JSS UNIVERSITY
SRI SHIVARATHREESHWARA NAGAR,
MYSORE-570 015

SYLLABUS
MASTER OF PHARMACY

M.Pharm-Drug Discovery
&
M.Pharm-Biopharmaceutics & Pharmacokinetics

2013
## M. PHARM: DRUG DISCOVERY

<table>
<thead>
<tr>
<th>Paper</th>
<th>Subjects</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paper I</td>
<td>Modern Bioanalytical Techniques</td>
<td>MBT</td>
</tr>
<tr>
<td>Paper II</td>
<td>Drug Design and Drug Research</td>
<td>MDD01</td>
</tr>
<tr>
<td>Paper III</td>
<td>Pharmacology in Drug Discovery</td>
<td>MDD02</td>
</tr>
<tr>
<td>Paper IV</td>
<td>Product Development and Commercialization</td>
<td>MDD03</td>
</tr>
</tbody>
</table>
PAPER I
MODERN BIOANALYTICAL TECHNIQUES
THEORY

Scope: This subject is designed to provide detailed knowledge about the importance of analysis of drugs in biological matrices.

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

- Extraction of drugs from biological samples
- Separation of drugs from biological samples using different techniques
- Bioanalytical method validation
- Guidelines for BA/BE studies.
- GLP and GCP

1 Analysis of drugs in biological matrices 07 Hrs
Analysis of drugs in use and drugs in Research and Development

2 Problems with analysis of biological matrices 10 Hrs
Properties of the biological media, small organic molecules, peptides and protein drugs, prodrugs, formulations, drug metabolites, other drugs, safety considerations.

3 Extraction of drugs and metabolites from biological matrices 10 Hrs
General principle and procedure involved in the bio-analytical methods such as Protein precipitation, Liquid - Liquid extraction and Solid phase extraction with special emphasis on Therapeutic Drug Monitoring.

4 Separation techniques 15 Hrs
Bio molecules separation by chromatography, thin layer chromatography, ion exchangers, molecular sieves, gel & capillary electrophoresis, western blot polymerase chain reaction, Gas chromatography, HPLC and LC MS/MS

5 Thermal Analysis and Tracer Techniques 15 Hrs
Principles of Thermal Analysis, Instrumentation Requirements, Applications
of Thermal Analysis, Concept of Radioactivity & Half life, $\alpha$, $\beta$, $\gamma$ emitters and their biological applications, Using tracers in assays, Detectors and counters, Concept of autoradiography, Radio labeled probes and their uses.


7 CHAPTER VII: An introduction to GLP and GCP

Good Laboratory Practice (GLP): Practicing GLP, Guidelines to GLP, Documentation of Laboratory work, Preparation of SOPs, Calibration records, Validation of methods, Transfer of methods, Documentation of results, Audits, Audit reports.

Good Clinical Practice (GCP): Origin of GCP, Requirements of GCP compliance, Guidelines for GCP, guidelines of ICH, guidelines of ICMR, Ensuring GCP, Documentation of GCP practice, Audit of GCP compliance
PAPER I  
MODERN BIOANALYTICAL TECHNIQUES

Practicals  75Hrs

Minimum 15 experiments to be conducted

1. Biomolecules separation utilizing various sample preparation techniques and Quantitative analysis of components by TLC and HPTLC techniques.
2. Biomolecules separation utilizing various sample preparation techniques and Quantitative analysis of components by HPLC techniques.
4. Protocol preparation for the conduct of BA/BE studies according to guidelines.

REFERENCES:

10. ICH guidelines
**PAPER: II**
**DRUG DESIGN AND DRUG RESEARCH**

**THEORY**

**Scope:** This subject is designed to provide detailed knowledge about the importance of lead compounds from natural and synthetic sources, different techniques of rational drug design and designing drugs for various biological targets.

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

- Discovery of lead molecules
- The different targets for drug discovery
- Chemistry and medicinal importance of different bioactive natural and synthetic compounds
- Various strategies to develop new drug like molecules.
- The design of new drug molecules using molecular modeling software
- Isolation, purification and characterization of important bioactive compounds.

