

## PHARMACOLOGY AND TOXICOLOGY

M.S. (Pharm.)

<b>SEMESTER-I</b>		
<b>Course Code</b>	<b>Course Name</b>	<b>Credits</b>
PC-511	Pathophysiology	1
PC-520	General Pharmacology	2
PC-530	Experimental Pharmacology	1
PC-540	Chemotherapy of Parasitic and Microbial Infections	1
NP-510	Separation Techniques	1
PE-520	Biopharmaceutics and Pharmacokinetics	2
BT-510	Biotechnology in Pharmaceutical Sciences	1
GE-510	Biostatistics	2
GE-520	Fundamentals of Intellectual Property (IP) and Technology Management	1
GE-511	Seminar	1
LG-510	General Lab Experience	3
<b>Total Credit</b>		<b>16</b>
<b>SEMESTER-II</b>		
<b>Course Code</b>	<b>Course Name</b>	<b>Credits</b>
PC-610	Drug Metabolism	1
PC-611	Pharmacological Screening and Assays	1
PC-620	CNS and Respiratory Pharmacology	2
PC-630	Autonomic, CVS, Blood, Renal and GI Pharmacology	2
PC-640	Autocoid and Endocrine Pharmacology	1
PC-650	Clinical Pharmacology and Regulatory Toxicology	2
PC-660	Chemotherapy and Immunopharmacology	2
GE-611	Seminar	1
LS-610	General Lab Experience in the Area of Specialization	2
<b>Total Credit</b>		<b>14</b>
<b>Semester-III [Project (22 weeks)]</b>		
<b>Course Code</b>	<b>Course Name</b>	<b>Credits</b>
TH-598	Synopsis	5
TH-599	Presentation	3
<b>Total Credit</b>		<b>8</b>
<b>Semester-IV</b>		
<b>Course Code</b>	<b>Course Name</b>	<b>Credits</b>
TH-698	Thesis	9
TH-699	Defence of Thesis	3
<b>Total Credit</b>		<b>12</b>

**Grand Total (I to IV semesters): 50**

# Pharmacology and Toxicology

## SEMESTER-I

PC-511

Pathophysiology

(1 credit)

1. Factors influencing the disease conditions such as sex, age, nutritional status, genetic make up etc.
2. Pathogenesis, symptoms and signs, laboratory findings and complications of respiratory, urinary tract, venereal and meningial infections.
3. Pathogenesis, symptoms and signs, laboratory findings and complications of Congestive heart failure, hypertension, cardiac arrhythmias.
4. Pathogenesis, symptoms and signs, laboratory findings and complications of Ulcer, pancreatitis.
5. Pathogenesis, symptoms and signs, laboratory findings and complications of hepatitis and cholecystitis.
6. Pathogenesis, symptoms and signs, laboratory findings and complications of Bronchial asthma.
7. Pathogenesis, symptoms and signs, laboratory findings and complications of depression, schizophrenia, epilepsy.
8. Pathogenesis, symptoms and signs, laboratory findings and complications of Parkinsonism and Alzheimer disease.
9. Pathogenesis, symptoms and signs, laboratory findings and complications of Hypo and hyperthyroidism, diabetes mellitus and other endocrine diseases.
10. Pathogenesis, symptoms and signs, laboratory findings and complications of Rheumatoid arthritis, gout and anemia.

### ***Recommended books:***

1. Pharmacotherapy: A Pathophysiologic Approach by Dipiro and others
2. The Pharmacological Basis of Therapeutics by Goodman and Gilman's

**PC-520****General Pharmacology**

(2 credits)

1. Concept of receptors as a drug target.
2. GPCR- Classification, structure, drug receptor interaction, G-protein, receptor characterization, receptor theories, agonist, antagonist.
3. Receptor regulation: GPCR desensitization, down regulation, up regulation
4. Regulators of G-protein signaling
5. Ion channels and Ion channel linked receptors and their regulation
6. Nuclear receptors
7. Transmembrane signaling mechanisms
8. Second messenger system
9. Transcription factors: Nrf2 Mechanism of action, pharmacological target and role in different diseases conditions
10. Dose response relationship and different type of antagonism
11. Efficacy and Toxicity evaluation using different experimental models, dose-response analysis, margin of safety in pre-clinical development
12. Chronopharmacology

***Recommended Books:***

1. The Pharmacological Basis of Therapeutics by Goodman & Gilman
2. Casarett&Doull's Essentials of Toxicology, edited by CD Klassen and JB Watkins
3. Scientific journals in the area of pharmacology(Trends in Pharmacological Sciences, Annual Reviews of Pharmacology and Toxicology, British Journal of Pharmacology, European Journal of Pharmacology, Pharmacology and Therapeutics, Nature Review Drug Discovery, Nature Review Neuroscience, Brain Research)

**PC-530****Experimental Pharmacology**

(1 credit)

1. Introduction to pharmacological research
2. Research ethics and publication ethics
3. Common laboratory animals and their physiological parameters, factors affecting the nature and degree of pharmacological responses; Handling and care of different animals; Bleeding and different routes of administration, anaesthetics used in animal research and chemical euthanasia.

4. Animal experimentation: Advantages and disadvantages; Anaesthesia used in laboratory animals, common agents, dose calculations, cannulation methodology, ventilation rate, recording of arterial blood pressure, intestinal motility etc.
5. Conscious animal experimentation, precautions to be taken in behavioural experiments.
6. Humanized mouse
7. Imaging techniques in pharmacological research
8. Drug solution preparations: Storage, concentration expression, common solvents, stabilizing agents, storage conditions, reference standards, methods of procurement of reference standards. False positive and false negative response.
9. In vitro experimentation: Advantages and disadvantages
10. Animal cell-culture techniques: Aseptic handling, cell counting and cell viability assays. Tissue isolation, tissue fixation, common fixatives, preparation of single cell suspension.
11. Protein and DNA gel electrophoresis: Western, northern, southern blot hybridization and PCR techniques.
12. Protein purification and identification by two dimensional gel electrophoresis, LCMS-MS, MALDI.

