Pharmaceutics Syllabus- 1st semester

PE-510 **(1 credit)**

Pharmaceutical Preformulation – I

1. **Preformulation studies:** Preformulation studies of drug substances, proteins and peptides. Fundamental and derived properties in preformulation profiling. Preformulation work-sheet.
2. **Role of pre-formulation in drug discovery:** material properties in lead selection, 'drugability' of new chemical entities, *in silico* and high throughput pre-formulation studies.
3. **Role of preformulation in drug development**: Preformulation as a support for formulation development, identification of 'developmental challenges' during pharmaceutical development, dosage form specific studies.
4. **Salt selection:** Role of salt selection in drug discovery and development, theoretical concepts for selection of counter ions for salt formation, 'pKa rule' for salt formation, decision tree for salt selection, appropriate case studies.
5. **Solubilization:** Solubility and solubilization of non-electrolyte, drug solubilization in surfactant systems, use of co-solvents for development of liquid formulations, solid-state manipulations including use of metastable solid forms like amorphous state.

PE-520 **(2 credits)**

Biopharmaceutics and Pharmacokinetics

1. **Introduction:** Definitions, ADME, concentration time profile, plotting the data, different fluid compartments and blood flow rate compartment models, biological half-life, elimination rate constant. Biopharmaceutics and pharmacokinetics in drug research.
2. **GIT Absorption of drugs:** Mechanism, physico-chemical, biological and pharmaceutical factors affecting drug absorption through GIT. Techniques for the GIT absorption assessment.
3. **Drug disposition:** Total body clearance, renal clearance, mechanism of clearance, clearance ratio, factors affecting renal clearance, hepatic clearance, volume of distribution and its significance.
4. **Protein and tissue binding:** Factors affecting protein binding, kinetics of protein binding, determination of rate constant and different plots (direct, scatchard and reciprocal), Implication of protein binding on pharmacokinetic parameters.
5. **Bioavailability and bioequivalence:** Definitions, federal requirements, methods of determination of bioavailability using blood and urinary excretion data. Protocol design for bioavailability assessment. Methods for bioequivalence determination.
6. **Pharmacokinetic characterization of drugs:** Pharmacokinetics of drugs following one/two compartment open models with first order elimination kinetics as applied to rapid intravenous injection, Intravenous transfusion and oral administration. Determination of absorption rate constant using Wagner-Nelson, Loo Riegelman methods. Flip-flop models, method of

residual. Urinary excretion data and its application in pharmacokinetic characterization of drugs. Pharmacokinetics of multiple dosing.

7. **Dosage regimen:** Dosage regimen adjustment in patients with renal and hepatic diseases. Drug dosage in elderly, children and obese patients.
8. **Non Linear Pharmacokinetics:** Various causes of non-linearity, Michaelis-Menten kinetics, In-vivo estimation of Km and Vm. Case studies.
9. **Physiologic pharmacokinetics models:** Mean Residence Time; Statistical Moment Theory; Application and limitations of physiologic pharmacokinetic models.
10. **Miscellaneous Topics:** Chronopharmacokinetics, Drug toxicity and forensic pharmacokinetics, kinetics of maternal-fetal drug transfer, pharmacokinetics v/s pharmacological/ clinical response, metabolic kinetics.

Recommended books:

1. Applied Biopharmaceutics& Pharmacokinetics, by Shargel, L., S. Wu-Pong
2. Biopharmaceutics and Pharmacokinetics: An Introduction by Notari, R. E.
3. Introduction to Biopharmaceutics, by Gibaldi, M.
4. Biopharmaceutics and Relevant Pharmacokinetics, by Wagner, J. G.
5. Textbook of Biopharmaceutics and Clinical Pharmacokinetics by Niazi, S.K.
6. Handbook of Bioequivalence Testing, by Niazi, S. K.
7. Modelling in Biopharmaceutics, Pharmacokinetics, and Pharmacodynamics: Homogeneous and Heterogeneous Approaches, by Macheras, P. and A. Iliadis
8. Comparative Pharmacokinetics: Principles, Techniques and Applications, by Riviere, J. E
9. Foundations of Pharmacokinetics, by Rescigno, A.
10. Clinical Pharmacokinetics and Pharmacodynamics: Concepts and Applications, by Rowland, M. and T. N. Tozer

PE-530 **(1 credit)**

Pharmaceutical Preformulation – II

1. **Complexation:** Metal and organic molecular complexes, inclusion compounds with reference to cyclodextrins, chemical characteristics of inclusion complexes, methods of preparation of cyclodextrin complexes, applications in solubilization / taste masking / enhancement of permeability / enhancement of oral bioavailability.
2. **Rheology:** Methods for evaluation of viscosity, concept of Viscoelastic, Newtonian/ non-Newtonian flow properties, thixotropy and their applications in development of dosage form, implications of viscosity on performance of liquid dosage forms like suspensions and emulsions, advanced techniques / equipment employed in the rheological characterization of pharmaceutical products.

