# Pharmacology and Toxicology

**M.S. (Pharm.)**

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<th>Course Name</th>
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<td>PC-511</td>
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<td>Chemotherapy of Parasitic and Microbial Infections</td>
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<td>NP-510</td>
<td>Separation Techniques</td>
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<td>PE-520</td>
<td>Biopharmaceutics and Pharmacokinetics</td>
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<td>BT-510</td>
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<td>LG-510</td>
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**Semester-II**

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<td>Drug Metabolism</td>
<td>1</td>
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<tr>
<td>PC-611</td>
<td>Pharmacological Screening and Assays</td>
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<td>PC-620</td>
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<td>PC-640</td>
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<td>PC-650</td>
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<td>LS-610</td>
<td>General Laboratory Experience in the area of Specialization</td>
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<td><strong>Total Credits</strong></td>
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**Semester-III**

- Project (22 weeks)
  - TH-598  Synopsis                                                               | 5       |
  - TH-599  Presentation                                                          | 3       |
  - **Total Credits**                                                           | **8**   |

**Semester-IV**

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<td>TH-698</td>
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<tr>
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<td><strong>Total Credits (I to IV semesters)</strong></td>
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**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; Congestive heart failure, hypertension, cardiac arrhythmias: Ulcer, pancreatitis, hepatitis and cholecystitis; Bronchial asthma, depression, schizophrenia, epilepsy, Parkinsonism and Alzheimer disease; Hypo and hyper thyroidism, diabetes mellitus and other endocrine diseases; Rheumatoid arthritis, gout and anemia.

**PC-520 General Pharmacology (2 credits)**

1. Drug receptor interaction theories, occupation theory, rate theory.

2. Receptor occupation and response relationship, spare receptors, silent receptors, orphan receptors, presynaptic and postsynaptic receptors.

3. **Receptor characterization methods:** Pharmacological characterization, radioligand methods, monoclonal anti-bodies, receptor subtypes, IUPHAR nomenclature, clinical significance of receptor subclassification.

4. Receptor down regulation and upregulation.

5. Structure activity relationships, pharmacodynamic and pharmacokinetic aspects of chiral drugs, allosteric binding, thermodynamics of drug interactions with the receptors.

6. Transmembrane signal mechanisms, second messengers, viz., cAMP, cGMP, calcium.

7. Dose response relationship and different types of antagonisms.

8. Desensitization and tachyphylaxis.


10. Non therapeutic uses of drugs.

**PC-530 Experimental Pharmacology (1 credit)**

1. Common laboratory animals and their physiological parameters, breeding types, inbred strains, F1 hybrids; Random breeding, selective breeding, breeding methods, factors affecting the nature and degree of pharmacological responses; Handling and care of different animals; Bleeding and different routes of administration and chemical euthanasia.

2. **In vitro experimentation:** Advantages and disadvantages; Physiological salt solutions, recording transducers, resting tensions, equilibrium, dose cycles; Methods of stimulation, stimulating devices, operation of recording devices, superfusion, cascade superfusion, perfusion, some commonly used isolated preparations.

3. **In vivo 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.

4. Conscious animal experimentation precautions to be taken in behavioural experiments.

5. Animal cell-culture techniques, aseptic handling, cell counting and cell viability assays.

6. Protein and DNA gel electrophoresis, western, northern, southern blot hybridization and PCR techniques.

7. Ultra, differential and analytical centrifugation, protein purification and identification by RF-HPLC, LCMS-MS, MALDI.

8. **Radiochemical methods of analysis:** Principle of radiation and radioactivity, decay of radioactivity, units, isotopes detection, scintillation detector (crystal and liquid), quenching, radioimmunoassay.


10. Data collection, data reduction, data representation, cumulative and noncumulative dose response curves, transformation of data logit, probit, pA scale, pD scale.
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.
7. Mechanism of action anti-amoebic drugs.
10. Targets of anti-filarial drug development.
11. Biology of viral infection.
20. Targets of anti-leishmanial drug development.

NP-510 Separation Techniques (1 credit)
1. Chromatography: General principles, classification of chromatographic techniques, normal and reversed phase, bonded phase, separation mechanisms.
2. Column chromatography: Merits and demerits, short-column chromatography and flash chromatography, vacuum liquid chromatography (VLC), medium pressure liquid chromatography, high pressure liquid chromatography (HPLC).
3. TLC, HPTLC, over pressure layer chromatography (OPLC), centrifugal chromatography.
4. Counter-current chromatography, droplet counter-current chromatography, ion-exchange, affinity, size exclusion and ion-pair chromatography.
5. Gas chromatography, introduction to GC-MS and LC-MS techniques.

