M.Pharm. First Semester

MPC-01 Modern Analytical Techniques

Prerequisite knowledge: Basic knowledge of chemistry, structure of organic compounds, basics and instrumentation of UV, IR, NMR, Mass, HPLC, TLC, GC.

1. UV-Spectroscopy:- Woodward-Fischer rule, Multi-component analysis (Simultaneous equation, Absorbance ratio, Derivative spectroscopy, Dual wave length, Chemical derivatization, Difference spectroscopy, Geometric corrections, Orthogonal Polynomial ) and Kinetic Studies.

2. Basics of FT-IR, Recent advances in instrumentation, Interpretation of IR spectrum.

3. Mass: Modes of ionization (Electron bombardment, arc and spark, thermal, chemical, negative chemical, fields ionization and desorption, laser induced, photoelectric ionization, ionization by ionic bombardment, ionization by atomic bombardment), Analyzers (TOF, Quadrupole, HRMS, Ion cyclotron resonance), Use of heavier isotope peaks, Fragmentation (Basics including Nitrogen rule, Mc Lafferty arrangement and index of hydrogen deficiency and factors affecting Fragmentation), Fragmentation and interpretation of mass spectra.

4. NMR: First order and non first order spectra, Factors affecting chemical shifts, Chemical shift equivalence of protons replacement test (Homotopic, enantiotopic and diastereotopic protons), Test of symmetry for chemical shift equivalence of protons (Homotopic, enantiotopic and diastereotopic protons), shape and nature of multi-plets, magnitude of coupling constant, Spin-spin splitting of complex spectra, simplification of complex spectra, applications of 13C NMR and 2D NMR, Cosy, Hector, comparison between PMR and CMR, NMR shift reagent. Interpretation of NMR spectra.

5. Chromatography:

TLC and HPTLC: Criterion for identification of an analyte, Method development (Plates; handmade and pre coated plates, plate size, sequential steps, selection of solvent, mobile phase and stationary phase), Common detectors and visualizing agents.

HPLC: Measurement of column performance, recent advances in instrumentation, Mobile phase: Characteristics, NP and RP mobile phase, selection and optimization of mobile phase), different types of column and their application, pre and guard column, selection of
solvent for analyte, modes of HPLC, selection criterion for detectors and selection of suitable wave length in UV and PDA detector, filter membrane, strategy for the development of HPLC method for Ionic and non ionic compounds, extra column effect, common HPLC trouble shooting

GLC: Instrumentation: Carrier gas, sample injection systems, column, tubing, gas chromatographic detectors (TCD, FID, ECS FPD, etc) recorders, integrators and computers. Column selection and column efficiency: solid support, open tubular column, liquid phases. Effect of Temperature and flow rate. Optimization of experimental conditions.

GSC: Adsorbent, multicolumn system. Qualitative analysis, quantitative analysis, peak area determination, peak height determination, relative precision of peak size, measurement techniques, data interpretation, Pharmaceutical applications. Columns used in ion pair chromatography, ion exchange chromatography, Gel permeation chromatography.

6. Principle, data interpretation and pharmaceutical application of DSC, X-ray diffraction, Scanning electron microscope and TEM

7. Principle and applications of LC-MS, GC-MS, GC-MS-MS, LC-MS-MS, UPLC, Flash chromatography, finger printing.

Reference Books
1. Snyder, Practical HPLC Method Development
2. Stahl, Thin Layer Chromatography
4. Pavia, Introduction to Spectroscopy
5. Connors, A Textbook of Pharmaceutical Analysis
7. Willard, Merrit, Dean& Settle, Instrumental methods of analysis.
10. Skoog, West & Holler, Fundamentals of analytical chemistry.
MPC-02: Product Development and Quality Assurance

1. Pre-formulation studies: Study of physical, chemical and pharmaceutical factors influencing formulation of drugs. Drug stability, stability study programs for formulations.

2. Study of different formulation additives: Diluent, binders, disintegrates, lubricants, vehicles, antioxidants, preservatives, organoleptic agents, suspending agents emulsifying agents, and drug-excipient interactions.


5. Basic concept of quality, quality control, quality assurance and total quality management. In process quality control test for pharmaceuticals.

6. Concept of validation, types, process validation of pharmaceutical dosage forms (Sterile and Non sterile dosage forms). Equipment validation, validation of analytical and manufacturing equipment.

7. Sampling, sampling procedures, types of sample and sampling plan.

8. Optimization techniques.

References:
1. Remington’s Pharmaceutical sciences
2. Banker and Rhodes, Modern Pharmaceutics
3. Lachman, Theory and Practice of Industrial Pharmacy
6. Arthur H.Kibbe, Handbook of Pharmaceutical Excipient
7. OPPI, Quality Assurance.
8. Chien, Novel Drug Delivery systems.
11. N.K. Jain, Controlled and Novel Drug Delivery
12. Robinson and Lee, Controlled Drug Delivery
MPC-03 Drug Regulatory Affairs & Intellectual Property Rights

2. GLP, WHO guideline, ISO 9000 and ISO 14000 series.
3. Documentation: MFR, BPR, Packaging records, SOP, Site Master File, Annual Product review, validation protocol, forms, maintenance of record in pharmaceutical industry.
5. Patent and intellectual property rights: Importance, application, processing, Indian Patent Act

Books Recommended:
5. WHO GMP guidelines, www.who.int
MPC-04 Biotechnology and Biostatistics

1. **Vaccine technology**: Traditional vaccine, Modern vaccine technologies, the impact of genetic engineering on vaccine technology, peptide vaccine, vaccine vectors, and difficulties associated with vaccine development, recombinant vaccines, Pharmaceutical application.


