M.PHARM
PHARMACEUTICAL CHEMISTRY

AIMS:

A post-graduate in Pharmaceutical Chemistry while undergoing the course in the institution should acquire adequate knowledge and necessary practical skills and attitude required for understanding reaction mechanisms, identification of lead molecules and their eventual refinement for development as drugs, knowledge of natural and synthetic molecules used as therapeutic agents.

OBJECTIVES:

The objectives are dealt under two headings namely
(a) Knowledge and understanding
(b) Attitudes

a) Knowledge and understanding:

A postgraduate student should acquire detailed theoretical knowledge and practical techniques of the following during the period of his/her course. He/she should acquire thorough theoretical knowledge and practical skills in Pharmaceutical Chemistry with special emphasis on all modern analytical instruments and techniques. He/she should acquire adequate theoretical knowledge and practical skills in QSAR, Computer Aided Drug Design and design of drugs targeted to act at specific sites. He/she should acquire adequate theoretical and practical knowledge about structure elucidation of natural products of medicinal interest and also mechanism of different reactions involved in the synthesis of various classes of drugs used in therapy.

b) Attitude:

A postgraduate student must inculcate attitude for applying his acquired knowledge of reaction mechanisms and drug design in the synthesis of new molecules to provide a cure for diseases of mankind. He/she has to maintain a high standard of professional ethics. He/she should continuously upgrade the acquired knowledge by keeping in touch with contemporary research through national and international journals and should be willing to participate in continuing education programs.

M. Pharm. I	**TITLES OF PAPERS**	**Total Hours**	**Hours per week**	
			Theory	**Practical**
PAPER-I	Modern Pharmaceutical Analysis	**75**	**3**	**6**
PAPER-II	Advanced Pharmaceutical Chemistry	**50**	**2**	**6**
PAPER-III	Medicinal Chemistry–I (Drug Design)	**50**	**2**	**6**
PAPER-IV	Medicinal Chemistry–II (Natural Products)	**50**	**2**	**6**
M. Pharm. II	Dissertation Work	**One Year**		

PAPER-II. ADVANCED PHARMACEUTICAL CHEMISTRY (Theory)

Total Hours: 50 (2 hr/week),	**Examination**	**Max Marks**
	Annual	100
	Internal Assessment Exam:	30
	Seminar Evaluation:	20
	Total:	150

GOAL:
The goal is to train the postgraduate students in various reaction mechanisms involved in the synthesis of various drug molecules.

OBJECTIVES:

1. To train a student in necessary skills involved in the synthesis of drug molecules in the laboratory and to ensure higher competence in the synthesis of newer molecules.
2. Each student has to achieve a high degree of proficiency and develop competence involved in the structural modification aimed at improved activity.

S.N	**Syllabus**	**Hr/Week**
1.	**Reaction intermediates in organic synthesis.**	**23**
a)	Carbocations: Formation, structure and stereochemistry, stability and reactivity of carbocations. Reactions (addition and substitution) involving carbocations, study of rearrangement reactions like, Wagner-Meerwein, Pinacol-pinacolone & trans-annular rearrangements.	5
b)	i) Carbanions: Formation, structure and stereochemistry, stability and reactivity of carbanions. Reactions (addition and substitution) involving carbanions, study of Perkin, Claisen, Benzoin, Aldol condensation, Cannizzaro reactions and Favorskii rearrangement.	5
	ii) Aromatic Nucleophilic reactions: Cyclohexadienyl anions and benzyne mechanism (cine substitution)	3
c)	Free radicals: Formation, structure and stereochemistry, stability and reactivity of free radicals. Reactions (addition and substitution) detection. Study of reactions involving free radicals including biological, addition to carbon – carbon multiple bonds.	4

