SYLLABUS

M.Pharm
Pharmaceutical Technology
(Formulations)

NATIONAL INSTITUTE OF PHARMACEUTICAL EDUCATION AND RESEARCH
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M.Pharm
Pharmaceutical Technology (Formulations)

Course No.	Course Name	Credits
Semester-I		
PE-510	Pharmaceutical Preformulation-I	1
PE-520	Biopharmaceutics and Pharmacokinetics	2
PE-530	Pharmaceutical Preformulation-II	1
PT-580	Regulatory Consideration for Formulation Development	1
MC-511	Spectral Analysis	2
GE-510	Biostatistics	2
GE-520	Fundamentals of Intellectual Property (IP) and Technology Management	1
GE-511	Seminar	1
LG-510	General Laboratory Experience	3
Elective		2
TOTAL CREDITS		**16**
Semester-II		
PT-620	Pharmaceutical Production Technology	1
PT-660	Formulation Development Concepts as applied in Industry	2
PE-630	Pharmaceutical Product Development-I	1
PT-670	Industrial Pharmaceutical Processing (Scale up and validation)	1
PE-650	Drug Delivery II (Targeted drug delivery)	2
PE-660	Solid State Pharmaceutics	1
PA-630	Stability Testing	1
GE-611	Seminar	1
LS-610	General Lab Experience in the Area of Specialization	2
Elective		2
TOTAL CREDITS		**14**
Semester-III		
Project (22 weeks)		
TH-598	Synopsis	5
TH-599	Presentation	3
TOTAL CREDITS		**8**
Semester-IV		
TH-698	Thesis	9
TH-699	Defence of Thesis	3
TOTAL CREDITS		**12**
GRAND TOTAL CREDITS (I to IV Semesters)		**50**

M.Pharm Pharmaceutical Technology (Formulation)
Semester - I

PE-510:- Pharmaceutical Preformulation - I (1 Credits)

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, 'drug ability' 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.

Recommended Books

- Mark Gibson Pharmaceutical Preformulation and Formulation- A Practical Guide from Candidate Drug Selection to Commercial Dosage Form.
- Simon Gaisford, Mark Saunders(auth.) Essentials of Pharmaceutical Preformulation.
- Moji C Adeyeye H G Brittain Preformulation solid dosage form development.
- Jens T. Carstensen Pharmaceutical Preformulation

PE-520:- Biopharmaceutics and Pharmacokinetics (2 Credits)

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.

Protocol design for bioavailability and bioequivalence assessment. Methods for bioequivalence determination. Regulatory perspective of design acceptance and BE determination - BCS based approach to avoid human PK study for BE 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. Pharmacokinetics of modified/sustained release dosage forms.

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. Lineweaver Burk equation.

9. **Physiologic pharmacokinetics models:** Mean Residence Time (MRT); Statistical moment theory; Mean absorption time (MAT); Mean dissolution time (MDT); Lagrange and spline method 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

- Applied biopharmaceutics pharmacokinetics. LEON SHARGEL AND ANDREW B.C. YU, 2016, 7th Edition.
- Foundation of Pharmacokinetics. Rescigno, A. 2003.
- Handbook of Bioequivalence Testing. Sarfaraz K. Niazi. 2007, 1st Edition.
- Biopharmaceutics and Relevant Pharmacokinetics. Wagner, J. G. 1970.
- Textbook of Biopharmaceutics and Clinical Pharmacokinetics. Niazi, S.K. 1980.
- Modeling in Biopharmaceutics, Pharmacokinetics, and Pharmacodynamics: Homogeneous and Heterogeneous Approaches. Macheras, P. and A. Iliadis, 2016, 2nd Edition.
- Comparative Pharmacokinetics: Principles, Techniques and Applications. Riviere, J.E., 2011, 2nd Edition.
- Introduction to Biopharmaceutics. Gibaldi, M. 1971.
- Biopharmaceutics and Pharmacokinetics: An Introduction. Notari, R. E. 2008
- BA/BE guidance of US FDA and EMEA, BCS waiver guidance by USFDA.