3. **Fermentation Technology**: Sources of microbial strains, basic fermentors, design and types of fermentations, control of fermentations parameters, downstream processing for product recovery.

4. **Microorganism in drug synthesis and development**: Microbial conversion of drugs like steroids, prostaglandins, anti-biotics.

5. **Measures of Central Tendency**: Mean, Median, Mode. Dispersion in Frequency Distributions- Mean Deviation, Standard Deviation, Coefficient of Variation.


7. **Experimental Design**: Introduction to full and factorial design, central composite designs, evolution to full and reduced mathematical models in experimental designs.

**Books recommended:**
1. Zito : Pharmaceutical Biotechnology
2. Prescott and Dunn: Industrial Biotechnology
3. Peppler: Microbial technology

**Practicals of the MPC 05, MPC 06 and MPC 07 will be based upon the respective subjects.**
1. **Receptors:**

Receptors and their types, structure, agonist, antagonist, signal transduction mechanism: G-protein coupled receptor, G-protein coupled receptor and cAMP, G-protein coupled receptor and phospholipase C; kinase linked 1TM receptor, Ion channels, ligand gated ion channels, drug-receptor interaction forces and drug receptor theories (occupancy, modified occupancy, rate, induced-fit, macromolecular perturbation, activation aggregation, two state model for receptor activation theories).

2. **Receptor Agonists and Antagonists**

An advanced study of the following types of receptor agonists, antagonists, their design, biochemical mechanism and biological evaluation methods:

(a) Opioid receptor
(b) Cannabinoid receptor
(c) Angiotensin receptor
(d) Histamine receptor
(e) Serotonin receptor

3. **Enzymes:**

Enzymes as catalysts, mechanisms of enzyme catalysis, co-enzyme catalysis, enzyme inhibition and inactivation, reversible and irreversible enzyme inhibitors.

4. **Enzymes Inhibitors:**

A detailed study of the following types of enzyme inhibitors, their design, biochemical mechanism and biological evaluation methods:

a) Cyclooxygenase inhibitors
b) Phosphodiesterase (PDE) inhibitors
c) Matrix metalloproteinase Inhibitors
d) Topoisomerase and Telomerase inhibitors
e) Protein tyrosine kinase inhibitors
5. **Drug Metabolism and Prodrugs:**
   Pathways for drug deactivation and elimination: Phase-I and Phase-II transformations, Prodrug design and applications.

6. **Case studies on the discovery of new drugs:**
   a) Proton-pump Inhibitor-Omeprazole as antiulcer agents.
   b) Antiviral agent- Ritonavir
   c) H2 Receptor Antagonist- Cimetidine

**Books Recommended:**
3. Lemke, Foye's Principles of Medicinal Chemistry, Lippincott Williams & Wilkins.
4. Wilson & Gisvold's Textbook Of Organic Medicinal And Pharmaceutical Chemistry by John Block and John M. Beale
7. P.N. Kourounakis and E.Rekka, Advanced drug design and development: A medicinal Chemistry approach,
8. Ledinicer: Organic Drug synthesis Vol. 1,2,3,4 (John Wiley & Sons N.Y.)
12. Monographs and relevant review articles appearing in various periodicals and journals.
MPC-09 Drug Design


2 Molecular modeling: Introduction, Molecular mechanics, force-field, molecular dynamics, molecular simulation, monte carlo, quantum mechanics (semi empirical; CNDO, MNDO, INDO, NDDO, AM1, PM3, MOPAC, empirical; Ab initio, Gaussian, hybrid QM/MM, Energy minimization; steepest descent, conjugate gradient, conformational analysis.

3 Analog based drug design: Introduction, Bio-isosteric replacement, rigid analogue, Alteration of chain branching, changes in ring size, ring position isomers, alteration of stereochemistry and design of stereoisomer and geometric isomers, fragmentation of a lead molecule. Methodologies in analog drug design: Topliss Tree approach, Craig Plot.

3 Ligand based drug design: Background and historical perspective of QSAR. Methodologies and applications of QSAR (Traditional : Hansch, Free-Wilson, Fujita Ban, Tolpolgical : Kier-Hall method, Modern methods: 3D-QSAR, Pharmacophore Mapping, Molecular Shape analysis, Receptor surface analysis, CoMFA, CoMSIA, HASL, H-QSAR. Statistical methods for development of QSAR Models and validation. Interpretation of QSAR models. Physicochemical descriptors in QSAR (Lipophilicity; clogP, polarizability; MR, Es, verloop sterimol parameter, electronic σ+,σ-, ionization constant, HOMO, LUMO, and topological descriptors). Introduction to 4D and 5D QSAR.

