Department	Pharmacy

Course Name	Medicinal Chemistry I & Drug Design	Course No.	0201318
Prerequisite	0201313, 0201335	Credit Hours	3
Number & date of course plan approval		Brief Description	See form QF02/0409

Course Objective	This course will explore the role of organic chemistry in the design and action of drugs. It will address principles of drug discovery, drug development, and drug/receptor interactions, types of chemical bonds involved in drug-receptor interactions, drug mechanism of action, and drug metabolism. Aspects of biochemistry and physical organic chemistry will be covered as necessary to understand the chemistry of drug action and metabolism in the body. This course is designed to introduce the knowledge of the relationship between different classes of pharmaceutical compounds and their physicochemical properties (relation to absorption, distribution, and elimination). It will emphasize on the stereochemical background necessary to understand the drugs activity: optical isomerism, geometric, and conformational. Students will earn basic knowledge of prodrugs concept and their actions. This course is designed to impart the knowledge in computational methods and drug design approaches. It will explore computational chemistry methods and their application in drug design. It is proposed to introduce the knowledge of hit discovery, lead identification, lead optimization, target selection, and molecular recognition employing computer-aided drug design software. And, it will shed the light on computer-based methods, combinatorial chemistry, high-throughput screening, and database mining.
Intended Learning Outcomes	- To recognize the physicochemical properties that affect drug bioavailability. - To classify the functional groups into acidic, basic, and neutral moieties. - To understand the significance of prodrug and its aim. - To perceive isosterism and bioisosterism concept in drug modification. - To address the metabolic pathways and distinguish between the metabolic phases and their corresponding enzymes. - To predict and draw the chemical structures of drug metabolites. - To understand drug/receptor complex formation and differentiate between the bonding forces mediating complex formation. - To differentiate between enzyme and protein as drug targets. - To understand the mechanism of ligand as agonist, antagonist, partial agonist, activator, (reversible and irreversible) inhibitor, suicide inhibitor, transition-state analogue.

	- To suggest chemical modification for metabolic susceptible moieties. - To optimize lead structure to enhance access to the target. - To emphasize on the general principles of drug design and drug action from an organic chemical perspective rather than from the perspective of specific classes. - To discuss new trends in drug discovery and development. - To be familiar in recent developments in key issues such as combinatorial chemistry, QSAR, recombinant technology, and molecular modeling. - To distinguish drug design approaches and their applications. - To recognize computational methods categories and their applications
Course Topics	1. Physicochemical Properties in Relation to Biological Action 2. Prodrugs 3. Drug Metabolism (Phase I and Phase II) 4. Making Drugs More Resistant to Enzymatic and Chemical Hydrolysis 5. Making Drugs Less Resistant to Enzymatic and Chemical Hydrolysis 6. Optimizing Hydrophilic/Hydrophobic Properties 7. Receptors as drug targets 8. Enzymes as drug targets 9. Computational Chemistry 10. Conformational Analysis 11. Ligand-based drug design 12. Structure-based drug design 13. Combinatorial Chemistry 14. Quantitative Structure Activity Relationship 15. Case Study: Design of ACE Inhibitors 16. Case Study: Current Research into Antidepressant Agents
Text Books	1- An Introduction of Medicinal Chemistry, 4th edition, Graham Patrick, Oxford Universtiy Press, 2008. 2- Foye's Principles of Medicinal Chemistry, 6th edition, Thomas L. Lemke and David A. Williams, Lippincott Williams & Wilkins, 2008. 3- Wilson and Gisvold's Textbook of Organic Medicinal and Pharmaceutical Chemistry, 11th edition, J. N. Delgado and W. A. Remers, Lippincott-Raven, 2005. 4- The Organic Chemistry of Drug Design and Drug Action, 2nd edition, Richard B. Silverman, Elsevier, 2004.

