SAVITRIBAI PHULE PUNE UNIVERSITY, PUNE

SYLLABUS FOR
University Department

Master of Science
In
Medicinal Chemistry

PART-I and II
(Semester I, II, III and IV-choice based Credit system**)**
w.e.f. July 2020-21

Total Number of Credits: 80

Semester I		
Core Courses		
Subject Code	**Subject Title**	**Number of Credits**
MC – 100	Coordination and Medicinal Chemistry	4
MC – 101	Reaction Mechanisms in Organic Chemistry I	4
MC-102	Kinetics, Thermodynamics and Drug Action	4
Elective Courses (any one)		
IC 125	Physical Methods in Inorganic Chemistry and Main Group Chemistry	4
OC 135	Reaction Mechanisms in Organic Chemistry II	4
PC 145	Chemical Mathematics and Elements of Computer Programming	4
Practical Courses:		
MC-108	Physical Chemistry Practicals and Computer Applications in Medicinal Chemistry and Instrumentation	4
Semester II		
Core Courses		
Subject Code	**Subject Title**	**Number of Credits**
MC-200	Advanced Organic Chemistry and Spectroscopy	4
MC-201	Bioactive Heterocyclic Chemistry	4
MC-202	Basic Biochemistry, Biomolecules and Bioinorganic Chemistry	4
Practical Courses:		
MC-208	Experiments in Organic Chemistry	4
MC-209	Biochemistry Practicals and Computer Applications in Medicinal Chemistry and Instrumentation (4 Credits).	4
Elective Courses (any one)		
Subject Code	**Subject Title**	**Number of Credits**
MC-205	Biostatistics and Cheminformatics	4
MC-206	Drug, Targets and Diseases	4
Total Number of Credits: 40		

Semester-III		
Core Courses		
Subject Code	**Subject Title**	**Number of Credits**
MC -300	Spectroscopic Methods in Structure Determination of Organic and Medicinal Compounds	4
MC -306	Advanced Reaction Mechanism	4
Elective Courses (any three)		
Subject Code	**Subject Title**	**Number of Credits**
MC-305	Carbanions and Aromaticity in Chemistry	4
MC-301	Stereochemistry of Organic/Medicinal compounds	4
MC -307	Drug Designing and Medicinal Biochemistry	4
MC-308	Research Project	4

Semester IV		
Core Courses		
Subject Code	**Subject Title**	**Number of Credits**
MC - 400	Synthetic Strategies in the Total Synthesis of Complex Drug Molecules	4
MC -401	Fundamentals of Chiral Drug Synthesis	4
Practical Courses:		
MC-408	Drug Intermediate Synthesis	4
MC-409	Medicinal Chemistry	4
Elective Courses (any one)		
Subject Code	**Subject Title**	**Number of Credits**
MC-405	Structure Determination and Chromatographic Technics	4
MC-406	Origin of Secondary Metabolic Drugs in Plants and Pharmacokinetics	4
Total Number of Credits: 40		

UGC recommended courses (Additional 10 credits)		
Subject Code	**Subject Title**	**Number of Credits**
	Cyber Security/Information Security	4
	Skill Based Credits	4
	Human Rights Education	4

Courses which can be opted by students from outside departments:

Subject Code	**Subject Title**	**Number of Credits**
Core courses:	**Semester-I**	
MC – 100	Coordination and Medicinal Chemistry	4
	Semester-II	
MC-202	Basic Biochemistry, Biomolecules and Bioinorganic Chemistry	4
	Semester-III	
MC -307	Drug Designing and Medicinal Biochemistry	4
	Elective course:	
MC-305	Carbanions and Aromaticity in Chemistry	4
	Semester-IV	
MC - 400	Synthetic Strategies in the Total Synthesis of Complex Drug Molecules	4
	Elective course:	
MC-406	Origin of Secondary Metabolic Drugs in Plants and Pharmacokinetics	4

Semester I

Core Course:

MC- 100 Coordination and Medicinal Chemistry (4 credits) (60L)

Coordination Chemistry (2 Credits) (30L)

1 Concept & Scope of ligand Fields.

2 Energy levels of transition metal ions, Free ion terms, term wave functions, spin –orbit coupling

3 Effect of ligand fields on energy levels of transition ions, weak cubic ligand field effect on Russell-Saunders terms, strong field effect, correlation diagrams,Tanabe-Sugano diagrams, Spin-pairing energies.

4 Electronic spectra of complexes band intensities, band energies, band width & shapes, spectra of 1^{st},2^{nd}& 3^{rd} row ion and rare earth ion complexes, spectrochemical & Nephelauxetic series, charge transfer & luminescence spectra, calculations of Dq,B, Racah parameters.

5 Magnetic properties of complexes paramagnetism,1^{st} & 2^{nd} ordered Zeeman effect, quenching of orbital angular momentum by Ligand fields, Magnetic properties of A,E,T ground terms in complexes ,spin free–spin paired equilibria

6 Definitions and theorems of group theory, subgroups, classes.

7 Molecular symmetry and symmetry groups - symmetry elements and operations,. Symmetry planes, reflections, inversion center, proper / improper axes and rotations, products of symmetry operations, equivalent symmetry elements and atoms, symmetry elements and optical isomerism, symmetry point groups, classes of symmetry operations, classification of molecular point groups.

8 Representations of groups. Great orthogonality theorem, character tables, properties of characters of representations.

9 Group theory and quantum mechanics. Wave function as bases for irreducible representation

10 Symmetry Adapted Linear Combinations -(SALC) - projection operators and their use to construct SALC.

11 Molecular Orbital Theory -

a) Principle, Symmetry factoring of secular equation, Carbocyclic systems, LCAO-MO π bonding, Worked example-Naphthalene, Three center bonding, symmetry based "selection rules" for cyclization.

b) Transformation properties of atomic orbital, MO's for Sigma bonding AB_n molecules, tetrahedral AB_4case, Hybrid orbital, MO's for pi bonding in AB molecules, cage and cluster compounds, MO's for metal sandwiched compounds

12 Mechanism of metal complexes.

Ligand substitution reactions, substitution of square - planar complexes, substitution in octahedral complexes, redox reactions and photochemical reactions

Medicinal Chemistry, (2 Credits) (30L)

History and classification, drug targets- lipids, carbohydrates, proteins, and nucleic acids; **(06L)**

Selected examples of drugs and their mechanism of action, identification of diseases and corresponding targets **(12L)**

Lead and analogue synthesis and actions: Antibacterial- sulphonamides and derivatives, quinolones and fluoroquinolones- nalidixic acid, ciprofloxacin, enoxacin, grepafloxacin, metronidazole, nitrofurazone, pyrazinamide, Anticancer- ethambutol, lomustine, carmustine, procarbazine, 5-fluorouracil, 6-mercaptopurine,tamoxifen **(12L)**

Text Books:-

1. An Introduction to Medicinal chemistry: Graham, Patric third edition

MC – 101 Stereochemistry and Organic Reactions. (4 Credits) (60L)

Stereochemistry of Organic and biomolecules (16L)

a) Symmetry properties of organic compounds, Chirality of organic compounds, chiral centre, configuration of chiral centre, enantiomerism, diastereomerism, pseudo-asymmetric carbon
b) Homotopic and heterotopic ligands and faces, Prochirality of center and faces
c) Stereochemistry of Natural products as exemplified by the study of stereochemistry of menthol
d) Conformational concepts, conformations of acyclic molecules, cyclohexane and mono, di-substituted cyclohexane, Conformational effect on physical properties of the molecules

Stereochemistry and drug action **(2L)**

Stereochemistry of Addition and Elimination reactions (12L)

Mechanistic and Stereochemical aspects of addition reactions of C-C multiple bonds including allenes, Ionic and free radical additions of halogens, halogen halides, hydration and related addition reactions, Electrophilic addition involving metal ions, Regio and Chemoselectivity, Orientation and reactivity, conjugate additions.

Mechanistic and Stereochemical aspects of elimination reactions, E2, E1, E1cb, eliminations not involving C-H bonds, reactivity effect of attacking and leaving groups, competition between substitution and elimination , anti and syn eliminations.

Ref. 1 (Page no. 341 – 396)

Books –

1. F. A. Carey and R. J. Sundberg. (Ed. IV), Part A – Adv. Organic Chemistry, Kluwer Academic pub., 2001.

2. E. L. Eliel, Stereochemistry of carbon compounds.

Organic Reactions

Nucleophilic Substitution Reactions at saturated carbon **(15L)**

The S_N2, S_N1, mixed S_N1 and S_N2 and SET mechanism.

The neighboring group mechanism, The Neighboring group participation by π & σ bonds, anchimeric assistance, classical and non classical carbocations, phenonium ions, norbornyl system, carbocation rearrangements in neighboring group participation. The S_Ni, ion pair mechanism, Nucleophilic substitution at an allylic, aliphatic trigonal and vinylic carbon. Reactivity effects of structure, attacking nucleophile, leaving group and reaction mechanism, solvent effect, phase transfer catalyst, ambident nucleophile and regio-selectivity.

Aromatic electrophilic and nucleophlic substitution Reactions **(15L)**
Aromaticity, Arenium ion mechanism, orientation and reactivity, energy profile diagram, calculation of partial rate factor, the ortho/ para ratio ipso attack, orientation in other ring systems such as Naphthalene, Anthracene, Six and five membered heterocycles, Diazonium coupling Vilsmeier reaction, Gattermann – Koch reaction, and other named reactions of carbocyclic rings. The ArS_N1, Benzyne and SNAr1, Mechanisms, Reactivity effect of substrate structure, leaving group and attacking nucleophile. Ref. 1 (page no. 539 to 594)

Books –

Texts –

1. F. A. Carey and R. J. Sundberg. (Ed. IV), Part A and part B – Adv. Organic Chemistry, Kluwer Academic pub.

2. J. March, (Ed IV), Adv. Organic Chemistry.

3. R.O.C. Norman, Organic Chemistry.

4. R. T. Morrison and R. N. Boyd, Organic Chemistry

References –

1. J. Clayden, N. Greeves. et. al Organic Chemistry , Oxford Univ. Press, 2001.

2. Gould E.S., Mechanism and Structure in Organic Chemistry.

3. H.O. House, Synthetic Organic Chemistry.

MC – 102 Kinetics, Thermodynamics and Drug Action (4 Credits) (60L)

Kinetics (30L)

1) Recapitulation, First, Second, Third and n^{th} order reactions, reactions of fractional order, complex reactions, parallel and consecutive reactions, reversible reactions, autocatalysis, oscillatory reactions.
2) Techniques and Methods, Fast reactions, flow techniques, relaxation methods, flash photolysis, Kinetic isotopic effect
3) Reactions in gas phase, Collision theory, unimolecular reactions, Lindemann mechanism, potential energy surface, Transition state theory, Free radical and chain reactions, explosive reactions
4) Reactions in solutions, effect of solvation, ionic strength on rates, Linear free energy relationships, correlation of rate with solubility parameters, Enzyme catalysis, Michaleis and Menton analysis

Text Books

Principle of Chemical Kinetics, J. C. House, Wm C Brown Publishers, (1997)

i) Chemical Kinetics, K. J. Laidler, Mc Graw Hill, Third Edition (1987).

