PHARMACEUTICAL ANALYSIS

UNIT I - QUALITY ASSURANCE

a. Introduction to quality assurance, various sources of quality variation and methods for control of quality variation.
b. Concept of statistical quality control for the control of quality variation and construction of quality control charts, methods and importance of sampling.
c. Introduction and importance of Validation, Validation methods for quality of equipment, validation of equipment and validation of analytical instruments and their calibration.
d. Importance and guidelines of GLP, importance and standards for ISO 9000.
e. Concepts, objectives and responsibilities of Total quality management, quality review and documentation of various quality aspects.
f. Origin, history, importance, types of International Conference for Harmonization (ICH) guidelines.
g. Concepts of Regulatory control.

UNIT II - CHROMATOGRAPHY

Introduction, history, classification, separation techniques, choice of methods. The following techniques are to be discussed with relevant examples of pharmaceutical products involving principles and techniques of separation of drugs from excipients.

a. **Column Chromatography**: Adsorption column chromatography, Operational techniques, frontal analysis and elution analysis. Factors affecting column efficiency, applications and partition chromatography.
b. **TLC**: Introduction, principle, techniques, detailed method of operation of Thin Layer Chromatography, importance of Rf value and applications.
c. **PC:** Introduction, principle, types of paper chromatography, preparation techniques, development techniques, applications.
d. **Ion-exchange chromatography**: Introduction, principles, types of ion exchange synthetic resins, physical properties, factors affecting ion exchange, methodology and applications.
e. **HPLC**: Introduction, theory, instrumentation with describing each component, and applications.
f. **HPTLC**: Introduction, theory, instrumentation, and applications.

g. **Gas Chromatography**: Introduction, theory, instrumentation-carrier gases, types of columns, stationary phases in GLC & GSC. Detectors-Flame ionization detectors, electron capture detector, thermal conductivity detector. Typical gas chromatogram, derivatisation techniques, programmed temperature gas chromatography, applications.

h. **Electrophoresis**: Principles of separation, equipment for paper and gel electrophoresis, and application.

i. **Gel filtration** and **affinity chromatography**: Introduction, operational technique, applications.

UNIT III - ELECTROMETRIC METHODS

Theoretical aspects, instrumentation, interpretation of data/spectra and analytical applications are to be discussed on the following topics.

a. **Potentiometry**: Electrical potential, electrochemical cell, reference electrodes, indicator electrodes, measurement of potential and pH, construction and working of electrodes, Potentiometric titrations, methods of detecting end point, Karl Fischer titration.

b. **Conductometry**: Introduction, conductivity cell, conductometric titrations and applications.

c. **Polarography**: Instrumentation, DME, residual current, diffusion current and limiting current, polarographic wave, Ilkovic's equation, Effect of oxygen on polarographic wave, Polarographic maxima and suppressors and applications.

d. **Amperometric Titrations:** Introduction, types of electrodes used, reference and indicator electrode, instrumentation, titration procedure, advantages and disadvantages of Amperometry over Potentiometry. Pharma applications.

UNIT IV - SPECTROSCOPY

Theoretical aspects, instrumentation, elements of interpretation of data/spectra and application of analytical techniques are to be discussed:

a. **Absorption Spectroscopy:**

Theory of electronic, atomic and molecular spectra. Fundamental laws of photometry, Beer-Lambert's Law, application and its deviation, limitation of Beer law, application of the law to single and multiple component analysis, measurement of equilibrium constant and rate constant by spectroscopy. Spectra of isolated chromophores, auxochromes, batho-chromic shift, hypsochromic shift, hyperchromic and hypochromic effect, effect of solvent on absorption spectra, molecular structure and infrared spectra.

Instrumentation – Photometer, U.V.-Visible spectrophotometer – sources of U.V.- Visible radiations, collimating systems, monochromators, samples cells and following detectors- Photocell, Barrier layer cell, Phototube, Diode array, applications of U.V.-Visible spectroscopy in pharmacy and spectrophotometric titrations.

Infrared Spectroscopy: Vibrational transitions, frequency – structure correlations, Infrared absorption bands, Instrumentation of IR spectrometer – sources of IR, Collimating systems, monochromators, sample cells, sample handling in IR spectroscopy and detectors– Thermocouple, Golay Cells, Thermistor, Bolometer, Pyroelectric detector, Applications of IR in pharmacy.