4 Structure based drug design: Introduction, methods to derive the three dimensional structure in drug design; crystallography and nuclear magnetic resonance. Docking; rigid, flexible and induced fit. Virtual screening.

5 Pharmacokinetics in drug design: pharmacophore, metabolism induced toxicity, structure related toxicity, insilico toxicity prediction, Toxicogenomics, high through put ADME studies and Physiologically-Based Pharmacokinetic (PBPK) Modelling.
Books recommended

2. **Carbohydrates in Drug Design** Edited by Z. J. Witczak and K. A. Nieforth, Marcel Dekker: New York, NY.
5. **Structure based Drug Design** Pandi Veerapandian, Taylor and Francis
6. **Smith and Williams Introduction to Principles of Drug Design and Action** Edited by H. John Smith, Taylor and Francis
7. **Textbook of Drug Design and Discovery** Edited by Povl Krogsgard-Larson, Taylor and Francis
9. **Ariens, Drug design-**
10. **Burger’s Medicinal Chemistry and Drug Discovery**
11. **Hansch Comprehensive Medicinal Chemistry**
1. Basic Concepts of aromaticity involving ring systems, hydrogen bonding and other weaker bondings, EDA complexes, crown ethers and inclusion compounds, Study of stability and reactivity of reaction intermediates: carbocations, carbonions, carbenes, nitrenes, and free radicals.

2. Carbanion Chemistry:
   Generation of carbanions by deprotonation and other means of generating enolates. Alkylation of enolates, oxygen versus carbon as the site of alkylation, alkylation of aldehydes, ester, amides,& nitrile. The nitrogen analogs of enols & enolate enamines and imine anions.

3. Substitution and Elimination reactions:
   Free radical substitution, Nucleophilic Aliphatic (S_{\text{N}1}, S_{\text{N}2}, S_{\text{N}1} \text{ vs } S_{\text{N}2}, S_{\text{Ni}}, Neighboring group effect), Nucleophilic Acyl substitution, Nucleophilic Aromatic Substitution. 1, 2 Elimination reactions:  E1, E2, E_{1\text{cb}}, E1 \text{ vs } E2, Elimination \text{ vs } Substitution.

4. A study of reaction mechanism of following Synthetically Important reactions:
   a) Arndt-Eistert Synthesis
   b) Baylis-Hillman Reaction
   c) Favorskii rearrangement
   d) Lawesson's Reagent
   e) Ring Closing Metathesis
   f) Ring Opening Metathesis (Polymerization)
   g) Suzuki Coupling reaction

5. Synthetic strategies:
   Disconnection approach, Protection & deprotection of various functional groups, Synthans for carbon- carbon bond formation, difunctional compounds, selective functional group interconversion (FGI) , retrosynthetic analysis (The disconnection approach, Consecutive versus convergent synthesis), Degradation techniques as a tool for
Retro-synthesis, synthetic approaches for attaching heterocyclic ring system in drug molecules having five, six membered hetero aromatic rings, fused ring systems and bio-conjugates synthesis.

6. **Stereochemistry:**
Stereoisomerism, enantiomers, elements of symmetry, chirality, racemic modification, resolution, configuration, specification of configuration, sequence rule, conformational isomers, reactions involving stereoisomers, asymmetric synthesis. Optical isomerism in compounds containing no chiral atom: biphenyls, allenes, compounds with exocyclic double bonds, spirans, chirality due to helical shape, chirality caused by restricted rotation of other types, “cis” “trans” isomerism resulting from double bonds, mono cyclic compounds, fused ring systems.

**Books Recommended:**
8. Theodara W.Greene, Greene’s protective groups in organic synthesis, A Wily and Sons, Inc.
MPC-11: Advances in Pharmaceutical Chemistry

1 Theory and application of techniques involved in extraction and isolation with specific reference to herbal products
   i Supercritical fluid extraction
   ii Solid phase micro extraction
   iii Microwave extraction


3 Green Chemistry: principal concept of green chemistry, application of green chemistry in catalysis, production of pharmaceuticals, polymer supported reactions, bio-catalysis and application of microwave in environmentally benign organic chemistry, ultrasonic based synthesis and ionic liquids.

4 Click Chemistry: Introduction, features, process chemistry and types of reactions, applications.

5 Bioinformatics in Drug Design: Introduction to Bioinformatics and Molecular biology. Information flow, sequence acquisition and analysis, archives and information retrieval: Genome and protein data base. Alignment: Pair wise, sequence and multiple. Protein structure prediction and homology modeling and In-silico screening methods.

1. K. C. Nicolaou, R. Hanko, W. Hartwig, Handbook of Combinatorial Chemistry

Practicals in the subject MPC 05, MPC 06, MPC 07 and MPC 12 will be based on theory.