THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY
CHENNAI-600 032

SYLLABUS – M.PHARMACY 2006-2007
BRANCH IV - PHARMACOLOGY

M. PHARMACY

I YEAR

SYLLABUS FOR PHARMACOLOGY – BRANCH IV

COMMON TO ALL BRANCHES - PAPER – I

MODERN PHARMACEUTICAL ANALYTICAL TECHNIQUES

THEORY **75 Hours(3 hrs./week)**

1. UV-VISIBLE SPECTROSCOPY : 6 Hours.

Brief review of electromagnetic spectrum and absorption of radiations. The chromophore concept, absorption law and limitations. Theory of electronic spectroscopy, absorption by organic molecules, choice of solvent and solvent effects, modern instrumentation – design and working principle. Applications of UV-Visible spectroscopy (qualitative and quantitative analysis), Woodward – Fischer rules for calculating absorption maximum, Photometric titrations and its applications.

2. FLAME EMISSION SPECTROSCOPY AND ATOMIC ABSORPTION SPECTROSCOPY : 3 Hours.

Principle, instrumentation, interferences and applications in Pharmacy.

3. SPECTROFLUORIMETRY : 3 Hours.

Theory, instrumentation, advantages, relationship of chemical structure to fluorescence spectra, solvent effect, effect of acids and bases on fluorescence spectra, concentration effects, factors affecting fluorescence intensity, comparison of fluorescence and UV-Visible absorption methods and applications in Pharmacy.

4. INFRARED SPECTROPHOTOMETRY : 6 Hours.

Introduction, basic principles, vibrational frequency and factors influencing vibrational frequency, instrumentation and sampling techniques, interpretation of spectra, applications in Pharmacy. FT-IR-theory and applications, Attenuated Total Reflectance (ATR).

5. NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY : 8 Hours.

Fundamental Principles and Theory, Instrumentation, solvents, chemical shift, and factors affecting chemical shift, spin-spin coupling, coupling constant, and factors influencing the value of coupling constant, spin-spin decoupling, proton exchange reactions, FT-NMR, 2D -NMR, NMDR, NOE, NOESY, COSY and applications in Pharmacy, interpretation of spectra, C13 NMR-Introduction, Natural abundance, C13 NMR Spectra and its structural applications.

6. ELECTRON SPIN RESONANCE SPECTROSCOPY : 2 Hours.

Theory and Principle, Limitations of ESR, choice of solvent, g-values, hyperfine splitting, instrumentation, difference between ESR & NMR and applications.

7. MASS SPECTROSCOPY : 8 Hours.

Basic principles and instrumentation, ion formation and types, fragmentation processes and fragmentation pattern, Chemical ionization mass spectroscopy (CIMS), Field Ionization Mass Spectrometry (FIMS), Fast Atom Bombardment MS (FAB MS), Matrix Assisted laser desorption / ionization MS (MALDI-MS), GC-MS, interpretation of spectra and applications in Pharmacy.

8. X-RAY DIFFRACTION METHODS : 4 Hours.

Introduction, generation of X-rays, X-ray diffraction, Bragg's law, X-ray powder diffraction, interpretation of diffraction patterns and applications.

9. OPTICAL ROTARY DISPERSION : 4 Hours.

Principle, Plain curves, curves with cotton effect, octant rule and its applications with example, circular dichroism and its relation to ORD.

10. THERMAL METHODS OF ANALYSIS : 5 Hours.

Theory, instrumentation and applications of Thermo Gravimetric Analysis (TGA), Differential Thermal Analysis (DTA), Differential Scanning Calorimetry (DSC) and Thermo Mechanical Analysis (TMA).

11. CHROMATOGRAPHIC TECHNIQUES : 15 Hours.

a) Classification of chromatographic methods based on mechanism of separation: paper chromatography, thin layer chromatography, ion exchange chromatography, column chromatography and affinity chromatography – techniques and applications.

b) Gas Chromatography : Theory and principle, column operation, instrumentation, derivatisation methods and applications in Pharmacy.

c) High Performance Liquid Chromatography : Principle, instrumentation, solvents used, elution techniques, RP-HPLC, LC-MS and applications in Pharmacy.

d) HPTLC and Super Critical Fluid Chromatography (SFC) : Theory and Principle, instrumentation, elution techniques and pharmaceutical applications.