Fluorimetric Analysis: Theory, luminescence, factors affecting fluorescence, quenching. Instrumentation, Applications, fluorescent indicators, study of pharmaceutically important compounds estimated by fluorimetry.

b. **Flame Photometry:** Theory, nebulisation, flame and flame temperature, interferences, flame spectrometric techniques and instrumentation and pharmaceutical applications.
c. **Atomic Absorption Spectrometry:** Introduction, Theory, types of electrodes, instrumentation, interferences and applications.
d. **Atomic Emission Spectroscopy**: Spectroscopic sources of radiation, atomic emission spectrometers, photographic and photoelectric detection, interferences and applications.
e. **NMR & ESR (introduction only):** Introduction, theoretical aspects and applications.
f. **Mass Spectrometry**: (**Introduction only**) – Introduction, Instrument components, fragmentation, types of ions produced, study of mass spectrum and applications.
g. **Polarimetry: (Introduction only**) – Introduction to optical rotatory dispersion, circular dichroism, optical activity, instrumentation of polarimeter and applications of polarimetry.
h. **X-RAY Diffraction: (Introduction only**) – Theory, reciprocal lattice concept, diffraction patterns and applications.
i. **Thermal Analysis**: Introduction, instrumentation, applications of Differential Scanning Calorimetry and Differential Thermal Analysis.

Text Books:

1. Text Book of Chemical Analysis, by A.I.Vogel, ELBS with Macmillan press, Hampshire.
2. Pharm Analysis by Skoog and West, Sounders Manipal College Publishing.
3. Textbook of Pharm. Analysis (Practical) by Beckett & Stenlake, CBS Publishers, Delhi
4. Introduction to Instrumental Analysis by Robert. D. Braun
5. How to practice GMP-A Plan for total quality control by P.P. Sharma, Vandana Publications, Agra.

Reference Books:

1. Text Book of Pharm. Analysis by Higuchi. Tand Hasen. E. B., New York Inter Science Publishers.
2. Quantitative Pharma. Analysis by Jenkins, The Blakiston division, New York.
3. Quantitative Drug Analysis, by Garrot. D, Chapman & Hall Ltd., London.
4. Undergraduate Instrumental Analysis by James. E., CBS Publishers.
5. Instrumental Analysis by Willard and Merritt, EWP, East West Press Ltd., Delhi/Madras.
6. Textbook of Pharm. Analysis by K.A.Connors, John Wiley & Sons, New York, Brisbane, Singapore.
7. Textbook of Drug Analysis by P.D. Sethi., CBS Publishers, Delhi.
8. Spectroscopy by Silverstein, John & Wiley & Sons. Inc., Canada & Singapore.
9. The Science & Practice of Pharmacy by Remington Vol-I & II, Mack Publishing Co. Pennsylvania.

Shri Vishnu College of Pharmacy (Autonomous) :: Bhimavaram

LESSON PLAN

COURSE: Pharm. D **BRANCH:**

CLASS: III Year **YEAR:** 2019-20

SUBJECT: Pharmaceutical Analysis (3.2 T)

The students can acquire complete knowledge on various analytical instruments regarding the construction, working principle, operational methodology and pharmaceutical applications. The course can also provide brief concepts regarding the concepts of quality in the manufacturing industry with respect to the total quality management and control of quality variations. The students can also be benefited by the concepts like regulatory control, GLP, ISO and ICH which will provides International guidelines for quality for producing quality products.

The course provides thorough knowledge in the separation techniques including all the basic and advanced chromatographic and electrophoresis and analytical measurement techniques in the electrochemical and spectroscopic divisions.

The students will gets exposed to the concepts of the various separation techniques including TLC, HPLC, HPTLC, GC, Ion exchange, Gel filtration and Affinity chromatographic techniques and brief introduction in the paper and gel electrophoresis techniques.

Students can learn the concepts, construction, working methods and applications aspects of various spectroscopic techniques like UV-Vis, IR, Fluorimetry, Flame photometry, AAS and AES and Potentiometry, Conductometry, Polarography and Amperometry like basic electrochemical measurement techniques. The course also provides basic skills and concepts in the advanced instruments like NMR, ESR, DSC, DTA, Mass Spectrometry and X-ray diffraction methods.