***Recommended books:***

1. Drug Discovery and Evaluation: Pharmacological Assays by Vogel& Vogel
2. CPCSEA guidelines (<http://cpcsea.nic.in>)

**PC-540**

**Chemotherapy of Parasitic and Microbial Infections**

(1 credit)

1. Introduction to parasitic and infectious diseases.
2. Biology of tuberculosis.
3. Mechanism of action of anti-tuberculosis drugs.
4. Targets for anti-tuberculosis drug development.
5. Mechanism of drug-resistance in tuberculosis.
6. Biology of human amoebiasis.

7. Mechanism of action of anti-amoebic drugs.
8. Biology of filarial infections.
9. Mechanism of action of anti-filarial drugs.
10. Targets of anti-filarial drug development.
11. Biology of HIV infection.
12. Mechanism of action of anti-HIV drugs.
13. Targets for anti-HIV drug development.
14. Biology of malaria.
15. Mechanism of action of anti-malarial drugs.
16. Targets for anti-malarial drug development.
17. Mechanism of drug-resistance in malaria.
18. Biology of leishmaniasis.
19. Mechanism of action of anti-leishmanial drugs.
20. Targets for anti-leishmanial drug development.
21. Drug-resistance in leishmaniasis.

***Recommended books:***

1. Chemotherapy by Frank Hawking
2. Parasitic Protozoa by Julius P. Kreier and Ristic
3. Malaria by Julius P. Kreier
4. Chemotherapy and Drug Resistance in Malaria by Wallace Peter
5. Atlas of Tropical Medicine and Parasitology by Wallace Peter and Geoffrey Pasvol
6. Manson's Tropical Diseases: Expert Consult Basic by Gordon C. Cook
7. Tropical Infectious Diseases: Principles, Pathogens and Practice by Richard L. Guerrant, David H. Walker and Peter F. Weller
8. Essentials of Tropical Infectious Disease by Richard L. Guerrant, David H. Walker, Peter F. Weller
9. History of Human Parasitology by F. E. G. Cox
10. Malaria Parasites and other Haemosporidia by P. C. C. Garnham
11. Diagnostic Microbiology by Bailey & Scott
12. Medical Microbiology by Samuel Baron
13. Textbook of Microbiology by P. C. Baveja
14. Human Parasitic Infections of Pharmaceutical & National Importance edited by Prati Pal Singh and V. P. Sharma

**NP-510**

**Separation Techniques**

(1 credit)

1. Separation Techniques: Need for learning separation techniques, separation techniques in natural product research and drug discovery, extraction techniques.
2. Chromatography: General principles, classification of chromatographic techniques, normal and reverse phase, bonded phase chromatography, stationary phases, activity of stationary phases, elutropic series, and separation mechanisms.
3. Column Chromatography and Short column chromatography: Column packing, sample loading, column development, detection.
4. Flash chromatography and Vacuum liquid chromatography: Objectives, optimization studies, selecting column and stationary phases, selecting suitable mobile phases, automated flash chromatography, and reverse phase flash chromatography.
5. High performance liquid chromatography: Principles, instrumentation, peak shapes, capacity factor, selectivity, plate number, plate height, resolution, band broadening, pumps, injector, detectors, columns, column problems, gradient HPLC, HPLC solvents, trouble shooting, sample preparation, method development.
6. Planar Chromatography - TLC/HPTLC/OPLC: Basic principles, sample application, development of plates, visualization of plates, 2D TLC, densitometry, Over pressure layer chromatography.
7. Counter current chromatography: Basic principles, droplet counter current chromatography, centrifugal partition chromatography, choice of solvents for SP and MP.
8. Gas Chromatography: Principles, instrumentation, split-splitless injector, head space sampling, columns for GC, detectors, quantification.
9. Biochromatography: Size exclusion chromatography, ion exchange chromatography, ion pair chromatography, affinity chromatography general principles, stationary phases and mobile phases.
10. Hyphenated techniques: Introduction to GC-MS and LC-MS techniques and their applications in natural products.

***Recommended books:***

1. Methods in Biotechnology, Natural Product Isolation by Sarker, Latif, Gray
2. Methods in Biotechnology, Natural Product Isolation by Richard Canell
3. Various Reviews and Research Papers

PE-520

**Biopharmaceutics and Pharmacokinetics**

(2 credits)

1. **Introduction:** Definitions, ADME, concentration time profile, plotting the data, different fluid compartments and blood flow rate compartment models, biological half-life, elimination rate constant. Biopharmaceutics and pharmacokinetics in drug research.

2. **GIT Absorption of drugs:** Mechanism, physico-chemical, biological and pharmaceutical factors affecting drug absorption through GIT. Techniques for the GIT absorption assessment.

3. **Drug disposition:** Total body clearance, renal clearance, mechanism of clearance, clearance ratio, factors affecting renal clearance, hepatic clearance, volume of distribution and its significance.

4. **Protein and tissue binding:** Factors affecting protein binding, kinetics of protein binding, determination of rate constant and different plots (direct, scatchard and reciprocal), Implication of protein binding on pharmacokinetic parameters.

5. **Bioavailability and bioequivalence:** Definitions, federal requirements, methods of determination of bioavailability using blood and urinary excretion data. Protocol design for bioavailability assessment. Methods for bioequivalence determination.

6. **Pharmacokinetic characterization of drugs:** Pharmacokinetics of drugs following one/two compartment open models with first order elimination kinetics as applied to rapid intravenous injection, Intravenous transfusion and oral administration. Determination of absorption rate constant using Wagner-Nelson, Loo Riegelman methods. Flip-flop models, method of residual. Urinary excretion data and its application in pharmacokinetic characterization of drugs. Pharmacokinetics of multiple dosing.

7. **Dosage regimen:** Dosage regimen adjustment in patients with renal and hepatic diseases. Drug dosage in elderly, children and obese patients.

