

MANAV BHARTI UNIVERSITY

SYLLABUS OF

M. PHARMA

(PHARMACEUTICAL CHEMISTRY)

COURSE STRUCTURE

2010

Semester I

	Subjects
1	Organic Chemistry and Drug Research
2	Spectral Analysis
3	Advanced organic chemistry
4	Pharmaceutical Chemistry Lab-I

Semester II

	Subjects
1	Advanced Medicinal Chemistry
2	Advanced Chemistry of Natural Products
3	Advanced Bio-organic Chemistry
4	Pharmaceutical Chemistry Lab-II

Semester III & IV

Project and Dissertation work

Every student for the degree of Master of Pharmacy shall be required to undertake a project involving methodical research under the supervision of a guide and submit copies of thesis.

SEMESTER-I

1. Organic chemistry and selected aspects of drug research

1. Reaction Intermediates

Formation, structure, stability and reactions of Carbocation, Carbanions, Free radicals, Nitrenes, Carbenes, Benzynes.

2. Concept of Acids and bases

Hard and soft acids and bases, effect of structure and medium on strength of acids and bases. pH, pKa, pKb, Henderson- Hassenbelch equation, buffer solutions.

3. Organic reactions:

Substitution, Addition, Elimination reactions, Rearrangement; Pinacol – Pinacolone rearrangement, Beckmann rearrangement, Fries rearrangement, Schimidt rearrangement, Hofmann- martius aniline rearrangement, Favorskii rearrangement, Claisen Condensation and rearrangement.

4. Organic Synthetic techniques involved in Drug Research

- Protection Deprotection of functional groups
- Introduction to asymmetric synthesis
- Microwave reactions

5. Separation Techniques:

Chromatography: general principles, classification, chromatographic techniques, normal and reversed phase bonded phase, column chromatography, High pressure liquid chromatography, thin layer and high performance thin layer chromatography, counter current chromatography, Droplet counter chromatography, ion exchange chromatography, principle application and Instrumentation of Gas chromatography; Introduction to chiral chromatography

6. Physico- Chemical parameters and drug action:

Inter and Intramolecular interaction : covalent, dipole, hydrogen bonding, Dihydrogen bonding, van der waals interaction.

7. Stereochemistry and Drug action

Molecular isomerism, chirality, molecular symmetry, racemic resolution procedure, conformational analysis.

Reading Material Recommended

- M. E. Wolff, Burger's Medicinal Chemistry and Drug discovery, Principle and Practice, John Wiley & Sons, New York. (Latest edition).
- Nogrody, Medicinal Chemistry, A Bio Chemical Approach, Oxford University Press, Oxford.

3. J. March, Advanced Organic Chemistry, Reactions, Mechanism and Structures, John Wiley & Sons, New York. (Latest edition).
4. Eliel and H. Samuel, Stereochemistry of Organic compounds, John Wiley & Sons, New York. (Latest edition).
5. E. Stahl, Thin Layer Chromatography, A laboratory handbook, Springer verlag- Berlin (Latest edition).
6. E. Heftman, A laboratory handbook of Chromatography. (Latest edition).

2. Spectral Analysis

1. Ultraviolet and Visible spectroscopy:

Introduction, energy levels, selection rules; Woodward Fieser, Fieser Kuhn and Nelson rule, Influence of substituents, ring Size and strain on spectra characteristics, solvent effect, methodology, spectral correlation with structure.

2. Infrared Spectroscopy:

Introduction, types of vibrations, characterstics regions of the spectrum, influence of substituents, ring size, hydrogen bonding, vibrational coupling, field effects on frequency, methodology, spectral interpretation with example.

3. Nuclear Magnetic Resonance spectroscopy:

Introduction, magnetic nuclear, chemical shift, shielding, relaxation process, chemical & magnetic non equivalence, local dia magnetic shielding and magnetic anisotropy, spin splitting, Pascal triangle, coupling constant, mechanism of coupling, quadrapoule broadening and decoupling. Effect of stereochemistry on the spectrum, shift reagent, application of ¹HNMR with some examples.

