NIRMA UNIVERSITY

Institute of Pharmacy

(M.Pharm. - Pharmacology)
(Semester - II)

L	T	P	C
4	-	-	4

Course Code	**MPL201T**
Course Title	**Advanced Pharmacology-II**

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, this subject helps the students to understand the concepts of drug action and mechanisms involved.

Objectives:

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

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

Course Learning Outcomes (CLO):

At the end of the course, students will be able to -

1. Explain mechanisms of action, adverse effects, contraindications and clinical uses of drugs used in treatment of diseases.
2. Relate pathogenesis of various diseases with their treatment
3. Utilize the knowledge of chronopharmacology for treatment of various diseases.
4. Develop understanding of role of oxidative stress in various disease and their treatment
5. Discuss pharmacological actions of different drugs useful for therapy of various diseases.

Syllabus: **Teaching hours**: 60 hr

UNIT I **12 Hours**

- **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

UNIT II **18 Hours**

- **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. Drugs used in Protozoal Infections Drugs used in the treatment of Helminthiasis Chemotherapy of cancer

UNIT III **06 Hours**

- **Immunopharmacology**
  Cellular and biochemical mediators of inflammation and immune response. Allergic or hypersensitivity reactions. Pharmacotherapy of asthma and COPD. Immunosuppressants and Immunostimulants

UNIT IV **12 Hours**

- **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

UNIT V **12 Hours**

- **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

Suggested Readings^: (Latest Edition)

1. Goodman Gilman A., Rall T.W., Nies A.I.S. and Taylor, P. Goodman and Gilman's The Pharmacological Basis of Therapeutics, New York: Mc Graw Hill, Pergamon Press.
2. Golan, D.E., Tashjian, A.H., Armstrong, E.J., Armstrong, A.W. Principles of Pharmacology. The Pathophysiologic Basis of Drug Therapy. Philadelphia: Lippincott Williams & Wilkins Publishers.
3. Katzung, B.G. Basic and Clinical Pharmacology, New York: McGraw Hill.
4. Gibaldi, M., Prescott, L. Hand book of Clinical Pharmacokinetics. ADIS Health Science Press
5. Herfindal, E.T., Gourley. Text book of Therapeutics, Drug and Disease Management. Williams and Wilkins Publication.
6. Shargel, L. Andrew B.C. Yu. Applied biopharmaceutics and Pharmacokinetics. New York: Mc Graw Hills Publishers.
7. Kwon, Younggil. Handbook of Essential Pharmacokinetics, Pharmacodynamics and Drug Metabolism for Industrial Scientists. New York: Kluwer Academic/Plenum.
8. Kumar, V. Abbas, A.K., Aster, J.C. Robbins & Cortan Pathologic Basis of Disease. Elseveir Publishers.
9. Srivastava, S.K. Complete Textbook of Medical Pharmacology. APC Avichal Publishing Company
10. Tripathi, K.D. Essentials of Medical Pharmacology. New Delhi: Jaypee Brothers Medical Publishers (P) Ltd.

L= Lecture, T= Tutorial, P= Practical, C= Credit

^ this is not an exhaustive list

(M.Pharm: Pharmacology)

(Semester - II)

L	T	P	C
4	-	-	4

Course Code	**MPL202T**
Course Title	**Pharmacological and Toxicological Screening Methods- II**

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.

Course Learning Outcomes (CLO):

At the end of the course, students will be able to -

1. Define various types of toxicity studies and their mechanism of action.
2. Demonstrate toxicity of various drugs qualitatively and quantitatively
3. Illustrate the skills and understanding required to conduct preclinical toxicity studies as per the regulatory and ethical requirements.
4. Interpret results of toxicokinetics of novel drugs
5. Evaluate various drugs for their safety pharmacological and toxicological actions using animal models to extrapolate them with human beings.

Syllabus: **Teaching hours: 60 Hours**

UNIT I **12 Hours**

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

UNIT II **12 Hours**

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

UNIT III **12 Hours**

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

UNIT IV **12 Hours**

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

UNIT V **12 Hours**

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

Suggested Readings^: (Latest Edition)

1. World Health Organization. Handbook: good laboratory practice (GLP): quality practices for regulated non-clinical research and development. World Health Organization.
2. Schedule Y Guideline: drugs and cosmetics (second amendment) rules, 2005, ministry of health and family welfare (department of health) New Delhi
3. Ng, R. Drugs: from discovery to approval. John Wiley & Sons, New Jersey.
4. Lower, G. M., & Bryan, G. T., Animal Models in Toxicology, 3rd Edition, OECD test guidelines.
5. Stine, K. E., & Brown, T. M. Principles of toxicology. CRC Press, United states.
6. 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)

L= Lecture, T= Tutorial, P= Practical, C= Credit

^ this is not an exhaustive list

(M. Pharm)

(Semester - II)

L	T	P	C
4	-	-	4

Course Code	**MPL203T**
Course Title	**Principles of Drug Discovery**

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 various stages of drug discovery.
2. Appreciate 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

Course Learning Outcomes (CLO):

At the end of the course, students will be able to -

1. Describe the flow and methods of drug discovery and development process and their challenges
2. Demonstrate role of genomics, proteomics and bioinformatics in drug discovery
3. Explain rational drug design based on the understanding of three-dimensional (3D) structures and physicochemical properties of drugs and target.
4. Apply various CADD in-silico techniques like pharmacophore modeling, QSAR, molecular docking, homology modeling etc for the lead identification and optimization
5. Make use of rationale and practical considerations for prodrug designing.

Syllabus: **Teaching hours: 60 Hours**

UNIT I **12 Hours**

- **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.

UNIT II **12 Hours**

- **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

UNIT III **12 Hours**

- **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,

UNIT IV **12 Hours**

- **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.

