M.Pharm

Pharmaceutical Quality Assurance-Syllabus

I SEMESTER

1. Methods of Drug Analysis
2. Modern Analytical Techniques-I
3. Quality Assurance of Pharmaceuticals
4. Good Manufacturing Practice

PRACTICALS

5.Methods of Drug analysis

6. Quality assurance of pharmaceuticals

1.Methods of Drug Analysis

Unit I

Different methods of analysis; reference standards;method development and validation.

Unit II

An advanced study of the principles involved in the determination of the official compounds in IP with the following analytical techniques

A. Non-aqueous,

B. Complexometric,

C. Oxidation-reduction

D. Diazotization methods

Unit III

An advanced study of the principles involved inthe determination of following organic functional groups:

A. Amines

B. Carbonyl compounds

C. Esters

D. Hydroxyland carboxyl

Unit IV

Principles involved in using the following reagents in pharmaceutical analysis with suitable examples:

A. MBTH(3-methyl-2-benzothizolone hydrazone)

B. F.C Reagent (Folin-Ciocalteau)

C. PDAB (Para Dimethyl Amino Benzaldehyde)

D. 2, 3, 5 - Triphenyl tetrazolium salt

E. 2, 6 - Dichloroquinone Chlorimide

Unit V

Principles involved in quantitative determination of

A. Alkaloids

B. Antibiotics

C. Vitamins

D. Steroids (including cardiac glycosides)

Unit VI

Principles involved in quantitative determination of the following classes of drugs listed in IP

A. Analgesic and Antipyretics

B. Antihypertensives

C. Antihistamines

D. Diuretics

E. Reverse transcriptase inhibitors

REFERENCES

1. Remington's Pharmaceutical Sciences by Alfonso and Gennaro
2. Pharmaceutical chemistry by Becket and Stenlake
3. Quantitative analysis of Drugs in Pharmaceutical Formulations by P. D. Sethi
4. Pharmaceutical Analysis by Higuchi, Bechmman Hassan
5. Theory and Practice of Industrial Pharmacy by Lieberman and Lachman
6. Indian Pharmacopoeia (latest)
7. Instrumental Methods of Chemical Analysis by B.K. Sharma
8. A Text book of Pharmaceutical Analysis by Kerrenth A.Conners
9. Journals (Indian Drugs, IJPS etc.)

Modern Analytical Techniques -I

Unit -I

UV-VISIBLE SPECTROSCOPY : Brief review of electromagnetic spectrum and absorption of radiations. The chromophore concept, absorption law and limitations. Theory of electronic spectroscopy, absorption by organic molecules. Choice of solvent and solvent effects. Applications of UV - Visible spectroscopy, Woodward-Fieser rules for calculating absorption maximum, interpretation of spectra, multi-component assay, diifference spectra.

Examples of drugs analysed by this technique.

Unit - II

INFRARED SPECTROPHOTOMETRY : Introduction, basic principles and sampling techniques, interpretation of spectra, applications in pharmacy, FT-IR, Attenuated Total Reflectance (ATR). Near infra red Spectroscopy (NIR) - theory and applications.

Examples of drugs analysed by this technique.

Unit -III

Potentiometry, Conductometry and Fluometry.

Examples of drugs analysed by this technique.

Unit - IV

NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY : Fundamental Principles and Theory, Instrumentation, solvents, chemical shift and factors affecting chemical shift, spin-spin coupling, coupling constant and factors influencing the value of coupling constant, spin-spin decoupling, protonexchange reactions, simplification of complex spectra. FTNMR: interpretation of spectra. C^{13} NMR- Introduction, Natural abundance, C^{13} NMR Spectra and its structural applications.

Examples of drugs analysed by this technique.

Unit -V

MASS SPECTROSCOPY : Basic principles and instrumentation, ion formation and types, fragmentation processes and fragmentation pattern, Chemical ionization Mass Spectroscopy (CIMS), Field ionization Mass Spectroscopy (FIMS), Fast Atom Bombardment Mass Spectroscopy (FABMS), Matrix Assisted laser desorption / ionization Mass Spectroscopy (MALDI-MS), interpretation of spectra and applications in Pharmacy.

