Maharshi Dayanand University, Rohtak

Department of Pharmaceutical Sciences

M. PHARM. PHARMACEUTICAL CHEMISTRY (MPC)

PROGRAM SPECIFIC OUTCOMES

PSO1 Acquinted with the principle of different types of titrimetric and gravimetric analysis. He /she will also be well versed in sampling, analysis of data, ready to perform different types of titrimetric and gravimetric analysis .

PSO2 Acquinted with the principle of limit tests, different classes of inorganic pharmaceuticals and their analysis. The practical paper deals with identification of different anions, cations and different inoganic pharmaceuticals.

PSO3 Able to use the knowledge obtained on various states of gases, liquids; colloids, thermodynamics etc in the ensuing fields like pharmaceutical engineering, physical pharmacy and medicinal chemistry.

PSO4 Get the knowledge of mode of action , structural correlation and use of different cardioactive classes of drugs along with steriods are taught to the students. This helps them in understanding the pharmacology of this processes.

PSO5 Learn about heterocyclic compounds, and electrophillic and nucleophillic reactions, which helps them in acquiring further knowledge in biochemistry, pharmacology and medicinal chemistry.

SCHEME OF EXAMINATION

Table- Schemes for internal assessments and end semester examinations (Pharmaceutical Chemistry)

Course Code	Course	Internal Assessment				End Semester Exams		Total
		Continuous Mode	Sessional Exams		Total	Marks	Duration	Marks
			Marks	Duration				
SEMESTER I								
MPA101T	Modern Pharmaceutical Analytical Techniques	10	15	1 Hr	25	75	3 Hrs	100
MPC101T	Advanced Organic Chemistry -I	10	15	1 Hr	25	75	3 Hrs	100
MPC102T	Advanced Medicinal chemistry	10	15	1 Hr	25	75	3 Hrs	100
MPC103T	Chemistry of Natural Products	10	15	1 Hr	25	75	3 Hrs	100
MPC104P	Pharmaceutical Chemistry Practical I	20	30	6 Hrs	50	100	6 Hrs	150
-	Seminar /Assignment	-	-	-	-	-	-	100
							Total	**650**

SEMESTER II								
MPC201T	Advanced Spectral Analysis	10	15	1 Hr	25	75	3 Hrs	100
MPC202T	Advanced Organic Chemistry -II	10	15	1 Hr	25	75	3 Hrs	100
MPC203T	Computer Aided Drug Design	10	15	1 Hr	25	75	3 Hrs	100
MPC204T	Pharmaceutical Process Chemistry	10	15	1 Hr	25	75	3 Hrs	100
MPC205P	Pharmaceutical Chemistry Practical II	20	30	6 Hrs	50	100	6 Hrs	150
-	Seminar /Assignment	-	-	-	-	-	-	100
							Total	**650**

Table- Schemes for internal assessments and end semester examinations (Semester III& IV)

Course Code	Course	Internal Assessment				End Semester Exams		Total
		Continuous	Sessional Exams		Total	Marks	Duration	Marks
		Mode	Marks	Duration				
SEMESTER III								
MRM101T	Research Methodology and Biostatistics	10	15	1 Hr	25	75	3 Hrs	100
-	Journal club	-	-	-	25	-	-	25
-	Discussion / Presentation (Proposal Presentation)	-	-	-	50	-	-	50
-	Research work	-	-	-	-	350	1 Hr	350
							Total	**525**
SEMESTER IV								
-	Journal club	-	-	-	25	-	-	25
-	Discussion / Presentation (Proposal Presentation)	-	-	-	75	-	-	75
-	Research work and Colloquium	-	-	-	-	400	1 Hr	400
							Total	**500**

SYLLABUS

SEMESTER-1

MODERN PHARMACEUTICAL ANALYTICAL TECHNIQUES (MPA101T)

Course outcomes

After completion of course student is able to know,

CO1 The analysis of various drugs in single and combination dosage forms

CO2 Theoretical and practical skills of the instruments

CO3 Application of the analytical techniques

THEORY **60 HOURS**

1 UV-Visible spectroscopy: Introduction, Theory, Laws, Instrumentation associated with UV-Visible spectroscopy, Choice of solvents and solvent effect and Applications of UV-Visible spectroscopy.

