

DEPARTMENT OF PHARMACEUTICAL SCIENCES
MAHARSHI DAYANAND UNIVERSITY, ROHTAK.

REVISED SYLLABUS

M. PHARMACY PHARMACEUTICAL CHEMISTRY
1ST SEMESTER

MPPCHM – 02: Pharmaceutical Chemistry - I
(Advanced Organic Chemistry – I)

THEORY

Lectures: 2 hrs / week

Unit I

Rearrangements-

- Carbon to carbon migration- Wagner-Meerwein, Pinacol-pinacolone, Benzilic acid, Favorskii.
- C to N migration -Hoffmann, Curtius, Beckmann, Schmidt, Lossen.
- C to O migration- Bayer-Villiger, hydroperoxides.

Pericyclic reactions- Molecular orbital symmetry, Woodward-Hofmann rules. Electrocyclic (Diels-Alder reaction) and sigmatropic reactions-Cope, Benzidine rearrangements. Cycloaddition.

Unit II

Miscellaneous reactions.

- Electrophilic Aromatic Substitution –Nitration, halogenation, sulphonation, Friedel-Crafts reactions.
- Nucleophilic Aromatic Substitution –via diazonium ions.
- Electrophilic addition to C=C double bond- halogens, halogen halides, water.
- Carboxylic acids- formation from alcohols and aldehydes, interconversions of carboxylic acid derivatives.

Synthon approach- Concept, half-reactions, FGI, analysis of target molecule, synthetic strategies. Application to synthesis of benzocaine, propranolol, haloperidol, salbutamol, chlorphoramine.

Practicals:

(6 hrs / week)

Number of Practicals / assignments based on aforementioned theory.

RECOMMENDED READINGS:

- Advanced Organic Chemistry — Reactions, Mechanisms & Structure, Jerry March
- Organic Chemistry — Vol I to III, S.P. Mukherji, S.P.Singh and R.S.Kapoor
- Reaction Mechanisms in Organic Chemistry, S.M. Mukherjee and S.P.Singh
- A Guide Book to Mechanisms in Organic Chemistry, Peter Sykes
- Stereochemistry of Carbon Compounds, Eliel
- Structure and Mechanism in Organic Chemistry, C.K.Ingold
- Organic Chemistry — Vols I & II, I.L. Finar
- Molecular Reactions and Photochemistry, C.H.Depny and O.L.Chapman
- Physical Organic Chemistry, Jack Hynes
- Vogel's Text Book of Practical Organic Chemistry .
- Practical Organic Chemistry, F.G.Mann and B.C.Saunders
- Combinatorial Chemistry — Synthesis and Applications, Stephen R. Wilson and Anthony W. Czarnik
- Remington — The Science and Practice of Pharmacy — Vol. I & II, A.R. Gennard
- Applications of Absorption Spectroscopy, John R.Dyer
- Organic Chemistry, Morrison & Boyd
- Experimental Methods in Organic Chemistry, Moore and Dalrymple
- Stereochemistry- R.S. Kalsi
- Organic Chemistry-Solomons G. and Fryhle C., Wiley, New York
- Organic Chemistry-Mc Murry J., Books/Cole, Pacific Grove (USA)
- Synthon approach –Stuart Warren
- Organic Chemistry- Pine, Hendrickson

(Advanced Medicinal Chemistry – I)

THEORY

Lectures: 2 hrs / week

Unit I

Drug Design: Approaches to drug design, method of variation, biochemical and physiological approaches. **Lead compound - Search & Optimization :** Search of lead compound from natural products and other sources, selection of test compounds. Methods of lead optimization – synthesis of analogs, variation of substituents, extension of structure, ring versus chain structures, bioisosterism, ring contraction and expansion. Case study of Cimitidine and pantaprazole.

Prodrugs: Objectives of Prodrug Design – increasing bioavailability, improving membrane permeability, prolonging activity, reducing side effects, removing undesirable properties. Prodrugs from different functional groups-carboxyl, amino, hydroxyl etc.

Unit II

Combinatorial chemistry: solid phase synthesis, Solution phase synthesis, deconvolution techniques and applications of combinatorial chemistry.

Antineoplastic agents-molecular mechanism of cancer, oncogenes, alkylating agents, antimetabolites, antibiotics, natural products.; Drugs through microbial transformation.

Nitric oxide- interplay of NO & biological systems. NO biosynthesis and cytotoxicity, NO synthetase inhibitors and their therapeutic significance.

Practicals:

(6 hrs / week)

Number of Practical / assignments based on aforementioned theory.