Examples of drugs analysed by this technique.

Unit - VI

Immunochemical techniques: Immunoelectrophoresis, immunoprecipitation, ELISA, Radioimmuno assay

Examples of drugs analysed by this technique.

REFERENCE BOOKS :

1. Instrumental methods of analysis- Scoog and West
2. Spectrometric identification of Organic compounds- Silverstein et.al.,
3. Instrumental Methods of Analysis- Willard Dean & Merrit
4. Text book of Inorganic Chemistry- A.I.Vogel.
5. Pharmaceutical Chemistry Vol. I & II- Becket and Stanlake.
6. Pharmaceutical Chemistry Vol. I & II- L.G.Conners
7. Text book of Pharmaceutical Analysis - K. A. Conners
8. Pharmaceutical Analysis- Hiquichi, Bechmann, Hassan.
9. Methods of Drug Analysis - Gearien, Graboski.
10. Pharmaceutical Analysis --Modern Methods -- Part A and B -- Munsen James,W
11. Quantitative analysis of Drugs -- Garrot
12. Quantitative Analysis of Drugs in Pharmaceutical Formulations --P.D.Sethi
13. IP, BP, USP
14. Application of Absorption Spectroscopy of organic compounds --Dyer.
15. Analytical Profiles of Drug Substances --Florey [Volume 13]
16. Spectroscopy of Organic compounds -P.5. Kalsi, Wilely Eastern Ltd, New Delhi.

3. Quality Assurance of Pharmaceuticals

Unit I

Quality of assurance of tablets: Weight variation; test for hardness; friability; chipping, capping; mottling; Test for disintegration and dissolution; Tests for coated and sustained release tablets; sampling techniques; difference in methods if any mentioned in IP,BP,USP and EP.

QA of capsules

Unit II

QA of injectables: sterility testing for pyrogens; particulate matter; volume/weight testing; testing of containers and caps used for packing of injectibles; testing for alkalinity: fibres etc.

Unit III

QA of liquid orals and related formulations:

Unit IV

QA of ointments, creams, gels, lotions, solution for external applications.

Unit V

QA of ophthalmic preparations

Unit VI

QA of metered dosage forms and transdermal implants.

References:

1. Lachman L, Lieberman HA,Kanig JL. The theory and practice of industrial pharmacy.3

ed.,Varghese Publishers, Mumbai 1991.

2. Sinko PJ. Martin's Physical Pharmacy and Pharmaceutical Sciences, 5th edi. B.I. Publications Pvt .Ltd.Noida, 2006.

3. Lachman L, Lieberman HA, Schwartz JB. Pharmaceutical dosage forms : Tablets Vol.1-III, 2 nd ed., CBS Publishers & distributers, New Delhi, 2005.

4. Conners KA., A Text book of Pharmaceutical Analysis Wells JI Pharmaceutical Preformulation : The Physicochemical properties of drug substances. Ellis Horwood Ltd. England, 1998.

5. Yalkowsky SH. Techniques of solubilization of drugs Vol - 12. Marcel Dekker Inc., New York, 1981.

6. Dressman J, Kramer J. Pharmaceutical dissolution testing. Saurah Printer Pvt. Ltd., New Delhi, 2005.

7. Sethi PD., Quantitative analysis of drugs in Pharmaceutical formulations, 3rd de., CBS publications, New Delhi, 2008.

8. Carstensen JT, Rhodes CT. Drug stability principles and practices, 3rd ed., CBS publishers & distributers, New Delhi, 2005.

9. Yoshioka S., Stella VJ. Stability of drugs and dosage forms. Springer (India) Pvt Ltd, New Delhi, 2006.

10. Banker GS, Rhodes CT. Modern Pharmaceutics. 4th ed., Marcel Dekker Inc. New york, 2005.

11. W. Grimm- Stability testing of drug products.

12. Mazzo DJ. International stability testing. Eastern Press Pvt Ltd Bangalore, 1999

13. Beckett AH, Stenlake JB. Practical Pharmaceutical chemistry. Part I & II. 4th ed., CBS publishers & distributers, New Delhi, 2004.