IR spectroscopy: Theory, Modes of Molecular vibrations, Sample handling, Instrumentation of Dispersive and Fourier – Transform IR Spectrometer, Factors affecting vibrational frequencies and Applications of IR spectroscopy

Spectroflourimetry: Theory of Fluorescence, Factors affecting fluorescence, Quenchers, Instrumentation and Applications of fluorescence spectrophotometer.

Flame emission spectroscopy and Atomic absorption spectroscopy: Principle, Instrumentation, Interferences and Applications.

12 Hrs

2 NMR spectroscopy: Quantum numbers and their role in NMR, Principle, Instrumentation, Solvent requirement in NMR, Relaxation process, NMR signals in various compounds, Chemical shift, Factors influencing chemical shift, Spin-Spin coupling, Coupling constant, Nuclear magnetic double resonance, Brief outline of principles of FT-NMR and 13C NMR. Applications of NMR spectroscopy.

12 Hrs

3 Mass Spectroscopy: Principle, Theory, Instrumentation of Mass Spectroscopy, Different types of ionization like electron impact, chemical, field, FAB and MALDI, APCI, ESI, APPI Analyzers of Quadrupole and Time of Flight, Mass fragmentation and its rules, Meta stable ions, Isotopic peaks and Applications of Mass spectroscopy

12 Hrs

4 Chromatography: Principle, apparatus, instrumentation, chromatographic parameters, factors affecting resolution and applications of the following: a) Paper chromatography b) Thin Layer chromatography c) Ion exchange chromatography d) Column chromatography e) Gas chromatography f) High Performance Liquid chromatography g) Affinity chromatography

12 Hrs

5 Electrophoresis: Principle, Instrumentation, Working conditions, factors affecting separation and applications of the following: a) Paper electrophoresis b) Gel electrophoresis c) Capillary electrophoresis d) Zone electrophoresis e) Moving boundary electrophoresis f) Iso electric focusing

X ray Crystallography: Production of X rays, Different X ray methods, Bragg‘s law, Rotating crystal technique, X ray powder technique, Types of crystals and applications of X-ray diffraction.

12 Hrs

REFERENCES

1. Spectrometric Identification of Organic compounds - Robert M Silverstein, Sixth edition, John Wiley & Sons, 2004.

2. Principles of Instrumental Analysis - Doglas 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. Practical Pharmaceutical Chemistry – Beckett and Stenlake, Vol II, 4th edition, CBS Publishers, New Delhi, 1997.

5. Organic Spectroscopy - William Kemp, 3rd edition, ELBS, 1991.

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-1 (MPC101T)

Course outcomes

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

CO1 The principles and applications of retero-synthesis

CO2 The mechanism & applications of various named reactions

CO3 The concept of disconnection to develop synthetic routes for small target molecule.

CO4 The various catalysts used in organic reactions

CO5 The chemistry of heterocyclic compounds

THEORY **60 Hrs**

1. Basic Aspects of Organic Chemistry

a. Organic intermediates: Carbocations, carbanions, free radicals, carbenes and nitrenes. Their method of formation, stability and synthetic applications.

b. Types of reaction mechanisms and methods of determining them,

c. Detailed knowledge regarding the reactions, mechanisms and their relative reactivity and orientations.