Plan:

Sl. No.	No. of Hrs.	Date	Topic (s) planned	Reference (Books with page numbers)	Remarks
1	**1**		Introduction to Pharmaceutical Analysis, Quality Assurance and Quality Systems	T1(1-36), T4(159-170), T5(1-13),	
2	**1**		Various sources of quality variation and methods for control of quality variation.	R4(804-815)	
3	**2**		Concept of statistical quality control for the control	T5(169-170,174-208),	
4	**1**		Introduction and importance of Validation	T4(413-423),T5(141-143)	
5	**1**		Validation methods for quality of equipment, validation and calibration of analytical equipment	T4(437-451)	
6	**1**		Importance and guidelines of GLP	T5(55-77), T6(2.80-2.89, 2.383-2.392),	
7	**1**		Importance and standards for ISO 9000	T5(19-52)	
8	**1**		Concepts Total quality management, quality review and documentation	T4(151-158, 230-240), T62(2.355-2.362),	
9	**1**		International Conference for Harmonization (ICH) guidelines	T2(2.58-2.71),	
10	**1**		Concepts of Regulatory control	R4(856-882)	
11	**1**		**Assignment topics discussion I**		
12	**5**		Introduction, history, classification, separation techniques, choice of methods of chromatography	T1(836-855), T2(85-86), T3(821-838)	
12	**3**		Adsorption column chromatography & partition chromatography	T2(86-96)	
14	**4**		Introduction, principle, techniques, detailed method and applications of TLC	T1(927-929, 930-931), T2(115-120), T3(875-878)	
15	**3**		Introduction, principle, types, method and applications of paper chromatography	T2(106-111),T3(869-872)	
16	**2**		Introduction, principles, types, factors affecting ion exchange, methodology and applications of Ion Exchange Chromatography	T1(918-920), T2(96-99), T3(850-855)	
17	**1**		**Assignment topics discussion II**		

18	**5**		Introduction, theory, instrumentation and applications of HPLC	T1(893-895), T2(1157-173), T3(859-865)	
19	**2**		Introduction, theory, instrumentation, and applications of HPTLC	T1(896-910), T2(123-125)	
20	**5**		Introduction, theory, instrumentation, method and applications of Gas Chromatography	T1(865-890), T2(128-157), T3(890-926)	
21	**3**		Principles, equipment and application of Paper and Gel Electrophoresis	T3(882-886)	
22	**3**		Introduction, operational technique, applications of Gel Filtration & Affinity Chromatography	T1(927), T3(882)	
23	**1**		**Assignment topics discussion III**		
24	**1**		Introduction to Electro analytical methods of Analysis	T1(690-698),	
25	**4**		Electrochemical cell, reference electrodes, indicator electrodes, measurement of potential and pH, applications of Potentiometry	T1(724-735, 755-761), T2(183-205, 246-247), T3(697-754)	
26	**3**		Introduction, conductivity cell, conductometric titrations and applications	T2(175-183)	
27	**3**		Introduction, DME, Instrumentation, method and applications of Polarography	T2(209-220), T3(761-784)	
28	**3**		Introduction, types of electrodes used, titration procedure, applications of Amperometric titrations	T2(238-243)	
29	**1**		**Assignment topics discussion IV**		
30	**1**		Introduction to spectroscopy	T1(158-159), T2(255, 257-264)	
31	**5**		Theory, fundamentals, Beer-Lambert's law, concepts of Absorption Spectroscopy	T1(159-188, 248-262, 378-383), T2(312-315, 379-383)	
32	**4**		Introduction, Instrumentation, methodology and applications of UV-Vis Spectroscopy	T1(198-227, 274-275, 392-406, 411-436), T2(264-285), T3(261-284)	
33	**3**		Introduction, Instrumentation, methodology and applications of IR Spectroscopy	T1(230-243, 477-502, 505-516), T2(379-391), T3(346-374)	
34	**3**		Introduction, Instrumentation, methodology and applications of Fluorimetry	T1(443-468), T2(358-371), T3(316-343)	

