COURSES OF STUDY

M.S. (Pharm.)

&

Ph.D

In

Pharmaceutical Analysis

July 2019

NIPER HYDERABAD

National Institute of Pharmaceutical Education and Research

PHARMACEUTICAL ANALYSIS

M.S. (Pharm.)

Course Code	Course Name	Credits
Semester-I		
PA-510	Topics in Pharmaceutical Analysis	2
MC-511	Spectral Analysis	2
NP-510	Separation Techniques	1
PE-510	Pharmaceutical Preformulation-I	1
PE-530	Pharmaceutical Preformulation-II	1
BT-510	Biotechnology in Pharmaceutical Sciences	1
GE-510	Biostatistics	2
GE-520	Fundamentals of Intellectual Property (IP) and Technology Management	1
GE-511	Seminar	1
LG-510	General Lab Experience	3
	Total Credits	**15**
Semester-II		
PA-610	Pharmacopoeial Methods of Analysis	2
PA-620	Instrumental Techniques for Evaluation of APIs and Drug Products	2
PA-630	Stability Testing	1
PA-640	Quality Control and Quality Assurance	2
NP-640	Structure Elucidation	2
PC-611	Pharmacological Screening and Assays	1
PE-630	Pharmaceutical Product Development-I	1
PE-660	Solid State Pharmaceutics	1
GE-611	Seminar	1
LS-610	General Lab Experience in the Area of specialization	2
	Total Credits	**15**
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 Credits (I to IV semesters)	**50**

Semester I

PA-510

Topics in Pharmaceutical Analysis (2 credits)

1**. Introduction to pharmaceutical analysis and techniques**: Scope and range of modern pharmaceutical analysis. Listing of various techniques, with broad discussion on their applications.

2. Material and product specifications: Definition of specifications, study of ICH Q6 guidelines and understanding of specifications through study of pharmacopoeial monographs on drug substances and products.

3. Reference standards: Types (primary, secondary, working and test standards), preparation, containers, labelling, storage and use.

4. Documentation-STPs, certificate of analysis, laboratory books: Typical documents used in a GLP laboratory including standard test protocols, COA and laboratory notebooks. Electronic records & signatures (21CFR Part-11 requirement).

5. Introduction to method development: Method development concepts, steps involved, intricacies at each step.

6. Method validation: Definition and methodology, discussion on each parameter with examples, special considerations in bioanalytical method validation.

7. Calibration and qualification of equipment: Difference of definitions, calibration standards, calibration frequency, examples of calibration of pH meter, FTIR, UV spectrophotometer and HPLC. Definition of qualification process involving URS [user requirement specification], DQ, IQ, OQ, CQ and PQ.

8. Quality risk management in analytical laboratory: Definition of quality risk management in ICH Q9 guideline. Its importance and application to analytical laboratory with examples. Analytical quality by design.

9**. Impurity profiling**: Types of impurities in drug substances and products. Method development for impurity analysis, techniques, identification and quantitation.

10. Automation and computer-aided analysis, LIMS: The concept of auto samplers and high-throughput analysis, computer controlled instrumentation, and networked laboratory. Peculiarities of laboratory information management systems (LIMS).

11. Management of analytical laboratory: Organization of laboratories based on their types, staffing, skill development and training, budgeting and financing, purchase of costly equipment, qualities of laboratory manager and management styles.

12. Laboratory inspections and audit: Internal inspection, external audit, concepts, preparing for inspections and audits.