PE-520 Biopharmaceutics and Pharmacokinetics (2 credits)
1. Introduction, concentration time profile, plotting the data, different fluid compartments and blood flow rates compartment models.
2. Protein and tissue binding, factors effecting protein binding, kinetics of protein binding, determination of rate constants and different plots (direct, scatchard and reciprocal); Significance volume of distribution, implications and in vitro methodologies.
3. Pharmacokinetic characterization of drugs: Absorption rate constants (Wagner-Nelson, Loo-Reigelman methods), limitations, lag-time, pharmacokinetics in presence of lag-time; Flip-flop model.
4. Case studies.
5. Drug disposition, renal clearance, mechanism of clearance, clearance ratio, determination of clearance, hepatic clearance, % drug metabolized, relationship between blood flow, intrinsic
clearance, hepatic clearance and protein binding, different volumes of distribution, significance, and integration kinetics.

6. **Pharmacokinetics of multiple dosing, dosage regimen design based on mean average, minimum and maximum, plasma/serum concentrations, limited fluctuation methods; Repeated one point method; Dosage adjustment in disease patients.**

7. **Nonlinear pharmacokinetics, direct, liner and orbit graph methods of dosing. Non-linear pharmacokinetics due to drug-protein binding.**

8. **Topics:** Chronopharmacokinetics; Drug toxicity and forensic, pharmacokinetics; Case study; Pharmacokinetics in elderly; Drug dosage in children, obese patient; First dose size; Kinetics of maternal-fetal drug transfer; Pharmacokinetics- pharmacologic/clinical response; Distribution kinetics; Metabolic kinetics; Dose and time dependencies; Turnover concepts; Small volume of distribution; Dialysis.

9. **Biopharmaceutics and pharmacokinetics in drug research.**

**BT-510 Biotechnology in Pharmaceutical Sciences (1 credit)**


2. **Genomics in target discovery:** Concept of genome, genes and gene expression. Genome sequencing and sequence comparison methods (e.g. BLAST), gene expression 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. **Expression purification and assay:** Gene expression in E. coli, in baculovirus, in mammalian cells. Various protein purification methods. Enzymes based assay for small molecule screening.

5. **Bioprocess technology:** Introduction to microbial growth, media formulation, fermentation processes, design, operation and characteristics of fermentation processes, instrumentation and bioprocess control.

6. **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.

7. **Biotechnology in pharmaceutical industry:** Major areas for biotechnology in the pharmaceutical industry such as antibiotics, vaccines, diagnostics, antibodies, biopharmaceuticals (insulin, interferon, GSF, CSF & therapeutic proteins etc.); Commercial aspects, priorities for future biotechnological research.

8. **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.

**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.
Experimental design and analysis of variance: Completely randomized, randomized blocks. Latin square and factorial designs. Post-hoc procedures.

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.

Non-parametric tests: Sign; Mann-Whitney U; Wilcoxon matched pair; Kruskal wallis and Friedman two way ANOVA tests. Spearman rank correlation.

Statistical techniques in pharmaceutics: Experimental design in clinical trials; Parallel and crossover designs. Statistical test for bioequivalence. Dose response studies; Statistical quality control.

PT-560 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 / organizational rules in India and abroad; Thesis research paper publication, credit sharing by workers, financial incentives; Useful information sources for patents related information-internet sites, brouchers, periodicals, CD roms; Significance of copyright protection for researchers; Indian Copyright Law and digital technologies-Beme 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; filing 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, POST WTO 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.

**GE-511 Seminar (1 credit)**
1. Introduction, information retrieval systems
2. Writing term papers and reports.
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, spreadsheet, 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, acute toxicity testing of drugs, analgesic activity of a compound, estimation of protein and haematological parameters.
4. Biotechnology for pharmaceutical sciences (20 hours)
   - Day-1: Preparation for plasmid miniprep.
   - Day-2: Plasmid miniprep and restriction digestion.
   - Day-3: Gel electrophoresis and molecular weight calculation.
   - Day-4: Discussion of result and viva.
5. **Specialization** (95 hours)

   ECG recording in rat, pA2 value for atropine in G.pig ileum, strength of an unknown sample of histamine by four point assay, analgesic effect of pentazocine using hot plate method, demonstration of receptor binding studies, effects of a drug on food and water intake. Demonstration of recording of rat blood pressure, anticonvulsive activity of a drug, locomotor activity, muscle relaxant activity using rotarod apparatus; Working of physiograph, chlorpromazine induced catalepsy, anti-inflammatory property of indomethacin, plasma glucose levels in streptozotocin treated rats; histology, cell culture techniques, cell viability assay, isolation of DNA from sample, SDS PAGE and DNA gel electrophoresis, genotoxic effects of drugs.
Semester-II

PC-610 Drug Metabolism (1 credit)
2. Excretion of drugs, biliary and fecal excretion; Factors effecting drug metabolism; Drug metabolism in fetus and new born; Models to study drug metabolism; Dose effect relationships.

