THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY
CHENNAI-600 032

SYLLABUS – M. PHARMACY 2006-2007
BRANCH V – PHARMACEUTICAL ANALYSIS

M. PHARMACY

I YEAR

SYLLABUS FOR PHARMACEUTICAL ANALYSIS – BRANCH V

COMMON TO ALL BRANCHES - PAPER – I

MODERN PHARMACEUTICAL ANALYTICAL TECHNIQUES

THEORY **75 Hours(3 hrs./week)**

1. UV-VISIBLE SPECTROSCOPY : 6 Hours.

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, modern instrumentation – design and working principle. Applications of UV-Visible spectroscopy (qualitative and quantitative analysis), Woodward – Fischer rules for calculating absorption maximum, Photometric titrations and its applications.

2. FLAME EMISSION SPECTROSCOPY AND ATOMIC ABSORPTION SPECTROSCOPY : 3 Hours.

Principle, instrumentation, interferences and applications in Pharmacy.

3. SPECTROFLUORIMETRY : 3 Hours.

Theory, instrumentation, advantages, relationship of chemical structure to fluorescence spectra, solvent effect, effect of acids and bases on fluorescence spectra, concentration effects, factors affecting fluorescence intensity, comparison of fluorescence and UV-Visible absorption methods and applications in Pharmacy.

4. INFRARED SPECTROPHOTOMETRY : 6 Hours.

Introduction, basic principles, vibrational frequency and factors influencing vibrational frequency, instrumentation and sampling techniques, interpretation of spectra, applications in Pharmacy. FT-IR-theory and applications, Attenuated Total Reflectance (ATR).

5. NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY : 8 Hours.

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, proton exchange reactions, FT-NMR, 2D -NMR, NMDR, NOE, NOESY, COSY and applications in Pharmacy, interpretation of spectra, C13 NMR-Introduction, Natural abundance, C13 NMR Spectra and its structural applications.

6. ELECTRON SPIN RESONANCE SPECTROSCOPY : 2 Hours.

Theory and Principle, Limitations of ESR, choice of solvent, g-values, hyperfine splitting, instrumentation, difference between ESR & NMR and applications.

7. MASS SPECTROSCOPY : 8 Hours.

Basic principles and instrumentation, ion formation and types, fragmentation processes and fragmentation pattern, Chemical ionization mass spectroscopy (CIMS), Field Ionization Mass Spectrometry (FIMS), Fast Atom Bombardment MS (FAB MS), Matrix Assisted laser desorption / ionization MS (MALDI-MS), GC-MS, interpretation of spectra and applications in Pharmacy.

8. X-RAY DIFFRACTION METHODS : 4 Hours.

Introduction, generation of X-rays, X-ray diffraction, Bragg's law, X-ray powder diffraction, interpretation of diffraction patterns and applications.

9. OPTICAL ROTARY DISPERSION : 4 Hours.

Principle, Plain curves, curves with cotton effect, octant rule and its applications with example, circular dichroism and its relation to ORD.

10. THERMAL METHODS OF ANALYSIS : 5 Hours.

Theory, instrumentation and applications of Thermo Gravimetric Analysis (TGA), Differential Thermal Analysis (DTA), Differential Scanning Calorimetry (DSC) and Thermo Mechanical Analysis (TMA).

11. CHROMATOGRAPHIC TECHNIQUES : 15 Hours.

a) Classification of chromatographic methods based on mechanism of separation: paper chromatography, thin layer chromatography, ion exchange chromatography, column chromatography and affinity chromatography – techniques and applications.

b) Gas Chromatography : Theory and principle, column operation, instrumentation, derivatisation methods and applications in Pharmacy.

c) High Performance Liquid Chromatography : Principle, instrumentation, solvents used, elution techniques, RP-HPLC, LC-MS and applications in Pharmacy.

d) HPTLC and Super Critical Fluid Chromatography (SFC) : Theory and Principle, instrumentation, elution techniques and pharmaceutical applications.

12. ELECTROPHORESIS : 3 Hours.

Theory and principles, classifications, instrumentation, moving boundary electrophoresis, Zone Electrophoresis (ZE), Isoelectric focusing (IEF) and applications.

13. RADIO IMMUNO ASSAY : 3 Hours.

Introduction, Principle, Theory and Methods in Radio Immuno Assay, Related Immuno Assay procedures and Applications of RIA Techniques.

