

Punjab Technical University, Jalandhar
M. Pharm (Pharmaceutics)
Study Scheme

1st Semester

Sr. No.	Course Code	Subject	Exam Hours	Maximum Marks	
				Int.	Ext.
1	PHCEU 511	Advanced Pharmacokinetics and Biopharmaceutics	3	20	80
2	PHCEU-513	Dosage - forms Design, Development and Process Validation	3	20	80
3	PHCEU-515	Novel Drug Delivery Systems	3	20	80
4	PHCEU-517	Pharmaceutics Laboratory-I	12	20	80
Total				80	320

2nd Semester

Sr. No.	Course Code	Subject	Exam Hours	Maximum Marks	
				Int.	Ext.
1	PHCEU 512	Pharmaceutical Technology	3	20	80
2	PHCEU-514	Drug Regulatory Affairs and IPR	3	20	80
3	PHCEU-516	Molecular Biology and Pharmaceutical Biotechnology	3	20	80
4	PHCEU-518	Pharmaceutics Laboratory – II	12	20	80
Total				80	320

M. Pharm (3rd & 4th Semester)**(Research work for one year)**

The thesis shall be presented by the candidate at the end of record academic year. The thesis shall be evaluated as under:

Evaluation of written thesis	:	Maximum Marks: 200
Presentation of Seminar on thesis & Viva Vice	:	Maximum Marks: 100
		Total Marks: 300

PHCEU-511 ADVANCED PHARMACOKINETICS AND BIOPHARMACEUTICS**External Marks: 80****4 Hrs/Week****Internal Marks: 20****Total Marks: 100****1. Compartmental pharmacokinetics (6 lectures)**

Review of fundamentals, Terminology, Basics of kinetics of single and multiple dose administration following instantaneous and non-instantaneous routes, one and two compartment body model kinetics, limitations of compartmental analysis.

Non-compartmental Pharmacokinetic Modeling Approach (7 lectures)

Merits of model-independent non-compartmental approaches, definition and significance, statistical moments, AUC, AUMC and their determination using trapezoidal and log-trapezoidal techniques, MRT and its significance in pharmacokinetics, computation of statistical moments from plasma and urine data, cut-off error, MDT, MTT, MAT, problem solving.

2. Nonlinear Pharmacokinetics (6 lectures)

Definition, significance and applications with literature examples, recognition of non-linearity, computation of nonlinear pharmacokinetic parameters (V_m , K_m , AUC, etc.) by single Michaelis Menten kinetics.

3. Clinical Pharmacokinetics (8 lectures)

Introduction; pharmacokinetic relationships; duration of response; kinetics of pharmacological response; explanation of clinical response via pharmacokinetics; monitoring plasma concentrations of drugs during clinical use, Therapeutic drug monitoring (TDM), turnover concepts, individualization of dosage and dosage regimen, variability, Effect of genetics, age, weight, pharmacokinetics, disease and interacting drugs, use of creatinine clearance, problem solving.

4. Protein Binding (4 lectures)

Theory of plasma protein binding and implications, elements of Scatchard, Klotz and Rosenthal analyses for computation of binding parameters, experimental techniques to determine protein binding with their merits and limitations, factors influencing protein binding, effect of binding on drug pharmacokinetics.

5. Biopharmaceutics (5 lectures)

Review of physicochemical, pharmaceutical and physiological variables affecting drug absorption from gastrointestinal tract.

6. Bioavailability and Bioequivalence Concepts: (5 lectures)

Assessment of bioavailability from plasma and urine level data, design and analysis of bioequivalence trials, Crossover designs, bioavailability of oral and non-oral dosage forms, statistical analysis of bioavailability and bioequivalence, pharmacodynamic models, Federal perspectives.

7. *In vitro-In vivo* correlations (IVIVC) (5 lectures)

Concepts, Biopharmaceutical Classification Scheme (BCS), varied IVIVC approaches with applications and limitations, dissolution as a surrogate to bioavailability for immediate release and extended release formulations, Federal perspectives