d)	Carbenes: Formation, structure and stereochemistry, stability and reactivity. Reactions (addition and substitution) reactions involving carbenes. Study of Reimer – Tiemen reaction, Wolff rearrangement, ring expansion reaction-conversion of pyrrole to pyridine.	3
e)	Nitrenes: Formation, structure and stereochemistry, stability and reactivity. Reactions (addition and substitution). Study of reactions involving nitrenes, Hofman, Curtius- Schmidt- Lossen rearrangement.	3
2.	**Catalysis**	**6**
a)	Introduction, homogenous, heterogenous catalysis and their applications.	2
b)	Phase transfer catalysis in anhydride, epoxide, ester, nitrile and sulfide formation in ester hydrolysis and reduction reactions	2
c)	Stereospecific catalysis	2
3.	**Green Chemistry**	**5**
a)	Principles and various techniques of green chemistry, green reagents, green catalysts, ionic solvents, phase transfer catalysts (PTC) in green synthesis, applications of PTC in synthesis of heterocyclic compounds.	4
b)	Microwave enhanced organic synthesis and ultrasound enhanced organic synthesis (sonochemistry), introduction, instrumentation, advantages, synthetic applications and limitations.	1
4.	**Combinatorial chemistry.**	**8**
	i). Introduction to Combinatorial Libraries. Concepts and Terms	1
	ii). Parallel Organic Synthesis Technology	2
	iii) Polymer-Supported Synthesis of Organic Compounds and Libraries	2
	iv). Macro Beads in Solid-Phase Synthesis	2
	v). Combinatorial Libraries in Solution.	1
5.	**Strategies in Organic Synthesis**	**8**
a)	Introduction, Target Selection, disconnection approach, functional group interconversion (FGI), synthons, uses of synthon approaches in synthesis of Trimethoprim, Ibuprofen, Nifedipine and Ciprofloxacin. Retrosynthesis, Chemoselectivity, Regioselectivity, linear synthesis and convergent synthesis. Basic rules in disconnections, strategic bonds, disconnection of strategic bonds in carbocyclic and heterocyclic rings, biomimetic approach.	5

b) Protecting and deprotecting groups; protection and deprotection of hydroxyl, carboxy, carbonyl, amino groups and carbon-carbon multiple bonds, chemo and regioselective protection and deprotection, illustration of protection and deprotection in synthesis. 2

c) Study of polymorphism of few selected APIs like paracetamol, aspirin, barbiturates, chloramphenicol maleate. 1

PAPER-II. ADVANCED PHARMACEUTICAL CHEMISTRY (Practical)

Total Hours: 150 (6 hr/week),	**Examination**	**Max Marks**
	Annual	**100**
	Internal Assessment Exam:	**30**
	Practical record Evaluation:	**20**
	Total:	**150**

Part –1 Preparation: (Minor experiments)

a) Study of experimental technique such as solvent purification, distillation (vacuum, fractional, steam and simple), preparative, column and TLC, Crystallization and filtration.

b) Carryout the preparations of organic compounds by conventional as well as microwave assisted methods along with their purity, percentage yield, physical and spectral data(UV/ IR) for the following;

1) Preparation of benzanilide from benzophenone (Beckmann rearrangement) Benzophenone ———— Benzophenone oxime —— Benzanilide

2) Preparation of 2-Phenyl indole from acetophenone (Fischer indolisation) Actophenone ——— Acetophenone phenylhydrazine ——— 2-Phenylindole

3) Preparation of 2,5-dihydroxy acetophenone from hydroquinone(Fries rearrangement) Hydroquinone———Hydroquinone diacetate———2,5-Dihydroxy acetophenone

4) Preparation of Diethyl fumarate from maleic acid (conversion of cis isomer to trans isomer) Maleic acid——————Fumaric acid——————Diethyl fumarate

5) Preparation of 2, 2‘-Dihydroxy –1, 1‘-binapthyl from 2-naphthol (oxidation of 2-naphthol and free radical coupling)

6) Preparation of Benzilic acid from Benzoin (Benzilic acid rearrangement)

7) Preparation of 2-amino-3-cyano-4,5-tetrahydro(b)thiophene

8) Preparation of 2-amino-3-carbethoxy-4,5-diphenylfuran

9) Preparation of thiazolidine-2, 4-dione.

c) Carryout at least two experiments on protection and de-protection of functional groups like hydroxyl, amino etc suing Fmoc/BOC

Part-II Qualitative Analysis (Major experiment)

A minimum of six organic binary mixtures and four ternary mixtures should be analyzed systematically by ether/aqueous separation technique with the preparation of at least one derivative in each compound.