14. STATISTICAL ANALYSIS : 5 Hours.

Introduction, significance of statistical methods, normal distribution, probability, degree of freedom, standard deviation, correlation, variance, accuracy, precision, classification of errors, reliability of results, confidence interval, Test for statistical significance – students T-test, F-test, Chi-square test, correlation and regression.

PRACTICALS

1. Use of colorimeter for analysis of Pharmacopoeial compounds and their formulations.
2. Use of Spectro photometer for analysis for Pharmacopoeial compounds and their formulations.
3. Simultaneous estimation of combination formulations (minimum of 4 experiments).
4. Effect of pH and solvent on UV Spectrum of certain drugs.
5. Use of fluorimeter for analysis of Pharmacopoieal compounds.
6. Experiments on Electrophoresis.
7. Experiments of Chromatography.
    (a) Thin Layer Chromatography.
    (b) Paper Chromatography.
        1) Ascending Technique.

2) Descending Technique.
3) Circular Technique.
4) Two dimensional Paper Chromatography and TLC.

8. Experiments based on HPLC & GC.
9. IR, NMR and Mass Spectroscopy – Interpretation of spectra & Structural elucidation (atleast for 4 compounds each).
10. Any other relevant exercises based on theory.

REFERENCES

1. Spectrometric identification of Organic Compounds, Robert. M. Silverstein et al, 7th Edition, 1981.
2. Fundamentals of Mathematical Statistics, S.C. Gupta and V.K. Kapoor.
3. Principles of Instrumental Analysis by Donglas A. Skoog, James, J. Leary, 4th Edition.
4. Pharmaceutical Analysis – Modern Methods – Part A, Part B, James W. Munson – 2001.
5. Vogel's Text Book of Quantitative Chemical Analysis, 6th Edition, 2004.
6. Chromatographic Analysis of Pharmaceuticals, John A. Adamovics, 2nd Edition.
7. Practical Pharmaceutical Chemistry, Part two, A. H. Beckett & J. B. Stenlake – 4th Edition.
8. Instrumental Methods of Chemical Analysis – B. K. Sharma - 9th Edition.
9. Instrumental Methods of Analysis – Hobert H. Willard, 7th Edition.
10. Organic Spectroscopy – William Kemp, 3rd Edition.
11. Techniques and Practice of Chromatography – Raymond P. W. Scott, Vol. 70.
12. Identification of Drugs and Pharmaceutical Formulations by Thin Layer Chromatography – P. D. Sethi, Dilip Charegaonkar, 2nd Edition.
13. HPTLC – Quantitative Analysis of Pharmaceutical Formulations – P. D. Sethi.
14. Liquid Chromatography – Mass Spectrometry, W. M. A. Niessen, J. Van Der Greef, Vol. 58.
15. Stereo Chemistry – Conformation and Mechanism by P. S. Kalsi, 2nd Edition.
16. Spectroscopy of Organic Compounds by P. S. Kalsi.
17. Organic Chemistry by I. L. Finar Vol. II – 5th Edition.

SYLLABUS FOR PHARMACEUTICAL ANALYSIS

BRANCH - V

PAPER – II

PHARMACEUTICAL AND COSMETIC ANALYSIS

THEORY **75 Hours(3 hrs./week)**

A. Pharmaceutical Analysis :

1. Principle and procedures involved in following, including assays of official drugs in I.P by Non-aqueous Titration, Complexometric Titration, Gravimetric Methods, Diazotisation Titration, Potentiometry, UV-Visible Method, HPLC and TLC. **10 Hours.**

2. A detailed study on related substances and impurities present in drugs and their effect on drug stability and therapeutic action. ICH guidelines for impurity and related substances determination in drugs. **6 Hours.**

3. (a) Identification and quantitative determination of preservatives, Antioxidants, colouring materials, emulsifiers and stabilizers in Pharmaceutical formulation.
   (b) Quality control and in process Quality control of Tablets, Capsules, Liquid dosage forms - parenteral & sterile preparations, ointments, creams, suppositories and controlled release products. **5 Hours.**

4. Analysis of drugs from biological samples including, selection of biological sample, extraction of drugs by various methods as LLE, SPE and Membrane filtration. Factors affecting extraction of drugs. **5 Hours.**

5. Stability testing of formulation and shelf life prediction. ICH guidelines for stability studies of drugs. **6 Hours.**

6. Quality control of Radio Pharmaceuticals and radio chemical methods in analysis. **5 Hours.**

7. Various types of raw materials used in the cosmetic industry for the manufacture of finished products. **4 Hours.**

8. General method of analysis to determine the quality of raw materials used in cosmetic industry. **6 Hours.**

9. Indian Standard Specifications (ISI) laid down for sampling and testing of various cosmetics in finished form by the Bureau of Indian Standards. **7 Hours.**

10. Methods of analysis to determine the quality of cosmetics in the finished forms such as Hair care products, Skin care products, Baby care products, Dental products, Personal hygiene products, Colour cosmetics, Ethnic products, Colour makeup preparation, Lipsticks, Hair setting lotions and Eye shadows.

