# UNIVERSITÀ DEGLI STUDI DI PALERMO

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| **DEPARTMENT** | Scienze e Tecnologie Biologiche, Chimiche e Farmaceutiche | | |
| **ACADEMIC YEAR** | 2018/2019 | | |
| **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)** | 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** | **TUTONE MARCO**<br>Tuesday 11:00 13:00<br>Wednesday 11:00 13:00 | | |

**DOCENTE:** Prof. MARCO TUTONE

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| **PREREQUISITES** | Knowledges of organic chemistry and biochemistry. Basic knowledges of 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 oral or written examination for each module. The final evaluation consists of an oral examination which will take into account of the mean of the marks obtained in each module He/she must answer at least three/four questions covering all aspect of the program. The examination tends to evaluate whether 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 |

## MODULE
## ADVANCED PHARMACEUTICAL CHEMISTRY

*Prof. MARCO TUTONE*

**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: “The Practice of Medicinal Chemistry” fourth edition, Academic Press, Elsevier.
T.L.Lemke, D.A.Williams: “Foye’s Principi di Chimica Farmaceutica.” IV Edizione
Italiana 2005, Piccin Nuova Libraria S.p.A., Padova.
Wei Zhang, Berkeley Cue, "Green Techniques for Organic Synthesis and Medicinal Chemistry" second edition, Wiley
S.E. Manahan, "Green Chemistry and the ten commandaments of sustainability", second edition, ChemChar Research Inc.
TESTI DI CONSULTAZIONE:
AA.VV.: “Burger’s Medicinal Chemistry and Drug Discovery” 6th Edition, Wiley 2003.
AA.VV.: “Comprehensive Medicinal Chemistry II” Elsevier 2007.

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| **AMBIT** | 50323-Discipline Chimiche, Farmaceutiche e Tecnologiche |
| **INDIVIDUAL STUDY (Hrs)** | 102 |
| **COURSE ACTIVITY (Hrs)** | 48 |

**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 |
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| 10 | Explanation of educational objectives of the discipline: its organization and final exam. Evaluation of the Biological Activity of Compounds: Techniques and Mechanism of Action Studies |
| 20 | Drug Targets, Target Identification, Validation, and Screening. Strategies in the Search for New Lead Compounds or Original Working Hypotheses. Natural Products as Pharmaceuticals and Sources for Lead Structures. Molecular Variations Based on Isosteric Replacements. Theoretical Aspects of Ligand Binding. Hit Optimization Strategies. The Role of Functional Groups in Drug-Receptor Interactions. Systems Biology: A New Paradigm for Drug Discovery. Drug Nomenclature. Protection of Inventions in Medicinal Chemistry |
| 18 | Principles of Combinatorial chemistry. Basic ideas and concepts of Combinatorial Chemistry. Synthetic methods & techniques in combinatorial synthesis. Characterisation of the synthesized compounds. Flow chemistry. Green Chemistry, and Environmental Chemistry. Flow chemistry. |

**MODULE**
**DRUG DESIGN**

*Prof. MARCO TUTONE*

**SUGGESTED BIBLIOGRAPHY**

"In silico Drug Discovery and Design: Theory, methods, challenges and applications." Edited by Claudio Cavasotto.
"Computational drug discovery and design" Riccardo Baron Editor, Springer, Humana Press.
"Chemoinformatica" Mabilia et al, Springer BioMed.
C.G.Wermuth: “The Practice of Medicinal Chemistry” Fouth edition, Academic Press, Elsevier.
A. Leach, "Molecular Modelling - Principles and applications", Pearson education.
Y. Connoly Martin, "Quantitative Drug Design - A Critical Introduction", CRC Press.
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.
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.

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| **AMBIT** | 50323-Discipline Chimiche, Farmaceutiche e Tecnologiche |
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| **COURSE ACTIVITY (Hrs)** | 48 |

**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 |
|---|---|
| 4 | Focus and organization of the course .<br>Hardwares and softwares for drug design |
| 8 | 2D and 3D representation of molecules, Molecular properties . Protein cristallography.<br>Molecular Mechanics, exploration of the conformational space and search of energetic minimum.<br>Similarity and diversity, 1D 2D and 3D molecular descriptors. |
| 10 | 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 |
| 10 | 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 |
| 8 | Fragment-Based Drug Design. 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 |
| 2 | Web Alert: Using the Internet for Medicinal Chemistry |
| 4 | Tutorial Practice of drug design |