# PHARMACEUTICAL ANALYSIS
## M. S. (Pharm.)

| Course no. | Course Name | Credits |
|---|---|---|
| **Semester I** | | |
| **CORE SUBJECTS (ALL COMPULSORY)** | | |
| PA-510 | Advanced Separation Techniques and Allied Hyphenated Techniques | 2 |
| PA-520 | Advanced Analytical Techniques in Pharmaceutical R&D | 1 |
| PA-530 | Pharmacopoeial Methods | 1 |
| PA-540 | Pharmacokinetics and *In vitro- In vivo* correlation | 1 |
| MC-530 | Spectral Analysis | 1 |
| MC-540 | Principles and Applications of NMR | 1 |
| GE-510 | Biostatistics | 2 |
| GE-511 | Seminar | 0.5 |
| LG-510 | General Laboratory Experience | 2.5 |
| **ELECTIVE SUBJECTS (FOR 4 CREDITS)** | | |
| | | |
| EL-501 | Biochemical Engineering Fundamentals | 2 |
| EL-502 | Biotechnology in Pharmaceutical Sciences | 1 |
| EL-503 | Industrial safety and green chemistry | 1 |
| EL-504 | Computer Application in Biomedical Engineering | 1 |
| EL-505 | Biological System Analysis and Control | 1 |
| EL-506 | Productivity in management and reengineering (Neha | 1 |
| EL-507 | Biosynthesis of Natural Products | 1 |
| EL-508 | Chemotherapy of Parasitic and Microbial Infections | 1 |
| | Choose any core courses of other department (BT/MC/MD/NP/PC/PE) | |

| Course no. | Course Name | Credits |
|---|---|---|
| **Semester II** | | |
| **CORE SUBJECTS (ALL COMPULSORY)** | | |
| PA-610 | Analytical Method Development and Validation | 3 |
| PA-620 | Practical Understanding of Instrumental Techniques | 1 |
| PA-630 | Stability Testing | 1 |
| PA-640 | Technology Transfer, Quality Control and Quality Assurance | 2 |
| PA-650 | Testing and Analysis of Medical Devices | 1 |
| PE-660 | Solid State Pharmaceutics | 1 |
| GE-611 | Seminar | 0.5 |
| LS-610 | General Lab Experience in the Area of Specialization | 2.5 |

| ELECTIVE SUBJECTS (FOR 4 CREDITS) | | |
|---|---|---|
| | | |
| EL-601 | Biomechanics | 2 |
| EL-602 | Mathematical Methods in Biomedical Engineering | 1 |
| EL-603 | Logistics & distribution | 1 |
| EL-604 | Total quality control | 1 |
| EL-605 | Lean system, 6 sigma | 1 |
| EL-606 | Introduction to Ayurveda and Polyherbal Formulations | 1 |
| EL-607 | Chemotherapy and Immunopharmacology | 2 |
| EL-608 | Pharmacovigilance and Medical Writing | 2 |
| | Choose any core courses of other department (BT/MC/MD/NP/PC/PE) | |
| | **Total Credits** | **16** |
| | | |
| | **Semester III** | |
| TH- 598 | Synopsis, Presentation | **9** |
| | **Semester IV** | |
| TH-698 | Thesis Writing and Thesis Defense | **9** |
| | **TOTAL CREDITS (I TO IV SEMESTERS)** | **50** |

# Course Contents

| PA-510<br>Advanced Separation Techniques and Allied Hyphenated Techniques<br>(2 Credits) | hrs |
|---|---|
| **Introduction to Pharmaceutical Analysis:**<br>Role of Pharmaceutical Analysis in Pharma Sector; Difference between analytical chemistry and pharmaceutical analysis; Expectation of Analytical Scientists-Quality Gatekeeper; Major roles in Reverse Engineering; Complex characterization; General routine analysis for quality monitoring and DMPK | 2 |
| **Separation Techniques:**<br>General Principle of chromatography, Column Chemistry, PQRI/USP Approach for selection of column; HILIC interactions<br><br>**Liquid Chromatography:**<br>Principle of HPLC, UHPLC, Preparative HPLC; Applications in Assay, RS, Dissolution, Bioanalysis and Spiking Study for comparison<br><br>**Gas Chromatography:**<br>Principle of GC and HS-GC; Applications in Residual Solvent Analysis<br><br>**Ion Chromatography:**<br>Principle of IC; Applications in Pharm Analysis<br><br>**Gel Permeation Chromatography:**<br>Principle of GPC; Applications in Polymer Characterization and Reverse Engineering; Analyses of Large molecules.<br><br>**Super Critical Fluid Chromatography:**<br>Principle of SFC; Applications in drug discovery<br><br>**Capillary Electrophoresis:**<br>Principle of CE; Applications of CE in Biologics<br><br>**Principle of Chiral Separation:** Basics of chirality; chiral stationary phases; modes of chiral separations; mobile phase and buffers for chiral separations and restrictions of solvents as per column chemistry. | 20 |
| **Structural Characterization through Hyphenated Techniques:**<br>Need of Structure Characterization with respect to impurities and metabolites; General steps of structure characterization<br>**LC-MS:**<br>Working principle of LC-MS, Types of Mass Analyzer, Amalgation of different Mass | 18 |

| | |
|---|---|
| data for interpretation<br><br>**LC-NMR and selection of NMR methods:**<br>Working principle of LC- NMR, Selection of right NMR techniques for data interpretation through usefulness of 1H; 13C; NoE; COSY; HSQC, HMBC, 15N; 1H-15N HSQC.<br><br>**Specific Mass interpretation Guide:**<br>Elemental composition calculation, Isotopic Pattern, Multi charge calculations, Finding adducts from mass spectrum, Nitrogen rule, peptide mapping | |