8. **Non Linear Pharmacokinetics:** Various causes of non-linearity, Michaelis-Menten kinetics, In-vivo estimation of  $K_m$  and  $V_m$ . Case studies.

9. **Physiologic pharmacokinetics models:** Mean Residence Time; Statistical Moment Theory; Application and limitations of physiologic pharmacokinetic models.

10. **Miscellaneous Topics:** Chronopharmacokinetics, Drug toxicity and forensic pharmacokinetics, kinetics of maternal-fetal drug transfer, pharmacokinetics v/s pharmacological/ clinical response, metabolic kinetics

**Recommended books:**

1. Applied Biopharmaceutics & Pharmacokinetics, by Shargel, L., S. Wu-Pong
2. Biopharmaceutics and Pharmacokinetics: An Introduction by Notari, R. E.
3. Introduction to Biopharmaceutics, by Gibaldi, M.
4. Biopharmaceutics and Relevant Pharmacokinetics, by Wagner, J. G.
5. Textbook of Biopharmaceutics and Clinical Pharmacokinetics by Niazi, S.K.
6. Handbook of Bioequivalence Testing, by Niazi, S. K.
7. Modeling in Biopharmaceutics, Pharmacokinetics, and Pharmacodynamics: Homogeneous and Heterogeneous Approaches, by Macheras, P. and A. Iliadis
8. Comparative Pharmacokinetics: Principles, Techniques and Applications, by Riviere, J. E
  
9. Foundations of Pharmacokinetics, by Rescigno, A.
10. Clinical Pharmacokinetics and Pharmacodynamics: Concepts and Applications, by Rowland, M. and T. N. Tozer

### **BT-510**

#### **Biotechnology in Pharmaceutical Sciences**

(1 credit)

1. **Biotechnology in pharmaceutical Sciences perspective:** Biology in drug discovery; Traditional drug discovery vs rational drug discovery; rational drug discovery pipeline; concept of target based drug design and target discovery; role of plant biotechnology in edible vaccine development.
2. **Genomics in target discovery:** Concept of genome, genes and gene expression; genome sequencing and sequence comparison methods (microarray); comparative genomics and expression genomics for target discovery of communicable disease and lifestyle disease.
3. **Systems and methods of molecular biology:** Isolation and validation of targets; PCR, RT-PCR nucleic acid isolation; cloning vectors (some examples), enzymes used in molecular cloning methods (some examples); cloning and characterization of biopharmaceuticals.
4. **Protein expression systems:** Gene expression in bacteria, yeast, insect and mammalian cells.
5. **Enzyme purification and assay:** Various protein purification methods; enzyme based assay for small molecule screening.
6. **Bioprocess technology:** Upstream process: Introduction to microbial growth, media formulation; sterilization, inoculum preparation
7. **Bioprocess technology:** Fermentation: Fermentation process design, operation and characteristics of fermentation processes; batch, fed-batch and continuous culture systems, instrumentation and bioprocess control.
8. **Downstream process:** Introduction to various downstream process operations in biopharmaceutical manufacturing such as centrifugation, filtration, tangential flow filtration, cell disintegration, solvent-solvent extraction, supercritical fluid extraction etc.
9. **Biotechnology in pharmaceutical industry:** Major areas of biotechnology in the pharmaceutical industry such as antibiotics, vaccines, diagnostics, antibodies,

biopharmaceuticals (insulin, interferon, GSF, CSF and therapeutic proteins etc.); commercial aspects, priorities for future biotechnological research.

10. **Industrial enzymes in drug development:** Penicillin amidase, lipase, oxidoreductase, nitrilase, protease etc.; use of all these enzymes for enantioselective synthesis of pharmaceutically important drugs/drug intermediates, future directions.

#### **Recommended books:**

1. Analysis of Genes and Genomes by Richard J Reece. John Wiley & Sons
2. Molecular Biotechnology by Principles and Applications of Recombinant DNA by Bernard R. Glick, Jack J. Pasternak and Cheryl L. Patten, ASM Press
3. Principles of Fermentation Technology by P F Stanbury, A. Whitaker, S. J. Hall. Butterworth-Heinemann

#### **GE-510**

#### **Biostatistics**

(2 credits)

1. **Statistics:** Introduction, its role and uses. Collection; Organization; Graphics and pictorial representation of data; Measures of central tendencies and dispersion. Coefficient of variation.
2. **Probability:** Basic concepts; Common probability distributions and probability distributions related to normal distribution.
3. **Sampling:** Simple random and other sampling procedures. Distribution of sample mean and proportion.
4. **Estimation and Hypothesis testing:** Point and interval estimation including fiducial limits. Concepts of hypothesis testing and types of errors. Student-t and Chi square tests. Sample size and power.
5. **Experimental design and analysis of variance:** Completely randomized, randomized blocks. Latin square and factorial designs. Post-hoc procedures.
6. **Correlation and regression:** Graphical presentation of two continuous variables; Pearson's product moment correlation coefficient, its statistical significance. Multiple and partial correlations. Linear regression; Regression line, coefficient of determination, interval estimation and hypothesis testing for population slope. Introduction to multiple linear regression model. Probit and logit transformations.
7. **Non-parametric tests:** Sign; Mann-Whitney U; Wilcoxon matched pair; Kruskal-Wallis and Friedman two-way ANOVA tests. Spearman rank correlation.
8. **Statistical techniques in pharmaceuticals:** Experimental design in clinical trials; Parallel and crossover designs. Statistical test for bioequivalence. Dose response studies; Statistical quality control.

