PHARMACEUTICAL TECHNOLOGY

FIRST SEMESTER

Course No. 3101 BIOSTATISTICS (THEORY)
(Common paper for all specializations)

LEARNING OBJECTIVES:
Learning this subject must help the student
1. To perform easily the calculations involved in all the statistical procedures, to properly understand all the concepts involved in testing of hypothesis and experimental design.

2. To apply the knowledge gained through this subject in the design, data collection and analysis involved in his/her research project in second year M.Pharm.

3. To interpret properly the experimental data in an industry or research setting in his/her future career and to take decisions in a more scientific manner.

UNIT I Introduction to biostatistics and applications of biostatistics in pharmaceutical and medical research. Tests of significance: Testing hypotheses- principle and applications of Z, t test and F tests. **8 hours**
UNIT II Analysis of Variance: 1-way, 2-way and 3-way classification. **8 hours**
UNIT III Non-parametric tests: Chi square test, sign test, Wilcoxon signed rank test, Wilcoxon rank sum test, Kruskal Wallis test, run test and median tests. **8 hours**
UNIT IV Design of Experiments: Principles of randomization, replication and local control;CRD, RBD, LSD - their applications and analysis of data. **8 hours**
UNIT V Factorial Experiments-Principles and applications; Use of software such as design expert and origin in the design of experiment **8 hours**
UNIT VI Probit analysis-Dose-effect relationships, calculation of LD_{50}, ED_{50} **8 hours**
UNIT VII Regression and correlation: Method of least squares, Correlation Coefficient, rank correlation and multiple regression. **8 hours**
UNIT VIII Optimization Techniques: Basic principles and advantages of optimization, Optimization using factorial design, the simplex lattice and sequential optimization.
8 hours
REFERENCE BOOKS
1. Statistics (Theory, Methods & Application) by D.C. Sancheti and V.K. Kapoor ; Sultan Chand & Sons; Educational Publishers, New Delhi

2. Comprehensive Statistical Methods by P.N. Arora, Sumeeth Arora and S.Arora;S.Chand Publication

3. Biostatistics- An Introductory Text by Avram Goldstein; The Macmillan Company, New York

4. Pharmaceutical Statistics Practical and Clinical Applications by Stanford Bolton, Charles Bon; Marcel Dekker Inc.

Course No. 3102 BIOPHARMACEUTICS AND PHARMACOKINETICS (THEORY)
LEARNING OBJECTIVES:
1. The course will help the student in understanding the various factors that contribute towards the bioavailability of a drug.

2. The student would gain knowledge on topics like drug interactions and pharmacokinetics. The student would be able to correlate *in vitro* and *in vivo* data and design experimental models for bioavailability studies.

UNIT I Drug Absorption, Distribution, Biotransformation and Excretion: Absorption of drugs, Significance of metabolisms involved in the absorption and bio transformation of drugs. Effects of Physico-Chemical, Pharmaceutical and Biological Factors on absorption, distribution, metabolism and excretion. Renal and Non renal Excretion Concept of clearance. **10 hours**

UNIT II Bioavailability and Bioequivalence of Drug Products: Factors-Assessment-Experimental designs and protocol for bioavailability and bioequivalence studies as per CDSCO, Schedule Y guidelines and GCP guidelines, *in-vitro and in-vivo* correlation of bioavailability, methods to enhance bioavailability. Statistical considerations in comparative bioavailability studies. **8 hours**

UNIT III Drug Interactions: Interaction of drugs with food, Classification of food drug interactions, models for estimation of pharmacokinetic parameters in food drug interaction studies. Effect of alcohol, smoking on drugs. Drug-Drug Interactions: factors contributing to drug interactions, Mechanisms of drug interactions with emphasis on pharmacokinetic interactions. **8 hours**

UNIT IV Pharmacokinetics: Basic consideration, pharmacokinetic models, Pharmacokinetic Parameters, Compartment modeling: One compartment model- IV bolus, IVinfusion, Extravascular; MultiCompartmentmodels; Twocompartmentmodel- IV bolus, IV infusion, Extravascular. Application of pharmacokinetics in new drug development and designing of dosage forms and novel drug delivery systems. Kinetics of multiple dosing-dosage regimens-loading and maintenance doses of sustained release and continuous blood levels. Concepts of software used in the pharmacokinetic analysis Win Nonlin® and Kinetica. **10 hours**

UNIT V Non-linear and Clinical Pharmacokinetics: Concepts of linear and non-linear pharmacokinetics, Michaelis - Menten Kinetics characteristics. Basic kinetic parameters, possible causes of non-induction, non-linear binding, non-linearity of pharmacological responses. **7 hours**