PC-611 Pharmacological Screening and Assays (1 credit)
1. General principles of screening, correlations between various animal models and human situations, animal ethics.
2. Pharmacological screening models for therapeutic areas such as hypertension, cerebral ischaemia, pain, epilepsy, depression, Parkinson’s disease, Alzheimer’s disease, diabetis, leishmaniasis etc.
3. Correlation between in-vitro and in-vivo screens; Special emphasis on cell based assay, biochemical assay, radioligand binding assay, high through put screening, high through put pharmacokinetic analysis, specific use of reference drugs and interpretation of results.

PC-620 CNS and Respiratory Pharmacology (2 credits)
1. Chemical transmission and drug action in the central nervous system, emphasis on noradrenaline, dopamine, 5-HT, acetylcholine, excitatory amino acids, GABA, glycine and histamine.
2. Peptides as mediators.
3. Pharmacodynamic, pharmacokinetic, therapeutic and toxicological facets of the following: Benzo diazepines and its antagonists. Barbiturates, 5-HT agonists and antagonists, tricyclic antidepressants, MAOI, atypical antidepressants, lithium, antiepileptics, drugs used in the treatment of Parkinsonism, centrally acting muscle relaxants, narcotic analgesics, psychomotor stimulants and psychotomimetic drugs, antipsychotic drugs, drugs used in Alzheimer’s disease, local anesthetics.
4. Respiratory stimulants, bronchodilators and anti-inflammatory agents used in asthma, cough suppressants.

PC-630 Autonomic, CVS, Blood, Renal, and GI Pharmacology (2 credits)
1. Chemical transmission of the autonomic nervous system.
2. Pharmacodynamic, pharmacokinetic, therapeutic and toxicological facets of the following: Muscarinic cholinergic receptor agonists and antagonists. Ganglionic stimulants and blocking agents, neuromuscular blocking agents, drugs acting on adrenoceptors.
3. Cardiac glycosides and other cardiotonic agents, anti dysrhythmic drugs, antianginal drugs, antihypertensives, calcium channel antagonists, ACE inhibitors, endothelium derived relaxing factors, lipid lowering agents. Diuretics, drug altering the pH of urine, excretion of organic molecules.
5. H2 receptor antagonists, proton pump inhibitors, antacids, emetics, antiemetics and cancer chemotherapy, purgatives, drugs regulate the GI motility, cholagogues and drugs used in cholelithiasis.
PC-640 Autacoids and Endocrine Pharmacology (1 credit)

Pharmacodynamic, pharmacokinetic, therapeutic and toxicological facets of the following: Histamine and bradykinin agonist and antagonists, drugs acting through eicosanoids and platelet activating factor. Adenohypophyseal hormones and related substances, thyroid and antithyroid drugs, insulin and oral hypoglycemic agents and endocrine pancreas, adrenocortical hormones, adrenocortical steroids and inhibitors of the synthesis, agents affecting the calcification, estrogens and progesterone and their antagonists, oral contraceptive, androgens.

PC-650 Clinical Pharmacology and Regulatory Toxicology (2 credits)

1. Introduction to clinical pharmacology, importance of clinical pharmacokinetics, therapeutic monitoring of important drugs.

2. Drug-drug interactions; Drug-food interactions; Drug-pollutant interaction.

3. Investigational new drug application, new drug application requirements; FDA requirements.

4. Preclinical testing strategy; Vis a-vis envisaged clinical studies; Experimental clarification of possible human risk; Technical details of experiments; Flow chart for development of preclinical testing.

5. Design and organisation of phase-I to phase-IV clinical studies.

6. Single dose and repeat dose toxicity studies; Factors influencing such studies such as species, sex, size, route, dose level; Data evaluation and regulatory requirements.

7. Reproductive toxicology assessment of male reproductive toxicity, spermatogenesis; Risk assessment in male reproductive toxicity; Female reproductive toxicology; Oocyte toxicity; alterations in reproductive endocrinology; relationship between maternal and developmental toxicity.