i. Aliphatic and aromatic compounds,

ii. Nucleophilic uni- and bimolecular reactions (SN1 and SN2)

iii. Elimination reactions (E1 & E2; Hoffman & Saytzeff's rule)

iv. Rearrangement reaction

12Hrs

2. Study of mechanism synthetic applications of following named Reactions:

Ugi reaction, Brook rearrangement, Ullmann coupling reactions, Dieckmann Reaction, Doebner-Miller Reaction, Sandmeyer Reaction, Mitsunobu reaction, Mannich reaction, Vilsmeyer-Haack Reaction, Sharpless asymmetric epoxidation, Baeyer-Villiger oxidation, Shapiro & Suzuki reaction, Ozonolysis and Michael addition reaction

12 Hrs

3. Synthetic Reagents & Applications

Aluminiumisopropoxide, N-bromosuccinamide, diazomethane, dicyclohexylcarbodimide, Wilkinson reagent, Witting reagent. Osmium tetroxide, titanium chloride, diazopropane, diethyl azodicarboxylate, Triphenylphosphine, Benzotriazol-1-yloxy) tris (dimethylamino) phosphonium hexafluoro-phosphate (BOP).

Protecting groups

a. Role of protection in organic synthesis

b. Protection for the hydroxyl group, including 1,2-and1,3-diols: ethers, esters, carbonates, cyclic acetals & ketals

c. Protection for the Carbonyl Group: Acetals and Ketals

d. Protection for the Carboxyl Group: amides and hydrazides, esters

e. Protection for the Amino Group and Amino acids: carbamates and amides

12Hrs

4. Heterocyclic Chemistry

General methods of synthesis and applications of drugs of five, six membered and fused heterocylces such as imidazole, pyrazole, triazole, pyrimidine, quinoline, acridine, phenothiazine and purine. Synthesis of few representative drugs containing these heterocyclic nucleus

12Hrs

5. Synthon approach and retrosynthesis applications

i. Basic principles, terminologies and advantages of retrosynthesis; guidelines for dissection of molecules. Functional group interconvertion and addition (FGI and FGA)

ii. C- X disconnections; C- C disconnections – alcohols and carbonyl compounds; 1,2- , 1,3- ,1,4- , 1,5- , 1,6- difunctionalized compounds

iii. Strategies for synthesis of three, four, five and six- membered ring

12Hrs

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, NewYork.

3. "Organic Chemistry" Clayden, Greeves, Warren and Woihers., Oxford University Press 2001.

4. "Organic Chemistry" Vol I and II. I.L. Finar. ELBS, Sixth ed., 1995.

5. A guide to mechanisms in Organic Chemistry – Peter Skyes (Orient Longman, New Delhi).

6. Reactive intermediates in organic chemistry – Tandom and Gowel. 60

7. Combinational Chemistry – Synthesis and applications – Stephen R Wilson & Anthony W Czarnik.

8. Carey, Organic chemistry, 5th edition (Viva Books Pvt. Ltd.)

9. Organic synthesis-The disconnection approach, S. Warren, Wily India

10. Principles of organic synthesis, ROC Norman and JM Coxan, Nelson thorns

11. Organic synthesis- Special techniques VK Ahluwalia and R Agarwal, Narosa Publishers

12. Organic reaction mechanisms IV edtn, VK Ahluwalia and RK Parashar, Narosa Publishers

ADVANCED MEDICINAL CHEMISTRY (MPC102T)

Course outcomes

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

CO1 Different stages of drug discovery

CO2 Role of medicinal chemistry in drug research

CO3 Different techniques for drug discovery

CO4 Various strategies to design and develop new drug like molecules for biological targets

CO5 Peptidomimetics

THEORY **60 Hrs**

1. Drug discovery: Stages of drug discovery, lead discovery; identification, validation and diversity of drug targets. Chemistry of prostaglandins, leukotrienes and thromboxones.

Biological drug targets: Receptors, types, binding and activation, theories of drug receptor interaction, drug receptor interactions, agonists vs antagonists, artificial enzymes.