RECOMMENDED READINGS :

1. Medicinal Chemistry — A molecular and Biochemical Approach, Thomas Nogrady and Donald F. Weaver
2. Medicinal Chemistry, A. Burger Vols. I to V
3. Principles of Medicinal Chemistry, W. O. Foye
4. The Organic Chemistry of the Drug Design and Drug Action, Richard B. Silverman
5. Goodman and Gilman's Text book of Pharmacology.
6. Wilson and Gisvold's Text book of Medicinal Chemistry

THEORY

Lectures: 2 hrs / week

Unit I

Mechanistic and biosynthetic approach to plant secondary metabolites. Acetate-malonate pathway (Biosynthesis of plant fatty acids, biosynthesis and oxidation of ricinoleic acid.) Polyketides (Biosynthesis of 6-methylsalicylic acid, petulin, penicillanic acid, griseofulvin, tetracyclines). Acetate-mevalonate pathway (biosynthesis of psoralen, gibberellic acid, cholesterol, conessine). Shikimic acid pathway (Biosynthesis of chlorogenic acid, cichorin). Mixed biogenesis of plant products:

Unit II

Flavonoids and anthocyanins. Biosynthesis of alkaloids: Hyoscyamine, Morphine, Vindoline. Compounds derived from Amino acids: Colchicine, Cephalosporin C. Biosynthesis of porphyrins: Cobalamine. Plant hormones including brassinosteroids. Marine products with therapeutic potential.

- a. Drug regulatory authorities in European Union (EU) -- Introduction, Organization and General Guidelines.
- b. Regulatory consideration for pre-clinical testing and clinical testing in EU.

Practicals:

(6 hrs / week)

Number of experiments based upon aforementioned theory, including the following :

1. Isolation and characterization of medicinally active constituents e.g.
 - (a) Eugenol from clove
 - (b) Curcumin from Turmeric
 - (c) Hesperidin from Orange Peel
 - (d) Glycyrrhizin from Glycyrrhiza
 - (e) Piperine from Black Pepper
 - (f) Trimyristin and Myristicin from Nutmeg
 - (g) Pectin from Orange Peel
 - (h) Ascorbic acid from Lemon
 - (i) Sennoside from Senna
 - (j) Menthol from Peppermint oil
 - (k) β -sitosterol from edible oils
 - (l) Glycosides
 - (m) Alkaloids
 - (n) Terpenoids from natural sources

RECOMMENDED READINGS:

1. Structure Elucidation of Natural Products by Mass Spectroscopy — Vol I & II, H. Budzikiewicz, C. Djerassic and D.H. Williams
2. Tables of Spectral Data for Structural Determination of Organic Compounds- E. Pretsch, T. Clerc, J. Seibl and W. Simon
3. Heterocyclic Chemistry-Albert
4. Biogenesis of Natural Compounds - Bernfeld
5. An Introduction to the Chemistry of Terpenoids and Steroids-Templeton
6. Organic Chemistry of secondary Plant Metabolism-Geissman and Crout
7. Chemistry of the Alkaloids-Pelletier
8. The Chemistry of the Natural Products- Butterworths.
9. Pharmacognosy and Pharmacobiotechnology - J.E. Robbers, M.K. Speedie and V.E. Tyler.

IIND SEMESTER

MPHPCHM – 05: Pharmaceutical Chemistry - IV (Advanced Organic Chemistry – II)

THEORY

Lectures: 2 hrs / week

Unit I

Stereochemistry: Optical isomerism- Plane, centre & axis of symmetry, chiral molecules-test and biological importance of chirality. Stereospecific and stereoselective synthesis. Resolution of racemic mixtures. Geometric isomerism- Resulting from double bonds, monocyclic compounds, fused ring systems. Conformational isomerism-conformations in cyclic compounds.

Reactive intermediates - structure, generation, stability and reactivity of carbocations, carbanions, carbenes, nitrenes and free radicals.

Unit II

Alkylation - Alkylation of nucleophilic carbon; enolates and enamines: generation & alkylation of enolates, dianions; oxygen vs. carbon as site of alkylation. Alkylation of aldehydes, esters, amides & nitriles. Enamines and imine anions.

Reduction reactions of carbonyl and other functional groups-Catalytic hydrogenation, reduction by Group III and Group IV hydride donors, dissolving metal reductions, reductive deoxygenation of carbonyl groups.

Kinetic and thermodynamic requirements for reaction, kinetic versus thermodynamic control. Non-kinetic and kinetic methods for determining mechanisms.

Practicals:

(06 hrs / week)

Number of Practical / assignments based on aforementioned theory.