35	**3**		Introduction, Instrumentation, methodology, interferences and applications of Flame Photometry	T2(339-346), T3(218-222)	
36	**1**		**Assignment topics discussion V**		
37	**3**		Introduction, Instrumentation, methodology, interferences and applications of Atomic Absorption Spectroscopy	T1(264-285), T2(346-354), T3(175-215)	
38	**3**		Introduction, Instrumentation, methodology, interferences and applications of Atomic Emission Spectroscopy	T1(291-311), T2(338), T3(222-232)	
39	**4**		Introduction, theoretical aspects and applications of NMR & ESR Spectroscopy	T1(551-571, 585), T2(408-425, 446-460), T3(465-494, 515-535)	
40	**4**		Introduction, theoretical aspects and applications of Mass Spectrometry	T1(606-620, 636-643), T2(468-495), T3(679-691)	
41	**2**		Introduction, theoretical aspects of Optical activity, ORD, CD, Instrumentation and applications of Polarimeter	T2(30-39)	
42	**2**		Theory, reciprocal lattice concept, diffraction patterns and applications of X-ray Diffraction	T2(78-84)	
43	**4**		Introduction, instrumentation, applications of Differential Scanning Calorimetry and Differential Thermal Analysis	T1(980-987), T2(69-75)	
44	**1**		**Assignment topics discussion VI**		

Text Books:

1. Pharm Analysis by Skoog and West, Sounders Manipal College Publishing.
2. Textbook of Pharm. Analysis (Practical) by Beckett & Stenlake, Volume II, CBS Publishers, Delhi
3. Introduction to Instrumental Analysis by Robert. D. Braun
4. CGMP for Pharmaceuticals by Manohar A. Potdar
5. Quality Assurance and Quality Management in Pharmaceutical Industry by Y. Anjaneyulu, R.marayya
6. Pharma Pathway – Industrial and Applied Pharmacy by D.A.Savant

Reference Books:

1. Instrumental Analysis by Willard and Merritt, EWP, East West Press Ltd., Delhi/Madras.
2. Textbook of Pharm. Analysis by K.A.Connors, John Wiley & Sons, New York, Brisbane, Singapore.
3. How to practice GMP-A Plan for total quality control by P.P. Sharma, Vandana Publications, Agra.
4. The Theory and Practice of Industrial Pharmacy by Leon Lachman, H.A. Liberman and Joseph L. Kanig, 3rd Edition.

QUESTION BANK

Short answer questions

Unit I: Quality Assurance

1. Define the terms Quality Assurance, Quality Control and Quality Variation
2. What are the various sources of Quality variation
3. Construction of Range charts
4. Different methods of sampling
5. Explain the terms Validation and Calibration
6. Objectives of Total Quality Management
7. Functions of contract lab Coordinator
8. Importance of Documentation
9. Objectives of Regulatory control
10. State the importance of ICH guidelines

Unit II: Chromatography

1. Classify different types of chromatographic techniques
2. Brief history of chromatography
3. State different types of separation techniques
4. Different types of elution in partition chromatography
5. Differentiate between Adsorption and Partition
6. Describe about a typical chromatogram
7. Define R_f and R_m
8. Selection of mobile phase for TLC analysis
9. Applications of paper chromatography
10. Classification of ion exchange resins
11. Advantages of TLC over Paper Chromatography
12. Differentiate HPLC with HPTLC
13. Advantages of HPTLC over TLC
14. Principle of separation by HPTLC
15. Define and classify Electrophoresis

16. Principle of Affinity Chromatography
17. Applications of Gel Filtration Chromatography
18. Temperature programming Gas Chromatography
19. Principle of separation by Paper Electrophoresis
20. Differentiate normal phase HPLC and reverse phase HPLC

Unit III: Electrometric Methods

1. Define the terms potential and salt bridge
2. Classify different electrodes used in Potentiometry
3. Define conductance, specific conductance, equivalent conductance and molar conductance
4. Factors affecting conductance
5. Explain about a typical polarogram
6. Add a note on polarographic suppressors
7. Differentiate potentiometric titrations with amperometric titrations
8. Applications of Amperometric titrations
9. Factors affecting conductance
10. Define residual current, diffusion current, limiting current and migration current