Recommended books (latest available edition):

1. Chemical Analysis: Modern Instrumentation Methods and Techniques by Francis Rouessac and Annick, Rouessac

2. Principles of Analytical Chemistry by Miguel Valcarcer

3. Analytical Method Development and Validation by Michael E. Swartz, Ira S. Krull

4. Good Laboratory Practices by Jurg P. Seiler

5. Principles of Instrumental Analysis by Douglas A. Skoog, F. James Holler, Timothy A. Nineman

6. Handbook of Modern Pharmaceutical Analysis by SatinderAhuja, Stephen Scypinski

7. Principles and Practice of Bioanalysis by Richard F. Venn

MC 511

Spectral Analysis (2 credits)

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 origin of 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 hetero atoms, quadrupole broadening and decoupling, effect of conformations and stereochemistry on the spectrum, Karplus relationship, diastereomeric protons, Heteronuclear 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) C NMR, correlation of structure with spectra: Chemical environment, shielding and carbon-13 chemical shift, calculation, proton-coupled C Spectra, Proton-decoupled Cspectra, Nuclear Overhauser Enhancement (NOE), Problem with integration, Distortion less 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. Webster & 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

Separation Techniques (1 credit)

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, ion pair chromatography, affinity chromatography general principles, stationary phases and mobile phases.

10. Hyphenated techniques: Introduction to GC-MS and LC-MS techniques and their applications in natural products.

Recommended Books:

1. Methods in Biotechnology, Natural Product Isolation by Sarker, Latif, Gray

2. Methods in Biotechnology, Natural Product Isolation by Richard Canell

3. Various Reviews and Research Papers

PE-510

Pharmaceutical Preformulation - I (1 credit)

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-530 (1credit)

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.

BT-510 {Not offered to M.S. (Pharm.) Biotechnology}

Biotechnology in Pharmaceutical Sciences (1 credit)

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, inoculums 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-solventextraction, supercriticalfluid 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.); commercialaspects, priorities forfuture biotechnologicalresearch.

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:

1. Analysis of Genes and Genomes by Richard J Reece. John Wiley & Sons

2. Molecular Biotechnology by Principles and Applications of Recombinant DNA by Bernard R. Glick, Jack J. Pasternak and Cheryl L. Patten, ASM Press

3. Principles of Fermentation Technology by P F Stanbury, A. Whitaker, S. J. Hall. Butterworth-Heinemann

4. Bioprocess Engineering Principles by Pauline M. Doran, Academic Press

5. Pharmaceutical Biotechnology by Concepts and Applications by Gary Walsh, John Wiley & Sons

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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 linearregression model.Probitand logit transformations.

7. **Non-parametric tests**: Sign; Mann-Whitney U;Wilcoxon matched pair; Kruskal wallis and Friedman two wayanova 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 (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 gentic 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 personnel;

TOT agencies in India-APCTD, NRDC, TIFAC, BCIL, TBSE/SIDBI; TOT related documentation-confidentiality agreements, licensing, MOUs, legal issues; Compulsory licensing excess to medicine issues; DOHA declaration, POSTWTO 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 benefits of modern biotechnology; Voluntary adoption of pollution control strategies.

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

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LG-510

General Laboratory Experience-15 hours/week (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, computer languages with emphasis to FORTRAN language and programming, hands on experience in pharmaceutical soft- ware 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 minirep.

Day-2: Plasmid minirep and restriction digestion.

Day-3: Gel electrophoresis and molecular weight calculation.

Day-4: Discussion of result and viva.

5. Specialization (50 hours)

a) To calibrate thermometer

b) To calibrate the common glassware (volumetric flask, burette and pipette) found in an analytical laboratory

c) Calibration of pH meter

d) To determine Water content in the given sample by Karl Fischer reagent

e) To determine moisture content in the given sample using infrared moisture balance

f) To construct calibration curve for a drug by UV spectrophotometer

g) To perform dissolution test on the given sample

I) Determination of pKa of given sample by spectrophotometric method.

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.

Semester II

PA-610

Pharmacopoeial Methods of Analysis (2 credits)

1. ICH Q4 Pharmacopoeial harmonization process: Current Status.

2. Study of different parts of various pharmacopoeias.

3. Critical comparative analysis of the following tests in IP, BP/EP and USP:

Physical tests: Viscosity, melting point, boiling point/range, water content and water analysis including loss on drying, loss on ignition, optical rotation, pH, specific gravity, osmolality/osmolarity, refractive index, MVTR, etc.