Thermodynamics: **(30L)**

1. Recapitulation of fundamental concepts in Thermodynamics **(6L)**

Work, Heat, Temperature, Mechanical Equivalent of Heat, Heat Capacities (C_p & C_v), Ideal Gas, Equation of State, Thermodynamic Equilibrium, Different types of Thermodynamic Processes- (Reversible, Irreversible, Adiabatic, Isothermal, Isobaric, etc.) Reservoir, Molecular Energies, State Functions and Path Functions, Exact & Inexact Differentials, Condition for Exact Differentials.

2. Laws of Thermodynamics and Thermodynamics Functions **(6L)**

Zeroth-, First-, Second- and Third Laws -Conceptual Development & Implications. Internal Energy (U), Enthalpy (H), Entropy (S), Helmholtz and Gibb's Free Energies (A & G), Absolute Entropy, Work under various conditions. Maxwell's Equations and their application, Various relationships for (C_p -Cv) & Cp/Cv, Conditions for Equilibrium and Spontaneity, Relationship between Free Energy change (ΔG) and Equilibrium Constant (K), Concept of Partial Molar Quantities -Chemical Potential *(*μ*).*

3. Applications **(10L)**

Heat Engine, Refrigeration, Joule-Thompson effect, Liquefaction of Gases. Flame Temperatures, Explosion Temperature and Pressure. Phase Equilibria (melting, vaporisation, sublimation, crystal modifications). Calculation of , □H , □S, □G & K and effect of Temperature & Pressure thereon for various types of Chemical Reactions -(Combustion, Hydrogenations, Bond Dissociation, Hydration/(Solvation), Ionisation, Isomerisation, Decomposition, Reduction of Metal Oxides, Ammonia synthesis, etc.). Electrochemical Cells- Electrode Potentials and Cell E.M.F., Determination of □G from cell E.M.F. Ideal & Non-ideal Solutions.

4. Statistical Thermodynamics (**8L**)

Microscopic point of view. Thermodynamic Probability (W)- Distinguishable and Indistinguishable Particles, Different ways of Arrangements and Maximisation ofW, Maxwell-Boltzmann Distribution Law, Partition Function (Q), Fermi-Dirac and Bose-Einstein Statistics.

Applications in Drug Actions

Books & References*:*

(1). Physical Chemistry -RA.Alberty & R.J.Silby, 1st ed. (1995), John Wiley.

(2). Physical Chemistry -G.B.Castellan, 3rd ed.(1986), Narosa Publishers, Mumbai.

(3). Physical Chemistry -G.M.Barrow, 5th ed. (1988), Tata McGraw Hill.

(4). Physical Chemistry -P.W.Atkins, 4th ed. ( ), E.L.B.S.

Practical Courses

MC – 108 :- Physical Chemistry Practicals and Computer Applications in Medicinal Chemistry and Instrumentation (4 Credits)

Physical Chemistry Practicals (3 Credits)

Measurement of pKa of phenols and its application

Influence of pH and pKa on ionization and solubility of Drugs

Determination of oil / water partition coefficient

Determination of lipophilicity substituent constant of sulphonamides by means of reversed-phase TLC

Determination of the free salisylic acid concentration inn asprin by forming Fe3+ complexes

Solvatometric studies on coumarins or other drugs.

Analysis of drug component from drug

A) Conductometry:

i) Hydrolysis of NH4Cl or CH3COONa or aniline. hydrochloride.

ii) Determination of λ0 or λα and dissociation constant of acetic acid.

iii) Hydrolysis of ethylacetate by NaoH.

iv) Determination of ..G, ..H, and .. S of Silver Benzoate by conductometry.

B) Potentiomerty:-

1. Stability Constant of a complex ion.
2. Solubility of a sparingly soluble salt.
3. To determine the ionic product of H2O
4. Estimation of halide in mixure.

C) pH metry:-

1. Determination of the acid and base dissociation constant of an amino acid and hence the isoelectric point of the acid.

D) Polarography

1. Determination of half wave potential E 1/2 and unknown concentration of anion.
2. Amperometric titration of Pb(NO3)2 with K2Cr2 O7

E) Colorimetric :-

1. Analysis of a binary mixture.
2. Copper EDTA photometric titration.

F) Radioactivity:-

1. Estimation of Mn in tea leaves by NAA
2. Half – life of a radioactive nuclide and Counting errors.
3. Determination of Emax of beta radiation and absorption coefficients in Al.

G) Chemical Kinetics:

1. Kinetic decomposition of diacetone alcohol by dilatometry.
2. Determination of an order of a reaction.
3. Bronsted primary salt effect.

H) Non- Instrumental :-

1) Freundlich and Longmuir isotherms for adsorption of acetic acid on active charcoal

2) Statistical treatment of experiemntal data

3) Molecular weight by steam distillation.

4) Glycerol radius by viscosity.

5) Partial Molar Volume (Polynometry) Determination of the densities of a series of solutions and to calculate the molar volumes of the components.

Each candidate should perform a minimum of 10 experiments with at least one experiment form each techniques.

References:-

1. *Practical physical chemistry, A. Findary, T.A. kitchner (Longmans, Green*
2. *and Co.)*
3. *Experiments in Physical Chemistry, J.M. Wilson, K.J. Newcombe, A.r.*
4. *Denko. R.M.W. richett (Pergamon Press)*
5. *Senior Practical Physical Chemistry, B.D. Khosla and V.S. Garg (R. Chand*
6. *and Co., Delhi.)*

Computer Applications in Medicinal Chemistry and Instrumentation (1 Credits)

1. Molecular Modeling: Energy minimization, geometry optimization, conformational analysis, global conformational minima determination; Approaches and problems; Bioactive vs. global minimum conformations; Automated methods of conformational search; Advantages and limitations of available software; Molecular graphics; Computer methodologies behind molecular modeling including artificial intelligence methods.
2. QSAR: Electronic effects; Hammett equation, Lipophilicity effects; Hansch equation, Steric Effects; Taft Equation; Experimental and theoretical approaches for the determination of physico-chemical parameters, parameter inter-dependence; Case studies; Regression analysis, extrapolation versus interpolation, linearity versus non-linearity; The importance of biological data in the correct form;

Semester II

MC 200 Advanced Organic Chemistry and Spectroscopy (4 credits) (**60 L)**

Oxidation and reduction **(17L)**

a) Oxidation reactions:
CrO_3, PDC, PCC, $KMnO_4$, MnO_2, Swern, SeO_2, $Pb(OAc)_4$, Pd-C, OsO_4, mCPBA, O_3, $NaIO_4$, HIO_4

b) Reduction reactions
Boranes and hydroboration reactions, R_3SiH, Bu_3SnH, MVP, H_2/Pd-C, Willkinsons, $NaCNBH_3$, NH_2NH_2, DIBAl

c) Rearrangements: **[08]**
a) Reactive intermediates:carbocations, carbaions, carbenes, niterenes
b) Beckmann, Hofmann,,Curtius, Smith, Wolf, Lossen, Bayer-villiger, Sommelet, Favorskii, Pinacol-pinacolon, Benzyl-benzilic acid, Calsien, Cope, Fries

d) Ylides:Phosphorus, Nitrogen and Sulphurylides **[07]**

e) Addition to carbon-heteroatom multiple bonds: **[08]**
Grignard, organo zinc, organo copper, organo lithium, reagents to carbonyl and unsaturated carbonyl compounds.

References:

1.Advanced Organic Chemistry, F. A. Carey and R J Sundberg, Part B (for autonomous centers).

2.Basic principles of organic chemistry, J D Roberts and M C. Caseiro Benjamin (1964).

3.Advanced organic chemistry, J. March 4th edition. Wiley-Interscience publication 1999.

4.Mechanism and structure in organic chemistry, E S Gould, Holt, Rinehart and Winston.

Organic Spectroscopy (20L)

a) UV: Factors affecting UV absorption and interpretation of UV spectra
b) IR: Ideas about IR frequencies, interpretation of IR spectra
c) ^{1}H NMR: Fundamentals of NMR, CW and FT-NMR, factors affecting chemical shift, integration coupling (1st order analysis)
d) Problems on UV, IR and ^{1}H NMR

References:

1. *Organic Chemistry –by J. Clayden, N. Greeves, S. Warren and P. Wothers (Oxford)*
2. *Modern Synthetic reactions-by H.O. House*
3. *Organic Synthesis –by M.B. Smith*
4. *Organic chemistry –by Cram, Hammond, Handricson*
5. *Introduction to spectroscopy –by D.l. Pavia, G.M. Lampman, G.S. Kriz, 3rd Edition*
6. *Spectroscopic methods in organic melecules –by D.h. William & I FlemmingMcGraw Hill*

MC 201 Bioactive Heterocyclic Chemistry (4 credits) (60 L)

a. Structure of heterocyclics; Introduction; Relationship of heterocyclic and carbocyclic aromatic compounds.; Systematic nomenclature. The relation between benzene ring and the heterocyclic rings **(10L)**

b. Heterocycles with three members with one heteroatom. **(5L)**

c. Structure of Five-membered Rings with One Heteroatom; Reactivity of five-membered rings with one heteroatom; Electrophilic attack; Nucleophilic attack; Nucleophilic attack at nitrogen heteroatom; Nucleophilic attack at hydrogen attached to ring carbon or ring nitrogen.; Benzoderivatives of five-membered heterocycles with one heteroatom.**(10L)**

d. Structure of five-membered rings with two or more heteroatoms; Azoles with heteroatoms in the 1,2-positions; Azoles with heteroatoms in the 1,3-positions; Reactivity of five-membered rings with two or more heteroatoms. **(10L)**

e. Structure of six-membered rings with one heteroatom; Reactivity of six-membered rings with one heteroatom (Pyran, thiopyran, Pyridine); Electrophilic attack; Nucleophilic attack; Nucleophilic attack at nitrogen heteroatom; Nucleophilic attack at hydrogen attached to ring carbon or ring nitrogen.; Benzoderivatives of six-membered heterocycles with one heteroatom. **(10L)**

f. Heterocycles with Six-members with two or more heteroatoms. Structure and reactivity of 1,2- and 1,4- and 1,3 diazines ; triazines, tetrazines, oxadiazines and oxathiazines.