15 Hours.

11. Toxicity testing in cosmetics and Safety and Legislation of Cosmetic products.

6 Hours.

PRACTICALS

1. Assay of Ibuprofen Tablet I.P., Tolbutamide Tablet I.P., Calcium Lactate and Ferrous Fumerate I.P.
2. Determination of Water in Sorbitol, Sodium Citrate & Ampicillin.
3. Determination of Total Chloride in Thiamine Chloride Hydrochloride.
4. Assay of Piperazine citrate as picrate derivative by Gravimetry.
5. Quality control Tests for Tablets, Capsules, Injections, Ointments and Suppositories.
6. Detection and Determination of Preservatives, Antioxidants and Colouring materials in Pharmaceuticals.
7. Determination of related substances in Albendazole, Amiloride, Metronidazole, Betamethazone, Carbamazepine, Diclofenac, Ephedrine, Ibuprofen, Paracetamol, Eucalyptus oil, Phenylbarbitone and Sulphafurazone as per I.P.
8. Based on topics covered in theory with emphasis on analysis of cosmetics and their adulteration with reference to Drugs and Cosmetic rules 1945.
9. Quality Control tests for some cosmetics. (e.g.,) Determination of SLS in Shampoo.

REFERENCES

1. Comprehensive Pharmacy Review 5th Edition by Leon Shargel, Alan H. Mutnick, Paul F. Souney, Larry N. Sawnson – 2004.
2. Applied Biopharmaceutics and Pharmacokinetics, 4th Edition by Leon Shargel / Andrew B.C., Yu – 1999.
3. A. H. Beckett and J. B. Stenlake Practical Pharmaceutical Chemistry, Part I and Part II, 4th Edition.
4. G. H. Jeffery, J. Basset, J. Mendham, R. C. Denny (Rev. by) Vogels Text Book of Quantitative Chemical Analysis, 5th Edition 1989, ELBS.
5. The Controller of Publications; New Delhi, Govt. of India, Indian Pharmacopoeia, Vol. I and Vol. II - 1996.
6. J. B. Wilkinson and R. J. Moore : Herry's Cosmeticology; Longman Scientific and Technical Publishers, Singapore.
7. P.D. Sethi; Quantitative Analysis of Drugs in Pharmaceutical Formulations, 3rd Edition - 1997,
8. ICH guideline for impurity determination and stability studies.
9. Practical HPLC method development by Lloyd R. Snyder, Joseph J. Kirkland, Joseph I. Glajch, John Wiley and Sons 2nd Edition – 1997.

10. Classification of cosmetics raw materials and adjuncts IS 3958 of Indian Standards Institution (BIS).
11. Cosmetic and toilet goods – methods of sampling IS 3958 of Indian Standards Institution (BIS).
12. Methods of sampling and test for various cosmetics as laid down by Indian Standard Institution (BIS).

SYLLABUS FOR PHARMACEUTICAL ANALYSIS

BRANCH - V

PAPER - III

ADVANCED PHARMACEUTICAL ANALYSIS

THEORY **75 Hours(3 hrs./week)**

1. Application of instrumental methods in the development of medicines, concept of Analytical Methods development. **5 Hours.**

2. Validation and calibration of various instruments used for drug analysis such as UV-Visible Spectrophotometer, IR Spectrophotometer, Spectrofluorimeter, HPLC, HPTLC and GC. **10 Hours.**

3. Principles and procedures involved in quantitative determination of following groups **5 Hours.**
   (a) Hydroxyl, (b) Aldehyde, (c) Ketone, (d) Ester (e) Amine.

4. A detailed study of principle and procedures involved in various physico-chemical methods of analysis including instrumental methods of analysis of Pharmaceutical dosage forms containing the following classes of drugs: **20 Hours.**
   a. Sulphonamides.
   b. Barbiturates – i.e., Barbituric acid derivatives and Xanthine derivatives.
   c. Steroids such as Adrenocortical steroids, Progesterone, Androgens and Cholesterol.
   d. Vitamins like Vitamin A, B1, B2, B12, C & E.
   e. Antibiotics like Chloramphenicol, Erythromycin, Penicillin & Streptomycin.
   f. Alkaloids of Cinchona, Ergot, Opium & Rauwolfia.
   g. Glycosides such as Digitoxin, Digoxin & Strophanthin.

