



## Pharmaceutical Analysis



# I Semester

## 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 Q6 guidelines and understanding of specifications through study of pharmacopoeial monographs on drug substances and products.
3. Reference standards: Types, preparation, containers, labeling, 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.
5. Introduction to method development: Method development concepts, steps involved, intricacies at each step, use of software.
6. Methods validation: Definition and methodology, discussion on each parameter with examples.
7. Calibration and qualification of equipment: Difference of definitions, calibration standards, calibration frequency, examples of calibration of pH meter, FTIR and a UV spectrophotometer. Definition of qualification process involving DQ, IQ, OQ, CQ and PQ. Brief discussion on protocol of each.
8. Bioanalysis and bioanalytical method validation: Types of body fluids, requirement of analysis, matrix effects, sample preparation, non-biological analytical samples. Acceptance criteria in comparison to non-biological samples.
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: Internal inspection, external audit, concepts, preparing for inspections and audits.

### Recommended books:

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. Nieman
6. Handbook of Modern Pharmaceutical Analysis by Satinder Ahuja, Stephen Scypinski
7. Principles and Practice of Bioanalysis by Richard F. Venn

### **MC-511 Spectral Analysis**

**(2 credits)**

**(Refer to Page No. 03)**

### **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 Dosage Form Design Parameters (1 credit)**  
**(Refer to Page No. 42)**

**BT-510 Biotechnology in Pharmaceutical Sciences (1 credit)**  
**(Refer to Page No. 28)**

**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 pharmaceuticals: 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 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; Penalties 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 attorneys technical aspects, criteria for selection, addresses, fee, rights and responsibilities of a patentee; Practical aspects regarding maintaining of a PATENT FILE; Patent infringement- 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, brochures, periodicals, CD roms; Significance of copyright protection for researchers; Indian Copyright Law and digital technologies-Berne 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 personnel; 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 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

### **GE-511 Seminar**

**(1 credit)**

1. Introduction, Information retrieval systems.
2. Writing term papers and reports.
3. Organization of scientific material, thesis, dissertation and refernces.
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-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, 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 haemological parameters.
4. Biotechnology for 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.
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 pHmeter
  - d) To determine water content in the given sample by Karl Fisher 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.

**II Semester****PA-610 Pharmacopoeial Methods of Analysis (2 credits)**

The course shall cover critical comparative analysis of the following selected tests in IP, BP/EP and USP:

1. Physical tests: Viscosity, melting point, boiling point/range, water content, osmolality/osmolarity, refractive index, loss on drying, loss on ignition, optical rotation, pH and specific gravity.
2. Limit tests: Tests for arsenic, lead, chloride, sulfate, and heavy metals.
3. Special tests: Inorganic impurities, residual solvents, etc.

4. Microbiological assays: Antimicrobial effectiveness testing, microbial limit tests, sterility test.
5. Biological tests: Antibiotics-microbial assays, bacterial endotoxins test.
6. Dissolution tests: Types of dissolution apparatus, dissolution test requirements for immediate release, delayed release, extended release dosage forms; coated, uncoated and enteric-coated tablets; gelatin capsules, etc.
7. Miscellaneous tests: Test for epianhydrotetracycline and epitetracycline (USP).

**Recommended books:**

1. The Indian Pharmacopoeia, Indian Pharmacopoeia Commission, Ghaziabad, 2010.
2. The British Pharmacopoeia, Stationary Office British Pharmacopoeia Commission, London, 2008.
3. The United States Pharmacopoeia-National Formulary, Board of Trustees, Rockville, 2006.
4. The European Pharmacopoeia, Directorate for Quality of Medicines of the Council of Europe, 2007.