3. **Micromeritics:** Particle size distribution, evaluation methods including advanced techniques like atomic force microscopy, significance of particle size in different dosage forms including aerosols, parenterals and solid dosage forms.
4. **Dissolution:** Theories of dissolution, release rates and constants, selection of dissolution media, bio-relevant media, Mechanisms of conventional release and controlled release, Dissolution data handling and correction factors, Dissolution equipments and IVIVC.

PE 540 **(1 credit)**

Regulatory Considerations for Formulation Development

1. International regulatory trends in pharmaceutical industry
2. **Role of regulatory affairs department in pharmaceutical organization:** regulatory audits, interactions with various other departments, single point contact with regulatory agencies.
3. **Types of regulatory filings for pharmaceutical products:** goals of regulatory registration procedures investigational new drug applications, introduction to various type of regulatory filings.
4. **New drug applications:** stages involved in NDA, different phrases of clinical trials, purpose of IND, types and categories of IND applications information to be given in IND applications.
5. **Chemistry, manufacturing and control (CMC) information in NDA:** information related to drug substance like manufacturing process, specifications, description of tests methods. Information related to drug product: description of method of manufacturing, specifications and acceptable limits. Information related to placebo.
6. **Hybrid NDA:** a difference from NDA, historical background, literature based hybrid NDAs and other sources of information for hybrid NDA, examples of types of products considered under hybrid NDA.
7. **Abbreviated New Drug applications (ANDAs):** historical developments leading to creation of ANDA process, Hatch Waxman Act, patent term restoration, criteria for patent term extension, various types of Hatch Waxman Exclusivities, concept of therapeutic equivalence, ANDA review process.
8. **Paragraph IV certification ANDAs:** different ANDA Patent certification options, Medicare Modernization Act, implications of this act on 30 month stay period and 180 day exclusivity, triggering and forfeiture of 180 day exclusivity, shared exclusivity
9. **ANDA with suitability petition:** case studies of drug products considered appropriate for filing under suitability petition.

MC-511 **(2 credits)**

Spectral Analysis

1. Ultra Violet (UV) and visible spectroscopy:

a) Energy levels and selection rules: Definitions, molecular orbital approach for energy absorption, various modes of transitions.

b) Correlation of structural variation with UV absorption: Factors influencing the position and intensity of absorptions, Inductive and resonance effects, effect of ring size, influence of stereochemical factors.

c) Predicting UV absorption: Woodward- Fieser, Fieser-Kuhn and Nelson rules;

d) Other factors: Non-conjugative effect, solvent effect, S-Cis band.

2. Infrared (IR)spectroscopy:

a) Characteristic regions of the spectrum: Various modes of vibrations, Energy levels

b) Correlation of structure with IR spectra: Influence of substituents, ring size, hydrogen bonding, vibrational coupling and field effect on frequency.

c) Applications: Determination of stereochemistry. Spectral interpretation with examples.

3. Nuclear Magnetic Resonance (NMR)spectroscopy:

a).Fundamentals: Physical basis, magnetic nuclei, resonance, relaxation processes, signal-sensitivity.

b) Instrumentation: Continuous-Wave (CW) instrument, Pulsed Fourier Transform (FT) instrument, Functions, Relation with sensitivity, Sampling.

c) **1H NMR, correlation of structure with spectra:** Chemical environment and shielding chemical shift and originof its concept, reference compound, local diamagnetic shielding and magnetic anisotropy, relation with chemical shift, chemical and magnetic non equivalence, spin-spin splitting and its origin, Pascal's triangle, coupling constant, mechanism of coupling, integral, NMR solvents and their residual peaks, protons on heteroatoms, quadrupole broadening and decoupling, effect of conformations and stereochemistry on the spectrum, Karplus relationship, diastereomeric protons, Hetero nuclear coupling to 19F and 31P, virtual coupling, long range coupling -epi, peri, bay effects. Shift reagents-mechanism of action, spin decoupling and double resonance. Explanation of spectra of some compounds and drugs.

d)**13C NMR, correlation of structure with spectra:** Chemical environment, shielding and carbon-13chemical shift, calculation, proton-coupled 13C Spetra, Proton-decoupled C spectra, Nuclear Overhauser Enhancement (NOE), Problem with integration,

Distortionless Enhancement by Polarization Transfer (DEFT), Heteronuclear coupling for carbon to deuterium, carbon to ^{19}F, carbon to P. Explanation of spectra of some compounds and drugs.