12 Hrs

2. Prodrug Design and Analog design:

 Prodrug design: Basic concept, Carrier linked prodrugs/ Bioprecursors, Prodrugs of functional group, Prodrugs to improve patient acceptability, Drug solubility, Drug absorption and distribution, site specific drug delivery and sustained drug action. Rationale of prodrug design and practical consideration of prodrug design.

 Combating drug resistance: Causes for drug resistance, strategies to combat drug resistance in antibiotics and anticancer therapy, Genetic principles of drug resistance.

 Analog Design: Introduction, Classical & Non classical, Bioisosteric replacement strategies, rigid analogs, alteration of chain branching, changes in ring size, ring position isomers, design of stereo isomers and geometric isomers, fragments of a lead molecule, variation in inter atomic distance.

12Hrs

3 Chemistry of Synthetic drugs: Systematic study, SAR, Mechanism of action and synthesis of new generation molecules of following class of drugs: Anti-hypertensive drugs, Psychoactive drugs, Anticonvulsant drugs, H1 & H2 receptor antagonist, COX1 & COX2 inhibitors, Adrenergic & Cholinergic agents, Antineoplastic and Antiviral agents.

Stereochemistry and Drug action: Realization that stereo selectivity is a pre-requisite for evolution. Role of chirality in selective and specific therapeutic agents. Case studies, Enantio selectivity in drug adsorption, metabolism, distribution and elimination.

12 Hrs

4. Rational Design of Enzyme Inhibitors: Enzyme kinetics & Principles of Enzyme inhibitors**,**Enzyme inhibitors in medicine, Enzyme inhibitors in basic research, rational design of non-covalently and covalently binding enzyme inhibitors.

12 Hrs

5. Peptidomimetics: Therapeutic values of Peptidomimetics, design of peptidomimetics by manipulation of the amino acids, modification of the peptide backbone, incorporating conformational constraints locally or globally.

Combinatorial chemistry and High throughput screening: Different techniques, Solid phase synthesis, Solution phase synthesis, Parallel synthesis, applications of combinatorial chemistry. High Throughput Screening- general outline, importance and application.

12 Hrs

REFERENCES:

1. Medicinal Chemistry by Burger.

2. Wilson and Gisvold's Text book of Organic Medicinal and Pharmaceutical Chemistry.

3. Comprehensive Medicinal Chemistry – Corwin and Hansch.

4. Computational and structural approaches to drug design edited by Robert M Stroud and Janet. F Moore

5. Introduction to Quantitative Drug Design by Y.C. Martin.

6. Principles of Medicinal Chemistry by William Foye.

7. Drug Design Volumes by Arienes.

8. Principles of Drug Design by Smith.

9. The Organic Chemistry of the Drug Design and Drug action by Richard B.Silverman.

10. An Introduction to Medicinal Chemistry –Graham L.Patrick, (III Edition.)

11. Biopharmaceutics and pharmacokinetics by DM.Brahmankar, Sunil B .Jaiswal.

12. Peptidomimetics in Organic and Medicinal Chemistry by Antonio Guarna and Andrea Trabocchi, First edition, Wiley publishers.

CHEMISTRY OF NATURAL PRODUCTS (MPC103T)

Course outcomes

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

CO1 Different types of natural compounds and their chemistry and medicinal importance

CO2 The importance of natural compounds as lead molecules for new drug discovery

CO3 The concept of rDNA technology tool for new drug discovery

CO4 General methods of structural elucidation of compounds of natural origin

CO5 Isolation, purification and characterization of simple chemical constituents from natural source

THEORY **60 Hrs**

1. Study of Natural products as leads for new pharmaceuticals for the following class of drugs:

a. Drugs Affecting the Central Nervous System: Morphine Alkaloids

b. Anticancer Drugs: Paclitaxel and Docetaxel, Etoposide, and Teniposide

c. Cardiovascular Drugs: Lovastatin, Teprotide and Dicoumarol

d. Neuromuscular Blocking Drugs: Curare alkaloids

e. Chemistry of macrolid antibiotics: Erythromycine, Azithromycine, Cephalosporins(New generation)

12Hrs

2. Alkaloids- General introduction, classification, isolation, purification, stereochemistry, molecular modification and biological activity of alkaloids, general methods of structural determination of alkaloids, structural elucidation of ephedrine, morphine, ergot, emetine and reserpine.