Unit IV: Spectroscopy

1. Differentiate atomic and molecular spectroscopy
2. Applications of Beer-Lambert's law
3. Define batho chromic shit, hypso chromic shift, hypo chromic and hyper chromic effects.
4. Wavelength regions of UV, Visible, IR and Radio frequency radiations
5. Construction of Phototube
6. Monochromators used in spectroscopy
7. Various transitions observed in UV-Vis spectroscopy
8. Different transitions observed in IR spectroscopy
9. Sample handling techniques in IR spectroscopy
10. Construction and working of Interferometer
11. Differentiate time domain and frequency domain IR spectrum

12. Applications of IR spectroscopy in Pharmacy
13. Define luminescence, Fluorescence and Quenching
14. Add a note on fluorescent indicators
15. Different type of fuels used for flame photometry
16. Principle of flame photometry
17. Applications of flame photometry
18. Interferences observed in Atomic Absorption Spectroscopy
19. Different types of atomization sources used in AAS
20. Applications of Atomic Emission Spectroscopy in Pharmacy
21. Explain shielding and deshielding effects in NMR
22. Define chemical shift and how can it be calculated
23. Different types of ions produced in Mass spectrometry
24. Define optical rotation, Circular Dichroism and Optical Rotatory Dispersion
25. Principle of DSC
26. Principle of DTA
27. Various sources of ionization in Mass Spectrometry
28. The information one can obtain from a typical NMR Spectrum
29. The information one can obtain from a typical Mass Spectrum
30. The information one can obtain from a typical DSC Thermogram

Long Answer Questions

Unit I: Quality Assurance

1. Enumerate various methods for control of Quality variation
2. Construction and uses of $\bar{X}$ charts
3. Explain equipment validation in detail
4. Concepts and role of Total quality Management
5. Write in detail about ISO 9000
6. ICH stands for? State the objectives of ICH guidelines and describe about few types of ICH guidelines
7. The role of Quality Assurance in the review and documentation process
8. Explain the various aspects of GLP

Unit II: Chromatography

1. Factors for choosing a suitable chromatographic method for drug analysis
2. Theories of Adsorption and Partition
3. Construction, method and applications of Column Chromatography
4. Detailed operational procedure of TLC
5. Classification of Paper Chromatography
6. Preparation and activation TLC plates, activation of TLC chamber
7. Factors affecting ion exchange separation and preparation of ion exchange resins
8. Method of separation and applications of ion exchange chromatography
9. Explain various components of HPLC instrument with a labeled diagram
10. Explain about various injectors and detectors used in HPLC systems
11. Instrumentation of HPTLC with a neat diagram
12. Differentiate GC with LC, explain various columns and detectors used in GC instrument
13. Principle and applications of GSC
14. Explain operational procedure and applications of Gel Electrophoresis
15. Method of separation and applications of Affinity Chromatography
16. Principle and operational method of Gel Filtration Chromatography

Unit III: Electrometric Methods

1. Construction, operation and applications of glass electrode
2. Measurement of pH and potential by Potentiometry
3. Classify electrodes used in Potentiometry by explaining one for each class
4. Principle, method and applications of conductometric titrations
5. State principle of polarography and derive Ilkovic's equation
6. Types of electrodes used and method of Amperometric titrations

Unit IV: Spectroscopy

1. Define and derive Beer-Lambert's law. State the applications and deviations of the law
2. Enumerate various components present in a double beam UV-Vis Spectrophotometer with a labeled diagram
3. Explain in detail the working and applications of UV-Vis Spectroscopy
4. Explain different transitions observed in UV-Vis Spectroscopy and add a note on detectors used in UV-Vis Spectrophotometer
5. Explain the construction and applications of a FT-IR Spectrophotometer
6. Principle, sample handling techniques of IR Spectroscopy, add a note on Interferometer
7. Principle, Instrumentation and applications of Flourimeter
8. Define quenching, importance and applications of quenching in pharmacy. Add a note on fluorescent indicators
9. Instrumentation, interferences observed and applications of Flame Photometry
10. Principle, Instrumentation, Interferences and applications of Atomic Emission Spectroscopy
11. Explain different atomization sources and detectors used in Atomic Absorption Spectroscopy, add a note on Interferences observed in AAS.
12. Explain ESR spectroscopy in detail
13. Principle and applications of NMR Spectroscopy, add a note on interpretation of a typical NMR Spectrum
14. Explain different fragmentation patterns observed in Mass Spectrometry with examples
15. Draw neat labeled diagram of a Polarimeter, explain its working mechanism with applications in Pharmacy
16. Define Diffraction, derive Bragg's equation and discuss about lattice concept of crystals
17. Principle, instrumentation and applications of DSC
18. Principle, instrumentation and applications of DTA