4. Mass Spectrometry:

Introduction, Essential components of a mass spectrometer, types of ions, molecular ion, fragment ion, rearrangement ion, metastable ion, Isotopic ions and their corresponding peaks, rules of fragmentation Mc Lafferty rearrangement, Retro Diels Alder and other fragmentation patterns.

Reading Material Recommended

1. R. M. Silverstein and F. X. Webster, Spectrometric identification of Organic compounds, John Wiley & Sons, New York. (Latest edition).
2. William kemp, Organic Spectroscopy, ELBS Mac millan, Hampshire, (U. K).
3. D. L. Pavia, G. M. Lampman and G. S. Kriz, Introduction to spectroscopy- A guide for students of Organic chemistry, Harcourt college publishers. (Latest edition).
4. D. H. Williams and I. Fleming, Spectroscopic methods in Organic chemistry, Tata Mc Graw Hill publishing company Ltd, New Delhi, India. (Latest edition).

3. Advances in Organic Chemistry

1. Photochemical Reaction:

Light absorption, electronic transition, Jablonski diagram, intersystem crossing, photosensitization, excited states of ketones & cleavage hydrogen abstraction, photochemistry of conjugated dienes, enones.

2. Pericyclic reaction;

Concepts of molecular orbital symmetry, Woodward Hofman rules of conservation of orbital symmetry and its applications to electrocyclic (Diels Alders reactions)

Sigmatropic, cycloaddition and ene reaction.

3. Name reactions; their mechanism and applications in drug synthesis

i) Grignard viii) Mannich

ii) Wittig ix) Knorr Pyrazole synthesis

iii) Reformatsky x) Strecker amino acid synthesis

iv) Claisen Schmidt xi) Merrifield solid phase synthesis

v) Perkin xii) Oppenauer oxidation

vi) Knoevenagel xiii) Wolf Kishner reduction

vii) Darzen xiv) Meerwein Ponndorf- verley reduction

4. **Stereochemistry:** Elements of symmetry Kinds of molecules displaying optical activity, compounds with chiral carbon atom, compound with other quadrivalent chiral atoms, compound with tervalent chiral atoms, 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, chirality and importance of chiral drugs.

5. 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

6. Synthetic strategies:

Protection & deprotection of various groups, disconnection approach, Synthans for carbon- carbon bond formation, difunctional compounds, selective functional group interconversion (FGI), retrosynthetic analysis, synthetic approaches for attaching heterocyclic ring system in drug molecule having two and six members hetero aromatic rings, fused ring systems.

Reading Material Recommended

1. J. March, Advanced Organic Chemistry, Reactions, Mechanism and Structures, John

Wiley & Sons, New York. (Latest edition).

2. R. M. Silverstein and F. X. Webster, Spectrometric identification of Organic compounds, John Wiley & Sons, New York. (Latest edition).

3. William Kemp, Organic Spectroscopy, ELBS Macmillan, Hampshire, (U. K).

4. D. L. Pavia, G. M. Lampman and G. S. Kriz, Introduction to spectroscopy- A guide for students of Organic chemistry, Harcourt college publishers. (Latest edition).

5. D. H. Williams and I. Fleming, Spectroscopic methods in Organic chemistry, Tata Mc Graw Hill publishing company Ltd, New Delhi, India. (Latest edition).

4. Pharmaceutical Chemistry Laboratory- 1

1. Separation of Organic compounds from their mixture and their identification.

2. Synthesis of Organic compounds of medicinal interest

3. Workshop/ Tutorials/ Seminars on

(a) Stereomodel use:- Exercise involving preparation of stereomodels with view to assess the importance of stereochemistry in drug action. Examples of Pharmacopoeial substance of stereochemical importance should be taken for illustration

(b) Interpretation of spectra of organic compounds- Workshop involving interpretation of IR, NMR and Mass spectra of Organic compounds to elucidate their chemical structure.

