M.PHARMACY

PHARMACEUTICAL CHEMISTRY

I SEMESTER

Paper 101 - Modern Analytical Techniques
Paper 102 - Research Methodologies
Paper 103 - Advanced Pharmaceutical Organic Chemistry
Paper 104 - Advanced Chemistry of Natural Products
Paper 105 - Advanced Pharmaceutical Organic Chemistry - LAB
Paper 106 - Advanced Chemistry of Natural Products - LAB
Paper 107 - Seminar

II SEMESTER

Paper 201 - Advanced Medicinal Chemistry-I
Paper 202 - Advanced Medicinal Chemistry-II
Paper 203 - Bioassays & Pharmacological Screening Methods
Paper 204 - Drug Regulatory Affairs
Paper 205 - Advanced Medicinal Chemistry-I - LAB
Paper 206 - Advanced Medicinal Chemistry-II - LAB
Paper 207 - Seminar

III SEMESTER

Paper 301 - Project Seminar-I (On the proposed project work with aims and objectives) - 50 Marks
Paper 302 - Project work - I

IV SEMESTER

Paper 401 - Project Seminar-II (On the experimentation and results of the project work) – 50 Marks
Paper 402 - Project work - II

SCHEME OF INSTRUCTIONS AND EVALUATION

PHARMACEUTICAL CHEMISTRY

FIRST SEMESTER

Paper No.	Title of the Paper	Evaluation / Marks				Total	Credits
		Theory		Practical			
		Mid Examination	University End Examination	Mid Examination	University End Examination		
Paper – 101	Modern Analytical Techniques	40	60			100	3
Paper – 102	Research Methodologies	40	60			100	3
Paper – 103	Advanced Pharmaceutical Organic Chemistry	40	60			100	3
Paper – 104	Advanced Chemistry of Natural Products	40	60			100	3
Paper – 105	Advanced Pharmaceutical Organic Chemistry Practical			40	60	100	2
Paper – 106	Advanced Chemistry of Natural Products Practical			40	60	100	2
Paper – 107	Seminar					100	2
	TOTAL					700	18

SECOND SEMESTER

Paper No.	Title of the Paper	Evaluation / Marks				Total	Credits
		Theory		Practical			
		Mid Examination	University End Examination	Mid Examination	University End Examination		
Paper – 201	Advanced Medicinal Chemistry-I	40	60			100	3
Paper –202	Advanced Medicinal Chemistry-II	40	60			100	3
Paper – 203	Bioassays & Pharmacological Screening Methods	40	60			100	3
Paper – 204	Drug Regulatory affairs	40	60			100	3
Paper – 205	Advanced Medicinal Chemistry-I Practical			40	60	100	2
Paper – 206	Advanced Medicinal Chemistry-II Practical			40	60	100	2
Paper – 207	Seminar					100	2
	TOTAL					700	18

THIRD AND FOURTH SEMESTERS

Paper No.	III Semester	Total	Credits ***
Paper - 301	Project Seminar – I (On the proposed project work with aims and objectives)	50	2
Paper - 302	Project work - I	----	20
	Total	50	22

Paper No.	IV Semester	Total	Credits ***
Paper - 401	Project Seminar – II (On the Completed project work)	50	2
Paper - 402	Project work - II	---	20
	TOTAL MARKS	50	22
	GRAND TOTAL FOR THE COURSE	1500	80

SCHEME OF INSTRUCTION AND EVALUATION FOR

M. PHARM- PHARMACEUTICAL CHEMISTRY

I SEMESTER

PAPER 101: MODERN ANALYTICAL TECHNIQUES
(Paper Common for all Specializations)

Principles, instrumentation and applications of the following Instruments and Chromatography techniques

Unit- I

i. UV- Visible spectrophotometry
ii. Infrared spectroscopy
iii. Spectrofluorimetry

Unit- II

i. NMR spectroscopy
ii. Electron Spin Resonance spectroscopy
iii. Atomic Emission spectroscopy

Unit- III

i. HPLC
ii. HPTLC
iii. Exclusion chromatography
iv. Super critical fluid chromatography