14. IP. Controller of Publication,Delhi. 1996.

15. BP, British Pharmacopoeia Commission office, London, 2008.

16. USP, United States Pharmacopoeial Convention. Inc. USP.

4. GOOD MANUFACTURING PRACTICE (THEORY)

Unit I

Concepts of GMP; Basic Components of GMP: Legal requirements pertaining to GMP:GMP

For manufacturing unit in general.

Unit II

GMP for tablets, capsules, liquid oral manufacturing section.

Unit III

GMP for Parenteral manufacturing section.

Unit IV

GMP for external preparations manufacturing section (ointments, creams, lotions etc.)

Unit V

GMP of section dealing with analysis of various formulations and raw materials.

Unit VI

GMP for stores, packing, and labelling section.

References:

1. Good Manufacturing Practices for Pharmaceuticals. Sidney H, Willig. Drugs and Pharm. Sci. Series. Vol. 109. Marcel Dekker Inc. New York.

2. Good Manufacturing Practices for Pharmaceuticals. Joseph D. Nally. Drugs and Pharm. Sci. Series, Vol.169, Informa healthcare.

3. Modern Pharmaceutics, G.S Banker & C.T. Rhodes, Drugs and Pharma. Sci. Series. Vol,121, Maracel Dekker Inc., New York.

4. How to Practice GMPs, P. P Sharma, Vandana Publication, Delhi.

5. Bulletin of World Health Organization (BLT)

6. (http://www.who.int/bulletin/downloads/en/indexl.html)

7. Remington's Pharmaceutical Sciences, J. P. Remington, Mack Pub. Co., Pennsylvania.

8. Pharmaceutical Packaging Technology, Dean, D.A. Evans, E. R. and Hall, J. H., Taylor and Francis, London.

9. Handbook of Package Engineering by Joseph. F. Handlon.

10. Relevant articles from Journals.

11. Environmental Protection Act 1986.

Methods of Drug Analysis Practical-I:

1. Use of colorimeter for analysis of Pharmacopoeial compounds and their formulations.

2. Use of Spectrophotometer for analysis for Pharmacopoeial compounds and their formulations.

3. Simultaneous estimation of combination formulations (minimum of 4 experiments).

a. Vitamins

b. Oral antidiabetics

c. NSAIDs

d. Antimicrobials

e. Antihistamines

f. Antihypertensive etc.

4. Effect of pH and solvent on UV spectrum of certain drugs.

5. Experiments on flame photometry.

6. Use of fluorimeter for analysis of Pharmacopoeial compounds.

7. IR, NMR and Mass spectroscopy - Interpretation of spectra & structural elucidation (atleast for 4 compounds each).

8. Any other relevant exercises basd on theory.

References:

1. Instrumental Methods of Analysis- Scoog and West.
2. Spectrometric Identification of organic Compounds- Silverstein et., al.
3. Instrumental Methods of Analysis - Willard Dean & Merrit.
4. Text Book of Inorganic Chemistry - A. I. Vogel.
5. Pharmaceutical Chemistry Vol.I & II - Becket and Stanlake.
6. Pharmaceutical Chemistry Vol.I & II - L.G. Chatten.
7. Text Book of Pharmaceutical Analysis - K.A. Connors.
8. Pharmaceutical Analysis - Hiquchi, Bechman, Hassan.
9. Methods of Drug Analysis - Gearien, Graboski.
10. Text Book of Biopharmaceutic Analysis - Robert Smith and James Stewart.
11. Pharmaceutical Analysis - Modern Methods- Part A and B - Munson James, W.
12. Quantitative Analysis of Drugs -Garrot.
13. Quantitative Analysis of Drugs in Pharmaceutical Formulations - P. D. Sethi.
14. IP/ BP/ USP.
15. Application of Absorption Spectroscopy of Organic Compounds - Dyer.
16. Analytical Profiles of Drug Substances - Florey [Volume 13].
17. Spectroscopy of Organic Compounds - P. 5. Kalsi, Wiley Eastern Ltd., New Delhi.

Quality Assurance of Pharmaceuticals Practical - II:

1. Friability testing
2. Hardness testing
3. Disintegration test
4. Dissolution test
5. Test for sterility
6. Test for pyrogens
7. Test for alkalinity of containers
8. Test for rubber/plastic caps
9. Test for allergens
10. Test for particulate matter

References:

1. Lachman L. Lieberman HA, Kanig JL. The theory and Practice of industrial pharmacy, 3rd ed. Varghese Publishers, Mumbai 1991.