PE-530:- Pharmaceutical Preformulation – II (1 Credit)

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. Specific Surface Area - its evaluation and importance in drug product development.

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 equipment and IVIVC. IVIVC correlation levels, procedure for IVIVC correlation. Multimedia dissolution profile and applicability for biowaiver to be added. ICH Q8 reference to be included for pharmaceutical development for regulatory requirement. Setting of dissolution specification - the regulatory expectation.

Recommended Books:

1. Physical Pharmacy by Alfred Martin, 06th Edition.
2. Martin's Physical Pharmacy and Pharmaceutical Sciences, Fifth Edition, edited by Patrick J. Sinko, BI Publications Pvt. Ltd.
3. M.E. Aulton, Pharmaceutics, The Science & Dosage Form Design, Churchill Livingstone, Edinburgh.
4. Remington's Pharmaceutical Sciences, Mack Publishing Company, Pennsylvnia
5. EMEA reflection paper for setting the dissolution specification.

PT-580: - Regulatory considerations for Formulation Development (1 Credit)

1. International regulatory trends in pharmaceutical industry

2. Harmonizing formulation development of global filings

3. Product development information in regulatory filings development pharmaceutics guidelines. Chemistry Manufacturing Guidelines (CMC)

4. Global requirements on stability studies, residual solvents and impurities.

5. Dealing with post approval changes.

Recommended Books:

1. New Drug Approval Process, Edited by Richard A. Guarino, Marcel Dekker

2. The Pharmaceutical Regulatory Process, Edited by Ira R. Berry, Marcel Dekker

3. Medical Product Regulatory Affairs, Edited by J. J. Tobin and G. Walsh, Wiley VCH

MC-511 :- Spectral Analysis (2 Credits)

1. **Ultraviolet (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, the effect of the ring size, the 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) **^{1}H NMR, correlation of structure with spectra:** Chemical environment and shielding, chemical shift and origin of its concept, reference compound, local diamagnetic shielding, and magnetic anisotropy, relation with the 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, the effect of conformations and stereochemistry on the spectrum, Karplus relationship, diastereomeric protons, Heteronuclear coupling to ^{19}F and ^{31}P, 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) **^{13}C NMR, correlation of structure with spectra:** Chemical environment, shielding and carbon-13 chemical shift, calculation, proton-coupled C Spectra, 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 ^{31}P. Explanation of spectra of some compounds and drugs

4. **Mass spectrometry (MS)**

a) Basic principles of Mass Spectrometry
b) Instrumentation: Ionization techniques: Electron ionization, Chemical ionization, Atmospheric pressure ionization (Electrospray ionization, APCI, and APPI), other sources: MALDI, ICP, etc.
c) Mass Analyzers: Quadrupole, Time of flight, Ion traps, LIT, FTICR, Orbitrap, High-Resolution Mass Spectrometry
d) Hyphenated Mass Spectrometry: GC/MS, HPLC/UPLC-MS and Tandem Mass Spectrometry (Product ion scan, Precursor ion scan, neutral loss scan, SIM and MRM)

e) Interpretation of mass spectra: Isotopes and ion abundances, the fragmentation pattern of organic molecules with different functional groups, qualitative analysis, Quantitative analysis

1. Applications: Application of mass spectrometry in Pharmacology/Toxicology, Environmental Monitoring/Analysis and Organic chemistry (Structure elucidation of organic molecules, A brief outline of metabolomics study including the scope of biomarkers study.