(10L)

g. Biologically important heterocycles. **(5L)**

Textbook:

1.John A. Joule, Keith Mills.; Heterocyclic Chemistry, 5th Edition , April 2010, ©2010, Wiley-Blackwell, ISBN: 978-1-4051-3300-5, 718 pages

References:

1. Gilchrist, T. L. Heterocyclic chemistry; 3rd ed.; Addison Wesley Longman: Edinburgh Gate, 1997.

2. Joule, J. A.; Mills, K.; Heterocyclic chemistry; 4th ed.; Blackwell Science: Oxford, 2000.

MC 202 Basic Biochemistry, Biomolecules, Bioinorganic Chemistry (4 Credits) (60 L)

Basic Biochemistry and Biomolecules I: Carbohydrates, Lipids and Vitamins (2 credits) (30 L)

1. **Introduction of Biochemistry:** The molecular logic of life; Structural hierarchy in the molecular organization of Cells. The chemical unity of diverse living organisms, prokaryotic and Eukaryotic. Scope of the subject in pharmaceutical Sciences.
2. **Carbohydrates:** Classification, basic chemical structure, monosaccharides, aldoses, and ketoses, cyclic structure of monosaccharides, stereoisomerisms, anomers and epimers. Reducing properties of monosaccharides, disaccharides, oiligosaccharides, polysaccharides, structural studies methylation and periodate oxidation. Polysaccharides-structure and function of complex carbohydrates, proteoglycans, glycoproteins, glycolipids, mucopolysaccharides.
3. **Lipids:** Classification, structure and function of major lipid subclasses-acylglycerols, circulating lipids: lipoproteins, chylomicrons, LDL, HDL, and VLDL. Pathalogical changes in lipid levels. Formation of micelles, monolayers, bilayter, liposomes.
4. **Vitamins and Co-enzymes:** Classification, water-soluble and fat-soluble vitamins. Structure, dietary requirements, deficiency conditions, coenzyme forms.

Biomolecules II: Amino acids, Proteins and Nucleic Acids (1 credit) **(15 L)**

1. **Amino acids**: Classification, Properties, reactions of amino acids
2. **Proteins:** Peptide bond, properties, functions

(a) Protein structure: Primary structure, Secondary structure; alpha-helix and beta pleated sheets, beta-turns, super secondary structure, and Tertiary structure: forces stabilizing and prediction of tertiary structure, fibrous and globular proteins, and Quaternary structure – hemoglobin.

(b) Working with proteins: Fractionation and purification by gel filtration and chromatographic techniques. Characterization by gel electrophoresis and isoelectric focusing.

(c) Protein sequencing: end group analysis, Sangers method and Edman degradation method

(d) Solid phase peptide synthesis

3. Nucleic acids

(a) Molecules of Heredity: Structure of dexoyribonucleic acid (D NA) and ribonucleic acid (RNA), DNA double helix, major groove and minor groove, A, B, and Z forms of DNA.

(b) DNA as genetic material, genetic code, flow of genetic information, DNA replication, transcription and translation

(c) Drugs acting on DNA: nucleoside analogues, Intercalating agents, Alkylating agents, UV radiations and thymine dimers, Drugs acting by chain 'cutting

***Reference Books**:*

1. *Principle of Biochemistry, Lehinger D.L. Nelson and M.M. Cox. Macmillan worth Publishers.*
2. *Biochemistry, L. Stryer, W.H. Freeman, San Francisco.*
3. *Schaum's Outline Steries of Theory and Problems of Biochemistry, Philip W. Kuchel and G.B.Ralston. Int. Ed., McGraw-Hill Book Co.*
4. *Problem Approaches in Biochemistry. Wood and Hood*

Bioinorganic Chemistry (1 credit) **(15 L)**

1. Principles of coordination Chemistry related to Bioinorganic–Proteins, nucleic acids and other metal binding biomolecules.
2. Choice, uptake and assembly of metal containing units in Biology
3. Control and utilization of metal ion concentration in cells.
4. Metal ion folding and cross –linking of biomolecules.
5. Binding of metal ions and complexes to biomolecular active centers

Text Books:

1. *Ligand field theory & its application: B.N.Figgis & M.A. Hitchman (2000) Wiely VCH publ. Chapters 5, 6, 8, 9, 11.*
2. *Principles of Bioinorganic Chemistry: S.J. Lippard & J.M Berg (1994), University science books, Mill Valley, California Chapters- 1,2,3,5,6,7,8.*
3. *Inorganic Chemistry: Shriver & Atkins (1999) Oxford.*
4. *Inorganic Electronic spectroscopy: A.B.P.Lever ,2nd edn (1984), Elsevier Science Publishers, New York.*
5. *Biological Chemistry of the Elements: R.J.P.Williams & F.R.deSalvia, Oxford University, Press-(1991)*
6. *Bioinorganic Chemistry : Inorganic elements in the Chemistry of life: An introduction & guide : W.Kaim,B.Schwederski, VCH,(1991)*

***Reference Books**:*

1. *Principle of Biochemistry, Lehinger D.L. Nelson and M.M. Cox. Macmillan Worth Publishers.Biochemistry, L. Stryer, W.H. Freeman, San Francisco.*
2. *Schaum's Outline Steries of Theory and Problems of Biochemistry, Philip W. Kuchel and G.B. Ralston. Int. Ed., McGraw-Hill Book Co.*
3. *Problem Approaches in Biochemistry. Wood and Hood*

Practical Courses:

MC – 208 Organic Chemistry practical (4 Credits)

1. **Techniques:** Crystallization, fractional crystallization, fractional distillation, sublimation, steam distillation, column chromatography, thin layer chromatography, GC, HPLC.
2. **Derivatives** of functional groups such as acetyl, 2,4-DNP, anilide, amide and aryloxy acetic acid
3. **Single stage preparations** (minimum 6 preparations) Synthesis of pain relieving drugs

   Asprin, benzocaine, phenacetin, acetoaminophenone, methyl salicylate, ibuprophen
4. **Two stage preparations** (minimum 4 preparations)

   Benzoin → Benzil → Benzilic acid

   ↓ Quinoxaline

   Substituted aniline → acetanilide → Bromination

   Substituted aniline → acetanilide-→ nitration

   Phthalic anhydride → *o*-benzoyl benzoic acid → anthraquinone

   Acetophenone → benzalacetophenone → epoxide

   Hydroquinone →quinone → 1,2,4-triacetoxybenzene
5. **Three stage preparations** (minimum one preparation)

   1. *alpha naphthol* → *o-alkylation with epichlorohydrin* →epoxide opening with amine→N- alkylation

   2. Pthalic acid → pthalic anhydride → phthalimide → anthranilic acid

Reference Books. Vogel's Text book of Practical Organic Chemistry, 5th Edition

MC-209 Biochemistry Practicals and Computer Applications in Medicinal Chemistry and Instrumentation (4 Credits)

Biochemistry Practicals (3 Credits)

1) Estimation of carbohydrates
2) Estimation of proteins
3) Molar extinction coefficient of molecules
4) Extraction and estimation of lipids
5) Direct microscopic counts
6) Total viable counts
7) Control of microbial growth
8) Determination of MIC (plate method)
9) Isolation of Bacterial, animal, plant and plasmid DNA
10) Agarose gel electrophoresis of DNA

Reference Book:

i. Biochemical Methods by Dr. S. Sadasivam and Dr. A. Manikam, 3rd Edition New Age International, 2006.

ii. Practical Biochemistry, Principles and Techniques (1995). Ed. Kelth Wilson and John Walker.

iii. Introductory Practical Biochemistry (2001). Ed. S.K. Sawhny and Randhir Singh

Computer Applications in Medicinal Chemistry and Instrumentation (1 Credits)

1. Molecular docking and dynamics: Rigid docking, flexible docking, manual docking;
2. Pharmacophore: Concept, pharmacophore mapping, methods of conformational search used in pharmacophore mapping

Instrumentation:

1. *HPTLC analysis of medicinal plants.*
2. *HPLC analysis of lipids and sugars*
3. *GC-MS of fatty acid esters*
4. *IR & NMR of simple organic compound synthesized in the lab.*
5. *Fluorescence interaction of drug with BSA.*

Elective Courses (any one)

MC 205 Biostatistics and Cheminformatics (4 Credits) (60 L)

Biostatistics (2 Credit) (30L)

1. Statistics: Introduction, its role and uses. Collection; Organization; Graphics and pictorial representation of data; Measures of central tendencies and dispersion. Coefficient of variation.
2. Probability: Basic concepts; Common probability distributions and probability distributions related to normal distribution.
3. Sampling: Simple random and other sampling procedures. Distribution of sample mean and proportion.
4. Student- t and Chi square tests. Sample size and power.
5. Experimental design and analysis of variance: Completely randomized, randomized blocks. Latin square and factorial designs. Post- hoc procedures.
6. Correlation and regression: Graphical presentation of two continuous variables; Pearson's product moment correlation coefficient, its statistical significance. Multiple and partial correlations. Linear regression; Regression line, coefficient of determination, interval estimation and hypothesis testing for population slope.
7. Statistical techniques in Pharmaceutics: Experimental design in clinical trials; Parallel and crossover designs. Statistical test for bioequivalence. Dose response studies; Statistical quality control.

Cheminformatics (2 Credits) (30L)

Informatics methods in drug design: Bioinformatics, cheminformatics, genomics, proteomics, Chemo genomics, pharmainformatics; ADME databases, chemical biochemical and pharmaceutical

Databases; Drug design techniques using these databases, advantages and disadvantages; Theoretical aqueous solvation calculations for the design of ligands.

