UNIVERSITÀ DEGLI STUDI DI PALERMO

DEPARTMENT	Scienze e Tecnologie Biologiche, Chimiche e Farmaceutiche		
ACADEMIC YEAR	2016/2017		
MASTER'S DEGREE (MSC)	PHARMACEUTICAL CHEMISTRY AND TECHNOLOGIES		
INTEGRATED COURSE	ADVANCED MEDICINAL CHEMISTRY AND DRUG DESIGN - INTEGRATED COURSE		
CODE	13186		
MODULES	Yes		
NUMBER OF MODULES	2		
SCIENTIFIC SECTOR(S)	CHIM/08		
HEAD PROFESSOR(S)	TUTONE MARCO	Professore Associato	Univ. di PALERMO
OTHER PROFESSOR(S)	MARTORANA ANNAMARIA	Professore Associato	Univ. di PALERMO
	TUTONE MARCO	Professore Associato	Univ. di PALERMO
CREDITS	12		
PROPAEDEUTICAL SUBJECTS	01870 - MEDICINAL AND TOXICOLOGICAL CHEMISTRY 2		
MUTUALIZATION			
YEAR	4		
TERM (SEMESTER)	2° semester		
ATTENDANCE	Not mandatory		
EVALUATION	Out of 30		
TEACHER OFFICE HOURS	**MARTORANA ANNAMARIA** Monday 11:00 13:00 Viale delle Scienze, edificio 17 studio 1/A9 Wednesday 11:00 13:00 Viale delle Scienze, edificio 17 studio 1/A9 **TUTONE MARCO** Tuesday 11:00 13:00 Wednesday 11:00 13:00		

DOCENTE: Prof. MARCO TUTONE

PREREQUISITES	Knowledges on organic chemistry and biochemistry Basic knowledges on geometry of small molecules and proteins
LEARNING OUTCOMES	Knowledge and comprehension abilities Acquisition of advanced tools for the development of studies to clarify the molecular mechanisms of drug action . Ability to use the specific language of this very specialized discipline . Applying knowledge and comprehension Ability to recognize and apply independently, methodologies necessary to study, also quantitative, the drug-receptor interactions . Autonomy of judgement
ASSESSMENT METHODS	The student is evaluated through two oral examinations. He/she must answer at least three/four questions covering all aspect of the program. The oral examination tends to evaluate wheter the student has developed knowledge, understanding and the ability to integrate the topics within the program. The threshold of sufficiency will be achieved if the student shows knowledge and understanding of the topics at least in general terms with sufficient communicative skills. Below this threshold the exam will be unsatisfactory and student will not pass it. On the contrary, the more the student will interact with the examining board with better expositive skill and deeper knowledge, the more the evaluation will be positive. The assessment is carried out of thirty.
TEACHING METHODS	Frontal lectures, Practice

MODULE
DRUG DESIGN

Prof. MARCO TUTONE

SUGGESTED BIBLIOGRAPHY

C.G.Wermuth: “Le applicazioni della Chimica Farmaceutica” EdiSES, 2000.
A.Gasco, C.Silipo, A.Vittoria: “Le basi chimico-fisiche della progettazione dei farmaci” SES, 1990.
H. Kubinyi in Methods and Principles in Medicinal Chemistry, “QSAR: Hansch Analysis and Related Approaches” VCH, 1993.
AA.VV.: “Burger’s Medicinal Chemistry and Drug Discovery” 6th Edition, Volume 1, Wiley 2003.
AA.VV.: “Comprehensive Medicinal Chemistry II” Volume 4, Elsevier 2007.
“Molecular ConceptorTM” Drug Design Courseware, Version 2.11, Synergix Ltd, 2009 (www.molecular-conceptor.com).
Bultinck, De Winter, Langenaeker, Tollenaere “Computational Medicinal Chemistry for Drug Discovery”, Marcel Dekker Inc., New York Basel, 2004
Gasteiger, Engel “Chemoinformatics a textbook”, Wiley-VCH
Todeschini “Introduzione alla chemiometria”, Edises
Articoli recenti di letteratura chimica reperibili sul web.

AMBIT	50323-Discipline Chimiche, Farmaceutiche e Tecnologiche
INDIVIDUAL STUDY (Hrs)	105
COURSE ACTIVITY (Hrs)	45

EDUCATIONAL OBJECTIVES OF THE MODULE

The student have to acquire the skills necessary to understand the problems related to the development and design of drugs, using quantitative structure - activity relationships, also applying mathematical methods, statistics and computer-aided methods to the pharmaceutical field .