Limit tests: Tests for arsenic, lead, chloride, sulfate, and heavy metals.

Impurities: Tests for epianhydrotetracycline and epitetracycline (USP), elemental impurities, residual solvents, etc.

Microbiological tests and assays: Antimicrobial (preservative) effectiveness testing, microbial limit tests, sterility test, vitamins assay (zone of exhibition), antibiotics assays, bacterial endotoxin test. Leachables and extractables.

Recommended books:

1. The Indian Pharmacopoeia, Indian Pharmacopoeia Commission, Ghaziabad.

2. The British Pharmacopoeia, Stationary Office British Pharmacopoeia Commission, London.

3. The United States Pharmacopeia-National Formulary, Board of Trustees, Rockville.

4. The European Pharmacopoeia, Directorate for Quality of Medicines of the Council of Europe.

PA-620 (2 credits)

Modern Instrumental Techniques for Evaluation of APIs and Drug Products

1. Non-destructive analysis and pharmaceutical visualization: Principle, instrumentation, qualitative and quantitative applications (including PAT and/or visualization) for the following equipment:

FT-NIR, ATR, FT-Raman, Terahertz Pulse Spectroscopy, Quadrupole Resonance Spectroscopy, Frequency Modulation Spectroscopy (FMS), X-Ray Diffraction (XRD), Optical Coherence, Tomography, Time-of-Flight Secondary Ion Mass Spectrometry

2. Thermal techniques:

DSC: Principle, thermal transitions, instrumentation (heat flux and power-compensation designs), modulated DSC, hyper DSC, experimental parameters (sample preparation, experimental conditions, calibration, heating and cooling rates, resolution, source of errors) and their influence, pharmaceutical applications.

TGA: Principle, instrumentation, factors affecting results, pharmaceutical applications.

3. Particle sizing: Static & dynamic laser light scattering.

4. Analysis of trace components: Techniques employed for the qualitative and quantitative evaluation of impurities, degradation products, drug-drug and drug-excipient interaction products, metabolites, elemental impurities, residual solvents, etc.

LC-MS: Variety of mass systems available, their essential differences, strategy for qualitative and quantitative analysis of trace components, specific case studies.

LC-NMR: Nature of interfaces, qualitative and quantitative applications.

Other Hyphenated Systems: Utility for the same purpose of GC-MS, CE-MS, SFC-MS, CE-NMR, LC-FT-IR, ICP-MS, GC-HS, etc.

Recommended books (latest available edition):

1. Principles of Instrumental Analysis by Dougla A. Skoog, F. James Holler, Timothy A. Nieman

2. Instrumental Method of Analysis by Hobart H. Willard, Lynne L. Merrit, John A. Dean, Frank A. Settle

3. Fundamentals of Fourier Transform Infrared Spectroscopy by Brian C. Smith

4. Modern Raman Spectroscopy: A Practical Approach by Ewen Smith, Geoffery Dent

5. Chemical Analysis: Modern Instrumental Methods and Techniques by FranscisRouessac and Annick Rouessac

6. Handbook of Pharmaceutical Analysis by Lena Ohannesian, Antony J. Streeter

7. HPLC for Pharmaceutical Scientists, Edited by Yuri Kazakevich and Rosario LoBrutto

8. Introduction to Thermal Analysis Techniques and Applications by Michael E. Brown

9. Modern Methods of Particle Size Analysis, Edited by Howard G. Barth

10. Electrophoresis: The Basics by David M. Hawcroft

PA-630 (1 credit)

Stability Testing

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:

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

Stability testing of phytopharmaceuticals: Regulatory requirements.

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

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

Stability testing of drug delivery systems.