UNIT VI Time Dependent Pharmacokinetics: Introduction, classification, physiologically induced time dependency, Chromo pharmacokinetics. **6 hours**

UNIT VII Non Compartmental Analysis based on Statistical Moment Theory Statistical Moments, Bioavailability, Clearance, half-life, Absorption kinetics, Apparent volume of distribution, fraction metabolites, Predicting Steady State Concentrations, Predicting time to steady state. **7 hours**

UNIT VIII Clinical Pharmacokinetics: Altered Kinetics in Paediatrics, Geriatrics, Kinetics in GI, Liver, Cardiac, Renal and Pulmonary Disease State. **7 hours**

REFERENCE BOOKS:

1. Pharmacokinetics, Milo Gibaldi, 2nd Ed.
2. Applied Biopharmaceutics and Pharmacokinetics, Leon Shargel, 5th Ed.
3. Biopharmaceutics and Clinical Pharmacokinetics, Robert E. Notari, 4th Ed.
4. Modern Pharmaceutics, Gilbert S. Banker, Christopher T. Rhodes, 4th Ed.
5. Clinical Pharmacokinetics and Pharmacodynamics – Concepts and Applications, Malcolm Rowland and Thomas N. Tozer, 4th Ed.
6. Drug Disposition and Pharmacokinetics, Stephen H. Curry, 3rd Ed.
7. Current concepts in the Pharmaceutical Sciences-Biopharmaceutics, James Swarbrick
8. Current concepts in the Pharmaceutical Sciences-Dosage Form Design and Bioavailability, James Swarbrick

Course No. 3103 BIOPHARMACEUTICS AND PHARMACOKINETICS (PRACTICAL)

1. Effect of particle size on the drug dissolution using drugs like aspirin, salicylic acid, nitrofurantoin

2. Effect of surfactant on the drug dissolution using drugs like sulfamethoxazole, nefidipine.

3. Effect of ointment base on drug diffusion using agar plate method and diffusion membrane.
4. Determination of protein binding effect on drugs by using dialysis sac method using protein bound drugs.

5. Improvement in the dissolution of drugs by solid dispersion, cyclodextrin complexation etc.

6. To study the effect of sink condition on dissolution of drugs using discriminatory dissolution medium

7. To study the effect of permeation enhancers on drug diffusion using Franz-diffusion cell using suitable biomembranes.

8. Calculation of pharmacokinetic parameters using reported data.

9. Calculation of bioavailability and bioequivalence from the given data using different approaches.

10. In vitro-in vivo correlations using experimental data.

11. Preparation of experimental protocols for carrying out pharmacokinetic, pharmacodynamic, bioavailability and bioequivalence studies using suitable experimental designs for the given data.

Course No.3104 ADVANCED PHYSICAL PHARMACEUTICS (THEORY)
LEARNING OBJECTIVES:
On learning this subject, the student must understand
1. The concepts of solubility, solubilization, dissolution, compression, granulation, stability, stability testing, polymers and biodegradable polymers.

2. The student must be able to apply these concepts in preparing dosage forms that have enhanced dissolution and bioavailability, and in performing operations like tablet compression, stability testing and polymer characterization, required in the industry.

UNIT I Solubilisation of drugs in aqueous media:
Solubility, ideal solubility, activity coefficient, Hildebrand solubility approach, solubility parameter, estimating solubility and dissolution rate, apparent solubility enhancement from different solid phases, pH control, salt formation, buffers, cosolvents, dependence of solubilisation on solute properties, dependence of solubilisation on cosolvent properties, multiple cosolvents, surfactants, complexation, self-association and stacking complexation, inclusion complexes, combination of pH and complexation. **8 hours**
UNIT II Solubilising excipients in pharmaceutical formulations:
Introduction, oral formulations(water soluble organic solvents, surfactants, water insoluble organic solvents, water insoluble solids, cyclodextrins, microemulsion oral formulations); injectable formulations (water soluble organic solvents, surfactants, cyclodextrins, phospholipids, emulsions), oily injectable formulations and transdermal formulations.
8 hours
UNIT III Granulation and tablet characteristics: Granule formation and structure, particle size measurement and interpretation, shape determination, surface area, densities and packings, granule strength and friability, electrostatic properties, flow properties, ease of consolidation and mechanisms; control of tablet characteristics, such as , size and shape, tablet thickness, hardness, friability, disintegration, weight variation and content uniformity. **8 hours**
UNIT IV Compression: properties of tablets influenced by compression (elastic deformation, plastic deformation, brittle fracture, micro squashing, density and porosity, hardness and strength, specific surface, disintegration, dissolution); measurement of compressional force, energy expenditure,

transmission of force. Consolidation, role of moisture, compression and consolidation under high loads, effect of friction, force distribution, development of radial force die wall lubrication, Heckle plots, energy involved in compaction, force-displacement curves, instrumentation of tablet machines, single station presses, multistation presses and signal processing. **8 hours**

