Department of chemistry

University of Pune, Pune

Syllabus of Medicinal Chemistry: II

Semester III: 4 courses 19 credits (one course is optional) + practicals of 8 credits =26 credits.

CHM 301-Medical Biochemistry, drugdesign and development 5 credit

Medical Biochemistry 2.5 credits

1) 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 syntheis.
2) Plasma membrane antiseptics and antiotics mechanism of antiseptics, disinffectants, catonic antibiotics, polypeptide antibiotics ionophoric and polyene antibiotics.
3) Mechanism of inhibition of Nucleic acids synthesis: inhibitors of nucleotide synthesis, inhibitor of polymerization of nuclic acids, inhibitors of polymerases.
4) Mechanism of inhibiton of protein synthesis: inhibitors of amnoacetyl tRNA formation, t RNA ribosome interaction inhibitors, 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, antiHIV etc, analgesic drugs.
6) Mechanism of resistance to antibiotics and other drugs: mechamism 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, synthesis of additional enzymes.

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 – 2.5 credits

1. Structure Activity Relationships in drug design: Qualitative versus quantitative approaches, advantages and disadvantages; Random screening, nonrandom screening, drug metabolism studies,clinical observations, rational approaches to lead discovery; Homologation, chain branching, ringchain transformations, bioisosterism; Insights into molecular recognition phenomenon; Structure based drug design, ligand based drug design**.(6)**

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. (4)

3. 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; 2D – QSAR; 3D-QSAR-examples CoMFA and CoMSIA.(4)

4. Molecular docking and dynamics: Rigid docking, flexible docking, manual docking; Advantages and disadvantages of flex-X, flex-S, autodock and dock softwares with successful examples; Monte Carlo simulations and molecular dynamics in performing conformational search, docking etc. (2)

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.(2)

6. Electronic structure methods and quantum chemical methods: Semi-empirical and ab initio methods; Conformational analysis, energy minimization, comparison between global minimum conformation and bioactive conformation; 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(3) 7. De novo drug design techniques.(1)

8. *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. (2)

advantages and disadvantages; Theoretical aqueous solvation calculations for the design of ligands. Conformational interconversion, transition-state determination and their role in designing rigid analogs (3)

CHM302: Spectroscopic Methods in Structure Determination of organic and medicinal compounds 5 credits

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

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 (10)

based on joint application of UV, IR, 1H and 13C NMR, 2D and Mass (including reaction

sequence.

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 and Sons.

3. Spectroscopic methods in organic chemistry – D. H. Williams and I. Flemming McGraw 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 Ltd.

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

CHM303: Stereochemistry of organic/medicinal compounds 5 **credits**

Conformation and reactivity in acyclic compounds **(06)**

Meaning of conformation and physical properties, conformational effects on the stability and

Reactivity Stereochemistry of six membered rings **(12)**

Shape of cyclohexane ring, monsubstuted and disubstited cyclohexane, physical properties, 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 rings **(06)**

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, Occerence, availbility, sterochemical restrictions and reactions of

norbornyl system Allenes, spiranes and biphenyls **(06)**

Enantiomerism in allenes, alkylidene cycloalkane, spiranes- configurational nomencalture, correlation of axial dissymmtry and centrodissymmetry.

Resolution methods **(04)**

Resolution by mechanical separtion of crystals, resolution by formation of diasteremers, second order asymmtric transformation, resolution by equilibrium asymmtric transformation, biochemical asymmtric transformation, criteria of optcal puriy, ORD and CD (**08)**

(Stereochemistry of natural products, strychnine, podophyllotixin **(04)**

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
5. Molecules of Nature
6. Organic Chemistry, Cram, Hammond, Hendrickson

CHO-304: Carbanions and Heterocyclic Chemistry 4 credits

Carbanions in organic synthesis (18)

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, Mannich, Cannizzaro, Darzens, Dieckmann, Claisen Baylis-Hillman reactions, Knoevenagel, benzoin condensation, alkylation of enolates and Stereo chemistry thereof, Conjugate additions.(15) Enamines and imine anions in organic synthesis etc.(03)

Free Radicals (8) 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

Synthesis of Heterocyclic natural product and drugs (8)

Chemistry heterocylics containing two hetroatoms: Pyrazines, pyradiazins, pyrimidines. ,1,2;1,3, and 1,4 diaoxazines and thiazines: pyrazole pyrazolines and imidazoles, imidazolines.