### Recommended books:

1. Fundamentals of Biostatistics by Bernard Rosner
2. Pharmaceutical Statistics: Practical and Clinical Applications by Bolton and Bon
3. Statistical Misconceptions by Huck GE-520 Fundamentals of Intellectual Property (IP) and Technology

### GE-520

#### Fundamentals of Intellectual Property (IP) and Technology Management (1 credit)

1. **Intellectual property:** Concepts and fundamentals; Concepts regarding intellectual property (IP), intellectual property protection (IPP) and intellectual property rights (IPR); Economic importance, mechanisms for protection of intellectual property-patents, copyrights, trademark; Factors effecting choice of IP protection; Penalties for violation; Role of IP in pharmaceutical industry; Global ramifications and financial implications.
2. **Trade related aspects of intellectual property rights:** Intellectual property and international trade; Concept behind WTO (World Trade Organisation), WIPO (World Intellectual Property Organisation) GATT (General Agreement on Tariff and Trade), TRIPs (Trade Related Intellectual Property Rights), TRIMS (Trade Related Investment Measures) and GATS (General Agreement on Trade in Services); Protection of plant and animal genetic resources; Biological materials; Gene patenting; Biotechnology / drug related IPR issues; Status in India and other developing countries; Case studies and examples; TRIPS issues on herbal drugs.
3. **Nuts and bolts of patenting, copyright and trademark protection criteria for patentability, types of patents; Indian Patent Act, 1970; WTO and modifications under TRIPS:** Filing of a patent application; Precautions before patenting-disclosures / non-disclosures, publication-article / thesis; Prior art search-published patents, internet search patent sites, specialized services-search requests, costs; Patent application-forms and guidelines, fee structure, time frames, jurisdiction aspects; Types of patent applications- provisional, non provisional, PCT and convention patent applications; International patenting-requirement procedures and costs; Financial assistance for patenting- introduction to schemes by NRDC and TIFAC; Publication of patents-gazette of India, status in Europe and US; Patent annuity; Patent attorneys technical aspects, criteria for selection, addresses, fee, rights and responsibilities of a patentee; Practical aspects regarding maintaining of a PATENT FILE; Patent infringement- meaning, scope, litigation, case studies and examples; Patenting by research students, lecturers and scientists University / organisational rules in India and abroad; Thesis research paper publication, credit sharing by workers, financial incentives; Useful information sources for patents related information-internet sites, brochures, periodicals, CD roms; Significance of copyright protection for researchers; Indian Copyright Law and digital technologies-Berne convention, WIPO copyright treaty (WCT), WIPO performance and

Phonogram Treaty (WPPT); Protection for computer data bases, multi media works; Trade marks legislation and registration system in India-an introduction, meaning of trademark criteria for eligibility; filling application for trademark registration; Trade secrets-scope modalities and protection; Case studies-drug related patents infringements.

4. **Technology development / transfer / commercialisation related aspects:** Technology development-meaning; Drug related technology development; Toxicological studies, bioequivalence (BU), clinical trials-phase-I, phase-II and phase-III; Approved bodies and agencies; Scale-up, semi-commercialisation and commercialisation-practical aspects and problems; Significance of transfer of technology (TOT), bottlenecks; Managing technology transfer-guidelines for research students, scientists and related personnel; TOT agencies in India-APCTD, NRDC, TIFAC, BCIL, TBSE/SIDBI; TOT related documentation-confidentiality agreements, licensing, MOUs, legal issues; Compulsory licensing excess to medicine issues; DOHA declaration, POSTWTO product patent regime

from 2005; Challenges for Indian pharmaceutical industry in the context of globalisation of IP; Drug registration and licensing issues-national and global; Drug master file submissions, SOPS; Related registration and marketing issues; Case studies antiretroviral drugs and others.

5. **Funding sources for commercialization of technology:** Preparation of a project report, financial appraisal, business models; GOI schemes and incentives; NRDC, TePP, HGT, TDB schemes. PATSER; Venture capitalists, banks. Incubator concept-Case studies with respect to IIT, CCMB, IMTECH, NIPER. Documentation and related aspects.
6. **Ethics and values in IP:** IP and ethics-positive and negative aspects of IPP; Societal responsibility; Avoiding unethical practices; Echo-responsibility-economic, social and environmental benefits of modern biotechnology; Voluntary adoption of pollution control strategies. 49 60 Courses of Study 2015

### ***Recommended books:***

1. Law Relating to Intellectual Property by B.L.Wadhera
2. IPR Handbook for Pharma Students and Researchers by P.Bansal
3. The Patents Act, 1970 (Bare Act with Short Notes) (New Delhi: Universal Law Publishing Company Pvt. Ltd. 2012)
4. Patent Agent Examination by Sheetal Chopra and Akash Taneja
5. Making Innovation Happen- A simple and Effective Guide to Turning Ideas into Reality by Michael Morgan
6. Making Breakthrough Innovation Happen by Porus Munshi
7. Innovation X- Why a Company's Toughest Problems are its Greatest Advantage by Adam Richardson
8. Legal Drafting for the Layman by Nabhi Kumar Jain
9. How to Write and Publish a Scientific Paper by Rober A Day
10. Concise Law Dictionary-with Legal Maxims, Latin Terms and Words and Phrases by Justice Y.V.Chandrachud
11. Biomedical Research- From Ideation to Publication by G.Jagadeesh and others

**GE-511****Seminar**

(1 credit)

1. Introduction, Information retrieval systems.
2. Writing term papers and reports.
3. Organization of scientific material, thesis, dissertation and refernces.
4. Reading research papers
5. Skills in oral presentation.

Each student has to present a seminar before end of the semester.

**LG-510****General Laboratory Experience-15 hours/week**

(3 credits)

1. **Analytical Techniques (30 hours):** Separation techniques.
2. **Computer and application in pharmaceutical sciences (100 hours):** Introduction to computers, basic unit and functions, H/W and S/W, operating systems, word processing, spread sheet, graphic programs, dbase, windows, statistical S/W programs and packages. Steps involved in S/W development, computer languages with emphasis to FORTRAN language and programming, hands on experience in pharmaceutical software systems. Use of computers in information retrieval systems.
3. **Pharmacology (25 hours):** Animal handling, route of administration of drugs, dose response relationship, analgesic activity of a compound, estimation of protein and haematological parameters.
4. **Biotechnology in pharmaceutical sciences (20 hours):** Day -1: Preparation for plasmid minirep. Day-2: Plasmid minirep and restriction digestion. Day-3: Gel electrophoresis and molecular weight calculation. Day-4: Discussion of result and viva.
5. **Specialization (95 hours):** Introduction to lab. experience and animal experimentation, blood glucose estimation, IC50 determination, demonstration of motor coordination, microscopic techniques, to study effect of drug on food and water intake, histopathological study, SDSPAGE demonstration, cell culture demonstration, cell viability assay.

