

JAWAHARLAL NEHRU TECHNOLOGICAL UNIVERSITY, KAKINADA

SYLLABUS for M.PHARMACY

PHARMACOLOGY AND TOXICOLOGY

I SEMESTER

Paper 101	-	Modern Analytical Techniques
Paper 102	-	Research Methodologies
Paper 103	-	Systemic Pharmacology
Paper 104	-	Pharmacokinetics and Drug Metabolism
Paper 105	-	Systemic Pharmacology – LAB
Paper 106	-	Pharmacokinetics and Drug Metabolism – LAB
Paper 107	-	Seminar

II SEMESTER

Paper 201	-	Advanced Pharmacology
Paper 202	-	Toxicology
Paper 203	-	Bioassays & Pharmacological Screening Methods
Paper 204	-	Drug Regulatory Affairs
Paper 205	-	Toxicology - LAB
Paper 206	-	Bioassays & Pharmacological Screening Methods - 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

PHARMACOLOGY AND TOXICOLOGY

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	Systemic Pharmacology	40	60			100	3
Paper – 104	Pharmacokinetics and drug Metabolism	40	60			100	3
Paper – 105	Systemic Pharmacology – Lab			40	60	100	2
Paper – 106	Pharmacokinetics and drug Metabolism - Lab			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 Pharmacology	40	60			100	3
Paper –202	Toxicology	40	60			100	3
Paper – 203	Bioassays and Pharmacological Screening Methods	40	60			100	3
Paper – 204	Drug Regulatory affairs	40	60			100	3
Paper – 205	Toxicology – Lab			40	60	100	2
Paper – 206	Bioassays and Pharmacological Screening Methods - Lab			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

M.PHARM - I SEMESTER

PAPER 101: MODERN ANALYTICAL TECHNIQUES

(Paper Common for all Specializations)

Principles, instrumentation and applications of the following Instruments and Chromatographic 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 Scoog 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. Connors.

REFERENCE BOOKS

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

PAPER 102: RESEARCH METHODOLOGIES

(Paper common for all Specializations)

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.

Recommended Books:

1. Fundamentals of Biostatistics by Khan & Khanum, 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).
5. Introduction to Biostatistics – A text book of biometry By Pranab Kumar Banerjee

PAPER 103: SYSTEMIC PHARMACOLOGY

Unit – I

Basic principles of Pharmacology, Mechanisms of drug action, Receptor proteins, Types and their molecular structure, Targets for G-Protein coupled receptors, protein phosphorylation and kinase cascade mechanisms, cellular aspects-excitation, contraction and secretion.

Pharmacology of Autonomic Nervous System

- Introduction and Physiology of autonomic nervous system, synthesis, release and metabolism of ANS neurotransmitters.
- Muscarinic receptor agonists and antagonists.
- Anticholinergic agonists and antagonists.
- Agents acting at neuromuscular junction and autonomic ganglia.
- Neuromuscular blockers.

Unit – II

Drugs acting on Central Nervous System:

- Neurotransmitters and neurotransmission in central nervous system.
- Anti epileptics.
- Anti psychotics.
- Antidepressants.
- CNS stimulants.
- Hypnotics and sedatives.
- Opioid analgesics.
- Drug addiction and drug abuse.
- Analgesic, Antipyretic and Anti-inflammatory agents.
- Drugs acting on Parkinson's disease.

Unit – III

Drugs acting on cardiovascular and renal systems:

- Cardiotonics.
- Anti – arrhythmics.
- Anti – hypertensives.
- Anti – anginal drugs.
- Anti – hyperlipidemic.
- Diuretics.

Drugs acting on the blood and blood – forming organs

- Hematopoietic agents : growth factors, minerals and vitamins.
- Blood coagulation and anti – coagulants, thrombolytics and anti – platelet drugs.

Unit – IV

Pharmacology of Chemotherapeutic and Anti-microbial agents

- General considerations of antimicrobial therapy.
- Sulfonamides, Trimethoprim, Quinolones, other related agents.
- Penicillins, Cephalosporins and other beta lactum anti-bacterial agents.
- Anti-fungal agents.
- Anti-viral agents.