**Reference Study Material:**


1) Book: Chemical Analysis: Modern Instrumentation Methods and Techniques by Francis Rouessac and Annick Rouessac, Wiley Publisher
2) Book: Fundamentals of Analytical Chemistry. Douglas A. Skoog/Donald M. West/F. James Holler/Stanley R. Crouch, Cengage Learning publisher.
3) Book: Practical pharmaceutical chemistry. By. A. H. Beckett and J. B. Stenlake. The Athlone Press.
4) Book: HPLC Made to Measure: A Practical Handbook for Optimization, Stavros Kromidas, Wiley-VCH.
5) Book: The HPLC-MS Handbook for Practitioners. Stavros Kromidas, Wiley Publisher
6) Book: LC-MS in Drug Analysis- Methods and Protocols, Langman, Loralie J., Snozek, Christine L. H, Springer Publisher.
7) Book: Chromatographic Analysis of Pharmaceuticals, John A. Adamovics, CRC Press
8) Recent Review Articles (published in last 5 years) of JPBA, JMS and Trends in Analytical Chemistry in the field of LC-MS and LC-NMR.


**Outcomes:**

On completion of the course, the student should be able to:

- Create analytical students ready for research and make transition from their B. Pham basic learning
- Enable students to visualize the applications of different separation technology
- Enable students to learn modern hyphenated techniques, which are useful during their future research
- Enable students to interpret structure characterization of impurities and metabolites

| PA-520<br>Advanced Analytical Techniques in Pharmaceutical R&D<br>(1 Credit) | hrs |
|---|---|
| **Solid State Characterization Techniques:**<br><br>**DSC:**<br>Working Principle, Application for Polymorphic Screening and Drug: Excipient interaction<br><br>**TGA:**<br>Working Principle, Application for understanding of Hydrate, Solvate and Residual volatile content calculation<br><br>**SXRD and PXRD:**<br>Working Principle of single crystal XRD; Application in solving structure; Working Principle of powder XRD; Application in polymorph Screening<br><br>**Particle Size Analyzer:**<br>Working Principle, Selection between Powder and Suspension Methods<br><br>**Microscopic Allied techniques:**<br>Basics of hot stage microscopic technique in particle size measurements; Applications of advanced Microscopic techniques in Drug Development including FE SEM | 12 |
| **Process Analytical Techniques:**<br>Basics of PAT, Snapshot on different PAT techniques and highlight of QbD need<br><br>**NIR:**<br>Working Principle and Application in process monitoring of API and Formulation<br><br>**Raman:**<br>Working Principle and Application in process monitoring in API synthesis<br><br>**FBRM/PVM:**<br>Working Principle and Application in Crystallization process | 6 |
| **Wet Analytical Techniques:**<br>Working principle of Titrations, pH, KF, LOD, ROI. Applications on specific titrations like EDTA; pKa determination, HS-KFC etc. | 2 |

**Reference Study Material:**


1) Book: Introduction to Thermal Analysis Techniques and Application, M. E. Brown, Kluwer Academic Publishers.
2) Book: Chemical Analysis: Modern Instrumentation Methods and Techniques by Francis Rouessac and Annick Rouessac, Wiley Publisher
3) Book: Handbook of Modern Pharmaceutical Analysis, Satinder Ahuja Stephen Scypinski, Academic Press.
4) Book: Instrumental Methods of Analysis, Hobart H. Willard, Lynne L. Merrit, John A. Dean and Frank A. Settle, CBS Publishers.
5) Book: Introduction to instrumental analysis, Robert. D. Braun, PharmaMed Press/BSP

Books.
6) Book Chapter: Process Analytical Technology from Pharmaceutical Quality by Design-A practical Approach, Walkiria S Schlindwein and Mark Gibson, Wiley Publisher.
7) Book: Differential Scanning Calorimetry-An Introduction for Practitioners, Höhne, G.W.H., Hemminger, W., Flammersheim, H.-J, Springers Publisher
8) Book: Pharmaceutical Microscopy, Carlton Robert Allen, Springers Publisher

**Outcomes:**

On completion of the course, the student should be able to:

- Demonstrate the importance of process analytical technology to students
- Derive the need of pharmaceutical product analysis
- Analyze the principles and practices of solid state analysis
- Identify different types of microscopic techniques and learn utilization of these techniques for 'fit-for-purpose' needs

| PA-530<br>Pharmacopeial Methods (1 Credit) | hrs |
|---|---|
| **Introduction to Indian Pharmacopeia and other Pharmacopeia (USP and EP/BP):** Importance of general chapters and guidance to regulatory filling.<br>Note: For holistic view, it is important to compare the contents of general chapters between Pharmacopeias | 1 |
| **Reference standards** | 1 |
| **Balances, Weighing Procedures and Uncertainty** | 2 |
| **Antimicrobial effectiveness testing** | 1 |
| **Sterility assurance** | 1 |
| **Identification tests—general** | 0.5 |
| **Loss on drying and Residue on ignition** | 1 |
| **Light diffraction measurement of particle size** | 1 |
| **Botanical extracts** | 0.5 |
| **Chromatography** | 2 |
| **Density of solids** | 1 |
| **Disintegration and Tablet friability** | 1 |
| **pH** | 0.5 |
| **Refractive index** | 1 |
| **Specific gravity** | 0.5 |
| **Specific surface area** | 1 |
| **Uniformity of dosage units** | 1 |
| **Viscosity** | 0.5 |
| **Water determination** | 0.5 |
| **Analytical data—interpretation and treatment** | 1 |
| **Application of water activity determination to nonsterile pharmaceutical products** | 1 |

**Reference Study Material:**


1) Current Version of USP
2) Current Version of EP
3) Current Version of IP
4) Current Version of BP
5) The International Pharmacopoeia, General Methods of Analysis and Quality Specification for Pharmaceutical Substances, Excipients and Dosage Forms. World Health Organization


**Outcomes:**

On completion of the course, the student should be able to:

- Demonstrate the importance of Pharmacopoeia in Pharmaceutical Industry
- Analyze the principles and practices of Pharmacopoeial methods
- Generate thought-process to distinguish pharmaceutical analysis from general analytical methods

| **PA-540**<br>**Pharmacokinetics and *In vitro- In vivo* correlation (1 Credit)** | **hrs** |
|---|---|
| **Basics Understanding of Bioavailability fundamentals, bioequivalence and therapeutic equivalence** | 2 |
| **Study design for Bioequivalance: Parellel and Cross over (brief about requirements through Clinicaltrial.org)**<br>Highly variable drugs with respect to Bioavailability with example | 2 |
| **Factors affecting bioavailability and bioequivalence:**<br>Physiological factors, disease state,<br>physicochemical properties of drugs,<br>Drug delivery factors. | 2 |
| **Introduction to IVIVC**:<br>Importance of IVIVC;<br>Application in drug development;<br>Definitions of ADME, $C_{max}$, $T_{max}$, AUC, $K_{EL}$ | 2 |
| **Calculation of PK parameters from Preclinical or Clinical data:**<br>$C_{max}$;<br>$T_{max}$,<br>AUC ($0 \rightarrow t$ and $0 \rightarrow \infty$),<br>$K_{EL}$, [Impact of changes on second decimals due to selection of data and statistical consideration would be included]<br>$T_{half}$ | 4 |
| **Dissolution as in-vitro evaluation:**<br>Biorelavaent dissolution media;<br>Physiology of GI track; Dissolution with different USP apparatus, their advantages and disadvantages;<br>Modified dissolution method for in-vivo simulation | 5 |
| **Regulatory requirement for bioequivalence:**<br>FDA guidance documents and F1 and F2 calculation,<br>Waiver of bioequivalence studies | 3 |

**Reference Study Material:**


1) Book: Pharmaceutical Dissolution Testing, Umesh V. Banakar, Marcel Dekker.
2) Book: Pharmaceutical Dissolution Testing, Jennifer Dressman and Johannes Kramer,Taylor and Francis.
3) Book: Biopharmaceutics and Pharmacokinetics,Brahmankar and D. M. Jaiswal, Vallabh Prakashan.
4) Book: Pharmacokinetics in Drug Development- Clinical Study Design and Analysis (Volume 1), Bonate, Peter L., Howard, Danny R, Springers Publication
5) Book: Pharmacokinetics in Drug Development- Regulatory and Development Paradigms (Volume 2), Bonate, Peter L., Howard, Danny R, Springers Publication
6) Book: Pharmacokinetics in Drug Development- Advances and Applications (Volume 3), Bonate, Peter L., Howard, Danny R, Springers Publication

**Outcomes:**

On completion of the course, the student should be able to:

- Demonstrate the principles of drug distribution in the body
- Interpret Pharmacokinetic data and correlate with absorption and elimination principles
- Demonstrate the importance of dissolution to correlate pharmaceutical performance of dosage form
- Analyze and create biorelavant dissolution media as in-vitro surrogate to understand absorption of drug in the body
- Ability to calculate Pharmacokinetic parameters
- Demonstrate the importance of bioquivalance and regulatory requirements