Conformational interconversion, transition-state determination and their role in designing rigid analogs: Predicting the mechanism of organic reactions using electronic structure.
Methods: Complete and constrained conformational search methods their advantages and disadvantages.
Theoretical aqueous solvation calculations for the design of ligands. Conformational De novo drug design techniques.
Practical sessions and seminars

MC 206 Drugs, targets and Diseases (4 Credits) (60 L)

1. Molecular Recognition in Drug-Receptor Binding a. Molecular forces b. Binding energetics
2. Enzyme Inhibitors a. Modes of inhibition
3. b. General approaches. Antibacterial Drugs i. Major drug classes ii. Drug resistance
4. Anticancer Drugs i. Major cancer drug targets ii.MOA of anticancer drugs iii.Drug resistance
5. Analgesic Drugs
6. Neurotransmitters (adrenergic, cholinergic effects; psychopharmacology)
7. CNS depressants (sedative/hypnotic, major/minor tranquilizers)h. CNS stimulants
8. Drug Metabolism a. Phase I metabolism b. Phase II metabolism
9. Prodrug Design a. Bioprecursor prodrugs b. Carrier-linked prodrugs
10. Case Studies

Reference Books

1. *An Introduction to Medicinal Chemisty by Graham L Patrick, 4th Edition, 2009, ISBN 978-0-19-923447. Oxford University Press*
2. *Fundamentals of Medicinal Chemistry by Gareth Thomas, 1st Edition, December 2003. ISBN 0-470-84307-1. John Wiley & Sons Inc.*
3. *Molecules and Medicines E.J.Corey, Laszlo Kurti, Barbara Czako 1st Edition, 2007 ISBN 3-13558-406-6.*

Semester III

MC 300: Spectroscopic Methods in Structure Determination of organic and medicinal Compounds (4 credits, 60 L)

1H NMR (16)

Recapitulation of basic principle, Fourier Transform technique, Pulse sequence, relaxation processes. Use of Integration in the quantative determination of isomers, Factors affecting chemical shifts (inductive, resonance and anisotropic effect with examples), chemical shift of different types of protons (alkane, alkene, alkyne and allene), aromatic protons and effect of substituent, different types of spin coupling, first order analysis of spectra, Ramsay mechanism of spin coupling, roofing effect with example, different spin systems (AB, AM, AX, ABX/AMX spin systems with examples), calculations of line intensities and chemical shifts in AB spin system, factors affecting coupling constants (dihedral angle, Karplus equation-graph, electronegativity, bond order, hybridization, bond angle with examples), non equivalence due to restricted rotations, rate processes. Effect of high field NMR for simplification of spectra, Shift reagents. Spin decoupling and Nuclear Overhauser effect with examples. NMR of Intra & intermolecular hydrogen bond, C….H---N, C—H….O, Ar-H…o=c etc., explaination of NMR with x-ray, determination of stereoisomer using NMR,

13C NMR (10)

Elementary ideas, instrumental difficulties, FT technique advantages and disadvantages. Proton Noise Decoupling technique advantages and disadvantages, off-resonance technique, Chemical shifts of solvents, factors affecting chemical shifts, analogy with 1H NMR, calculations of chemical shift of hydrocarbons, effect of substituents on chemical shifts, different types of carbons (alkene, alkyne and allene), chemical shift of aromatic carbons and effect of substituent. Chemical shifts of carbonyl, nitrile, oxime carbons.

Two dimensional (2D) (08)

NMR techniques, principle and pulse technique, DEPT with 3 different angles, 1H-1H COSY, 1H-13C COSY (HETCOR, HMQC), interpretation of 2D spectra and examples.

Mass spectrometry (16)

Theory, instrumentation various methods of ionization (field ionization, FAB, MALDI, californium plasma), different detectors [magnetic analyzer, ion cyclotron analyzer, quadruple mass filter, time of flight (TOF)]. Importance of HRMS, Rules of fragmentation of different functional groups, factors controlling fragmentation. Fragmentation of different types of compounds like alkanes alkenes, aromatic compounds, carbonyl compounds, nitriles etc.

Problems -based on joint application of UV, IR, 1H and 13C NMR, 2D and Mass (including reaction Sequence). **(10 L)**

Books:

1. Introduction to Spectroscopy – D. L. Pavia, G.M. Lampman, G. S. Kriz, 3rd Ed. (Harcourt college publishers).

2. Spectrometric identification of organic compounds R. M. Silverstein, F. X. Webster,6th Ed. John Wiley

3. Spectroscopic methods in organic chemistry – D. H. Williams and I. Flemming Mc Graw Hill.

4. Absorption spectroscopy of organic molecules – V. M. Parikh

5. Nuclear Magnetic Resonance – Basic Principles- Atta-Ur-Rehman, Springer- Verlag (1986).

6. One and Two dimensional NMR Spectroscopy- - Atta-Ur-Rehman, Elsevier (1989).

7. Organic structure Analysis- Phillip Crews, Rodriguez, Jaspars, Oxford University Press (1998).

8. Organic structural spectroscopy- Joseph B. Lambert, Shurvell, Lightner, Cooks, Prentice-Hall (1998).

9. Organic structures from spectra- Field L. D., Kalman J.R. and Sternhell S. 4th Ed. John Wiley and sons

10. NMR spectroscopy of Organic compounds. Jackmann and Sternhell S

MC 306: Advanced Reaction Mechanism (4 Credits) (60 L)

Pericyclic reactions analysis and their applications in synthesis, Recapitulation of Molecular Orbitals, their symmetry properties **(2)**

Woodward –Hoffmann's Conservation of orbital symmetry property rule. **(6)**

Application of Woodward –Hoffmann's Conservation of orbital symmetry property rule to the ground state and excited state Electrocyclic reactions, Cycloaddition reactions Chelotropic reactions, and Sigmatropic reactions

Fukui's HOMO and LUMO orbitals **(12)**

Application of Fukui's HOMO and LUMO orbitals analysis to the ground state and excited state Electrocyclic reactions, Cycloaddition reactions, Chelotropic reactions and Sigmatropic reactions

Synthesis of Endiandric acid (using pericyclic reactions) **(4)**

Synthesis of Citral (using pericyclic reactions) (BASF symthesis) **(1)**

Photochemistry: **(20)**

Principles of photochemical reactions; orbital symmetry considerations, Excited states and their properties; experimental set up for photochemical reactions; Several useful photochemical reactions-olefin, carbonyl, aromatic phochemical reactions and their applications in organic synthesis (isomerization, Patterno-Buchi reaction, Barton reaction, Norrish type I and II reaction, Photoreduction, Rearrangements: di-π-methane, oxa di-π- and aza di-π-methane rearrangements, Photocycloaddition, Photochemical aromatic substitution reaction, Reactions with singlet oxygen. Applications of photochemical methods in synthesis: Isocumene, Cedrene, Hirsutene**.**

Free radicals in organic synthesis **(15)**

Formation, stability and detection of long and short lived radicals, homolysis and free radical displacements, addition and rearrangement of free radicals, radical cyclizations and their applications in synthesis

Books/References:

1. *Mechanism and structure in Organic Chemistry – E. S. Gould (Holt, Rinehart and Winston)*
2. *Advanced Organic Chemistry, Part A – F. A. Carey and R. J. Sundberg, 5th Ed. Springer (2007).*
3. *Radicals in Organic Synthesis B. Giese, Pergamon press (1986)*
4. *a) Organic photochemistry: A visual approach-Jan Kopecky, VCH publishers (1992).*

b) Excited states in Organic Chemistry- J.A. Barltrop and J.D.Coyle, John Wiley & sons

c) Oganic Photochemistry-O. Kan

5. *Conservation of orbital symmetry – R. B. Woodward and R. Hoffmann; Verlag chemie,weinheim (1970).*
6. *Orbital Symmetry : A problem solving approach- R. E. Lehr and A. P. Marchand; Academic (1972).*
7. *Organic reactions and orbital symmetry, 2nd Ed. T. L. Gilchrist and R. C. Storr; Cambridge University Press.*
8. *Classics in total synthesis- K. C. Nicolaou and E. J. Sorensen; VHC (1996)*
9. *P. A. Wender and J. J. Howbert J. Am. Chem. Soc. 103, 688-690 (1981)*
10. *Henning Hopf et al Eur. J. Org. Chem., 567-581, (2005)*

and references cited therein.

11 Mehta, G.; Reddy, A. V. J. Chem. Soc., Chem. Commun. 1981, 456-457. and references cited therein

Elective Courses (any three)

MC-305: Carbanions and Aromaticity in Chemistry (4 credits) **(60 L)**

(i) **Designing Organic Synthesis-**

Synthons and Chiron's, retrosynthetic analysis and synthesis. **(18)**

Chiron-definition, types, application of Chiron- use of carbohydrates, alpha-amino acid, alphahydroxy acids and terpenes in selected natural product (iii) Umpolung in organic synthesis **(**04**)**

(iv) Protection, deprotection for functional groups hydroxyl, amino, carboxyl and carbonyl, alkene and alkyne (04**)**

Carbanions in organic Chemistry **(20)**

Ionization of carbon hydrogen bond and prototopy, Base and acid catalysed halogenation of ketones, keto-enol equilibria, structure and rate in enolisation, concerted and carbanion mechanism for tautomerism,carbanion character in phenoxide and pyrrolyl anions, geometry of carbanions,

hydrolysis of haloforms, Aldol, alkylation of enolates and stereochemistry thereof, Conjugate additions. directed enaolate alkylation, aldol reaction and its application natural product synthesis, enols, enamines and imine in organic synthesis, Carbenes in organic synthesis

Aromaticity **(14)**

Criteria of Aromaticity- (1)The Energy Criterion (2) Structural Criteria, (3) Electronic Criteria, Relationship among the Energetic, Structural, and Electronic Criteria of Aromaticity, Inscribed polygon method for monocyclic compounds The Annulenes-Cyclobutadiene, Benzene, Cyclooctatetraene, [10]Annulenes, [12], [14], and [16] Annulenes, [18] Annulene and Larger Annulenes,Other Related Structures-Kekulene, Fullerene, Aromaticity in Charged Rings, Heteroaromatic Systems, Fused-Ring Systems, compounds with exocyclicdouble bonds, substituted aromatics Other aromatic compounds-Mesoionic Compounds, The Dianion of Squaric Acid, 1 Mobius aromaticity, Homoaromaticity, Pi-Pi interaction

Neighboring Group Participation **(08)**

Concept of neighboring group participation (anchimeric assistance) with mechanism, neighboring group participation by π & σ bonds, classical and non classical carbocations, Intramolecular displacement by hydrogen, Oxygen,nitrogen, sulphur and halogen. Alkyl, cycloalkyl, Aryl participation, participation in bicyclic system, migartory aptitude, intimate and solvent separted ion-pair, transannular, pinacole and carbocation rearrangements and related rearrangements in neighboring group participation, NGP in elimination and addition.