Synthesis of chloroquine, papavarine, amlodipine, bromouidine, ranitidine, Vit-B6, tryptophan,

thiamine, histidine. (v)

Aromatcity (10)

Criteria of Aromaticity- (2)(1)The Energy Criterion (2) Structural Criteria, (3) Electronic Criteria, Relationshipamong the Energetic, Structural, and Electronic Criteria of Aromaticity, Inscribed

polygon method for monocyclic compounds

The Annulenes-Cyclobutadiene, Benzene, Cyclooctatetraene, (4)[10]Annulenes, [12], [14], and [16] Annulenes, [18] Annulene and Larger Annulenes,Other Related Structures-Kekulene, Fullerene, Aromaticity in Charged (3)Rings, Heteroaromatic Systems, Fused-Ring Systems, compounds with exocyclicdouble bonds, substituted aromatics

Other aromatic compounds-Mesoionic Compounds, (1) The Dianion of Squaric Acid, 1 Mobius aromaticity, Homoaromaticity

Green Chemistry, *Multicomponent reactions:* Ugi, Passerini, Biginelli, Hantzsch, Mannich, Petasis, Strecker, Kabachnik-fields reactions;and their chiral version.
Cascade reactions, click chemistry. (4)

Optional to 330 (4credits)/CHO336 Organic reaction Mechanism and NGP

Organic reaction mechanism : . (4)

Methods of determining reaction mechanisms (kinetic and non-kinetic methods; Energy profile

diagrams, reaction intermediates, crossover experiments and isotopic labelling; Order of reactions,

reversible, consecutive and parallel reactions, solvent, ionic strength and salt effects; Acid-base

catalysis; Hammett eq.

Stereoelectronic effect on reactivity-(12)

geometric constraint on SN2 reaction, E1,E2, E1cB reactions, dioxiranes and peracid reactions, Cope /Coreys Winter reaction, Bayer Villiger rearrangements, Baldwins rules of ring closer, Exocyclic enolate alkylations, intramolecular aldol reactions.Introduction of hyperconjugation and NBO analysis, Rple of hyperconjugation in cyclohexane, sigma acceptor abilities, Epimerization equilibrium heterocycles some recent examples.

Hydrogen bonding **(**08)

Weak and strong H..bond, Hydrogen bonding-Classical vs nonclassical intermolecular forces, donar –accetor vs electronic views, prototypical H-bonds, charge and resonance assisted h-bonds, optimal geometry, cooperative and anticooperative network, symmetric h-bond. H-bond lenths by x-ray.

Spectroscopy -Nmr, ir, cmr, Raman, x-ray of N-H..N, N-H..O.N-H…X, NH….C, C-H...N/O/X etc, C-H pi interactions

Use of H..bonding in explaining reaction Mechanism, H. bond assisted organic reactions, application of H..bonding in drug interactions peptides and proteins.

Aldol reaction, **(**6)

soft enolaisation, Chiral auxillaries in aldol reactions Aldehyde and enolate facial selectivity, double stereodifferentiating aldol reactions, Zimmerman traxler transition state, Polar Felkin vs Comforth, application of aldol reaction. natural produt synthesis.

Transion metals in heterocyclic synthesis **(**18)-

Chemistry heterocylics containing two hetroatoms: Pyrazines, pyradiazins, pyrimidines. ,1,2;1,3, and 1,4 diaoxazines and thiazines: pyrazole pyrazolines and imidazoles, imidazolines.

