PHARMACOLOGY

MODERN PHARMACEUTICAL ANALYTICAL TECHNIQUES

THEORY

1. UV-Visible spectroscopy: Introduction, Theory, Laws, Instrumentation associated with UV-Visible spectroscopy, Choice of solvents and solvent effect and Applications of UV-Visible spectroscopy, Difference/ Derivative spectroscopy.
   IR spectroscopy: Theory, Modes of Molecular vibrations, Sample handling, Instrumentation of Dispersive and Fourier - Transform IR Spectrometer, Factors affecting vibrational frequencies and Applications of IR spectroscopy, Data Interpretation.
   Spectroflourimetry: Theory of Fluorescence, Factors affecting fluorescence (Characterestics of drugs that can be analysed by flourimetry), Quenchers, Instrumentation and Applications of fluorescence spectrophotometer.
   Flame emission spectroscopy and Atomic absorption
   spectroscopy: Principle, Instrumentation, Interferences and Applications.

2 NMR spectroscopy: Quantum numbers and their role in NMR, Principle, Instrumentation, Solvent requirement in NMR, Relaxation process, NMR signals in various compounds, Chemical shift, Factors influencing chemical shift, Spin-Spin coupling, Coupling constant, Nuclear magnetic double resonance, Brief outline of principles of FT-NMR and 13C NMR. Applications of NMR spectroscopy.

3 Mass Spectroscopy: Principle, Theory, Instrumentation of Mass Spectroscopy, Different types of ionization like electron impact, chemical, field, FAB and MALDI, APCI, ESI, APPI Analyzers of Quadrupole and Time of Flight, Mass fragmentation and its rules, Meta stable ions, Isotopic peaks and Applications of Mass spectroscopy.

4

4. Chromatography: Principle, apparatus, instrumentation, chromatographic parameters, factors affecting resolution, isolation of drug from excipients, data interpretation and applications of the following:
   j) Thin Layer chromatography
   k) High Performance Thin Layer Chromatography
   l) Ion exchange chromatography
   m) Column chromatography
   n) Gas chromatography
   o) High Performance Liquid chromatography
   p) Ultra High Performance Liquid chromatography
   q) Affinity chromatography
   r) Gel Chromatography

5 Electrophoresis: Principle, Instrumentation, Working conditions,factors affecting separation and applications of the following:
a) Paper electrophoresis b) Gel electrophoresis c) Capillary electrophoresis d) Zone electrophoresis e) Moving boundary electrophoresis f) Iso electric focusing
X ray Crystallography: Production of X rays, Different X ray methods, Bragg's law, Rotating crystal technique, X ray powder technique, Types of crystals and applications of X-ray diffraction.

6 Potentiometry: Principle, working, Ion selective Electrodes andApplication of potentiometry.
Thermal Techniques: Principle, thermal transitions and Instrumentation (Heat flux and power-compensation and designs), Modulated DSC, Hyper DSC, experimental parameters (samplepreparation, experimental conditions, calibration, heating and cooling rates, resolution, source of errors) and their influence,advantage and disadvantages, pharmaceutical applications. Differential Thermal Analysis (DTA): Principle, instrumentation and advantage and disadvantages, pharmaceutical applications, derivative differential thermal analysis (DDTA). TGA: Principle, instrumentation, factors affecting results,advantage anddisadvantages, pharmaceutical applications.

ADVANCED PHARMACOLOGY - I

THEORY

1. 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.

2 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

Autonomic Pharmacology

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

3 Central nervous system Pharmacology

General and local anesthetics

Sedatives and hypnotics, drugs used to treat anxiety.

Depression, psychosis, mania, epilepsy, neurodegenerativediseases.

Narcotic and non-narcotic analgesics.

4 Cardiovascular Pharmacology

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

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

5 Autocoid Pharmacology

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

Pharmacology of antihistamines, 5HT antagonists.

PHARMACOLOGICAL AND TOXICOLOGICAL SCREENING METHODS - I

THEORY

1. Laboratory Animals

Common laboratory 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.

Bioassay-Principle, scope and limitations and methods

2 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: behavioral and muscle co ordination, CNS stimulants and depressants, anxiolytics, anti-psychotics, anti epileptics and nootropics. Drugs for neurodegenerative diseases like Parkinsonism, Alzheimers and multiple sclerosis. Drugs acting on Autonomic Nervous System.