Recommended Books:

1. Donald L Pavia, Gary M Lampman, George S Kriz, James A Vyvyan; Introduction to Spectroscopy, 5th Edition, Cengage Learning, USA, 2013
2. William Kemp; Organic spectroscopy, 3rd Edition; Palgrave Publishers Ltd (formerly Macmillan Press Ltd). 2002
3. Spectroscopic Methods in Organic Chemistry by Dudley H. Williams & Ian Fleming
4. Robert M. Silverstein, Francis X. Webster & David J. Kiemie, Spectrometric Identification of Organic Compounds, 7th edition, John Wiley and Sons, Inc. 2005
5. Applications of Absorption Spectroscopy of Organic Compounds by Dyer
6. Colin N. Banwell & Elaine M. McCash; Fundamentals of Molecular Spectroscopy, 4th Edition, McGraw Hill Education, 1994.

GE-510 :- Biostatistics (2 Credits)

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:

1. Fundamentals of Biostatistics by Bernard Rosner.
2. Pharmaceutical Statistics: Practical and Clinical Applications by Bolton and Bon.
3. Statistical Misconceptions by Huck GE-520 Fundamentals of Intellectual Property (IP) and Technology

GE-520 :- Fundamentals of Intellectual Property (IP) and Technology Management (1 Credit)

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 IPin 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 infringements.
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, POSTWTO product patentregime 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. 49 60 Courses of Study 2015.

Recommended Books:

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

GE-511 :- Seminar (1 Credit)

1. Introduction, Information retrieval systems.
2. Writing term papers and reports.
3. Organization of scientific material, thesis, dissertation and references.
4. Reading research papers.

5. Skills in oral presentation.
   Each student has to present a seminar before end of the semester.

LG-510 :- General Laboratory Experience (3 Credits)

1. **Analytical Techniques (75 hours):**
   a) Spectral analysis workshop (45 hours).
   b) Separation techniques (30 hours).
2. **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.
3. **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.
4. **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.

M.Pharm Pharmaceutical Technology (Formulation) Semester - II

PT-620: Pharmaceutical Production Technology (1 credit)

1. Design of Pharmaceutical Plants- HVAC systems: Introduction, Clean room, US Federal Standards, European community guidelines and ISO guidelines and requirements for clean rooms; factors to be considered in designing HVAC in pharmaceutical plant
2. Improved tablet production systems. Benefits, tablet production, production process, improvement in unit processes; development in the area of granulation
3. Tablet coating- process, coating equipment, fluid bed coating, particle coating, application techniques and applications
4. Parenteral production design: Design concepts, area planning and environmental control, wall and floor treatment, fixtures, personnel flow, utilities and equipment location.
5. Latest advancements such as isolator barrier technology, trends in aseptic filtration, blow fill seal and pre-filled syringe technology
6. Lyophilization: Advantages and application of lyophilization, Principles of lyophilization, process of freeze-drying, equipment used-its principle and working
7. Advances in dispersion technology: Nano-systems (R), Dissocubes (R), Nanoedge (R) technologies, Dynomill principle and working
8. Specialized solid dosage form technologies: Zydis (R), Orasolv and Durasolv
9. Supercritical fluid technology and application in pharmaceutical field

Recommended Books/Literature:

1. Pharmaceutical Dosage Forms: Disperse Systems by Herbert A. Lieberman, Leon Lachman, Kenneth E. Avis.

2. Pharmaceutical Dosage Forms: Tablets by Herbert A. Lieberman, Leon Lachman, Kenneth E. Avis.

3. Pharmaceutical Dosage Forms: Parenteral Medications by Herbert A. Lieberman, Leon Lachman, Kenneth E. Avis

4. Modern Pharmaceutics, Marcel Dekker by Banker, G.S. and C.T. Rhodes

5. The Theory and Practise of Industrial Pharmacy by Lachman, Lieberman and Kanig

PT-660:- Formulation Development Concepts as Applied in Industry (2 Credits)

1. **Systems in formulation development:** Components of project initiation; Global versus market specific products; SOPs; Stages of development; Inputs and outputs at each stage. Characterization

2. **Prototype formulation development:** Strategy for generics and drug products for NCEs; Innovator product characterization

3. **API sourcing; Formulation additives**: Study of different types of additives e.g. Semester-II antioxidants and preservatives, coloring and flavouring agents, emulsifying and suspending agents, basic materials for ointment bases, diluents and pharmaceutical solvents, regulatory perspectives: GRAS, IIG;

