VNIVERSITAT DE VALÈNCIA

Course Guide
44613 Medicinal chemistry

COURSE DATA

Data Subject	
Code	44613
Name	Medicinal chemistry
Cycle	Master's degree
ECTS Credits	5.0
Academic year	2018 - 2019

Study (s)

Degree	Center	Acad. year	Period
2218 - Master's Degree in Chemistry	Faculty of Chemistry	1	Second term

Subject-matter

Degree	Subject-matter	Character
2218 - Master's Degree in Chemistry	8 - Medicinal chemistry	Optional

Coordination

Name	Department
ANDREU MASIA, CECILIA	325 - Organic Chemistry

SUMMARY

The subject of Medicinal Chemistry in the Master of Chemistry is fundamentally directed to graduates in Chemistry or other related technological sciences who wish to acquire basic knowledge of this branch of Chemistry. Medicinal Chemistry, as an interdisciplinary science, connects with other branches of science such as Physiology and Pharmacology. For this reason, the specific aspects related to the physiological and pharmacological bases that are essential for the understanding of the processes involved in the action of the drugs will be first studied. In the following themes, fundamental aspects of the subject will be developed, such as pharmacokinetics and pharmacodynamics, drug metabolism, qualitative and quantitative structure-activity relationship, novel drug design strategies, synthesis scaling problems, etc. Subsequently, specific therapeutic groups based on metals of special relevance, such as cisplatin and other similar anticancer agents, antimicrobial and antiparasitic, antiarthritic, antiviral, etc. will be studied in a specific way. Finally, the subject will be completed with the study of different analytical techniques that allow the estimation of biomedical parameters of interest and high-throughput screening techniques. Metabolomics will be introduced as a diagnostic and prognostic technique, and its application in vivo in the clinical diagnosis, prognosis and follow-up of therapy will be considered.

PREVIOUS KNOWLEDGE

Relationship to other subjects of the same degree

There are no specified enrollment restrictions with other subjects of the curriculum.

Other requirements

Chemistry knowledge acquired during the Chemistry Degree are required.

COMPETENCES (RD 1393/2007) // LEARNING OUTCOMES (RD 822/2021)

2218 - Master's Degree in Chemistry

- Be able to solve complex chemistry problems, whether in the academic, research or industrial application areas at a specialization or masters-level.
- Possess the necessary skills to develop multidisciplinary activities within the field of chemistry at the master's level.
- Be able to design, perform, analyse and interpret experiences and complex data in the environment of chemistry at a specialization level.
- Acquire advanced knowledge to assess the importance of chemistry in health, the environment, new materials and energy.
- Acquire the necessary advanced knowledge to assess the importance of chemistry in economic and social development in a context of specialization.

LEARNING OUTCOMES (RD 1393/2007) // NO CONTENT (RD 822/2021)

• Select the most appropriate analytical techniques for the estimation of biomedical parameters of interest based on their characteristics and applicability.

• Know the fundamentals of structure-activity relationships, demonstrate a critical knowledge of QSAR methods and their application.

• Know and understand how to use *in silico* drug design methods based on molecular topology or on the drug-receptor interaction.

• Know experimental quantitative methods for the determination of the metabolic profile, as well as to analyze NMR spectra.

• Introduce Metabolomics as a diagnostic and prognostic technique and its *in vivo* application in the clinical diagnosis, prognosis and follow-up of the therapy.

• Know the general biosynthetic pathways of the secondary metabolites and apply the fundamental knowledge of organic reactivity to the understanding of the mechanisms of biosynthetic reactions.

• Predict metabolic changes in drugs.

• Recognize chemical and biochemical processes based on the structure / activity relationship.

• Describe and apply some computational techniques used in the design of drugs and combine NMR data with those obtained by computational chemistry techniques to understand the structural requirements of ligand-receptor molecular recognition processes.

• Know how to design effective drug syntheses.

DESCRIPTION OF CONTENTS

1. Introduction

Medicinal Chemistry and its field of study. Phases in the development of a drug. Drug nomenclature systems. From the drug to the medicine.