SYLLABUS

Hrs	Frontal teaching
2	Focus and organization of the course . Hardwares and softwares for drug design
2	Drug discovery: rational drug design
8	2D and 3D representation of molecules. Molecular properties (surfaces, volumes, MEP, electron density, partition coeffiecient logP, accessible surface area, molecular connectivity, etc.). Molecular Mechanics, exploration of the conformational space and search of energetic minimum. Similarity and diversity, 1D 2D and 3D molecular descriptors.
12	Ligand-based drug design, pharmacophore modelling, problem analysis (data collecting, pharmacophore hypothesis generation). QSAR and 3D-QSAR models, models validation , application of predictive QSAR and 3D-QSAR models to database mining
8	Structrure-based drug design. Homology modelling, threading, ab initio modelling of proteins, model validation, Ramachandran plot. Docking, Induced-Fit Docking, MM-GBSA, FEP and Covalent Docking. Site Mapping
5	Molecular Dynamics
2	Semi-empirical methods, quantum-mechanical methods, DFT (Functional density theory), hybrid methods QM/MM. Accuracy and applicability of quantum-mechanical methods to pharmaceutical science

Hrs	Practice
6	Tutorial Practice of drug design

MODULE
ADVANCED PHARMACEUTICAL CHEMISTRY

Prof.ssa ANNAMARIA MARTORANA

SUGGESTED BIBLIOGRAPHY

Manuale di Chimica Farmaceutica - Progettazione, meccanismo d'azione e metabolismo dei farmaci (a cura di A.M.Almerico, A.Di Stilo, R.Fruttero, A.Lauria, G.Murineddu, G.Pinna, F.Pinnen) 2015, Edizioni EDRA SpA. Edizione Italiana di: R.B.Silverman, M.W.Holladay: "The organic chemistry of drug design and drug action." Third Edition., 2014, Elsevier
C.G.Wermuth: "Le applicazioni della Chimica Farmaceutica" 2000, EdiSES.
T.L.Lemke, D.A.Williams: "Foye's Principi di Chimica Farmaceutica." IV Edizione Italiana 2005, Piccin Nuova Libraria S.p.A., Padova.
TESTI DI CONSULTAZIONE:
AA.VV.: "Burger's Medicinal Chemistry and Drug Discovery" 6th Edition, Wiley 2003.
AA.VV.: "Comprehensive Medicinal Chemistry II" Elsevier 2007.
"Molecular

AMBIT	50323-Discipline Chimiche, Farmaceutiche e Tecnologiche
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COURSE ACTIVITY (Hrs)	45

EDUCATIONAL OBJECTIVES OF THE MODULE

The expected educational objective of this discipline is to let the student acquire the skills needed to understand the relevant topics in the study of drug-receptor interactions and lead optimization, in order to identify new targets and to develop new drug molecules.

SYLLABUS

Hrs	Frontal teaching
6	Explanation of educational objectives of the discipline: its organization and final exam. Definition of Medicinal Chemistry. Generation of new drug molecule: discovery phase, optimization phase, development phase. Definitions: xenobiotic, drug, active molecule, medicament. Names of drugs, codes: CAS, EINECS. Classification of drugs. Molecular action of drugs.Characterization of biophases from a molecular point of view. Aqueous phase. Lipid phase. Lipids of membrane: phospholipids, glycolipids, cholesterol.
10	Study of the targeted receptor. Visualization of the proteins of membrane in 3D: peptide bonds, amino acids. Chemistry of the ligand-receptor complex: cell response, physiological response. Non-catalytic receptors. Ligand-gated ion channels. G protein-coupled receptors. 3D evaluation of receptors coupled to G proteins: effectors modulated by G proteins. Membrane receptors with intrinsic enzymatic activity. Intracellular receptors. Catalytic receptors: enzymes, DNA. Molecular Mechanism of Drug Action. Chemistry of drug binding to receptors: chemical bond (covalent and noncovalent), the free energy associated to a biochemical reaction. Study and analysis of examples of drug-receptor complex preparatory for the in silico evaluation of a lead compound.
11	Strategies in the search of new lead compounds: improvement of existing drugs, systematic screening, exploitation of biological information, planned research and rational approaches (computer-assisted drug design). Natural products as pharmaceuticals and sources for lead structures. New developments in medicinal chemistry: nutraceuticals and functional foods.
18	Combinatorial chemistry and high-troughtput synthesis. Flow chemistry. Lead compounds generation. Primary exploration of structure-activity relationships. Isostery. Bioisostery. Molecular variations in homologous series. Vinylogues and benzologues. Molecular variations based on isosteric replacements. Ring transformations. Qualitative and quantitative aspects of structure-activity relationships: specific substituent effects, stereochemical aspects, chiral switching. Application strategies for primary structure-activity relationship exploration.