TEACHING AND LEARNING ACTIVITIES

Journal Club:

Each student is required to present any two recent articles relevant to the Advanced Pharmaceutical chemistry from any of the journals in a year.

Seminars:

Each student is required to give two seminars relevant to the subject in a year.

Field/ Industrial Visits:

It is desirable to make to one visit to the relevant Laboratory / Industry in a year.

Conference / Meetings:

Each student has to be encouraged to attend at least one relevant national conference.

Scheme of Practical Examination

Sl. No	Synopsis	Experiments		Viva-voce	Total
		Major	Minor		
1	20	35	25	20	**100**

Reference Books:

1. A Guide Book to Mechanisms in Organic Chemistry- Peter Sykes (Orient Longman, New Delhi)
2. Advanced Organic Chemistry- Reactions, Mechanism and Structure- Jerry March (Wiley Interscience Publication; 4th Edition, New York)
3. Advanced Practical Organic Chemistry-O.P. Agarwal
4. Combinatorial Chemistry- Synthesis and Applications S.R. Wilson & Anthony W. Czarnik (John Wiley and Sons, USA)
5. Designing Organic Syntheses: A Programmed Introduction to the Synthon Approach. Stuart Warren. John Wiley & Sons.
6. Elemental Practical Organic Chemistry Part I & II A. I. Vogel
7. Experimental Organic Chemistry Vol-I & II –P. R. Singh *etal*.
8. F. A. Cary and R. I. Sundberg, Advanced Organic Chemistry, Part A and B, 5th Edition, Springer, 2009.
9. Green solvents for chemistry; perspective and practice, Oxford University Press, Willium M Nelson.

10. H G Brittain. Polymorphism in Pharmaceutical Solids. Marcel Dekker Inc. NY,1999
11. Handbook of green chemistry and technology, Blackwell Science ltd. James Clarke & Duncan Macquarrie, 2002
12. M. B. Smith, Organic Synthesis, 2nd Edition, 2005
13. Microwaves in organic and medicinal Chemistry, C.O. Kappe, A. Stadler, (Wiley-Vch) June 2005
14. Organic Chemistry by Morison & Boyd (Prentice Hall), New Delhi
15. Organic Chemistry of Synthetic Drugs- Lednicer (Wiley, Interscience Publications, New York)
16. Organic Chemistry Vol-I and II by I. L. Finar, 5th Edition (ELBS, Longman, London).
17. Organic Synthesis: the discpnnection approach, Stuart Warren, Paul Wyatt.
18. Physical Organic Chemistry – Jack Hine
19. Protective groups in organic synthesis, Green and Wuts, Iain Edn, John Wiley & sons.
20. Reaction Mechanisms in Organic Chemistry-S. Mukharjee and S P. Singh (Mc Millan India Ltd., New Delhi), 3rd Edition, Reprinted
21. Reactive Intermediates in Organic Chemistry – Tandon and Goel (Oxford and IBH Publisher)
22. Vogel's Text Book of Practical Organic Chemistry 4th Edition (ELBS, Longman, London).

Journals:

1. Indian Journal of Chemistry Section - B
2. Indian Journal of Heterocyclic Chemistry
3. Indian Journal of Pharmaceutical Sciences.
4. At least one International Journal is to be subscribed.

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PAPER-III. MEDICINAL CHEMISTRY-I (DRUG DESIGN)(Theory)

Total Hours: 50 (2 hr/week),	**Examination**	**Max Marks**
	Annual	100
	Internal Assessment Exam:	30
	Seminar Evaluation:	20
	Total:	150

GOAL:

The goal of studying this paper is to train the candidates to ensure that he/she develops the skill in the designing of target specific molecules.