| **MC-530**<br>**Spectral Analysis**<br>**(1 credit)** | **hrs** |
|---|---|
| **UV-Vis Spectroscopy:**<br>Energy levels and selection rules: Definitions, molecular orbital approach for energy absorption, various modes of transitions.<br>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 stereo chemical factors.<br>Predicting UV absorption: Woodward-Fieser, Fieser-Kuhn and Nelson rules.<br>Other factors: Non-conjugated interactions, Solvent effect, S-Cis band | **4** |
| **Infrared (IR) spectroscopy:**<br>Characteristic regions of the spectrum: Various modes of vibrations, Energy levels;<br>Correlation of structure with IR spectra: Influence of substituents, ring size, hydrogen bonding, vibrational coupling and field effect on frequency.<br>Applications: Determination of stereochemistry, structural elucidations of biomolecules (conformation of secondary structure of peptides), Spectral interpretation with examples | **4** |
| **Mass-Spectrometry:**<br>Molecular ion and metastable peak, fragmentation patterns, nitrogen and ring rules, McLafferty rearrangement, electron and chemical ionization modes, applications.<br>Basics of Instrumentation (Ionization sources, Mass filters/analyzers and detectors), Tandem Mass analyzers, High Resolution and Accurate Mass<br>Applications in biomolecules | **9** |
| **Introduction to ORD, CD, Atomic absorption spectroscopy (AAS) and Inductively Coupled Plasma-Mass spectrometry (IPC-MS)** Basic principles with one examples from each | **3** |
| Note: All chapters should include at least one example as case study from current research articles | |

**Reference Study Material:**


1) Introduction to Spectroscopy: A Guide for Students of Organic Chemistry Donald L. Pavia, Gary M. Lamlman and George S. Kriz Thomson
2) R. S. Drago, Physical Methods for Chemists, W. B. Saunders,1992.

3) Fundamentals of Molecular Spectroscopy, C. N. Banwell, McGraw-Hill, 1966
4) Instrumental Methods of Analysis, Seventh Edition Hobart H. Willard, Lynne L. Merrit, John A. Dean and Frank A. Settle CBS Publishers
5) Spectrometric Identification of Organic Compounds, Sixth Edition Robert M. Silverstein and Webster Fransis Wiley-VCH
6) Spectroscopy by Donald L Pavia, Gary M Lampman, George S Kriz, James A Vyvyan
7) Organic spectroscopy by William Kemp
8) Spectroscopic Methods in Organic Chemistry by Dudley H. Williams & Ian Fleming
9) Spectrometric Identification of Organic Compounds by Robert M. Silverstein, Francis X. Webster & David J. Kiemie
10) Applications of Absorption Spectroscopy of Organic Compounds by Dyer
11) Edmond de Hoffmann, Vincent Stroobant: *Mass Spectrometry, Principles and applications*, 3rd Edition, Wiley, 2007
12) E. de Hoffmann and V.Stroobant, *Mass Spectrometry: Principles and Applications*, 3rd edition, Wiley Interscience (2007).

**Outcomes:**

On completion of the course, the student should be able to:

This course will make students of diverse background to understand the basic principle of various spectroscopic/spectrometric methods and other modern tools to characterize molecules therapeutic molecules. The course provides the student with knowledge about: (1) Basic concept of UV spectroscopy and its various applications. (2) Basic concept of IR spectroscopy and its various applications (3) Basic concept of various Mass spectrometric techniques and its various applications (4) Applications of other various techniques towards structural determination and identifications of molecule. The course should enable the student to assess the basics of how to elucidate the chemical structure of synthetic, semisynthetic or naturally isolated molecules. Analyse the samples of interest.

| **MC-540**<br>**Principles and Applications of NMR-Spectroscopy**<br>**(1 credit)** | **hrs** |
|---|---|
| **Fundamentals of NMR spectroscopy**:<br>Physical basis, Magnetic nuclei, resonance, relaxation processes, signal sensitivity $^{1}$H NMR: 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 heteroatoms, quadrupole broadening and decoupling, effect of conformations and stereochemistry on the spectrum, Karplus relationship, diastereomeric protons, Heteronuclear coupling to 19F and 31P. $1^{3}$C NMR: Chemical environment, shielding and carbon-13 chemical shift, calculation, proton-coupled 13C spectra, Proton- | **12** |

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|---|---|
| decoupled 13C spectra, Nuclear Overhauser Enhancement (NOE), Problem with integration, Heteronuclear coupling for carbon to deuterium, carbon to 19F, carbon to 31P, Introduction of qNMR with examples | |
| **NMR Instrumentation:**<br>Component of NMR spectrometer, operation of NMR spectrometer, Fourier transform NMR instruments | **2** |
| **Distortionless Enhancement by Polarisation Transfer (DEFT):**<br>Introduction of DEPT Spectroscopy, Types of DEPT NMR, Examples and applications | **2** |
| **2D NMR spectroscopy:**<br>Introduction of 2D NMR with examples and its applications in elucidation of complex natural products and biomolecules | **4** |
| Note: All chapters should include at least one example as case study from current research articles | |

**Reference Study Material:**


1) R. S. Macomber, A Complete introduction to modern NMR techniques, 1st Ed, John Wiley & Sons, England (1998).
2) M. H. Levitt, Spin dynamics: Basics of Nuclear Magnetic Resonance, 2nd Ed, John Wiley & Sons, England (2008).
3) C. P. Slichter, Principles of Magnetic Resonance, 3rd Ed, Springer Verlag, Berlin (1996)


**Outcomes:**

On completion of the course, the student should be able to:

**The course gives the student insight about:** How to assess the structural analysis of a molecule The course should enable the student to: Assess the basics of how to elucidate the chemical structure of synthetic, semisynthetic or naturally isolated molecules.