12. ELECTROPHORESIS : 3 Hours.

Theory and principles, classifications, instrumentation, moving boundary electrophoresis, Zone Electrophoresis (ZE), Isoelectric focusing (IEF) and applications.

13. RADIO IMMUNO ASSAY : 3 Hours.

Introduction, Principle, Theory and Methods in Radio Immuno Assay, Related Immuno Assay procedures and Applications of RIA Techniques.

14. STATISTICAL ANALYSIS : 5 Hours.

Introduction, significance of statistical methods, normal distribution, probability, degree of freedom, standard deviation, correlation, variance, accuracy, precision, classification of errors, reliability of results, confidence interval, Test for statistical significance – students T-test, F-test, Chi-square test, correlation and regression.

PRACTICALS

1. Use of colorimeter for analysis of Pharmacopoeial compounds and their formulations.
2. Use of Spectro photometer for analysis for Pharmacopoeial compounds and their formulations.
3. Simultaneous estimation of combination formulations (minimum of 4 experiments).
4. Effect of pH and solvent on UV Spectrum of certain drugs.
5. Use of fluorimeter for analysis of Pharmacopoieal compounds.
6. Experiments on Electrophoresis.
7. Experiments of Chromatography.
    (a) Thin Layer Chromatography.
    (b) Paper Chromatography.
        1) Ascending Technique.
        2) Descending Technique.
        3) Circular Technique.

4) Two dimensional Paper Chromatography and TLC.

8. Experiments based on HPLC & GC.
9. IR, NMR and Mass Spectroscopy – Interpretation of spectra & Structural elucidation (atleast for 4 compounds each).
10. Any other relevant exercises based on theory.

REFERENCES

1. Spectrometric identification of Organic Compounds, Robert. M. Silverstein et al, 7th Edition, 1981.
2. Fundamentals of Mathematical Statistics, S.C. Gupta and V.K. Kapoor.
3. Principles of Instrumental Analysis by Donglas A. Skoog, James, J. Leary, 4th Edition.
4. Pharmaceutical Analysis – Modern Methods – Part A, Part B, James W. Munson – 2001.
5. Vogel's Text Book of Quantitative Chemical Analysis, 6th Edition, 2004.
6. Chromatographic Analysis of Pharmaceuticals, John A. Adamovics, 2nd Edition.
7. Practical Pharmaceutical Chemistry, Part two, A. H. Beckett & J. B. Stenlake – 4th Edition.
8. Instrumental Methods of Chemical Analysis – B. K. Sharma - 9th Edition.
9. Instrumental Methods of Analysis – Hobert H. Willard, 7th Edition.
10. Organic Spectroscopy – William Kemp, 3rd Edition.
11. Techniques and Practice of Chromatography – Raymond P. W. Scott, Vol. 70.
12. Identification of Drugs and Pharmaceutical Formulations by Thin Layer Chromatography – P. D. Sethi, Dilip Charegaonkar, 2nd Edition.
13. HPTLC – Quantitative Analysis of Pharmaceutical Formulations – P. D. Sethi.
14. Liquid Chromatography – Mass Spectrometry, W. M. A. Niessen, J. Van Der Greef, Vol. 58.
15. Stereo Chemistry – Conformation and Mechanism by P. S. Kalsi, 2nd Edition.
16. Spectroscopy of Organic Compounds by P. S. Kalsi.
17. Organic Chemistry by I. L. Finar Vol. II – 5th Edition.

SYLLABUS FOR PHARMACOLOGY

BRANCH – IV

PAPER – II

PHARMACOLOGY AND TOXICOLOGY

THEORY **75 Hours(3 hrs./week)**

1. DRUG ABSORPTION : 3 Hours.

Gastro intestinal, percutaneous and rectal kinetics.
Factors affecting drug absorption.