1. **Lead discovery and Analog Based Drug Design**
   
   Rational approaches to lead discovery based on traditional medicine, Random screening, Non-random screening, serendipitous drug discovery, lead discovery based on drug metabolism, lead discovery based on clinical observation.

   **Analog Based Drug Design:** Bioisosteric replacement, rigid analogs, alteration of chain branching, changes in ring size, ring position isomers, design of stereo isomers and geometric isomers, fragments of a lead molecule, variation in interatomic distance.

2. **Lead pharmaceuticals of natural origin**
   
   a. Anticancer drugs: Taxols, Etoposide, Tenoposide
   
   b. Cardiovascular drugs: Statins, Teprotide, Dicoumarol
   
   c. Anti inflammatory drugs: Khellin, Sodium chromoglycate
d. Drugs affecting CNS : Morphine alkaloids

e. Antiparasitic drugs : Artemisinin, Quinine

f. Neuromuscular blocking drugs : Curare alkaloids

g. Anti asthmatic drugs : Vasicine

3  Quantitative Structure Activity Relationship (QSAR)  10 Hrs

SAR versus QSAR, History and development of QSAR, Types of physicochemical parameters, experimental and theoretical approaches for the determination of physicochemical parameters such as Partition coefficient, Hammet's substituent constant and Taft's steric constant. Hansch analysis, Free Wilson analysis, 3D-QSAR approaches like COMFA and COMSIA.

4  Molecular Modeling and virtual screening techniques  10 Hrs

**Molecular Modeling:** Introduction to molecular mechanics and quantum mechanics. Energy Minimization methods and Conformational Analysis, global conformational minima determination, Bioactive as global minimum conformations.

**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.

5  Informatics & Methods in drug design  8 Hrs

Introduction to Bioinformatics, pharmainformatics, chemoinformatics, chemogenomics, ADME databases, chemical biochemical and pharmaceutical databases; Drug design techniques using these databases.

6  Design of drugs for the following biological targets  10 Hrs

Agent acting on enzymes: DHFR, HMG-CoA Reductase, Phosphodiesterase, ACE, Transpeptidase, β-lactamase.

Agents acting on receptors: PPAR, protein kinases.

Agents acting on Nucleic acids: Topoisomerase, DNA and RNA polymerase,
Reverse transcriptase.

7  **Photochemical study and bioactive guided fractionation**  
10 hrs

General process of drug discovery from traditional system of medicine. General and advanced methods of extraction, isolation of bioactive moieties and their characterization by spectral methods for the following class of compounds.

- **Alkaloids**: Caffeine, Piperine
- **Glycosides**: Bacosides, Andrographolides
- **Resins**: Curcumin,
- **Essential oils**: Menthol, Citral, Dawana oil
- **Polyphenols/Flavonoids**: Quercetin, Rutin
- **Proteins**: Spirulina
- **Tannins**: Gallic acid, Ellagic acid
- **Saponins**: Ginseng, Diosgenin

8  **Tissue culture methods for the production of important secondary metabolites.**  
7 Hrs

Definition, type, media preparation, advantages and disadvantages. Hairy root culture, Biotransformation and transgenic plants. Production of important secondary metabolites.
PAPER: II  
DRUG DESIGN AND DRUG RESEARCH  

Practicals:  

1. Synthesis and characterize medicinally important compounds involving at least 2 steps  
2. 2D QSAR based experiments.  
3. 3D QSAR based experiments.  
4. Docking based experiments.  
5. Virtual screening based experiments  
6. Isolation and characterization of the following natural products  
   a. Caffeine form tea  
   b. Piperine form black pepper  
   c. Starch, amylase and amylopectin form potato  
   d. Curcumin from turmeric  
   e. Oleoresins from ginger  

7. Determination of ash and extractive / ash values, bitterness value, moisture content, hemolytic activity, foaming index  
8. Application of chromatographic techniques such as TLC/HPTLC/HPLC/GC in the analysis of herbal raw materials/extracts/formulations.  

