Gujarat Technological University

Master of Pharmacy

Semester – II

Paper code -2920201

Specialization paper - IV

Drug Design and Discovery

Theory
(Six hours per week, 8 credits)

1. General Introduction to drug discovery concept/process and importance of drug design approaches in drug discovery.
2. Various targets for drug action and theory of drug action –agonist, antagonism/ blockers and enzyme inhibition (IC50, EC50 concept)- an overview
3. A general study of stereochemistry and physicochemical properties of the drug/drug-like molecules and their importance in drug action. Correlation between physicochemical properties and drug action, establishing structure activity relationship (SAR) and its analysis. Isosterism and bio-isosterism as guides to structural variations and Prodrug design its application in lead optimization.
4. Various approaches to drug discovery
5. Quantitative Structure Activity Relationship QSAR- brief introduction to various methods of QSAR – Physicochemical parameters – lipophilic, electronic and steric. Detail study on Hansch LFER model, Free Wilson analysis and mixed approach. Various basic statistical methods useful in QSAR development.
    a. 3D QSAR – importance and various models (COMFA, MSA, HASL, Apex 3D, DISCO, GFA) used for it.
6. Computer Aided Drug Design (CADD) – Molecular modeling
    a. Basic concepts of computational chemistry like Quantum Mechanics, Molecular Mechanics, Force Field, Energy minimization, Conformational generation and analysis, geometry optimization, Molecular Dynamics
    b. Ligand based drug design, Analogue approach, Pharmacophore Mapping, importance of ligand shape and Excluded volume techniques, Artificial intelligence methods.
    c. Structure based drug design, requirement of SBDD, utilization of target structure derived from NMR and X-ray Crystallography techniques, understanding of drug–receptor/enzyme/target interactions, preparation of protein/target along with active site analysis, docking process, various docking methods. De-novo drug design.
    d. Drug design based on antagonism and enzyme inhibition. Various software used in CADD
7. Virtual screening of huge compound databases by using Pharmacophore mapping as well as docking methods
8. Pharmacokinetics (Absorption, Distribution, Metabolism Elimination i.e. ADME) in drug discovery.

References Books:

1. Ariens – Drug Design, vol. VII, Academic Press.
2. H Smith & H J William – Introduction to the Principal of Drug Design, John Wright & Sons Ltd.
3. Burgers Medicinal Chemistry – The Basis of Medicinal Chemistry by Manfred S. Wolff, Part – I , John Wiley & Sons

4. Copmuter assisted Drug Design by Edward C. Olson (America Chemical Society, ACD symposium series 112).
5. W. O. Foye - Principles of Medicinal Chemistry, Lipincott Williams and Wilkins.
6. C. Hansch and Leo - Comprehensive Medicinal Chemistry Vol. 4, Pergamon Press.
7. Molecular Modeling in Drug Design by Cohen N. C.
8. C. G. Wermuth - The Practice of Medicinal Chemistry, Elsevier publication.
9. E. H. Kerns and L. Di - Drug like properties, concepts, structure design and methods, Academic Press.