2. DRUG DISTRIBUTION : 3 Hours.

a. Plasma Protein binding – factors affecting plasma protein binding.
b. Tissue binding.
c. Transfer of drugs through biological barriers, their therapeutic implication in drug action with emphasis on drug transporters.

3. ELIMINATION OF DRUGS : 3 Hours.

a. Routes of elimination of drugs.
b. Concept of hepatic and renal clearance.
c. Biological half life.

4. BIOAVAILABILITY AND BIOEQUIVALENCE OF DRUG PRODUCTS : 2 Hours.

Factors affecting bioavailability & importance of bioequivalence studies.

5. BIOTRANSFORMATION OF DRUGS : 4 Hours.

a. Phase-I and Phase-II metabolic reactions, microsomal and non-microsomal biotransformation reactions.
b. Drug metabolism in liver, kidney, intestine and placenta.
c. Drug metabolism in fetus, new born and aged.

6. FACTORS INFLUENCING DRUG METABOLISM : 3 Hours.

a. Stereochemical, Physicochemical and biological factors.
b. Physiological and environmental factors, species , strain, sex, and age difference.
c. Pathological states.
d. Genetic factors – Introduction to bacterial genetics, evaluation of pharmacogenetics, heritable factors recognized in the use of drugs.

7. PHARMACODYNAMICS : 3 Hours.

a. General aspects of receptor pharmacology.
b. Structural and functional aspects of receptors.
c. Regulation of receptors.
d. Classification of receptors.

8. NEUROTRANSMISSION : 3 Hours.

a. General aspects and steps involved in neurotrasmision.
b. Neurohumoral transmission in autonomic nervous system.
c. Neurohumoral transmission in central nervous system.
d. Non-adrenergic non-cholinergic transmission (NANC).

9. SYSTEMIC PHARMACOLOGY : 33 Hours

A detailed study of the mechanism of action, pharmacology and toxicology of drugs used in

a. ANS- Parasympathomimetics and lytics, sympathomimetics and lytics, agents acting at neuromuscular junction and ganglia.
b. Local and general anesthetics.
c. CNS – General anesthetics, sedatives, hypnotics. Drugs used to treat anxiety, depression, psychosis, mania, epilepsy, neurodegenerative diseases, drug dependence and addiction.
d. CVS- Diuretics, anti ischemics antihypertensives, antiarrythmics,drugs for heart failure and dyslipidiemia.
e. Effect of drug on blood constituents.
f. Autocoid Pharmacology- A study of the mechanisms involved in the formation, release, pharmacological actions and possible physiological role of histamine, serotonin, kinins, prostaglandins, opioidautocoids and cyclic 3' – 5' AMP. Systemic pharmacology of drugs acting as agonists and antagonist to the autocoids.
g. Immunopharmacology- Cell and biochemical mediators involved in allergy, immunomodulation and inflammation. Classification of hypersentitivity reactions and diseases involved. Therapeutic agents for allergy, asthma, COPD and other immunological diseases with emphasis on immunomodulators.
h. GIT pharmacology- Antiulcer, prokinetics, antiemetics, antidiarrhoeal and drugs for constipation and irritable bowel syndrome.
i. Analgesics and anti-inflammatory agents.
j. Hormone and hormone antagonists.
k. Antibiotics & Chemotherapeutic agents.

10. FREE RADIALS PHARMACOLOGY 3 Hours.

a. Generation of free radicals.
b. Role of free radicals in etiopatholgy of various diseases.
c. Protective activity of certain important antioxidants.

11. TOXICOLOGY 5 Hours.

a. Principles of toxicology.
b. Abnormal action of drugs such as tolerance, addiction, habituation, idiosyncracy, allergy, hypersensitivity, antagonism, synergism, potentiation, tachyphylaxis.
c. Adverse drug reactions and its monitoring.
d. Heavy metals poisoning.

12. DRUG INTERACTIONS & RATIONALE FOR DRUG COMBINATIONS:

5 Hours.

Its implications and possible means to avoid them. Drug – Drug interactions involving antibiotics, cardiovascular drugs, antihistaminic drugs and analgesic, anti-inflammatory agents. Various mechanisms of drug interaction, drug-food interaction and drug - drug interaction.

