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


## SYLLABUS – M.PHARMACY 2006-2007
## BRANCH II – PHARMACEUTICAL CHEMISTRY

**M. PHARMACY**

**I YEAR**

**SYLLABUS FOR PHARMACEUTICAL CHEMISTRY – BRANCH II**

**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.

## BRANCH II

## PHARMACEUTICAL CHEMISTRY

## ADVANCED ORGANIC CHEMISTRY

## PAPER - II

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

**I. Techniques in drug development and synthesis will be dealt at advanced level. These include a deep knowledge of the following topics: 8 Hours**

a) Chemical bonding (localized, delocalized and Bonding weaker than covalent)
b) Reaction intermediates (carbocations, carbanions, free radicals, carbenes and nitrenes)
c) Various types of mechanisms and methods of determining them.
d) Acids and Bases.
e) Effect of structure on Reactivity.

**II. Detailed knowledge to be imparted in the following topics: 14 Hours.**

a) Substitution reactions (aliphatic neucleophilic, aromatic electrophilic, aliphatic electrophilic, aromatic nucleophilic and free radical).
b) Addition reactions (both carbon-carbon and carbon-heteroatom multiple bonds).
c) Elimination reactions and Rearrangement reactions.
d) Oxidation – reduction reactions and the reagents used for such reactions.
e) Protection and deprotection of various groups.

**III.** a) Chirality and the importance of chiral drugs. **6 Hours.**
b) Techniques for preparing chiral drugs (chirality pool, enzymatic transformation and asmmetric synthesis).
c) Symphoria : Introduction, neighbouring group effects with reference to stereo chemistry, intra molecular neucleophilic attack, rate of reaction anchimeric assistance.

**IV. Synthetic methodologies for obtaining drugs: 8 Hours.**

a) Disconnection approach.
b) Synthones for carbon-carbon bond formation.
c) Difunctional compounds.
d) Selective functional group interconversions (FGI).
e) Retrosynthetic analysis.

**V. Heterocyclic Chemistry: 8 Hours.**

Synthetic approaches for attaching heterocyclic ring systems in drug molecules having five membered and six membered heteroaromatic rings and fused ring systems.

**VI. Photochemical Reactions: 5 Hours.**

Basic theory, orbital symmetry rules and their applications.

**VII. Catalysis: 5 Hours.**

Introduction, phase transfer catalysis in anhydride, epoxide, ester, nitryl, sulphide formation, ester hydrolysis and reduction reaction.

**VIII. Pericyclic reactions: 5 Hours.**

Mechanism, Types of pericyclic reactions – cyclo addition, elctrocyclic reaction, sigmatrophic rearrangement.

**IX. A study of the following reactions of synthetic importance: 12 Hours.**

a) Birch reduction.
b) Mannich reaction.
c) Meerwin-Pondroff's reduction.
d) Oppeneaur oxidation.
e) Beckmann rearrangement.
f) Grignard reaction.
g) Hoffman rearrangement.
h) Ozonolysis.
i) Reformatsky reaction.
j) Michael reaction.

**X. Introduction to combinatorial chemistry 4 Hours.**

## PRACTICALS

I. Synthesis of the following heterocyclic compounds

a) Benzimidazole.
b) Benzotriazole.
c) 2,3 diphenylquinoxaline.
d) Oxadiazole.
e) Thiadiazole.
f) Isatin.

II. To perform the following reactions of synthetic importance

a) Birch reduction.
b) Clemmenson reduction.
c) Meerwin-Pondroff's reduction.

d) Grignard reaction.
e) Oppeneaur oxidation.
f) Benzyllic acid rearrangement.
g) Beckmann rearrangement.
h) Photochemical reaction.

## REFERENCES


1. "Advanced Organic chemistry, Reaction mechanisms and structure", J. march, John Wiley and sons, N.Y.
2. "Mechanism and structure in organic chemistry", E.S.Gould, Hold Rinchart and Winston,NewYork.
3. "The Organic Chemistry of Drug Design and Action" R.B.Silverman, Academic press Inc., San Diego, 1992.
4. "Chitotechnology" R.A. Steldon, Marcell Dekker Inc., Newyork 1993.
5. "Asymmetric synthesis", R.A. Aitken and S.M.Kilengi, Ed., Blackie Academic and professional London, 1992.
6. "Organic Chemistry" Clayden, Greeves, Warren and Woihers., Oxford University Press 2001.
7. "Organic Chemistry" Vol I and II. I.L. Finar. ELBS, Sixth ed., 1995.
8. A guide to mechanisms in Organic Chemistry – Peterskyes (Orient Longman, New Delhi).
9. Reactive intermediates in organic chemistry – Tandom and Gowel.
10. Molecular reaction and Photochemistry – C.H. Depuy and O.L.Chapman.
11. Combinational Chemistry – Synthesis and applications – Stephen R. Wilson &
12. Anthony W. Czarnik

## BRANCH II – PHARMACEUTICAL CHEMISTRY

## ADVANCED MEDICINAL CHEMISTRY

## PAPER-III

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

### 1. MICROBIAL TRANSFORMATION TECHNOLOGY IN THE PREPARATION OF DRUGS 6 Hours.

Theoretical and practical aspects of microbial transformations in the production of certain drugs.