4. **Mass spectrometry (MS)**: Molecular ion and metastable peak, fragmentation patterns, nitrogen and ring rules, McLafferty rearrangement, electron and chemical ionization modes, applications.

Recommended Books:

1. Spectroscopy by Donald L Pavia, Gary M Lampman, George S Kriz, James A Vyvyan
2. Organic spectroscopy by William Kemp
3. Spectroscopic Methods in Organic Chemistry by Dudley H. Williams & Ian Fleming
4. Spectrometric Identification of Organic Compounds by Robert M. Silverstein, Francis X. W ebster & David J. Kiemie
5. Applications of Absorption Spectroscopy of Organic Compounds by Dyer
6. Fundamentals of Molecular Spectroscopy by Colin N. Banwell & Elaine M. McCash
7. Spectroscopy by Pavia, Donald L. Lampman, Gary M. Kriz, George S.

NP-510 **(1 credit)**

Separation Techniques

1. Separation Techniques: Need for learning separation techniques, separation techniques in natural product research and drug discovery, extraction techniques.
2. Chromatography: General principles, classification of chromatographic techniques, normal and reverse phase, bonded phase chromatography, stationary phases, activity of stationary phases, elutropic series, and separation mechanisms.
3. Column Chromatography and Short column chromatography: Column packing, sample loading, column development, detection.
4. Flash chromatography and Vacuum liquid chromatography: Objectives, optimization studies, selecting column and stationary phases, selecting suitable mobile phases, automated flash chromatography, and reverse phase flash chromatography.
5. High performance liquid chromatography: Principles, instrumentation, peak shapes, capacity factor, selectivity, plate number, plate height, resolution, band broadening, pumps, injector, detectors, columns, column problems, gradient HPLC, HPLC solvents, trouble shooting, sample preparation, method development
6. Planar Chromatography - TLC/HPTLC/OPLC: Basic principles, sample application, development of plates, visualization of plates, 2D TLC, densitometry, Over pressure layer chromatography.
7. Counter current chromatography: Basic principles, droplet counter current chromatography, centrifugal partition chromatography, choice of solvents for SP and MP

8. Gas Chromatography: Principles, instrumentation, split-splitless injector, head space sampling, columns for GC, detectors, quantification.
9. **Biochromatography:** Size exclusion chromatography, ion exchange chromatography, ionpair chromatography, affinity chromatography general principles, stationary phases and mobile phases.
10. **Hyphenated techniques:** Introduction to GC-MS and LC- S techniques and their applications in natural products.

Recommended Books:

- Methods in Biotechnology, Natural Product Isolation by Sarker, Latif, Gray
- Methods in Biotechnology, Natural Product Isolation by Richard Canell
- Various Reviews and Research Papers

BT-510 **(1 credit)**

Biotechnology in Pharmaceutical Sciences

1.Biotechnology in pharmaceutical Sciences perspective: Biology in drug discovery; Traditional drug discovery vs rational drug discovery; rational drug discovery pipeline; concept of target based drug design and target discovery; role of plant biotechnology in edible vaccine development.

2.Genomics in target discovery: Concept of genome, genes and gene expression; genome sequencing and sequence comparison methods (microarray); comparative genomics and expression genomics for target discovery of communicable disease and lifestyle disease.

3.Systems and methods of molecular biology: Isolation and validation of targets; PCR, RT-PCR nucleic acid isolation; cloning vectors (some examples), enzymes used in molecular cloning methods (some examples); cloning and characterization of biopharmaceuticals.

4.Protein expression systems: Gene expression in bacteria, yeast, insect and mammalian cells.

5.Enzyme purification and assay: Various protein purification methods; enzyme based assay for small molecule screening.

6.Bioprocess technology: Upstream process: Introduction to microbial growth, media formulation; sterilization, inoculum preparation

7. Bioprocess technology: Fermentation: Fermentation process design, operation and characteristics of fermentation processes; batch, fed-batch and continuous culture systems, instrumentation and bioprocess control.

8.Downstream process: Introduction to various downstream process operations in

biopharmaceutical manufacturing such as centrifugation, filtration, tangential flow filtration, cell disintegration, solvent-solvent extraction, supercritical fluid extraction etc.

9.Biotechnology in pharmaceutical industry: Major areas of biotechnology in the pharmaceutical industry such as antibiotics, vaccines, diagnostics, antibodies, biopharmaceuticals (insulin, interferon, GSF, CSF and therapeutic proteins etc.); commercial aspects, priorities for future biotechnological research.

