.

MC-540 - Industrial Process and Scale-up Techniques (1 Credit)

1. **Status of the pharmaceutical industry:** Status of the bulk drugs(APIs and KSMs), 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 synthetic and natural products of commercial interest, *e.g.*sulfadiazine, aspirin, 4-hydroxyisoleucine, lutein, gymnemic acids, etc.
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 nutraceuticals and pharmaceuticalformulations
9. **Drug Development Processes and Regulatory Role:**New Drug Application (NDA), Investigational New Drug Application (INDA), Abbreviated New Drug Application (ANDA), Biologic License Application (BLA), Marketing Authorization Application (MAA), Drug Master File (DMF), etc.
10. **National and International Pharmaceutical Industries Regulatory Agencies and Organizations:**Food and Drug Administration (FDA/USFDA), Medicines and Healthcare Products Regulatory Agency (MHRA), Central Drug Standard Control Organization (CDSCO), Drugs Controller of India (DCI), European Medicines Agency (EMEA), International Conference on Harmonization (ICH), etc.

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 pharmaceutics:** 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, spreadsheet, 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 glycidicester 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. **Quantum Mechanics and Molecular Mechanics.** Hamiltonian of DrugsConcept of force fields. Absolute and relative energies of drugs and 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. **Applications of Quantum mechanics, and molecular mechanics methods.**Prediction of molecular properties of drugs (bond distance, angles, torsions, and conformations), the study of reaction mechanism and potential energy diagrams (transition state and product stabilities), drug metabolism and toxicity of troglitazone, conversion of proguanil to cycloguanil
4. **QSAR**: Steric and electronic effects: Hammett equation, lipophilicity effects. Hansch equation. Experimental and theoretical approaches for the determination of physicochemical parameters, and descriptors. Regression analysis, extrapolation versus interpolation, linearity versus nonlinearity. Descriptor calculation. The importance of biological data in the correct form; 2D QSAR; 3D QSAR. Introduction to modern Artificial Intelligence and Machine learning methods: data curation, model building, assessment, and end-use. Modern lead optimization concepts like ligand efficiency, multiparameter optimization.
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 are used in pharmacophore mapping. Comparison between the popular pharmacophore methods with practical examples.
7. **Molecular Dynamics:** Introduction to MD methodology and software, 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. Residue-wise interaction energy estimation using MD simulations. Case study on Hemoglobin, human vs. bacterial CYP450 ligand interaction energy difference.
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 the 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 drug design using CADD methods, Antidiabetic agent design (PPAR gamma), anti-cancer agent design (PARP-1 inhibitors).

Recommended Books:

1. Goodman, J. M.; Royal Society of Chemistry (Great Britain). Chemical Applications of Molecular Modelling. **1998**, 216.
2. Silverman, R. B.; Holladay, M. W. The Organic Chemistry of Drug Design and Drug Action: Third Edition. *The Organic Chemistry of Drug Design and Drug Action: Third Edition***2015**, 1–517.
3. Güner, O. F. Pharmacophore Perception, Development, and Use in Drug Design. **2000**, 537.
4. Leach, A. R. Empirical Force Field Models: Molecular Mechanics. *Molecular Modelling: Principles and Applications***2001**, 165–252.
5. *Young, D. C. Computational Drug Design: A Guide for Computational and Medicinal Chemists*; Wiley, 2009.
6. Foye, W. O.; Lemke, T. L.; Williams, D. A. *Foye's Principles of Medicinal Chemistry*; Wolters Kluwer Health/Lippincott Williams & Wilkins, 2013.
7. Laurence, L. B.; Bruce, A. C.; Bjorn, C. K. *Goodman and Gilman's the Pharmacological Basis of Therapeutics*, Twelfth Ed.; The McGraw-Hill Companies, 2011.
8. Cramer, C. J. *Essentials of Computational Chemistry: Theories and Models*; Wiley, 2004.
9. Silverman, R. B.; Holladay, M. W. *The Organic Chemistry of Drug Design and Drug Action.*
10. Davis, A.; Ward, S. E. *The Handbook of Medicinal Chemistry*; Davis, A., Ward, S. E., Eds.; Royal Society of Chemistry: Cambridge, 2015. https://doi.org/10.1039/9781782621836.

MC 620 - Logic in Organic Synthesis-ll (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-metalcatalyzed 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 umpoledsythons:** Concept, acyl, and glycine cation/anion, homoenolate anion, vicinyldicarbonian, 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 stereochemical effects, 1,3 -dipolar cycloadditions, chelotropic reactions; Sigmatropicrearangements-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. Michael B. Smith, and Jerry March; March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure, 6th Edition, WILEY-INTERSCIENCE A JOHN WILEY & SONS, INC., PUBLICATION 2007
2. Francis A. Carey; Richard J. Sundberg; Advanced Organic Chemistry: Reactions and Synthesis, Part A: Structure & Mechanism, 5th edition, Springer 2008
3. Francis A. Carey; Richard J. Sundberg; Advanced Organic Chemistry: Reactions and Synthesis, Part B: Reaction & Mechanism; 5th edition, Springer 2008
4. Jonathan Clayden, Nick Greeves and Stuart Warren; Organic Chemistry; 2nd edition, Oxford 2012
5. Modern Synthetic Reactions by Herbert O. House
6. William Carruthers, Iain Coldham, Modern Methods of Organic Synthesis, 4th edition, Cambridge University Press 2004
7. Morrison and Boyd; Organic Chemistry; 6th edition; Prentice-Hall of India Private Limited 2002
8. Asymmetric Synthesis, Vol 3, Editor: J. D. Morrison Advanced Organic Chemistry by March
9. Mechanism and Structure in Organic Chemistry by Gould
10. F. A. Cotton and G. Wilkinson; Advanced Inorganic Chemistry (A comprehensive text); 3rd edition; Wiley, 1978
11. Fundamentals of Medicinal Chemistry by Thomas