Transion metals in heterocyclic synthesis-C-N, C-O bond formations **(**6) Reaction of metals with heterocyclic **(**4) Synthesis of chloroquine, papavarine, amlodipine, bromouidine, ranitidine, Vit-B6, tryptophan, thiamine, histidine. (12)

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)

7. Aromaticity , P. Garratt

8. Crbocyclic non-benzenoid aromatic compounds, D. Lloyd

CHM-301 Medicinal Biochemistry, Drug Design& Development

CHM-310- Drug Intermediates organic synthesis (4)

CHM- 320 Medicinal chemistry. (4)

Semester IV 3 Courses **16 credits** + 2 courses inter sectional option 4 **credits**= **23 credits**

CHM-401: Synthetic Strategies in the Total Synthesis of Complex drug Molecules
6 credits

(i) Transitional metals complexes and Boron, Si and Sn in organic synthesis

Transition metal complexes in organic synthesis-Introduction-oxidation states of transition metals, 16-18 rule, dissociation, association, insertion, oxidative addition, reductive elimination of transition metal **(1)**

Organopalladium in organic synthesis- Heck arylation, allylic activation, carbonylation, wacker oxidation, isomarization formation N-aryl and N-alkyl bond transmetalation, allyl deprotection in peptides, coupling reactions: Stille coupling, Sonogashira and Suzuki coupling reactions and their importance (6),Organo nickels- coupling carboxylation, amination, carbonylation **(1)**

Chromium carbonyls regioselective alkylation and acylation of aromatics, nucleophilc substitution, lithiation reaction **(2),** Reactions Iron carbonyls, ferrocenes, Fe-cyclopentadiene complex, protection of dienes,**,** Isomerization **(2)** Manganese and Co-carbonyls in hydroformylation, carboxylations, synthesis of silane complexes and their applications Pausal-khand reactions and its applications protection of alkynes by Co2CO8 **(2)**Wilkinson, Noyori, Knowls catalyst of Ruthenium and Rhodium – synthesis and uses its use in hydrogenation reactions-deallylation, C-C, C-O, C-N bond cleavages **(1)**

Organoboranes- preparation and properties of organoborane reagents e.g. RBH2,R2BH, R3B, 9-BBN,catechol borane. Thexyl borane, cyclohexyl borane , ICPBH2, IPC2BH, Hydrborationmechanism, stereo and regeoselectivity, uses in synthesis of primary, secondary tertiary alcohols, aldehydes, ketones, alkenes. Synthesis of EE, EZ, ZZ dienes and alkyenes. Mechanism of addition of IPC2BH. Allyl boranes- synthesis, mechanism and uses **(6)** Synthesis and uses of organo silane and organo tin compounds **(1),** Olefin metathesis by Ist , and IInd generation catalyst, reaction mechanism and application in the synthesis of homo and heterocyclic compounds **(2)**

(ii) **Designing Organic Synthesis**- Synthons and Chirons **(16)**

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 **(**00**)**

(iv) Protection, deprotection for functional groups hydroxyl, amino, carboxyl and carbonyl (06**)**

Natural Product Synthesis-Synthesis of biologically active Natural products: on the basis of disconnection and direct associative approaches. Strychnine (Overmann , Woodward), prostoglandins F2a((Corey and Stokes), Cephalosporin

(Woodward), Penicillins, Estrone, Mifepristone (Vollard), Taxol (12)

Pericyclic reaction, Chelotropic reactions, and Sigmatropic reactions (8)

Fukui's HOMO and LUMO orbitals
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

supramolecules **(**02**)**

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)

Classics Total in Synthesis by Nicolaou, Sorensen

CHM-402: Fundamentals of Chiral Drug Synthesis **6 credits**

Assymetric synthesis **(24)**

Recapitulation of Stereochemical concepts- enantiomers, diastereomers, homotopic and heterotopic ligands, stereoselective and stereospecific reactions, prochirality, Chemo-, regio-, diastereo- and enantio-controlled approaches; Chirality transfer, Asymmetric inductions; Chiral pools, Chiral auxiliaries, chiral reagents and catalysts, and templates;

Asymmetric oxidations: Sharpless asymmetric epoxidation, dihydroxylation, aminohydroxylation, Asymmetric reduction reactions: Reduction of ketones, imines and olefins (use of BINOLS)

Asymmetric C-C bond forming reaction: Simmon-Smith reaction, aldol reaction and alkylationbased on Evans method, 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.

Stereoselective addition of nucleophiles to carbonyl group: Re-Si face concepts, Cram's rule, Felkin Anh rule, Houk model, Cram's chelate model. Asymmetric synthesis use of chiral auxiliaries, asymmetric hydrogenation, asymmetric epoxidation and asymmetric dihydroxylation.