Books:

1. Mechanism and structure in Organic Chemistry – E. S. Gould (Holt, Rinehart and Winston)
2. . Advanced organic chemistry part-A. F. A. Carey and R. J. Sundberg, 5th Ed. Springer (2007)
3. Advanced organic chemistry by J. March, 6th Ed.
4. Organic Chemistry – J. Clayden, N. Greeves, S. Warren and P. Wothers. Oxford University Press (2001)
5. Modern Heterocyclic chemistry – L. A. Paquette (Benjamin).
6. Heterocyclic chemistry – J. A. Joule and K. Mills 4th edition Blackwell publishing (2007)

MC 301 Stereochemistry of organic/medicinal compounds 4 credits (60 L)

Conformation and reactivity in acyclic compounds **(10)**

Meaning of conformation and physical properties, conformational effects on the stability and Reactivity Stereochemistry of six membered rings **(14)**

Conformation and chemical reactivity in cyclohexanes, conformational effects in six membered rings containing unsaturation. Six membered heterocyclic ring

The shapes of rings other than six membered ring, five membered, rings larger than 6-membered medium rings, conformational effects in medium rings, transannular effects, concept of I strain

Fused rings and bridged rings **(14)**

Bicyclic and polycyclic, Occurrence, availability, stereochemical restrictions and reactions of norbornyl system, Enantiomerism in allenes, alkylidene cycloalkane, spiranes- configurational nomenclature, correlation of axial dissymmetry and center of dissymmetry. **(06)**

ORD and CD and its application in determination of stereoisomers **(10)**

Stereochemistry of natural products, strychnine, podophyllotixin **(10)**

Energy minimization and geometry optimization of conformers conformational analysis of cyclohexane etc using computational methods. **(04)**

Skill development in stereochemistry-Problems/ workshop/ seminars **(06)**

Books:

1. Stereochemistry of carbon compounds - E. L. Eliel

2. Stereochemistry of carbon compounds - E. L. Eliel and S. H. Wilen

3. Organic Chemistry – J. Clayden, N. Greeves, S. Warren and P. Wothers (Oxford Press.)

4. Stereochemistry of organic compounds –Nasipuri

Organic Chemistry, Cram, Hammond, Hendrickson

MC – 307 : Drug Designing and Medicinal Biochemistry (4 Credits) (60 L)

Medicinal Biochemistry (20)

Introduction to development of antimicrobial agents, historical development of antimicrobials, chemotherapy, use of synthetic compounds and antibiotic revolution .Mechanism of action at molecular level of selected antibiotics: inhibitors of cell wall :introduction to bacterial cell wall, peptidoglycan structure synthesis , mechanism of antibiotics inhibiting cell wall synthesis. Plasma membrane antiseptics, mechanism of antiseptics, disinfectants, cationic antibiotics, polypeptide antibiotics ionophoric and polyene antibiotics. Mechanism of inhibition of Nucleic acids synthesis: inhibitors of nucleotide synthesis, inhibitor of polymerization of nucleic acids, inhibitors of polymerases. Mechanism of inhibition of protein synthesis: inhibitors of amnoacetyl tRNA formation, t RNA ribosome interaction inhibitors, and inhibitors of peptide bond formation. 5) Mechanism of action of Antiviral, antifungal, antiprotozoal, analgesic drugs: mechanism of action at molecular level of some antiprotozoal: antimalarial, antiviral antiflu, anti HIV etc, analgesic drugs. 6) Mechanism of resistance to antibiotics and other drugs: mechanism of resistance at biochemical level of some antibiotics: conversion of active drug to inactive, modification of drug sensitive site, loss of cell permeability to drug.

Immunology (10)

Reference books:

1. Biochemistry of antimicrobial action (4 th ed) t J Franklin, chapman hall (1989)

2. Mechanism of micrbial dieases, M Schaechter et. al. Williams and Willkino Int. Ed (1989)

3. Medicinal Chemistry,- Molecular and Biochemical approach – Thomas Mogardy and Donald Weaver (3rd ed) Oxford press.

4. Biochemistry- L, Stryer (3rd ed) Freeman and Co.

5. Text book Biochemistry with clinical corelations Thomas Devlin (2nd ed) John wiley and sons.

6. General microbiology, pelczar, Rard chan (1987).

Drug Design and Development – (30)

1. Structure Activity Relationships in drug design: Qualitative versus quantitative approaches

2. Molecular Modeling: Energy minimization, geometry optimization, conformational analysis, global conformational minima determination; Approaches and problems; Bioactive vs. global minimum conformations; Automated methods of conformational search; Advantages and limitations of available
software; Molecular graphics; Computer methodologies behind molecular modeling including artificial
intelligence methods.

3. QSAR: Electronic effects; Hammett equation, Lipophilicity effects; Hansch equation, Steric Effects; Taft Equation practical examples

4. Molecular docking and dynamics: Rigid docking, flexible docking, manual docking; Advantages and Disadvantages of flex-X, flex-S, auto dock and dock software's with successful examples; Monte Carlo Simulations and molecular dynamics in performing conformational search, docking etc. practical examples

5. Pharmacophore: Concept, pharmacophore mapping, methods of conformational search used in pharmacophore mapping; Comparison between the popular pharmacophore methods like Catalyst/HipHop, DiscoTech, GASP, etc. with practical examples.

MC– 308 Research Project (4- credits)

Students are required to submit written record and present details of the project to be pursued in semester-III. This should include the purpose and basis of the project, stating aims, objectives and probable outcomes, be able to supplement these with necessary information, literature review towards it, and process for the project itself.

Semester IV

MC – 400: Synthetic Strategies in the Total Synthesis of Complex drug Molecules (4 credits)

(60L)

(i) Synthetic Organic Chemistry using Transition metals and Boron (30)

Introduction, basic concepts, TS metal complexes, 16-18 electron rule, oxidation states, ligands, oxidative addition, reduction elimination, association, dissociation, transmetallation, migratory insertion.

Wacker, Trost-Tsuji, Heck, Sonogashira, Stille, Suzuki, carbonylative Suzuki and stile, Negishi, Kumada, **Hiyama**, Buchwald-Hartwig, Buchwald-Goldberg, **carbonylative amination**.

Ni-catalyzed homo coupling and carbonylation, Ni-allyl complexes. Alkene-alkene metathesis, En-yne metathesis, **alkyne-alkyne metathesis**. Hydrogenation: Wilkinson's, Knowles, Noyori etc.

Hydroformylation, Hydrocarboxylation, Pausan-Khand, Nicholas, Mn & Co catalyzed carbonylation.

Fe-cat. Carbonylation, protection of diene, Cr. Metal-arene complexes.

Jacobsen, Sharples epoxidation, Sharples **dihydroxylation**.

Organo-Bornes: Preparation and there reactivity, Applications in synthesis of alcohol, amine, halognation, protonolysis and C-C bond formation. Reactions with alkyne, synthesis of E and Z alkene, Z,Z diene, E,E diene, preparation of allyl borane and their application.

(ii) Retro-synthesis and synthesis of Natural products and drug molecules (on the basis of disconnection and direct associative approaches. Juvobione (minimum 4 approaches) Strychnine (Overmann , Woodward), prostoglandins F2 (Corey and Stokes), Penicillins, Estrone, Mifepristone (Vollard), Taxol

(iii) Structure determination of Natural products. Structure elucidation of natural products by spectroscopy and degradative methods: Examples of natural products from following classes of secondary metabolites Alkaloids, Flavonoids. Sterols; Coumarins Triterpenes; Xanthones - each 2-3 examples **(15L)**

(iv) Stereo-selective reaction Carbocuperation, carboalumination, Tebbe, Petasis Olefinations, Takai Reaction, Alkyne bond forming reactions, cyclopropanation reaction. Application in the synthesis of drug and natural products **(15L)**

Books/References:

1. Modern synthetic reactions – H. O. House (Benjamin)

2. Organic chemistry – J. Clayden, N. Greeves, S. Warren and P. Wothers (Oxford Press)
3. Designing of organic synthesis – S. Warren (Wiley)
4. Some modern methods of organic synthesis – W. Carruthers (Cambridge)
5. Organic synthesis – M. B. Smith
6. Organometallics in organic synthesis – J. M. Swan and D. C. Black (Chapman and Hall)
7. Advanced organic chemistry, Part B – F. A Carey and R. J. Sundberg 5th edition (2007)
8. Palladium in Organic Synthesis Richard Heck
9. Organonickel compounds, Jolly
10. Comprehensive organometallic chemistry-Vol. 1-8
11. Chiron approach in organic synthesis – S. Hanessian (Relavent chapters For Chirons)
12. Aromaticity , P. Garratt
13. Carbocyclic non-benzenoid aromatic compounds, D. Lloyd

MC 401 Fundamentals of Chiral Drug Synthesis 4 credits (60 L)

Assymetric synthesis (20 L)

Recapitulation of Stereochemical concepts- enantiomers, diastereomers, homotopic andheterotopic ligands, stereoselective and stereospecific reactions, prochirality, Chemo-, regio-, diastereo- and enantio-controlled approaches; Chirality transfer, Asymmetric inductions; Chiralpools, Chiral auxiliaries, chiral reagents and catalysts, and templates; Self-regeneration of stereo-center **Asymmetric reduction reactions**: Reduction of Ketones and Imines: Hydrogenation of Ketones, Hydrogenation and Transfer Hydrogenation of Imines and , Transfer Hydrogenation of Ketones, Reduction of Ketones Using Enantioselective Borohydride Reagents, Diseteroselective reduction of olefins, Reduction by BINAL-H, Diastereoselective Syn-Reduction of β-Hydroxy -Ketones, Diastereoselective Anti-Reduction of β-Hydroxy Ketones,

Asymmetric C-C bond forming reaction: Simmon-Smith reaction, aldol reaction, Mukayama aldol reaction, Shibasaki bi-metallic catalyst system; RAMPSAMP based alkylation strategy, Meyers oxazoline and bis-lactam based methods; Michael reaction, Henry reaction (Nitro aldol), Baylis- Hillman-Morita reactions, Asymmetric allylation, Asymmetric cycloaddition reactions, Asymmetric hydroformylation.