| **PA-610**<br>**Analytical Method Development and Validation**<br>**(3 Credits)** | **hrs** |
|---|---|
| **Introduction to method development**:<br>Method development concepts,<br>steps involved,<br>intricacies at each step,<br>use of software and analytical quality by design. | 2 |
| **HPLC method development**:<br>**Assay Method development**:<br>Selection of diluent;<br>'fit-for-purpose' specificity;<br>selection of concentration;<br>Selection of Mobile phase<br>**RS Method development**:<br>Impurity Specification as per ICH and MAPP guideline;<br>Gradient selection;<br>Calculation for elution prediction;<br>Resolution calculation;<br>Robustness of method<br>RRF calculation<br>Selection of wavelength and other detector<br>Beware of co-elution<br>**Cleaning method development:**<br>Understanding of MOC;<br>Calculation of MACO (History and New requirements); Changing scenario when new product is introduced in plant;<br>Selection of concentration;<br>Factors to increase sensitivity | 12 |
| **GC Method development for residual volatiles:**<br>Selection of Column;<br>Selection of Liquid injection and head space injection;<br>Temperature gradient selection;<br>Split ratio and sensitivity | 3 |
| **LC-MS method development:**<br>Selection of ESI and APCI;<br>Selection of ionization mode;<br>Selection of MS parameters;<br>Selection of LC condition;<br>Basics of MRM and SRM | 6 |
| **Analytical Methods validation (Including Limit test)**:<br>Definition and methodology,<br>discussion on each parameter (specificity, accuracy, precision, range, LOD/LOQ, Robustness, Solution Stability) with examples.<br>Exercise for making validation protocol | 12 |
| **Bioanalysis and bioanalytical method validation**:<br>Types of body fluids,<br>requirement of analysis,<br>matrix effects,<br>sample preparation,<br>Bioanalytical method validation as per USFDA guidance; | 12 |

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|---|---|
| Difference between USFDA and other guidelines through comparision | |
| **qNMR method development:**<br>Basics of qNMR;<br>Selection of transfer/delay time and method development;<br>Selection of internal standards; Understaning and usage of ERATIC methods (interal signals)<br>Calculation of potency | 3 |
| **QbD principles in method development:**<br>Risk assessment for false positive and false negative results;<br>Approaches to be considered during method development like factorial design | 5 |
| **GTI method development:**<br>Types of GTIs;<br>Limit and TTC levels;<br>Purging study and method development criteria;<br>Partial method validation with respect to GTI control strategy | 5 |

**Reference Study Material:**


1) Book: Practical HPLC Method Development, Lloyd R. Snyder, Joseph J. Kirkland and Joseph I. Glajch , John Wiley and Sons
2) Book: HPLC Method Development for Pharmaceuticals (Volume 8), Satinder Ahuja Henrik Rasmussen, Academic Press
3) Book: Genotoxic Impurities: Strategies for Identification and Control, Andrew Teasdale, Wiley Publication
4) Current ICH M7 (https://www.fda.gov/media/85885/download)
5) Book: Pharmaceutical Quality by Design-A practical Approach, Walkiria S Schlindwein and Mark Gibson, Wiley Publisher
6) Book: HPLC, LC-MS and GC Method Development and Validation-Guideline for academic and industrial scientists involved in method development and validation, Ghulam Shabir, Lap Lambert Academic Publishing.
7) Book: Handbook of LC-MS Bioanalysis: Best Practices, Experimental Protocols, and Regulations, Wenkui Li , Jie Zhang and Francis L. S. Tse, Wiley Publisher.
8) Book: Sample Preparation in LC-MS Bioanalysis, Wenkui Li, Wenying Jian and Yunlin Fu, Wiley Publisher
9) Quantitative NMR information sheet and Calculation (Accessed by www.bruker.com/potency/determination or any recent documents available from Bruker).


## Outcomes:

On completion of the course, the student should be able to:

- Enable students to visualize research problem and train to tackle with appropriate selection of techniques
- Enable students to develop analytical methods for ‘fit-for-purpose’ need with understanding of false positive and false negative results
- Interpret principles and procedures underlying QbD aspects of method development
- Derive the method capability through define robustness check
- Produce analytical method validation protocols as per ICH requirements

| PA-620<br>Practical Understanding of Instrumental Techniques<br>(1 Credit) | hrs |
|---|---|
| **UV and IR:**<br>Instrumentation and working flow diagram;<br>Role of each module/assosories<br>Instrument operating procedure<br>Calibration/performance verification | 2 |
| **DSC**<br>Instrumentation and working flow diagram;<br>Role of each module/assosories<br>Instrument operating procedure<br>Calibration/performance verification | 1 |
| **TGA**<br>Instrumentation and working flow diagram;<br>Role of each module/assosories<br>Instrument operating procedure<br>Calibration/performance verification | 1 |
| **Dissolution Appratus I; II and IV**<br>Instrumentation and working flow diagram;<br>Role of each module/assosories<br>Instrument operating procedure<br>Calibration/performance verification | 3 |
| **Hot Stage Microscope**<br>Instrumentation and working flow diagram;<br>Role of each module/assosories<br>Instrument operating procedure<br>Calibration/performance verification | 2 |
| **HPLC and GPC**<br>Instrumentation and working flow diagram;<br>Role of each module/assosories<br>Instrument operating procedure<br>Calibration/performance verification | 2 |
| **LC-MS**<br>Instrumentation and working flow diagram;<br>Role of each module/assosories<br>Instrument operating procedure<br>Calibration/performance verification | 2 |
| **SEM**<br>Instrumentation and working flow diagram; | 1 |

| | |
|---|---|
| Role of each module/assosories<br>Instrument operating procedure<br>Calibration/performance verification | |
| **Particle size analyzer (including Zetasizer)**<br>Instrumentation and working flow diagram;<br>Role of each module/assosories<br>Instrument operating procedure<br>Calibration/performance verification | 4 |
| **GC**<br>Instrumentation and working flow diagram;<br>Role of each module/assosories<br>Instrument operating procedure<br>Calibration/performance verification | 2 |

