# Maharshi Dayanand University, Rohtak

# Department of Pharmaceutical Sciences

## M. PHARM. PHARMACOLOGY (MPC)

### PROGRAM SPECIFIC OUTCOMES

**PSO1** Demonstrate the use of the pharmacological principles into clinical decision-making

**PSO2** Predict and demonstrate the pharmacodynamics and pharmacokinetics of drugs and other therapeutic agents of the different origins.

**PSO3** Get the knowledge of the various guidelines to find the safe, toxic and lethal dose of the drugs.

**PSO4** Understand various techniques and methods to prevent the adverse effects of the drugs to ensure safety and to minimize the adverse drug events.

**PSO5** Understand the methods of assessment and reporting of the adverse effects of the drugs.

### SCHEME OF EXAMINATION

**Table- Schemes for internal assessments and end semester examinations (Pharmacology)**

| Course Code | Course | Internal Assessment | | | | End Semester Exams | | Total |
|---|---|---|---|---|---|---|---|---|
| | | Continuous | Sessional Exams | | Total | Marks | Duration | Marks |
| | | Mode | Marks | Duration | | | | |
| **SEMESTER I** | | | | | | | | |
| MPA101T | Modern Pharmaceutical Analytical Techniques | 10 | 15 | 1 Hr | 25 | 75 | 3 Hrs | 100 |
| MPL101T | Advanced Pharmacology-I | 10 | 15 | 1 Hr | 25 | 75 | 3 Hrs | 100 |
| MPL102T | Pharmacological and Toxicological Screening Methods-I | 10 | 15 | 1 Hr | 25 | 75 | 3 Hrs | 100 |
| MPL103T | Cellular and Molecular Pharmacology | 10 | 15 | 1 Hr | 25 | 75 | 3 Hrs | 100 |
| MPL104P | Pharmacology Practical I | 20 | 30 | 6 Hrs | 50 | 100 | 6 Hrs | 150 |
| - | Seminar /Assignment | - | - | - | - | - | - | 100 |
| | | | | | | | **Total** | **650** |
| **SEMESTER II** | | | | | | | | |
| MPL201T | Advanced Pharmacology II | 10 | 15 | 1 Hr | 25 | 75 | 3 Hrs | 100 |

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|---|---|---|---|---|---|---|---|---|
| MPL202T | Pharmacological and Toxicological Screening Methods-II | 10 | 15 | 1 Hr | 25 | 75 | 3 Hrs | 100 |
| MPL203T | Principles of Drug Discovery | 10 | 15 | 1 Hr | 25 | 75 | 3 Hrs | 100 |
| MPL204T | Clinical Research and Pharmacovigilance | 10 | 15 | 1 Hr | 25 | 75 | 3 Hrs | 100 |
| MPL205P | Pharmacology Practical II | 20 | 30 | 6 Hrs | 50 | 100 | 6 Hrs | 150 |
| - | Seminar /Assignment | - | - | - | - | - | - | 100 |
| | | | | | | | **Total** | **650** |

## Table- Schemes for internal assessments and end semester examinations

## (Semester III& IV)

| **Course Code** | **Course** | **Internal Assessment** | | | | **End Semester Exams** | | **Total** |
|---|---|---|---|---|---|---|---|---|
| | | **Continuous** | **Sessional Exams** | | **Total** | **Marks** | **Duration** | **Marks** |
| | | **Mode** | **Marks** | **Duration** | | | | |
| **SEMESTER III** | | | | | | | | |
| MRM101T | Research Methodology and Biostatistics | 10 | 15 | 1 Hr | 25 | 75 | 3 Hrs | 100 |
| - | Journal club | - | - | - | 25 | - | - | 25 |
| - | Discussion / Presentation (Proposal Presentation) | - | - | - | 50 | - | - | 50 |
| - | Research work | - | - | - | - | 350 | 1 Hr | 350 |
| | | | | | | | **Total** | **525** |
| **SEMESTER IV** | | | | | | | | |
| - | Journal club | - | - | - | 25 | - | - | 25 |
| - | Discussion / Presentation (Proposal Presentation) | - | - | - | 75 | - | - | 75 |
| - | Research work and Colloquium | - | - | - | - | 400 | 1 Hr | 400 |
| | | | | | | | **Total** | **500** |

**SYLLABUS**

## SEMESTER-1

## MODERN PHARMACEUTICAL ANALYTICAL TECHNIQUES (MPA101T)

**Course outcomes**

After completion of course student is able to know,

CO1 The analysis of various drugs in single and combination dosage forms

CO2 Theoretical and practical skills

CO3 Understand the requirement of the different analytical techniques wherever required.