Recommended books:

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

PA-640

Quality Control and Quality Assurance (2 credits)

1. Good manufacturing practices [Schedule M] and Good laboratory practices [Schedule L-I]: Their applications to pharmaceutical industry.

2**. Basic principles and concepts of quality management**: Quality control, quality assurance, quality auditing, ISO system, electronic quality management system (eQMS).

3. Control of raw & packaging material and labelling, sampling, testing, release and distribution of finished products.

4. Document control: Preparation, review, approval, issuance, storage and retrieval (e.g., master manufacturing and packaging records, site master file, etc.), electronic document management system (e-DMS).

5. Standard operating procedures: SOP on SOPs, Change control procedure, annual product review/product quality review, handling of deviations & non conformity, corrective & preventive actions (CAPA), handling of laboratory incidents and OOS test results.

6. Qualification of facility and utilities: Concepts of facility validation, qualification of HVAC and water systems.

7. Process validation, product change over, basic requirements of cleaning and its validation

8. Technology transfer from R&D to manufacturing, including product life-cycle approach.

9. Handling of market complaints, recalls and returned goods.

10. Quality risk management in production area, data integrity management.

11. Introduction to concepts of QbD, PAT and continuous manufacturing.

Recommended books (latest available edition):

1. Quality Assurance of Pharmaceuticals: A Compendium of Guidelines and Related Materials, Volume 1

2. Quality Assurance of Pharmaceuticals: A Compendium of Guidelines and Related Materials, Volume 2

3. Q.A. Manual by D.H.Shah,

4. Good Pharmaceutical Manufacturing Practice: Rationale and Compliance by John Sharp

5. WHO Expert Committee on Specifications for Pharmaceutical Preparations

6. Handbook of Pharmaceutical Quality Assurance by Dr. Premnath Shenoy

NP-640

Structure Elucidation (2 credits)

1. Structure elucidation of natural products: General strategies for structure elucidation of natural products with few examples.

2. Chemical methods: Determination of carbon skeleton, dehydrogenation, oxidative methods in structure elucidation, reductive methods in structure elucidation.

3. Chemical methods: General methods for structure elucidation of steroids, terpenoids, alkaloids with few examples.

4. Ultraviolet spectroscopy: Basic principles, rules to calculate max, applications in structure elucidation with examples.

5. Infra red spectroscopy: Basic principles, various factors affecting frequency, functional group identification, applications in structure elucidation with examples.

6. Mass Spectrometry: Basic principles, various ionization modes EI, CI, FAB etc. fragmentation patterns, HRMS,applications in structure elucidation with examples.

7. ^{1}H and ^{13}C NMR Spectroscopy: basic principles, chemical shift, factors affecting chemical shift, prediction of chemical shifts, coupling constants, Karplus curve, advanced 1D NMR experiments such as NOE,DEPT etc

8. 2D NMR: ^{1}H- ^{1}H COSY, HSQC, HMBC, NOESY experiments: Their use in structure elucidation.

9. Structure elucidation: Examples from alkaloids, flavaonoids, and sterols.

10. Structure elucidation - examples from coumarins, triterpenes, and xanthones.

Recommended books:

1. Spectroscopy by Pavia, Lampman, Kriz, Vyvyan

2. Spectrometric Identification of Organic Compounds by RM Silverstein

3. Organic Spectroscopy by William Kemp

4. Spectral Data for Structure Elucidation

PC-611

Pharmacological Screening and Assays (1 credit)

1. Role of pharmacology in drug discovery

2. General principles of pharmacological screening.

3. Animal ethics, regulations for conducting animal experimentation.

4. 3 R's concept, alternatives to animal experimentations, Organs-on-chips

5. Pharmacological screening models

6. Correlations between various animal models and human situations.

7. Correlation between in-vitro and in-vivo screens.

8. Cell- based assay, CaCo-2 cell permeability assay. Single cell gel electrophoresis assay(COMET) assay.

9. Zebra fish model to screen pharmaceutical molecules.

10. Biochemical assays.

11. Introduction to cell culture, role of genomic and proteomic techniques in the process of target identification in drug discovery, MALdiTof., microarray.