### 2. QUANTITATIVE ANALYSIS OF STRUCTURE ACTIVITY RELATIONSHIP 7 Hours.

a) History and development of QSAR.
b) Drug receptor interactions.
c) Physicochemical parameters.
d) Hansch analysis, Fee Wilson analysis, relationship between them.
e) Statistical methods – regression analysis, partial least square analysis (PLS) and other multivariate statistical methods.
f) 3D QSAR approaches.

### 3. MOLECULAR MODELING IN DRUG DESIGN 6 Hours.

Molecular mechanics, quantum mechanisms, known receptor sites, calculation of affinity, unknown receptors – pharmacophore models. Searching for similarity, molecular comparison, finding common pattern.

### 4. ANALOG DESIGN FROM LEAD MOLECULE 6 Hours.

Introduction, Bioisosteric replacement, rigid analogs, alteration of chain branching, changes in ring size, ring position isomers, design of stereo isomers and geometric isomers, fragments of a lead molecule, variation in inter atomic distance.

### 5. PRODRUG DESIGN. 6 Hours.

Introduction, chemical bond, gastro intestinal absorption, parenteral administration, distribution, transdermal absorption, pharmacokinetic and biopharmaceutical aspects, rationale of prodrug design and practical considerations.

**6. APPROACHES TO THE RATIONAL DESIGN OF ENZYME INHIBITORS 6 Hours.**

Enzyme inhibitors in medicine, Enzyme inhibitors in basic research, rational design of non covalently and covalently binding enzyme inhibitors.

**7. GASTRIC PROTON PUMP INHIBITORS. 6 Hours.**

Introduction, gastric acid secretion and its inhibitors, test assay for studying gastric acid inhibitors, irreversible gastric proton pump inhibitors.

**8. AGENTS AFFECTING IMMUNE RESPONSE. 6 Hours.**

Immune response, immuno suppressants, immuno stimulants.

**9. MEDICINAL CHEMISTRY OF THE FOLLOWING GROUP OF DRUGS 12 Hours.**

a) Antiviral agents and agents under development of HIV infection.
b) Antineoplastic agents.
c) Antihypertensive agents.
d) Prostaglandins, leukotrienes and other eicosanoids.

**10. A STUDY OF THE MANUFACTURE OF THE FOLLOWING DRUGS 6 Hours.**

a) Paracetamol.
b) Diphenhydramine.
c) Indomethacin.
d) Sulphamethoxazole.
e) Pheniramine maleate.

**11. STEREOCHEMISTRY AND DRUG ACTION 8 Hours.**

Realization that stereoselectivity is a pre-requeisite for evolution. Role of chirality in selective and specific therapeutic agents. Case studies, Enantio selectivity in drug adsorption, metabolism, distribution and elimination.

## PRACTICALS

1. Synthesis of various barbiturates and determination of pKa value of barbiturates in relation to their biological activity.
2. Determination of partition co-efficient and calculation of values of a series of drugs like barbiturates.
3. Synthesis of local anesthetic and evaluation of their biological activity.
4. Synthesis of some anticonvulsants (other than barbiturates) and their evaluation.
5. Synthesis of some anti-inflammatory agents and their evaluation.

6. Synthesis of non-narcotic analgesics and evaluation in comparision to narcotic analgesics.
7. Suitable synthesis and the evaluation of drugs based on theory topics.

## REFERENCES


1. A Biomedical basis – Medicinal chemistry by Thomas Nogrady.
2. Introduction to Quantitative Drug Design by Y.C. Martin.
3. Selective toxicity by Aldrein Albert.
4. Comprehensive Medicinal Chemistry – Corwin and Hansch.
5. Medicinal Chemistry by Burger.
6. Principles of Medicinal Chemistry by William Foye.
7. Drug Design Volumes by Arienes.
8. Principles of Drug Design by Smith.
9. Strategy of Drug Design by Brucell.
10. The Organic Chemistry of the Drug Design and Drug action by Richard B. Silverman.
11. Remington's Text book of Pharmaceutical Sciences.
12. Wilson and Gisvold's Text book of Organic Medicinal and Pharmaceutical Chemistry.