2. Sinko PJ, Martin's Physical Pharmacy and Pharmaceutical Sciences 5th ed. B.I. Publications Pvt. Ltd. Noida, 2006.

3. Lieberman HA, Lachman L, Schwartz JB. Pharmaceutical dosage forms : tablets Vol I-III, 2nd ed. CBS Publishers & Distributors, New Delhi. 2005.

4. Conners KA. A Text Book of Pharmaceutical Analysis Wells JI.

5. IP/ BP/ USP.

M.Pharm II Semester

Paper I : Modern Analytical Techniques -II

UNIT - I

HPLC and UPLC/UFLC : Principle, instrumentation, column material and sizes; detectors - their scope and limitations ; elution techniques; solvents and solvent mixtures used for elution; use in the analysis of drugs and APIs; LC-MS.

UNIT - II

GAS CHROMATOGRAPHY: Principles, instrumentation, column material; applications; derivatization; GC-MS.

UNIT - III

Other chromatographic techniques: Ion-exchange, ion-pair, affinity, size exclusion, chiral and super critical fluid chromatography: Principle, material used, application in the analysis.

UNIT - IV

Theory, instrumentation and applications of the following thermal methods of analysis: Thermo Gravimetric Analysis (TGA) ; Differential thermal analysis (DTA) ; Differential scanning calorimetry (DSC); and Thermo mechanical analysis (TMA).

UNIT - V

ELECTROPHORESIS: Theory and principle, classification, instrumentation, material, capillary electrophoresis , moving boundary eletrophoresis, isoelectric focussing (IEF); applications

UNIT - VI

Principle and applications of the following techniques in the analysis of Drugs and APIs :

1. Flame photometry
2. Polarimetry
3. Scanning Electron Microscopy
4. Transmission Electron Microscopy
5. Zeta Meter
6. Powder X-ray diffraction

Recommended books:

1. Skoog DA, Holler FJ, Crouch SR, Principles of instrumental analysis, 6th ed. Baba Barkha Nath Printers, Haryana, 2007.

2. Silverstein RM, Webstar FX, Spectrometric identification of organic compounds. 6th ed. John Wiley & sons (Asia) Pvt Ltd., Singapore,2005.

3. Willard HR, Merritt LL, Dean JA, Settle FA. Instrumental methods of analysis, 7th ed., CBS Publishers & distributers, New Delhi, 1986.

4. Ewing GW, Instrumental methods of chemical analysis, 5th ed., McGraw Hill Book Company, New York, 1985.

5. Schirmer RE. Modern methods of Pharmaceutical analysis, Vol. I & II, 2nd ed., CRC Press, Florida, 2000.

6. Whoston C. X-ray methods, John Wiley & Sons, New York, 1987.

7. Lee DC, Webb M. Pharmaceutical Analysis, Blackwell publishing, Australia, 2004.

8. Gurdeep R. Chatwal, Instrumental Methods of Chemical analysis, Himalaya Publishing House, 2006.

Paper-II: Quality Assurance of Pharmaceuticals-II

Unit-I

Quality assurance of: Large volume parenterals (transfusion fluids etc)

Unit-II

Quality Assurance of biological Products: Biological assays of the following.

1. Vaccines: diphtheria, tetanus, rabies.
2. Enzymes: streptokinase, urokinase.
3. Antitoxins: diphtheria, tetanus.
4. Hormones: chronic gonadotropin, oxytoxin, insulin.
5. Monoclonal antibodies

Unit-III

Quality assurance of Antibiotics: Raw materials (APIs) and formulations.