12. High throughput screening and high content screening, transgenic animal model for drug screening.

13. Specific use of reference drugs

14. Interpretation of results.

15. Pharmacogenomics and Personal medicine

Recommended book/journals:

1) Drug Discovery and Evaluation: Pharmacological Assays by Vogel & Vogel

2) CPCSEA guidelines (http://cpcsea.nic.in)

3) Scientific journals in the area of pharmacology

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.

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.

4. Methods of optimization – OVAT and Design of experiments (DOE).Experimental designs, screening designs, factorial designs, composite designs, 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.

9. Case studies or regulatory guidelines related to above topics shall be discussed after each topic.

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, definition, 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, enatiotropy / 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

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.

Books recommended:

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

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GE-611 (1 credit)

Seminar

Students are required to submit 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-10 hours/week (2 credits)

Practical's in lab :

1. Analysis of a drug sample by a pharmacopoeial method and preparation of its certificate of analysis.

2. Determination of viscosity of given samples using Ostwald viscometer and rotoviscometer.

3. Estimation of the given drug in urine and blood samples using HPLC and identification of metabolites.

4. Stress study of a drug sample in proposed conditions and establishment of a stability indicating assay using HPLC.

5. Separation of an impurity in a sample on a preparative HPLC.

6. Establishment of dissolution characteristics of a given controlled release preparation using an automated dissolution tester.

7. Particle size and shape analysis using of an automated particle size analyzer.

8. Determination of tapped and bulk density.

9. Study of different packaging materials and their evaluation.

10. Determination of osmolality of given solutions.

11. Moisture determination of given substances using infrared moisture balance.

Practical's in CIL:

1. Determination of instrument calibration, melting behaviour and polymorphic behaviour of various compounds by DSC.

2. Spectrofluorimetric analysis of a given sample.

3. Study of hydrate forms of ampicillin trihydrate using TGA.

4. Study of the given sample by AAS.

5. Freeze drying of a sample.

6. Separation of impurities of betamethasone velerate on LC-MS using BP method and study the mass values of impurities.

7. Study of a given mixture by GC-MS.

8. Study of given sample on polarimeter.

9. ATR analysis of a given drug sample.

10. Conduct of a titration using an autotitrator

Pharmaceutical Analysis

Ph.D Course

Semester –I

PA-710:	**Impurity and Metabolite Profiling**	**(2 Credits)**
PA-720:	**Development and troubleshooting of GC and HPLC methods**	**(2 Credits)**
PA-730:	**CE and SFC in Pharmaceutical Analysis**	**(2 Credits)**

Semester –II

PA-740:	**Liquid Chromatography in Pharmaceutical Analysis**	**(2 Credits)**
PA-750:	**Analytical Chemometrics**	**(2 Credits)**
PA-760:	**Mass Spectrometry in Pharmaceutical Analysis**	**(2 Credits)**

Semester –I

PA-710:

Impurity and Metabolite Profiling (2 Credits)

1. Introduction: Basic of impurity and Metabolite profiling.

2. Impurity profiling: Practical Approach

3. Metabolite identification: In-vitro/ In-vivo approaches and sample preparation.

4. Regulatory perspectives.

5. Basics of instrumentation techniques: HPLC, LC-MS, LC-IR, LC-NMR and metabolite identification using radio ligand technique.

6. Case studies: Impurity profiling, isolation and characterization.

7. Case studies: Metabolite profiling, isolation and characterization.

PA-720:

Development and troubleshooting of GC and HPLC methods (2 Credits)

1. Preparation of drug sample for analysis-Introduction, compatibility with the instrumental method, fundamental theories controlling preparation techniques.