Flavonoids. Introduction, isolation and purification of flavonoids, General methods of structural determination of flavonoids; Structural elucidation of quercetin.

12Hrs

3. Steroids- General introduction, chemistry of sterols, sapogenin and cardiac glycosides. Stereochemistry and nomenclature of steroids, Structure elucidation of male & female sex hormones(testosterone, Estradial, progesterone), Adrenocortcoids (carsisone) and contraceptive agents.

Terpenoids – Classification, isolation, isoprene rule and general methods of structural elucidation of Terpenoids; Structural elucidation of drugs belonging to mono, di and tri terpenoids, carotinoids.

12Hrs

4. Recombinant DNA technology and drug discovery:

rDNA technology, hybridoma technology, New pharmaceuticals derived from biotechnology; Oligonucleotide therapy. Gene therapy: Introduction, Clinical application and recent advances in gene therapy, principles of RNA & DNA estimation

Active constituent of certain crude drugs used in Indigenous system.

Diabetic therapy – *Gymnema sylvestre*, *Salacia reticulate*, *Pterocarpus marsupiam*, *Swertia chirata*, *Trigonella foenum graccum*; Liver dysfunction – *Phyllanthus niruri*; Antitumor – *Curcuma longa* Linn.

12Hrs

5. Structural Characterization of natural Products

Structural characterization of natural compounds using IR, 1HNMR, 13CNMR and MS Spectroscopy

12Hrs

REFERENCES

1. Modern methods of plant analysis – Peech and M.V.Tracey.
2. Phytochemistry Vol. I and II by Miller, Jan Nostrant Rein Hld.
3. Recent advances in Phytochemistry Vol. I to IV – Scikel Runeckles.
4. Chemistry of natural products Vol I onwards IWPAC.
5. Natural Product Chemistry Nakanishi Gggolo.
6. Natural Product Chemistry "A laboratory guide" – Rapheal Khan.
7. The Alkaloid Chemistry and Physiology by THF Manske.
8. Introduction to molecular Phytochemistry – CHJ Wells, Chapmannstall.
9. Organic Chemistry of Natural Products Vol I and II by Gurdeep and Chatwall.
10. Organic Chemistry of Natural Products Vol I and II by O.P. Agarwal.
11. Organic Chemistry Vol I and II by I.L. Finar
12. Elements of Biotechnology by P.K. Gupta.
13. Pharmaceutical Biotechnology by S.P.Vyas and V.K.Dixit.
14. Biotechnology by Purohit and Mathoor.
15. Phytochemical methods of Harborne.
16. Burger's Medicinal Chemistry.

PHARMACEUTICAL CHEMISTRY PRACTICAL-I (MPC104P)

Course outcomes

After completion of the course, student is able to

CO1 Synthesize the compounds

CO2 Standardization of the compounds

CO3 Use different techniques in the area of the Pharmaeutical chemistry.

Practicals

1. Analysis of pharmacopoeial compounds and their formulations by UV Vis spectrophotometer, RNA & DNA estimation

2. Simultaneous estimation of multi component containing formulations by UV spectrophotometry

3. Experiments based on HPLC

4. Experiments based on Gas Chromatography

5. Estimation of riboflavin/quinine sulphate by fluorimetry

6. Estimation of sodium/potassium by flame photometry

To perform the following reactions of synthetic importance

7. Purification of organic solvents, column chromatography

8. Claisen-schimidt reaction.

9. Benzyllic acid rearrangement.

10. Beckmann rearrangement.

11. Hoffmann rearrangement

12. Mannich reaction

13. Synthesis of medicinally important compounds involving more than one step along with purification and Characterization using TLC, melting point and IR spectroscopy (4 experiments)

14. Estimation of elements and functional groups in organic natural compounds

15. Isolation, characterization like melting point, mixed melting point, molecular weight determination, functional group analysis, co-chromatographic technique for identification of isolated compounds and interpretation of UV and IR data.