8. Mutagenicity; Mechanisms of mutagenesis, point mutations; Individual chromosomes and complete genome mutations, germ cell mutations, somatic cell mutation; Tests systems in vitro, test for gene mutation in bacteria, chromosome damage, gene mutation, in vivo micronucleus tests in rodent, metaphase analysis.

9. Carcinogenicity; Principles of carcinogenicity, prechronic studies for dose testing, chronic study, transplacental carcinogenesis; Cocarcinogenesis/tumor promotion, estimation of carcinogenicity of complex mixtures.

10. Toxicokinetics, animals and dose groups; Exposure measurement; determination of metabolites complicating factors in exposure interpretation, analytical method, good laboratory practices; Stereoisomerism vis-à-vis regulatory requirements; Single enantiomers; Racemate enantiomer switch; Regulatory requirements.

11. Toxicokinetic methods validation; assay development; Assay validation, study monitoring, calibration of standards; validation report.

12. Preclinical toxicological requirements for biologicals and biotechnological products; safety analysis; problems specific to recombinant products – secondary pharmacology, antibodies, transmission of viral infections, residual DNA, etc.

PC-660 Immunopharmacology and Chemotherapy (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 the following: Quinolones, sulphonamides, penicillins, cephalosporins, clavulanic acid, aminoglycosides, broad spectrum antibiotics, chemotherapeutic agents used in tuberculosis, antifungal agents, antiprotozoal agents, antimalarial agents, antiparasitic drugs, antiviral drugs, drugs used in the treatment of AIDS, antineoplastic agents.
GE-611 Seminar (1 credit)

Students are required to submit written record and present details of the project to be pursued in semester-III and 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 Laboratory Experience in the area of Specialization-10 hours/week (2 credits)

Effect of drugs on rat blood pressure, estimation of blood glucose in normal and diabetic rats, OGTT test, effect of unknown drug on food and water intake, effect of unknown drug on rat ECG, effect of cyclophosphamide on neutrophil counts, in vitro experiment on rat prostrate, in vitro experiment on rat vas deferens, effect of drug on passive avoidance apparatus, effect of drug on TFL using analgesiometer, demonstration of ischemic model, effect of antioxidants on lipid peroxidation, genotoxic effect of unknown drug (micronucleus test and chromosomal aberration), demonstration of nerve conduction velocity in rats, effect of antidepressant on tail suspension test, identification of stages of estrus cycle in rats, antinflammmtory activity of unknown compounds using carrageenan induced paw oedema in rats, finding out pA2 value of atropine, antihistaminic activity of unknown drug in g.pig cell culture techniques, effect of drug on locomotor activity, to study motor incoordination using rota rod apparatus, effect of unknown drug on PTZ seizure, effect of unknown drug on MES seizure, effect of unknown drug on gastric emptying, effect of NSAIDs on gastric mucosa, effect of unknown drug using elevated plus maze, effect of unknown drugs on gastric acid secretion in pylorus ligated rats, demonstration of brain oedema/ BBB disruption, demonstration of blood flow, measurement of cholesterol and TGs in rats, radioligand binding demonstration, effect of unknown agent on hot plate test, demonstration of molecular biology technique, SDS PAGE, DNA GEL electrophoresis, MALDI and LCMS. Microarray technique, effect of cyclophosphamide on neutrophil counts; Microscopic techniques, blood cell counting and histopathological studies.
Ph.D. courses

**PC-710 Receptor Mechanisms** (2 credits)

1. Molecular and chemical characterization of membrane receptors; Use of monoclonal antibodies in receptor characterization and purification; Immunoprecipitation and electrophoretic analysis of membrane proteins; Peptide mapping; Molecular weight determination by radiation inactivation; Solubilization of the receptors; Reconstitution of membrane receptors.

2. Biochemical mechanisms of cell signalling; Plasma membrane and cytosolic receptor structure; Plasma membrane as a signal transduction element; Mechanisms of receptor mediated signalling; Ion gated channels; Ligand activated receptors with intrinsic enzyme activity; Amplification of transmembrane signals.

3. Structure of G proteins, subclassification of G proteins; Role of heterotrimeric G proteins in signalling; Generation of intracellular second messengers; Modulation of G protein activity.

4. Calcium as second messenger, PIP2, IP3 receptors, calcium influx and efflux, intracellular sources of calcium and release, calcium oscillations; Intracellular calcium determinations in cell suspensions; Development of fluorescent indicators, fura-2, fluo-3, BAPTA; Digital ratio imaging in single cells.

