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RAJIV GANDHI PROUDHYOGIKI VISHWAVIDYALAYA

M. Pharm (Pharmaceutical Analysis)

III Semester Elective Course Contents

ELECTIVE I

MPY 301 (Pca) : IMPURITY PROFILING

Unit I

Introduction: Classification of impurities in pharmaceutical products, origin of impurities, types of impurities: process impurities, degradation impurities, and contamination impurities. Nature of impurities: organic, inorganic, and residual solvent impurities. Differences between impurities and degradation products. Pharmacopoeial limits of impurities in drug substance and drug products.

Unit II

Application of hyphenated characterization techniques in impurity profiling: LC-MS, LC-MS-MS, GC-MS, TLC-MS, CE-MS, MEKC-MS, CEC-MS, LC-NMR, LC-IR etc.

Toxicological perspectives of impurities in pharmaceutical products: Classes of genotoxic impurity, analytical challenge of genetic toxins, determination of genotoxic impurities.

Unit III

Application of analytical techniques in impurity profiling: Chromatography: HPLC, preparative chromatography, flash chromatography, column chromatography, gas chromatography; Spectroscopy: UV/Visible, FTIR, Raman, NIR, MS, and NMR spectroscopy; Electrophoretic and Related Methods: Capillary electrophoresis, micellar electrokinetic chromatography (MEKC), microemulsion electrokinetic chromatography (MEEKC) and capillary electrochromatography (CEC).

Unit IV

Impurity identification & structure elucidation: Introduction of systematic approaches for isolation, identification, and structure elucidation of unknown impurities. Case studies for impurity identification and structure ilucidation. Setting of limits for impurities in drug products.

Unit V

Regulatory requirements of impurity profiling: ICH guidelines, EMEA guideline, PhRMA approach, USFDA guidance, European pharmacopoeial guidance, Guidance for oncology products, Identification, qualification, and quantification threshold of impurities, Regulatory perspective of impurities for different New Drug Applications (NDA).

Books and references recommended:

1. R.J. Smith, M. L. Webb, *Analysis of drug impurities*, Blackwell Publishing.
2. M. V. N. Kumar Talluri, *Impurity profiling of drugs and pharmaceuticals*, Lambert Academic Publishing.
3. ICH harmonized tripartite guideline, *Impurities in new drug products Q3B(R2)*
4. ICH harmonized tripartite guideline, *Impurities: guideline for residual solvents Q3C(R3)*
5. USFDA, Guidance for Industry ANDAs: *Impurities in drug products.*
6. USFDA, Guidance for Industry ANDAs: *Impurities in drug substances.*
7. *United states pharmacopoeia*.

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III Semester Elective Course Contents

ELECTIVE II

MPY 302 (Pca) : BIOANALYTICAL METHODS & METABOLITE PROFILING

Unit I

Role of drug metabolism research in drug discovery: Types of metabolites, assessment of potential toxicity of metabolites, metabolic clearance in body. Study of detailed procedure of i*n-vitro* drug metabolism studies, *in-vivo* ADME studies. Impact of metabolic information in investigational new drug application (IND) and new drug application (NDA).

Unit II

Liquid radiochromatography techniques: Introduction, instrumentation, and application of new radiochromatography techniques in drug metabolism studies: HPLC-RFD, HPLC-LSC, HPLC-MSC, Stop-Flow HPLC-RFD, dynamic flow HPLC-RFD, UPLC-radiodetection, HPLC-AMS, LC-RFD-MS, stop-flow and dynamic flow LC–RFD–MS, LC-MSC-MS. Profiling of radiolabeled metabolites in plasma, analysis of metabolites of nonradiolabeled drugs using radiolabeled cofactors or trapping agents, determination of structures and formation pathways of sequential metabolites, enzyme kinetic studies.

Unit III

Metabolite identification & structure determination: Application of various analytical techniques for improving metabolite detection and identification, software-assisted metabolite identification, MS-related techniques for metabolite identification, characterization of unstable metabolites, detection and characterization of reactive metabolites and intermediates, examples of metabolite structure determination from known biotransformations.

Unit IV

Common experimental approaches & protocols: Metabolic stability, characterization of enzyme kinetics, quantitative analytical methods, prediction of human hepatic clearance, protocols for assessment of in-vitro & in-vivo bioactivation potential of drug candidates, reaction phenotyping, analysis of *in-vitro* cytochrome P450 inhibition in drug discovery and development, testing drug candidates for CYP3A4 induction.

Unit V

ADME studies in animals and humans: Objectives, rational, and regulatory compliance, experimental design, sample analysis, metabolite profiling and identification, and data presentation, examples of data presentation. Bioanalytical method development & validation.

Books and references recommended:

1. Donglu Zhang, Mingshe Zhu, W. Griffith Humphreys*; Drug Metabolism in Drug Design and Development,* Wiley Interscience.
2. Roger M. Smith; *Handbook of analytical separations: Bioanalytical Separation, Volume 4,* Elsevier Sciences Publication.
3. D. A. Welis: *High throughput bioanalytical sample preparation: Methods and automation strategies,* Elsevier Sciences Publication.
4. Sarfaraz K. Niazi; *Handbook of Bioequivalence Testing,* Informa Healthcare.