OBJECTIVES:

1) To train candidates with different theoretical aspects involved in drug design.
2) To know about the various basic molecules useful in designing newer compounds for the treatment of different disease conditions.
3) Ability to master the different techniques used in the synthesis of dug molecules.
4) Use information technology tools to carry out research.
5) update his/her knowledge by self-study and by attending advanced courses, conferences and seminars in drug design.

S.N	**Syllabus**	**Hr/Week**
1.	**Theoretical aspects of Drug Design** Introduction to drug design and discovery. Conventional methods of drug design. Lead, discovery of lead, lead optimization, objectives of lead optimization, pharmacophore identification and analog approach of drug discovery	**4**
2.	**Targets in Drug Discovery and Development** Introduction, Different biological targets for drug discovery: enzymes, nucleic acids, and polysaccharides. Cellular Communication, Receptor Nomenclature, Receptor Classes- G-Protein-Coupled Receptors, Ligand-Gated Ion Channels, Steroid Receptors, Orphan Receptors, Defining the Receptor-Ligand Interaction, Receptor Binding Assays, Functional Assays, Receptor Sources.	**8**
3.	**History and development of QSAR.**	**8**
a)	Theoretical compartment model for relationship between physical properties and biological activity(Hammet, Taft)	3
b)	Mathematical methods for the analysis of QSAR i) Diagnosis mechanism ii) Prediction of activity	

iii) Optimization
iv) Refinement of synthetic Targets 3

c) Application of Hansh Analysis 1

d) Application of Free-Wilson Analysis 1

4. In-silico and Computer Aided Drug design **10**

Molecular Mechanics, force fields (Potential energy function), Energy Minimization Methods, Conformational Analysis. Concepts of Virtual Screening, Drug likeness, Screening-Counting Schemes, Functional Group Filters, Topological Drug Classification-Pharmacophore Point Filter-Focused Screening Libraries for Lead Identification, Pharmacophore Screening, Structure-Based Virtual Screening, Protein Structures, Computational Protein-Ligand Docking Techniques, Rigid Docking, Flexible or induced fit Docking, i*n silico* De Novo design.

5. Designing and applications of Prodrugs **5**

Basic concept, Prodrugs of functional group, Prodrug design 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.

6. Rational design of enzyme inhibitors **8**

a) Enzyme inhibitors- Reversible, irreversible, Kcat inhibitors, transition state analogs and their application with respect to drug design. 3

b) Enzyme inhibitors of ACE, leukotrienes Lipoxygenase, Cycloxygenase, Aromatase, Xanthine oxidase, Cytochrome P-450 Inhibitors, DHFR Inhibitors, and Gastric proton pump Inhibitors. 3

c) HIV-Protease / Reverse Transcriptase, Integrase and DNA polymerase Inhibitors, 2

7. Recent advances in the development of Immuno modulators **2**

8. Recombinant DNA technology **5**

a) Introduction; New drugs from Recombinant DNA technology 1

b) Protein engineering and site directed mutagenesis. 2

c) Development of t-PA as a therapeutic agents Epitope mapping and Human growth hormone. 1

d) Screening of recombinant DNA libraries and development of HIV-tat inhibitor. 1

PAPER-III. MEDICINAL CHEMISTRY-I (DRUG DESIGN)(Practical)

Total Hours: 150 (6 hr/week),	**Examination**	**Max Marks**
	Annual	**100**
	Internal Assessment Exam:	**30**
	Practical record Evaluation:	**20**
	Total:	**150**

Part 1: Synthesis of the following important medicinal compounds involving more than one step and characterization using TLC. M.P. and IR spectroscopy.

1. INH
2. Methaqualone
3. Saccharin Sodium
4. Dapsone
5. Phenytoin from Benzoin
6. Sulfanilamide
7. 2-Methyl Benzimidazole from OPDA (Phillips synthesis)
8. 2-Mercapto Benzimidazole/Benzimidazolyl-2-thiol
9. Antipyrine

Part 2:

1. Determination of Partition coefficient by shake flask method (Diazepam,Pheytoin and Caffeine)
2. Determination of *pKa* value by potentiometric method (Phenobarbitone, Ibuprofen)
3. In vitro screening of medicinally important compounds for Anti-inflammatory, Antimicrobial and Antioxidant study.
4. In Silico QSAR based experiments (Three experiments)

TEACHING AND LEARNING ACTIVITIES

Journal Club:

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Seminars:

Each student is required to give two seminars relevant to the subject in a year.