READING MATERIAL RECOMMENDED

1. J.G. Wagner, Fundamentals of Clinical Pharmacokinetics, Drug Intelligence Publications, Hamilton, Ill, 1975.
2. J.G. Wagner, Pharmacokinetics for the Pharmaceutical Scientist, Technomic, Pa, 1993.
3. L. Shargel, and A. Yu, Applied Biopharmaceutics and Pharmacokinetics, Appleton and Large, Norwalk, CT, 1993.
4. M. Gibaldi and D. Perrier, Pharmacokinetics, J. Swarbrick, ed., Marcel Dekker, NY
5. M. Gibaldi, Biopharmaceutics and Clinical Pharmacokinetics, Lea & Febiger, Philadelphia.
6. W.R. Gillespie, Non-compartmental versus Compartmental Modeling in Clinical Pharmacokinetics, Clinical Pharmacokinetics, 20, 253-262 (1991).
7. R.D.Purves, "Optimum Numerical integration methods for the estimation of area under the curve (AUC) and area under the moment curve (AUMC)". J.Pharmac. Biopharma., 20 (3), 211-226,1992.
8. P.G.Welling, F.L.S. Tse and S.V. Dighe (eds) *Pharmaceutical Bioequivalence*, Marcel Dekker Inc. New York, USA 1991.
9. A.Yacobi, J.P.Skelly and V.K.Batra (ed.) Toxicokinetics and new drug development, Pergamon Press, New York USA., 1989.
10. Singh, B. Protein binding of drugs: A review, Pharmacos, 1991.
11. www.fda.gov/cder/guidance

PHCEU – 513 Dosage- forms Design, Development and Process Validation

External Marks: 80

4 Hrs/Week

Internal Marks: 20

Total Marks: 100

1. Preformulation (6 lectures)

Introduction, aims of preformulation, physicochemical properties, criteria for selection of drug and excipients, Excipient compatibility.

2. Solubility and solubilization (5 lectures)

Solubility and solubilization; techniques to improve drug solubility including surfactant system, cosolvent, solid state manipulation, complexation and chemical modification.

3. Partition coefficient (6 lectures) Partition coefficient; pharmaceutical significance of partition coefficient, correlation with *in vivo* performance, experimental and theoretical techniques to estimate log P values including shake flask, chromatography, Hansch & Leo/Rekker principle, effect of pH and temperature on partition coefficient**4. Solid state Pharmaceutics (5 lectures)**

Crystallinity, crystal habit, polymorphism, amorphous state, solvates, hydrates, thermal methods (DSC, DTA, TGA, TMA) and other analytical techniques such as X-Ray diffraction analysis for characterization.

5. Complexation (4 lectures)

Metal and organic molecular complexes, Inclusion complexes with reference to cyclodextrins, types of cyclodextrins their pharmaceutical applications.

6. Pharmaceutical Rheology (5 lectures)

Modern concept of rheology, viscoelastic analysis of semisolids, application and practice of rheology, selection of most suitable viscometer for a given sample.

7. Polymers (7 lectures)

Polymer classification, physicochemical properties and polymer solutions. Biodegradable and Nonbiodegradable polymers. Application of polymers in controlled release of drugs, transport of small molecules in polymers, ionic polymers as drug carriers.

8. Pharmaceutical Process Validation (12 lectures)

Basic concept, definition and regulatory basis of validation. Benefits of validation. Phases of equipment validation such as pre-purchase, post-purchase (IQ, OQ and PQ) and qualification of established /in-use equipment. Types of process validation related to prospective, retrospective and concurrent process validation. Re-validation of validation process and scale-up and post approval changes (SUPAC). Validation of tablets, liquids and sterile products. Validation of steam, dry heat, gaseous, radiation and filtration sterilization processes. Analytical Validation.

READING MATERIAL RECOMMENDED

1. S H Yalkowsky (Ed), Techniques of Solubilization of Drugs, Marcel Decker Inc., Newyork USA
2. A Martin, Physical Pharmacy, 3rd Edition. B. I. Waverly Pvt. Ltd., New Delhi, India 1995.
3. J.I. Wells, Pharmaceutical Preformulation: The Physicochemical Properties of Drug Substances, Ellis Horwood, Chiechester (UK), 1998.
4. R. Berry and R. A. Nash, Pharmaceutical Process Validation, Marcel Dekker, N.Y. (1993)
5. N. K. Jain (Editor), Pharmaceutical Product Development, Ist Edition, CBS Publisers and Distributer, New Delhi.
6. N. K. Jain (Editor), Controlled and novel drug delivery systems. Ist Edition, CBS Publisers and Distributer, New Delhi.
7. G.S Banker and C.T. Rhodes, Modern Pharmaceutics, second edition, Marcel Decker Inc., Newyork USA
8. S.P.Vyas and R.K.Khar, controlled drug delivery, concept and advances, first edition 2002, vallabh prakashan , Delhi.