UNIT V **12 Hours**

- **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

Suggested Readings^: (Latest Edition)

1. Sioud, M. Target Discovery and Validation Reviews and Protocols: Emerging Molecular Targets and Treatment Options, Volume 2. Totowa: Humana Press Inc., New Jersey.
2. León, D., & Markel, S. (Eds.). In Silico Technologies in Drug Target Identification and Validation. CRC Press, United States
3. DiStefano, J. K., Disease Gene Identification. Methods and Protocols. Springer New York Dordrecht Heidelberg, London.
4. Mannhold, R., Krogsgaard-Larsen, P., & Timmerman, H. QSAR: Hansch analysis and related approaches (Vol. 1). John Wiley & Sons, New Jersey.
5. Bures, M. G. Structure-based Ligand Design Edited by K. Gubernator and H.-J. Bohm. Wiley-VCH, Weinheim.
6. Parrill, A. L., & Reddy, M. R. (Eds.). Rational drug design: novel methodology and practical applications. American Chemical Society, United States
7. Turner R. J. New drug development design, methodology and, analysis. John Wiley & Sons, Inc., New Jersey.
8. Stroud, R. M. & Moore, J. M. Computational and Structural Approaches to Drug Discovery: Ligand-Protein Interactions. RCS Publishers.
9. Smith, H. J. & Williams, H. Introduction to the principles of drug design and action. CRC Press, Taylor & Francis.
10. Patrick, G. L. An introduction to medicinal chemistry. Oxford University Press.

L= Lecture, T= Tutorial, P= Practical, C= Credit

^ this is not an exhaustive list

(M. Pharm)

(Semester - II)

L	T	P	C
4	-	-	4

Course Code	**MPL204T**
Course Title	**Clinical Research and Pharmacovigilance**

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:

After completion of course student is able to know about –

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

Course Learning Outcomes (CLO):

At the end of the course, students will be able to -

1. Understand regulatory perspectives of clinical trials and research
2. Explain pharmacoepidemiology, pharmacoeconomics, safety pharmacology
3. Summarize basic aspects, terminologies and establishment of pharmacovigilance
4. Discuss methods, ADR reporting and tools used in Pharmacovigilance
5. Develop clinical trial documentation including ADR reporting
6. Elaborate about clinical trials

Syllabus: **Teaching hours: 60 Hours**

UNIT I **10 Hours**

- **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

UNIT II **12 Hours**

- **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

UNIT III **12 Hours**

- **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.

UNIT IV **10 Hours**

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

UNIT V **10 Hours**

- **Methods, ADR reporting and tools used in Pharmacovigilance**

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.

UNIT VI **06 Hours**

- **Health Economics and Outcomes Research**
  Pharmacoepidemiology, pharmacoeconomics, safety pharmacology

Suggested Readings^: (Latest Edition)

10. Central Drugs Standard Control Organization- Good Clinical Practices, Guidelines for Clinical Trials on Pharmaceutical Products in India. New Delhi: Ministry of Health; 2001.
11. International Conference on Harmonization of Technical requirements for registration of Pharmaceuticals for human use. ICH Harmonized Tripartite Guideline. Guideline for Good Clinical Practice.E6; June 2016.
12. Ethical Guidelines for Biomedical Research on Human Subjects 2000. Indian Council of Medical Research, New Delhi.
13. Machin, D., Simon D., and Sylvan G., eds. Textbook of Clinical Trials. USA. John Wiley & Sons.
14. Rondel, R. K., Varley, S. A., & Webb, C. F. (Eds.). Clinical Data Management. New York: Wiley.
15. Lloyd, J., & Raven, A. (Eds.). Handbook of Clinical Research. Churchill Livingstone.
16. Di Giovanna, I., & Hayes, G. Principles of Clinical Research. UK, Routledge
17. Verma, S., Gulati, Y. Fundamentals of Pharmacovigilance. New Delhi, Paras Medical Publishers.
18. Arora, D. Pharmacovigilance: An Industry Perspective. Mumbai, Pharmapublishers.

L= Lecture, T= Tutorial, P= Practical, C= Credit

^ this is not an exhaustive list

(M. Pharm)

(Semester - II)

L	T	P	C
-	-	12	6

Course Code	**MPL205P**
Course Title	**Pharmacological Practical-II**

Syllabus: **Teaching hours**: 180 hrs

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 the strength of unknown sample by matching bioassay by using suitable tissue preparation
4. To determine the strength of unknown sample by interpolation bioassay by using suitable tissue preparation
5. To determine the strength of unknown sample by bracketing bioassay by using suitable tissue preparation
6. To determine 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 and heart rate.
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

Suggested Readings^: (Latest Edition)

1. Ghosh, M. N. Fundamentals of Experimental Pharmacology. Kolkatta: Hilton & Company
2. Kulkarni, S. K. Hand book of Experimental Pharmacology. Delhi: Vallabh Prakashan
3. Kitchen, Von Ian. Textbook of in Vitro Practical Pharmacology. Oxford: Blackwell Scientific Publications.
4. Bioassay techniques for drug development. Atta-ur-Rahman - M. Iqbal. Choudhary - William J. Thomsen - Harwood Acad. Publ.
5. Shargel, L. Andrew B.C. Yu. Applied biopharmaceutics and Pharmacokinetics. New York: Mc Graw Hills Publishers.
6. Kwon, Younggil. Handbook of Essential Pharmacokinetics, Pharmacodynamics and Drug Metabolism for Industrial Scientists. New York: Kluwer Academic/Plenum, Print.
7. https://www.who-umc.org/

L= Lecture, T= Tutorial, P= Practical, C= Credit

^ this is not an exhaustive list