UNIT V Stability: physical, chemical and microbiological stability, quantitation of rate of degradation (zero order kinetics, first order kinetics, shelf life calculation), factors influencing reaction rate(temperature, pH, ionic strength, dielectric constant), methods of stabilizing dosage forms. **8 hours**

UNIT VI Stability testing: ICH guidelines for stability testing, selection of batches and container closure systems, matrixing and bracketing design, storage conditions and testing frequency, climatic zones concept, stability testing in different stages of drug product life cycle, specific stability tests for various dosage forms. Photo stability studies, expiration dating, overages calculation. **8 hours**

UNIT VII Polymers: Definitions, molecular weight averages, determination of molecular weight from solution viscosity, polymers as thickening agents, polymers in solutions, preparing polymer solutions, thermodynamics of polymer solutions, gel formation, coacervation and microencapsulation, Pharmaceutical application of polymers.

8 hours

UNIT VIII Hydrogels (over view, synthesis, structure and properties, swelling ratio and water content, use in drug delivery, mucoadhesive hydrogels, sensitivity to pH changes, Polyethylene oxides), lipids(physical and chemical properties, applications in drug delivery), Biodegradable polymers as drug carriers (overview, factors affecting selection of polymer, factors affecting drug release, degradation mechanisms, polyesters, polyanhydrides). **8 hours**

REFERENCE BOOKS:

1. Encyclopedia of Pharmaceutical Technology, edited by James swarbrick, Third Edition, Informa Healthcare publishers.

2. Pharmaceutical Dosage Forms, Tablets, Volume II, edited by Herbert A. Lieberman and Leon Lachman; Marcel Dekker, Inc.

3. The Theory and Practice of Industrial Pharmacy, Fourth Edition, edited by Roop k Khar, S P Vyas, Farhan J Ahmad, Gaurav K Jain; CBS Publishers and Distributors Pvt. Ltd.

4. Martin's Physical Pharmacy and Pharmaceutical Sciences, Fifth Edition, edited by Patrick J. Sinko, BI Publications Pvt. Ltd.

Course No. 3105 ADVANCED PHYSICAL PHARMACEUTICS (PRACTICAL)

1. Stability studies on commercial tablets containing drugs like aspirin over two months at room temperature, 37°C and 45°C.

2. Stability studies on suspensions containing drugs like aspirin over 20 days at room temperature, 37°C and 45°C.

3. Determination of molecular weight by viscosity method, by Mark- Houwink equation for gelatin, methyl cellulose and polyvinyl alcohol.

4. Effect of temperature on the decomposition of bromophenol blue at three temperatures and two pH values

5. Effect of pH on the decomposition of aspirin.

6. Preparation of granules, drying by conventional dryer and fluidized bed dryer and comparing the granules by their flow properties.

7. Preparation of tablets by two different sets of granules with different flow properties; and finding the effect of variability in flow rate of granules on the weight variation of resultant tablets using drugs like Metronidazole.

8. Drawing the coacervation curve on a three component system graph (gelatin, sodium sulphate and water) for gelatin, sodium sulphate system.

9. Determination of bloom strength of gelatin.

10. Preparation of liquid paraffin emulsion in a colloid mill; determining the effect of duration of milling (up to 10 minutes), on the heat developed in the emulsion (temperature) and on the extent of micronization (globule size analysis).

11. Visiting a pharmaceutical industry and observing the modern equipment used in production and quality control.

12. Carrying out accelerated stability studies of disperse systems using freeze thaw technique and centrifugation techniques and prediction of shelf life.