**THEORY** **60 HOURS**

**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.

**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

**Spectroflourimetry:** Theory of Fluorescence, Factors affecting fluorescence, Quenchers, Instrumentation and Applications of fluorescence spectrophotometer.

**Flame emission spectroscopy and Atomic absorption spectroscopy**: Principle, Instrumentation, Interferences and Applications.

**12 Hrs**

**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.

**12 Hrs**

**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

**12 Hrs**

**4 Chromatography**: Principle, apparatus, instrumentation, chromatographic parameters, factors affecting resolution and applications of the following:

a) Paper chromatography b) Thin Layer chromatography c) Ion exchange chromatography d) Column chromatography e) Gas chromatography f) High Performance Liquid chromatography g) Affinity chromatography

**12 Hrs**

**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.

**12 Hrs**

**REFERENCES**

1. Spectrometric Identification of Organic compounds - Robert M Silverstein, Sixth edition, John Wiley & Sons, 2004.

2. Principles of Instrumental Analysis - Doglas A Skoog, F. James Holler, Timothy A. Nieman, 5th edition, Eastern press, Bangalore, 1998.

3. Instrumental methods of analysis – Willards, 7th edition, CBS publishers.

4. Practical Pharmaceutical Chemistry – Beckett and Stenlake, Vol II, 4th edition, CBS Publishers, New Delhi, 1997.

5. Organic Spectroscopy - William Kemp, 3rd edition, ELBS, 1991.

6. Quantitative Analysis of Drugs in Pharmaceutical formulation - P D Sethi, 3rd Edition, CBS Publishers, New Delhi, 1997.

7. Pharmaceutical Analysis- Modern methods – Part B - J W Munson, Volume 11, Marcel Dekker Series

## ADVANCED PHARMACOLOGY-I (MPL101T)

**Course outcomes**

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

CO1 Discuss the pathophysiology and pharmacotherapy of certain diseases

CO2 Explain the mechanism of drug actions at cellular and molecular level

CO3 Understand the adverse effects, contraindications and clinical uses of drugs used in treatment of diseases

**THEORY** **60HOURS**

**UNIT-I**

**General Pharmacology**

**12 Hrs**

a. Pharmacokinetics: The dynamics of drug absorption, distribution, biotransformation and elimination. Concepts of linear and non-linear compartment models. Significance of Protein binding. 06 hrs

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. 06 hrs

**UNIT-II**

**12 Hrs**

**Neurotransmission**

**06 Hrs**

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**

**06 Hrs**

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

**UNIT-III**

**12 Hrs**

**Central nervous system Pharmacology**

General and local anesthetics 02 hrs

Sedatives and hypnotics, drugs used to treat anxiety. 02 hrs

Depression, psychosis, mania, epilepsy, neurodegenerative diseases. 05 hrs

Narcotic and non-narcotic analgesics. 03 hrs

**UNIT-IV**

**Cardiovascular Pharmacology**

**12 Hrs**

Diuretics, antihypertensives, antiischemics, anti- arrhythmics, drugs for heart failure

and hyperlipidemia. 07 hrs

Hematinics, coagulants , anticoagulants, fibrinolytics and anti-platelet drugs 05 hrs

**UNIT- V**

**Autocoid Pharmacology**

**12 Hrs**

The physiological and pathological role of Histamine, Serotonin, Kinins Prostaglandins

Opioid autocoids. 08 hrs

Pharmacology of antihistamines, 5HT antagonists. 04 hrs

**REFEERENCES**

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.

6. 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

## PHARMACOLOGICAL AND TOXICOLOGICAL SCREENING METHODS-I (MPL102T)

**Course outcomes**

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

CO1 Appraise the regulations and ethical requirement for the usage of experimental animals.

CO2 Describe the various animals used in the drug discovery process and good laboratory practices in maintenance and handling of experimental animals

CO3 Describe the various newer screening methods involved in the drug discovery process

CO4 Appreciate and correlate the preclinical data to humans

**THEORY** **60 HOURS**

**Unit-I**

**12 Hrs**

**Laboratory Animals**

Common lab animals: Description, handling and applications of different species and strains of animals. 02 hrs

