ADVANCED PHARMACOLOGY - II

MPL 201T

Scope: The subject is designed to strengthen the basic knowledge in the field of pharmacology and to impart recent advances in the drugs used for the treatment of various diseases. In addition, the subject helps the student to understand the concepts of drug action and mechanism involved

Objectives: Upon completion of the course the student shall be able to:

1. Explain the mechanism of drug actions at cellular and molecular level
2. Discuss the Pathophysiology and pharmacotherapy of certain diseases
3. Understand the adverse effects, contraindications and clinical uses of
4. drugs used in treatment of diseases

THEORY **60 Hrs**

1. Endocrine Pharmacology: **12 hrs**

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.

2. Chemotherapy: **12 hrs**

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: **12 hrs**

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.

4. GIT Pharmacology **12 hrs**

Antiulcer drugs, Prokinetics, antiemetics, anti-diarrheals and drugs for constipation and irritable bo

Chronopharmacology

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

5. Free radicals Pharmacology **12 hrs**

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*.

REFERENCES

1. The Pharmacological basis of therapeutics- Goodman and Gill man's
2. Principles of Pharmacology. The Pathophysiologic basis of drug therapy by David E Golan et al.
3. Basic and Clinical Pharmacology by B.G -Katzung
4. Pharmacology by H.P. Rang and M.M. Dale.
5. Hand book of Clinical Pharmacokinetics by Gibaldi and Prescott.
6. Text book of Therapeutics, drug and disease management by E T. Herfindal and Gourley.
7. Applied biopharmaceutics and Pharmacokinetics by Leon Shargel and Andrew B.C.Yu.
8. Handbook of Essential Pharmacokinetics, Pharmacodynamics and Drug Metabolism for Industrial Scientists
9. Robbins & Cortan Pathologic Basis of Disease, 9th Ed. (Robbins Pathology)
10. A Complete Textbook of Medical Pharmacology by Dr. S.K Srivastava published by APC Avichal Publishing Company.
11. KD.Tripathi. Essentials of Medical Pharmacology.
12. Principles of Pharmacology. The Pathophysiologic basis of drug Therapy by David E Golan, Armen H, Tashjian Jr, Ehrin J,Armstrong, April W, Armstrong, Wolters, Kluwer-Lippincott Williams & Wilkins Publishers

PHARMACOLOGICAL AND TOXICOLOGICAL SCREENING METHODS-II

MPL 202T

Scope: This subject imparts knowledge on the preclinical safety and toxicological evaluation of drug & new chemical entity. This knowledge will make the student competent in regulatory toxicological evaluation.

Objectives:

Upon completion of the course, the student shall be able to,

1. Explain the various types of toxicity studies.
2. Appreciate the importance of ethical and regulatory requirements for toxicity studies.
3. Demonstrate the practical skills required to conduct the preclinical toxicity studies.

THEORY **60 Hrs**

1. **Basic definition and types of toxicology:** **12 hrs**
   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 **12 hrs**
   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, **12 hrs**
   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.
4. IND enabling studies (IND studies) - Definition of IND, importance of IND, **12 hrs**
   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 **12 hrs**

Importance and applications of toxicokinetic studies.

Alternative methods to animal toxicity testing.

REFERENCES

1. Hand book on GLP, Quality practices for regulated non-clinical research and development (http://www.who.int/tdr/publications/documents/glphandbook. pdf).
2. Schedule Y Guideline: drugs and cosmetics (second amendment) rules, 2005, ministry of health and family welfare (department of health) New Delhi.
3. Drugs from discovery to approval by Rick NG.
4. Animal Models in Toxicology, 3rd Edition, Lower and Bryan.
5. OECD test guidelines.
6. Principles of toxicology by Karen E. Stine, Thomas M. Brown.
7. Guidance for Industry M3(R2) Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals (http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm073246.pdf).

PRINCIPLES OF DRUG DISCOVERY

MPL 203T

Scope: The subject imparts basic knowledge of drug discovery process. This information will make the student competent in drug discovery process

Objectives: Upon completion of the course, the student shall be able to,

1. Explain the various stages of drug discovery.
2. Appreciate the importance of the role of genomics, proteomics and bioinformatics in drug discovery
3. Explain various targets for drug discovery.
4. Explain various lead seeking method and lead optimization
5. Appreciate the importance of the role of computer aided drug design in drug discovery

THEORY **60 Hrs**

1. **An Overview of Modern Drug Discovery Process:** **12 hrs**

   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-** **12 hrs**

   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** **12 hrs**

   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,

4. **Molecular docking:** **12 hrs**

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.

5. **QSAR Statistical Methods:** **12 hrs**

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.

REFERENCES

1. MouldySioud. Target Discovery and Validation Reviews and Protocols: Volume 2 Emerging Molecular Targetsand Treatment Options. 2007 Humana Press Inc.

2. Darryl León. Scott MarkelIn. Silico Technologies in Drug Target Identification and Validation. 2006 by Taylor and Francis Group, LLC.

3. Johanna K. DiStefano. Disease Gene Identification. Methods and Protocols. Springer New York Dordrecht Heidelberg London.