5. Elemental analysis such as determination of sodium, potassium, calcium, phosphorous, sulphur, chlorine, bromine and iodine. **6 Hours.**

6. Principles and procedures involved in the use of the following reagents in Pharmaceutical analysis : **10 Hours.**
   a. N, 1-naphthyl ethylene diamine.
   b. Para – dimethyl amino Benzaldehyde (PDAB).
   c. 2, 6 – Dichloro quinone chlorimide.
   d. 1, 2 – Naphtho quinone 4 – sulphonate.
   e. 2, 3, 5 – Triphenyl Tetrazolium Salt.
   f. Ninhydrin.
   g. Folin – Ciocalteau reagent.

h. Para dimethyl amino cinnamaldehyde.
i. 3 – methyl 2 – benzothiazoline hydrazone (MBTH).
j. 2, 4 – dinitro phyenyl hydrazine.

7. Analysis of Drugs and Excipients in solid state – Particle size analysis, X-ray powder diffraction. **6 Hours.**

8. A detailed study of Principles and Procedures involved in the following Biological tests and assays : **13 Hours.**
Test for effectiveness of Antimicrobial preservatives, Adsorbed Diphtheria Vaccine, Adsorbed Diphtheria Antitoxin, Microbiological Assay of Cyanocobalamine, Microbiological Assay of Neomycin sulphate, Oxytocin, Tetanus Antitoxin, Rabies vaccine, Rabies Antiserum and Tetanus Antitoxin.

PRACTICALS

1. Calibration and validation of UV-Visible, IR, Flourimeter, HPLC & HPTLC.
2. Assays of official compounds by fluorimetry :
   a) Quinine b) Codeine c) Thiamine and d) Riboflavin.
3. Study of Quenching effect in fluorimetry : quenching of quinine by potassium Iodide.
4. Determination of 'Sodium' in Sodium chloride injection.
5. Colorimetric estimation of Sulphacetamide in 'eye drops' using NED.
6. Assay of Reserpine injection IP.
7. Quantitative Analysis of drugs in the following 'Multicomponent dosage form' - Ibuprofen & Paracetamol Tablet, Paracetamol and Nimusulide Tablet, Ciprofloxacin and Tinidazole Tablet.
8. Quantitative Determination of following groups :
   a) Hydroxyl group b) Carbonyl group c) Amine.
9. Quantitative Colorimetric determination of suitable drugs using following reagents :
   a) Paradimethyl Amino cinnamaldehyde b) MBTH c) F C reagent
   d) 2,6 dichloro quinone chlorimide e) Ninhydrin.
10. Assay of the following official formulations :
    a) Frusemide Tablet b) Metformin Tablet c) Chloroquine Tablet
    d) Chloramphenicol Capsule e) Digoxin Tablet.
11. Verification of Standards for a sample of castor oil I.P
12. HPLC & HPTLC analysis of drugs.

REFERENCE

1. Vogel's : Text book of quantitative chemical analysis revised by G. H. Jeffery, J. Bassett, J. Mendham, R. C. Denney, 6th Edition, Pearson Education Publishers – New Delhi, 1989, India.3.
2. H. Beckett and Stenlake, Practical Pharmaceutical Chemistry, Vol. I and Vol. II, 4th Edition CBS Publishers, 1997, New Delhi.

3. K.A Connors : Text Book of Pharmaceutical Analysis, 3rd Edition, Wiley- inter Science Publication, 1999, New York.
4. Indian Pharmacopoeia, Vol. I & II, 1996, the Controller of Publications, Government of India.
5. John H. Kennedy, Principles of Analytical Chemistry, 2nd Edition, Saunders College Publishing, 1990, New York.
6. Higuchi, Bechmman and Hassan : Pharmaceutical Analysis, 2nd Edition, John Wiley and Sons, New York.
7. D. C. Garratt, The Quantitative Analysis of Drugs, CBS Publishers, 2001, New Delhi.
8. P. D. Sethi, Quantitative Analysis of Drugs in Pharmaceutical Formulation, 3rd Edition.
9. J. W. Munson, Pharmaceutical Analysis – Modern Methods, Part – A & B, 2001.