Use of chiral auxiliaries in asymmetric hydrogenation, asymmetric epoxidation and asymmetric dihydroxylation(other than sharpless). Epoxidation of Cyclic Enones and Acyclic Enones, Epoxidation with Metal(salen) Complexes, Epoxidation Using Metal–Porphyrin-Based Catalysts, Epoxidation of Electron-Deficient Alkenes, Epoxidation with Iminium, Epoxidation of Aldehydes

synthesis of chiral natural products - Erythronolide , 6-Deoxyerythronolide, Rifamycin S , (Kishi's Synthesis in 1980 , Kishi's Synthesis in 1981), Masamune's Synthesis, Synthesis of the o- Side Chain of the taxol, The Enantioselective Synthesis of (R)-4-Hydroxy-2-Cyclopentenone

Advanced Carbohydrate Chemistry (12 L)

Introduction of sugars, structures of triose, tetrose, pentose, hexose. Fisher projection, D- and L- configuration, Conversion of Fisher projection to furanose and pyranose form, Haworth

Structure, 4C1 and 1C4 Conformations, anomeric effect, Reactions of five and six carbon sugars, glycoside formation, acetonide formation, reduction, synthesis of D-glyceraldehyde, Killani- Fischer Synthesis, glucal formation and reactions, Ferrier and Hanesian Reaction, Ferrier rearrangement. Utilisation of the basic concepts of carbohydrate chemistry in the synthesis of (S) Propanediol, (R) and (S) – Epichlorohydrin, L (+)-Alanine, 11-Oxaprostaglandin F2 (-) Multistratin, (-) Pentenomycin, (-) Shikimic acid, Carbonolide B.

Organocatalyst: Synthesis and applications (08 L)

Imine and enamine cat reaction, thiourea and urea cat reaction, counter ion catalyzed reaction, hydrogen bonding and somo activation, cascade reaction, organo catalyzed and metal catalyzed reactions, heterocyclic carbenes and metal catalyzed reactions. Synthesis of drug and natural products using organo catalyzed reaction.

Chemistry of amino acids, peptides, nucleotides, nucleosides (16 L)

Chiral Synthesis of alpha and Beta amino-acid , Difficulties involved in synthesis of peptides, Importance of peptides in drug discovery, Protection and Deprotection of amino acids General aspects, need for protection, minimal versus global protection, protection of amino group by acid and base labile groups, protection of carboxyl group, concept of orthogonal protection in peptide synthesis, importance of side-chain functional group protection and details of protective groups used for masking individual amino acids, methods used for deprotection. Coupling reactions in peptide synthesis Side reactions in peptide synthesis: Deletion peptides, side reactions initiated by proton abstraction, protonation, over-activation and side reactions of individual amino acids

Principle of solid phase peptide synthesis, t-BOC and FMOC protocols, various solid supports and linkers: Activation procedures, peptide bond formation, deprotection and cleavage from resin, low and high HF cleavage protocols, formation of free peptides and peptide amides, purification and case studies, site-specific chemical modifications of peptides Chemistry of nucleosides and nucleotides

Synthesis of Antibiotics-penicillins, cephalosporins, macrolides, aminosides, cyclins, oflaxacin (Nicolaeue) **(04)**

Books:

1. Asymmetric Reactions and Processes in Chemistry: Ernest L. Eliel

2. Catalytic Asymmetric Synthesis: 2nd Ed., Iwao Ojima

3. Asymmetric Organocatalysis: From Biomimetic Concept to Applications in Asymmetric Synthesis: David MacMillan

4. Organic Chemistry – J. Clayden, N. Greeves, S. Warren and P. Wothers (Oxford Press.)

5. Asymetric synthesis Vol.1-5 by J. D. Morrison

6. Chirotechnology:Industrial synthesis of optcally active compounds, R. A. Sheldon

7. Organic Chemistry - R. P. Morrison and R. N. Boyd

8. Organic Chemistry – I. L. Finar, volume II

9. Chiron approach in organic synthesis – S. Hanessian

10. An introduction to medicinal chemistry-Grham L. Patric oxoford press

11. The organic chemistry of drug design and drug action- R.B. Silverman

12. *Exploring OSAR fundamentals and applications in chemistry and biology-Corwin Hansch and Albert Leo* Practicals

MC-408- Drug Intermediates synthesis (4 Credits)

i) Two stage Preparations based on stereo selective reaction (minimum six)

ii) Three stage preparations based on name reactions with chemoselective, and stereoselective reaction

MC- 409: Medicinal chemistry. (4 credits)

1. Screening of synthesized compounds for
   a. Antioxidant activity
      (i) DPPH assay
      (ii) NBT assay
      (iii) Pulse Radiolysis
   b. Antibacterial activity
      (i) Zone of Inhibition
      (ii) Minimal Inhibitory concentration (MIC)
      (iii) Colony count
   c. Anticancer activity
      (i) Cytotoxicity by MTT assay
      (ii) Cell count using Haemocytometer

Elective Courses (Any One)

MC 405: Structure Determination and Chromatographic techniques (4 Credits) (60 L)

Structure determination (30 L)

A. Molecular Formula Determination (EA and MS)
   1. Elemental Analysis (EA)
   2. Mass Spectrometry (MS - EI)
   3. Index of Hydrogen Deficiency (IHD)

B. Functional Groups (IR and NMR)
   1. Infrared Spectroscopy (IR)
   2. Nuclear Magnetic Resonance Spectroscopy (^{13}C NMR)
   3. Chemical Equivalence, Symmetry

C. Connectivity – Carbon-Hydrogen Framework (^{1}H NMR and MS)
   1. ^{1}H NMR
      a. Chemical Equivalence and Non-equivalence
      b. Topicity
      c. Spin-spin Splitting (*J* Coupling)
      d. The Chemical Shift
   2. MS Fragmentation patterns

Advanced NMR Methods: ^{31}P, ^{11}B, and other Nuclei, Through-bond Coupling, DEPT/APT/INEPT,^{1}H–^{1}H Decoupling (1D) and COSY (2D), HMQC, HMBC, HSQC, INADEQUATE, Through-space Coupling, NOE (1D) and NOESY (2D), ROESY

MS Methods: EI, CI, FAB, Negative Ion Modes, MALDI, (APCI, Electrospray) $(MS)^{n}$

Textbooks:

1. *Crews, Phillip, Jaime Rodríguez, and Marcel Jaspars. Organic Structure Analysis. New York: Oxford University Press, 1998. ISBN: 0195101022.*
2. *Pretsch, E., P. Bühlmann, and C. Affolter. Structure Determination of Organic Compounds: Tables of Spectral Data. Berlin; New York: Springer, 2000. ISBN: 3540678158.*

Chromatographic techniques (30 L)

1. Gas Chromatography:

Gas chromatography theory and Instrumentation, Column types, Solid/Liquid Stationary phases, Column switching techniques, Basic and specialized detectors, elemental detection, chiral separations, Pyrolysis gas chromatography, High temperature techniques, Applications (Clinical, petrochemical etc.) and problems.

2. High Performance Liquid Chromatography:

HPLC theory and instrumentation, Adsorption chromatography, Liquid-Liquid partition chromatography, Microbore and capillary chromatography, Affinity techniques, Size exclusion, Ion pair separations, Chiral and Isotope separations, Applications and problems.

3. Ion-Chromatography
4. Electrophoresis:

Separation by Adsorption-Affinity techniques, Affinity elution from Ion exchangers and other Adsorbents, Pseudo affinity adsorbents, Polyacrylamide gel electrophoresis, Isoelectric focusing, Isotachophoresis, Two-dimensional gel electrophoresis, Crossing immuno- and affinity techniques, Capillary electrophoresis in rotation-stabilized media, Electrophoresis in stabilized salts, blotting techniques, Applications in Nuclei acids, clinical and capillary zone electrophoresis of carbohydrates.

5. Hyphenated Techniques:

Mass spectrometry principle, Instrumentation, Ionization methods-

EI, CI, FAB, arc & spark, photoionization, thermal ionization, FI & FD, Laser induced, Photoelectric ionization, SIMS, Mass analyzers-Magnetic, Double foucusing, Time of flight, Quadrupolar, Ion cyclotron resonance analyzer. Coupled techniques, GC-FTIR, GC-MS (Use of stable isotopes), HPLC-MS, Tandem mass spectroscopy, MS-MS, Principle, Instrumentation & analysis of micronutrients.

Books:

1. *Practical Aspects of Gas Chromatography/Mass Spectrometry. G.M.Message, John Wiley & Sons, New York, (1984).*
2. *HPLC: Analytical Chemistry by Open Learning John Wiley & Sons, New York, (1991).*
3. *Protein Purification: Principles & Practice. Springer International, 3rd Edition, New Delhi, Students Edn. (1994).*
4. *Organic Spectroscopy: Principles & Applications, Jag Mohan, Narosa Publishing House, Chapters 5 &7.*
5. *Instrumental Methods of Chemical analysis, H. H. Willard, L. L. Merrit, Jr. J. A. Dean & F. A. Settle Jr., 6th Edition, (1986)*

MC-406: Origin of secondary metabolic drugs in plants and pharmacokinetics (4 credits) (60L)

Biogenesis (24)

of terpenes: sesquiterpenes, triterpenes and chloesterol, alkaloids : polyketide Biogenesis of terpenes – mono terpenes, Sesquiterpenes**,** Triterpenes, Steroids, Biogenesis of Alkaloidsornithine based(pyrrolizidine), Lysine based(quinolizidine and indolizidine),Pyridine based**,** Tyrosine and modified tetrahydroisoquinoline based alkaloids, Phenethylisoquinoline and terpinoid tetrahydroisoquinoline (Amaryllidaceae alkaloids, anthranilic acid base simple Indole and terpinoid indole.

Biogenesis of polyketides – saturate and unsaturated fatty acids Arachidonic acid cascades – prostaglandins, Aromatics derived from polyketides.Synthesis of Prostaglandins, Thromboxane, Leukotriene in nature and lab

Mechanism of biological processes (6)

Selectivity of enzyme mediated reactions and its comparison with synthetic reactions

Mechanisms involving vit. B1, B2, B6, Biotin, NAD/NADP – NADH/NADPH, Folic acid, Riboflavin

Pharmocokinetics, pharmacodynamics (30)

Principal of pharmacokinetics . Concepts of drug disposition: Absorption : Distribution: Metabolism: Excretion (ADME). Application of pharmacokinetis principals to the calculations of drugs doses. Chemical aspect of drug metabolism. Drug toxicology concepts: carcinogenesis: mutagenesis: teratogenesis: and organ/ systemic toxicity. Analysis of drug n biological fluids and clinical pharmacokinetics applications.

Concepts and clinical roals of pharmacogenetics. Pharmacodynamics, concept and application of therapeutic drug monitoring (TDM). Pharmacokinetics consideration for adverse effect and drug interaction. Clinical pharmacokinetics of selected drugs. Including amino- glycosides, digoxin and anticonvulsants.