4. Hugo Kubiny. QSAR: Hansch Analysis and Related Approaches. Methods and Principles in Medicinal Chemistry. Publisher Wiley-VCH

5. Klaus Gubernator, Hans-Joachim Böhm. Structure-Based Ligand Design. Methods and Principles in Medicinal Chemistry. Publisher Wiley-VCH

6. Abby L . Parrill. M . Rami Reddy. Rational Drug Design. Novel Methodology and Practical Applications. ACS Symposium Series; American Chemical Society: Washington, DC, 1999.

7. J. Rick Turner. New drug development design, methodology and, analysis. John Wiley & Sons, Inc., New Jersey.

CLINICAL RESEARCH AND PHARMACOVIGILANCE

MPL 204T

Scope: This subject will provide a value addition and current requirement for the students in clinical research and pharmacovigilance. It will teach the students on conceptualizing, designing, conducting, managing and reporting of clinical trials. This subject also focuses on global scenario of Pharmacovigilance in different methods that can be used to generate safety data. It will teach the students in developing drug safety data in Pre-clinical, Clinical phases of Drug development and post market surveillance.

Objectives: Upon completion of the course, the student shall be able to,

1. Explain the regulatory requirements for conducting clinical trial
2. Demonstrate the types of clinical trial designs
3. Explain the responsibilities of key players involved in clinical trials
4. Execute safety monitoring, reporting and close-out activities
5. Explain the principles of Pharmacovigilance
6. Detect new adverse drug reactions and their assessment
7. Perform the adverse drug reaction reporting systems and communication in Pharmacovigilance

THEORY **60 Hrs**

1. **Regulatory Perspectives of Clinical Trials:** **12 hrs**

   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 **12 hrs**

   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-** **12 hrs**

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** **12 hrs**

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 centers in Hospitals, Industry and National programmes related to pharmacovigilance. Roles and responsibilities in Pharmacovigilance.

5. **Methods, ADR reporting and tools used in Pharmacovigilance** **12 hrs**

International classification of diseases, International Nonproprietary 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** **12 hrs**

REFERENCES

1. Central Drugs Standard Control Organization- Good Clinical Practices, Guidelines for Clinical Trials on Pharmaceutical Products in India. New Delhi: Ministry of Health;2001.
2. International Conference on Harmonization of Technical requirements for registration of Pharmaceuticals for human use. ICH Harmonized Tripartite Guideline. Guideline for Good Clinical Practice.E6; May 1996.
3. Ethical Guidelines for Biomedical Research on Human Subjects 2000. Indian Council of Medical Research, New Delhi.
4. Textbook of Clinical Trials edited by David Machin, Simon Day and Sylvan Green, March 2005, John Wiley and Sons.
5. Clinical Data Management edited by R K Rondels, S A Varley, C F Webbs. Second Edition, Jan 2000, Wiley Publications.
6. Handbook of clinical Research. Julia Lloyd and Ann Raven Ed. Churchill Livingstone.
7. Principles of Clinical Research edited by Giovanna di Ignazio, Di Giovanna and Haynes.

PHARMACOLOGICAL PRACTICAL - II

MPL 205P

1. To record the DRC of agonist using suitable isolated tissues preparation.
2. To study the effects of antagonist/potentiating agents on DRC of agonist using suitable isolated tissue preparation.
3. To determine to the strength of unknown sample by matching bioassay by using suitable tissue preparation.
4. To determine to the strength of unknown sample by interpolation bioassay by using suitable tissue preparation
5. To determine to the strength of unknown sample by bracketing bioassay by using suitable tissue preparation
6. To determine to the strength of unknown sample by multiple point bioassay by using suitable tissue preparation.
7. Estimation of PA2 values of various antagonists using suitable isolated tissue preparations.
8. To study the effects of various drugs on isolated heart preparations
9. Recording of rat BP, heart rate and ECG.
10. Recording of rat ECG
11. Drug absorption studies by averted rat ileum preparation.
12. Acute oral toxicity studies as per OECD guidelines.
13. Acute dermal toxicity studies as per OECD guidelines.
14. Repeated dose toxicity studies- Serum biochemical, haematological, urine analysis, functional observation tests and histological studies.
15. Drug mutagenicity study using mice bone-marrow chromosomal aberration test.
16. Protocol design for clinical trial.(3 Nos.)
17. Design of ADR monitoring protocol.
18. In-silico docking studies. (2 Nos.)
19. In-silico pharmacophore based screening.
20. In-silico QSAR studies.
21. ADR reporting

REFERENCES

1. Fundamentals of experimental Pharmacology-by M.N.Ghosh
2. Hand book of Experimental Pharmacology-S.K.Kulakarni
3. Text book of in-vitro practical Pharmacology by Ian Kitchen
4. Bioassay Techniques for Drug Development by Atta-ur-Rahman, Iqbal choudhary and William Thomsen
5. Applied biopharmaceutics and Pharmacokinetics by Leon Shargel and Andrew B.C.Yu.
6. Handbook of Essential Pharmacokinetics, Pharmacodynamics and Drug Metabolism for Industrial Scientists.