



**DEPARTMENT: PHARMACOLOGY
SUB: PHD ENTRANCE SYLLABUS**

SUBJECT: ADVANCED PHARMACOLOGY

General Pharmacology

- a. Pharmacokinetics: The dynamics of drug absorption, distribution, biotransformation and elimination. Concepts of linear and non-linear compartment models. Significance of Protein binding.
- b. Pharmacodynamics: Mechanism of drug action and the relationship between drug concentration and effect. Receptors, structural and functional families of receptors, quantitation of drug receptors interaction and elicited effects.

Neurotransmission

- a. General aspects and steps involved in neurotransmission.
- b. Neurohumoral transmission in autonomic nervous system (Detailed study about neurotransmitters- Adrenaline and Acetyl choline).
- c. Neurohumoral transmission in central nervous system (Detailed study about neurotransmitters- histamine, serotonin, dopamine, GABA, glutamate and glycine].
- d. Non adrenergic non cholinergic transmission (NANC). Co-transmission

Systemic Pharmacology

A detailed study on pathophysiology of diseases, mechanism of action, pharmacology and toxicology of existing as well as novel drugs used in the following systems

a. Autonomic Pharmacology

Parasympathomimetics and lytics, sympathomimetics and lytics, agents affecting neuromuscular junction

Central nervous system Pharmacology

General and local anesthetics

Sedatives and hypnotics, drugs used to treat anxiety

Depression, psychosis, mania, epilepsy, neurodegenerative diseases.

Narcotic and non-narcotic analgesics.

Cardiovascular Pharmacology

Diuretics, antihypertensives, antiischemics, anti-arrhythmics, drugs for heart failure and hyperlipidemia.

Hematinics, coagulants, anticoagulants, fibrinolytics and anti-platelet drugs

Autocoid Pharmacology

The physiological and pathological role of Histamine, Serotonin, Kinins Prostaglandins Opioid autocoids.

Pharmacology of antihistamines, 5HT antagonists.

Endocrine Pharmacology

Molecular and cellular mechanism of action of hormones such as growth hormone, prolactin, thyroid, insulin and sex hormones

Anti-thyroid drugs, Oral hypoglycemic agents, Oral contraceptives, Corticosteroids. Drugs affecting calcium regulation

Chemotherapy

Cellular and molecular mechanism of actions and resistance of antimicrobial agents such as β -lactams, aminoglycosides, quinolones, Macrolide antibiotics. Antifungal, antiviral, and anti-TB drugs.

Chemotherapy

Drugs used in Protozoal Infections Drugs used in the treatment of Helminthiasis
Chemotherapy of cancer

Immunopharmacology

Cellular and biochemical mediators of inflammation and immune response. Allergic or hypersensitivity reactions. Pharmacotherapy of asthma and COPD.

Immunosuppressants and Immunostimulants

GIT Pharmacology

Antiulcer drugs, Prokinetics, antiemetics, anti-diarrheals and drugs for constipation and irritable bowel syndrome.

Chronopharmacology

Biological and circadian rhythms, applications of chronotherapy in various diseases like cardiovascular disease, diabetes, asthma and peptic ulcer

Free radicals Pharmacology

Generation of free radicals, role of free radicals in etiopathology of various diseases such as diabetes, neurodegenerative diseases and cancer. Protective activity of certain important antioxidant

Recent Advances in Treatment:

Alzheimer's disease, Parkinson's disease, Cancer, Diabetes mellitus

SUBJECT: PHARMACOLOGICAL AND TOXICOLOGICAL SCREENING METHODS

Laboratory Animals Common lab animals:

Description, handling and applications of different species and strains of animals.

Transgenic animals: Production, maintenance and applications

Anaesthesia and euthanasia of experimental animals.

Maintenance and breeding of laboratory animals.

CPCSEA guidelines to conduct experiments on animals

Good laboratory practice.

Preclinical screening of new substances for the pharmacological activity using in vivo, in vitro, and other possible animal alternative models.

General principles of preclinical screening.

CNS Pharmacology: behavioural and muscle coordination, CNS stimulants and depressants, anxiolytics, anti-psychotics, anti-epileptics and nootropics. Drugs for neurodegenerative diseases like Parkinsonism, Alzheimer's and multiple sclerosis. Drugs acting on Autonomic Nervous System.

