UNIVERSITY OF PUNE

Revised Syllabus for M. Sc. (Part – II)

Semester III and IV

For the year 2009-2010

Subject: Drug Chemistry

Semester III

CH-361 : - Chemistry of Heterocycles and Biologically active Compounds-
CH-362 :- Advance Analytical methods.
CH-363: - Drug Development (Immunology and Microbiology)
CH-364:- Stereo chemical Principles and applications.

SemesterIV

CH-461 - Synthetic Methods in Organic Chemistry.
CH-462:- Chemotherapy.
CH-463 : - Drug Design
Practical Courses

CH-367: - Practical Course-I
CH468:- Practical Course-II
CH469:- Practical Course-III /Project work/Industrial Training

CH361:- CHEMISTRY OF HETEROCYCLES AND BIOLOGICALLY ACTIVE COMPOUNDS

1 Synthesis and reactions of furan, Thiophene, Pyrrole, Pyridine, Benzofuran, Benzothiophene, Indole, Quinoline, Isoquinoline, Imidazole, Pyrazole Isoxazo1e, Thiazoles, Coumarins, Purines and pyrimidines,

2 Synthesis of biolog1cally active natural products e.q . Prostaglandins, Cephalosporin -C Reserpine , Taxol, Cortisone, Estrone. Epothiolone, Penicillin.

3 Synthetic Drugs. Ciprofloxacin, ibuprofen, Atenolol, Captopril, Diazepam, Chloroquine Barbiturates, Miconazole, Vit -B_6, Vitamin- A, Biotin,Ethambutol, Ranitidine, Omeprazole.

4 Synthesis of drugs of current Interest.

References

1 Heterocyclic Chemistry- Joule and Mills.
2 Modem Heterocyclic Chemistry- Paquette LA and Benjamin
3 Organic Chemistry of Drug synthesis-D Led nicer and L.A. Mitcher Vol I to III
4 Drug of today, Drugs of future (Journals)
5 Principles of Medicinal Chemistry -Foye.
6 Medicinal Chemistry-Burger

CH-362 ADVANCED ANALYTICAL METHODS.

1 PMR- Principle and Instrumentation, FT, Chemical Shifts, spin-spin Coupling Different spin systems, mechanism of spin coupling.
e.q. AB, ABX, factors affecting vicinal and Geminal Couplings, Rate processes, long Range Couplings, spin decoupling, Shift reagents, Solvent Shifts,
Nuclear Overhauser effect. 2D NMR, (COSY and HETCOR) applications.

2 C^{13}-NMR- Elementary ideas, instrumental problems , Chemical shift features of hydrocarbons, Effect of substituent on Chemical shifts Olefinic, acetylenic. aromatic and Carbonyl Carbons, Effects of Coupling.

3 Mass Spectrometry- Theory, instrumentation, Modes of Ionisation, Types of detectors, modes of fragmentation. Different types of ions,Molecular ions ,isotopic peaks, factors controlling fragmentation.

4 Structural elucidation of drug molecules based on joint application of UV, IR, PMR, CMR, and mass spectroscopy.

5 Separation Techniques- Fundamental Principles, Theory, Instrumentation and applications of GLC, HPLC, GCMS, HPTLC,

References

1 Spectroscopic methods in organic Chemistry, D.H.Williams and Ian Fleming

2 Spectrometric Identification of Organic compounds-T.C.Morril R M Silverstein and G. Bassler, 6th Edn., John Wiley & Sons
3. Introduction to Spectroscopy, D.L.Pavia, G.M.Lampman and G.S.Kriz, 3rd Edn. Harcourt College Publishers.

4 Absorption spectroscopy of Organic molecules- VM Parikh, (Addision Wesley.)

5 Applications of NMR spectroscopy in Organic Chemistry L.N.Jackman and S.Stemhell, Pergaman press.

5 NMR Basic Principles , Atta Ur Rehman , Springer Verlag (1986)
6. Organic Structure Analysis, Phillip Crew, Rodriques, Jaspars, Oxford Univ. Press(1998)

7 13 C- NMR Spectroscopy G.C.Levy, R.L.Licher, G.LNelson (Wiley Inter science)