10.Industrial enzymes in drug development: Penicillin amidase, lipase, oxidoreductase, nitrilase, protease etc.; use of all these enzymes for enantioselective synthesis of pharmaceutically important drugs/drug intermediates, future directions.

Recommended books:

- Analysis of Genes and Genomes by Richard J Reece. John Wiley & Sons.
- MolecularBiotechnology by Principles and Applications of Recombinant DNA by Bernard R. Glick, Jack J. Pasternak and Cheryl L.Patten, ASM Press.
- Principles of Fermentation Technology by PF Stanbury,A.Whitaker,S.J.Hall. Butterworth-Heinemann
- Bioprocess Engineering Principles by Pauline M.Doran, Academic Press.
- Pharmaceutical Biotechnology by Concepts and Applications by Gary Walsh, John Wiley & Sons.

GE-510 **(2 credits)**

Biostatistics

1.Statistics: Introduction, its role and uses. Collection; Organization; Graphics and pictorial representation of data; Measures of central tendencies and dispersion. Coefficient of variation.

2.Probability: Basic concepts; Common probability distributions and probability distributions related to normal distribution.

3.Sampling: Simple random and other sampling procedures. Distribution of sample mean and proportion.

4.Estimation and Hypothesis testing: Point and interval estimation including fiducial limits. Concepts of hypothesis testing and types of errors. Student- t and Chi square tests. Sample size and power.

5.Experimental design and analysis of variance: Completely randomized, randomized blocks. Latin square and factorial designs. Post- hoc procedures.

6.Correlation and regression: Graphical presentation of two continuous variables; Pearson's product moment correlation coefficient, its statistical significance. Multiple and

partial correlations. Linear regression; Regression line, coefficient of determination, interval estimation and hypothesis testing for population slope. Introduction to multiple linear regression model. Probit and logit transformations.

7.Non-parametric tests: Sign; Mann-Whitney U; Wilcoxon matched pair; Kruskal wallis and Friedman two way anova tests. Spearman rank correlation.

8.Statistical techniques in pharmaceutics: Experimental design in clinical trials; Parallel and crossover designs. Statistical test for bioequivalence. Dose response studies; Statistical quality control.

Recommended books:

- Fundamentals of Biostatistics by *Bernard Rosner*
- Pharmaceutical Statistics: Practical and Clinical Applications by *Bolton and Bon*
- Statistical Misconceptions by *Huck*

GE-520 **(1 credit)**

Fundamentals of Intellectual Property (IP) and Technology Management

1. **Intellectual property:** Concepts and fundamentals; Concepts regarding intellectual property (IP), intellectual property protection (IPP) and intellectual property rights (IPR); Economic importance, mechanisms for protection of intellectual property-patents, copyrights, trademark; Factors effecting choice of IP protection; Penalities for violation; Role of IP in pharmaceutical industry; Global ramifications and financial implications.

2. Trade related aspects of intellectual property rights: Intellectual property and international trade; Concept behind WTO (World Trade Organisation), WIPO (World Intellectual Property Organisation) GATT (General Agreement on Tariff and Trade), TRIPs (Trade Related Intellectual Property Rights), TRIMS (Trade Related Investment Measures) and GATS (General Agreement on Trade in Services); Protection of plant and animal genetic resources; Biological materials; Gene patenting; Biotechnology / drug related IPR issues; Status in India and other developing countries; Case studies and examples; TRIPS issues on herbal drugs.

3. Nuts and bolts of patenting, copyright and trademark protection criteria for patentability, types of patents; Indian Patent Act, 1970; WTO and modifications under TRIPS: Filing of a patent application; Precautions before patenting-disclosures / non-disclosures, publication-article / thesis; Prior art search-published patents, internet

search patent sites, specialized services-search requests, costs; Patent application-forms and guidelines, fee structure, time frames, jurisdiction aspects; Types of patent applications- provisional, non provisional, PCT and convention patent applications; International patenting-requirement procedures and costs; Financial assistance for patenting- introduction to schemes by NRDC and TIFAC; Publication of patents-gazette of India, status in Europe and US; Patent annuity; Patent attomeys technical aspects, criteria for selection, addresses, fee, rights and responsibilities of a patentee; Practical aspects regarding maintaining of a PATENT FILE; Patent infrigment- meaning, scope, litigation, case studies and examples; Patenting by research students, lecturers and scientists-University / organisational rules in India and abroad; Thesis research paper publication, credit sharing by workers, financial incentives; Useful information sources for patents related information-internet sites, brouchers, periodicals, CD roms; Significance of copyright protection for researchers; Indian Copyright Law and digital technologies-Beme convention, WIPO copyright treaty (WCT), WIPO performance and Phonogram Treaty (WPPT); Protection for computer data bases, multi media works; Trade marks legislation and registration system in India-an introduction, meaning of trademark criteria for eligibility; filling application for trademark registration; Trade secrets-scope modalities and protection; Case studies-drug related patents infringments.