References:

1. *Screening methodology in pharmacology –II by Turner and Hebborn*
2. *Evolution of drug activity by Laurence and Bacharach- Vol I and II.*
3. *In vitro toxicity testing by john M. Fraizer.*
4. *Combination drugs : Their use and regulation- Louis lasanga*
5. *Drug receptor and their Effctors ed. By Nigel J. M. Birdsall.*
6. *Receptor binding in drug research by robert A.O. Brien.*
7. *General and applied toxicology by Bryan Ballantyne T. Marrs and P. Turner*
8. *Safety evolution of drugs and chemicals by W. Eugene Lloyd.*

Books

1. Peptides: Sythesis, structure and applications, Bernd Gutte
2. Organic Chemistry, H. Dugas
3. Biochemistry by Zubay Chapter 11.
4. Organic Chemistry Chapter 50– J. Clayden, N. Greeves, S. Warren and P. Wothers (Oxford Press.)
5. Secondary metabolism by J.Mann
6. Medicinal Natural products by P.M. Dewick

Courses which can be opted by students from outside departments:

Core courses Semester-I

MC- 100 Coordination and Medicinal Chemistry (4 credits) (60L)

Coordination Chemistry (2 Credits) (30L)

1 Concept & Scope of ligand Fields.

2 Energy levels of transition metal ions, Free ion terms, term wave functions, spin –orbit coupling

3 Effect of ligand fields on energy levels of transition ions, weak cubic ligand field effect on Russell-Saunders terms, strong field effect, correlation diagrams,Tanabe-Sugano diagrams, Spin-pairing energies.

4 Electronic spectra of complexes band intensities, band energies, band width & shapes, spectra of 1^{st},2^{nd}& 3^{rd} row ion and rare earth ion complexes, spectrochemical & Nephelauxetic series, charge transfer & luminescence spectra, calculations of Dq,B, Racah parameters.

5 Magnetic properties of complexes paramagnetism,1^{st} & 2^{nd} ordered Zeeman effect, quenching of orbital angular momentum by Ligand fields, Magnetic properties of A,E,T ground terms in complexes ,spin free–spin paired equilibria

6 Definitions and theorems of group theory, subgroups, classes.

7 Molecular symmetry and symmetry groups - symmetry elements and operations,. Symmetry planes, reflections, inversion center, proper / improper axes and rotations, products of symmetry operations, equivalent symmetry elements and atoms, symmetry elements and optical isomerism, symmetry point groups, classes of symmetry operations, classification of molecular point groups.

8 Representations of groups. Great orthogonality theorem, character tables, properties of characters of representations.

9 Group theory and quantum mechanics. Wave function as bases for irreducible representation

10 Symmetry Adapted Linear Combinations -(SALC) - projection operators and their use to construct SALC.

11 Molecular Orbital Theory -

a) Principle, Symmetry factoring of secular equation, Carbocyclic systems, LCAO-MO π bonding, Worked example-Naphthalene, Three center bonding, symmetry based "selection rules" for cyclization.

b) Transformation properties of atomic orbital, MO's for Sigma bonding AB_n molecules, tetrahedral AB_4case, Hybrid orbital, MO's for pi bonding in AB molecules, cage and cluster compounds, MO's for metal sandwiched compounds

12 Mechanism of metal complexes.

Ligand substitution reactions, substitution of square - planar complexes, substitution in octahedral complexes, redox reactions and photochemical reactions

Medicinal Chemistry, (2 Credits) (30L)

History and classification, drug targets- lipids, carbohydrates, proteins, and nucleic acids; **(06L)**

Selected examples of drugs and their mechanism of action, identification of diseases and corresponding targets **(12L)**

Lead and analogue synthesis and actions: Antibacterial- sulphonamides and derivatives, quinolones and fluoroquinolones- nalidixic acid, ciprofloxacin, enoxacin, grepafloxacin, metronidazole, nitrofurazone, pyrazinamide, Anticancer- ethambutol, lomustine, carmustine, procarbazine, 5-fluorouracil, 6-mercaptopurine,tamoxifen **(12L)**

Text Books:-

2. An Introduction to Medicinal chemistry: Graham, Patric third edition

Semester-II

MC 202 Basic Biochemistry, Biomolecules, Bioinorganic Chemistry (4 Credits) (60 L)

Basic Biochemistry and Biomolecules I: Carbohydrates, Lipids and Vitamins (2 credits) **(30 L)**

5. **Introduction of Biochemistry:** The molecular logic of life; Structural hierarchy in the molecular organization of Cells. The chemical unity of diverse living organisms, prokaryotic and Eukaryotic. Scope of the subject in pharmaceutical Sciences.
6. **Carbohydrates:** Classification, basic chemical structure, monosaccharides, aldoses, and ketoses, cyclic structure of monosaccharides, stereoisomerisms, anomers and epimers. Reducing properties of monosaccharides, disaccharides, oiligosaccharides, polysaccharides, structural studies methylation and periodate oxidation. Polysaccharides-structure and function of complex carbohydrates, proteoglycans, glycoproteins, glycolipids, mucopolysaccharides.
7. **Lipids:** Classification, structure and function of major lipid subclasses-acylglycerols, circulating lipids: lipoproteins, chylomicrons, LDL, HDL, and VLDL. Pathalogical changes in lipid levels. Formation of micelles, monolayers, bilayter, liposomes.
8. **Vitamins and Co-enzymes:** Classification, water-soluble and fat-soluble vitamins. Structure, dietary requirements, deficiency conditions, coenzyme forms.

Biomolecules II: Amino acids, Proteins and Nucleic Acids (1 credit) **(15 L)**

1. **Amino acids**: Classification, Properties, reactions of amino acids
2. **Proteins:** Peptide bond, properties, functions

(a) Protein structure: Primary structure, Secondary structure; alpha-helix and beta pleated sheets, beta-turns, super secondary structure, and Tertiary structure: forces stabilizing and prediction of tertiary structure, fibrous and globular proteins, and Quaternary structure – hemoglobin.

(b) Working with proteins: Fractionation and purification by gel filtration and chromatographic techniques. Characterization by gel electrophoresis and isoelectric focusing.

(c) Protein sequencing: end group analysis, Sangers method and Edman degradation method

(d) Solid phase peptide synthesis

(e)

3. Nucleic acids

(a) Molecules of Heredity: Structure of dexoyribonucleic acid (D NA) and ribonucleic acid (RNA), DNA double helix, major groove and minor groove, A, B, and Z forms of DNA.

(b) DNA as genetic material, genetic code, flow of genetic information, DNA replication, transcription and translation

(c) Drugs acting on DNA: nucleoside analogues, Intercalating agents, Alkylating agents, UV radiations and thymine dimers, Drugs acting by chain 'cutting

***Reference Books**:*

5. *Principle of Biochemistry, Lehinger D.L. Nelson and M.M. Cox. Macmillan worth Publishers.*
6. *Biochemistry, L. Stryer, W.H. Freeman, San Francisco.*
7. *Schaum's Outline Steries of Theory and Problems of Biochemistry, Philip W. Kuchel and G.B.Ralston. Int. Ed., McGraw-Hill Book Co.*
8. *Problem Approaches in Biochemistry. Wood and Hood*

Bioinorganic Chemistry (1 credit) (15L)

Principles of coordination Chemistry related to Bioinorganic–Proteins, nucleic acids and other metal binding biomolecules.

1. Choice, uptake and assembly of metal containing units in Biology
2. Control and utilization of metal ion concentration in cells.
3. Metal ion folding and cross –linking of biomolecules.
4. Binding of metal ions and complexes to biomolecular active centers

Text Books:

7. *Ligand field theory & its application: B.N.Figgis & M.A. Hitchman (2000) Wiely VCH publ. Chapters 5, 6, 8, 9, 11.*
8. *Principles of Bioinorganic Chemistry: S.J. Lippard & J.M Berg (1994), University science books, Mill Valley, California Chapters- 1,2,3,5,6,7,8.*
9. *Inorganic Chemistry: Shriver & Atkins (1999) Oxford.*
10. *Inorganic Electronic spectroscopy: A.B.P.Lever ,2nd edn (1984), Elsevier Science Publishers, New York.*
11. *Biological Chemistry of the Elements: R.J.P.Williams & F.R.deSalvia, Oxford University, Press-(1991)*
12. *Bioinorganic Chemistry : Inorganic elements in the Chemistry of life: An introduction & guide : W.Kaim,B.Schwederski, VCH,(1991)*

***Reference Books**:*

5. *Principle of Biochemistry, Lehinger D.L. Nelson and M.M. Cox. Macmillan Worth Publishers.*
6. *Biochemistry, L. Stryer, W.H. Freeman, San Francisco.*
7. *Schaum's Outline Steries of Theory and Problems of Biochemistry, Philip W. Kuchel and G.B. Ralston. Int. Ed., McGraw-Hill Book Co.*
8. *Problem Approaches in Biochemistry. Wood and Hood*

Semester III

MC – 307 : Drug Designing and Medicinal Biochemistry (4 Credits) (60 L)

Medicinal Biochemistry (20)

Introduction to development of antimicrobial agents, historical development of antimicrobials, chemotherapy, use of synthetic compounds and antibiotic revolution .Mechanism of action at molecular level of selected antibiotics: inhibitors of cell wall :introduction to bacterial cell wall, peptidoglycan structure synthesis , mechanism of antibiotics inhibiting cell wall synthesis. Plasma membrane antiseptics, mechanism of antiseptics, disinfectants, cationic antibiotics, polypeptide antibiotics ionophoric and polyene antibiotics. Mechanism of inhibition of Nucleic acids synthesis: inhibitors of nucleotide synthesis, inhibitor of polymerization of nucleic acids, inhibitors of polymerases. Mechanism of inhibition of protein synthesis: inhibitors of amnoacetyl tRNA formation, t RNA ribosome interaction inhibitors, and inhibitors of peptide bond formation. 5) Mechanism of action of Antiviral, antifungal, antiprotozoal, analgesic drugs: mechanism of action at molecular level of some antiprotozoal: antimalarial, antiviral antiflu, anti HIV etc, analgesic drugs. 6) Mechanism of resistance to antibiotics and other drugs: mechanism of resistance at biochemical level of some antibiotics: conversion of active drug to inactive, modification of drug sensitive site, loss of cell permeability to drug.