## SEMESTER-II

### PC-610

#### Drug Metabolism

(1 Credit)

1. Biotransformation of drugs.
2. Enzymes responsible for bio-transformations, microsomal and non-microsomal mechanisms.
3. Factors influencing enzyme induction and inhibition.
4. Factors effecting drug metabolism.
5. Drug metabolism in fetus and new born.
6. Models of study drug metabolism.
7. Dose-effect relationships.
8. Excretion of drugs, biliary and fecal excretion.
9. Adverse drug reactions and drug interactions; Toxic reactions, allergic reactions, idiosyncrasy.
10. Acute poisoning and its treatment.

#### ***Recommended books:***

- 1) Introduction to Drug Metabolism, by G. Gordon Gibson and Paul Skett
- 2) Drug Metabolism Handbook Concepts and Applications Edited by Ala F. Nassar, Wiley

### PC-611

#### Pharmacological Screening and Assays

(1 credit)

1. Role of pharmacology in drug discovery
2. General principles of pharmacological screening.
3. Animal ethics, regulations for conducting animal experimentation.
4. 3 R's concept, alternatives to animal experimentations, Organs-on-chips
5. Pharmacological screening models

6. Correlations between various animal models and human situations.
7. Correlation between in-vitro and in-vivo screens.
8. Cell- based assay, CaCo-2 cell permeability assay. Single cell gel electrophoresis assay (COMET) assay. 9. Zebrafish model to screen pharmaceutical molecules.
10. Biochemical assays.
11. Introduction to cell culture, role of genomic and proteomic techniques in the process of target identification in drug discovery, MALdiTof., microarray.
12. High throughput screening and high content screening, transgenic animal model for drug screening. 13. Specific use of reference drugs
14. Interpretation of results.
15. Pharmacogenomics and Personal medicine

***Recommended book/journals:***

- 1) Drug Discovery and Evaluation: Pharmacological Assays by Vogel & Vogel
- 2) CPCSEA guidelines (<http://cpcsea.nic.in>)
- 3) Scientific journals in the area of pharmacology

**PC-620**

**CNS and Respiratory Pharmacology**

(2 credits)

1. CNS drug discovery and challenges.
2. Neurotransmitters: dopamine, 5-HT, excitatory amino acids, GABA, glycine, cannabinoids, melatonin etc; Neurotransmitters receptors, their agonist and antagonists
3. Neuromodulators, neuromediators and transporters
4. Peptides as mediators: Substance P, neuropeptide Y, somatostatin, cholecystokinin, neurotensin, enkephalin, Orexin, CGRP etc
5. Pharmacology of antianxiety drugs, antidepressants, antipsychotic drugs and psychomotor stimulants.
6. Pharmacology of antiepileptics.

7. Pharmacology of antimigraine drugs
8. Pharmacology of local anaesthetics, general anaesthetics, sedatives and hypnotics, centrally acting muscle relaxants.
9. Pharmacology of narcotic analgesics, Drug dependence and withdrawal responses
10. Pharmacology of drugs used in neurodegenerative disorders such as Parkinson's disease, Alzheimer's disease, Huntington's disease, Multiple sclerosis
11. Drugs for stroke
12. Pharmacology of nerve growth factors
13. CNS disease models for evaluation of effects of NCEs
14. Gene therapy and cell based therapy for CNS disorders
15. CNS disease models: Evaluation of effect of NCEs
16. Respiratory pharmacology: Pharmacology of bronchodilators, pharmacology of anti-inflammatory agents used in asthma& COPD and cough suppressants.
17. Asthma/COPD models for evaluation of effects of NCEs

***Recommended books/journals:***

- 1) The Pharmacological Basis of Therapeutics by Goodman and Gilman's
- 2) Pharmacology by Rang and Dale
- 3) Pharmacotherapy: A Pathophysiologic Approach by DiPiro and others
- 4) Pharmacology by Lippincott
  
- 5) Drug Discovery and Evaluation: Pharmacological Assays by Vogel & Vogel
- 6) Scientific journals (Trends in Pharmacological Sciences, Annual Reviews of Pharmacology and Toxicology, British Journal of Pharmacology, European Journal of Pharmacology, Pharmacology and Therapeutics, Nature Review Drug Discovery, Nature Review Neuroscience, Brain Research)

**PC-630**

**Autonomic, CVS, Blood, Renal and GI Pharmacology**

(2 credits)

1. Introduction to Autonomic Pharmacology: Chemical transmission of in the ANS (cholinergic and adrenergic)
2. Pharmacology of muscarinic cholinergic receptor agonists and antagonists. anticholinesterase agents,

3. Pharmacology of sympathomimetic drugs.
4. Ganglionic stimulants and blocking agents, neuromuscular blocking agents
5. Introduction to CVS Pharmacology: CVS drug discovery and challenges
6. Antihypertensives drugs and newer targets for hypertension
7. Antianginal drugs and newer targets for MI
8. Drugs for Heart failure and antiarrhythmic drugs.
9. Pharmacology of Lipid lowering and antiobesity agents
10. Factors necessary for erythropoiesis: Homopoietic growth factors. Mechanism of blood clotting, hematopoietic agents, Oral anticoagulants: Factors increase/decrease the efficacy of oral anticoagulants, Heparin,
11. Platelet adhesion and activation: Antiplatelet agents, thrombolytic agents and antifibrinolytic agents and hemostatic agents, integrins as therapeutic agents.
12. Renal Pharmacology: Diuretics, vasopressin
13. Gene therapy and cell based therapy for CVS disorders
14. CVS disease models: Evaluation of effect of NCEs
15. Pharmacology of GI drugs: Drugs for peptic ulcer, emetics, antiemetics, drug regulating GI motility
16. GI disease models for evaluation of effects of NCEs