Field/ Industrial Visits:

It is desirable to make to one visit to the relevant Laboratory / Industry in a year.

Conference / Meetings:

Each student has to be encouraged to attend at least one relevant national conference.

Scheme of Practical Examination

Sl. No	Synopsis	Experiments	Viva-voce	Total

		Major	Minor		
1	20	35	25	20	**100**

Reference Books:

1. A Biochemical basis – Medicinal chemistry by Thomas Nogrady
2. Introduction to quantitative drug design by Y.C.Martin
3. Selective Toxicity by Drein Albert
4. Comprehensive Medicinal Chemistry by Corwin and Hansch.
5. Medicinal Chemistry by Burger, 4th Edition.
6. Principles of Medicinal Chemistry by William O. Foye, 3rd Edition.
7. Drug design volumes by Ariens
8. Principles of Drug design by Smith
9. Strategy of Drug design by Brucell
10. The Organic Chemistry of the Drug design and Drug action by Richard B.Silverman

Journal: At least one international journal is to be subscribed

1. Indian Journal of Chemistry Section B
2. Indian Journal of Heterocyclic Chemistry
3. Indian Journal of Pharmaceutical Sciences

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PAPER-IV: MEDICINAL CHEMISTRY–II (NATURAL PRODUCTS)(Theory)

Total Hours: 50 (2 hr/week),	**Examination**	**Max Marks**
	Annual	100
	Internal Assessment Exam:	30
	Seminar Evaluation:	20
	Total:	150

GOAL:

- To train the student to learn in detail about different biological constituents of plants and to study their biosynthetic path ways.
- To train the student to isolate and identify the different principles from plant source.

OBJECTIVES:

1. To impart a thorough knowledge to the student about different medicinally active principles, their formation, isolation and identification.
2. The candidate is trained to improve the yield of the active principles by suitable bio-chemical modifications.
3. The candidates are trained to modify the chemical structure of the active constituents to improve their pharmacological activity.

S.N	**Syllabus**	**Hr/Week**
1	**A) General chemical methods of structural elucidation of natural products.** **B) Structure elucidation of the following compounds based on chemistry, chemical degradation and synthesis of the compounds;**	**15**
a)	Morphine alkaloids: Morphine, Papavarine	3
b)	Cardiac glycosides: Lanatoside C, Ouabain	3
c)	Rauwolfia alkaloid: Reserpine	3
d)	Vinca alkaloids: Vinblastine and vincristine	3
e)	Ipecacuanha alkaloid: Emetine	3
2.	**Microbial conversions as tools in the preparation of drugs**	**4**
a)	Introduction	
b)	Practical aspects of microbial transformation	
c)	Some theoretical aspects of microbial transformation	
d)	Conversion by microorganism	
3.	**A) General introduction and classification of steroids** **B) Hormones:**	**9**
a)	Female and male sex hormones –development of antifertility agents.	3
b)	Adrenal cortex hormones and their derivatives	3
c)	Carotenoids and their therapeutic importance.	1
d)	Development of anabolic steroids and antifertility agents	2

4.	**Antiboitics :**	**10**
a)	Penicillins and Cephalosporins:	
	i) Early Penicillins and cephalosporins	1
	ii) AmidoPenicillins	1
	iii) Beta lactamase stable cephalosporins	1
	iv) Antipsuedomonalpenicillins and cephalosporins	2
	v) New oral compounds and future prospects	1
b)	Other betalactam agents	
	i) Nocardins and monobactams	1
	ii) Clavulanic acid analogs	1
	iii) Carbapenams	1
	Other fused Betalactam systems	1
5.	**Purine,Pyrimidines and their applications**	**8**
a)	The metabolism of purines and pyrimidines, allopurinol and xanthine oxidase	2
b)	Purine and pyrimidine antimetabolites as antineoplastic agents	2
c)	Purine and pyrimidine related Antiparasitic agents	2
d)	Purine and pyrimidine related Antifungal agents	2
6.	**Chemistry of vitamins**	**4**
a)	Water soluble vitamins: Vitamin B_1, B_2, B_6 and Vitamin C	2
b)	Fat soluble vitamins: Vitamin A, D, E and K	2