**PA-620 Modern Instrumental Techniques for Evaluation of APIs and Drug Products (2 credits)**

1. Spectroscopic techniques: Specific discussion on the following shall be preceded by overview on many newer techniques that allow non-destructive analysis and visualization. Also students shall be made aware of the concepts of chemometrics, lasers, and charged coupled devices.
  - a) FT-NIR: Principle (overtones, combinations, fermi resonance, interferences etc.), instrumentation (dispersion spectrometer and FT-NIR), advantage and disadvantage, qualitative and quantitative applications, including PAT and non-destructive analysis.
  - b) ATR: Principle (total internal reflection, evanescent wave, etc.), instrumentation (ATR crystal, IR beam), advantages and disadvantages, pharmaceutical applications.
  - c) FT-Raman: Principle (absorption, diffraction, scattering and emission of wave, molecular interaction), instrumentation (Dispersive Raman, FT-Raman), advantage and disadvantage, pharmaceutical applications including detection of counterfeits.
2. Thermal techniques:
  - a) 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, sources of errors) and their influence, advantages and disadvantages, pharmaceutical applications.
  - b) DTA: Principle, instrumentation, advantage and disadvantage, pharmaceutical application, derivative differential thermal analysis (DDTA).
  - c) TGA: Principle, instrumentation, factors affecting results, advantages and disadvantages, pharmaceutical application.
3. Particle sizing: Light interaction methods: Rayleigh or static laser light scattering, photon correlation spectroscopy or dynamic laser light scattering, single particle light scattering, multi-angle light scattering.
4. Electrophoresis: Capillary electrophoresis: Basic principle (zeta potential), instrumentation, different modes of CE, advantages and disadvantages, pharmaceutical applications.



5. Chromatographic techniques:
  - a) HPLC: Principle, instrumentation, pharmaceutical applications.
  - b) UPLC: Principle and applications.
  - c) LC-MS and LC-NMR: Nature of interfaces, applications.

### Recommended books:

1. Principles of Instrumental Analysis by Douglas 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, Geoffrey Dent
5. Chemical Analysis: Modern Instrumental Methods and Techniques by Francis Rouessac 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 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. Stress testing: Role, regulatory aspects, protocols/approaches, practical considerations.
3. Stability-indicating methods: Definition, regulatory requirement, steps in development, practical considerations.
4. Role of kinetics studies: Important mechanistic and stability-related information provided by results of study of factors like temperature, pH, buffering species, ionic strength, dielectric constant, etc. on the reaction rates.
5. Stability testing protocols: Selection of batches, container orientation, test parameters, sampling frequency, specifications, storage conditions, recording of results, concept of stability commitment, etc.
6. Retest period/shelf life determination: Evaluation of stability data.
7. Photostability: Photostability testing of new active substances and medicinal products, light sources and options, types of chambers, presentation of samples, practical considerations, confirmatory testing.
8. Stability testing of biotechnological products: Typical stability testing issues of biotechnological vis-à-vis conventional products, considerations in ICH Q5C guideline.
9. Stability testing of phytopharmaceuticals: Regulatory requirements, protocols, HPTLC/HPLC finger printing, Interactions and complexity.
10. Post-approval changes: Nature of post-approval changes. Regulatory requirements of stability re-workup.

11. Reduced stability-testing plans: Bracketing and matrixing designs for multiple strength, packaging, etc.
12. Ongoing and follow-up stability testing: Definitions, applicability, requirements in WHO 2009 stability testing guideline.
13. Stability test equipment: Types of stability chambers (walk-in, stand-alone, photostability), design considerations, qualification and other critical issues.

**Recommended books:**

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

**PA-640 Quality Control and Quality Assurance****(2 credits)**

1. Good manufacturing practices and its applications to pharmaceutical industry.
2. Basic principles and concepts of quality management viz. quality control, quality assurance, quality auditing and ISO system etc.
3. Sampling, finished products labeling, distribution records.
4. Document control: Issuance, storage and retrieval.
5. Standard operating procedures: Change control procedure and annual product review.
6. Basic principles of validation: Validation protocols, analytical method validation and process validation.
7. Technology transfer from R & D to manufacturing.
8. Product change over, basic requirements of cleaning and its validation.
9. Market complaint and handling of returned goods.

**Recommended books:**

1. Quality Assurance of Pharmaceuticals: A Compendium of Guidelines and Related Materials
2. Quality Assurance of Pharmaceuticals: A Compendium of Guidelines and Related Materials by D.H. Shah, Q.A. Manual
3. Good Pharmaceutical Manufacturing Practice: Rationale and Compliance by John Sharp

**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. <sup>1</sup>H and <sup>13</sup>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: <sup>1</sup>H-<sup>1</sup>H COSY, HSQC, HMBC, NOESY experiments: Their use in structure elucidation.
9. Structure elucidation: Examples from alkaloids, flavonoids, and sterols.
10. Structure elucidation - examples from coumarins, triterpenes, and xanthenes.

**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)****(Refer to Page No. 30)****PE-630 Pharmaceutical Product Development-I****(2 credits)****(Refer to Page No. 46)****PE-660 Solid State Pharmaceutics****(1 credit)****(Refer to Page No. 48)**

**GE-611 Seminar****(1 credit)**

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)****Practicals 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.

**Practicals 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.