Transgenic animals: Production, maintenance and applications 02 hrs

Anaesthesia and euthanasia of experimental animals. 03 hrs

Maintenance and breeding of laboratory animals. 02 hrs

CPCSEA guidelines to conduct experiments on animals 02 hrs

Good laboratory practice. 01 hrs

**Unit-II**

**12 Hrs**

**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.

**Unit-III**

**12 Hrs**

**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.

**Unit-IV**

**12 hrs**

**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, antihyperlipidemic, and agents. Anti cancer agents

**Unit V**

**12 hrs**

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

Immunosuppressants and immunomodulators 02 hrs

**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 08 hrs

Limitations of animal experimentation and alternate animal experiments. 01 hr

Extrapolation of *in vitro* data to preclinical and preclinical to humans. 01 hr

**REFERENCES**

1. Biological standardization by J.H. Burn D.J. Finney and I.G. Goodwin
2. Indian Pharmacopeia and other Pharmacopeias
3. Screening methods in Pharmacology by Robert Turner. A
4. Evaluation of drugs activities by Laurence and Bachrach
5. Methods in Pharmacology by Arnold Schwartz.
6. Fundamentals of experimental Pharmacology by M.N.Ghosh
7. Pharmacological experiment on intact preparations by Churchill Livingstone
8. Drug discovery and Evaluation by Vogel H.G.
9. Experimental Pharmacology by R.K.Goyal.
10. Preclinical evaluation of new drugs by S.K. Gupta

## CELLULAR AND MOLECULAR PHARMACOLOGY (MPL103T)

**Course outcomes**

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

CO1 Explain the receptor signal transduction processes.

CO2 Explain the molecular pathways affected by drugs.

CO3 Appreciate the applicability of molecular pharmacology and biomarkers in drug discovery process.

CO4 Demonstrate molecular biology techniques as applicable for pharmacology

### Unit I

**12 Hrs**

**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.

### Unit II

**12Hrs**

**Cell signaling**

Intercellular and intracellular signaling pathways. Classification of receptor family and molecular structure ligand gated ion channels; Gprotein 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.

**Unit III**

**12Hrs**

**Principles and applications of genomic and proteomic tools 06 hrs**

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 06 hrs**

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

**Unit IV**

**12Hrs**

**Pharmacogenomics 08 hrs**

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 **04 hrs**

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

**Unit V**

**12Hrs**

**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

**Unit VI**

Biosimilars

**References:**

1. The Cell, A Molecular Approach. Geoffrey M Cooper.

2. Pharmacogenomics: The Search for Individualized Therapies. Edited by J. Licinio and M -L. Wong

**Immunotherapeutics**

3. Handbook of Cell Signaling (Second Edition) Edited by Ralph A. et.al

4. Molecular Pharmacology: From DNA to Drug Discovery. John Dickenson et.al

5. Basic Cell Culture protocols by Cheril D.Helgason and Cindy L.Miller

6. Basic Cell Culture (Practical Approach ) by J. M. Davis (Editor)

7. Animal Cell Culture: A Practical Approach by John R. Masters (Editor)

8. Current porotocols in molecular biology vol I to VI edited by Frederick M.Ausuvel et la.

## PHARMACOLOGY PRACTICAL-I (MPL104P)

**Course outcomes**

After completion of the course, student is able to

CO1 Understand the requirements of the animals study for the drug develooment

CO2 Understand the mechanism of the action and interactions of the drugs.

CO3 Calculate the dose and dose frequency of drugs.

**Practicals**

1. Analysis of pharmacopoeial compounds and their formulations by UV Vis spectrophotometer

2. Simultaneous estimation of multi component containing formulations by UV spectrophotometry

3. Experiments based on HPLC

4. Experiments based on Gas Chromatography

5. Estimation of riboflavin/quinine sulphate by fluorimetry

6. Estimation of sodium/potassium by flame photometry

**Handling of laboratory animals.**

1. Various routes of drug administration.

2. Techniques of blood sampling, anesthesia and euthanasia of experimental animals.

3. Functional observation battery tests (modified Irwin test)

4. Evaluation of CNS stimulant, depressant, anxiogenics and anxiolytic, anticonvulsant activity.

5. Evaluation of analgesic, anti-inflammatory, local anesthetic, mydriatic and miotic activity.

6. Evaluation of diuretic activity.

7. Evaluation of antiulcer activity by pylorus ligation method.

8. Oral glucose tolerance test.

9. Isolation and identification of DNA from various sources (Bacteria, Cauliflower, onion, Goat liver).

10. Isolation of RNA from yeast

11. Estimation of proteins by Braford/Lowry's in biological samples.

12. Estimation of RNA/DNA by UV Spectroscopy

13. Gene amplification by PCR.

14. Protein quantification Western Blotting.

15. Enzyme based *in-vitro* assays (MPO, AChEs, α amylase, α glucosidase).

16. Cell viability assays (MTT/Trypan blue/SRB).

17. DNA fragmentation assay by agarose gel electrophoresis.

18. DNA damage study by Comet assay.

19. Apoptosis determination by fluorescent imaging studies.

20. Pharmacokinetic studies and data analysis of drugs given by different routes of administration using softwares

21. Enzyme inhibition and induction activity

22. Extraction of drug from various biological samples and estimation of drugs in biological fluids using different analytical techniques (UV)

