

MEDICINAL CHEMISTRY

UNIT-I: Introduction to Drugs and Their Action

Drugs: Historical background-sources and classification of drugs-important terminologies in medicinal chemistry. Drug Action: role of intermolecular forces-drug targets: lipids, carbohydrates, proteins (enzymes, receptor) and nucleic acids as drug targets. Pharmacokinetics and pharmacodynamics: administration, absorption, distribution, metabolism, elimination of drugs-bioavailability of drugs-side effects.

UNIT-II: Selected Examples of Drugs and Their Mechanism of Action

Antibacterial agents-mechanism of action-antibacterial agents that act against cell metabolism (sulfonamides), inhibit cell wall synthesis (penicillins, cephalosporins), interact with plasma membrane (valinomycin and gramicidin A), impair protein synthesis (tetracyclines, chloramphenicol) and act on nucleic acids (quinolones and fluoroquinolones, rifamycins). Antiviral agents-general principles-nucleic acid synthesis inhibitors (HIV), host cell penetration inhibitors, inhibitors of viral protein synthesis. Antifungal agents-azoles, allyamines and phenols. Anticancer drugs and their mechanism of action- role of antimetabolites, antisense drugs, alkylating agents and interchelating agents in cancer chemotherapy. Cardiovascular drugs: antiarrhythmic and antihypertension drugs.

UNIT-III: Drug Discovery, Design and Development

Identification of diseases and corresponding targets, bioassays and leads. Stereochemistry and solubility issues in drug design. Structure activity relationships (SARs): changing size and shape-introduction of new substituents. Quantitative structure activity relationships (QSARs): lipophilicity-electronic and steric effects-Hansch Analysis-Topliss decision tree. Chemical and process development of drugs. Preclinical trials: pharmacology, toxicology, metabolism and stability studies-formulation. Clinical trials: phase I-IV studies-ethical issues. Patent protection. Regulation

UNIT-IV: Lead and Analogue Synthesis-1

Designing organic synthesis-disconnection approach-synthons and synthetic equivalents-one group disconnections: alcohol, olefin, ketone, acids-two group disconnections: 1,2-, 1,3-, 1,4- and 1,5-difunctional compounds-convergent synthesis-functional group interconversions- functional group additions-carbon-heteroatom bonds-methods for 3- to 6-membered rings.

UNIT-V: Lead and Analogue Synthesis-2

Combinatorial synthesis in medicinal chemistry: Solid phase techniques-methods of parallel synthesis-mix and split techniques-dynamic combinatorial chemistry-screening and deconvolution-limitations of combinatorial synthesis

Asymmetric synthesis: basic principles-stereoselective and stereospecific reactions- methods for determining enantiomeric excess-chiral auxiliary, reagents and catalysts and their applications (wherever applicable) in alkylation, hydrogenation, hydroxylation, epoxidation and hydroboration of alkenes, reduction of ketones-Cram and Felkin-ahn models. Noyori's BINAP – Jacobson catalyst – Evans catalyst.

References:

- 1) Fundamentals of Medicinal Chemistry by Gareth Thomas, John Wiley & Sons: Chichester, **2003**.
- 2) Medicinal Chemistry: An Introduction by Gareth Thomas, Wiley-Interscience, 2nd edition, **2008**.
- 3) An introduction to Medicinal Chemistry by Graham L. Patric, Oxford University Press, USA, 3rd edition, **2005**.
- 4) Wilson and Giswald's Textbook of Organic Medicinal and Pharmaceutical Chemistry by John Block and John M Beale (Eds), Lippincott Williams & Wilkins, 11th edition, **2003**.
- 5) The Organic Chemistry of Drug Design and Drug Action by Richard B. Silverman, Academic press, 2nd edition, **2004**.
- 6) Designing Organic Synthesis: The Disconnection Approach by Stuart Warren, Wiley, 2nd edition, **1984**.
- 7) Asymmetric Synthesis by H. B. Kagan, Thieme Medical Publishers, **2003**.
- 8) Advanced Organic Chemistry: Part-A and Part-B by Francis A. Carey and Richard B. Sundberg, Springer, 5th edition, **2007**.