Self regeneration of sterecentre

Advanced Carbohydrate Chemistry (12)

Introduction of sugars, structures of triose, tetrose, pentose, hexose. Fisher projection, D- and Lconfiguration,

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. **(06)** 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. **(06)**

Development of organocatalyst: (08) Type of organocatalyst, structure of organo catylyst, factors influencing organo -catalytic reactions, Hydrogen bonding in organo-catalysis.Mechanisms of organo catalytic reactions (imines and enamines), DFT studies Development of proline as organocatalyst, various reactions of proline, their stereochemistry and mechanisms, importance of transition states, comparison of prolines catalyzed reactions with transition metal catalyzed reactions, application of organocatalysts in the synthesis of natural products and drug molecules

Chemistry of amino acids, peptides, nucleotides, nucleosides (**12)**

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

Photochemistry (8)

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.

Mechanism of biological processes **(8)**

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

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

alkaloids : polyketide Biogenesis of terpenes – mono terpenes **(**02**)** Sesquiterpenes**(**04**)**

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

CHM-403: This course is intersectional optional

Pharmaceutical analysis and pharmacodynamics 4-credits

1. Structure Elucidation of natural product **(10)**

Some typical structure elucidation insights for natural products by combination of

Classical, spectroscopic, synthetic and degradative methods depicting examples

1. Use of spectroscopic techniques such as 1H NMR, 13C NMR, NOE, DEPT, HMQC, HMBC, COSY, NOESY, HRMS and FAB mass for structural elucidation of selected natural products.

2. 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, indoles, carbazoles each 2-3 examples

2. Spectrometry in Pharmaceutical Analysis **(10)**

Importance of chromatographic separation, mass analyzers, atmospheric pressure ionization techniques: ESI, APPI, APCI. Interpretation of API mass spectra: Molecular weight determination, typical fragmentation behavior for individual functional groups: (i) phosphorous (ii) sulfur (iii) nitrogen (iv) oxygen (5) halogen substituent's (6) alkyl and aryl substitution on the aromatic ring, polycyclic aromatic hydrocarbons, alkenes and alkynes. 3. Liquid chromatography - electrospray ionization - mass spectrometry (LC-ESI-MS) to the detection and determination of antibiotics drugs, antidiabetics, antitumour, antiretroviral drugs. EI-MS of small molecular mass of selected drugs- fragmentation information.

X-Ray, IR, NMR, Raman spectra in pharma analysis **(4)**

(Workshops on structural determinations)

3. **Chromatographic techniques in Organic/Medicinal chemistry (8)**

General principles, classification of chromatographic techniques, normal and

reversed phase, bonded phase, separation mechanisms.

TLC, HPLC, HPTLC, over pressure layer chromatography (OPLC), centrifugal chromatography.

. Counter-current chromatography, droplet counter-current chromatography, ion-exchange, affinity, size exclusion and ion-pair chromatography. Gas chromatography, introduction to GC-MS and LC-MS techniques., Chiral coulums and its applications

Pharmocokinetics, pharmacodynamics(16)

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: carciogenesis: mutagenesis: teratogenesis: and organ/ systemic toxicity. Analysis of drug n biological fluids and clinical pharmaokinetics applications. Concepts and clinical roals of pharmacogenetics. Pharmacodynamics, concept and application of therapetic drug monotoring (TDM). Pharmacokinetics consederation for adverse effect and drug interaction. Clinical pharmacokinetics of selected drugs. Including amino- glycosides, digoxin and antoconvulsants.

1Screening methodology in pharmacology –II by Turner and Hebborn

1) Evolation of drug activity by Laurence and Bacharach- Vol I and II.
2) In vitro toxicity testing by john M. Fraizer.
3) Combination grugs : Their use and regulation- Louis lasanga
4) Drug receptor and their Effctors ed. By Nigel J. M. Birdsall.
5) Hypersencetivity drugs vol I by max Samter and C.W. parker
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) Safty evolution of drugs and chemicals by W. Eugene Lloyd.
9) Pharmacology 3rd ed – H.p. Rang and M.M. dale.

CHM-410 :Research Project 7 **credits**

Experimental work – Cont. Based on synthesis of natural Products.7 credits

Each student has to present a 2 seminars before end of the each semester.