**Reference Study Material:**


1) Book: Instrumental Methods of Analysis, Willard M H, CBS publishers
2) Book: Text Book of Pharmaceutical Analysis, K. A. Connors, Wiley Interscience.
3) User Manuals of Malvern [https://www.malvernpanalytical.com/en/learn/knowledge-center/user-manuals/]
4) User Manuals of Agilent LC
5) User Manuals of Agilent LC-MS
6) User Manuals of Agilent GC
7) User Manuals of Distek Dissolution Apparatus
8) User Manuals of Distek Dissolution Apparatus
9) User Manuals of Distek Dissolution Apparatus
10) User Manuals of HSM and SEM (Carl Zeiss and Leica)


**Outcomes:**

On completion of the course, the student should be able to:

- Enable students to develop skill set to handle instruments independently
- Derive methodology for instrument operating procedure and best practices for use
- Interpret principles and procedures of calibration and setting-up acceptance criterion for each test

| PA-630<br>Stability Testing (1 Credit) | hrs |
|---|---|
| **Drug development cycle and stability-testing**: Role and types of stability studies during different stages of drug and product development. | **2** |
| **Stress testing of drug substances:** Role, regulatory aspects, protocols / approaches, practical considerations. | **2** |
| **Stability-indicating assays:** Definition, regulatory requirement, steps in development, practical considerations. | **2** |
| **Role of kinetic 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. Temp and RH based prediction through recent advancement. | **3** |
| **Stability-testing protocols:** Selection of batches, container orientation, test parameters, sampling requency, specifications, storage conditions, recording of results, concept of stability commitment, etc. | **2** |
| **Retest period/shelf-life determination**: Evaluation of stability data. | **1** |
| **Photo stability testing**: Photostability testing of new active substances and medicinal products, light sources and options, types of chambers, presentation of samples, practical considerations, confirmatory testing. | **1** |
| **Stability testing of biotechnological products**: Typical stability testing issues of biotechnological vis-à-vis conventional products, considerations in ICH Q5C guidelines. | **2** |
| **Stability testing of phytopharmaceuticals**: Regulatory requirements, protocols, HPTLC / HPLC fingerprinting, interactions and complexity. | **1** |
| **Post-approval changes**: Nature of post-approval changes. Regulatory requirements of stability re-workup. | **1** |
| **Reduced stability-testing plans:** Bracketing and matrixing designs for multiple strength, packaging, etc. | **1** |
| **Ongoing and follow-up stability testing:** Definitions, applicability, requirements in WHO 2009 stability testing guideline. | **1** |
| **Stability-test equipment:** Types of stability chambers (walk-in, stand-alone, photostability), design considerations, qualification and other critical issues. | **1** |

**Reference Study Material:**


1) Pharmaceutical Stress Testing: Predicting Drug Degradation, Steven W Baertschi, Robert A Reed, Karen Mills Alsante. Informa Healthcare.
2) ICH Guidelines for Impurity Determination and Stability Studies.
3) Identification and Determination of Impurities in Drugs, S. Gorog, Elsevier.
4) Analysis of Drug Impurities, R. J. Smith and M. L. Webb. Blackwell Publishing.
5) Handbook of Isolation and Characterization of Impurities in Pharmaceuticals, S. Ahuja, K. M. Alsante and Academic Press.


**Outcomes:**

On completion of the course, the student should be able to:

- Enable students to interpret requirement of stability study with respect to shelf-life determination
- Enable students to design stability study as per regulatory requirements
- Perform stress study for API and dosage form as prerequisite to understand degradation profile
- Generate predictive ability to calculate shelf-life

| **PA-640**<br>**Technology Transfer, Quality Control and Quality Assurance**<br>**(2 Credit)** | **hrs** |
|---|---|
| **Good manufacturing practices and its applications to pharmaceutical industry:**<br>ICH Q7 in brief;<br>Quality Management;<br>Personnel;<br>Buildings and Facilities,<br>Materials Management<br>ISO systems | 4 |
| **Document control and change control-**<br>Issuance;<br>Controlled distribution;<br>Archival;<br>Tracking of revisions;<br>Change control procedure | 3 |
| **Breif introduction for documents used in GLP/GMP:**<br>SMF;<br>DRP;<br>CoA;<br>Job Description and Training Document;<br>SOP; IOP; GAM;<br>Deviations;<br>BMR/BPR,<br>Method development reports;<br>method transfer reports;<br>Specification and STP;<br>Impurity justification Reports;<br>Calibration Schedule | 5 |
| **Standard operating procedures/Instrument operating procedures**:<br>Writing requirements for SOP/IOP;<br>Content of SOP and IOP;<br>Format/Annexure numbering;<br>Excersise with one example | 5 |
| **Online Documentation and 21 CFR Part 11 requirements:**<br>Electronic lab note book;<br>Date and Time stamping;<br>Risk identification with respect to data integrity | 5 |
| **Technology transfer**<br>Working environment change from R & D to manufacturing;<br>Priciple of TT and Need; | 8 |