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;DNAdamage 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. Glasel, J. A.; Deutscher, M. P. Introduction to Biophysical Methods for Protein and Nucleic Acid Research. 1995, 510.
2. Khan, S. H.; O'Neill, R. Alan. Modern Methods in Carbohydrate Synthesis. 1996.
3. Varki, A.; Cummings, R. D.; Esko, J. D.; Stanley, P.; Hart, G. W.; Aebi, M.; Darvill, A. G.; Kinoshita, T.; Packer, N. H.; Prestegard, J. H.; Schnaar, R. L.; Seeberger, P. H. Essentials of Glycobiology. Cold Spring Harbor (NY) 2017, 823.
4. P. M. Collins, Robin Ferrier, R. J. F. Peter M. Collins, Robert J. Ferrier-Monosaccharides_Their Chemistry and Their Roles in Natural Products-Wiley%2.Pdf. 1995, 594.
5. Nölting, B. Methods in Modern Biophysics: Third Edition. Methods in Modern Biophysics: Third Edition 2010, 1–273. https://doi.org/10.1007/978-3-642-03022-2.
6. Freifelder, D. Physical Biochemistry : Applications to Biochemistry and Molecular Biology. 1982, 761.
7. Nelson, D. L., & Cox, M. M. Lehninger Principles of Biochemistry, 7th ed.; W.H. Freeman., 2017.

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, gauch 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. Ernest L. Eliel, Samuel H. Wilen; *Stereo Chemistry of Organic Compounds*; Wiley 1994
2. Ernest L. Eliel; *Stereo Chemistry of Carbon Compounds*; McGraw Hill Education; 2001
3. F. Albert Cotton; *Chemical Application of Group Theory*; 3rd edition; John Wiley and Sons 1990
4. Jonathan Clayden, Nick Greeves and Stuart Warren; *Organic Chemistry*; 2nd edition, Oxford 2012

MC-640: Synthetic Aspects of Process Chemistry (2 Credit)

1. **Reaction progress kinetic analysis:** Streamlining reaction steps, route selection, characteristics of expedient routes, characteristics of cost-effective routes, reagent selection, families of reagents useful for scale-up, solvent selection, selecting solvents based on physical characteristics, selected solvent impurities.
2. **Green chemistry:** 12 Principles of green chemistry, examples of greener routes to chemical reactions, designing robust reaction conditions, reaction media for green chemistry, organic reactions in water, sustainable development of a process.
3. **Catalysis in organic synthesis:** Metal-catalyzed reactions, asymmetric organo-catalysis, phase transfer catalysis, photocatalysis, electrocatalysis, biocatalyst,benefits and challenges of applying phase transfer catalysis technology in the pharmaceutical industry.
4. **Emerging trends in process chemistry:** Use of Domino, Cascade, and Tandem reactions, multi-component reactions, development of efficient one-pot process with examples, lithium-halogen exchange reactions in process chemistry.
5. **Click chemistry:** Beyond the paradigm of carbonyl chemistry, Click chemistry reaction types, Click chemistry in water, Click reactions in "solid-phase synthesis", examples of Click Chemistry sequences-diversity with ease, its application in the synthesis of heterocycles and macromolecules.
6. **Microwave reactions:** Discovery and advantages of its use, increased reaction rates, mechanism, superheating effects of microwave, effects of solvents in microwave-assisted synthesis, microwave technology in process optimization, its applications in various organic reactions and heterocycles synthesis.
7. **Impurity consideration:** Introduction, steps to optimizing reactions, minimizing impurity formation by identifying impurities first, method development for separation, synthesis, and isolation of impurities and their characterization, Statistical design of experiments.
8. **Troubleshooting:** Physical and chemical causes of processing problems, steps for troubleshooting a process, debottlenecking a problem, Stereoselective enzymatic synthesisof APIs.

Recommended Books:

1. Process Chemistry in the Pharmaceutical Industry by Kumar Gadamasetti, Marcel Dekker
2. Inc.
3. Practical Process Research &Development by Neil G. Anderson, Academic Press
4. Principles of Process Research and Chemical Development in the Pharmaceutical Industry
5. by O. Repic, John Wiley &Sons, Inc
6. Pharmaceutical Process Chemistry for Synthesis by Peter J. Harrington

GE 611 - Seminar (1 Credit)

Students are required to submit the written record and present deta.ls of the project to be pursued in semester-Ill & 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