SYLLABUS FOR PHARMACEUTICAL ANALYSIS

BRANCH – V

PAPER – IV

QUALITY CONTROL AND QUALITY ASSURANCE

THEORY **75 Hours(3 hrs./week)**

1. Concepts and Philosophy of TQM, GMP (orange guide), ISO-9000. **5 Hours.**

2. Organisation and personnel, responsibilities, training, hygiene. **3 Hours.**

3. Premises : **4 Hours.**

   Location, Design, Plan Layout, Construction, Maintenance and Sanitations. Environmental control, Sterile areas, control of contamination.

4. Equipments : **4 Hours.**

   Selection, purchase specifications, maintenance, sterilization of an area (TP & STP)

5. Raw Materials : **3 Hours.**

   Purchase specifications, Maintenance of stores, Selection of vendors, Controls on Raw materials.

6. Manufacture of and controls on dosage forms : **5 Hours.**

   Manufacturing Documents, Master Formula, Batch Formula Records, Standard operating procedure, Quality audits of manufacturing processes and facilities.

7. Standard operating procedures for various operations like cleaning, filling, drying, compression, coating, disinfection, sterilisation, membrane filtration etc., **4 Hours.**

8. Packaging and labeling controls, line clearance, reconciliation of labels; cartons and other packaging material; types and tests assuring quality of glass. Types of plastics used, permeation, leaching, sorption, chemical reactions, biological tests, modification of plastics by drugs; Different types of closures and closure liners; film wrapper; Blister packs, Bubble packs, shrink handling; foil / plastic pouches, bottle seals, tape seals, breakable seals and sealed tubes; Quality control of packaging material and filling equipment. **10 Hours.**

9. Quality control Laboratory : **8 Hours.**

   Responsibilities, Good Laboratory Practices, Routine controls, Instruments, Protocols, Non-clinical testing, Controls on animal house, Application of Computers in Quality control laboratory.

10. Finished product release : **3 Hours.**

    Quality review, Quality audits, Batch release document.

11. Warehousing : **2 Hours.**

    Good warehousing practice, Materials, Managements.

12. Distribution : **3 Hours.**

    Distribution of records, Handling of returned goods, Recovered materials and Reprocessing.

13. Complaints and Recalls : **2 hours.**

    Evaluation of complaints, Recall procedures, Related records and documents.

14. Waste disposal, Scrap disposal procedure and records. **2 Hours.**

15. Regulatory aspects of Pharmaceuticals and Bulk drug Manufacturing, Regulatory drug analysis. **3 Hours.**

16. Loan License Auditing – Concepts, Auditing. **3 Hours.**

17. Recent Amendments to drugs and cosmetics act and other relevant rules, Consumer protection, Environmental protection act, Certification and Licensing procedure. **5 Hours.**

18. WHO Certification, Globalisation of Drug Industry, Introduction to Export of Drugs and Import Policy **4 Hours.**

19. Patent regime. **2 Hours.**

PRACTICALS

1. Calibration of volumetric glass wares.
2. Testing containers, closures, liners, glass, plastics used for packing.
3. Test of packaging materials, cartons, aluminium foils, strip packing, blister packing, ampoules, vials, etc.
4. Sterility testing of areas.
5. Testing of related substances and foreign substances in raw materials as per I.P.
6. Assay for the raw materials, calculated either on anhydrous or hydrous basis as per I.P.

7. Estimation of the Acid value, Iodine value, Ester value, Saponification value for the raw materials as per I.P.
8. Microbiological evaluation of waste water.

REFERENCES

1. Quality Assurance Guide by Organisation of Pharmaceutical products of India.
2. Good Laboratory Practice Regulations, 2nd Edition, Sandy Weinberg, Vo. 69, Decker Series.
3. Quality Assurance of Pharmaceuticals – A compendium of guidelines and related materials – Vol. I – WHO Publications.
4. A guide to Total Quality Management – Kaushik Maitra and Sedhan K.Ghosh.
5. How to practice GMPs – P. P. Sharma.
6. ISO 9000 and Total Quality Management – Sadhank. G. Ghosh.
7. The International Pharmacopoeia Vol. 1,2,3,4 - 3rd Edition, General Methods of Analysis and Quality specification for Pharmaceutical Substances, Excipients and Dosage forms.
8. Controller of Publication, Govt. of India - Indian Pharmacopeia, Vol. I and II - 1996.
9. Burn, Finiey and Godwin : Biological Standardisation, 2nd Edition, Oxford University Press, London.
10. Dr. A. Patani : The Drugs and Cosmetics Act 1940, Eastern Book Company, Lucknow.