

ADVANCED SPECTRAL ANALYSIS (MPC 201T)

Scope

This subject deals with various hyphenated analytical instrumental techniques for identification, characterization and quantification of drugs. Instruments dealt are LC-MS, GC-MS, ATR-IR, DSC etc.

Objectives

At completion of this course it is expected that students will be able to understand–

- Interpretation of the NMR, Mass and IR spectra of various organic compounds
- Theoretical and practical skills of the hyphenated instruments
- Identification of organic compounds

THEORY

60Hrs

- | | | |
|----|--|-----------|
| 1. | UV and IR spectroscopy:
Wood ward – Fieser rule for 1,3– butadienes, cyclic dienes and α , β -carbonyl compounds and interpretation compounds of enones.
ATR-IR, IR Interpretation of organic compounds. | 12
Hrs |
| 2 | NMR spectroscopy:
1-D and 2-D NMR, NOESY and COSY, HECTOR, INADEQUATE techniques, Interpretation of organic compounds. | 12
Hrs |
| 3 | Mass Spectroscopy

Mass fragmentation and its rules, Fragmentation of important functional groups like alcohols, amines, carbonyl groups and alkanes, Meta stable ions, Mc Lafferty rearrangement, Ring rule, Isotopic peaks, Interpretation of organic compounds. | 12
Hrs |
| 4 | Chromatography:
Principle, Instrumentation and Applications of the following :
a) GC-MS b) GC-AAS c) LC-MS d) LC-FTIR e) LC-NMR f) CE-MS g) High Performance Thin Layer chromatography h) Super critical fluid chromatography i) Ion Chromatography j) I-EC (Ion-Exclusion Chromatography) k) Flash chromatography | 12
Hrs |

5	a). Thermal methods of analysis Introduction, principle, instrumentation and application of DSC, DTA and TGA.	12 Hrs
	b). Raman Spectroscopy Introduction, Principle, Instrumentation and Applications.	
	c). Radio immuno assay Biological standardization , bioassay, ELISA, Radioimmuno assay of digitalis and insulin.	

REFERENCES

1. Spectrometric Identification of Organic compounds – Robert M Silverstein, Sixth edition, John Wiley & Sons, 2004.
2. Principles of Instrumental Analysis – Douglas A Skoog, F. James Holler, Timothy A. Nieman, 5th edition, Eastern press, Bangalore, 1998.
3. Instrumental methods of analysis – Willards, 7th edition, CBS publishers.
4. Organic Spectroscopy – William Kemp, 3rd edition, ELBS, 1991.
5. Quantitative analysis of Pharmaceutical formulations by HPTLC – P D Sethi, CBS Publishers, New Delhi.
6. Quantitative Analysis of Drugs in Pharmaceutical formulation – P D Sethi, 3rd Edition, CBS Publishers, New Delhi, 1997.
7. Pharmaceutical Analysis- Modern methods – Part B – J W Munson, Volume 11, Marcel Dekker Series

ADVANCED ORGANIC CHEMISTRY - II (MPC 202T)

Scope

The subject is designed to provide in-depth knowledge about advances in organic chemistry, different techniques of organic synthesis and their applications to process chemistry as well as drug discovery.

Objectives

Upon completion of course, the student shall be able to understand

- The principles and applications of Green chemistry
- The concept of peptide chemistry.
- The various catalysts used in organic reactions
- The concept of stereochemistry and asymmetric synthesis.

THEORY

60 Hrs

1. Green Chemistry:

12

- a. Introduction, principles of green chemistry
- b. Microwave assisted reactions: Merit and demerits 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
- c. Ultrasound assisted reactions: Types of sonochemical reactions, homogenous, heterogeneous liquid-liquid and liquid-solid reactions, synthetic applications
- d. Continuous flow reactors: Working principle, advantages and synthetic applications.

Hrs

2 Chemistry of peptides

12

- a. Coupling reactions in peptide synthesis
- b. Principles of solid phase peptide synthesis, t-BOC and Fmoc protocols, various solid supports and linkers: Activation procedures, peptide bond formation, deprotection and cleavage from resin, low and high HF cleavage protocols, formation of free peptides and peptide amides, purification and case studies, site-specific chemical modifications of peptides
- c. Segment and sequential strategies for solution phase peptide synthesis with any two case studies
- d. Side reactions in peptide synthesis: Deletion peptides, side

Hrs

reactions initiated by proton abstraction, protonation, over-activation and side reactions of individual amino acids.