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|---|---|
| Workflow;<br>R&R of each CFT;<br>Excersise with one example<br>Method transfer excersise | |
| **Laboratory investigations and Inspections**:<br>Out of specification;<br>Out of trend;<br>CAPA<br>Deviation (plan and unplan),<br>Root cause analysis;<br>Internal inspection,<br>external audit, concepts, preparing for audits and inspections | 5 |
| **Product changeover, basic requirement of cleaning** | 3 |
| **Market complaint and handling of returned goods** | 2 |

**Reference Study Material:**


1) Technology Transfer Introduction and Objectives, Mark Gibson, [https://store.pda.org/TableOfContents/Tech_Transfer_Ch01.pdf]
2) WHO guidelines on transfer of technology in pharmaceutical manufacturing [https://www.who.int/medicines/areas/quality_safety/quality_assurance/TransferTechnology PharmaceuticalManufacturingTRS961Annex7.pdf]
3) USP 1224 for Transfer of Analytical Methods and Procedures
4) Book: Good Laboratory Practice Regulations, Sandy Weinberg , Marcel Dekker Inc.
5) Quality Assurance of Pharmaceuticals – A Compendium of Guidelines and Related Materials, World Health Organization.
6) Book: A Guide to Total Quality Management, Kaushik Maitra and Sedhan K.Ghosh.
7) Book: Pharmaceutical Quality Assurance, M A Potdar ,Nirali/ Pragati
8) Book: Quality Assurance and Good Laboratory Practices, Y Anjaneyulu
9) Book: Quality Control and Applications, B L Hanser
10) Book: Quality Assurance in Analytical Chemistry, Werner Funk


**Outcomes:**

On completion of the course, the student should be able to:

- Enable students to interpret requirement of technology transfer
- Enable students to visualize QC and QA work responsibility
- Familiarize students with quality language and connectivity with respect to QMS
- Enable students to draft SOP
- Design of audits and familiarization with investigations

| PA-650<br>Testing and Analysis of Medical Device (1 credit) | hrs |
|---|---|
| Brief Introduction to Medical Devices and types of medical devices (Include Hybrid drug-device combinations) | 1 |
| **Regulatory Requirement**:<br>Premarket Approval; Investigational Device Exemption. | 1 |
| **GLP requirement with respect to Analytical facility in medical device**:<br>Equipment installation: DQ, IQ, OQ and PQ; SOP/IOP preparation; Site Master file and QMS | 2 |
| **Physical and Mechanical Testing of medical device**: The regulatory perspectives of physical and mechanical properties of medical devices and implant materials. Physical properties: testing parameters; porosity & surface area (ISO 9277:2010), zeta potential & size (ISO/TR 19997:2018 & ISO 22412:2017); morphology & particle size by image analysis methods (ISO 13322-1:2014); Method for contact angle and surface tension (ISO15989:2004). Mechanical properties: tensile, compressive, shear, wear and fatigue testing of implants (cardiovascular, orthopedic and dental) and different implant materials (ISO 19213:2017, ISO 12106:2017, ISO 5840-1: 2015 and ISO 14801, etc.) | 6 |
| **Performance Indicators and CQAs:**<br>Setting specifications; Example with two medical devices | 2 |
| **Quality Guidelines:**<br>ISO 13485 Quality Management System for Medical Devices | 2 |
| **Chemical Testing of Medical Device materials**:<br>Identification of Extractable and Leachable chemicals; Forced Degradation Studies and Degradation Product Characterization for identification and quantification of potential degradation products from medical devices; Determination of Active Pharmaceutical Ingredient (API) Drug Release Characteristics; Stability studies including Accelerated and Stressed studies; Imaging of the phase distribution of Drug Components | 2 |
| **Biological Testing of Medical Devices:** Introduction to Biological testing, International Standard ISO 10993 and principles for biological evaluation of medical devices, Biological evaluation process (general biocompatibility testing considerations and test-specific considerations), Endpoints of biocompatibility testing (ISO 10993-1: 2018) as per the category of medical device (nature of body contact as well as the time period of contact) | 4 |