13. CLINICAL PHARMACOLOGY : 5 Hours.

a. Basics in clinical pharmacology.
b. Clinical trials of drugs, design of clinical trials and testing of drugs in humans.
c. Therapeutic drug monitoring :- Criteria for TDM, Specific examples :
d. Digoxin, aminoglycosides & theophylline.

PRACTICAL

1. Experiments for studying the effects of the more important biogenic agents like histamine, acetylcholine, 5HT, oxytocin and their effect in the presence of antagonist on suitable isolated tissue preparations.
2. Estimation of PA_2 values of various antagonists under suitable isolated tissue preparations.
3. Experiments on CVS- Effect of various drugs on isolated heart preparations on various animal models under normal arrhythmic and hypodynamic conditions.
4. Drugs acting on Gastro intestinal tract. To study the drug activity on oesophagal motility.
5. Monitoring of drug concentration in saliva/urine /blood.
6. Action of CNS stimulants and depressants using suitable experimental model.
7. Evaluation of antidepressant and antianxiety drugs.
8. Drug absorption and elimination studies.
9. Any other experiment based on the topics mentioned in theory.

REFERENCES

1. The Pharmacological basis of therapeutics – Goodman and Gilman's.
2. Pharmacotherapy – DiPiro.
3. Pharmacology – Katzung.
4. Fundamentals of experimental pharmacology by M.N.Ghosh.
5. Handbook of experimental pharmacology by S.K.Kulkarni.
6. Text book of In vitro practical pharmacology by IanKitchen.
7. Pharmacological experiments on intact preparations by Churchill Livingstone.
8. Hand book of clinical pharmacokinetics- Gibaldi and Prescott.
9. Principles of drug action by Goldstein, Amaow and Kalman.
10. Clinical pharmacology by Molmon and Morrelli.
11. Clinical trails and tribulations by Allen E. Cato.
12. Drug interactions by Ivan H. Stockley.
13. Text book of therapeutics- drug, disease and management by Herfindal and Gourley.

SYLLABUS FOR PHARMACOLOGY

BRANCH –IV

PAPER – III

BIOLOGICAL STANDARDIZATION & PHARMACOLOGICAL SCREENING METHODS

THEORY **75 Hours(3 hrs./week)**

1. LABORATORY ANIMALS: 8 hours.

a. Commonly used laboratory, transgenic and other genetically prone animal models (viz., nude mice, SH rats etc).

b. Techniques of blood collection, anesthesia and euthanasia of experimental animals.

c. Various routes of drug administration.

d. Maintenance and breeding of Laboratory animals.

e. Regulations and ethics requirements.

2. PRINCIPLES OF BIOLOGICAL STANDARDIZATION : 6 hours.

a. Statistical treatment of model problems in evaluation of drugs.

b. Methods of biological assay, principles of biological assays with certain examples.

c. Development of new bioassay methods.

3. IMMUNOASSAY : 8 Hours.

a. General principles of immunoassay :
Theoretical basis, optimization of immunoassay, Heterogeneous immunoassay system, Homogeneous immunoassay systems.

b. Production of Immunoassay reagents :
Introduction, receptors or binders, unlabelled ligands calibrators, Labelled ligands and receptors, separation techniques, buffers.

c. Immunoassay methods evaluation :
Protocol outline, objectives and preparation, evaluation of precision, standard tracer, sensitivity, evaluation of accuracy, antibody characteristics monitoring, reaction conditions, Clinical evaluation.

4. NEW APPROACHES IN DRUG DISCOVERY : 4 Hours.

a. Combinatorial chemistry.
b. Pharmacogenomics.
c. Proteonomics.
d. Array technology.