- | | | |
|---|---|-----|
| 3 | Photochemical Reactions | 12 |
| | Basic principles of photochemical reactions. Photo-oxidation, photo-addition and photo-fragmentation. | Hrs |
| | Pericyclic reactions | |
| | Mechanism, Types of pericyclic reactions such as cyclo addition, electrocyclic reaction and sigmatropic rearrangement reactions with examples | |
| 4 | Catalysis: | 12 |
| | a. Types of catalysis, heterogeneous and homogenous catalysis, advantages and disadvantages | Hrs |
| | b. Heterogeneous catalysis - preparation, characterization, kinetics, supported catalysts, catalyst deactivation and regeneration, some examples of heterogeneous catalysis used in synthesis of drugs. | |
| | c. Homogenous catalysis, hydrogenation, hydroformylation, hydrocyanation, Wilkinson catalysts, chiral ligands and chiral induction, Ziegler-Natta catalysts, some examples of homogenous catalysis used in synthesis of drugs | |
| | d. Transition-metal and Organo-catalysis in organic synthesis: Metal-catalyzed reactions | |
| | e. Biocatalysis: Use of enzymes in organic synthesis, immobilized enzymes/cells in organic reaction. | |
| | f. Phase transfer catalysis - theory and applications | |
| 5 | Stereochemistry & Asymmetric Synthesis | 12 |
| | a. Basic concepts in stereochemistry - optical activity, specific rotation, racemates and resolution of racemates, the Cahn, Ingold, Prelog (CIP) sequence rule, meso compounds, pseudo asymmetric centres, axes of symmetry, Fischers D and L notation, cis-trans isomerism, E and Z notation. | Hrs |
| | b. Methods of asymmetric synthesis using chiral pool, chiral auxiliaries and catalytic asymmetric synthesis, enantiopure separation and Stereo selective synthesis with examples. | |

REFERENCES

1. "Advanced Organic chemistry, Reaction, mechanisms and structure", J March, John Wiley and sons, New York.
2. "Mechanism and structure in organic chemistry", ES Gould, Hold Rinchart and Winston, New York.
3. "Organic Chemistry" Clayden, Greeves, Warren and Wothers., Oxford University Press 2001.
4. "Organic Chemistry" Vol I and II. I.L. Finar. ELBS, Sixth ed., 1995.
5. Carey, Organic chemistry, 5th edition (Viva Books Pvt. Ltd.)
6. Organic synthesis—the disconnection approach, S. Warren, Wiley India
7. Principles of organic synthesis, R.C. Norman and J.M. Coxon, Nelson Thornes
8. Organic synthesis— Special techniques VK Ahluwalia and R Aggarwal, Narosa Publishers.
9. Organic reaction mechanisms IV edtn, VK Ahluwalia and RK Parashar, Narosa Publishers.

COMPUTER AIDED DRUG DESIGN (MPC 203T)

Scope

The subject is designed to impart knowledge on the current state of the art techniques involved in computer assisted drug design.

Objectives

At completion of this course it is expected that students will be able to understand

- Role of CADD in drug discovery
- Different CADD techniques and their applications
- Various strategies to design and develop new drug like molecules.
- Working with molecular modeling softwares to design new drug molecules
- The in silico virtual screening protocols

Theory

60 Hrs

1. Introduction to Computer Aided Drug Design (CADD)

12

Hrs

History, different techniques and applications.

Quantitative Structure Activity Relationships: Basics

History and development of QSAR: Physicochemical parameters and methods to calculate physicochemical parameters: Hammett equation and electronic parameters (σ), lipophilicity effects and parameters ($\log P$, π -substituent constant), steric effects (Taft steric and MR parameters) Experimental and theoretical approaches for the determination of these physicochemical parameters.

2 Quantitative Structure Activity Relationships: Applications

12

Hrs

Hansch analysis, Free Wilson analysis and relationship between them, Advantages and disadvantages; Deriving 2D-QSAR equations.