Course No. 3106 Comprehensive viva

PHARMACEUTICAL TECHNOLOGY

SECOND SEMESTER

Course No. 3207 MODERN ANALYTICAL TECHNIQUES (THEORY)
(Common paper for all specializations)
Course No. 3208 QUALITY ASSURANCE AND DRUG REGULATORY AFFAIRS (THEORY)(Common paper for all specializations)
Course No. 3209 NOVEL DRUG DELIVERY SYSTEMS (THEORY)
LEARNING OBJECTIVES:
On learning this subject, the student will understand the concepts in parenteral controlled release and will be able to design sustained or controlled or novel drug delivery systems
UNIT I Introduction to Parenteral Drug Delivery: Basic requirements of Parenteral Controlled release products; release profiles and biofate of intravenously administered systems and intramuscularly administered systems. **4 hours**
UNIT II Targeted Drug Delivery: Concepts of Targeting, Rationale of Drug Targeting, Carriers, Passive Targeting, Inverse Targeting, Active Targeting, First, Second, and Third order Targeting, Ligand Mediated Targeting, Physical Targeting, Dual Targeting, Double Targeting, Combination Targeting and problems associated with Targeted Delivery Systems. **4 hours**
UNIT III Targeting to the Brain, Targeting to the tumour and Targeting to the colon. **4 hours**
UNIT IV Sustained release formulations (encapsulated slow release granules, tableted slow release granulations, matrix tablets, drug complexes, ion activated systems, pH independent systems, altered density systems, colonic release systems). **8 hours**
UNIT V Controlled release formulations (osmotic pressure activated systems, hydrodynamic pressure activated systems, hydrodynamically balanced systems, the synchron system, the Penn kinetic system and bio adhesive system); *In vitro* and *in vivo* product evaluation and testing.
10 hours

UNIT VI Design and Evaluation of Novel drug delivery systems: Ocuserts, transdermal drug delivery systems, *In situ* gelling systems, stimuli-sensitive "smart" polymers as drug delivery systems, glucose-responsive insulin delivery, polymer drug conjugates.
10 hours
UNIT VII Novel carriers for controlled targeted drug delivery: Liposomes, Niosomes, Ethosomes, Transferosomes, Virosomes, polymeric nanoparticles, solid lipid nanoparticles, inorganic nanoparticles. **10 hours**
UNIT VIII Supra molecular systems, micelles/reverse micelles, lipoproteins, liquid crystals, resealed erythrocytes, carbon nanotubes, self-emulsifying drug delivery systems, Aquasomes, DQA somes, nanosuspension, nanocapsules. **10 hours**
REFRENCE BOOKS:
1. Targeted and Controlled Drug Delivery, Novel Carrier Systems by S. P. Vyas and R. K. Khar, CBS Publishers and Distributors Pvt. Ltd, First Edition 2012
2. Lachman/Lieberman's The Theory and Practice of Industrial Pharmacy, Fourth Edition, Editors: Roop K Khar, S P Vyas, Farhan J Ahmed, and Gaurav K Jain, CBS Publishers and Distributors Pvt ltd, 2013.

Course No.3210: PRODUCT FORMULATION AND DEVELOPMENT (THEORY)
LEARNING OBJECTIVES:
The course gives a foundation on
1. Pre-formulation aspects involved in product development.
2. The student will be able to carry out the functions in the production division of a pharmaceutical industry by understanding the production, scale up techniques, quality control and packaging aspects of large scale manufacture of different dosage forms like oral liquids, tablets, capsules, parenterals etc.

UNIT I Pharmaceutical Product Development: Introduction to product development. Goals of preformulation, preformulation drug characterization in a structured program for different dosage forms. Influence of the parameters like intrinsic solubility, dissociation constant (pK_a), salts, solvents, partition coefficient, dissolution, polymorphism, particle size, shape and surface area, bulk density, flowability, hygroscopicity, stability indicating assays, and stability. **10 hours**
Formulation Development of the following dosage forms:
UNIT II Oral Liquids: Monophasic Systems, Solutions: Vehicles, Additives Used in Formulation of Solutions, Oral Solution Products, Equipment, and Compounding, Filling of Liquids.
Biphasic Systems: Suspensions: Formulation and Manufacture of Suspension, Evaluation of Stability.
Emulsions: Microemulsions, Multiple Emulsions, Nanoemulsions Theories of Emulsification, Preparation of Emulsion, Equipment's Used for Emulsification, Stability, evaluation of Emulsions and their applications in drug delivery. **8 hours**
UNIT III Tablets: Types of Tablets, Components of a Tablets, Excipients, Granulation Methods, Mechanisms and Equipment, Processing Problems of Tablets, working of tablet Machines.
Tablet Coating: Comparison of different coating techniques procedures. Problems involved in each coating and trouble shooting. Equipment used for sugar coating, film coating, aqueous film coating, compression coating, enteric coating. Novel Drug Delivery. Technologies: Mouth Dissolving Tablets (Orasolv, Durasolv and Zydis Oral Fast Dissolving Dosage Forms), Oral Controlled Release Drug Delivery Systems, Osmotically Controlled release dosage forms, Nanocrystal Technology, IDD Formulations, Self-Repairing Tablets, Effervescent Tablets, Dissocubes. **10 hours**