8 Introduction to high performance liquid Chromatography RS.Haimilton, Chapman and Hall, London

9 Introduction to separation Science L.R..Snyder and CH Howarth
10 Monographs from American Chemical Society

CH-363 DRUG DEVELOPMENT

Part A: **Immunology and Microbiology**

1 Microbial Drug Development - Introduction to Microbiology and classification of Microbes. Characterisation and Screening of Microbes fermentation process, Microbia1growth, kinetics, Isolation and Improvement of Individual micro- organism, fermenter designing, Media designing, antimicrobial assays; Down Stream process and effluent treatment (Microbial and Chemical)

2 Immunology and Immunopharmacology- Overview of the immune system and its role, Adaptive and innate Immunity.Immune response and the undcrlymg mechanisms, Regulation of immune response. Hypersensitivity, immunodeficiency, Autoimmunnity, Immunzation, Immunosuppresants, Immunomodulators, Immunological techniques.

Part B: **Drug discovery and Development**

3 Introduction to the different systems of medicines

4 Sources of drugs, Microbial, Plant, Marine, synthetic, A historical perspective.

5 Discovery and Development of Drugs- History of drug discovery,Strategies in drug discovery, lead discovery, pharmacophore identification, lead development, Bioassays, screening of compounds. Toxicological evaluation of new drugs, Pre-Clinical testing, Clinical trials, Patents and intellectual property rights, Bioavailabability of drugs, Bioequivalance, Pharmacokinetics. From R & D to plant. Strategies in process development, scale up process. GMP, QA, QC, FDA, Documentation, pharmacoepia, Industrial hygiene and safety, Routes of drug administration, formulation of Dosage forms.

References

1 Introduction to Microbiogy- II^{dn}. Edn Ingraham and Ingraham(Thomson Books)

2 Microbiogy-Stanies,

3 Microbiology- Pleczar.

4 Immunology-Roitt Bostolf,Malc (2001) Mosby

5 Physiology and Anatomy -Carolla.

6 Industrial Microbiology-Cassida.

7 The Chemical Industry-Healton CA (hapman end Hall)

8 Comprehensive Medicinal Chemistry Vol-I (Hansch (1990) Pergamon pres

9 Basic and Chemical Immunology-Stites(1987) Prentice Hall.

10 Principle of Drug action-Goldstein.

11 Bioavailabinty and Bio equivalence-H.P.Tinis.

12 Pharmacoepia of India, British pharmecoepia, US Pharmacoepia

13 Introduction to medicinal Chemistry, III Edn. Patrick (2001) Oxford

14 Pharmaceutical Dosage forms and Drug Delivery system VIth Edn. .Arnel (Wessley)

15 Organic Chemistry of Drug Design and Drug Action. R.B.Silverman (1993) Academic

CII-364- STEREOCHEMICAL PRINCIPLES AND APPUCATIONS

1 Stereochemistry of six membered rings-Physical properties, Conformation and Chemical reactivity, Conformational effects in six membered rings containing Unsaturation.
2 The shape of rings other than six membered, Conformational effects in medium size rings,Trans annular effects, concept of I-strain
3 Stereochemistry of fused, bridged and caged rings.
4 An Overview of stereochemistry of pericyclic reactions. Electrocyclic, Cycloaddition and Sigmatropic reactions and their analysis.(FMO, Correlation diagrams and ATS approach)
5 Chiron approach —An Overview with applications
6 Asymmetric synthesis and Asymmetric Induction overview, Importance of Chiralitity in

drugs. Chiral Auxilliaries, Chiral reagents and Chiral catalysis with examples.

7 Asymmetric catalysis in target oriented synthesis.

References

1 Stereochemistry of carbon compounds –E L Eliel

2 Stereochemistry of Organic compounds-D Nassipuri (Wiley Interscience)

3 Conformational Analysis —E.L.Eliel, N.L. Allinger, S Allinger and GA Morrison.

4 Chiron Approach to Organic synthesis-P. S.Hanessian.

5 Asymmetric Synthesis-J.D.Morrison.

6 Asymmetric Synthcsis-Simpkins.

7 Asymmetric Synthesi-Aitken RA.

8 Chirality in Drug Design end synthesis-C. Brown(Academic Press)

9 Conservation of orbital symmetry RB. Woodward and Hoffmann.

10 Organic Reactions and Orbital symmetry -Gilchrist.

CH-461 SYNTHETIC METHODS IN ORGANIC CHEMISTRY

1 Organolithium, Aluminium, Phosphorous and Boranes, Synthetic applications

2 Transition metal complexes in Organic synthesis.

3 Enamines in Organic synthesis.

4 Umpolung in Organic synthesis

5 Designing Organic synthesis.

6 Protecting groups for hydroxyl, amino, carboxyl and aldehyde ketonefunctions as illustrated in the synthesis of polypeptide and polynucleotide