3D-QSAR approaches and contour map analysis.

Statistical methods used in QSAR analysis and importance of statistical parameters.

3 Molecular Modeling and Docking

12

Hrs

a) Molecular and Quantum Mechanics in drug design.

b) Energy Minimization Methods: comparison between global

c) Molecular docking and drug receptor interactions: Rigid docking, flexible docking and extra-precision docking. Agents acting on enzymes such as DHFR, HMG-CoA reductase and HIV protease, choline esterase (AChE & BChE)

- ### In Silico Drug Design and Virtual Screening Techniques
- Similarity based methods and Pharmacophore based screening, structure based In-silico virtual screening protocols.

1. Computational and structural approaches to drug discovery, Robert M Stroud and Janet. F Moore, RCS Publishers.
2. Introduction to Quantitative Drug Design by Y.C. Martin, CRC Press, Taylor & Francis group..
3. Drug Design by Ariens Volume 1 to 10, Academic Press, 1975, Elsevier Publishers.
4. Principles of Drug Design by Smith and Williams, CRC Press, Taylor & Francis.
5. The Organic Chemistry of the Drug Design and Drug action by Richard B. Silverman, Elsevier Publishers.
6. Medicinal Chemistry by Burger. Wiley Publishing Co.

7. An Introduction to Medicinal Chemistry –Graham L. Patrick, Oxford University Press.
8. Wilson and Gisvold's Text book of Organic Medicinal and Pharmaceutical Chemistry, Ippincott Williams & Wilkins.
9. Comprehensive Medicinal Chemistry – Corwin and Hansch, Pergamon Publishers.
10. Computational and structural approaches to drug design edited by Robert M Stroud and Janet. F Moore

PHARMACEUTICAL PROCESS CHEMISTRY (MPC 204T)

Scope

Process chemistry is often described as scale up reactions, taking them from small quantities created in the research lab to the larger quantities that are needed for further testing and then to even larger quantities required for commercial production. The goal of a process chemist is to develop synthetic routes that are safe, cost-effective, environmentally friendly, and efficient. The subject is designed to impart knowledge on the development and optimization of a synthetic route/s and the pilot plant procedure for the manufacture of Active Pharmaceutical Ingredients (APIs) and new chemical entities (NCEs) for the drug development phase.

Objectives

At completion of this course it is expected that students will be able to understand

- The strategies of scale up process of APIs and intermediates
- The various unit operations and various reactions in process chemistry

THEORY

60 Hrs

1. Process chemistry

12

Introduction, Synthetic strategy

Hrs

Stages of scale up process: Bench, pilot and large scale process.

In-process control and validation of large scale process.

Case studies of some scale up process of APIs.

Impurities in API, types and their sources including genotoxic impurities

2 Unit operations

12

- a) Extraction: Liquid equilibria, extraction with reflux, extraction with agitation, counter current extraction.
- b) Filtration: Theory of filtration, pressure and vacuum filtration, centrifugal filtration,
- c) Distillation: azeotropic and steam distillation
- d) Evaporation: Types of evaporators, factors affecting evaporation.
- e) Crystallization: Crystallization from aqueous, non-aqueous solutions factors affecting crystallization, nucleation. Principle and general methods of Preparation of polymorphs, hydrates, solvates and amorphous APIs.