16. Some typical degradation reactions to be carried on selected plant constituents

SEMESTER-II

ADVANCED SPECTRAL ANALYSIS (MPC201T)

Course outcomes

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

CO1 Interpretation of the NMR, Mass and IR spectra of various organic compounds

CO2 Theoretical and practical skills of the hyphenated instruments

CO3 Identification of organic compounds

THEORY **60Hrs**

1. **UV and IR spectroscopy**: Wood ward – Fiesure rule for 1,3- butadienes, cyclic dienes and α, β-carbonyl compounds and interpretation compounds of enones. ATR-IR, IR Interpretation of organic compounds.

12Hrs

2. **NMR spectroscopy**: 1-D and 2-D NMR, NOESY and COSY, HECTOR, INADEQUATE techniques, Interpretation of organic compounds.

12Hrs

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.

12Hrs

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.

12Hrs

5. **Thermal methods of analysis** – Introduction, principle, instrumentation and application of DSC, DTA and TGA.

Raman Spectroscopy: Introduction, Principle, Instrumentation and Applications.

Radio immuno assay: Biological standardization , bioassay, ELISA, Radioimmuno assay of digitalis and insulin

12Hrs

REFERENCES

1. Spectrometric Identification of Organic compounds - Robert M Silverstein, Sixth edition, John Wiley & Sons, 2004.

2. Principles of Instrumental Analysis - Doglas 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 (MPC202T)

Course outcomes

Upon completion of course, the student shall able to understand

CO1 The principles and applications of Green chemistry

CO2 The concept of peptide chemistry.

CO3 The various catalysts used in organic reactions

CO4 The concept of stereochemistry and asymmetric synthesis.

THEORY **60 Hrs**

1. Green Chemistry

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.

12Hrs

2. Chemistry of peptides

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

12Hrs

3. Photochemical Reactions

Basic principles of photochemical reactions. Photo-oxidation, photo-addition and photo-fragmentation

Pericyclic reactions

Mechanism, Types of pericyclic reactions such as cyclo addition, elctrocyclic reaction and sigmatrophic rearrangement reactions with examples

12Hrs

4. Catalysis

a. Types of catalysis, heterogeneous and homogenous catalysis, advantages and disadvantages

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

12Hrs

5. Stereochemistry & Asymmetric Synthesis

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.

b. Methods of asymmetric synthesis using chiral pool, chiral auxiliaries and catalytic asymmetric synthesis, enantiopure separation and Stereo selective synthesis with examples.

12Hrs

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, NewYork.

3. "Organic Chemistry" Clayden, Greeves, Warren and Woihers., 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, Wily India

7. Principles of organic synthesis, ROCNorman and JMCoxan, Nelson thorns

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 (MPC203T)

Course outcomes

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

CO1 Role of CADD in drug discovery

CO2 Different CADD techniques and their applications

CO3 Various strategies to design and develop new drug like molecules.

CO4 Working with molecular modeling softwares to design new drug molecules

CO5 The *in silico* virtual screening protocols

Theory **60 Hrs**

1. Introduction to Computer Aided Drug Design (CADD): 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 (sigma), lipophilicity effects and parameters (log P, pi-substituent constant), steric effects (Taft steric and MR parameters) Experimental and theoretical approaches for the determination of these physicochemical parameters.

12 Hrs

2. Quantitative Structure Activity Relationships: Applications

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.