RECOMMENDED READINGS:

1. Advanced Organic Chemistry — Reactions, Mechanisms & Structure, Jerry March
2. Organic Chemistry — Vol I to III, S.P. Mukherji, S.P.Singh and R.S.Kapoor
3. Reaction Mechanisms in Organic Chemistry, S.M. Mukherjee and S.P.Singh
4. A Guide Book to Mechanisms in Organic Chemistry, Peter Sykes
5. Stereochemistry of Carbon Compounds, Eliel
6. Structure and Mechanism in Organic Chemistry, C.K.Ingold
7. Organic Chemistry — Vols I & II, I.L. Finar
8. Molecular Reactions and Photochemistry, C.H.Depny and O.L.Chapman
9. Physical Organic Chemistry, Jack Hyne
10. Vogel's Text Book of Practical Organic Chemistry .
11. Practical Organic Chemistry, F.G.Mann and B.C.Saunders
12. Combinatorial Chemistry — Synthesis and Applications, Stephen R. Wilson and Anthony W. Czarnik
13. Remington — The Science and Practice of Pharmacy — Vol. I & II, A.R. Gennard
14. Applications of Absorption Spectroscopy, John R.Dyer
15. Organic Chemistry, Morrison & Boyd
16. Experimental Methods in Organic Chemistry, Moore and Dalrymple
17. Stereochemistry- R.S. Kalsi
18. Organic Chemistry-Solomons G. and Fryhle C., Wiley, New York
19. Organic Chemistry-Mc Murry J., Books/Cole, Pacific Grove (USA)
20. Synthon approach –Stuart Warren
21. Organic Chemistry- Pine, Hendrickson

MPHPCHEM – 06: Pharmaceutical Chemistry - V

(Advanced Medicinal Chemistry – II)

THEORY

Lectures: 2 hrs / week

Unit I

Antiviral agents- DNA & RNA viruses, viral replication, retroviruses, strategies to design anti-HIV drugs, antiviral drugs.

Enzymes: Enzymes as catalyst, Mechanisms of enzyme catalysis, Enzyme inhibition and inactivation, Drug resistance and drug synergism with special reference to enzymes, Reversible enzyme inhibitors with reference to development of ACE inhibitors and sulphonamides, Transition state analogs and multisubstrate analogs, slow-tight binding inhibitors with special reference to the development of statins.

DNA-Interactive agents: Introduction, DNA structure and properties, classes of drugs that interact with DNA, Reversible DNA binders, DNA alkylators, DNA strand breakers.

Unit II

Quantitative structure activity relationship (QSAR): Physicochemical parameters – hydrophobicity, electronic and steric parameters, Hansch analysis – Steps involved, Facts to be considered, Development of one-target and multi-target QSAR models in case of antimicrobial agents, Free-Wilson analysis, Craig plot, Topliss scheme, CoMFA analysis.

Analogue based drug discovery – Analogues as means of discovering new drugs, Drug likeliness and Analogue based drug discovery, Privileged Structures and Analogue-Based Drug Discovery.

Molecular modeling: generation of 3D coordinates, sketch approach, conversion of 2D structures in 3D form, force fields, geometry optimization, energy minimization procedures. Quantum mechanical methods, conformational analysis, Pharmacophore identification, molecular modeling in 3D QSAR-CoMFA and related approaches.

Practicals: (6 hrs / week)

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2. Medicinal Chemistry, A. Burger Vols. I to V
3. Principles of Medicinal Chemistry, W. O. Foye
4. Wilson and Gisvold's Text book of Medicinal Chemistry
5. The Organic Chemistry of the Drug Design and Drug Action, Richard B. Silverman
6. Analogue based Drug Discovery, János Fischer and C. Robin Ganellin
7. Goodman and Gilman's Text book of Pharmacology.
8. Chemoinformatics - Concepts, Methods, and Tools for Drug Discovery, Jürgen Bajorath

THEORY

Lectures: 2 hrs / week

Unit I

Study of the chemistry of natural products using degradative and synthetic methods and spectral techniques. Biological significance will also be discussed.

Alkaloids: Quinine, Morphine, Reserpine.

Coumarins: psoralen, xanthotoxin and umbelliferone.

Flavonoids: Quercetin and Rutin.

Steroids: Cholesterol, Vitamin D and Cardiac glycosides.

Unit II

Terpenoids: Zingiberene, Abietic acid and β -amyrin.

Antibiotics: Chemistry of Cephalosporin, Polypeptides and Chloramphenicol.

Antineoplastic agents obtained from Plants: Catharanthus alkaloids; Paclitaxel and derivatives; Podophyllotoxin, Etoposide and Teniposide.

Practicals:

(6 hrs / week)

Number of experiments based upon aforementioned theory, including the following :

1. Degradation reactions of natural products and their identification by micro-TLC, qualitative tests and spectroscopic methods viz. Atropine, caffeine, ephedrine and nicotine.
2. Paper chromatography, electrophoresis of amino acids derived from plant sources.

RECOMMENDED READINGS:

1. Structure Elucidation of Natural Products by Mass Spectroscopy — Vol I & II, H. Budzikiewicz, C.Djerassi and D.H. Williams
2. Tables of Spectral Data for Structural Determination of Organic Compounds- E. Pretsch, T.Clerc, J. Seibl and W. Simon
3. Heterocyclic Chemistry-Albert
4. Biogenesis of Natural Compounds - Bernfeld
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