- | | | |
|---|--|-----------|
| 3 | Unit Processes - I | 12
Hrs |
| | <ul style="list-style-type: none"> a) Nitration: Nitrating agents, Aromatic nitration, kinetics and mechanism of aromatic nitration, process equipment for technical nitration, mixed acid for nitration, b) Halogenation: Kinetics of halogenations, types of halogenations, catalytic halogenations. Case study on industrial halogenation process. c) Oxidation: Introduction, types of oxidative reactions, Liquid phase oxidation with oxidizing agents. Nonmetallic Oxidizing agents such as H₂O₂, sodium hypochlorite, Oxygen gas, ozonolysis. | |
| 4 | Unit Processes - II | 12
Hrs |
| | <ul style="list-style-type: none"> a) Reduction: Catalytic hydrogenation, Heterogeneous and homogeneous catalyst; Hydrogen transfer reactions, Metal hydrides. Case study on industrial reduction process. b) Fermentation: Aerobic and anaerobic fermentation. Production of <ul style="list-style-type: none"> i. Antibiotics; Penicillin and Streptomycin, ii. Vitamins: B2 and B12 iii. Statins: Lovastatin, Simvastatin c) Reaction progress kinetic analysis <ul style="list-style-type: none"> i. Streamlining reaction steps, route selection, ii. Characteristics of expedient routes, characteristics of cost-effective routes, reagent selection, families of reagents useful for scale-up. | |
| 5 | Industrial Safety | 12
Hrs |
| | <ul style="list-style-type: none"> a) MSDS (Material Safety Data Sheet), hazard labels of chemicals and Personal Protection Equipment (PPE) b) Fire hazards, types of fire & fire extinguishers c) Occupational Health & Safety Assessment Series 1800 (OHSAS-1800) and ISO-14001 (Environmental Management System), Effluents and its management | |

REFERENCES

1. Process Chemistry in the Pharmaceutical Industry: Challenges in an Ever-Changing Climate–An Overview; K. Gadamasetti, CRC Press.
2. Pharmaceutical Manufacturing Encyclopedia, 3rd edition, Volume 2.
3. Medicinal Chemistry by Burger, 6th edition, Volume 1–8.
4. W.L. McCabe, J.C Smith, Peter Harriott. Unit operations of chemical engineering, 7th edition, McGraw Hill
5. Polymorphism in Pharmaceutical Solids .Dekker Series Volume 95 Ed: H G Brittain (1999)
6. Regina M. Murphy: Introduction to Chemical Processes: Principles, Analysis, Synthesis
7. Peter J. Harrington: Pharmaceutical Process Chemistry for Synthesis: Rethinking the Routes to Scale-Up
8. P.H.Groggins: Unit processes in organic synthesis (MGH)
9. F.A.Henglein: Chemical Technology (Pergamon)
- 10.M.Gopal: Dryden's Outlines of Chemical Technology, WEP East-West Press
- 11.Clausen,Mattson: Principle of Industrial Chemistry, Wiley Publishing Co.,
- 12.Lowenheim & M.K. Moran: Industrial Chemicals
- 13.S.D. Shukla & G.N. Pandey: A text book of Chemical Technology Vol. II, Vikas Publishing House
- 14.J.K. Stille: Industrial Organic Chemistry (PH)
- 15.Shreve: Chemical Process, Mc Grawhill.
- 16.B.K.Sharma: Industrial Chemistry, Goel Publishing House
- 17.ICH Guidelines
- 18.United States Food and Drug Administration official website www.fda.gov

PHARMACEUTICAL CHEMISTRY PRACTICALS – II
(MPC 205P)

1. Synthesis of organic compounds by adapting different approaches involving (3 experiments)
 - a) Oxidation
 - b) Reduction/hydrogenation
 - c) Nitration
2. Comparative study of synthesis of APIs/intermediates by different synthetic routes (2 experiments)
3. Assignments on regulatory requirements in API (2 experiments)
4. Comparison of absorption spectra by UV and Woodward – Fieser rule
5. Interpretation of organic compounds by FT-IR
6. Interpretation of organic compounds by NMR
7. Interpretation of organic compounds by MS
8. Determination of purity by DSC in pharmaceuticals
9. Identification of organic compounds using FT-IR, NMR, CNMR and Mass spectra
10. To carry out the preparation of following organic compounds
11. Preparation of 4-chlorobenzhydrylpiperazine. (an intermediate for cetirizine HCl).
12. Preparation of 4-iodotoluene from p-toluidine.
13. NaBH₄ reduction of vanillin to vanillyl alcohol
14. Preparation of umbelliferone by Pechmann reaction
15. Preparation of triphenyl imidazole
16. To perform the Microwave irradiated reactions of synthetic importance (Any two)
17. Determination of log P, MR, hydrogen bond donors and acceptors of selected drugs using softwares
18. Calculation of ADMET properties of drug molecules and its analysis using softwares
Pharmacophore modeling
19. 2D-QSAR based experiments
20. 3D-QSAR based experiments
21. Docking study based experiment
22. Virtual screening based experiment