2. Pharmacokinetic and pharmacodynamic phases in the drug action

Concept and chemical nature of the biological targets. Stages to consider in the action of the drugs: ADME. Nature of the cell membrane. Physicochemical models that explain the transport through membranes. Physicochemical properties influencing in the pharmacological action. Representative examples. Molecular topology and pharmacological action.

3. Drug metabolism

Phase I metabolic processes: Oxidations, reductions and hydrolysis. Phase II metabolic processes. Consequences of metabolism. Stereochemical selectivity of metabolic processes. Metabolic polymorphism. Metabolic interactions. Control of the activity of the drug by its metabolism. Design of biorreversible drugs: prodrugs and drugs of controlled inactivation.

4. General aspects of drug design (1)

Qualitative structure-activity relationships. Methods of finding and discovering new drugs. Biological structure-activity qualitative relationships: pharmacophoric groups and auxophores. Pharmacodynamic techniques. Biochemical design strategies.

5. General aspects of drug design (2)

Structure-activity quantitative relations. QSAR and QSPR methods. Types of properties (bulk and molecular. Specific and non-specific). Types of molecular descriptors (physical, geometrical and topological). Extra-thermodynamic approximation: Hansch-Fujita and Free-Wilson methods. Statistical methods of correlation. Molecular topology. Some results obtained by molecular topology. NMR applications in the ligand-target molecular recognition processes.
Molecular modelling: Molecular dynamics, molecular mechanics, quantum mechanics. Receptor-based

methods. Docking. Ligand-based methods. Application of QSAR methods. Alignment methods. CoMFA. Molecular-topology-based methods. Main concepts and results.

6. Synthesis of drugs: parallel and combinatorial synthesis

Introduction to combinatorial and parallel synthesis.
Chemical and process development: Factors to consider in the scaling processes. Selection of route, reagents and solvents. Optimization of processes to minimize impurities. Representative examples.

7. Therapeutic agents based on metals (1)

Anticancer agents. Cisplatino: history and mechanism of action. Second generation of platinum based drugs: carboplatin and oxaliplatin. Analog drugs of cisplatin for oral administration: satraplatin and gallium compounds. Anticancer drugs based on ruthenium and other elements. Radiopharmaceuticals based on metals: 89Sr, 90Y, 153Sm, 223Ra. Use of metal porphyrins in photodynamic therapy.

8. Therapeutic agents based on metals (2)

Antimicrobial and antiparasitic agents based on pnictogens. Antibacterial properties of silver ions. Antiproliferative properties of macrocyclic chelating agents. Antiarthritics and other gold based drugs. Vanadium salts in the treatment of diabetes. Polyoxometalates and other inorganic antiviral drugs. Treatment of trace element deficiencies: Menkes disease (Cu), anemia (Fe), osteoporosis (Ca). Treatment of superabundance of trace elements: chelation therapy. Cardiovascular diseases: NO, nitroprussiate and analogues of superoxydodismutasas. Antacids. Use of lithium salts in bipolar disorder.

9. Inorganic compounds for clinical diagnosis (1)

Magnetic resonance contrast agents. Physical Principles of NMR Imaging. Relaxation of Gd (III) complexes. Interactions of contrast agents with proteins. Stability and toxicity of Gd (III) compounds. Structure and molecular dynamics. Other contrast agents based on Mn (II) salts and magnetic nanoparticles. X-ray contrast agents: iodinated compounds.

10. Inorganic compounds for clinical diagnosis (2)

Fundamentals of neutron capture therapy: boron and gadolinium compounds. Use of 99mTc, 68Ga and other radionuclides in diagnosis and therapy: gamma ray and positron emission techniques. Luminescent compounds for clinical diagnosis based on transition metals and lanthanoids.

11. Estimation of biomedical parameters using analytical techniques

Analytical techniques for the estimation of biomedical parameters. Chromatographic and electrophoretic techniques in drug design. High performance screening techniques.