23. Extraction of drug from various biological samples and estimation of drugs in biological fluids using different analytical techniques (HPLC)

**References**

1. CPCSEA, OECD, ICH, USFDA, Schedule Y, EPA guidelines,

2. Fundamentals of experimental Pharmacology by M.N.Ghosh

3. Handbook of Experimental Pharmacology by S.K. Kulkarni.

4. Drug discovery and Evaluation by Vogel H.G.

5. Spectrometric Identification of Organic compounds - Robert M Silverstein,

6. Principles of Instrumental Analysis - Doglas A Skoog, F. James Holler, Timothy A. Nieman,

7. Vogel's Text book of quantitative chemical analysis - Jeffery, Basset, Mendham, Denney,

8. Basic Cell Culture protocols by Cheril D. Helgason and Cindy L.Mille

9. Basic Cell Culture (Practical Approach ) by J. M. Davis (Editor)

10. Animal Cell Culture: A Practical Approach by John R. Masters (Editor)

## SEMESTER-II

## ADVANCED PHARMACOLOGY-II (MPL201T)

**Course ouctomes**

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

CO1 Explain the mechanism of drug actions at cellular and molecular level

CO2 Discuss the Pathophysiology and pharmacotherapy of certain diseases

CO3 Understand the adverse effects, contraindications and clinical uses of drugs used in treatment of diseases

### UNIT-I

**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

### UNIT-II

**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.

### UNIT-III 12 Hrs

**Chemotherapy 06 Hrs**

Drugs used in Protozoal Infections

Drugs used in the treatment of Helminthiasis

Chemotherapy of cancer

**Immunopharmacology 06 Hrs**

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

Immunosuppressants and Immunostimulants

### UNIT-IV

**GIT Pharmacology 08 Hrs**

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

**Chronopharmacology 04 Hrs**

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

## UNIT-V

**Free radicals Pharmacology** **04 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:** **08 Hrs**

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

## PHARMACOLOGICAL AND TOXICOLOGICAL SCREENING METHODS-II (MPL202T)

**Course outcomes**

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

CO1 Explain the various types of toxicity studies.

CO2 Appreciate the importance of ethical and regulatory requirements for toxicity studies.

CO3 Demonstrate the practical skills required to conduct the preclinical toxicity studies.

### Unit I

**12 Hrs**

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 Hrs**

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 Hrs**

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 Hrs**

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 Hrs**

Toxicokinetics- Toxicokinetic evaluation in preclinical studies, saturation kinetics

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/glp-handbook.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 (MPL203T)

**Course outcome**

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

CO1 Explain the various stages of drug discovery.

CO2 Appreciate the importance of the role of genomics, proteomics and bioinformatics in drug discovery

CO3 Explain various targets for drug discovery.

CO4 Explain various lead seeking method and lead optimization

CO5 Appreciate the importance of the role of computer aided drug design in drug discovery

### Unit-I

**12 Hrs**

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 Hrs**

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 Hrs**

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 Hrs**

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 Hrs**

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

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., Hoboken, New Jeney.

## CLINICAL RESEARCH AND PHARMACOVIGILANCE (MPL204T)

**Course outcomes**

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

CO1 Explain the regulatory requirements for conducting clinical trial

CO2 Demonstrate the types of clinical trial designs

CO3 Explain the responsibilities of key players involved in clinical trials

## UNIT-I

**12 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

**12 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 centres in Hospitals, Industry and National programmes related to pharmacovigilance. Roles and responsibilities in Pharmacovigilance

## UNIT-V

**12 hours**

**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.

## UNIT-VI

Pharmacoepi Dermatology , pharmacoeconomics , safety pharmacology

**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.

## PHARMACOLOGY PRACTICAL-II (MPL205P)

**Course outcomes**

After completion of the course, student is able to

**CO1** Understand the need of the invitro studies before the use of the drugs on the living organism

**CO2** Standardize the unknown drug sample

**CO3** Report the ADRs

**Practicals**

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.

17. Protocol design for clinical trial.

18. Protocol design for clinical trial.

19. Design of ADR monitoring protocol.

20. In silico docking studies.

21. In silico pharmacophore based screening.

22. In silico QSAR studies.

23. ADR reporting

24. In silico docking studies.

**References**

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2. Hand book of Experimental Pharmacology-S.K.Kulakarni

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4. Bioassay Techniques for Drug Development by Atta-ur-Rahman, Iqbal choudhary and William Thomsen

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6. Handbook of Essential Pharmacokinetics, Pharmacodynamics and Drug Metabolism for Industrial Scientists.