Unit- IV

i. Mass Spectroscopy including LCMS & GCMS
ii. GLC

Unit- V

i. Plasma Emission spectroscopy
ii. X-Ray diffractometry
iii. Optical Rotatory Diffusion
iv. Vapor phase chromatography
v. Affinity chromatography
vi. Ion-exchange chromatography

TEXT BOOKS

1. Practical Pharmaceutical Chemistry Vol. 1 &II by Beckett & Stenlake.
2. Instrumental Methods of Analysis by Scog and West.
3. Instrumental Methods of Analysis by B.K.Sharma
4. Vogel's text book of Quantitative Chemical Analysis.
5. Instrumental methods of Analysis by Willard & Merrit.
6. A text book of Pharmaceutical Analysis by K. A. Conners.

REFERENCE BOOKS

1. I.P.
2. B.P.
3. U.S.P.
4. Remington's Pharmaceutical Sciences.
5. Spectroscopy b Silversterin

PAPER 102: RESEARCH METHODOLOGIES
(Paper common for all Specialization)

UNIT I

Statistical Methods:
Chance Variation – Probability Distribution - Normal Distribution – Sampling Distribution Error and its significance-Measures of Error- Control of Error in Experimental Investigations – Problem Solving.

UNIT II

Correlation and Regression, Multiple Regression - Problem Solving

UNIT III

Tests of Significance: Principles, t-test, z-test, F-ratio test, Chi-square test, Non-parametric tests- their applications in pharmacy research with examples – Problem Solving

UNIT IV

Design of Experiments
Criteria of a good design with examples.
Principles- Randomization, replication and local control.
Study of CRD, RBD, LSD and factorial designs- their applications in Pharmacy research with examples – Problem Solving

UNIT V

Analysis of Variance (ANOVA) – one way, two way and three way – principles and applications in pharmacy research- Problem Solving
Optimization Techniques: Optimization Techniques based on Factorial Experiments - Problem Solving.

Text & Reference Books:

1. Fundamentals of Biostatistics by Khan & Khanum, 3rd Revised Edition, Ukaaz Publications, Hyderabad
2. Theory & Practice of Industrial Pharmacy by Leon Lachman and Others
3. Remington's Practice of Pharmaceutical sciences, (Latest Edition)
4. Principles of Biostatistics by Marcello Pagnano, Published by Brooks/Cole, (Saurabh Printers Pvt. Ltd)

PAPER 103: ADVANCED PHARMACEUTICAL ORGANIC CHEMISTRY

Unit-I

Stereochemistry:
Elements of symmetry, Plane of symmetry, Centre of symmetry, Alternative axis of symmetry, Simple axis of symmetry, kinds of molecules displaying optical activity. Notation, Relative configuration and Absolute configuration .Compounds with a chiral carbon atom, compounds with other Quadrivalent chiral atoms. Optical isomerism in compounds containing no chiral atom, biphenyl, allenes, compounds with exocylic double bonds and spirans. Chirality due to helical shape, chirality caused due to restricted rotation (other types).

Cis / Trans, E – Z isomerism resulting from double bonds, monocyclic compounds, fused ring system. Racemic modifications and methods for resolution of racemic mixtures. Asymmetric synthesis and stereo – selective synthesis.

Unit-II

Reactive Intermediates:Definitions, Generation, stability, Structure and Reactivity of free radicals, carbocations, carbanions, carbenes, Nitrenes/Nitrenium ions.
Mechanisms of organic reactions: Free radicals (addition and substitution), Electrophilic (addition and substitution). Nucleophilic (addition and substitution).
Concepts of Aromaticity involving ring systems,. Aromatic Substitution reactions, Electrohilic aromatic substitution. Mechanisms, Orientation and Reactivity.

Unit-III

Elimination Reactions: E_2, E_1CB and E_2C mechanisms, Mechanisms and orientation in Pyrolytic eliminations, effect of substrate structure, Attacking base, leaving group and reaction bond,medium and reactivity addition to carbon – carbon multiple bond reactions. Mechanisms,Orientation and reactivity.
Electrocyclic, pericyclic and sigmotropic reactions: introduction, terminology and mechanism with suitable examples.