PHCEU-515 Novel Drug Delivery Systems**External Marks: 80****4 Hrs/Week****Internal Marks: 20****Total Marks: 100****1. Controlled Drug Delivery (8 lectures)**

Fundamentals of Controlled Release (CR) Drug Delivery: Rationale of sustained/controlled drug delivery; Physicochemical and biological factors influencing design and performance of CR products, therapeutic status of CDDS. Theory of mass transfer; Fick's first and second laws and their applications in drug release and permeation. Pharmacokinetic/ pharmacodynamic basis of controlled drug delivery; bioavailability assessment of CR systems

2. Design and fabrication of technology based CR systems (21 lectures)

- a. Strategies and design of oral controlled release delivery systems, oral systems based on dissolution, diffusion and dissolution, ion-exchange resins, pH-independent formulations, altered density formulations. Bucco/mucoadhesive systems. Osmotic controlled oral drug delivery
- b. Parenteral systems, biopharmaceutic considerations, design and development, polymeric microspheres, dispersed drug delivery.
- c. Implantable therapeutic systems, biocompatibility of polymers and carriers; Intrauterine devices and intravaginal devices.
- d. Transdermal therapeutic systems (TTS): Drug absorption through skin, permeation enhancers, basic components of TTS, approaches to development and kinetic evaluation, Testing of transdermal patches, pressure sensitive adhesives; iontophoresis, sonophoresis and electroporation.
- e. Novel ocular drug delivery systems: Ocular therapeutics and constraints to effective delivery, formulation considerations to improve the ocular bioavailability, ocular inserts including insoluble and soluble inserts, non-corneal routes and their use for systemic drug delivery.

3. Colloidal and supramolecular delivery systems (10 lectures)

- i. Closed bilayered system: Historical background, structural aspects, preparation, characterization, evaluation and applications, specialized liposomes and niosomes.
- ii. Nanoparticles, microspheres: Method of preparation, characterization, evaluation and pharmaceutical applications.
- iii. Multiple w/o/w emulsions as drug vehicles. Introduction, composition of the multiple emulsion and stability, influence of the nature of oily phase, methods for stabilizing w/o/w multiple emulsions, mechanisms of transport of solutes, *in vivo* studies.
- iv. Microemulsions: Introduction, structure of microemulsions, solubilization and formulation of microemulsions, Self-emulsifying drug delivery systems (SEDDS), transport properties and pharmaceutical applications of emulsions.

4. Protein and peptide drug delivery (5 lectures): Considerations in the physiological delivery of therapeutic proteins; carrier-mediated transport of peptides and peptide analogues, problems associated with the delivery of protein and peptides (5 lectures)**5. Targeted drug delivery (4 lectures):** History, concept, types and key elements; ideal carrier system and approach with special reference to organ targeting (e.g. brain, tumor, lung, liver and lymphatics); Basics of temperature, pH and magnetically induced targeting tactics.(5 lectures)**READING MATERIAL RECOMMENDED**

1. J.R. Robinson & V.H.L. Lee (Eds), Controlled Drug Delivery, Fundamentals and applications, Vol. 29&Vol. 31, 2nd Edition, Marcel Dekker, N.Y. 1987
2. Y.W. Chien (Ed.), Transdermal Controlled Systemic Medications, Marcel Dekker, N.Y. 1987.
3. S.D. Bruck, Controlled Drug Delivery, Vol.1 (Basic Concepts) CRC Press. Florida, 1983
4. S.D. Bruck, Controlled Drug Delivery, Vol. II (Clinical Applications) CRC Press. Florida, 1983.
5. P. Tyle and B. Ram, Targeted Therapeutic Systems, Marcel Dekker, N.Y., 1990.
6. L.F. Prescott and W.S. Nimmo, Novel Drug and its Therapeutic Applications, John Willy and Sons, Chichester (1990).
7. Targeted and controlled drug delivery by S. P. Vyas and R. K. Khar, 2001
8. N.K. Jain, Controlled and novel drug delivery, 1997, CBS, New Delhi.
9. N.K. Jain, Advances in Controlled and novel drug delivery, 2001, CBS, New Delhi.