4. New developments in excipient science, functional and co-processed excipients, international patented excipients.

5. Drug-excipient interaction: Drug-excipient interaction and incompatibilities, physical, chemical, pharmaceutical and therapeutic, analytical techniques to characterize drug excipient incompatibility. Implication of quantitative selection of each excipient in product development

6. Optimization studies for tablets, capsules, injectables, liquid orals, topicals, aerosols and NDDS products

7. Product and Process development: Pack strategies; Documentations- MFC, MF, specifications, development report, technology transfer dossier.

8 Early clinical trial formulations: Composition and further development stages during product development.

9 Design of experiments: Factorial design for product and process development. Fundamentals with case studies from literature.

10 Stability protocols: Formulation development-based stability protocols; Stability reports.

Recommended Books/Literature:

1. Modern Pharmaceutics by Gilbert S. Banker, Christopher T. Rhodes
2. Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems by L.V.Allen, N.C.Popovich and Howard C. Ansel
3. Remington's' Pharmaceutical Sciences
4. Pharmaceutical Dosage Forms: Disperse Systems by Herbert A. Lieberman, Leon Lachman, Kenneth E. Avis.
5. Pharmaceutical Dosage Forms: Tablets by Herbert A. Lieberman, Leon Lachman, Kenneth E. Avis.
6. The Theory and Practise of Industrial Pharmacy by Lachman, Lieberman and Kanig

PE-630:- Pharmaceutical Product Development – I (1 Credit)

1. **Development of dosage forms:** Four stage development including preformulation, prototype development, scale up studies and commercialization, Post commercial monitoring of the product (Pharmacovigilance) as product lifecycle management
2. **Design of materials and product specifications:** Creation and optimization of material and product specifications. In-process, product release and regulatory specifications.

3. **Quality by design (QbD):** Fundamentals of pharmaceutical quality by design, identification of critical quality attributes, critical material attributes, critical process parameters and quality risk management. Identification of QTPP; and formulation by design.
4. **Methods of optimization** – OVAT and Design of experiments (DOE). Experimental designs, Screening design and modelling design, factorial design(s) and Taguchi design, Central composite design, Box-Behnken Design and Plackett- Burman design, mixture designs, response surface methodology. Applications of systematic optimization techniques.
5. **Process analytical technology (PAT)** and other control strategies for QbD.
6. **Pharmaceutical Packaging:** Pack types for different dosage forms, packaging materials like glass and plastic, selection of proper material, labelling, preformulation screening of package components; barrier, child resistance and temper evident packaging systems; regulatory perspectives.
7. **Testing of packaging materials** – equipment used, extractable and leachable.
8. **Documentation protocols:** Forms and maintenance of records in product development department including clinical batches.

Recommended Books/Literature:

1. Javed Ali, Sanjula Baboota. Regulatory Affairs in the Pharmaceutical Industry, 2021, 1st Edition, Elsevier, ISBN: 9780128222119.
2. Sandy Weinberg. Guidebook for Drug Regulatory Submissions, Wiley, ISBN: 978-0-470-37138-1.
3. David Mantus, Douglas J. Pisano. FDA Regulatory Affairs: Third Edition, CRC Press; 3rd edition, ISBN: 978-1841849195.

PT-670: Industrial Pharmaceutical Processing 1 (Scale up and validation) **(1 Credit)**

1. Pilot Plant Scale-up: Introduction, stages of product development, stages of scale-up and pilot plant scale up.
2. Process scale-up for solid, liquid, topical and sterile dosage forms.
3. Scale up and Post Approval Changes (SUPAC) guidelines and Change-Control
4. Process Validation: General Principles and Practices (2011) guidelines, salient features of process validation and stages of process validation
5. Introduction to Quality by Design in development of pharmaceutical dosage forms, Design space definition and implication
6. Introduction to Risk Analysis-Salient features of risk analysis tool such Failure Mode and Risk Analysis (FMEA)in identification of critical process controls.
7. Pharmaceutical Equipment Qualification: Introduction, stages of equipment qualification, Design qualification, Installation qualification, operational qualification, performance qualification and installation qualification
8. Cleaning Validation: Introduction, validation methodology of pharmaceutical equipment; guidelines and essential requirement of good cleaning validation
9. Case studies of Quality by design in formulation of dosage forms