Unit-IV

Molecular Rearrangements & their applications:
Carbon to Carbon Migration: Wagner – Meerwin rearrangement, Claisen rearrangement and Benzil – Benzilic acid rearrangement.
Carbon to Nitrogen Migration: Hoffmann rearrangement, Curtius rearrangement and Lossen rearrangement, Beckman rearrangement.
Carbon to Oxygen Migration: Bayer – Villiger rearrangement, Rearrangement of hydro peroxides and Wittig rearrangement.
Synthetic Reagents & Applications: Lead Tetra Acetate (LTA), N- Bromosuccinimide (NBS), Osmium Tetroxide, Lithium Aluminum Hydroxide and Sodium Bromohydride.

Unit-V

Unit Process in Organic Synthesis: Catalytic hydrogenation, Nitration, Sulphonation, Halogenation, Amination, Acetylation, Esterification and Hydrolysis
Scale Up Techniques for process optimization, Maximization of productivity,
in – process control techniques with examples. Chemical Technology of selected bulk drugs – Ibuprofen, Paracetamol, Ciprofloxacin and Isosorbide Nitrate.
Synthetic Strategies: Introduction, Target selection , Retro synthesis , various strategic approaches, criteria or a disconnection of strategic bonds, strategic bonds in rings, Dégradation techniques for retro synthesis.

Recommended Books:

1. Francis A. Carey & Richard J. Sunberg, Advanced Org. Chemistry , III rd Edition , Par B; Reactions and synthesis , Plenum Press, new York , London , Latest Edition.
2. Eliel I. Ernest and Samuel h, Stereochemistry of Org. Compounds, John Wiley and sons, New York, 2003 Edition.
3. Roland E. Lehr & Alan P Marchard, Orbital Symmetry: A Problem solving approach, Academic Press, New York Latest Edition.
4. J. March , Advanced Org. Chemistry , Reactions Mechanisms and Structure , 4^{th} Edition, John Wiley & Sons , New York Latest Edition
5. I. L. Finar , Organic Chemistry , ELBS
6. Herbert O. Modern Synthesis Reactions II^{nd} Edition W.A. Beenamis Inc. Menco Park California
7. W. Carruthers , Some Modern Methods of Org. Synthesis , III rd Edition , Cambridge University Press, Cambridge(1988)
8. Groggins, Unit process in Org. Synthesis, McGraw Hill Book Crop.
9. S. Warren, Org. Synthesis. The Disconnection Approach, J. Wiley & Sons. NY
10. Gorgy Keri and Istarian Toth , Molecular Patho-mechanisms and New Trends in Drug Research – Taylor and Francis Group ,London 2003
11. R.K. Mackie , A Guidebook to Organic Thesis – Prentice Hall
12. T.W. Greene and PGM Warts ,Protecting Groups – John Willey
13. Michael B. Smith , Organic Synthesis

PAPER 104: ADVANCED CHEMISTRY OF NATURAL PRODUCTS

Unit-I

General Methods of Extraction, Qualitative chemical test for the detection of various natural product compounds. Study of herbal extracts – processing, equipment and analytical profile of extracts of drugs.
Isolation/Separation techniques –The technique and application of thin layer chromatography and Preparative TLC, Column chromatography – medium and high-pressure liquid column chromatography, Flash chromatography, HPTLC, HPLC and GC – normal and reverse phase techniques.

Unit-II

Alkaloids - Introduction, general methods of structure elucidation, chemistry and structure elucidation of Morphine, Reserpine and Quinine. Isolation procedure of Piperine and Quinine.

Unit-III

Steroids – Introduction, nomenclature and stereochemistry of different steroidal skeletons. Chemistry of cardiac glycosides, progesterone, oestradiol, cortisone, testosterone, bile acids. Chemistry and structural elucidation of cholesterol.. Synthesis of stilbesterol & hexesterol, Isolation procedures for diosgenin and sennosides.