Assignments

Assignment 1

Unit I & III: Quality Assurance & Electrometric Methods

1. Applications of Amperometry
2. Applications of Conductometry
3. Applications of Polarography
4. Applications of Potentiometry
5. Aspects of quality review and documentation.
6. Concept of statistical quality control
7. Concepts of regulatory control
8. Concepts of total quality management
9. Description of a polarogram
10. Good Laboratory Practices
11. Guidelines of International Conference for Harmonization
12. Instrumentation of Amperometry
13. Instrumentation of Conductometry
14. Instrumentation of Polarography
15. Instrumentation of Potentiometry
16. Introduction to quality assurance, sources of quality variation and control of quality variation
17. ISO 9000
18. Quality of equipment and Validation of equipment
19. Theoretical aspects of Amperometric Titrations
20. Theoretical aspects of Conductometry
21. Theoretical aspects of Polarography
22. Theoretical aspects of Potentiometry
23. Theoretical concepts of validation
24. Validation and calibration of analytical instruments

Assignment 2

Unit II: Chromatography

1. Introduction, history, classification of chromatography
2. Factors affecting ion exchange, methodology and applications of Ion-exchange chromatography
3. Instrumentation and methodology of HPLC
4. Instrumentation and methodology of HPTLC
5. Instrumentation, carrier gases and detectors for GLC
6. Instrumentation, carrier gases and detectors for GSC
7. Introduction, principle, techniques of paper chromatography
8. Introduction, principle, techniques of TLC
9. Introduction, principles, types of ion exchange synthetic resins, physical properties of resins
10. Introduction, technique, applications affinity chromatography
11. Introduction, technique, applications Gel filtration chromatography
12. Introduction, theory and applications of HPLC
13. Introduction, theory and applications of HPTLC
14. Introduction, theory, types of columns and stationary phases in GLC
15. Introduction, theory, types of columns and stationary phases in GSC
16. Operational technique of column chromatography and factors affecting column efficiency
17. Principles and techniques of separation of Adsorption column chromatography,
18. Principles and techniques of separation in partition chromatography
19. Principles of separation, equipment and applications of gel electrophoresis
20. Principles of separation, equipment and applications of paper electrophoresis
21. Procedure, Rf value and applications of paper chromatography
22. Procedure, Rf value and applications of TLC
23. Programmed temperature gas chromatography and applications of GC
24. Separation techniques, choice of methods for chromatography

Assignment 3

Unit IV: Spectroscopy

1. Applications of Infrared Spectroscopy in pharmacy
2. Applications of U.V.-Visible spectroscopy in pharmacy and spectrophotometric titrations
3. Applications of Fluorimetric Analysis and fluorescent indicators
4. Beer-Lambert's Law: Concept, deviation, limitation and applications of the law
5. Fragmentation, types of ions produced mass spectrum and applications of Mass spectrometry
6. Instrumentation of Flourometer and Spectroflouorometer
7. Instrumentation of IR spectrometer, sources of Irradiation
8. Instrumentation of Photometer and U.V.-Visible spectrophotometer, sources of UV & Visible radiation
9. Instrumentation and applications of Flame Photometry
10. Introduction, theoretical aspects and applications of ESR
11. Introduction, theoretical aspects and applications of NMR
12. Monochromators, detectors used in IR spectrometer
13. Monochromators, detectors used in Photometer and U.V.-Visible spectrophotometer
14. Theoretical aspects of Flame Photometry
15. Theoretical aspects of Infrared Spectroscopy
16. Theory of electronic, atomic and molecular spectra
17. Theory, Instrumentation and applications of Atomic Absorption Spectrometry
18. Theory, Instrumentation and applications of Atomic Emission Spectroscopy
19. Theory, Instrumentation and applications of circular dichroism
20. Theory, Instrumentation and applications of DSC
21. Theory, Instrumentation and applications of DTA
22. Theory, Instrumentation and applications of optical rotatory dispersion
23. Theory, Instrumentation and applications of polarimeter
24. Theory, luminescence, factors affecting fluorescence, quenching in Fluorimetric Analysis