2. Specific sample preparation techniques: Soxhlet extraction, Liquid –liquid extraction, solid phase extraction. Solid phase micro extraction, protein precipitation methods, Ultra filtration, direct injection methods, derivatization methods and applications to different pharmaceutical dosage forms: tablets, capsules, ointments etc.

3.GC Detectors, GC column characteristics, GC inlets and injectors, GC preparative maintenance and trouble shooting, residual samples preparation ,method development process, method validation and QA Processes.

4. HPLC Detectors: PDA, ELSD, Conductivity, UV, Refractive Index, Fluorescence, Mass spectrometry, HPLC column selection and mobile phases, mobile phase additives.

5. HPLC method development by using different stationary phases, mechanism of interactions, HPLC preventive maintenance and troubleshooting, case studies.

6. Calibration methods: external, internal and standard addition methods.

PA-730:

CE and SFC in Pharmaceutical Analysis (2 Credits)

1. Over view of CE in Pharmaceutical Analysis, Basic configuration, CE characteristics, principles of CE, methods and modes of CE.

2. Improve performance of CE methods –general considerations, method development, CE as orthogonal technique to chromatography. Crown ethers as buffer additives in capillary electrophoresis.

3. SFC Introduction, developing achiral separation methods in Pharmaceutical development, preps SFC, some case histories from Pharma.

4. Investigation into the use of atypical organic solvents with immobilized chiral stationary phases in SFC mode.

5. Use of chiroptical and ELSD detection in analysis and Prep.SFC.

6. Pharmaceutical Analysis applications.

Semester –II

PA-740:

Liquid Chromatography in Pharmaceutical Analysis (2 Credits)

1. HPLC method development for biomolecules, monolithic stationary phases-applications, chiral stationary phases, principle of chiral recognition, molecular imprinted polymers as sorbents for separation and extraction.

2. Assay and stability testing by HPLC, application of HPLC for cleaning validation, HPLC in dissolution testing, HPLC in chiral analysis of Pharmaceuticals.

3. New developments in HPLC role of Ultra, Nano liquid chromatography in Pharmaceutical Analysis, Immobilized Polysaccharide CSPs: advancement in enantiomeric separations, reversed phase chiral method development.

4. Preparative HPLC, practical aspects of Preparative HPLC: Equipment, sample solubility, effective of sample size: Touching –Band separations, column saturation capacity, gradient elution, heavily overload separations, unusual isothermal behavior and recovery.

5. Examples of preparative method developments: Normal, reversed phase and chiral phases, recent advances in preparative HPLC separations.

PA-750:

Analytical Chemometrics (2 Credits)

1. General introduction and its application in optimization, Modeling and parameter estimation, sampling.

2. Calibration ,Resolution ,Factor analysis, signal processing, structure-property relationship, pattern recognition.

3. Propagation of measurement uncertainties (Inaccuracy and imprecision).

4.Multivariate Calibration , Multivariate Curve Resolution, Chemo informatics, Library Searching, Data Preprocessing and Feature Selection, Image Analysis, Microarrays.

PA-760:

Mass Spectrometry in Pharmaceutical Analysis (2 Credits)

1. Importance of chromatographic separation, mass analyzers, atmospheric pressure ionization techniques: ESI, APPI, APCI.

2.Interpretation of API mass spectra: Molecular weight determination, typical fragmentation behavior for individual functional groups: (i) phosphorous (ii) Sulfur (iii) nitrogen (iv) oxygen (v) halogen substitute's (vi) alkyl and aryl substitution on the aromatic ring, polycyclic aromatic hydrocarbons, alkenes and alkynes.

3. Liquid chromatography-electro spray ionization-mass spectrometry (LC-ESI-MS) to the detection and determination of antibiotics drugs, antidiabetics, antitumour, antiretroviral drugs.

4. EI-MS of small molecular mass of selected drugs-fragmentation information.

5. Development, Validation and transfer for high throughput bioanalytical LC-MS/MS Methods.