12 Hrs

3. Molecular Modeling and Docking

a. Molecular and Quantum Mechanics in drug design

b. Energy Minimization Methods: comparison between global minimum conformation and bioactive conformation 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)

12 Hrs

4. Molecular Properties and Drug Design

a. Prediction and analysis of ADMET properties of new molecules and its importance in drug design.

b. *De novo* drug design: Receptor/enzyme-interaction and its analysis, Receptor/enzyme cavity size prediction, predicting the functional components of cavities, Fragment based drug design.

c. Homology modeling and generation of 3D-structure of protein.

12 Hrs

5. Pharmacophore Mapping and Virtual Screening Concept of pharmacophore, pharmacophore mapping, identification of Pharmacophore features and Pharmacophore modeling; Conformational search used in pharmacophore mapping. *In Silico* Drug Design and Virtual Screening Techniques Similarity based methods and Pharmacophore based screening, structure based *in silico* virtual screening protocols.

12 Hrs

REFERENCES:

1. Computational and structural approaches to drug design edited by Robert M Stroud and Janet. F Moore

2. Introduction to Quantitative Drug Design by Y.C. Martin.

3. Drug Design by Ariens Volume 1 to 10, Academic Press, 1975.

4. Principles of Drug Design by Smith and Williams.

5. The Organic Chemistry of the Drug Design and Drug action by Richard B. Silverman.

6. Medicinal Chemistry by Burger.

7. An Introduction to Medicinal Chemistry –Graham L. Patrick, (III Edition.)

8. Wilson and Gisvold's Text book of Organic Medicinal and Pharmaceutical Chemistry.

9. Comprehensive Medicinal Chemistry – Corwin and Hansch.

10. Computational and structural approaches to drug design edited by Robert M Stroud and Janet. F Moore

PHARMACEUTICAL PROCESS CHEMISTRY (MPC204T)

Course Outcomes

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

CO1 The strategies of scale up process of APIs and intermediates

CO2 The various unit operations and various reactions in process chemistry

CO3 Synthesis of APIs.

THEORY **60 Hrs**

1. Process chemistry

a. Introduction, Synthetic strategy

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

c. In-process control and validation of large scale process.

d. Case studies of some scale up process of APIs.

e. Impurities in API, types and their sources including genotoxic impurities

12 Hrs

2. Unit operations

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.

12 Hrs

3. Unit Processes

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.

12 Hrs

4. Unit Processes

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

i. Antibiotics; Penicillin and Streptomycin,

ii. Vitamins: B2 and B12

iii. Statins: lovastatin, simvastatin

Reaction progress kinetic analysis

a. Streamlining reaction steps, route selection,

b. Characteristics of expedient routes, characteristics of cost-effective routes, reagent selection, families of reagents useful for scale-up.

12 Hrs

5. Industrial Safety

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

12 Hrs

REFERENCES:

1. Process Chemistry in the Pharmaceutical Industry: Challenges in an Ever- Changing Climate-An Overview; K. Gadamasetti

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

11. Clausen,Mattson: Principle of Industrial Chemistry

12. Lowenheim & M.K. Moran: Industrial Chemicals

13. S.D. Shukla & G.N. Pandey: A text book of Chemical Technology Vol. II

14. J.K. Stille: Industrial Organic Chemistry (PH)

15. Srreve: Chemical Procress

16. B.K.Sharma: Industrial Chemistry

17. ICH Guidelines

18. United States Food and Drug Administration official website www.fda.gov

PHARMACEUTICAL CHEMISTRY PRACTICAL-II (MPC205P)

Course outcomes

After completion of the course, student is able to

CO1 Synthesize and compare the APIs

CO2 Interpret the data by using different analytical techniques

CO3 Use different softwares

Practicals

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 Wood ward – Fiesure 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-iodotolene from p-toluidine.

13. NaBH4 reduction of vanillin to vanillyl alcohol

14. Preparation of umbelliferone by Pechhman 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

22. Virtual screening based experiment