7 Biomimetic synthesis

8 Green Chemistry.

9 Domino Reactions

References

1 Principles of Organo metallic Chemistry- G.E.Coates, Green and K. Wade

2 Transition Metal Intermediates in Organic synthesis C W Bird, Logos (1967)

3 Organometallics in Organic synthesis- J. M. Swan and DC Black (Chapman Hall)

4 Designing Organic synthesis - S Warren (Wiley Interscience)

5 Some modern methods of Organic synthesis. W Carruthers (Cambridge)

6 Modem synthetic Reactions- HO House, Benjamin.

1 Organic Chemistry -Clayden, Greeves, Warrcn of wothers (Oxford press)

8 Organic synthesis M. B. Smith.

CH-462 CHEMOTHERAPY

1. Antimicrobial therapy -Development and mechanism of action for Penicillins, Cephalosporins.and Quinolones. An Overview of Aminoglycosides, Macrolides, peptide and miscellaneous antibiotics.
2 Antifungals, Antiviral, Antimalarial, Antimycobacterials
3 Cancer and its Chemotherapy. Developments in Immunotherapy
4 Cardiovascular system and its disorders: Hypertension, Heart Failure, Angina Pectoris, Arrythmia, Myocardial Infarction, Ischaemic heart diseases, Stroke, CVS disorder management with current drugs.
5 Central Nervous System, CNS disorders, A study of antidepresants, Hypnotics and sedatives, Tranquilizers and Anticonvulsants.
6 Pain , Inflammation ,Analgesics, anti- inflammatory agents.
7 Endocrine system and Hormonal therapy.
8 Gastrointestinal tract disorders and Drugs.
9 Emphasis on Organic Chemistry of Diseases and Drag action.
10 Diabetis and Management of Diabetis.

References

1 Medicinal Chemistry -Burger vols. I to IV (John Wiley)
2 Principles of Medicinal Chemistiy- W.Foye.
3 Comprehensive Medicinal Chemistry -C.Hansch (Pergaman Press).
4 Selective Toxicity –A. Albert (Chapman Hall)
5 Principles of Drug action - A. Goldstein.
6 Organic Chemistry of Drug action and Drug design -LB. Silverman (Acad press)
7 Physiology and Anatomy- Carolla.
8 Medicinal Chemistry-Biochemical approach, Thomas Nogardy.
9 Essential of pharmacology -K. D. Tripathi.
10 Pharmacology-Hanney
11 Pharmacology-Goodman and Gilman.

CH- 463 DRUG DESIGN

1. Membrane and Receptor- Structure, functions and the mechanism of drug action

(Receptor Response), Design of agonist and antagonists, Receptor theories, Models and their types.

2. Physicochemical principles of Drug action- Drug Receptor interactions, Quantitative description of physicochemical parameters and their calculation. QSAR, Hansch analysis, COMFA, COMSIA, Free Wilson Method, Topliss and Craig's models.

3 Design of Drugs based on pharmacokinetics, Bio activation and metabolism Pro-drug Design rational design of enzyme inhibitors.

4. Molecular Biology in Medicinal Chemistry and Drug discovery.

5. Combinatorial Chemistry and high throughput Screening.

6. Bio-informatics and applications in drug design.

7. Computers Aided Drug design: Basic concept of Computational chemistry like Quantum Mechanics, Molecular Mechanics, Force fields, Energy minimization, Conformational search, Molecular dynamics. Ligand based drug design, Receptor based drug design. Analog approach, pharmacophore mapping. Molecular-modeling etc. Virtual Screening.

8. Bio statistics.

9. Current trends in the field of drug discovery and design.

References

1. An Introduction to Medicinal Chemistry- IInd Edn. Patrick(Qxford 2001)
2. Medicinal Chemistry Vol. I Burger.
3. Molecular Modeling, Principles and applications -Andrew Leach(Longman) 1998.
4. Comprehensive Medicinal Chemistry vol.4 Corwin Hansch(1990) pergaman press.
5. Organic Chemistry of drug design and drug action-RB. Silverman (1993) Acad. press
6. Statistical MethodS in Biology-Norman Bailey(1995) Cambridge.
7. A Text book of Drug design and development IInd Edn. Povl..Krogsgaard-Larsen Tommy L. and U Madsen (1996) Harwood Acad. Publishers.