PAPER-IV: MEDICINAL CHEMISTRY–II (NATURAL PRODUCTS)(Practical)

Total Hours: 150 (6 hr/week),	**Examination**	**Max Marks**
	Annual	**100**
	Internal Assessment Exam:	**30**
	Practical record Evaluation:	**20**
	Total:	**150**

Part –1: Isolation and Characterization of following active constituents

1. Eugenol from Clove
2. Curcumin from Turmeric
3. Sennosides from senna
4. Hesperidine from Orange Peel
5. Embelin from Embelia Ribes
6. Glycyrrhizin from Glycyrrhiza Glabra
7. Plumbagin from Plumbago Rosea
8. Solanine from potatoes
9. Naringen from Grape Fruit Peel
10. Trimyristin and Myristin from Nutmeg
11. Azylic acid from Castor Oil
12. Pectin from Orange Peel
13. Lycopene from Tomato Peel

14. Epicatechin from Cashew Kernel outer covering
15. Piperine from Black pepper

Part-II: Degradation reaction of following natural products and the identification of the degraded intermediates by micro TLC and qualitative tests.

1. Atropine,
2. Caffeine,
3. Ephedrine,
4. Saponification of Trimyristin

Scheme of Practical Examination

Sl. No	Synopsis	Experiments		Viva-voce	Total
		Major	Minor		
1	20	35	25	20	**100**

TEACHING AND LEARNING ACTIVITIES

Journal club
Each student is required to present any two recent articles relevant to the Advanced Pharmaceutical Chemistry from any of the journals in an year.

Seminars
Each student is required to give two seminars relevant to this subject in a year.

Field/Industrial visits
It is desirable to make to one visit to the relevant / Laboratory / Industry

Conference / Meetings
Each student has to be encouraged to attend at least one relevant national conference.

Reference Books:

1. Modern Methods of Plant Analysis- Peech and M.V. Tracey
2. Phytochemistry Vol-I and II by Miller, Jan Nostrant Rein Hold.
3. Recent Advances in Phytochemistry-Vol-I-IV Scikel Runeckles
4. Chemistry of Natural Products Vol-I onwards IWPAC
5. Natural Products Chemistry Nakanishi Golo
6. Natural Products Chemistry "A Laboratory Guide"-Raphael Ikan, IInd Edition, Academic Press New York.
7. The Alkaloid Chemistry and Physiology- Volumes RHF Manske
8. Introduction to Molecular Phytochemistry-CHJ Wells, Chapmannstall.
9. Comparative Phytochemistry edited by T.Swain
10. Organic Chemistry of Natural Products- Vol-I & II – Gurdeep Chatwal, Himalaya publishing house, Mumbai..
11. Organic Chemistry Vol-I & II by I.L. Finar, ELBS Longman, 5th Edition , London
12. Elements of biotechnology by P.K. Gupta

13. Pharmaceutical Biotechnology by S.P.Vyas and V.K.Dixit, CBS publisher, New Delhi.
14. Biotechnology by Purohit and Mathur , Agro Botanical publishers, Bikaner.
15. Phytochemistry method by Harborne
16. Burger's Medicinal Chemistry, 5th Edition, Vol.I, II. John Wiley and Sons, New York.
17. Burger's Medicinal Chemistry, 4th Edition, Vol. II, Part-II, John Wiley and Sons, New York.
18. Comprehensive Medicinal Chemistry, Vol.II by Corwin Hansch, Pergamon Press, New York

Journals:

(At least one international journal is to be subscribed)

1. Indian Journal of Pharmaceutical Sciences
2. JMAPS
3. Indian Journal of Natural Products
4. Phytopharma
5. Journal of Natural Products.
6. Indian Journal of Chemistry.
7. Phytochemistry

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