Reference books:  

9. Advances in Medicinal Chemistry,
16. Bioinformatics; Methods and applications; Genomics, Proteomics and Drug Discovery; Rastogi, S. C. and Mendiratta and Rastogi, P.
PAPER III
PHARMACOLOGY IN DRUG DISCOVERY

THEORY
75Hrs (3Hrs/Week)

Scope: This subject is designed to provide comprehensive knowledge in the concepts of drug design and development process. The subject emphasizes on identification of endogenous mediators as drug targets, their validation, preclinical screening, toxicity studies of new chemical entities, clinical evaluation and regulatory aspects of drug development.

Objectives: On completion of this curriculum students shall be able to understand

- Comprehensive knowledge in Pharmacology
- Targets for Drug Discovery.
- Translational research.
- Regulatory aspects of drug development.

1 Drug discovery: Stages of drug discovery, identification, validation and diversity of drug targets. 4 Hrs

2 Biological targets: Structure and function of different enzymes, ion channels and receptors. Functional selectivity of receptors. Forces involved in Drug-Receptor Interaction. Principles and fractional occupancy, Drug-Receptor occupation, Schild analysis. Receptor polymorphism; Cell signaling and signal transduction pathways 14 Hrs

3 New Approaches in Drug Discovery: High-Throughput Screening, Pharmacogenomics, Proteomics, Array technology and Recombinant DNA technology of drugs. Disease targets for gene therapy. Monoclonal antibodies for diseases such as Diabetes, Cancer and neurodegenerative disorders. Biomarkers and its targets: Biosensors and Devices: Introduction and it’s applications 16 Hrs

4 Drug Development 35 Hrs

4.1. Laboratory animals 02 Hrs

Study of various laboratory animals and genetically modified animal species used in pre clinical research.
4.2. Pre Clinical development 11 Hrs

Selection of small molecules for potential targets to evaluate for therapeutic areas: Cancer, diabetes, pain and inflammation, cardiovascular, epilepsy, Parkinson’s disease and Alzheimer’s disease in animal models (both *in vitro* and *in vivo*).

4.3. Drug Safety Assessment 12 Hrs

Introduction to the *in vitro* toxicology: The importance of alternatives to animal testing and toxicity testing.

Detailed study of the principle behind the toxicity assessment using the following *in vitro* models: Phototoxicity, Cytotoxicity, AMES and HPRT Tests, Comet, Micronucleus and Chromosome Aberration Assays.

Introduction to Good Laboratory Practices and the role of regulatory guidelines (OECD and ICH)

Preclinical toxicity assessment: Systemic Toxicity (acute and repeated dose), Male Fertility, Female Reproduction and Developmental Toxicity, Local toxicity (dermal, ocular and inhalation), Allergenicity/Hypersensitivity, Genotoxicity and Carcinogenicity according to OECD and ICH guidelines.

Toxicokinetic study and its applications

4.4 Clinical trials 10 Hrs

Detailed study of various phases of clinical trials (Phase I, II, III and IV)

Pharmacoepidemiology; Case studies across therapeutic and disease areas, drug approvals and disapprovals: Concepts and applications of Pharmacovigilance

5 Biostatistics: Basic concepts of biostatistics: Mean, median, mode, standard deviation, Standard error of mean and probability, etc.

Parametric and non-parametric tests. Tests of significance (Student’s t-test, ANOVA, Kruskal-Wallis H-test, Wilcoxon’s Signed Rank test), Simple linear regression analysis.

6 Hrs
PAPER III
PHARMACOLOGY IN DRUG DISCOVERY

Practicals: 75Hrs

1. Preparation of cell culture media, primary and secondary cell cultures. Cell viability assays. Isolation of DNA from cells/tissues and separation using agarose gel electrophoresis.

2. *In vitro* screening of test compounds using suitable cell lines/enzymes for their potential activities against Cancer, diabetes, inflammation, cardiovascular, epilepsy, Parkinson’s and Alzheimer’s diseases, hepatotoxicity and oxidative stress.