**Reference Study Material:**


1) Indian Regulation: G.S.R. 102(E)_dated 11.02.2020_ Registration of certain medical devices
2) Indian Regulation: S.O. 648(E) dated 11.02.2020_ Medical Device Definition
3) Indian Regulation: 2019.10.18_G.S.R. 797(E)_Registration of Certain Medical Devices_chapter-IIIA
4) WHO regulation: Amendment in Environmental requirements for mfg. of Medical Devices Annexure- A of the Fifth Schedule of MDR, 2017 [https://www.who.int/medical_devices/publications/en/MD_Regulations.pdf]
5) Quality System Information-Guidance document From USFDA [https://www.fda.gov/medical-devices/postmarket-requirements-devices/quality-system-qs-regulationmedical-device-good-manufacturing-practices]
6) 21 CFR 820: [https://www.ecfr.gov/cgi-bin/text-

idx?SID=332944a20dfb1ca8fb05033d20caf52e&mc=true&tpl=/ecfrbrowse/Title21/21CIsubchapH.tpl
7) FDA Perspective on Leachable Impurities [https://www.fda.gov/media/84017/download]
8) Book: Leachables and Extractables Handbook: Safety Evaluation, Qualification, and Best Practices Applied to Inhalation Drug Products, Douglas J. Ball, Daniel L. Norwood, Cheryl L. M. Stults and Lee M. Nagao,
*9) International Medical Devices Regulators Forum http://www.imdrf.org/documents/documents.asp*
10) WHO perspective: https://www.who.int/medical_devices
11) Book: Medical Device 1st edition, Seeram Ramakrishna Lingling Tian Charlene Wang Susan Liao Wee Eong Teo, Woodhead Publishing
12) Book: Biomaterials, Medical Devices and Combination Products: Biocompatibility Testing and Safety Assessment, Shayne Cox Gad, Samanta Gad-McDonald, CRC Press

**Outcomes:**

On completion of the course, the student should be able to:

- Evaluate the need for medical devices to undergo physical, chemical or biological testing
- Perform physical, chemical or biological evaluation of a medical device based on the ISO guidelines.
- Evaluation of filling requirements like leachable and extractable
- Design of performance test of medical device

| PE-660<br>Solid State Pharmaceutics<br>(1 credit) | hrs |
|---|---|
| **Levels of solid-state properties**:<br>Molecular/particle/bulk level properties, the interdependence of various levels on each other, the role of different levels during pharmaceutical development and process development | 2 |
| **Molecular-level**:<br>Crystalline form, definition, the 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 software. Computational solid-state pharmaceutics and molecular dynamics. | 2 |
| **Polymorphism**:<br>Definition, the significance of polymorphism in drug product performance, packing / conformational polymorphism, thermodynamics of polymorphs, enatiotropy / monotropy, the concept of the transition temperature, Burger, and Ramberger rule. Regulatory concerns related to polymorphism, introduction to the latest regulatory position on polymorphism. | 2 |
| **Crystallization process**:<br>Basics of crystallization process applied in drug research, Molecular aggregation events in crystallization, energetic of crystallization, enthalpy entropy balance, types of nucleation, Ostwald's step rule, experimental protocols for polymorph screening, crystal design strategies; Co-crystals: Introduction, the formation of co-crystals and its applications in drug delivery | 2 |
| **Amorphous state**:<br>Definition, Role of amorphous state in drug delivery, long-range order versus short-range order, the disorder in the amorphous state, the concept of glass transition temperature (Tg), the thermodynamic necessity for Tg, entropy crisis. | 2 |
| **Role of amorphous state in drug delivery**:<br>Particulate level properties and its implications on product performance and processing, Solubility advantage, spring parachute effect during solubility studies, physical instability of the amorphous form, techniques for stabilization of amorphous form, amorphous solid solutions/dispersions | 2 |
| **Particulate level properties**:<br>Crystal habit, generation of different crystal habits, implications of crystal habit on product performance, and processing | 2 |
| **Bulk level**:<br>Bulk density, compressibility, flow properties, cohesivity, electrostatics, aggregation, agglomeration, role in formulation development, and processing | 2 |

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|---|---|
| **Testing of solid-state purity** | 2 |
| **Solid-state in light of nanocrystals.** | 2 |

**Reference Study Material:**


1) Advanced Pharmaceutical Solids, Jens T. Carstensen, Marcel Dekker, 2001.
2) Advanced Pharmaceutics *Physicochemical Principles*, Cherng-ju Kim, CRC Press, 2004.
3) Bentley's Textbook of Pharmaceutics An Adaptation, Sanjay K. Jain and Vandana Soni, Elsevier, 2012.
4) Crystal Engineering: A textbook, Edited by G. R. Desiraju, J. J.Vittal and A. Ramanan
5) Handbook of Preformulation *Chemical, Biological, and Botanical Drugs*, Sarfaraz K. Niazi, CRC Press, 2nd Edition, 2019.
6) Integrated Pharmaceutics *Applied Preformulation, Product Design, and Regulatory Science*, Antoine Al-achi, Mali Ram Gupta, William Craig Stagner, Wiley, 2013.
7) Pharmaceutics *Basic Principles And Application To Pharmacy Practice*, Alekha K. Dash, Somnath Singh, Justin Tolman, Academic Press (Elsevier), 2014.
8) Physicochemical Principles of Pharmacy, Alexander T Florence and David Attwood, Pharmaceutical Press, 4th Edition, 2006.
9) Polymorphism in Pharmaceutical Solids Edited by Harry Brittain
10) Polymorphism in Pharmaceutical Solids, Harry G. Brittain, Informa Healthcare, 2nd Edition, 2009.
11) Solid State Characterization of Pharmaceuticals Edited by Angeline and Mark Zarkrzewski
12) Solid State Characterization of Pharmaceuticals, Richard A. Storey and Ingvar Ymen, Wiley, 2011.