UNIT IV Capsules and Microencapsulation: Types of gelatin and excipients used in the preparation of soft and hard gelatin capsules. Related advantages of soft and hard gelatin capsules. Methods and equipment involved in the manufacturing of soft and hard gelatin capsules. Powder Filling, Choice of Excipients, Non Powder Filling, Storage, packaging and Stability Considerations of hard gelatin capsules. Micro encapsulation**:** Methods and Applications of Microencapsulation. **10 hours**

UNIT V Parenteral Products: Routes of administration, categories of Parenteral Products based on volume, formulation additives, development of Parenteral Products, Important parameters for Parenterals development, manufacturing of Parenterals, Quality Control requirements for Parenterals. **7 hours**

UNIT VI Opthalmic Products: Absorption of drugs in the Eye, product development of ophthalmic products, general safety considerations, conventional ophthalmic dosage forms, Packaging and Storage, approaches for efficient drug delivery.

Ophthalmic implants and shunts, Inserts, Non erodible ocular inserts, Erodible Ocular inserts, Contact lens, recent development of contact lenses (bandage lenses, therapeutic contact lenses in drug delivery, Silicone hydrogel based lenses), Collagen Shields and Implants, An anopthalmos and orbital implants, glaucoma shunts, particulate based drug carriers. **6 hours**

UNIT VII Topical Products: Structure of skin, Mechanisms of skin penetration, Percutaneous Absorption, Design of topical drug products (Gels, Liquid-Preparations, powders, Ointments), Novel Drug Delivery Systems for topical Drug Delivery (Micro emulsion, liposome, Transferons, Ethosones, Hydrogels), Evaluation of topical dosage forms.Rectal Products: Advantages, Rectal preparations. **6 hours**

UNIT VIII Pharmaceutical Packaging: Packaging Materials, Glass, Plastic, Metals, Rubber, Evaluation of Packaging materials. Special problems of container product interactions, pharmacopoeial specifications tests and standards for packaging materials. **6 hours**

REFERENCE BOOKS:

1. Lachmen/Liberman - Theory and Practice of Industrial Pharmacy, Roop K. Khar, S.P. Vyas, Farhan J. Ahmad, Gaurav K. Jain, 4th Ed.
2. Pharmaceutical Dosage Forms and Drug Delivery Systems, Loyd V. Allen Jr., Nicholas B. Popovich, Howard C. Ansel, 9th Ed. 40
3. Aulton's Pharmaceutics – The Design and Manufacture of Medicines, Michael E. Aulton, 3rd Ed.
4. Remington – The Science and Practice of Pharmacy, 20th Ed.
5. Encyclopedia of Pharmaceutical Technology, James Swarbrick, 3rd Ed.
6. Pharmaceutical Dosage Forms – Tablets Vol 1 to 3, A. Liberman, Leon Lachman and Joseph B. Schwartz
7. Pharmaceutical Dosage Forms – Disperse Systems Vol 1 to 3, H.A. Liberman, Martin, M.R. and Gilbert S. Banker.
8. Pharmaceutical Dosage Forms – Parenteral Medication Vol 1 & 2, Kenneth E. Avis and H.A. Libermann.

Course No. 3211 PRODUCT FORMULATION AND DEVELOPMENT (PRACTICAL)

1. Preformulation studies of drugs like aspirin, sulfamethoxazole, nefidipine etc. using different excipients as per ICH guidelines.

2. Preparation and evaluation of matrix controlled drug delivery systems using suitable drugs like theorphylline, diclofenac, aceclofenac.

3. Formulation and evaluation of oral disintegrating tablets using suitable drugs.

4. Formulation and evaluation of transdermal patches

5. Preparation and evaluation of microcapsules using techniques like coacervation-phase separation, ionic gelation method.

6. Formulation of dry syrup and its evaluation.

7. Formulation and evaluation of gastric floating drug delivery system

8. Comparison of different gels using diclofenac/aceclofenac like drugs

9. Formulation of liposomes and their characterization using microscopy.

10. Formulation and evaluation of suspensions containing suitable drugs.

11. Studies on effect of emulsifying agents on the stability of emulsion.

Course No. 3212 Comprehensive Viva

THIRD SEMESTER

Course No.3313 Seminar on the objectives and work plan of the proposed project to be completed within one month from the commencement of the project.

Course No.3314 Mid-term project review at the end of third semester.

Course No.3315 Seminar on the selected topic.

FOURTH SEMESTER

Course No.3416 Thesis evaluation.

Course No.3417 Thesis viva-voce.