(c) Basic Chromatographic techniques.

SEMESTER-II

1. Medicinal Chemistry

1. Drug design and approaches to drug discovery:

Analogue synthesis versus rational design; discovery of lead compounds; pharmacophore identification, structure modification, physicochemical alterations, prodrug approach, Quantitative structure activity relationship, molecular modeling, combinatorial chemistry and high throughput screening, innovations in drug delivery.(Basic concept only)

2. Drug effectors theories:

Receptor concept, nature and types of receptor, receptor characterization.

3. Structure of Cell membrane:

Membrane lipids, membrane proteins, membrane carbohydrates, passage through membrane.

4. Rational design of enzyme inhibitors.

a. Design of non – covalently binding enzymes inhibitors, rapid reversible inhibitors, slow, tight & slow tight inhibitors, transition state analogs, multisubstrate inhibitors.

b. Current development with respect to the inhibition of the following enzymes, reverse transcriptase, catechol- methyl transferase, ACE, glycinamide ribonucleotide transformylase, HMG Co A reductase inhibitors, antimetabolites, dihydrofolate reductase inhibitors ,PDE, protein kinase.

c. Design of covalently binding enzyme inhibitors, mechanism based inhibitors, affinity labels, pseudoreversible inhibitors. One representative example each from pyridoxyl phosphate dependent enzyme, Gaba transferases, ornithine decarboxylase, MAO, Thymidylate synthase, creatine kinase and B- glucosidase inhibitors.

5. **Nitric oxide:** second messenger, introduction chemical properties of nitric oxide , reaction of nitric oxide with metals, interplay between the reactions of nitric oxide in biological system , nitric oxide synthetase isoenzymes , nitric oxide synthetase inhibitors, cytotoxic role of nitric oxide , therapeutic significance of NOS inhibitors & nitric oxide..

6. Advances in Chemotherapy of parasitic, microbial and viral infection

Antimalarials, Antiamoebics, Antifilarials, Antileishmanials, Antituberculars, Anti HIV drugs

7. Advances in Psychotherapeutic agents

Biochemical basis of mental disorder, antipsychotics, antidepressants and anti anxiety drugs.

8. Advances in therapeutic agents for cardiovascular disorders

Antihypertensive, Antiarrhythmics , Antihyperlipidemics.

Reading Material Recommended

1. M. E. Wolff, Burger's Medicinal Chemistry and Drug discovery, Principle and Practice, John Wiley & Sons, New York. (Latest edition).
2. Nogrady, Medicinal Chemistry, A Bio Chemical Approach, Oxford University Press, Oxford.
3. Matridale, The extra Pharmacopoeia, Pharmaceutical press, London. (Latest edition)
4. R. B. Silverman, The Organic Chemistry of Drug design and Drug action, Academic press, New York. (Latest edition).
5. Monographs and relevant review articles appearing in various Periodicals and Journals.

2. Chemistry of Natural Products

1. Natural Products:

Introduction, sources (Plant, animal, microbial, marine), classification on chemical basis. Role of natural products in development of medicinal chemistry, providing "leads". Selected example taken from Antimalarials, Local anaesthetics and Anticholinergics.