Immunology (10)

Reference books:

1. Biochemistry of antimicrobial action (4 th ed) t J Franklin, chapman hall (1989)

2. Mechanism of micrbial dieases, M Schaechter et. al. Williams and Willkino Int. Ed (1989)

3. Medicinal Chemistry,- Molecular and Biochemical approach – Thomas Mogardy and Donald Weaver (3rd ed) Oxford press.

4. Biochemistry- L, Stryer (3rd ed) Freeman and Co.

5. Text book Biochemistry with clinical corelations Thomas Devlin (2nd ed) John wiley and sons.

6. General microbiology, pelczar, Rard chan (1987).

Drug Design and Development – (30)

1. Structure Activity Relationships in drug design: Qualitative versus quantitative approaches

2. Molecular Modeling: Energy minimization, geometry optimization, conformational analysis, global conformational minima determination; Approaches and problems; Bioactive vs. global minimum conformations; Automated methods of conformational search; Advantages and limitations of available software; Molecular graphics; Computer methodologies behind molecular modeling including artificial intelligence methods.

3. QSAR: Electronic effects; Hammett equation, Lipophilicity effects; Hansch equation, Steric Effects; Taft Equation practical examples

4. Molecular docking and dynamics: Rigid docking, flexible docking, manual docking; Advantages and Disadvantages of flex-X, flex-S, auto dock and dock software's with successful examples; Monte Carlo Simulations and molecular dynamics in performing conformational search, docking etc. practical examples

5. Pharmacophore: Concept, pharmacophore mapping, methods of conformational search used in pharmacophore mapping; Comparison between the popular pharmacophore methods like Catalyst/HipHop, DiscoTech, GASP, etc. with practical examples.

Elective Courses

MC-305: Carbanions and Aromaticity in Chemistry (4 credits) (60 L)

(i) **Designing Organic Synthesis**-

Synthons and Chiron's, retrosynthetic analysis and synthesis. **(18)**

Chiron-definition, types, application of Chiron- use of carbohydrates, alpha-amino acid, alphahydroxy acids and terpenes in selected natural product (iii) Umpolung in organic synthesis **(**04**)**

(iv) Protection, deprotection for functional groups hydroxyl, amino, carboxyl and carbonyl, alkene and alkyne **(04)**

Carbanions in organic Chemistry (20)

Ionization of carbon hydrogen bond and prototopy, Base and acid catalysed halogenation of ketones, keto-enol equilibria, structure and rate in enolisation, concerted and carbanion mechanism for tautomerism,carbanion character in phenoxide and pyrrolyl anions, geometry of carbanions, hydrolysis of haloforms, Aldol, alkylation of enolates and stereochemistry thereof, Conjugate additions. directed enaolate alkylation, aldol reaction and its application natural product synthesis, enols, enamines and imine in organic synthesis, Carbenes in organic synthesis

Aromaticity (14)

Criteria of Aromaticity- (1)The Energy Criterion (2) Structural Criteria, (3) Electronic Criteria, Relationship among the Energetic, Structural, and Electronic Criteria of Aromaticity, Inscribed polygon method for monocyclic compounds The Annulenes-Cyclobutadiene, Benzene, Cyclooctatetraene, [10]Annulenes, [12], [14], and [16] Annulenes, [18] Annulene and Larger Annulenes,Other Related Structures-Kekulene, Fullerene, Aromaticity in Charged Rings, Heteroaromatic Systems, Fused-Ring Systems, compounds with exocyclicdouble bonds, substituted aromatics Other aromatic compounds-Mesoionic Compounds, The Dianion of Squaric Acid, 1 Mobius aromaticity, Homoaromaticity, Pi-Pi interaction

Neighboring Group Participation (08)

Concept of neighboring group participation (anchimeric assistance) with mechanism, neighboring group participation by π & σ bonds, classical and non classical carbocations, Intramolecular displacement by hydrogen, Oxygen,nitrogen, sulphur and halogen. Alkyl, cycloalkyl, Aryl participation, participation in bicyclic system, migartory aptitude, intimate and solvent separted ion-pair, transannular, pinacole and carbocation rearrangements and related rearrangements in neighboring group participation, NGP in elimination and addition.

Books:

1. Mechanism and structure in Organic Chemistry – E. S. Gould (Holt, Rinehart and Winston)

2. . Advanced organic chemistry part-A. F. A. Carey and R. J. Sundberg, 5th Ed. Springer (2007)

3. Advanced organic chemistry by J. March, 6th Ed.

4. Organic Chemistry – J. Clayden, N. Greeves, S. Warren and P. Wothers. Oxford University Press (2001)

5. Modern Heterocyclic chemistry – L. A. Paquette (Benjamin).

6. Heterocyclic chemistry – J. A. Joule and K. Mills 4th edition Blackwell publishing (2007)

Semester IV

MC – 400: Synthetic Strategies in the Total Synthesis of Complex drug Molecules (4 credits)

(60L)

(i) Synthetic Organic Chemistry using Transition metals and Boron (30)

Introduction, basic concepts, TS metal complexes, 16-18 electron rule, oxidation states, ligands, oxidative addition, reduction elimination, association, dissociation, transmetallation, migratory insertion.

Wacker, Trost-Tsuji, Heck, Sonogashira, Stille, Suzuki, carbonylative Suzuki and stile, Negishi, Kumada, **Hiyama**, Buchwald-Hartwig, Buchwald-Goldberg, **carbonylative amination**.

Ni-catalyzed homo coupling and carbonylation, Ni-allyl complexes. Alkene-alkene metathesis, En-yne metathesis, **alkyne-alkyne metathesis**. Hydrogenation: Wilkinson's, Knowles, Noyori etc. Hydroformylation, Hydrocarboxylation, Pausan-Khand, Nicholas, Mn & Co catalyzed carbonylation.

Fe-cat. Carbonylation, protection of diene, Cr. Metal-arene complexes.

Jacobsen, Sharples epoxidation, Sharples **dihydroxylation**.

Organo-Bornes: Preparation and there reactivity, Applications in synthesis of alcohol, amine, halognation, protonolysis and C-C bond formation. Reactions with alkyne, synthesis of E and Z alkene, Z,Z diene, E,E diene, preparation of allyl borane and their application.

(ii) Retro-synthesis and synthesis of Natural products and drug molecules (on the basis of disconnection and direct associative approaches. Juvobione (minimum 4 approaches) Strychnine (Overmann , Woodward), prostoglandins F2 (Corey and Stokes), Penicillins, Estrone, Mifepristone (Vollard), Taxol

(iii) Structure determination of Natural products. Structure elucidation of natural products by spectroscopy and degradative methods: Examples of natural products from following classes of secondary metabolites Alkaloids, Flavonoids. Sterols; Coumarins Triterpenes; Xanthones -each 2-3 examples **(15L)**

(iv) Stereo-selective reaction Carbocuperation, carboalumination, Tebbe, Petasis Olefinations, Takai Reaction, Alkyne bond forming reactions, cyclopropanation reaction. Application in the synthesis of drug and natural products **(15L)**

Books/References:

1. Modern synthetic reactions – H. O. House (Benjamin)
2. Organic chemistry – J. Clayden, N. Greeves, S. Warren and P. Wothers (Oxford Press)
3. Designing of organic synthesis – S. Warren (Wiley)
4. Some modern methods of organic synthesis – W. Carruthers (Cambridge)
5. Organic synthesis – M. B. Smith
6. Organometallics in organic synthesis – J. M. Swan and D. C. Black (Chapman and Hall)
7. Advanced organic chemistry, Part B – F. A Carey and R. J. Sundberg 5th edition (2007)
8. Palladium in Organic Synthesis Richard Heck
9. Organonickel compounds, Jolly
10. Comprehensive organometallic chemistry-Vol. 1-8
11. Chiron approach in organic synthesis – S. Hanessian (Relavent chapters For Chirons)
12. Aromaticity , P. Garratt
13. Carbocyclic non-benzenoid aromatic compounds, D. Lloyd

Elective courses;

MC-406: Origin of secondary metabolic drugs in plants and pharmacokinetics (4 credits) (60L)

Biogenesis (24)

of terpenes: sesquiterpenes, triterpenes and chloesterol, alkaloids : polyketide Biogenesis of terpenes – mono terpenes, Sesquiterpenes**,** Triterpenes, Steroids, Biogenesis of Alkaloidsornithine based(pyrrolizidine), Lysine based(quinolizidine and indolizidine),Pyridine based**,** Tyrosine and modified tetrahydroisoquinoline based alkaloids, Phenethylisoquinoline and terpinoid tetrahydroisoquinoline (Amaryllidaceae alkaloids, anthranilic acid base simple Indole and terpinoid indole.

Biogenesis of polyketides – saturate and unsaturated fatty acids Arachidonic acid cascades – prostaglandins, Aromatics derived from polyketides.Synthesis of Prostaglandins, Thromboxane, Leukotriene in nature and lab

Mechanism of biological processes (6)

Selectivity of enzyme mediated reactions and its comparison with synthetic reactions

Mechanisms involving vit. B1, B2, B6, Biotin, NAD/NADP – NADH/NADPH, Folic acid, Riboflavin

Pharmocokinetics, pharmacodynamics (30)

Principal of pharmacokinetics . Concepts of drug disposition: Absorption : Distribution: Metabolism: Excretion (ADME). Application of pharmacokinetis principals to the calculations of drugs doses. Chemical aspect of drug metabolism. Drug toxicology concepts: carcinogenesis: mutagenesis: teratogenesis: and organ/ systemic toxicity. Analysis of drug n biological fluids and clinical pharmacokinetics applications.

Concepts and clinical roals of pharmacogenetics. Pharmacodynamics, concept and application of therapeutic drug monitoring (TDM). Pharmacokinetics consideration for adverse effect and drug interaction. Clinical pharmacokinetics of selected drugs. Including amino- glycosides, digoxin and anticonvulsants.

References:

9. *Screening methodology in pharmacology –II by Turner and Hebborn*
10. *Evolution of drug activity by Laurence and Bacharach- Vol I and II.*
11. *In vitro toxicity testing by john M. Fraizer.*
12. *Combination drugs : Their use and regulation- Louis lasanga*
13. *Drug receptor and their Effctors ed. By Nigel J. M. Birdsall.*
14. *Receptor binding in drug research by robert A.O. Brien.*
15. *General and applied toxicology by Bryan Ballantyne T. Marrs and P. Turner*
16. *Safety evolution of drugs and chemicals by W. Eugene Lloyd.*

Books

1. *Peptides: Sythesis, structure and applications, Bernd Gutte*
2. *Organic Chemistry, H. Dugas*
3. *Biochemistry by Zubay Chapter 11.*
4. *Organic Chemistry Chapter 50– J. Clayden, N. Greeves, S. Warren and P. Wothers (Oxford Press.)*
5. *Secondary metabolism by J.Mann*
6. *Medicinal Natural products by P.M. Dewick*