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M. Pharm (Pharmaceutical Analysis)
III Semester Elective Course Contents
ELECTIVE III
MPY 303 (Pca) : QUALITY CONTROL TESTING OF HERBAL PRODUCTS

Unit I

Evaluation of herbal drugs: Concept, considerations, parameters and methods of quality control for medicinal plant materials as per different pharmacopoeias and other guidelines. Regulations of ayurvedic pharmacopoeia of India, Ayurvedic formulary of India, and WHO guidelines with respect to herbal product testing.

Unit II

Quantitative and qualitative testing of herbal products: Microscopic identification, foreign matter, ash, extractive, moisture content (LOD), Volatile oil in drugs. Determination of refractive index, specific gravity, *p*H value, melting and congealing range, boiling range, optical rotation, viscosity, total solids, solubility, saponification value, iodine value, acid value, peroxide value, unsaponifiable matter, mineral oil (Holde's test), rancidity test (Kreis test), alcohol content.

Methods of estimation of starch, fatty oil, protein, alkaloid, pesticide residues, aflatoxin, total phenolics, total tannins, reducing sugars, total sugars, non-reducing sugars, curcumin, densitometer, aluminium, borax, calcium, copper, iron, magnesium, mercury, silica, sodium and potassium, sulphur. Limit tests, microbial limit tests.

Unit III

Application of chromatographic techniques: Separation and identification of herbal products. Application of UV, IR, NMR, 1H NMR, 13C NMR & Mass spectroscopy data for purification and structure elucidation of phytoconstituents. Herbal fingerprint profile of single and multicomponent herbal drugs. Stability testing of natural products. Isolation of marker compound and their characterization.

Unit IV

Analysis of ayurvedic formulations and crude drugs: Identity, purity, and quality of crude drugs. Determination of pesticide residues, determination of arsenic and heavy metals, determination of microbial load in crude drugs. Identification of aflatoxins in crude drugs. Quantitative microscopy, including lycopodium spore method as applied to drug evaluation and pollen grain analysis.

Unit V

Regulatory requirements: Importance of crude drug standardization and application of biomarkers. Standardization, quality, efficacy and safety requirements & assessment procedures for herbal medicines as per USFDA. Guidelines on quality of herbal medicinal products/traditional herbal medicinal products, test procedures and acceptance criteria for herbal medicinal products as per EMEA requirements.

Books and references recommended:

1. P. Houghton, P. K. Mukherjee, *Evaluation of Herbal Medicinal Products Perspectives on quality, safety and efficacy*, Pharmaceutical Press.
2. P. K. Mukherjee, *Quality control of herbal drugs: an approach to evaluation of botanicals*, Business Horizons.
3. European Medicines Agency (EMEA), evaluation of medicines for human use: *Guidance on Herbal products.*
4. *The Ayurvedic Pharmacopoeia of India, First edition*, Government of India Ministry of Health And Family Welfare Department of Ayush, 2007.

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M. Pharm (Pharmaceutical Analysis)

III Semester Elective Course Contents

ELECTIVE IV

MPY 304 (Pca) : STABILITY TESTING OF DRUG SUBSTANCES & DRUG PRODUCTS

Unit I

ICH and WHO stability guidelines: Stress testing, Selection of batches, container and closures system, specification, testing frequency, storage conditions, Stability commitments and evaluation. Photostability testing conditions and procedures.

Unit II

Stress testing program: Approches and conditions for stress testing i.e temperature, humidity, pH etc. Possible drug degradation pathways, Generic approach for stress testing. Reporting and documentation. Protocols for stress testing program of a drug substances and drug product.

Unit III

Stability prediction: Applications of Arrhenius theory for stability prediction, activation energy calculation and its application in shelf life prediction, Q10 value calculation. Shelf life determination, calculation of overages.

Unit IV

Statistical and regulatory aspect of drug stability studies: Current regulations and guidance, statistical model building, evaluating stability batches. Matrixing and bracketing designs for stability studies. Overview on reduction of testing plans. Variations and changes in stability conditions in India, ASEAN, Arab countries, Brazil and Europe. Stability variations. Extention of retest date and its data requirements. Postapproval FDA stability requirements.

Unit V

Physical stability testing: Requirement, study parameters, and applications of physical stability testing for tablets, dispersed systems, semisolids and liquid dosage forms.

Preservatives stability studies: Assesment of preservative activity, test design, efficacy testing, factors influencing reproduceability. Pharmacopoeial methods, acceptance criteria.

Books and references recommended:

1. *Q1 Stability*, ICH Guidelines.
2. David J. Mazzo, *International stability testing*, Interpharm Press.
3. L. Lachman, H. A. Lieberman, J. L. Kanig, *The theory and practice of industrial pharmacy.*
4. J. T. Carstensen, C. T. Rhodes, *Drug stability: principles and practices*, Informa Healthcare.
5. Kim Huynh-Ba, *Handbook of stability testing in pharmaceutical development: regulations, methodologies, and best practices*, Springer.
6. Banker and Rhodes, *Modern pharmaceutics*, Marcel Dekker.
7. *Remington's pharmaceutical sciences.*
8. *United states pharmacopoeia*.