Unit-IV

Polypeptides and Proteins – Introduction and general methods of separation, general methods of degradation and end group analysis, general methods of synthesis of peptides, Sequence analysis, secondary and tertiary structure of proteins, chemistry of insulin.

Unit-V

Natural Products as Leads for New Drugs:
Introduction, History, approaches to discovery and development of natural products as potential new drugs, selection and optimization of lead compounds for further developments from CNS, Anticancer, Antibiotic and Cardiovascular drugs.

Recommended Books:

1. Organic Chemistry Vol. 2nd by I. L. Finar
2. Org. Chemistry by Morrison & Boyd
3. Alkaloids – Chemical & Biological Prospective by S. W. Pelletier
4. Steroids by Fischer and Fischer
5. Pharmacognosy by Trease & Evans
6. Chemistry of Natural Products – Ata Ur Rehman
7. Natural Products – A Lab Guide by Raphael Ikon

Paper 105 - Advanced Pharmaceutical Organic Chemistry LAB

(Based on Theory at least 10 Experiments)

Paper 106 - Advanced Chemistry of Natural Products LAB

(Based on Theory at least 10 Experiments)

II[nd] SEMESTER

Paper 201: ADVANCED MEDICINAL CHEMISTRY – I

Unit-I

Theoretical Aspects of Drug Action:

Types of drug action, physicochemical parameters and pharmacological activity, Non empirical Electronic parameters, steric parameters and Stereo Chemical aspects of Drugs. Drug Receptors, Receptor types and isolation, Drug Receptor Interaction, theories of drug action, mechanism of drug action.

Unit-II

Targets for the development of following chemotherapeutic agents:

Anti-tubercular, Anti- HIV, anticancer, anti – fungal, Immuno- modulators, anti- amoebic drugs.

Targets for the development of following pharmacodynamic agents:

Anti-ulcer, Analgesic, Anti Inflammatory, Anti atherosclerotic, Anti- angiogenesis, Anti – hypertensives.

Unit-III

Biotransformation of drugs:

Prodrug approach, Soft Drug approach, enzymes responsible for biotransformation, microsomal and non microsomal mechanisms. Factors influencing enzyme induction and inhibition.

Unit-IV

Design of Local anesthetics:

Introduction, general considerations on the development of new drugs, classical and rational procedures for the development of local anesthetics

Unit-V

Antipsychotic Agents:

Role of Dopamine, Serotonin, Glutamate and their receptors. SAR and Pharmacokinetics of Ticyclic Neuroleptics, Butyrophenones and Benzamides. A brief account of non – benzodiazepine agonist.

Recommended Books:

1. Richard B. Silvermann, Org. Chemistry of Drug Design and drug Action.
2. Berger's Medicinal Chemistry and Drug Design. 6th Edition.
3. Korolkovas Essentials of Medicinal Chemistry
4. Purcell Strategies of Drug Design
5. Alfred Berger Biochemical Basis of Drug Design
6. Corwin , Hansen Comprehensive Medicinal Chemistry
7. William O Foye Medicinal Chemistry

8. Testa B and Jenner P. Drug Metabolism Chemical & Biochemical Aspects, Marcel Dekker
9. Gyorgy Keri & Istdan Toth Molecular Pathomechanism and New Trends in Drug Research, Taylor & Francis Pub.
10. Ariens. Drug design medicinal chemistry a series of monograph-volume 11- III, academic press, an imprint of Elsevier pub.

Paper 202: ADVANCED MEDICINAL CHEMISTRY – II

Unit-I

Genesis of New Drugs: Serendipity, Random Screening, Extraction of active principles from Natural Sources, Molecular Modification of Known Drugs, Selection or Synthesis of Soft Drugs, Drug Latentiation and rational drug design

Unit-II

Rational Drug Design: QSAR: Parameters involved in QSAR, lipophilicity (Polarisabiltiy, electronic and steric parameters). Quantitative models. Hansch Analysis, Free Wilson Analysis and their relationships, linear relationships and applications of Hansch and Free Wilson Analysis.