Preclinical screening of new substances for the pharmacological activity using in vivo, in vitro, and other possible animal alternative models.

Respiratory Pharmacology: anti-asthmatics, drugs for COPD and anti allergies.

Reproductive Pharmacology: Aphrodisiacs and antifertility agents Analgesics, anti-inflammatory and antipyretic agents.

Gastrointestinal drugs: anti-ulcer, anti -emetic, anti-diarrheal and laxatives.

Preclinical screening of new substances for the pharmacological activity using in vivo, in vitro, and other possible animal alternative models.

Cardiovascular Pharmacology: antihypertensives, antiarrhythmics, antianginal, antiatherosclerosis agents and diuretics. Drugs for metabolic disorders like anti-diabetic, antihyperlipidemic, and agents.

Anti-cancer agents

Preclinical screening of new substances for the pharmacological activity using in vivo, in vitro, and other possible animal alternative models.

Immunosuppressants and immunomodulators

General principles of immunoassay:

Theoretical basis and optimization of immunoassay, heterogeneous and homogenous immunoassay systems.

Immunoassay methods evaluation; protocol outline, objectives and preparation. Immunoassay for digoxin and insulin

Limitations of animal experimentation and alternate animal experiments.

Extrapolation of in vitro data to preclinical and preclinical to humans.

Basic definition and types of toxicology (general, mechanistic, regulatory and descriptive)

Regulatory guidelines for conducting toxicity studies OECD, ICH, EPA and Schedule Y
OECD principles of Good Laboratory Practice (GLP) History, concept and its importance in drug development

Acute, sub-acute and chronic- oral, dermal and inhalational studies as per OECD guidelines.

Acute eye irritation, skin sensitization, dermal irritation & dermal toxicity studies. Test item characterization- importance and methods in regulatory toxicology studies

Reproductive toxicology studies

Male reproductive toxicity studies, female reproductive studies (segment I and segment III), teratogenicity studies (segment II) Genotoxicity studies (Ames Test, in vitro and in vivo Micronucleus and Chromosomal aberrations studies) In vivo carcinogenicity studies

IND enabling studies (IND studies)- Definition of IND, importance of IND, industry perspective, list of studies needed for IND submission. Safety pharmacology studies- origin, concepts and importance of safety pharmacology. Tier1- CVS, CNS and respiratory safety pharmacology, HERG assay. Tier2- GI, renal and other studies

Toxicokinetics- Toxicokinetic evaluation in preclinical studies, saturation kinetics Importance and applications of toxicokinetic studies. Alternative methods to animal toxicity testing.

SUBJECT: CELLULAR AND MOLECULAR PHARMACOLOGY

Cell biology

Structure and functions of cell and its organelles

Genome organization. Gene expression and its regulation, importance of siRNA and micro RNA, gene mapping and gene sequencing

Cell cycles and its regulation.

Cell death– events, regulators, intrinsic and extrinsic pathways of apoptosis. Necrosis and autophagy.

Cell signaling

Intercellular and intracellular signaling pathways.

Classification of receptor family and molecular structure ligand gated ion channels; G-protein coupled receptors, tyrosine kinase receptors and nuclear receptors.

Secondary messengers: cyclic AMP, cyclic GMP, calcium ion, inositol 1,4,5- trisphosphate, (IP3), NO, and diacylglycerol.

Detailed study of following intracellular signaling pathways: cyclic AMP signaling pathway, mitogen-activated protein kinase (MAPK) signaling, Janus kinase (JAK)/signal transducer and activator of transcription (STAT) signaling pathway.

Principles and applications of genomic and proteomic tools

DNA electrophoresis, PCR (reverse transcription and real time), Gene sequencing, micro array technique, SDS page, ELISA and western blotting.

Recombinant DNA technology and gene therapy

Basic principles of recombinant DNA technology-Restriction enzymes, various types of vectors. Applications of recombinant DNA technology. Gene therapy- Various types of gene transfer techniques, clinical applications and recent advances in gene therapy

Pharmacogenomics

Gene mapping and cloning of disease gene.

Genetic variation and its role in health/ pharmacology.

Polymorphisms affecting drug metabolism.

Genetic variation in drug transporters Genetic variation in G protein coupled receptors Applications of proteomics science: Genomics, proteomics, metabolomics, functionomics, nutrigenomics.

