Universidad Zaragoza

Academic Year/course: 2021/22

68458 - Medicinal Chemistry

Syllabus Information

Academic Year: 2021/22
Subject: 68458 - Medicinal Chemistry
Faculty / School: 100 - Facultad de Ciencias
Degree: 626 -
ECTS: 6.0
Year: 01
Semester: Second semester
Subject Type: Optional
Module:

1. General information

1.1. Aims of the course

This course and its expected results respond to the following approaches and objectives:

One of the main objectives of this subject is to provide students with an overview of medicinal chemistry at the intersection between synthetic organic chemistry, pharmacology and medicine, directly related with other biological subjects which are also addressed in this master's degree. This subject will emphasize aspects such as the design, chemical synthesis and development of pharmaceutical agents or bioactive molecules, as well as the launch to the market of these compounds and their patentability. In addition, students are expected to become familiar with the synthesis of organic compounds used as drugs and to acquire knowledge of other more complex structures such as proteins and derivatives.

Students will be able to understand the use of synthetic organic chemistry and computational chemistry as tools closely related to biological chemistry, enzymology and structural biology, with the aim of discovering and developing new therapeutic agents.

Moreover, key chemical compounds and structural families will be identified for their subsequent therapeutic use. On the other hand, synthetic and computational aspects will be included in the study and development of drugs and their relationship with their biological activity, i.e., the understanding of their structure-activity relationship (SAR).

These approaches and objectives agree with the following Sustainable Development Goals (SDGs) of the United Nations Agenda 2030 (https://www.un.org/sustainabledevelopment/es/), in such a way that the acquisition of the learning results of this subject provides training and competence to contribute to a certain extent to its achievement:

Goal 3: *Health and wellness*
Goal 4: *Quality education*

1.2. Context and importance of this course in the degree

This elective subject, which belongs to the third module of the master's degree that includes the subjects of the second semester, will allow students to deepen their training as molecular biotechnologists, enabling them to configure a personalized curriculum in which they can combine instrumental, methodological, statistical, modeling and/or related to the creation and management of biotechnology companies.

This elective course is really necessary and coherent in this master's degree where, after the student has taken the obligatory courses of the first four-month period, he/she can study in depth the design, obtaining and improvement of new compounds for their biological evaluation, with the ultimate aim of establishing relationships between the chemical structure and the biological activity that contribute to the development of new drugs.

This course will make the student aware of the problems involved in the interaction of drugs with the biological environment (usually the human body) in which they must exert their effect.

It is also essential for students to acquire knowledge about how the pharmaceutical industry works. This is one of the most dynamic industrial sectors which, being related to health, continues growing due to the social demand for new, more effective, safer and personalized drugs.

This subject contributes to answer all these aspects that are not addressed in the other subjects of this master.

1.3. Recommendations to take this course

It is recommended that the students assist to the whole course.

2. Learning goals

2.1. Competences

Upon successful completion of the course, the student will be more competent to:

Basic competences of this subject:

CB6 ? To have and to understand knowledge that provides a basis or an opportunity to be original in the development and / or implementation of ideas, often in a research context.

CB7 ? The students know how to implement the acquired knowledge and their ability to solve problems in new or little-known environments within broader (or multidisciplinary) contexts related to their area of ??study.

CB8 ? The students are able to integrate knowledge and face the complexity of providing opinions based on information that, being incomplete or limited, includes reflections on social and ethical responsibilities linked to the application of their knowledge and opinions.

CB9 - The students know how to communicate their conclusions and the latest knowledge and reasons that support them to specialized and non-specialized audiences in a clear and unambiguous

way.

CB10 - The students have the learning skills that allow them to continue studying, largely self-directed or autonomously.

Specific competences of this subject:

CE05 ? To design cell and animal tests of toxicity, bioavailability and effectiveness of bioactive compounds.

CE06 ? Apply statistical techniques to carry out studies that relate molecular structure with biological activity and allow to generate predictive models.

CE018 - Evaluate the interest of a determined molecule or biological structure as a therapeutic target.

CE019 - Know the basic tools of Medical Chemistry.

CE020 - Design pharmacokinetic and pharmacodynamic tests adapted to specific compounds.

CE021 - Apply design principles to improve the ADMET properties of candidate compounds.

CE022 - Understand the approval and marketing process of a drug.

Generic competences of this subject:

CG01 ? To arrange, analyze critically, understand and synthesize information.

CG02 ? To obtain information from different types of sources and evaluate their reliability.

CG03 ? To learn efficiently through autonomous study and acquire a significant level of independence.

CG04 ? To implement the acquired knowledge and solve problems in new or unfamiliar environments within broader (or multidisciplinary) contexts related to the study area.

CG05 ? To formulate, analyze, evaluate and compare new or alternative solutions for different problems.

CG07 ? To develop capacity for criticism and self-criticism.

