GUJARAT TECHNOLOGICAL UNIVERSITY

Bachelor of Engineering
Subject Code: 3160415
6th Semester
Rational Drug Design

Type of course: B.E. (Biotechnology)

Prerequisite: Basic concepts of Biochemistry, Bioinformatics

Rationale: Computer aided drug development is need of pharmaceutical industries to cut the cost ,time and simplify the process of development of successful API . Drug development can be best accelerated by computer- assisted approaches. The subject will enable student to carry out research in pharmaceutical industry.

Teaching and Examination Scheme:

Teaching Scheme			Credits	Examination Marks				Total Marks
L	T	P	C	Theory Marks		Practical Marks		
				ESE (E)	PA (M)	ESE (V)	PA (I)	
4	0	2	5	70	30	30	20	150

Content:

Sr. No.	Content	Total Hrs	% Weightage
1	Unit-I Molecular Modelling in Drug Discovery: Drug discovery process, Role of Bioinformatics in drug design, Methods of computer aided drug design, ligand design methods, drug design approaches, Target identification and validation, lead optimization and validation, Structure and ligand based drug design, modelling of target-small molecule interactions, Molecular simulations. Protein Modelling.	**9**	**15**
2	Unit-II Quantum Mechanics and Molecular Mechanics: Features of molecular mechanics force fields; Bond structure and bending angles – electrostatic, van der Waals and non – bonded interactions, hydrogen bonding in molecular mechanics; Derivatives of molecular mechanics energy function; Application of energy minimization.	**9**	**15**
3	Unit-III Molecular Dynamics simulation methods: Molecular Dynamics using simple models; Molecular Dynamics with continuous potentials and at constant temperature and pressure; Time – dependent properties; Solvent effects in Molecular Dynamics; Conformational changes from Molecular Dynamics simulation and application.	**9**	**15**

4	Unit-IV Molecular Docking and lead optimization: Molecular Docking; Types of Molecular Docking, docking algorithms and programs, Structure-based methods to identify lead compounds; de novo ligand design; Applications of 3D Databases Searching and virtual Screening; Strategy for target identification and Validation, lead identification, optimization and validation. Combinatorial chemistry and library design, virtual screening, drug likeness and compound filtering, Absorption, distribution, metabolism, excretion and toxicity (ADMET) property prediction, computer based tools for drug design.	**14**	**23.3**
5	Unit-V Pharmacophore and QSAR: Pharmacophore derivation, 3D pharmacophore prediction and application in drug discovery; QSARs and QSPRs, QSAR Methodology, Various Descriptors used in QSARs: Electronic; Topology; Quantum Chemical based Descriptors. Use of Genetic Algorithms, Neural Networks and Principal Components Analysis in the QSAR equations.	**9**	15
6	Unit-VI Success of CADD: Elvitegravir, A New HIV-1 Integrase Inhibitor for Antiretroviral Therapy, Perampanel: A Novel, Noncompetitive AMPA Receptor Antagonist for the Treatment of Epilepsy	**10**	16.7

Suggested Specification table with Marks (Theory):

Distribution of Theory Marks					
R Level	**U Level**	**A Level**	**N Level**	**E Level**	**C Level**
24	20	20	12	12	12

Legends: R: Remembrance; U: Understanding; A: Application, N: Analyze and E: Evaluate C: Create and above Levels (Revised Bloom's Taxonomy)

Note: This specification table shall be treated as a general guideline for students and teachers. The actual distribution of marks in the question paper may vary slightly from above table.

TEXT BOOK:

1. Computational methods in drug design Fred E. Cohen, Walter Hamilton Moos Publisher: ESCOM Science, 1993.

2. Molecular Modelling for Beginners - Alan Hinchliffe Publisher: John Wiley & Sons Inc, 2008. ISBN: 978-0470513149.

3. Combinatorial Library Design and Evaluation: Principles, Software, Tools, Applications in Drug Discovery – Arup Ghose, Vellarkad Viswanadhan Publisher: CRC Press, 2001. ISBN: 0-8247-0487-8.

4. Molecular Modeling Basics - Jan H. Jensen Publisher: CRC Press, 2010. ISBN 978- 1420075267.

5. 3D QSAR in Drug Design: Recent Advances – Hugo Kubinyi, Gerd Folkers, Yvonne C. Martin Publisher: Springer Science & Business Media. ISBN: 0-306-46858-1.

6. Computational Chemistry and Molecular Modeling - K. I. Ramachandran, Gopakumar Deepa, Krishnan Namboori Publisher: Springer – Verlag Berlin Heidelberg. ISBN: 978- 3540773023.

7. Successful Drug Discovery, Volume I, - Janos Fischer & David P. Rotella, Wiley-VCH 2015

Reference Books

1. Andrew R Leach - Molecular modelling _ principles and applications-Prentice Hall (2001)

Course Outcomes:

Exposure to various methods of rational drug design such as modelling of protein and target-small molecule interactions, molecular docking, lead optimization, Combinatorial chemistry and library design, Virtual screening, Toxicity (ADMET) property analysis, Pharmacophore and QSAR.

Sr. No.	CO statement	Marks % weightage
CO-1	Apply docking methodology (Lead optimization, combinatorial chemistry, Toxicity analysis) & describe different types of protein-ligand interactions.	25
CO-2	Set up molecular dynamics simulations and free energy calculations.	20
CO-3	Design drugs based on 3D QSAR and pharmacophore derivation.	20
CO-4	Infer basics of quantum & molecular mechanics and dynamics for advanced application in drug discovery pipeline.	20
CO-5	Comprehend the current scenario in pharmaceutical industry research throgh case studies	15

List of Experiments:

1. Role of Bioinformatics in drug design
2. Structure Based Drug Design
3. Coordinate System
4. Quantum Mechanics
5. Energy concept and its importance in drug action
6. Pharmacophore hypothesis
7. ADME calculation
8. Solvent effects in Molecular Dynamics
9. Application of 3D Database searching in Molecular Docking

Major Equipments: Computer with Internet connectivity

List of Open Source Software/learning website:

Students can refer to video lectures available on the websites including NPTEL. Students can refer to the CDs which are available with some reference books.

Softwares : Pymol, AutoDock, Gold, FRED, GAMESS, SoMFA, GRID, ISISDraw