Immunotherapeutics

Types of immunotherapeutics, humanisation antibody therapy, Immunotherapeutics in clinical practice

Cell culture techniques

Basic equipments used in cell culture lab. Cell culture media, various types of cell culture, general procedure for cell cultures; isolation of cells, subculture, cryopreservation, characterization of cells and their application.

Principles and applications of cell viability assays, glucose uptake assay, Calcium influx assays

Principles and applications of flow cytometry

Biosimilars

SUBJECT: PRINCIPLES OF DRUG DISCOVERY

An overview of modern drug discovery process:

Target identification, target validation, lead identification and lead Optimization. Economics of drug discovery.

Target Discovery and validation-Role of Genomics, Proteomics and Bioinformatics. Role of Nucleic acid microarrays, Protein microarrays, Antisense technologies, siRNAs, antisense oligonucleotides, Zinc finger proteins. Role of transgenic animals in target validation

Lead Identification-

combinatorial chemistry & high throughput screening, in silico lead discovery techniques, Assay development for hit identification.

Protein structure, Levels of protein structure, Domains, motifs, and folds in protein structure. Computational prediction of protein structure: Threading and homology modeling methods. Application of NMR and X-ray crystallography in protein structure prediction.

Rational Drug Design

Traditional vs rational drug design, Methods followed in traditional drug design, High throughput screening, Concepts of Rational Drug Design, Rational Drug Design Methods: Structure and Pharmacophore based approaches.

Virtual Screening techniques: Drug likeness screening, Concept of pharmacophore mapping and pharmacophore-based Screening.

Molecular docking:

Rigid docking, flexible docking, manual docking; Docking based screening. De novo drug design. Quantitative analysis of Structure Activity Relationship History and development of QSAR, SAR versus QSAR, Physicochemical parameters, Hansch analysis, Fee Wilson analysis and relationship between them.

QSAR Statistical methods

Regression analysis, partial least square analysis (PLS) and other multivariate statistical methods. 3D-QSAR approaches like COMFA and COMSIA

Prodrug design

Basic concept, Prodrugs to improve patient acceptability, Drug solubility, Drug absorption and distribution, site specific drug delivery and sustained drug action. Rationale of prodrug design and practical consideration of prodrug design

SUBJECT: CLINICAL RESEARCH AND PHARMACOVIGILANCE

Regulatory Perspectives of Clinical Trials:

Origin and Principles of International Conference on Harmonization - Good Clinical Practice (ICH-GCP) guidelines.

Ethical Committee- Institutional Review Board, Ethical Guidelines for Biomedical Research and Human Participant-Schedule Y, ICMR.

Informed Consent Process

Structure and content of an Informed Consent Process Ethical principles governing informed consent process

Clinical Trials: Types and Design

Experimental Study- RCT and Non RCT, Observation Study: Cohort, Case Control, Cross sectional

Clinical Trial Study Team

Roles and responsibilities of Clinical Trial Personnel: Investigator, Study Coordinator, Sponsor, Contract Research Organization and its management

Clinical Trial Documentation

Guidelines to the preparation of documents, Preparation of protocol, Investigator Brochure, Case Report Forms, Clinical Study Report Clinical Trial Monitoring-Safety Monitoring in CT

Adverse Drug Reactions:

Definition and types. Detection and reporting methods. Severity and seriousness assessment. Predictability and preventability assessment, Management of adverse drug reactions; Terminologies of ADR.

Basic aspects, terminologies and establishment of pharmacovigilance

History and progress of pharmacovigilance, Significance of safety monitoring, Pharmacovigilance in India and international aspects, WHO international drug monitoring programme, WHO and Regulatory terminologies of ADR, evaluation of medication safety, establishing pharmacovigilance centres in Hospitals, Industry and National programmes related to pharmacovigilance. Roles and responsibilities in Pharmacovigilance

Methods, ADR reporting and tools used in Pharmacovigilance

International classification of diseases, International Non-proprietary names for drugs, Passive and Active surveillance, Comparative observational studies, Targeted clinical investigations and Vaccine safety surveillance. Spontaneous reporting system and Reporting to regulatory authorities, Guidelines for ADRs reporting. Argus, Aris G Pharmacovigilance, VigiFlow, Statistical methods for evaluating medication safety data.

Pharmacoepidemiology , Pharmacoeconomics , safety pharmacology