5. Organization of screening for the Pharmacological activity of new substances with emphasis on evaluation using *in vivo, in vitro, ex vivo, in situ, in silico* and other possible animal alternative models. 38 Hours.

a. General Principles and Safety Pharmacology Procedures.
b. Cardiovascular pharmacology– Anti-hypertensives, anti-arrythmics, vasodilators and diuretics.
c. CNS pharmacology – behavioural and muscle co-ordination, CNS stimulants and depressants, anxiolytics, anti-epileptics and Nootropics.
d. Drugs for neurodegenerative diseases like Parkinsonism, Alzheimers, multiple sclerosis, etc.
e. Drugs acting on Autonomic Nervous system.
f. Respiratory pharmacology – Anti- asthmatics, COPD, Anti- allergic and mucoactives.
g. Reproductive pharmacology – Aphrodisiacs and anti-fertility agents.
h. Analgesics ,anti-inflammatory and antipyretic agents.
i. Gastrointestinal drugs – Anti-ulcer, anti-emetic, anti-diarrhoeal and laxatives.
j. Anti-cancer agents.
k. Drugs for metabolic disorders like anti-diabetic, anti-hyperlipidemic ,anti-obesity, and hepatoprotective agents.
l. Models in drug absorption and metabolism.
m. Immunopharmacology - Specific (cell and humoral mediated) and non specific methods.
n. Screening of free radical scavenging activity.

6. ESSENTIALS OF TOXICOLOGY : 6 hours.

a. Physicochemical, Biochemical and genetic basis of toxicity, principles of toxicokinectics, mutagenesis and carcinogenesis.
b. Guidelines and regulatory agencies – CPCSEA, OECD, FDA, ICH, FHSA, EPA, EEC , WHO etc.,
c. Behavioural, Inhalation, cellular and sub-cellular toxicity hypersensitivity and immune response, range finding tests.
d. Acute, sub-acute and chronic toxicity studies according to guidelines.

7. Importance of alternative experimental models, its advantages and disadvantages. **5 hours.**

PRACTICALS

1. Biological standardization of drugs like Histamine, Acetylcholine, 5 - HT.
2. Experiments on CNS. General screening methods of drugs acting on CNS
    a. CNS stimulants and depressants.
    b. Anxiogenics and anxiolytics.
    c. Amnestics and Nootropics.
    d. Anticonvulsants.
    e. Analgesics.
    f. Safety pharmacology.
3. Drugs acting on Gastrointestinal tract :
    a. General screening methods for the anti ulcer activity, intestinal motility, and anti – diarrhoeals .
4. Experiments on CVS:
   General screening procedure of anti-arrhythmic agents, anti- hypertensives, anti –ischemics.
5. Experiments on Local anesthetics :
    a. General methods for evaluating local anesthetic activity.
6. Experiments on General Pharmacology :
    a. Enzyme induction activity.
    b. Drug dependence & withdrawal effects.
7. Experiments on Diuretics :
    a. General screening methods for evaluating the diuretic activity.
8. Screening procedure for antidiabetic drugs.
9. Experiments on Analgesic & Anti-inflammatory drugs :
    a. General screening methods for the evaluation of Analgesics and Anti-inflammatory agents (using both acute and chronic models for anti-inflammatory agents).
10. Experiments on Chemotherapy :
    a. General methods for evaluating the Antimicrobial activities of chemotherapeutic agents.
11. Experiments on toxicology :
    a. Oral & skin acute toxicity tests.
12. Estimation of biochemical and free radical scavengers.

REFERENCES

1. Biological standardization by J.H. Burn, D.J. Finney and L.G. Goodwin.
2. Indian Pharmacopoeia and other pharmacopoeias.
3. Screening methods in Pharmacology by Robert Turner, A.
4. Evaluation of drugs activities by Laurence and Bachrach.
5. Methods in Pharmacology by Arnold Schwartz.
6. Selected topics on the Experimental Pharmacology by Usha G. Kamat, Dadkar, N.K and Seth, U.K.

7. Fundamentals of experimental Pharmacology Ghosh, M.N.
8. Pharmacological experiment on intact preparations by Churchill Livingstone.
9. Drug Discovery and Evaluation by Vogel HG.
10. Animal models in toxicology by Shayne Cox Gad and Christopher P. Chengelis.
11. The UFAW Handbook on the care and management of laboratory animals by UFAW.
12. Principles and methods of toxicology by Hayes.
13. CRC Handbook of toxicology by Derelanko and Hollinger.