4.Technology development / transfer / commercialisation related aspects: Technology development-meaning; Drug related technology development; Toxicological studies, bioequivalence (BU), clinical trials-phase-I, phase-II and phase-III; Approved bodies and agencies; Scale-up, semi-commercialisation and commercialisation-practical aspects and problems; Significance of transfer of technology (TOT), bottlenecks; Managing technology transfer-guidelines for research students, scientists and related personnal;

TOT agencies in India-APCTD, NRDC, TIFAC, BCIL, TBSE/SIDBI; TOT related documentation-confidentiality agreements, licensing, MOUs, legal issues; Compulsary licensing excess to medicine issues; DOHA declaration, POST WTO product patent regime from 2005; Challenges for Indian pharmaceutical industry in the context of globalisation of IP; Drug registration and licensing issues-national and global; Drug master file submissions, SOPS; Related registration and marketing issues; Case studies-antiretroviral drugs and others.

5.Funding sources for commercialization of technology: Preparation of a project report,

financial appraisal, business models; GOI schemes and incentives; NRDC, TePP, HGT, TDB schemes. PATSER; Venture capitalists, banks. Incubator concept-Case studies with respect to IIT, CCMB, IMTECH, NIPER. Documentation and related aspects.

6. **Ethics and values in IP:** IP and ethics-positive and negative aspects of IPP; Societal responsibility; Avoiding unethical practices; Echo-responsibility-economic, social and environmental benifits of modern biotechnology; Voluntary adoption of pollution control strategies.

Recommended books:

- Law Relating to Intellectual Property by B.L.Wadhera
- IPR Handbook for Pharma Students and Researchers by P.Bansal
- The Patents Act, 1970 (Bare Act with Short Notes) (New Delhi: Universal Law Publishing
- Company Pvt. Ltd. 2012)
- Patent Agent Examination by Sheetal Chopra and Akash Taneja
- Making Innovation Happen- A simple and Effective Guide to Turning Ideas into Reality by Michael Morgan
- Making Breakthrough Innovation Happen by Porus Munshi
- Innovation X- Why a Company's Toughest Problems are its Greatest Advantage by
- Adam Richardson
- Legal Drafting for the Layman by Nabhi Kumar Jain
- How to Write and Publish a Scientific Paper by Rober A Day
- Concise Law Dictionary-with Legal Maxims, Latin Terms and Words and Phrases by
- Justice Y.V.Chandrachud
- Biomedical Research- From Ideation to Publication by G.Jagadeesh and others

LG-510

General Laboratory Experience (3 credits)

Analytical Techniques (75 hours):

a) Spectral analysis workshop (45 hours)

b) Separation techniques (30 hours)

Computer and application in pharmaceutical sciences (100 hours): Introduction to computers, basic unit and functions, H/W and S/W, operating systems, word processing, spread sheet, graphic programs, dbase, windows, statistical S/W programs and packages. Steps involved in S/W development, computer languages with emphasis to FORTRAN language and programming, hands on experience in pharmaceutical software systems. Use of computers in information retrieval systems.

Pharmacology (25 hours): Animal handling, route of administration of drugs, dose response relationship, acute toxicity testing of drugs, analgesic activity of a compound, estimation of protein and haematological parameters.

Biotechnology in pharmaceutical sciences (20 hours):

Day -1: Preparation for plasmid miniprep.

Day-2: Plasmid miniprep and restriction digestion.

Day-3: Gel electrophoresis and molecular weight calculation.

Day-4: Discussion of result and viva

Specialization (50 hours):

a) To prepare granules by dry granulation using Roller compactor.

b) To optimize wet granulation process and perform scale up using Rapid Mixer Granulator (RMG)

c) Study the dissolution behaviour/ drug release pattern of various conventional, sustained release, enteric coated and nanoparticulate dosage form and establishment of dissolution kinetics. Study of various factors affecting dissolution / drug release.

d) Study of drug protein binding and effect of competitive agent on binding kinetics.

e) Plotting and interpretation of pharmacokinetics data and calculation of various pharmacokinetic parameter.

GE-511 Seminar **(1 Credit)**