CH-367 PRACTICAL COURSE- I

1 Clemmensen/ Wolf kischner Reduction.
2 $NaBH_4$/ $LiAlH_4$ Reductions.
3 Hydroboration-Oxidation.

4 Synthesis of chiral auxiliary.
5 Asymmetric induction using Disopinanyl borane.
6 Oxidation using H_2CrO_4
7 Synthesis of Heterocycles.
8 Grignard reaction.
9 Synthesis of some Drug Molecu1es
10 Lithiation and other Metalation reactions
11 Determination of partition Coefficients and Ionisation constant of Drug molecules.

CH- 468 PRACTICAL COURSE-II

1. Microbiology - Differentiation, Gram staining Mophology, Protoplast fusion, Screening of bacterial substances, sterility testing. Micrrobial assays, Production of penicillin by fermentation

2. Phytochemistry- Techniques in isolation and extraction of crude drugs, purification and of various active principles having medicinal, industrial and chemical importance

3. Biochemistry- Isolation, purification and characterisation of Enzymes, stability studies, Kinetics determination of Km, Vmax, 1-50, Inhibition studies, reversible, irreversible and K Cat. Electrophoresis, Isolation and estimation of DNA, DNA-drug interaction studies, Determination of drug in blood and urine.

CH-469:- PRACTICAL COURSE III
PROJECT WORK / INDUSTRIAL TRAINING.

The students who will not do project course, shall carry out at least 12 experiments to illustrate the principles of Organic mechanism and synthesis.
Synthesis of Heterocycles Viz.
Quinoloine, Barbiturates, Acridines, Indole, Carbazole, Pyrazolle, Pyrolle, Coumarins, Thiazole, Imidazole, Triazole etc.
Synthesis involving following reactions.
Beckmann rearrangement, Hoffman rearrangement, Friedel Crafts acylation, Sandmeyer, Fries rearrangement. Biginelli reaction, Aldol Claisen condensation, Hydroboration etc.
Use of spectroscopic methods for structure determination and/or carryout biological activity studies for some of the compounds prepared during the course.

References

1. Practical Organic Chemistry, Al. Vogel (ELBS).
2. PharmacologiCal Basis of Therapeutics (Pergman press, New York) Goodman and Gilman.

3. Evaluation of Drug Activities- Pharmacometrics, Lawrence D. R. Bacharach AL. (Academic press London)
4 Screening Methods in Pharmacology, Turner R..A (Academic press London).
5 Physiological Chemistry, Hawk.
6 Clinical Biochemistry, Vol I and II Varley.
7 Fundamentals of Experimental Pharmacology, Ghosh M.N.(Scientific Book Agency, Calcutta)
8 Practical Biochemistry, Plummer.
9 Practical Microbiology. :
10 Practical Biochemistry, Jayaraman.
11 Microscale and Macro scale Preparations Williamson and Williamson.
12 Practical Heterocylic Chemistry, Fitton and Smalley (AP)
13 Organic Synthesis Collective Volumes, Vol I to VIII.

The following changes are suggested for the First year M.Sc. I Drug Chemistry syllabus. The Practical Course in Inorganic Chemistry will be replaced by:

CH-128: INORGANIC AND ANALYTICAL CHEMISTRY PRACTICALS

1. Inorganic synthesis and characterization by physical or chemical methods:
a) Cis-trans potassium diaquo dioxalate chromate (III)
b) Chloropentammino cobalt (III) chloride.

2. Colorimetry;
Keg of M-L systems such as:
i) Fe (III) Salicylic acid
ii) Fe (III) Sulphosalicylic acid
iii) Fe (III) resorcilic acid by Job's method and Mole ratio method

3. Photometric titration of systems such as:
a) Cu^{2+} - EDTA
b) Fe^{2+} - Sulphosalicylic acid
c) Co^{2+} - R-nitroso salt.