References	1. Burger's Medicinal Chemistry and Drug Discovery, 6th edition, M. E. Wolff, 2003. 2. The Organic Chemistry of Drug Synthesis, Vol. 1-6, D. Lednicer and L. A. Mitscher, John Wiley and Sons.		
Grade Determination	1st Exam = 25% 2nd Exam = 25% Final Exam = 50%	Practical Course Grade Determination	Course Work = 50% (Reports, Term Papers, Quizes) Final Exam = 50%

Course Outline

Week	Hours	Subjects	Chapters in Textbook	Notes
1-2	١ ١ ١ ١ ١ ١	**Physicochemical Properties in Relation to Biological Action** - Solubility in water. - Partition coefficient. - Acid/ base partition. - Bonding forces. - Isosterism & Bioisosterism. - Geometric isomers. - Conformational Isomerism. - Optical isomerism.	Textbooks 1-٤/	
3	1 1 1	**Prodrugs** - Basic concepts. - Prodrugs of functional groups. - Chemical delivery systems.	Textbooks 1-٤/	
3-5	١ ١ ١ ١ ١ ١ ١ ١ ١	**Metabolic Changes of Drugs and Related Organic Compounds** - General pathways of drug metabolism. - Sites of drug biotransformation. - Factors affecting drug metabolism. - Phase I metabolic pathways. - Phase II metabolic pathways	Textbooks 1-٤/	
6	١ ١ ١	**Making Drugs More or Less Resistant to Enzymatic and Chemical Hydrolysis** - Steric Shield - Electronic Effects of Bioisostere - Stereoelectronic Modification - Metabolic Blockers - Removal or Replacement of	Textbooks 1-٤/	

		Susceptible Groups - Self- destructive Drugs		
7	١ ١ ١	**Optimizing Hydrophilic/Hydrophobic Properties** - Variation of Alkyl or Acyl Substituents to vary polarity - Variation of Polar Substituents to vary polarity - Variation of *N*-alkyl to vary pKa - Variation of aromatic to vary pKa - Bioisosteres of Polar Groups	Textbooks 1-٤/	
8-9	١ ١ ١ ١ ١ ١	**Receptors as Drug Targets** - Design of Agonists: - Binding Groups - Position of the Binding Groups - Size and Shape - Allosteric Modulators - Design of Antagonists: - Antagonists acting at the binding site - Antagonists acting out with the binding site - Antagonists as Molecular Labels - Partial Agonist - Inverse Agonist	Textbooks 1-٤/	
10-11	١ ١ ١ ١ ١ ١	**Enzyme as Drug Targets** - Inhibitors acting at the active site of an enzyme - Reversible Inhibitors - Irreversible Inhibitors - Inhibitors acting at the allosteric binding site - Competitive and Non-competitive Inhibitors - Transition-state Analogues - Suicide Substrates - Isozyme selectivity of inhibitors - Medical Uses of Enzyme Inhibitors	Textbooks 1-٤/	
12	١ ١ ١	**Molecular Modeling** - Computational Methods. - Potential energy. - Molecular mechanics - Quantum Mechanics - Conformational analysis - Molecular Dynamic Simulation (MD) - X-ray crystallography	Textbooks 1-٤/	

		- Superposing		
13	1	**Structure-Based Drug Design (SBDD)** - Molecular Docking	Textbooks 1-٤/	
13	١ ١	**Combinatorial Chemistry** - General Aspects. - Parallel Synthesis. - Solid Phase Technique. - Split synthesis: peptide libraries. - Anchors. - Protecting Groups.	Textbooks 1-٤/	
14-15	١ ١ ١ ١ ١ ١	**Ligand-Based Drug Design (LBDD)** - Pharmacophore modeling - Quantitative Structure-Activity Relationships (QSAR) - Methods to correlate physicochemical parameters with biological activity. - Equations and Graphs - Physicochemical Parameters - Hydrophobicity - Electronic Property - Steric Property - Hansch Analysis. - De Novo Method. - Enhancement Factor. - Topliss Schemes. - COMFA	Textbooks 1-٤/	

Approved by Dept. Chair		Date of Approval	

Extra Information: (Updated every semester and filled by course instructor)

Course Instructor	Dima A. Sabbah, Ph.D.
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