CG09 - Be able to develop a project, participating in the stages of bibliographic search, experiment planning, obtaining results, interpretation, and dissemination of the same.

2.2. Learning goals

The student, in order to pass this subject, must demonstrate the following results:

1. To know the main therapeutic targets for which drugs exist.

2. To know the main design tools used in Medical Chemistry.

3. To know the ADMET tests that are carried out on a candidate molecule to evaluate its potential as a drug.

4. To know the strategies of Medical Chemistry to improve the ADMET properties of a compound.

5. To understand the pathway that a preclinically evaluated compound follows before it becomes a commercial drug.

2.3. Importance of learning goals

They serve, first of all, to introduce students into the world of medicinal chemistry and its relation with drugs, as well as to the entire route that the drugs follow until they reach the market.

They allow the student to face the synthesis of a given simple drug with the basic design tools in Medicinal Chemistry (organic synthesis and computational tools).

They provide students with tools for computational analysis of the characteristics of a biologically active molecule in order to establish its structure-activity relationships (SARs).

All of the above-mentioned will be of great help to successfully face the learning of other subjects of this master's degree and also during the future professional career of the students.

3. Assessment (1st and 2nd call)

3.1. Assessment tasks (description of tasks, marking system and assessment criteria)

The student must demonstrate the achievement of the learning outcomes through the following evaluation activities.

A continuous evaluation will be carried out. However, the students will also have the option of taking the global evaluations according to the UZ exam calendar for the two official calls.

The activities and evaluation criteria for the continuous evaluation and the global evaluation (first and second call) are described below.

Continuous Evaluation

1. Problem solving classes and case studies (20% of FG)

The resolution of these exercises constitutes an individual or group work of the students. The students must submit a report at the end of each session following the guidelines and presentation format to be indicated. The qualifications and the corrected exercises will be made available to students. These types of controls are framed within the concept of continuous evaluation, which will allow monitoring of the learning process.

2. Theoretical Exam (50% of FG)

The theoretical exam will consist of questions that require either short answers (limited response tests) or a broad development of the topic (essay tests or free and open answer). The first type will allow a comprehensive sampling of the student's knowledge of the subject, and the second type will allow an

assessment of their ability to express themselves, to present and keep arguments, and to make critical judgments. The written test will be based on the scheduled learning activities.

In order to take the exam, the student will be able to consult the bibliography that he/she considers appropriate (web pages or similar cannot be consulted).

3. Evaluation tests of the practical computer sessions (30% of FG)

The student must demonstrate that he/she is making good use of the internship sessions.

Compulsory attendance. The following will be valued: 1. The development of the practice by the student: that is, the way in which the student carries out the practice taking into account the following criteria: -The student is able to work autonomously following the protocol. 2. The report presented at the end of the practices, taking into account the following criteria: - Describe in a convenient way the methods used - Correctly interpret the results - In case of discrepancy in the results, find out the cause of the error and amend it.

4.Complementary activities (up to 1 extra point on the FG)
The activities (seminars, conferences, debates, etc.) that may be proposed as voluntary option may represent an extra mark on the final grade of the course up to a maximum of 1 point.

FG = 0.20 M$_{\text{Problem solving}}$ **+ 0.5 M**$_{\text{Theoretical Exam}}$**+ 0.30 N**$_{\text{Computer Sessions}}$

Global Evaluation (100% of FG)
1. Theoretical Exam (100% of FG)

The theoretical exam will consist of questions that require short answers (limited response tests) or that require a broad development of the topic (essay tests or free and open answer).

In order to take the exam in the global evaluation, the student will not be able to consult the bibliography.

FG = 1 M$_{\text{Theoretical Exam}}$

Therefore, the **overall grade (OG)** of the course will be the **final grade (FG)**, calculated as the weighted average of the evaluation activities described above + the possible extra grade derived from the complementary activities. The extra grade mentioned above will only be added to the GC if it is higher or equal to 4 points out of 10, both in first and second call. The GC will not be able in any case, to exceed the numerical qualification of 10.

OG** = FG + extra grade (CA)**

*** The **overall grade (OG)** will result from the addition to FG of the extra grade (up to 1 point), obtained from the complementary tasks performed on a voluntary basis. These will only be added if

FG is equal or higher than 4, in both calls.

In the evaluation of the tests described above, the accuracy, thoroughness and approach of the answers, as well as the argumentation and critical analysis of them will be positively valued. The understanding of concepts and processes, and the ability to interrelate them, as well as the concreteness, clarity, order and presentation will be also assessed.

If **plagiarism** or other fraudulent actions are detected and confirmed, this will be sufficient reason to evaluate the student with the lowest possible grade on the corresponding test.

The evaluation of this course is planned to be carried out face-to-face, whenever possible. Otherwise, and following the guidelines set out, the evaluation activities will be adapted to allow them to be carried out remotely, trying to maintain, as far as possible, the typology and criteria set out here.