Unit-III

Molecular Modeling: Introduction, molecular methods, Known receptors, unknown receptors.

Unit-IV

Enzyme Inhibitors: A detailed study of the following types of enzyme inhibitors ,related drugs and their pharmaceutical significance :

a. P.G. Synthetase (Cycloxygenase & Lipoxygenase Inhibitors)
b. Phosphodiesterase (PDE) Inhibitors
c. Carbonic Anhydrase Inhibitors.
d. Angiotensin Converting Enzyme (ACE) Inhibitors
e. Acetyl Cholinesterase (Ach E) Inhibitors.

Unit-V

Combinatorial Chemistry – Parallel Synthesis, real combinatorial chemistry and deconvolution methods.

Recommended Books:

1. Berger's Medicinal Chemistry and Drug Design. 6th Edition
2. Korolkovas Essentials of Medicinal Chemistry
3. William O Foye Medicinal Chemistry
4. Lednicer, Organic Chemistry of Drug Synthesis
5. Ariens ,Drug Design , Academic Press
6. Purcell Strategies of Drug Design
7. Corwin , Hansen Comprehensive Medicinal Chemistry
8. Richard B. Silvermann, Org. Chemistry of Drug Design and drug Action
9. Smith and Williams , Introduction to principles of Drug Design – Harwood Academy Press.

10. Gyorgy Keri & Istdan Toth Molecular Pathomechanism and New Trends in Drug Research, Taylor & Francis Pub
11. Thomas Nogrady, Medicinal Chemistry. A biochemical Approach, Oxford Univ. Press.

Paper 203: BIOASSAYS & PHARMACOLOGICAL SCREENING METHODS

Unit I:

Principles of Experimental Pharmacology and Drug Discovery:

Common laboratory animals in Pharmacological research, Limitations of animal tests, Alternatives to animal use, Anesthetics used in laboratory animals, some standard techniques used in handling laboratory animals, Euthanasia of experimental animals. Regulation for the care and use of laboratory animals.

Strategies and approaches employed in drug discovery. Basic concepts of Combinatorial chemistry, High throughput screening, Cell lines and their applications in drug discovery. Transgenic animal models in the development of new drugs.

Unit II:

Principles of Biological standardization: Statistical treatment of modern problems in the biological evaluation of drugs. Methods used in the bio-assays for antibiotics and microbiological assays. Bioassay for Diphtheria antitoxin; Tetanus; Cholera vaccine; Posterior Pituitary extract; Adrenaline; Heparin; Digitalis; d-Tubocurarine; Vitamins. Test for pyrogens.

Bioassay methods for autocoids – Development of new bio-assay methods. Assays using special designs for experiments to eliminate known source of variation. Toxicity tests, Determination of LD_{50}, Acute, Sub acute, and Chronic toxicity studies – Tests for freedom from undue toxicity of drugs.

Unit III:

Basic Principles of Screening and types – Simple, Blind and Programmed Screening. Need for isolated tissues in pharmacological evaluation of drugs.

Organization of screening for the Pharmacological activity and evaluation of new substances in CVS:

1. Diuretics
2. Antihypertensives
3. Antianginal agents
4. Anti arrhythmic agents and agents used in sudden cardiac failure
5. Druigs used in cardiomyopathies
6. Drugs used in hyperlipidemia and atherosclerosis
7. Anti infarct agents

Unit IV:

Organization of screening for the Pharmacological activity and evaluation of new substances in CNS:

1. Anti-epileptics
2. Anti-anxiety agents and Drugs used in mood and sleep disorders
3. Antipsychotics

4. Drugs affecting memory
5. Drugs used in Alzheimer's disease
6. Local Anesthetics
7. Skeletal muscle relaxants and Neuromuscular blockers

Unit V:

Organization of screening for the Pharmacological activity and evaluation of new substances

1. Anti-diabetic agents
2. Analgesics and Drugs used in arthritis and neuropathic pain
3. Anti-Inflammatory agents
4. Anti-asthmatic agents
5. Anti-ulcer agents
6. Hepatoprotective agents