Unit-IV

Quality assurance of:

1. Guazes (medicated and non-medicated), plasters, cotton
2. Containers and packing materials, caps and labels.

Unit - V

Quality control of Cosmeceuticals: Hair care products (shampoo and hair dyes), baby care products (oils, creams, powders and shampoos), personal hygiene products (shaving creams, after shave lotions and soaps), eye care products (eye shadows, eye liners, and eye brow pencils)

Unit -VI: Quality control of Herbal products: WHO guidelines for the quality control of raw materials used in herbal formulations. Quality control of crude drugs : proximate analysis, including ash and extractive values, crude fiber content, UV and fluorescence analysis of powdered drugs, quantitative microscopy and micro-chemical tests. Analysis of official formulations derived from crude drugs including some herbal preparations, alkaloids (ephedrine, reserpine and ergotamine).

Recommended books:

1. Commercial's manual on drugs & cosmetics, 2nd ed., Commercial Law Publishers (India) Pvt. Ltd, New Delhi, 2004.

2. Sharma PP, Cosmetics-formulation, Manufacturing and quality control, 3rd ed., Vandana Publications Pvt. Ltd., Delhi, 2005

3. Kokare CR. Pharmaceutical microbiology and biotechnology. 2nd ed., Nirali Prakashan, Pune, 2006.

4. Nanda S, Nanda A, KharRK. Cosmetic technology. Birla Publications Pvt. Ltd, Delhi, 2007.

5. Mukherjee PK, Quality control of herbal drugs : an approach to evaluation of botanical. Business horizons New Delhi, 2007.

6. Evans WC, Trease and Evans Pharmacognosy. 15th ed., Saunders, China, 2004.

7. Lachman L, Lieberman HA, Kanig JI. The theory and practice of industrial pharmacy, 3rd ed., Varghese Publishers, Bombay, 1991.

8. Remington: The science and practice of pharmacy, 21st ed., vol. I & II, Lippincott Williams & Wilkings, Noida, 2006.

9. Agarwal SS, Paridhavi M. Herbal drug technology. Universities Press (India) Pvt. Ltd, Hyderabad, 2007.

10. Nelson DL, Cox MM. Lehninger Principles of biochemistry, 4th ed., Replika Press Pvt. Ltd, India, 2006.

11. Murray RK, Granner DK, Rodwell VW, Harper's Illustrated biochemistry, 27th ed., McGraw-Hill, New Delhi, 2006.

12. David Pearson. The chemical analysis of foods, 7th ed., Churchill Livingstone, Edinburgh, 1976.

13. Nielson S, Introduction to the chemical analysis of foods. Jones & Bartlett Publishers, Boston, 1974.

Paper-III: Drug Regulatory Affairs

Unit-I:

1. Drug regulatory bodies in India, United States and European Union- Organization, structure, activities and responsibilities- An overview.

2. A study of compendia- An overview and a coparative picture of IP, BP, USP, EP.

3. Manufacture for sale or for distribution of drugs other than homeopathic medicines: Applications - for drugs in schedules C and C (1) and other than those specified in these schedules; conditions for issuing licenses; loan licenses; inspection; cancellation of licenses; special provisions relating to biological and other special products.

Unit-II:

Schedule M and rules connected with it (The new schedule M):

Part 1: Good manufacturing practices and requirements of premises, plant and equipment.

Part 1A: Specific requirements for manufacture of sterile products, parenterals preparations small volume injectables and large volume parenterals) and sterile ophthalmic preparations.

Part 1B: Specific requirements for manufacture of oral solid dosage forms (Tablets and Capsules).

Part 1C: Specific requirements for manufacture of oral liquids (Syrups, Elixirs, Emulsions and Suspensions).

Part 1D: Specific requirements for manufacture of topical products ie., external preparations (Creams, Ointments, Pastes, Emulsions, Lotions, Solutions, Dusting powders and identical products).

Part 1E: Specific requirements of premises, plant and materials for manufacture of active pharmaceutical ingredients (bulk drugs).

Unit - III:

1. Schedule M II: Requirements of factory premises for manufacture of cosmetics:

a) General requirements b) Requirement of plant and equipment c) Standards for cosmetics.

2. Schedule M III: Requirement of factory premises for manufacture of medical devices.

3. Provisions related to biological and other special products- Part X of D & C act

4. Labelling and packing of drugs other than homeopathic medicines- Part IX of D & C act

5. Standards for surgical dressings- Rule 124C and scheduleF2; methods of test

6. Standards for ophthalmic preparations-Rule 126A and schedule FF.

7. Particulars to be shown in manufacturing records-Schedule U and rules associated with it.

Unit IV:

A study of:

1.Narcotic drugs and psychotropic substances act 1985.