***Recommended books/journals:***

- 1) The Pharmacological Basis of Therapeutics by Goodman and Gilman's
- 2) Drug Discovery and Evaluation: Pharmacological Assays by Vogel & Vogel
- 3) Scientific journals (Trends in Pharmacological Sciences, Annual Reviews of Pharmacology and Toxicology, British Journal of Pharmacology, European Journal of Pharmacology, Pharmacology and Therapeutics, Cardiovascular journals, Nature Review Drug Discovery

**PC-640**

**Autacoids and Endocrine Pharmacology**

(1 credit)

1. Introduction to autacoids
2. Pharmacology of histamine: Histamine receptors, histamine agonists and antagonists

3. Pharmacology of bradykinin: Bradykinin receptors, bradykinin agonists and antagonists
4. Pharmacology of eicosanoids: COX inhibitors
5. Pain and inflammatory models for screening
6. Adenohypophyseal hormones and related substances.
7. Thyroid and antithyroid drugs.
8. Insulin and oral hypoglycemic agents, Endocrine pancreas.
9. Adrenocortical hormones: adrenocortical steroids and inhibitors of the synthesis.
10. Agents affecting the calcification,
11. Estrogens and progesterone and their antagonists, Oral contraceptive
12. Androgens

***Recommended books/journals:***

- 1) The Pharmacological Basis of Therapeutics by Goodman and Gilman's
- 2) Pharmacology by Rang and Dale
- 3) Basic and Clinical Pharmacology by Katzung
- 4) Drug Discovery and Evaluation: Pharmacological Assays by Vogel & Vogel

**PC-650**

**Clinical Pharmacology and Regulatory Toxicology**

(2 credits)

1. Introduction to clinical pharmacology
2. Investigational new drug (IND) application, clinical trials, new drug application (NDA) requirements; Regulatory agencies
3. Pharmacovigilance,
4. GCP Guidelines and GLP Guidelines
5. Individualization of drug therapy: Personalized medicine
6. Preclinical testing strategy; Vis-à-vis envisaged clinical studies; Experimental clarification of possible human risk; Technical details of experiments; Flow chart for development of preclinical testing.
7. Single dose and repeat dose toxicity studies: Factors influencing such studies such as species, sex, route, dose level; Data evaluation and regulatory requirements.

8. Reproductive toxicology assessment of male reproductive toxicity: Spermatogenesis; Risk assessment in male reproductive toxicity; Female reproductive toxicology; Oocyte toxicity.
9. Mutagenicity: Mechanisms of mutagenesis, germ cell mutations, somatic cell mutation; Tests systems in vitro, test for gene mutation in bacteria, chromosome damage, in vivo micronucleus tests in rodent, metaphase analysis.
10. Carcinogenicity: Principles of carcinogenicity, dose-setting for carcinogenesis bio assay, transplacental carcinogenesis; Cocarcinogenesis/tumor promotion.
11. Toxicokinetics, animals and dose groups: Exposure measurement; determination of metabolites complicating factors in exposure interpretation, analytical method, good laboratory practices; Stereiosomerism vis-à-vis regulatory requirements; Single enantiomers; Racemate enantiomer switch; Regulatory requirements.
12. Preclinical toxicological requirements for biological and biotechnological products: Safety analysis; problems specific to recombinant products secondary pharmacology.
13. Safety Pharmacology - ICH S7 and S7B guidelines
14. Safety pharmacological studies for pharmaceuticals
15. Safety pharmacological studies for biological products

***Recommended books/journals:***

- 1) Clinical Pharmacology by Lawrence
- 2) Basic and Clinical Pharmacology by Katzung
- 3) ICH Guidelines
- 4) Schedule Y
- 5) OECD Guidelines 6) US FDA Guidelines

**PC-660**

**Chemotherapy and Immunopharmacology**

(2 credits)

1. Introduction to immunopharmacology, immunomodulators, immunostimulants and immunosuppressants.
2. General considerations of antimicrobial agents.

3. Spectrum of activity, mechanism of action, ADME and therapeutic aspects of following Quinolones, sulphonamides, penicillinscephalosporins,clavulanic acid, aminoglycosides, broad spectrum antibiotics.
4. Spectrum of activity, mechanism of action, ADME and therapeutic aspects of Quinolones, and aminoglycosides.
5. chemotherapeutic agents used in tuberculosis.
6. Spectrum of activity, mechanism of action, ADME and therapeutic aspects of the antifungal agents.
7. Spectrum of activity, mechanism of action, ADME and therapeutic aspects of antiprotozoal agents.
8. Spectrum of activity, mechanism of action, ADME and therapeutic aspects of the antimalarial agents, antiparasitic drugs.
9. Spectrum of activity, mechanism of action, ADME and therapeutic aspects of antineoplastic agents.

***Recommended books:***

1. Chemotherapy by Frank Hawking
2. Parasitic Protozoa by Julius P. Kreier and Ristic
3. Maraia by Julius P. Kreier
4. Chemotherapy and Drug Resistance in Malaria by Wallace Peter
5. Atlas of Tropical Medicine and Parasitology by Wallace Peter and Geoffrey Pasvol
6. Manson's Tropical Diseases: Expert Consult Basic by Gordon C. Cook
7. Tropical Infectious Diseases: Principles, Pathogens and Practice by Richard L. Guerrant, David H. Walker and Peter F. Weller
8. Essentials of Tropical Infectious Disease by Richard L. Guerrant, David H. Walker, Peter F. Weller
9. History of Human Parasitology by F.E.G. Cox
10. Malaria Parasites and other Haemosporidia by P.C.C. Garnham
11. Diagnostic Microbiology by Bailey & Scott
12. Medical Microbiology by Samuel Baron
13. Textbook of Microbiology by P.C.Baveja
14. Human Parasitic Infections of Pharmaceutical and National Importance edited by Prati Pal Singh and V.P. Sharma
15. Quantitative Real-time PCR in Applied Microbiology edited by Martin Filion

**GE-611**  
**Seminar**

(1 credit)

Students are required to submit written record and present details of the project to be pursued in semester-III & IV. This should include the purpose and basis of the project, stating aims, objectives and probable outcomes, be able to supplement these with necessary information, literature review towards it and process for the project itself.