Recommended Books/Literature:

1. PharmaceuticalProcessValidation by Ira R.Berryand Robert Nash
2. TheTheoryandPractise of IndustrialPharmacy by Lachman, Lieberman andKanig
3. www.fda.gov
4. Www.who.org

PE-650 :- Drug Delivery -II (Targeted Drug Delivery and Novel Carrier Systems) (2 Credits)

1. Fundamentals of targeted drug delivery: Need of targeted drug delivery, ligand-receptor interaction, levels of targeting, active and passive targeting, EPR effects, receptor-mediated endocytosis, multifunctional approach in targeted drug delivery.
2. Chemical drug delivery systems: Prodrug concept for drug design, drug targeting and antibody-directed enzyme prodrug therapy (ADEPT), soft drug design, Lipid-drug/ polymer-drug conjugate.
3. Targeted brain delivery: Overview of brain, specific targets for brain delivery, concept of nose to brain delivery, types and key elements: Ideal carrier system and approach with case studies depicting utility in various brain diseases.
4. Targeted Tumor Delivery: Structural features of tumor vasculature, levels of tumor targeting, tumor ligands for targeted drug delivery, biopharmaceutical characteristics of delivery systems for tumor-specific delivery.
5. Colloidal and Supramolecular drug delivery systems: Preparation and characterization, biopharmaceutical considerations, evaluation, and applications in drug delivery of the following delivery vectors: a) Liposomes and niosomes b) Solid lipid nanoparticles and nanostructured lipid carriers c) Polymeric nanoparticles – PLGA, chitosan, albumin, gelatin, alginate etc. d) Carbon nanotubes, (e) microspheres (f) microemulsions (g) SEDDS and SNEDDS.
6. Overview of Specialized drug delivery systems: Transfersomes, Ethosomes, Layersomes, Bilosomes, Emulsomes, Virosomes, Cubosomes, Aquasomes, Pharmacosomes. Dendrimers, Polymeric micelles and Resealed Erythrocytes.
7. Stimuli-responsive drug delivery systems: Magnetically, thermal and pH-assisted drug delivery systems.
8. Miscellaneous targeting approaches: Fundamentals of gene delivery, Overview of colon, liver, macrophage, mitochondrial and M cells targeting.

Recommended Books/Literature:

1. Controlled and Novel Drug Delivery, Jain, N.K. 1997.
2. Advances in Novel and Controlled Drug Delivery, Jain, N.K., CBS publisher.
3. Novel Drug Delivery Systems Chien, Y.W, Taylor & Francis, Second Edition.
4. Controlled and Novel Drug Delivery, Robinson, J.R. & Lee, V.H.I. Taylor & Francis, 2nd edition.
5. Targeted & Controlled Drug Delivery, Vyas S.P. & Khar R.K, CBS Publisher.

PE-660:- Solid State Pharmaceutics (1 Credit)

1. **Levels of solid-state properties:** Molecular / particle / bulk level properties, interdependence of various levels on each other, role of different levels during pharmaceutical development and process development