2.Medical and toiletry preparations (the excise duties) act 1955 and rules 1976.

3.Pollution and environment control act.

Unit V:

1. Requirements and guidelines on clinical trials for import and manufacture of new drugs- Schedule Y. Appendices associated with the schedule.

2. GLP and cGLP, principles (OECD guidelines of GLP)

Unit VI

1. ICH guidelines for stability testing.

2. WHO guidelines- an overview.

3. USFDA and other certifying agencies.

Recommended books:

1. Drugs and Cosmetics act, rules and its amendments published by Govt. of India.

2. Forensic pharmacy, BS Kuchekar, AM Khadatare and SC Jitkar, 6th ed., Nirali Prakashan.

3. Textbook of Forensic pharmacy, BM Mittal, 9th ed., Vallabh Prakashan.

4. Drugs and Cosmetics act, 1940, SW Deshpande.

5. Law and Drugs, Law publications- SN Katju

6. Law of Drugs in India, Hussain.

7. Narcotic drugs and psychotropic sunstances act 1985.

8. Medicinal and toilet preparations (the excise duties) act 1955 and rules 1976.

9. Pollution and environment control act.

Paper- IV: Pharmaceutical Process Validation

UNIT-I

Introduction to pharmaceutical validation; definition; manufacturing process model; scope of validation; advantage of validation; organization for validation; validation master plan; types of process validation; prospective; concurrent; retrospective and revalidation. design qualification; installation qualification; operational qualification

And performances qualification of facilities.

UNIT-II

Process validation of dosage forms like tablets, capsules, liquid orals, transdermal preparations and equipment- dry powder mixers, tablet compression machine, fluidized bed dryer, dry heat heat sterilization tunnels, capsule filling machines, dissolution test apparatus.

UNIT-III

Process validation of parental formulations and sterile dosage forms: Validation of aseptic areas, processes and instruments- autoclave, filling machine.

UNIT-IV

General principles of analytical method validation; Need for validation of analytical methods; Validation of analytical instruments and methods-UV-VIS spectrophotometer, IR spectrometer, HPLC/UPLC, LC-MS.

UNIT-V

Utilities and cleaning validation: validation of pharmaceutical water system and pure steam; validation of HAVC system and air handling units; cleaning of equipment and cleaning of facilities, validation of computer systems.

UNIT-VI

A study of the following topics:

1. Validation of coating process
2. Validation of medical devices like stents, intra uterine devices, implants.
3. Change control and SUPAC.

Recommended books:

1. Pharmaceutical process validation, Ira. R. Berry & robert Nash, 2nd Ed., Marcel Dekker Inc.

2. Validation of Pharmaceutical process (Sterile products), F.J. Carleton and J.P. Agalloco, 2nd Ed. (Revised and Expanded), Marcel Dekker Inc.

3. Pharmaceutical Quality Assurance, M.A. Potda, Niali Prakashan, Pune.

4. Current Good Manufacturing Practices, M.A . Potda, Pharma-Med press, Hyderabad.

Practical-I: Quality Assurance of Pharmaceuticals-II

1. HPLC/ UPLC analysis of drugs in formulations
2. GC- and GC-MS analysis of drugs/ APIs
3. Capillary electrophoresis
4. Chiral separations
5. Gel electrophoresis
6. Experiments based on thermal methods of analysis
7. Flame photometric analysis
8. Polarimetry
9. Refractive index determination
10. Experiments based on TLC and Paper chromatography
11. Bioassays

Practical-II: Pharmaceutical Process Validation

1. Validation of analytical method (minimum of four exercises)
2. Validation of following equipment
    a. Autoclave
    b. Hot air oven
    c. Dry powder mixer
    d. Tablet compression machine
3. Validation of processing area
4. Validation of atleast two analytical instruments- HPLC, UV-Vs Spectrophotometer
5. Cleaning Validation of one equipment
6. Validation of sterile areas and sterilization methods- Aseptic filling area and membrane filtration.
7. Validation of laminar air flow unit
8. Validation of dissolution test apparatus.