## BRANCH II - PHARMACEUTICAL CHEMISTRY

## NATURAL PRODUCTS OF MEDICINAL INTEREST

## PAPER –IV

**THEORY: 75 Hours (3 Hrs./week)**

1. **Isolation, identification and application** of GLC, HPLC and counter current distribution to separation and analysis of plant constituents. Application of IR H1 NMR, MS, ORD and CD to structural studies of natural products. **8 Hours.**

2. **NATURAL PRODUCTS AS LEADS FOR NEW PHARMACEUTICALS : 7 Hours.**

   Cannabinoids, asperlicin, etoposide, teniposide, echinocandins, teprotide, khellin, cromoglycate, milbemycins.

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3. **The Natural products obtained by terrestrial and microbial sources by spectral data. Important members representing the following classes of natural products shall be discussed. 8 Hours.**

   a. **Alkaloids-** General introduction and classification, isolation and purification methods, general methods employed for determining the structure of alkaloids, constitution of morphine, reserpine and quinine.

   b. **Steroids-** General introduction, stereochemistry, nomenclature and structure elucidation of sterols (cholesterol), sapogenin (diosgenin) and cardiac glycosides. **9 Hours.**

   c. **Flavonoids -** Detailed chemical account of rutin and quercetin. **8 Hours.**

   d. **Triterpenoids –** A general chemical treatment and structural elucidation of terpenoids. **7 Hours.**

   e. **Coumarins –** General methods of isolation and purification and structural determination of Xanthotoxin and psoralene. **4 Hours.**

4. **STEROIDAL HORMONES : 4 Hours.**

   Steroid receptor, natural hormones and currently used synthetic derivatives, SAR, comparison of activity, transformation of phytosterols into steroidal drugs.

5. **ROLE OF RECOMBINANT DNA TECHNOLOGY AND DRUG DISCOVERY. 6 Hours.**

   Cloning DNA, expression of cloned DNA, manipulation of DNA sequence information new biological targets for drug developments, novel biotechnology derived pharmaceutical products. Antibody, antisense oligonucleotide therapy, gene therapy.

## 6. β – LACTUM ANTIBIOTICS. 4 Hours.

Mechanism of action, penicillins, cephalosporins, nocardicins and monobactums, carbapenems and penems, β-lactamase inhibitors and other β-lactum agents.

## 7. NON β-LACTUM ANTIBIOTICS. 4 Hours.

Amino glycosides, macrolides, linomycins and polypeptide antibiotics.

## 8. AWARENESS OF THE ACTIVE CONSTITUENT OF CERTAIN CRUDE DRUGS USED IN INDIGENOUS SYSTEM. 6 Hours.

a. Diabetic therapy – Gymnema sylvestre, Salacia reticulate, Pterocarpus marsupiam, Swertia Chirata, Trigonella Foenum – graccum.
b. Liver dysfunction – phyllanthus niruri.
c. Antitumor – curcuma longa Linn.

## PRACTICALS

1. Estimation of elements and functional groups in organic compounds.
2. Isolation, characterization like melting point, mixed melting point, molecular weight determination, functional group analysis, co-chromatographic technique for identification of isolated compounds and interpretation of UV and IR data.
3. Some typical degradation reactions to be carried on selected plant constituents.

## REFERENCES


1. Modern methods of plant analysis – Peech and M.V.Tracey.
2. Phytochemistry Voi. I and II by Miller, Jan Nostrant Rein Hld.
3. Recent advances in Phytochemistry Vol. I to IV – Scikel Runeckles.
4. Chemistry of natural products Vol I onwards IWPAC.
5. Natural Product Chemistry Nakanishi Gggolo.
6. Natural Product Chemistry "A laboratory guide" – Rapheal Khan.
7. The Alkaloid Chemistry and Physiology by THF Manske.
8. Introduction to molecular Phytochemistry – CHJ Wells, Chapmannstall.
9. Organic Chemistry of Natural Products Vol I and II by Gurdeep and Chatwall.
10. Organic Chemistry of Natural Products Vol I and II by O.P. Agarwal.
11. Organic Chemistry Vol I and II by I.L. Finar
12. Elements of Biotechnology by P.K. Gupta.
13. Pharmaceutical Biotechnology by S.P.Vyas and V.K.Dixit.
14. Biotechnology by Purohit and Mathoor.
15. Phytochemical methods of Harborne.
16. Burger's Medicinal Chemistry.