Recommended Books:

1. H.G.Vogel (ed),Drug Discovery and Evaluation- Pharmacological Assays, 2nd Edition, Springer verlag,Berlin,Germany,2002.
2. M.N.Gosh, Fundamentals of Experimental pharmacology, 2nd Edition, Scientific Book Agency,Culcutta,India,1985.
3. D.R.Laurence and A.L.Bacharach (Eds), Evaluation of Drug Activities: Pharmacometrics, Volume I and II, Academic press, London,U.K,1964.
4. Biological Standardization by J.H.Burn, D.J.Finney and L.G. Goodwin.
5. Pharmacopoeias: IP,BP,USP
6. Screening methods in pharmacology by Robert A.Turner.
7. Methods in Pharmacology by Swarbrick.

Paper 204: DRUG REGULATORY AFFAIRS:
(Paper Common for all Specializations)

Unit – I

Formulation development: Regulatory requirements involved in the preformulation studies, solid, liquid and semi-solid dosage forms, controlled release preparations, injections, ocular preparations as per the European community, United States and Indian regulatory authorities

Unit - II

Manufacturing: Regulatory requirements as per European community, United States and Indian regulatory authorities for manufacturing information, manufacturing formula, process, validation of manufacturing process, equipment, documentation, inspection requirement of regulatory guidelines for active ingredients, data requirement for new drug, International aspects of Excipients, approval as per guidelines of all the territories. Regulatory guidelines for packaging materials, test and evaluation of packaging materials, biological test, elastometer test, microbiological test and evaluation of closures.

Unit - III

Stability testing: Scientific and technical background to the design of stability testing regulatory requirements as per European community, United States and Indian regulatory authorities for testing of new active substances, bulk active drug substances, dosage form in their final packaging. Extension of shelf-life after authorization of drug international harmonization and current guidelines. Regulatory affairs in respect of residual solvents as per the ICH guidelines, analytical method validation, pharmacokinetic and toxicokinetic validation.

Biopharmaceutics: Different testing parameters and standards as per regulatory requirements of European community, United States and Indian regulatory authorities with respect to factors related to formulation, dosage form, manufacturing process, stability and storage.

Unit - IV

Preclinical aspects of Biopharmaceutics: Current guidelines and developments as per regulatory requirements of European community, United States and Indian regulatory authorities in respect of clinical bioavailability , study design, presentation documentation and statistical analysis

Clinical pharmacology and Pharmacodynamics: Regulatory guidelines as per European community, United States and Indian regulatory authorities on clinical study design, documentation, presentation and interpretation. Clinical trials: Definition, phase I, phase II, phase III and phase IV studies, design documentation, presentation and interpretation, statistical analysis of clinical data and factorial design.

Unit - V

Intellectual property rights and patents: Introduction, purpose, international scenario and Indian scenario, guidelines as per European community, United States and Indian regulatory authorities, documentation, presentation and application, procedure for obtaining and writing a patent and patenting rules and regulations

References:

1. Quality Assurance Guide by Organization of Pharmaceutical producers of India.
2. Drug formulation manual by D.P.S. Kohli and D.H.Shah. Eastern publishers, New Delhi.
3. How to practice GMPs by P.P.Sharma. Vandhana Publications, Agra.
4. Pharmaceutical Process Validation by Fra. R. Berry and Robert A. Nash.
5. Pharmaceutical Preformulations by J.J. Wells.
6. Applied production and operations management by Evans, Anderson, Sweeney and Williams.
7. Basic Principles of Clinical Research and Methodology by Gupta.
8. Biopharmaceutics and Clinical Pharmacokinetics-An introduction; 4th edition, Revised and expanded by Robert. E. Notari, Marcel Dekker Inc, New York and Basel, 1987

Paper 205: Advanced Medicinal Chemistry-I Practical

BASED ON THEORY AT LEAST 10 EXPERIMENTS

Paper 206: Advanced Medicinal Chemistry-II Practical

BASED ON THEORY AT LEAST 10 EXPERIMENTS