2. **Molecular level:** Crystalline form, concept of long-range order, supramolecular arrangements, building blocks of crystals, unit cell, basic types of unit cells, demonstration of unit cells using crystal visualization softwares.
3**. Polymorphism:** Definition, significance of polymorphism in drug product performance, packing / conformational polymorphism, thermodynamics of polymorphs, enantiotropy / monotropy, concept of transition temperature, Burger and Ramberger rule.
4. **Crystallization process:** Molecular aggregation events in crystallization, energetic of crystallization, enthalpy entropy balance, types of nucleation, Ostwald's step rule, experimental protocols for polymorph screening.
5. **Implications of polymorphism in pharmaceutical development:** Regulatory concerns related to polymorphism, introduction to latest regulatory position on polymorphism.
6. **Amorphous state:** Definition, long range order versus short range order, disorder in the amorphous state, concept of glass transition temperature (Tg), thermodynamic necessity for Tg, entropy crisis.
7. **Role of amorphous state in drug delivery:** Solubility advantage, spring parachute effect during solubility studies, physical instability of the amorphous form, techniques for stabilization of amorphous form, amorphous solid dispersions.
8. **Co-crystals:** Introduction, synthons used for formation of co-crystals and applications in drug delivery, Regulatory expectation of co-crystals.
9. Particulate level properties: Crystal habit, generation of different crystal habits, implications of crystal habit on product performance and processing.
10. **Bulk level:** Bulk density, compressibility, flow properties, cohesivity, electrostatics, aggregation, agglomeration, role in formulation development and processing.

Recommended Books:

1. Polymorphism in Pharmaceutical Solids Edited by Harry Brittain
2. Solid State Characterization of Pharmaceuticals Edited by Angeline and Mark Zarkrzewski
3. Crystal Engineering: A textbook, Edited by G. R. Desiraju, J. J.Vittal and A. Ramanan.
4. USFDA guidance for Co crystals

PA-630:- Stability Testing (1 Credit)

1. **Drug development cycles and stability testing:** Role and types of stability studies during different stages of drug and product development.
2. **Drug stability testing guidelines:** International, Regional, and National drug stability guidelines.
3. **WHO vs. ICH drug stability testing guidelines:** Comparison of different aspects in WHO guideline, and critical comparison with ICH parent guideline Q1A(R2).
4. **Specific discussion on following ICH guidelines:** Q1B, Q1C, Q1D, Q1E and Q5C.
5. **Additional topics:**

   a) **Stress testing and stability-indicating method development:** Role, regulatory aspects, protocols/approaches, practical considerations.

   b) Stability testing of phytopharmaceuticals and Herbal products: Regulatory requirements including EMA for herbal products.

   c) Stability test equipment: Types of stability chambers (walk-in, stand-alone), design considerations, qualification and other critical issues**.**

   d) Stability testing for Shipping & Distribution: Stability testing during transport.

   e) Stability testing of drug delivery systems.

Recommended Books/Literature:

1. ICH (www.ich.org) and WHO (www.who.int) guidelines
2. Pharmaceutical Stress Testing (Predicting Drug Degradation) by Steven Baertschi a. and Karen Alsante
3. Drug Stability (Principles and Practices) by S. James, Jens ThurØCarstensen
4. Stability-indicating HPLC Methods for Drug Analysis by Quanyun A. Xu, Lawrence A. Trissel
5. Stability of Drugs and Dosage Forms by Sumic Yoshioka, Valentino Stella
6. Physical Pharmacy and Pharmaceutical Sciences by Patrick Sinko, Alfred Martin
7. New Drug Approval Process (Chapter 7) by Richard Guarino
8. Handbook of Stability Testing in Pharmaceutical Development: Regulations, Methodologies, and Best Practices by Kim Huynh-Ba
9. Stability and Characterization of Protein & Peptide of Drugs by Y. John Wang
10. Peptide and Protein Drug Analysis by Ronald Reid

GE-611: - Seminar (1 Credit)

Students are required to submit a written record and present details of the project to be pursued in semester-III & IV. This should include the purpose and basis of the project, stating aims, objectives and probable outcomes, be able to supplement these with necessary information, literature review towards it and process for the project itself.

LS-610: - General Laboratory Experience-10hours/week (2 Credits)

Development and evaluation of drug delivery systems, formulation development and evaluation, transdermal drug delivery system development of control release delivery systems, HPLC method development, generation and characterization of solid-state forms, permeability studies.