PHCEU-517 PHARMACEUTICS LABORATORY-I

External Marks: 80

16 Hrs/Week

Internal Marks: 20

Total Marks: 100

1. Experiments based on Biopharmaceutics and Pharmecokinetics
2. Experiments based on dosage-forms –Design
3. Experiments based on drug delivery systems

PHCEU -512 PHARMACEUTICAL TECHNOLOGY

External Marks: 80

4 Hrs/Week

Internal Marks: 20

Total Marks: 100

1. Improved tablet production and coating systems (13 lectures)

Benefits, process design considerations; materials handling, processing step combination and elimination, tablet production equipment, layout and design of facilities, materials flow, quality assurance procedures including in-process quality control, construction, equipment and environmental considerations, materials management and inventory control. Advances in coating process, fluid-bed coating, particle coating.

2. Processing of parenteral and related sterile products (15 lectures)

Material management, humidity and temperature controls, air filtration systems, dust collectors, etc. manufacturing including various aspects of preparing SVP solutions, suspensions, powders/ freeze dried powders for reconstitution, filling, sealing, inspection and labeling, raw materials including water, stability, storage and inventory control, batch mixing, clarification by membrane filters and support systems. Environmental factors in the design of parenteral production facilities.

3. Capsules & microencapsulation (14 lectures)

3.1 Hard gelatin capsules: Development of hard geletin capsules as a dosage form . Manufacturing process and material used in the shell and the steps used in its manufacturing such as sorting, printing, size and shapes, sealing and self locking closures. Different materials used for automatetic filling based on auger, vibratory and piston tamp fill (Dosing Disk and Dosator Machines) principles. General considerations in the design of hard gelatin capsule for formulations ,storage, packaging and stability consideration.

3.2 Soft geletin capsules: General considerations of the development of soft geletin capsules as a dosage form composition of shell, formulation strategies and carriers of the drug used and their manufacturing devices.

3.3 Materials other than gelatin used for capsule formulation.

3.3 Microencapsulation: Microencapsules and microspheres as drug delivery systems. Different techniques and methods employed for micra encapsulation.

4. Spheronization (3 lectures)

Introduction, Extrusion-spheronization methods, Formulation, Process variable, Equipments, Evaluation of pellets.

5. Packaging developments (5 lectures)- Packaging material, unit dose packaging, blister packing, strip packing, FDA regulations, packs for tablets, capsules, ointments, child resistant packaging, evaluation of packaging material.

READING MATERIAL RECOMMENDED

1. Pharmaceutical dosage forms Lachman et al.,: Tablets, volume I,II,III
2. Pharmaceutical dosage forms Lachman et al. : Parenterals, volume I,II
3. Remington, Science and practice of Pharmacy, Vol.1, 2000, Lippincot williams and wilkins.
4. J.T. Carstensen, Drug Stability: Principles and Practices, Marcel Dekker, N.Y.
5. N.K. Jain , Pharmaceutical product development. CBS publication and distributors, New Delhi.
6. G.S. Banker and C.T.Rhodes, Modern Pharmaceutics, IInd edition , Marcel Dekker, INC, NewYork.

PHCEU -514 Drug Regulatory Affairs and IPR**External Marks: 80****4 Hrs/Week****Internal Marks: 20****Total Marks: 100**

1) Drug Regulatory Affairs (10 Lectures)- Harmonization of regulatory requirements including ICH activity. Regulatory requirements of different regions applicable to pharmaceutical developments, manufacturing, quality control on finished products, extended release products, biopharmaceutical and bioequivalence assessment and good clinical practices and Comparison with regulation in India. Filing of IND, NDA and ANDA for approval and registration.

2) Stability Testing (10 Lectures)- Role of stability testing, stability test guidelines. Protocol of stability testing including testing under different climatic zones and conditions. Conduct of stability testing. Presentation and recording of stability data, determination of shelf life. Stability test equipment and recent developments in this area.

3) Documentation (2 lectures)- Importance of documentation, statutory requirements and procedure for documentation, critical examination of documents.

4) GMP of Pharmaceuticals (10 Lectures)- Current GMP in manufacturing, processing, packaging of drugs. GMP for finished products. General provision, organization and personnel, building and facilities, equipment, control of components and drug product, container and closures, production and process, packaging and labeling, laboratory and control of records and reports.

5) Intellectual property (18 Lectures)- Concepts and fundamentals of Intellectual property protection (IPP) and Intellectual property Rights (IPR). Economic importance, important mechanism for protection of Intellectual property. Patents, Industrial and layout designs, Copyrights, Trademarks, Trade secrets, factors affecting IP protection, Penalties for violation or infringement. Trade related aspects of IPR. Concepts behind GATT, WTO, TRIPS, TRIMS and GATS. Salient features of Indian Patent act 1970, 1999, 2003, amendments and rules.