5. Receptor dynamics and signalling; The mobile receptor paradigm; Receptor microclustering, patching, internalization, receptor mobility and cell activation; Homologous and heterologous regulation of receptors, sequestration, receptor turnover.

6. Signal transduction of neurotransmitters and neuromodulators viz., norepinephrine

7. HT, pathophysiological implications of neurotransmitter receptors.

8. Introduction to mechanistic approach of drug design, receptor mapping, and computer aided drug design.

**PC-730 Free Radicals in Drug Research** (2 credits)

1. Introduction to free radicals: Free radicals, reacting oxygen species, production of free radicals in cells, damaging reactions of free radicals, defences against free radicals, free radicals in human disease.


3. Antioxidants: Endogenous antioxidants- enzymatic and nonenzymatic; Regulation of antioxidant defences, pharmacological antioxidants.


**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.


3. Different methods in toxicity testing: Dose determination, response characterization, NOAEL, MTD and threshold limitations; Hormesis, lower dose extrapolation, in vitro and in vivo correlation, animal to human extrapolation; Flow chart.

4. Mechanism of toxicity: Evaluation across different models; Target organs, cell death, necrosis, apoptosis, oxidative stress, chromosome and DNA damage.
5. 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.

6. Reproductive toxicity, germ cell toxicant, effect on gonads, F1 generation study. Neonatal toxicity; Transplacental mutagenesis and carcinogenesis.

7. Carcinogenicity, carcinogen identification: Carcinogenesis process, drug induced carcinogenicity, lifetime carcinogenicity bio assays, neonatal mouse models; Short and medium term bio assays, limitations and impacts.

8. Regulations, discovery-development gap: Risk characterization; Management and Communication; Future of regulatory toxicology in drug safety evaluation

**MC-740 Advanced Topics in Drug Action and Drug Design (2 credits)**

Molecular recognition and supra-molecular chemistry; Molecular associations involving weak interactions; Solvation effects on molecular associations; Metalloenzymes in medicinal chemistry; Metals in medicine- reversible and irreversible enzyme inhibition. Mechanisms of drug activation; Enzyme activation of drugs; Bioprocess prodrugs chemistry of metabolic reactions. Organic chemistry of drug metabolism- conjugation reactions, reductive reactions, oxidative reactions. Molecular interaction fields- Molecular electrostatic potentials in understanding drug action. Drug action on biomembranes- organic chemistry of drug permeability through membranes. Molecular similarity and molecular diversity in drug design.

**PC-910 Diabetes, Pathophysiology and discovery of new drugs (2 credits)**

1. Diabetes, Definition, Genetics and Pathogenesis: Definition, diagnosis and classification, Genetics of Type I and Type II diabetes, Insulin resistance and it pathogenesis of Type II diabetes, Beta cell dysfunction in Type II diabetes, Secondary forms of diabetes, syndromes of extreme insulin resistance


5. Discovery of anti diabetic drugs, animal models for studying type I and type II diabetes, insulin resistance models, ob/ob and db/db mice, zucker fatty rats, n-STZ rats, invitro screening models, insulin secretogogue activity in RIN cells, glucose uptake studies in 3T3L1 adipocytes, and muscle cells, GLUT4 translocation and PPAR gamma agonism

6. Newer targets for diabetes, role of SGLT1 and SGLT2 receptors DPP4 inhibition, Beta cell regeneration and GLP1 inhibitors.

7. Oxidative stress in diabetes and its markers, different pathways of oxidative stress in diabetic complications.
**PC-920 Current topics in Cancer Research (2 credits)**

1. Diagnosis of Cancer, Treatment of cancer, Chemotherapy and radiotherapy, DNA replication and cancer cell cycle, Regulation of Growth: Growth Factors, Receptors, and Signaling Pathways, Oncogenesis, tumor suppressor genes and apoptosis, tumor immunity and immunotherapy, angiogenesis.


3. The MTT assay, ELISA, DNA fragmentation assay, COMET assay, PARP cleavage as a means of apoptosis, different methods of detecting apoptosis, TUNEL Assay, Annexin V staining, cell adhesion assays.


5. Different animal models to study cancer, principles involved in mouse xenograft models in anticancer drug screening, pharmacokinetic knowledge based oncology drug development. Tumor targeting in cancer therapy.

**GE- 711 Seminar (1 credit)**

1. Introduction, information retrieval systems.

2. Writing term papers and reports.


4. Reading research papers.

5. Skill in oral presentation.

*Each student has to present a seminar.*