- Chemotherapy of Tuberculosis, Leprosy and Malaria.
- Chemotherapy of Protozoal infections.
- Antineoplastic agents, Immunosuppressants and Immunostimulants.

Unit – V

Hormones and their antagonists

- Pituitary hormones and their hypothalamic releasing factors.
- Thyroid and anti- thyroid drugs.
- Endocrine pancreas; Pharmacotherapy of Diabetes Mellitus.
- Estrogens and progestins.
- Androgens.

Recommended Books:

1. Pharmacology and Pharmacotherapeutics by R. S. Satoskar, S. D. Bhandarkar and S.S. Ainapure.
2. The Pharmacological basis of therapeutics by Joel G. Hardman, Lee E. Limbird and Alfred Goodman Gilman.
3. Pharmacology by H.P. Rang, M.M. Dale, J.M. Ritter & P.K. Moore.
4. Basic and Clinical Pharmacology by Bertram G. Katzung.
5. Pharmacology (Lippincott's) by Mary J. Mycer, Richard A. Harvey and Pamela C. Champe.
6. Essentials of Medical Pharmacology by K.D. Tripathi.

PAPER 104: PHARMACOKINETICS AND DRUG METABOLISM

UNIT – I: Absorption

- Factors affecting drug absorption
- Gastrointestinal, percutaneous and rectal absorption
- Absorption kinetics, Wagner Nelson & Loo Riegelman methods
- Invitro methods of drug absorption (PAMPA and CACO₂ models)
- Role of P- glycoprotein in drug absorption

Unit – II: Distribution

- Plasma protein binding , factors affecting plasma protein binding
- Tissue binding, kinetics of protein binding
- Transfer of drugs through biological membranes (Blood Brain Barrier, Placental Barrier)

Unit – III: Metabolism

- Microsomal & Non microsomal biotransformations of drugs(Liver, Kidney and kinetics)
- Physiological, Pathological factors affecting drug metabolism
- Genetic factors influencing drug metabolism
- First pass effect
- Human Cytochrome P450 enzyme ,Substrates,inducers and inhibitors of CYP 450 enzymes
- In Vitro methods of drug metabolism(Liver microsomes,Liver S9 fraction&Hepatocytes)

Unit – IV: Excretion

- Excretion of drugs by various routes
- Factors affecting excretion of drugs
- Enterohepatic recirculation
- Significance of elimination rate constant and elimination half life

Unit – V: Clinical Pharmacokinetics

- Basic concepts of clinical pharmacokinetics
- Therapeutic drug monitoring
- Population pharmacokinetics
- Drug interactions and their clinical significance
- Prediction of drug interactions
- Pharmacokinetic and pharmacodynamic modeling(PK/PD modelling)

Recommended Books:

1. Biopharmaceutics and pharmacokinetics - An Introduction by Robert E, Notari
2. Drug metabolism by Bernard Testa and Peter Jenner.
3. Selected chapters from Principles of drug action by Gold Stein, Aranow and Kalman.
4. Drug interaction by D. G. Grahme – Smith.
5. Remington's Pharmaceutical Sciences
6. The Pharmacological basis of therapeutics by Joel G. Hardman, Lee E. Limbird and

Alfred Goodman Gilman

PAPER 105: SYSTEMIC PHARMACOLOGY – LAB

(Practicals based on theory)

PAPER 106: PHARMACOKINETICS AND DRUG METABOLISM – LAB

(Practicals based on theory)

M.PHARM - II SEMESTER

PAPER 201: ADVANCED PHARMACOLOGY

Unit – I: Molecular Pharmacology

Pharmacology of receptors: Classification, cellular signaling systems, pharmacology of agonists and antagonists of the following receptors

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|------------------------------------|-----------------------------|
| i. Excitatory amino acid receptors | vi. Melatonin receptors |
| ii. Purinoreceptors | vii. Adrenergic receptors |
| iii. GABA and Glycine receptors | viii. Cholinergic receptors |
| iv. Neurosteroid receptors | ix. Dopaminergic receptors |
| v. Cannaboid receptors | x. Serotonergic receptors. |

Signalling Mechanisms: Physiological function, Pharmacological implications and therapeutic potential of the following target sites:

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|--|-------------------------|
| i. Phosphoinositide 3 – kinase (PI3K) | v. Protein kinases |
| ii. MAP Kinase | vi. Phospho diesterases |
| iii. Caspases | |
| iv. Peroxisome proliferator activator receptors (PPAR) – α and γ | |

Unit – II: Neuropeptides

A study of the mechanisms involved in the formation, release, possible physiological role, pharmacological actions, agonists, antagonists and therapeutic potential of

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|-------------------------------------|---------------------|
| i. Calcitonin gene related peptides | iii. Substance P |
| ii. Neuropeptide Y | iv. Cholecystokinin |

Unit – III: Endogenous Mediators

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|---------------------|-----------------|
| i. Histamine | v. Nitric Oxide |
| ii. Prostaglandins | vi. Kinins |
| iii. Leukotrienes | vii. 5-HT |
| iv. Opioid peptides | |

Unit – IV: Transporter Proteins

- i. Classification and biology of ATP binding cassette (ABC) transporter superfamily.
- ii. Multidrug resistance (MDR) proteins.

Unit – V:

- i. Principles of clinical pharmacology and designs for testing of drugs in humans. Clinical trials – Phases I, II, III, IV.
- ii. Stem cells – Basic concepts and therapeutic applications in medicine.
- iii. Free radicals, their biological role, endogenous anti-oxidant systems and their role in tissue protection.

Recommended Books:

1. The Pharmacological basis of therapeutics by Joel G. Hardman, Lee E. Limbird and Alfred Goodman Gilman.
2. Pharmacology by H.P. Rang, M.M. Dale, J.M. Ritter & P.K. Moore
3. Basic and Clinical Pharmacology by Bertram G. Katzung.

4. Text book of Pharmacology by W. C. Bowman, M. J. Rand.

PAPER 202: TOXICOLGY

Unit – I:

History, scope of toxicology, principles of toxicology, mechanisms and risk assessment, biotransformation of xenobiotics and toxicokinetics.

Unit – II:

Chemical Carcinogens:

Definitions, multistage carcinogenesis, mechanisms of action of chemical carcinogens {genotoxic, mutagenesis, inorganic carcinogens (arsenic, beryllium, cadmium, chromium, nickel, lead)}, test systems for carcinogenicity assessment (short-term tests for mutagenicity – invitro & invivo gene mutation assays, chromosomal alterations, DNA damage), chemical carcinogenesis in humans.

Unit - III

Target Organ Toxicity:

- Toxic responses of the blood.
- Toxic responses of immune system.
- Toxic responses of the liver.
- Toxic responses of the kidney.
- Toxic responses of the nervous system.
- Toxic responses of heart and vascular system.
- Toxic responses of the endocrine system.

Unit – IV:

Toxic Agents:

- Toxic effects of pesticides.
- Toxic effects of metals.
- Toxic effects of solvents and vapors.
- Toxic effects of plants.

Unit – V:

Environmental Toxicology:

- Air pollution.
- Ecotoxicology.
- Food toxicology.
- Clinical toxicology.

Recommended Books:

1. Casarett & Doull's Toxicology The Basic Science of Poisons, Seventh edition. Editor- Curtis D. Klaassen, Ph.D.
2. Niesink R.J.M. de Vries J and Hollingers M.A. Toxicology, Principal and Applications, CRC Press1996.
3. Harrisons Principles of Internal Medicine. Medical Toxicology (Ellen Horns).
4. Toxicology – Principles and Applications, Raymond J.M.Niesink, John de.Vries, Manfred A. Hollinger.
5. Basis of Toxicology Testing Edited by Douald J Ecobichon.

6. Ellenhorn's Medical toxicology 2nd Edition Williams and Wilkins, Baltimore, 1997.
7. Goldfrank's Toxicological Emergencies , ninth edition.

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 autocooids – Development of new bio-assay methods. Assays using special designs for experiments to eliminate known source of variation. Toxicity tests, Determination of LD₅₀, 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. Drugs 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, Calcutta, 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 and 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.

Recommended Books:

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 - TOXICOLOGY LAB

(Practicals based on theory)

PAPER 206 - BIOASSAYS & PHARMACOLOGICAL SCREENING METHODS LAB

(Practicals based on theory)