4. Methodology, learning tasks, syllabus and resources

4.1. Methodological overview

The learning process designed for this course is based on lectures of a participative nature that will be complemented with**problem classes, seminars (which may be given by professionals), practical computer sessions and tutorials.**

The theoretical contents of the course will be presented, as well as practical examples that clarify the concepts presented.

4.2. Learning tasks

The program provided to the student to help him/her achieve the expected results includes the following activities:

Master class

Master classes and participative lectures given by the professor, where external experts and/or the students themselves may also intervene.

Problem solving and case studies

The teacher will propose problems and practical cases to be solved individually or in groups. The possible solutions to the problems will be solved and discussed in class, promoting the participation of the students. In addition, the teacher will propose problems and case studies as tasks to be carried out by the student.

Laboratory practices

Students will perform computer practices corresponding to the practices program. These activities will instruct the student on how to approach experimental techniques or computational methods, present data and results provided by the application of these.

Finally, the results will be shared and discussed with the other students. This part of the course

requires individual work by the student. These activities will enable the student to acquire the capacity and skills necessary to describe, quantify, analyze and critically evaluate the results obtained, as well as to use the experimental techniques and methods related to this Master and to design technical and methodological alternatives, all of these by themselves.

Discussions, seminars and conferences

Personalized teacher-student mentoring

Independent student work

Evaluation tests

4.3. Syllabus

Theoretical Program

MIODULE I. Drug targets and drugs

1.- Enzymes and receptors as pharmacological targets

2.- Nucleic acids and other pharmacological targets

3.- Antimicrobial agents

4.- Anticancer agents

5.- Drugs for the central nervous system

6.- Other drugs

MODULE II. Basic tools in Medical Chemistry

7.- Find lead compounds

8.- Combinatorial synthesis

9.- Chiral drugs and their synthesis

10.- (Q)SARs to guide Medical Chemistry

11.- Computers in Medical Chemistry

MODULE III. Drug characterization: pharmacokinetics and pharmacodynamics

12.- Chemical characterization of the lead compounds

13.- Pharmacokinetics and pharmacodynamics

14.- Safety and Toxicology

15.- Animal models of disease

MODULE IV. Chemical strategies to improve drugs

16.- Improvement of solubility and affinity for the target

17.- Improvement of chemical and metabolic stability

18.- Improvement of protein binding and permeability

19.- Decreased toxicity

20.- Improved administration (prodrugs and encapsulation)

MODULE V. From the drug to the patient

21.- Intellectual property and patents in drug discovery

22.- Fundamentals of clinical trials

23.- Bringing the drug to the market

24.- Illustrative examples in drug discovery

Note: The order of these topics may be changed, depending on teaching and organizational needs.

Practices program. The student will perform a type A or type B practice.

Practice type A. During 7 computer sessions of 3 hours, the student will convert a molecule (hit), active against a target of known structure, into a lead, ideally addressing all of the following:
Design of a synthetic route for the hit to facilitate the synthesis of derivatives.

- Calculation of its solubility and its ADMET properties.
- In view of these properties and the desired pharmacological activity: proposal of improved variants by design of derivatives or by searching for analogues by similarity, substructure or pharmacophore.
- Proposal of a formulation and an administration protocol to test its pharmacological activity in an animal model.
- Writing a patent application.
- Design of a Phase I clinical trial.

Practice type B. During 7 computer sessions of 3 hours, the student will be in charge of redesigning a protein drug in order to achieve:

- Improving protein stability (solubility, conformational stability, tendency to aggregate, presence of proteolysis or modification sequences).
- Incorporating, if applicable, cellular vehiculation functionalities.
- Planning strategies to optimize target affinity.

The student will design a new protein drug sequence that, with as few changes as possible, solves the initial problems of the molecule. He/she will also design a suitable expression vector to produce the drug recombinantly. In the case of designing a vaccine, instead of an expression vector, an immunization vector will be designed.

Note: The practices program may be slightly altered, depending on teaching and organizational needs.

4.4. Course planning and calendar

Schedule of classroom sessions and presentation of homework

This is a 6 ECTS course that is scheduled within the group of electives that can be taken in the second semester of the first year of the Master in Biophysics and Quantitative Biotechnology.

All information about **timetables and exam schedules** is published on the website of the Faculty of Science.

In reprographics and/or through the Digital Teaching Ring, students will be provided with a variety of teaching materials.

The teaching of this course is planned to be carried out face-to-face, whenever possible. Otherwise, and following the guidelines set out, the evaluation activities will be adapted to allow them to be carried out remotely, trying to maintain, as far as possible, the typology and criteria set out here.

4.5. Bibliography and recommended resources

http://psfunizar10.unizar.es/br13/egAsignaturas.php?codigo=68458