3. *In vivo* screening of test compounds using suitable animal models for their potential activities against Cancer, diabetes, inflammation, cardiovascular, epilepsy, Parkinson’s and Alzheimer’s diseases hepatotoxicity and oxidative stress.

4. *In vitro* toxicity assessment of a test compound using suitable models such as AMES Test, HPRT Test, Comet Assay, Micronucleus Test and Chromosome Aberration Test

5. *In vivo toxicity* evaluation: Acute and repeated dose systemic toxicity studies

6. Statistical analysis exercises using appropriate statistical software’s (Graph Pad Prism, SPSS and Winolin).

7. Case studies of approvals and disapprovals of drugs

Reference Books:

4. Katzung, B.G; Basic and Clinical Pharmacology, 10th ed., 2007, Lange Medical Publisher, USA


10. Bacq Z.M., Cepek, Fundamentals of Biochemical Pharmacology


12. U. Satyanarayana. Biotechnology, Books and allied (P) Ltd., Kolkata


PAPER IV
PRODUCT DEVELOPMENT AND COMMERCIALIZATION

THEORY 75Hrs (3Hrs/Week)

Scope: Course designed to impart advanced knowledge and skills required to learn various aspects and concepts at pharmaceutical industries.

Objectives: On completion of this curriculum students shall be able to understand

- The elements of Preformulation studies & Pilot Plant Scale-up Techniques
- Material & Maintenance Management
- Biopharmaceutics & BA/BE, NDDS, IPR and Regulatory Filing

1 Preformulation 10Hrs

Physical characteristics: Particle size, shape, surface area, Solubilization, surfactants and its importance, temperature, pH, co-solvency; Techniques for the study of crystal properties and polymorphism.

Chemical characteristics: Degradation, Hydrolytic, oxidative, reductive, photolytic degradations;

Biopharmaceutics characteristics: Solubility, dissociation, Dissolution rate, diffusibility, and drug stability in GI tract. Physicochemical characteristics of new drug molecules with respect to different dosage forms.


Bioavailability: Objectives and considerations in bioavailability studies, Concept of equivalents, measurement of bioavailability, Determination of the rate of absorption, Bioequivalence and its importance, bioequivalence studies.
**Dosage Regimen:** Multiple dosing with respect to IV and oral route, Concept of loading dose, maintenance dose, Accumulation index, Adjustment of dosage in renal and hepatic impairment, Individualization of therapy, Therapeutic Drug Monitoring.

3 **Novel Drug Delivery Systems**

**Oral Drug Delivery Systems:** Introduction, development of novel DDS for oral controlled release drug administration, modulation of GI transit time. Approaches to extend GI transit time of DDS.

**Ocular Drug Delivery Systems:** Introduction, controlled ocular drug delivery-requisites & approaches for ocular drug delivery devices-matrix type, capsular type & implantable types.

**Transdermal Drug Delivery Systems:** Introduction, Permeation through skin, factors affecting permeation, permeation enhancers, basic components of TDDS formulation and evaluation of transdermal drug delivery systems.

**Targeted Drug Delivery Systems:** Concept. Advantages and disadvantages, biological processes and event involved in drug targeting, drug targeting through various systems like nanoparticles, liposomes, resealed erythrocytes, microspheres, magnetic microspheres, ethosomes, aquasomes, niosomes, phytosomes and monoclonal antibodies

**Protein and Peptide Drug Delivery:** Manifestation of protein instability and stability. Drug delivery systems for proteins and peptides with special reference to oral & nasal routes.

4 **Pilot Plant Scale up Techniques, Pharmaceutical Production Planning and Control** : Significance of pilot plant scale up study, Large scale manufacturing techniques (formula, equipment, process, stability and quality control) of solids, liquids, semisolid and parenteral dosage forms, General principles, Types of production systems, calculation of standard costs, production or process planning, Routing, Loading, Scheduling, Dispatching of records, Production control.
5 Pharmaceutical Pre-approval inspections, Post operational activities 10 Hrs