2. Natural products as medicinal agents along with their structurally modified form

a) Ephedrine b) Ergot alkaloids c) Vasicine d) Taxol

3. Medicinal agents obtained by chemical modification of natural products

Selected examples from the categories of antineoplastic agent (paclitaxel and its derivative)

podophyllotoxin and its derivative like etoposide and teniposide

4. Bioactive compounds from marine sources.

Marine natural products and drug development

5 Toxins used as Drugs and Pharmaceuticals.

6. Nutraceuticals

7. Significant biosynthetic pathway; Acetate- mevalonate shikimic acid.

Reading Material Recommended

1. M. E. Wolff, Burger's Medicinal Chemistry and Drug discovery, Principle and Practice, John Wiley & Sons, New York. (Latest edition).
2. Matridale, The extra Pharmacopoeia, Pharmaceutical press, London. (Latest edition).
3. K.B.G. Torsell, Natural products chemistry, John Wiley & Sons, New York. (Latest edition).
4. I.L Finar, Organic Chemistry Vol:2 The English language book society and Longman group Ltd, London. (Latest edition).
5. G. A. Cordell, Introduction to Alkaloids, John Wiley & Sons, New York. (Latest edition).

6. M. L. Wickery and D. Wickery, Secondary plant metabolism, Mac millan Pvt Ltd.
7. J. B. Harborne, Phytochemical methods, Chapman and Hall, London. (Latest edition).
8. Monographs and relevant review articles appearing in various Periodicals and Journals.

3. Advanced Bio organic Chemistry

1. Steroids:

Definition, structure, nomenclature, classification and medicinal importance of steroids.

Biosynthesis of Cholesterol. Chemistry of Cholesterol, Bile acids, and Sex-hormones.

2. Alkaloids:

Definition, sources, isolation, structure, nomenclature and classification of Alkaloids.

Synthesis, medicinal importance test for identity, structural elucidation including spectral data and pharmacopeal standards of following compounds; Morphine, and Reserpine.

3. Terpenoids:

Definition, structure, nomenclature, classification, isolation medicinal importance and structural elucidation of terpenoids. Isoprene rule; chemistry of α -pinene, camphor, abietic acid and β - amyryn.

4. Glycoside:

Definition structure nomenclature and classification of glycosides Chemistry mechanism of action and medicinal importance of cardiac glycosides, anthracene glycosides.

5 a) Chemistry and medicinal importance of following natural compounds

- i) Lignans along with their modified forms
 - ii) Anthocyanin and Flavanoids: Definition, structure, nomenclature and classification of flavanoids. Chemistry and therapeutic importance of flavanoids should be discussed.
 - iii) Carotenoids.
- b) Chiral resolution of some important drugs by
- i) classical methods
 - ii) by enzyme- resolution of Propranolol and Naproxen as example

6 Biotechnology and drug development :

Basics of biotechnology and biotechnologically produced drugs.

7. Purines and pyrimidines

Chemistry, synthesis, interrelationship and medicinal uses of caffeine, theophylline theobromine and uric acid.

Reading Material Recommended

1. M. E. Wolff, Burger's Medicinal Chemistry and Drug discovery, Principle and Practice, John Wiley & Sons, New York. (Latest edition).
2. Matrinale, The extra Pharmacopoeia, Pharmaceutical press, London. (Latest edition).
3. K.B.G. Torsell, Natural products chemistry, John Wiley & Sons, New York. (Latest edition).
4. I.L Finar, Organic Chemistry Vol:2 The English language book society and Longman group Ltd, London. (Latest edition).
5. G. A. Cordell, Introduction to Alkaloids, John Wiley & Sons, New York. (Latest edition).
6. M. L. Wickery and D. Wickery, Secondary plant metabolism, Mac millan Pvt Ltd.
7. J. B. Harborne, Phytochemical methods, Chapman and Hall, London. (Latest edition).
8. Monographs and relevant review articles appearing in various Periodicals and Journals.
9. R. M. Silverstein and F. X. Webster, Spectrometric identification of Organic compounds, John Wiley & Sons, New York. (Latest edition).

4. Pharmaceutical Chemistry Laboratory- 2

1. Synthesis of Organic compounds of medicinal interest, involving minimum two step synthesis.
2. Isolation of Natural products from Plant materials.
3. Workshop/ Tutorials/ Seminars on
 - (a) Stereomodel use
 - (b) Interpretation of spectra of organic compounds
 - (c) Chromatographic techniques