Students are required to submit written record and present details of the project to be pursued in semester-IV. Student has to present his outcome of the work in local and/or national, or international seminars.

LABORATORY SAFETY

The following safety rule applies **at all times** in the laboratory rooms.
• No open food or drink is permitted at any time, whether a lab is in progress or not.
• No eating, drinking, or chewing of gum or tobacco is permitted.
• Never taste anything at all while in the lab rooms.
The following additional rules apply **while a laboratory session is in progress**.
• The lab is restricted to the students enrolled in the course. Visitors, especially children, are not allowed.
• You must wear goggles for eye protection during every laboratory period, until all students have completed all their experiments. Even if you wear prescription glasses or contact lenses, you need to wear goggles as well.
• Report all accidents to your laboratory instructor immediately.
• Know the location of the two main exits from the room, eye washes, safety shower, fire alarms, fire blanket and fire extinguishers. (First Aid box, nearest hospital)
• If a chemical comes in contact with your eye, immediately flush the eye with a gently flowing source of water from the eyewash. If you wear contact lenses, remove them. Continue flushing for at least 15 minutes. Use your thumb and forefinger to hold your eyelids away from the eyeball, move your
eyes continuously—up and down and sideways—to flush out thoroughly behind the eyelids and behind the eyeball. Notify the laboratory instructor immediately. Promptly seek medical attention. If someone else in the lab has a chemical in their eye, help them get to the eyewash and help them operate it!
• Clothing must offer you good protection against chemical spills and splashes.
• No high heeled shoes, open toed shoes, sandals, or shoes made of loosely woven material not allowed.
• Legs must be covered by your clothing.
• No smoking is allowed in chemical laboratories.
• Every student must wear protective eye shields at all times in the laboratory. This is to protect you from your neighbour's mistakes as well as your own.

• Carry out experiments which produce toxic chemicals or vapours, and/or are likely to be violent, in a fume cupboard.
• Fire is a serious hazard in the laboratory and is usually caused by the careless handling of organic solvents. These must not be heated using a Bunsen burner.
• Do not peer into the mouth of a test tube which is being heated or in which a reaction may be occurring.
• If the clothing is splashed by a corrosive liquid, strip the clothing and treat the skin immediately. As a first treatment washing with water is generally appropriate, call a demonstrator to assist you.
• Wear a laboratory coat at all times in the practical laboratory to protect you and your cloths.
• Always carry a small towel to the laboratory to assist you in handling hot objects in addition to tongs.
• Bunsen burners may only be used in the fume cupboard or keep it away from the inflammable solvents.
• Most organic compounds are combustible. Those with low boiling points and high vapor pressure at room temperatures may present a serious fire hazard. Ether, for example, which has a boiling point of 35°C, may be ignited by a flame removed by sixteen feet. Hence, it is never permissible to heat over an open flame any substance in an open vessel containing such volatile liquids. Steam bath are ideal for this purpose.
• **Fire**

Fire is one of the most serious and most likely hazards to occur in a laboratory. The most generally
useful fire extinguisher in the laboratory is the Carbonodioxide cylinder which can be safely used with most chemicals and electric equipment, and is clean.
Asbestos blankets are useful for smoothening small fires and burning clothings.

• **Chemical Hazards**

Most compounds are highly toxic when injected orally. Many chemicals are poisonous, corrosive, carcinogenic or explosive.
• Corrosive chemicals such as acids and alkalis are stored in low shelves and opened with care.
• One should never taste any compound and odors of substances should be detected with extreme care.
• Mouth pipetting is always potentially dangerous and some form of safety pipette must be used instead.
• Sensitive tissues, for example, the eye should not be needlessly exposed to vapours. One should never place his/her face directly over a reaction mixture.
• It is mandatory that each student study each experiment prior to undertaking any laboratory
procedure in order to understand the implications of the particular experiment.
• Dangers chemicals obtained from commercial sources usually carry a warning printed in the bottle. These warnings should be followed.
• It is the duty of all members of laboratory staff to co-operate in the prevention of accidents.
• In addition to the welfare of the staff of the laboratory there is concern for preservation of the building, equipment, furnishing and apparatus.