READING MATERIAL RECOMMENDED

1. Pharmaceutical product development 2006, edited by N.K. Jain, CBS publishers and distributors. New Delhi, and references there in.
2. Good manufacturing practices for pharmaceuticals: A plan for total quality control from manufacturer to customer, Vth edition, revised and expanded by Sidney H. Willig, Marcel and Dekker.
3. <http://www.patentoffice.nic.in>
4. <http://www.patentmatics.com>
5. <http://www.iprlawindia.org>
6. <http://www.indianpatent.org.in>
7. <http://www.wipo.int>

PHCEU -516 MOLECULAR BIOLOGY AND PHARMACEUTICAL BIOTECHNOLOGY**External Marks: 80****4 Hrs/Week****Internal Marks: 20****Total Marks: 100****1) Introduction to Microbial Genetics (8 lectures)**

A brief Introduction and review of DNA and its structure, DNA polymerase and its role in DNA synthesis, Genetic code, Flow of genetic information, Types of mutations, Detection and isolation of mutants, Physical and chemical agents causing mutations, biological significance of mutations on translation process. DNA repair such as excision repair, removal of lesions, post-replication repair and recombination repair.

2) Microbial Recombination & Plasmids (5 lectures)

General principal of bacterial re-combination, Bacterial plasmids, Transposable elements, Bacterial conjugation, DNA transformation, Transduction, generalized and specialized.

3) Gene cloning (8 lectures)

Introduction to gene cloning. Main steps of gene cloning, Gene cloning procedures, Restriction endonucleases, Isolation of DNA to be cloned (Creation and screening of gene library), Plasmid cloning vectors and isolation of plasmid with DNA inserts. Application of genetic engineering with special reference to the production of proteins of pharmaceutical significance such as insulin, human growth hormone and tissue Plasminogen activator (t-PA).

4) Fermentation Technology (10 lectures)

The fermentation process and its mode operation with special reference to fed-batch culture. Strain improvement and selection procedures. Optimizing mutagenesis and isolation of mutants substrates for industrial production. Regulation and maximizing the production of secondary metabolites. Development of fermentation medium and control of physical parameters for production efficiency. Biosynthesis and the fermentation process for the production of cephalosporins and antitubercular antibiotics such as streptomycin and rifamycins, vitamins (B12), amino acids (lysine and glutamic acid) and citric acid.

5) Immobilised enzymes (5 lectures)

Definition, advantages over soluble enzymes, different methods of immobilization, effect on the stability of the enzymes, potential applications and uses of immobilized enzymes, Kinetics of immobilized enzyme catalysed reactions and different parameters like temperature, pH, enzyme and substrate concentration which influence the velocity of a reaction. Biosensors and their applications in medicine and pharmacy.

6) Monoclonal Antibodies (5 lectures)

Production of monoclonal antibodies, diagnostic, therapeutic and analytical applications and their role in drug targeting.

7) Gene Therapy (4 lectures)

An introduction to genetic disorders, concepts and principles of gene, viral and non- viral gene delivery systems, safety and ethical considerations.

READING MATERIAL RECOMMENDED

1. Molecular Biology and Biotechnology by Smith and Wood, 1991, Chapman and Hall, New York and London
2. Microbiology by L.M Prescott, J.P Harley and D.A Klein, Vth edition, Mc Graw-Hill.
3. A textbook of Industrial Microbiology by Wulf Crueger and Anneliese Crueger, 2nd edition, Sinauer Associates, INC, Sunderland MA01375
4. Martin's Physical Pharmacy and Pharmaceutical Sciences by Patrick J. Sinko, Vth edition, Lippincott Williams and Wilkins by Patrick J. Sinko
5. J. Woodward (Editor), Immobilized cells and Enzymes, A Practical Approach, IRL Press.
6. J.P. Remington, Science and Practice of Pharmacy, Vol I, 2000, Lippincott Williams and Wilkins.
7. S.P. Vyas, V.K. Dixit, Pharmaceutical Biotechnology, 1998, CBS New Delhi.
8. B. Albert, D. Bray, J. Lewis, M. Raff, K. Roberts, D Watson, Molecular Biology of the cell 1983, Garland, N.Y.

PHCEU -518 PHARMACEUTICS LABORATORY-II

External Marks: 80

16 Hrs/Week

Internal Marks: 20

Total Marks: 100

- 1. Experiments based Tablet Technology**
2. Experiments based on Micro-encapsulation
3. Experiments based on Enzyme Kinetics.