**LS-610**

**General Lab Experience in the Area of Specialization 10 hours/week**

(2 credits)

Ed50 calculation, working of stereotaxy apparatus, effect of drug on locomotor activity, demonstration of blood pressure recording, SDS PAGE, western blotting experiment, DNA Gel Electrophoresis experiment, MTT and LDH assay, effect of cyclophosphamide on neutrophil counts, Genotoxic effect of unknown drugs, histopathological evaluation and different target organ, microscopic techniques, blood cell counter.

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## PhD

### PHARMACOLOGY AND TOXICOLOGY

SEMESTER-II		
Course Code	Course Name	Credits
PC-810	Application of Biotechnology in Parasitic Disease Research	2
PC-820	Pharmacological Interventions for Ischemic Brain Injury	2
PC-830	Parasitology/Microbiology, Community and Pharmacy	2
PC-840	Regulatory Toxicology and Drug Safety Evaluation	2
PC-850	Cellular and Molecular Parasitology	2
PC-860	Epigenetics and Diseases	2

### SEMESTER-II

#### PC-810

#### Application of Biotechnology in Parasitic Disease Research

(2 credits)

- 1. Biotechnology and parasitic disease research - An introduction:** Role of genetic engineering in parasitic disease research, study of parasites and recombinant DNA technology, immuno technology and parasitology. Molecular biology of malaria parasites, leishmanidonorovani and entamoebahistolytica.
- 2. General techniques:** Cultivation and cloning of plasmodium falciparum, leishmanidonorovani and entamoebahistolytica. Preparation of malaria parasites from experimental animals. Isolation of different stages of malaria parasites and synchronization; Identification, counting, cryopreservation and recultivation of parasites.
- 3. Cellular and molecular basis of the pathogenesis of parasitic diseases:** Mechanisms of Ph.D. Courses pathogenesis in malaria-general considerations; Mechanism(s) of erythrocyte invasion, immune evasion, antigenic variation and cytoadherence in malaria; Mechanisms of the survival and growth of leishmanidonorovani in macrophages and, mechanisms of virulence in entamoebahistolytica. Role of cytokines in the pathogenesis of malaria, leishmaniasis and amoebiasis. Mechanisms of protective immunity in malaria

and leishmaniasis. Conventional and DNA vaccine development against malaria. In vitro correlates of protective immunity in vivo in parasitic diseases.

4. **Recombinant DNA technology in parasitic disease research:** Strategies for the use of rDNA technologies in the study of parasite antigens; Application of rDNA technology in the identification and exploitation of new drug targets in parasites; Biotherapy of parasitic diseases, detection and analysis of cytokine mRNA in cells and tissues using RT-PCR; Development of DNA probe based diagnostic tools for parasites; Construction of cDNA libraries and genomic DNA cloning and other related genetic engineering techniques.
5. **Hybridoma technology and analysis of proteins:** Basic principles of somatic cell hybridization; Production of monoclonal antibodies; Detection and characterization of monoclonal antibodies using immunofluorescence assay and ELISA; Applications of hybridoma technology in parasitic disease research; Metabolic and surface labeling of parasite antigens and SDS-PAGE and two-dimensional analysis of parasite antigens.

#### **PC-820**

##### **Pharmacological Interventions for Ischemic Brain Injury**

(2 credits)

1. Pathophysiology of ischemic brain injury, clinical manifestations and laboratory evaluation.
2. Excitotoxicity of ischemic brain injury: Glutamate excitotoxicity, excitatory amino acid (EAA) receptors EAA antagonists. Problems with EAA antagonists.
3. Oxidative stress in ischemic brain injury: FRs measurement and potential of free radical scavengers in brain injury, nitric oxide in ischemic brain injury.
4. Potential neuroprotective approaches for ischemic brain injury: Calpain inhibitors, PARP inhibitors, MAP kinase inhibitors, apoptosis inhibitors etc.
5. Animal models for focal and global ischemia. Neuronal culture and brain slices for testing neuroprotective drugs.

#### **PC-830**

##### **Parasitology/Microbiology, Community and Pharmacy**

(2 credits)

1. **Parasitic, microbial and viral infections, community and pharmacy:** The general perceptions, linkages and relevances; Basic principles of epidemiology; Epidemiology of infectious/tropical diseases; Community related issues involved in the epidemiological studies; Community participation in epidemiological studies; Role of epidemiological studies on disease treatment, control and prevention.

2. **Emerging and re-emerging infections:** Role of vectors and population migration; Impact of travel on the transmission patterns of infectious diseases; Mapping and managing of the drug-resistant pathogens.
3. **Biomedical and biocultural definitions of parasitic and microbial diseases:** The perceptions of community; Community or selected schools participation/involvement in the control and treatment of infectious diseases; Role of NGOs and media; Modern and traditional medicines for the treatment of tropical diseases.
4. **Mothers definition of malaria:** Mothers beliefs and behaviours in relation to malaria in children; Home management of childhood malaria, diarrhoea and respiratory infections; The decision-making dynamics in treatment seeking behaviours, antimalarials available in retail outlets and home; Impact of parasitic and microbial diseases on the education of children.
5. **Women and tropical diseases:** Introduction; Women's participation in the treatment and management of infectious diseases; The relationship between gender and tropical diseases: Risk factors of infection, social costs and access to care, knowledge and resources; Assessment of women' need as related to infectious diseases, their involvement in the identification of their own needs, setting their own goals and targets; Training of women to train themselves.
6. **Mass chemo and immunoprophylaxis against tropical diseases:** Evaluation of their impact and the understanding of the cost-effectiveness.
7. **Determination of disease burden, the disability-adjusted life years, and the understanding of the economical aspects of tropical diseases:** Details of studies the social and economic burden of malaria and tuberculosis.