4. Potentiometry:
a) Complexometric determination using disodium EDTA of
i) Co^{2+}
jj) Al^{3+}
iii) Cu^{2+}

5 Solvent extraction of Al / Mo usmg 8-hydroxy quinoline complex and determination by spectrophotometry

6. Solvent extraction of ferric thiocyanate complex and determination by colorimetry.

7. Separation and estimation of Fe and Al on a cation exchanger.

8. Separation and estimation of copper and cobalt on cellulose column.

9. Analysis of Vitamin C in juices and squashes.

10. Analysis of Vitamin A in food products.

11. Simultaneous determination by titanium and vanadium Pt and Pd using hydrogen peroxide by spectrophotometry.

12, Estimation of Na, K and Ca in binary mixture by flame photometry using Li as Internal standard and using standard addition method.

13. Determination of the strength of the following by fiourimetmy, beryllium, aluminium, vitamin B1, vitamin B2.

14. Determination of the strength of commercial phosphoric acid/vinegar by conductometric titration.

15. Analysis of malathion by colorimetry or polarography.

16. Estimation of nitrile, fluoride, dissolved chlorine, chloride, iron, chromium~, manganese colorimetrically.

17. Estimation of Hg, Pb, Cd spectrophotometrically/complexo-metrically.

18. Estimation of sulphadizine.

19. Estimation of mixtures of benzoic acid and salicylic acid in pharmaceutical preparations

20. Determination of iron, calcium and phosphorous in milk powder.

21. Partition coefficient.

References:

1) A textbook of Qualitative Inorganic Analysis3rd Edn., A. I. Vogel, ELBS.
2) A Textbook of Practical Organic Chemistry, 4th Edn. A. I. Vogel, ELBS.
3) Standard Methods of Chemical Analysis, 6th Edn. A series of volumes edited by F. J. Weicher, Robert E. Krieger Publishing co.
4) Pharmacoepoeia of India.

Practical Course in Physical Chemistry will be replaced by

CH-107 Practical Course in Separation, Purification & Analytical techniques in Drug Chemistry.

1. Purification of solvents and reagents
2. Mixture separation Two and Three components.
3. Isolation of Natural products from Clove, Cinnamom by steam distillation. Also use Soxhlet apparatus for one natural product.
4. Chromatographic techniques as TLC, Coloumn chromatography
5. Biomolecule separation and identification using Gel Electrophoresis, Paper chromatography Immunoelectrophoresis.
6. Separation and Identification of of active drug ingredients from commercial pharmaceutical preparations.
7. Try to use spectral data whenever possible.
8. Any current techniques as per need and demand.

Modifications in CH: 248 as shown below

CH - 248: ORGANTIC CHEMISTRY PRACTICALS

1. Techniques: Crystallization, fractional crystallizsation, fractional distillation, vacuum distillation, sublimation, steam distillation,
2. Single stage preparation involving different type of reactions (minimum 8 preparations).
3. Two-stage preparations (mininim 2 preparation).
4. Three-stage preparations (minimum 2 preparations).
5. Derivatives of functional groups such as acetyl, benzoyl, 2, 4-DNP, oxime, anilide, amide and aryloxy acetic acid (minimum one of each type)

Typical preparations from which the single and two stage preparations can be Chosen are:

1. Toluene —p-nitrotoluene —p-nitrobenzoic acid —p-amino benzoic acid
2. Benzene- Acetopheneone.- Acetophenone oxime -Acetanilide
3. Benzaldehyde-Benzoin -Benzil. Benzillic acid
4. Nitrobenzene -m-dinitrobenzene- m-nitroaniline- m-nitrophenol
5. Phthalic acid -~phthalic anhydride –phthalimide- Anthranilic acid
6. Anthranilic acid - pheylglycine - orthocarboxylic acid - indigo
7. Acetophenone - Benzalacetophenone - epoxide
8. Cyclohexanone - Cyclohexanone oxime -caprolactam
9. Phthalic anhydride - O-benzolylbenzoic acid - anthraquinone.
10. O-Cholobenzoinc acid - N-phenylanthranilic acid - acridone.
11. Cholrobenzene ~ 2, 4-dinitrochlorobenzene - 2, 4-dinitrophenol
12. Bromobenzene -~ triphenylcarbinol -tritylchloride
13. Resorcinol ~ resacetophenone — 4-ethyl resorcinol

14. Phenol - allylphenyl ether-+ o-allylphenol
15. Phenol - salicylaldehyde -~ coumarin