## ELECTIVE PAPER-B: DRUG DESIGN

| Semester | Subject Code | Category | Instruction Hours | | | | | | Credits |
|---|---|---|---|---|---|---|---|---|---|
| | | | Lecture | | Theory | | Practical | | |
| | | | Per Week | Per Semester | Per Week | Per Semester | Per Week | Per Semester | |
| I | 21CPCH1Da | Elective | 3 | 45 | 3 | 45 | 0 | 0 | 3 |

**COURSE OBJECTIVES:**

- To understand the concepts of drug design, drug metabolism, mechanism of drug –receptor binding and its structure activity relationship qualitatively and quantitatively.
- To enhance the knowledge in the various areas of molecular modelling, molecular docking and drug design techniques with detail concepts of all the mentioned areas.

**COURSE OUTCOME:**

- On completion of the course, the student should be able to:

| CO Number | CO statement | Knowledge level |
|---|---|---|
| **CO1** | Learn about the ligands based on its electronic level using computational quantum chemistry | **K2, K3 & K4** |
| **CO2** | Justify the role and importance of the various disciplines involved in the different phases of drug discovery and development, identification of gobal reactivity indicators of compounds using computer methodologies and molecular modeling including artificial intelligence methods. | **K2, K3 & K4** |
| **CO3** | Get clear idea about the use of computational chemistry in structure based drug design, drug development as a process involving target selection, lead discovery using computer-based methods and computational chemistry/high-throughput screening. | **K3 & K4** |
| **CO4** | Describe the safety evaluation, bioavailability, clinical trials, essentials used for drug development and also acquire knowledge about molecular recognition, computer aided drug design and toxicology as applied to the development of new medicines | **K2, K3 & K4** |
| **CO5** | Get knowledge about molecular docking, simulation and dynamic in drug designing and development process. | **K2, K3 & K4** |

*CO-Course Outcomes

Knowledge level K1-Remember; K2-Understand; K3-Apply; K4-Analyze

**MAPPING WITH PROGRAM OUTCOMES**

| COS | PO1 | PO2 | PO3 | PO4 | PO5 | PO6 |
|---|---|---|---|---|---|---|
| **CO1** | S | S | S | M | M | M |
| **CO2** | M | S | M | M | S | M |
| **CO3** | M | S | M | S | S | M |
| **CO4** | M | S | S | S | S | M |
| **CO5** | M | M | S | S | S | S |

**UNIT-I Electronic Structure methods** **9 hours**

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 design of ligands - Conformational interconversion, transition-state determination and their role in designing rigid analogs.

**UNIT-II Molecular modeling** **9 hours**

Molecular Mechanics, Quantum Mechanics, 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 - Molecular properties, reactivity, Homo, Lumo, Electrostatic potential - Solvent accessible surface - Computer methodologies behind molecular modeling including artificial intelligence methods.

**UNIT-III DRUG DESIGN** **9 hours**

Drug design strategies-rational drug design: Inhibitors of ACE; structure-based drug design: Anti-HIV agents; ligand based approach - Design of agonist and antagonist: β2-Agonists and the treatment of asthma - Discovery of the H2–receptor antagonist - Transition state analogues - Pro drug concept - prodrugs of ampicillin, enalapril and propranolol.

SAR: Qualitative versus quantitative approaches - advantages and disadvantages -Random screening - Non-random screening.

**UNIT-IV QSAR AND DRUG METABOLISM** **9 hours**

QSAR - Electronic effects - Hammett equation - lipophilicity effects - Hansch equation, steric effects - Taft equation - Experimental and theoretical approaches for the determination of physio-chemical parameters - parameter inter-dependence.

Adsorption, distribution, metabolism and elimination - Methods of drug administration, drug solubility and lipophilicity, clogP. cell membrane permeability, blood brain barrier Lipinski's

rule of five – Metabolism - first pass metabolism, chemical and metabolic stability- bioavailability and bioequivalence - concept of drug half life -therapeutic window.

**UNIT – V Molecular docking and dynamics** **9 hours**

Rigid docking, flexible docking, manual docking - Advantages and disadvantages of Flex-X, Flex-S, Autodock and Dock softwares, with successful examples.

Molecular dynamics: Dynamics of drugs, biomolecules, drug-receptor complexes, Monte Carlo simulations and Molecular dynamics in performing conformational search and docking - Estimation of free energy from dynamical methods

**Distribution of Marks**: Theory-80% and Problems-20%

**TEXT BOOKS**

| S. No | Authors | Title | Publishers | Year of publication |
|---|---|---|---|---|
| 1. | Burger | Medicinal Chemistry and Drug Discovery | 5th Edn | 1995 |
| 2. | R. B. Silverman | Chemistry of Drug Design and Drug action | Acad. press | 2004 |
| 3. | Graham Patrick | An Introduction to Medicinal Chemistry | 2nd Edn. Qxford | 2010 |
| 4. | N. K. Jain | Advances in Controlled and Novel Drug Delivery | CBS | 2001 |
| 5. | Lednicer | The Organic Chemistry of Drug Synthesis | Vol.1, 5th Edition, John Wiley & Sons | 2001 |
| 6. | Foye's | Principles of Medicinal Chemistry, | Sixth Edition, Wolters Kluwer | 2008 |
| 7. | G.R. Chatwal | Medicinal Chemistry | Himalaya Publishing House | 2007 |
| 8. | V.K. Ahluwalia and M. Chopra | Medicinal Chemistry | Ane Book Pvt. Ltd. | 2008 |

**REFERENCE BOOKS**

| S.No | Authors | Title | Publishers | Year of publication |
|---|---|---|---|---|
| 1. | R.B. Silverman | Organic Chemistry of Drug Design and Drug Action | Academic Press | 2012 |
| **2.** | William H, Malick JB | Drug Discovery and Development | Humana Press Clifton. | 2004 |

**TEACHING METHODOLOGY:**

- Board and chalk
- PowerPoint presentation
- Models
- Group discussion
- Seminar and Assignments
- Animated videos

**SYLLABUS DESIGNERS:**

1. Dr. T. Gomathi, Assistant Professor, Department of Chemistry
2. Mrs. J. Saranya, Assistant Professor, Department of Chemistry
3. Dr. D. Shakila, Assistant Professor, Department of Chemistry