Evaluation of FDA, Pre-new drug application approval inspection, FDA risk based approach to inspections, Critical role Pharmaceutical scientist in product development and preparing for pre-approval inspection, Training requirements in product development, System based pre-approval inspection, cGMP risk assessment, and Management strategy, concepts in quality by design for drug development manufacture, Equipment cleaning during pharmaceutical product development and its importance to pre-approval inspection, Distribution, Recalled products, Returned products, Complaints and adverse effects, Drug product salvaging documents and formats

6 Pharmaceutical Regulations 20 Hrs

Laws and Acts: An introduction of following laws with regard to drug product design, manufacture and distribution in India (with latest amendments):

a. Drugs and Cosmetics Act 1940 and its rules 1945

b. National Pharmaceutical Pricing Authority (NPPA)


d. Patent Procedure in India

Registration Requirements: Forms, Clinical Trial Registration, Test License, Commercial Import License, Sale License, Manufacture License, Certificate of Pharmaceutical Product (CoPP)

Regulatory requirements: For import and product registration of New Drugs, DCGI & RCGM requirements, Generics, Medical Devices, Biologics, Herbals, Cosmetics & Fixed Dose Combinations, Export of drugs, traditional drugs, narcotics etc.

USA: Organization and structure of FDA. Federal register and CFR, History and evolution of FDC act, Hatch Waxman act and Orange book, Regulatory Approval Process for IND, NDA, ANDA. Regulatory requirements for Orphan drugs and
Combination Products, SUPAC & PMS. Changes to an approved NDA / ANDA.

**European Union:** Organization of EMA & Marketing Authorization procedures in EU (CP, DCP, MRP, NP). Eudralex directives for human medicines, Variations & extensions, IMPD. Requirements for BA/BE studies, Compliance of European Pharmacopoeia (CEP)/ Certificate of Suitability (CoS)

**Emerging Markets:** Overview, Regulatory Requirements for generic drug registration, new drugs and post approval requirements in BRICS countries (Brazil, Russia, India, China, South Africa) and Egypt.
PAPER IV
PRODUCT DEVELOPMENT AND COMMERCIALIZATION

Practical: 75Hrs

1. To study the effect of pH on the solubility of drugs
2. Accelerated stability of drugs in various dosage forms
3. Effect of pH on the stability of drugs in solution at elevated temperature
4. Improved solubility of drugs using surfactant systems
5. Improvement of dissolution characteristics of slightly soluble drugs by Various techniques
6. Influence of polymorphism on solubility and dissolution
7. Protein binding studies of a highly protein bound drug & poorly protein bound drug. (2 experiments).
8. Bioavailability studies of Paracetamol
9. Preparation and evaluation of NDDS (5 experiments)
10. Preparation of clinical trial protocol for registering trial in India
11. Registration for conducting BA/BE studies in India
12. Import of medical devices into India
13. Preparation of regulatory dossier as per Indian CTD format
14. Registering for different Intellectual Property Rights in India
15. Preparation and documentation for Indian Patent
16. Preparation of checklist for registration of IND as per ICH CTD format.
17. Preparation of checklist for registration of NDA as per ICH CTD format.
18. Preparation of checklist for registration of ANDA as per ICH CTD format.
19. Case studies on response with scientific rationale to USFDA Warning Letter
22. Comparison study of DMF system in US and EU
23. Preparation of an IMPD for EU submission.
24. Checklist for submission of Category III applications (Post approval changes) for TGA
25. Registration requirement comparison study in emerging markets (BRICS)
References:

4. Lachman L Liberman. Theory and Practice of Industrial Pharmacy by 3rd edition
15. Guidance for Industry on Submission of Clinical Trial Application for Evaluating Safety and Efficacy by CDSCO (Central Drug Standard Control Organisation)
16. Guidance for Industry on Requirement of Chemical & Pharmaceutical Information including Stability Study Data before approval of clinical trials / BE studies by CDSCO
17. Guidelines for Import and Manufacture of Medical Devices by CDSCO
18. Guidelines from official website of CDSCO
19. Drugs: From Discovery to Approval, Second Edition By Rick Ng
22. Preparation and Maintenance of the IND Application in eCTD Format By William K.S
23. Country Specific Guidelines from official websites