## PC-840

### Regulatory Toxicology and Drug Safety Evaluation

(2 credits)

1. **Concept and development of regulatory toxicity testing models:** Bio assays and endpoints: Human pharmaceutical products; Exposure characterization; Routes of exposure; ADME profiles.
2. **Stages of drug development:** Drug laws, FDA, OECD, ICH, Schedule Y; Design of preclinical toxicity studies and clinical development, clinical risk/benefit analysis. Safety evaluation of medical devices and bio materials. Good Laboratory Practices (GLP), issues and implementation.
3. **Different methods in toxicity testing:** Dose determination, response characterization, NOAEL.
4. **MTD and threshold limitations:** Hormesis, lower dose extrapolation, in vitro and in vivo correlation, animal to human extrapolation; Flow chart.
5. **Mechanism of toxicity:** Evaluation across different models: Target organs, cell death, necrosis,apoptosis,oxidativestress,chromosomeandDNA damage.

6. **Acute and chronic toxicity, genetic toxicity:** Types of genetic toxicity testing; Principles of detection; Genotoxicity of marketed drugs, test batteries, Salmonella test, micronucleus test, chromosome aberration test, Comet assay, New-bio assays.
7. **Reproductive toxicity:** Germ cell toxicant, effect on gonads, F1 generation study. Neonatal toxicity; Transplacental mutagenesis and carcinogenesis.
8. **Carcinogenicity, carcinogen identification:** Carcinogenesis process, drug induced carcinogenicity, lifetime carcinogenicity bio assays, neonatal mouse models; Short and medium term bio assays, limitations and impacts.
9. **Regulations, discovery-development gap:** Risk characterization; Management and Communication.
10. Future of regulatory toxicology in drug safety evaluation.

## PC-850

### Cellular and Molecular Parasitology

(2 credits)

1. **Ultrastructure of parasites/microbes/viruses:** Plasmodium, leishmania, entamoeba, mycobacterium, candida, HIV, hepatitis B virus; Basic principles related to structure and function of the cell membranes; Biology of the cell membranes of plasmodium, leishmania and entamoeba; Cell wall of mycobacterium tuberculosis and its unique features; Structure of HIV.
2. **Disease processes and the definition of pathogenesis:** Modern concepts of the pathogenetic mechanisms with special reference to the underlying genetic basis; Mechanisms of virulence; Acute-phase response and proinflammatory mechanisms during infections; Mechanisms of mimicry; Cerebral malaria (CM) and mechanisms of sequestration; Experimental models of CM; Hematopoiesis and anaemia in malaria; Genetic factors that determine the susceptibility and resistance to malaria. *E. histolytica*: Mechanisms of encystation and excystation; Macrophage-mycobacteria interaction, and the mechanisms of latency during *M. tuberculosis* infection.
3. **Bioimmuno-therapy of infectious diseases and the development of protein drugs:** Brief introduction to carbohydrate, protein, lipid and nucleic metabolism in parasitic infections (plasmodium, leishmania and *M. tuberculosis*); Studies on some known potential drug targets in plasmodium, leishmania, *M. tuberculosis* and HIV. genes and antigens/proteins of plasmodium, leishmania, *M. tuberculosis* in the development of vaccines and drugs.
4. **Drug-resistance:** The definition; Drug-resistance in parasites and microbes; General mechanisms of drug-resistance; Detailed studies on mechanisms of resistance of (1) Plasmodium to chloroquine, artemisinin derivatives and pyrimethamine; (2) *M. tuberculosis* to isoniazid, rifampicin, pyrazinamide, ethambutol and streptomycin; Reversal of drug-resistance; Experimental selection of drug-resistant strains of

Plasmodium berghei (in vivo) and P. falciparum (in vitro); Role of cloning in experimental selection of drug-resistant strains.

5. **Basic principles of vaccinology:** Conventional (whole cell live, killed and attenuated), subunit and molecular vaccines. nucleic acid vaccines; Prime-boost vaccination;

Adjuvants and the mechanisms of their action; Experimental models of vaccination against malaria and tuberculosis; Latest knowledge in the human vaccine development against malaria, leishmania, tuberculosis and HIV.

6. **Fundamentals of the immunodiagnosis with special reference to torpical diseases; Immunodiagnosis:** Approaches, practices and research needs; Impact of immunodiagnosis on the disease control. Various serological tests (ELISA, IFA, IHA etc.); Studies on presently used diagnostic kits for malaria, tuberculosis and HIV; Molecular diagnosis: Weaknesses and strengths.

## PC-860

### Epigenetics and Diseases

(2 credits)

1. Toxicogenomics, pharmecogenomics, pharmecogenetics and personalized medicine.
2. **Proteomics in Drug Discovery:** Two dimension gel electrophoresis; in-gel digestion etc.
3. **Microarray technology:** Hybridization and types of arrays, tilling array, protein arrays.
4. **Chromatin structure and functions:** The Nucleosome, euchromatin& heterochromatin, regulation and alteration of chromatin higher order structure.
5. **Chromatin Immunoprecipitation:** Chip on chip technology.
6. **Epigenomics, Histone modifications:** Acetylation, methylation, phosphortylation, Ubiquitination, ribosylation etc.
7. Role of histone modifications in diseases in diabetes.
8. Role of histone modifications in cancer.
9. Neurodegenerative diseases.
10. The use of chromatin immunoprecipitation assays in genome-wide analysis of histone modifications.

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