3 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 allergics. Reproductive Pharmacology: Aphrodisiacs and antifertility agents Analgesics, antiinflammatory and antipyretic agents. Gastrointestinal drugs: anti ulcer, anti - emetic, anti- diarrheal and laxatives.

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

Cardiovascular Pharmacology: antihypertensives, antiarrythmics, antianginal, antiatherosclerotic agents and diuretics. Drugs for metabolic disorders like anti-diabetic, antidyslipidemic agents. Anti cancer agents. Hepatoprotective screening methods.

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

Iimmunomodulators, Immunosuppressants and immunostimulants

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 tohumans

CELLULAR AND MOLECULAR PHARMACOLOGY

THEORY

1. 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.

2 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, **J**anus kinase (**J**AK)/signal transducer and activator of transcription (STAT) signaling pathway.

3 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.

4. Pharmacogenomics

Gene mapping and cloning of disease gene.

Genetic variation and its role in health/ pharmacologyPolymorphisms 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

5. 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

b. Biosimilars

ADVANCED PHARMACOLOGY - II

THEORY

1. Endocrine Pharmacology

Molecular and cellular mechanism of action of hormones such asgrowth hormone,
prolactin, thyroid, insulin and sex hormones
Anti-thyroid drugs, Oral hypoglycemic agents, Oral contraceptives, Corticosteroids.
Drugs affecting calcium regulation

2 Chemotherapy

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

3 Chemotherapy

Drugs used in Protozoal Infections
Drugs used in the treatment of Helminthiasis
Chemotherapy of cancer
Immunopharmacology
Cellular and biochemical mediators of inflammation and immuneresponse. Allergic or
hypersensitivity reactions. Pharmacotherapy of asthma and COPD.
Immunosuppressants and Immunostimulants

4 GIT Pharmacology

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

Chronopharmacology

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

5 Free radicals Pharmacology

Generation of free radicals, role of free radicals in etiopathology ofvarious 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, Diabetesmellitus

PHARMACOLOGICAL AND TOXICOLOGICAL SCREENING METHODS-II

THEORY

1. 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

2 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

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

4 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
5	Toxicokinetics- Toxicokinetic evaluation in preclinical studies, saturation kinetics Importance and applications of toxicokinetic studies. Alternative methods to animal toxicity testing.

PRINCIPLES OF DRUG DISCOVERY

THEORY

1. 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.

2 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

3 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

4	Virtual Screening techniques: Drug likeness screening, Concept of pharmacophore mapping and pharmacophore based Screening, Molecular docking: Rigid docking, flexible docking, manualdocking; 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.
5	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

CLINICAL RESEARCH AND PHARMACOVIGILANCE

THEORY

1. 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
2. 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

3 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.

4 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

5 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.

6 Pharmacoepidemiology, pharmacoeconomics, safety pharmacology

Research Methodology & Biostatistics

UNIT – I

General Research Methodology: Research, objective, requirements, practical difficulties, review of literature, study design, types of studies, strategies to eliminate errors/bias, controls, randomization, crossover design, placebo, blinding techniques.

UNIT – II

Biostatistics: Definition, application, sample size, importance of sample size, factors influencing sample size, dropouts, statistical tests of significance, type of significance tests, parametric tests(students "t" test, ANOVA, Correlation coefficient, regression), non-parametric tests (wilcoxan rank tests, analysis of variance, correlation, chi square test), null hypothesis, P values, degree of freedom, interpretation of P values.

UNIT – III

Medical Research: History, values in medical ethics, autonomy, beneficence, non-maleficence, double effect, conflicts between autonomy and beneficence/non-maleficence, euthanasia, informed consent, confidentiality, criticisms of orthodox medical ethics, importance of communication, control resolution, guidelines, ethics committees, cultural concerns, truth telling, online business practices, conflicts of interest, referral, vendor relationships, treatment of family members, sexual relationships, fatality.

UNIT – IV

CPCSEA guidelines for laboratory animal facility: Goals, veterinary care, quarantine, surveillance, diagnosis, treatment and control of disease, personal hygiene, location of animal facilities to laboratories, anesthesia, euthanasia, physical facilities, environment, animal husbandry, record keeping, SOPs, personnel and training, transport of lab animals.

UNIT – V

Declaration of Helsinki: History, introduction, basic principles for all medical research, and additional principles for medical research combined with medical care.