SYLLABUS FOR PHARMACOLOGY

BRANCH – IV

PAPER – IV

DRUG DESIGN AND MOLECULAR PHARMACOLOGY

THEORY **75 Hours(3 hrs./week)**

1. **A general treatment of the approaches to drug design:** including the methods of variation, study of the use of biochemical and physiological information involving new drugs. **7 hours.**

2. **Drug Receptor theory:** **7 Hours.**

   Concept of receptors, theories of drug receptor interaction, forces involved in drug receptor interaction. Receptor polymorphism and dimerization and its importance in drug design.

3. **Physiochemical properties in relation to biological action and drug design.** **10 Hours**
   a. Complex of events between drug administration and drug action.
   b. Solubility & partition coefficient.
   c. Rational drug design.
   d. Selected physiochemical properties like isosterism, steric behaviour, ionization, hydrogen bonding, chelation, oxidation- reduction potential, surface actions.

4. **Guidelines for drug and analog drug design:** **7 hours.**
   a. Basic considerations of drug design, de- novo drug design, lead seeking methods, rational drug design.
   b. Structural factors in drug design.
   c. Prodrug concepts.

5. **Principles of Computer aided drug design.** **7 Hours.**

6. **The quantitative analysis of structure activity relationships** **7 Hours.**
   a. Fundamentals of QSAR- objectives, expressions of biological activity.
   b. QSAR parameters related to chemical structure, correlative methods and analysis of results.

7. **Molecular pharmacology** **10 Hours.**
   a. Application of molecular pharmacology to drug design.
   b. Introduction to cell structure and function.
   c. Cell signaling, organization of signal transduction pathway and biosensors.
   d. Protein structure prediction and molecular modeling.

8. Gene expression, regulation and gene mapping 5 Hours.

9. Recombinant DNA technology: Principles, process and its application. 5 Hours.

10. Gene Therapy 10 Hours.

a. Gene transfer technologies (viral and non viral vectors).
b. Clinical application of gene therapy.
c. Disease targets for gene therapy.
d. Pharmacodynamics, pharmacokinetics of peptide and protein drugs and immunogenicity of protein therapeutics.

PRACTICALS

1. Practicals related to physiochemical properties in relation to biological action including partition coefficient.
2. Cell cultures preparation and maintenance :
   Chick embryo fibroblast Lymphocyte culture.
3. Protein separation and isolation using gel electrophoresis.
4. DNA isolation, sequencing and PCR techniques.
5. Estimation of protein and nucleic acids.
6. RNA isolation from yeast.

REFERENCES

1. A guide to chemical basis of drug design by Alfred Burger (John Wiley & Sons).
2. Introduction to the principles of drug design by John Smith and Haywel Williams (Wright PSG).
3. Burgers Medicinal chemistry – The basis of Medicinal Chemistry by Manfred E. Wolff Part – 1 (John Wiley & Sons).
4. Computer assisted Drug Design by Edward. C. Olson (American Chemical Society- ACS symposium series 112).
5. Wilson & Giswold's text book of Organic, Medicinal and Pharmaceutical chemistry.
6. Goodman and Gilman's – The Pharmacological Basis of Therapeutics – 8th edition (Pergamon Press)
7. Medicinal Chemistry – The role of organic chemistry in drug research by S.M. Roberts and B.J. Price.
8. Principles of Medicinal chemistry by William Foye.
9. Vogel's text book of practical organic chemistry y Arthur I. Vogel (ELBS and Longman).
10. Current protocols in molecular biology by Frederick. M. Ausubel.
11. Human molecular genetics by Tomstracham & Andrew P. Read.
12. Bioinformatics: Genes, proteins & Computers by Christine Orengo.
13. The Cell – A molecular approach, Geoffrey M. Cooper.
14. Genetherapy, Therapeutic mechanism and strategies by NancySmyth, Templeton Danilo D. Lasic.