12. Introduction to metabolomics

Fundamentals. Chromatographic and electrophoretic techniques combined with mass spectrometry. Chemometric techniques. Applications in drug R & D.

WORKLOAD

ACTIVITY	Hours	% To be attended
Theory classes	40,00	100
Tutorials	5,00	100
Seminars	5,00	100
Development of individual work	35,00	0
Study and independent work	40,00	0
TOTAL	**125,00**	

TEACHING METHODOLOGY

The subject will be taught through participatory master lessons, seminars where practical problems will be solved and tutored classes oriented to evaluate the student's understanding of the subject. In addition, the Virtual Classroom platform will be used for communication and information exchange.

EVALUATION

First call:

The qualification of the subject in first call will be obtained from the notes resulting from the final exam (70%) and the continuous evaluation activities carried out during the course (30%). The minimum score for each item must be equal to or greater than 4.5 in order to make the average.

The exam will be unique and will consist of four parts, each of which will contribute to the final grade in proportion to the number of theoretical classes dedicated. In order to be able to average between the different parts, a minimum grade of 3.0 will be required in each one of them.

The minimum overall grade to pass the subject will be 5.0.

Second call:

The qualification of the subject, in second call will be obtained applying the same criteria as in the first call.

REFERENCES

Basic

- Patrick GL (2013) An Introduction to Medicinal Chemistry. Oxford Univ. Press, 5ª ed.
- Avendaño C (2001) Introducción a la Química Farmacéutica. Ed Interamericana - McGraw-Hill, 2ª ed.
- Dewick PM (2006) Essentials of Organic Chemistry. Ed Wiley.
- Anderson NG (2012) Practical Process Research & Development. A Guide for Organic Chemists. Academic Press, 2ª ed.
- Patrick GL (2014) An Introduction to Drug Synthesis. Oxford University Press.
- Devillers J y Balaban AT (1999) Topological Indices and Related Descriptors in QSAR and QSPAR. Gordon & Breach, New York.
- Young DC (2009) Computational Drug Design. A Guide for Computational and Medicinal Chemists. John Wiley & Sons, Inc., Hoboken, NJ.
- Castro EA (2010) QSPR-QSAR Studies on Desired Properties for Drug Design, Research Signpost.
- Dralle Mjos K, Orvig C (2014) Chem Rev 114, 4540.
- Wong E, Giandomenico CM (1999) Chem Rev 99, 2451.
- Ho Y-P, Au-Yeung SCF, To KKW (2003) Med Res Rev, 23, 633.
- Wheate NJ, Walker S, Craig GE, Oun R (2010) Dalton Trans, 39, 8113.
- Wilson JJ, Lippard SJ (2014) Chem Rev 114, 4470.
- Cutler CS, Hennkens HM, Sisay N, Huclier-Markai S, Jurisson SS (2013) Chem Rev 113, 858
- Scott LE, Orvig C (2009) Chem Rev 109, 4885.
- Caravan P, Ellison JJ, McMurry TJ, Lauffer RB (1999) Chem Rev 99, 2293.
- Soloway AH, Tjarks W, Barnum BA, Rong F-G, Barth RF, Codogni IM, Wilson JG (1998) Chem Rev 98, 1515.
- Anderson CJ, Welch M (1999) Chem Rev 99, 2219.
- McPherson RA, Pincus MR (2016) "Henry's Clinical Diagnosis and Management by Laboratory Methods", 23 ed, Elsevier, Amsterdam.
- Watson DG (2016) "Pharmaceutical Analysis", 4ª Ed, Elsevier.

- Lindon JC, Nicholson JK, Holmes E (2007) The Handbook of Metabonomics and Metabolomics, Elsevier

Additional

- Camps P, Vázquez S, Escolano C (2009, 2010) Química Farmacéutica I. Tomos 1 y 2. Publicacions i edicions Universitat de Barcelona.
- Avendaño C (1997) Ejercicios de Química Farmacéutica. Ed. Interamericana. Mc. Graw-Hill.