Pharmaceutical Chemistry(20346)

Qualification/course: Bachelor's Degree in Human Biology **Year:** 2 **Term:** 3 **Number of ECTS credits:** 6 **Number of study hours:** 150 **Course Language(s):** Catalan, Spanish, English **Teaching staff:** David Andreu (coordinator), Beatriz G. de la Torre and Ricardo Gutiérrez

1. Presentation of the course

Medicinal Chemistry is an obligatory subject in the degree course in Human Biology which has a value of 6 ECTS credits and is taught in the third term of the second year. The course will be taught by David Andreu (coordinator), Beatriz G. de la Torre and Ricardo Gutiérrez.

2. Competences to be achieved

The goal of the course, as defined in the syllabus, is to provide Human Biology students with a (basic) chemical view of drugs that will make them skilled in identifying chemico-structural patterns in biomolecules and drugs, and to understand how these relate to relevant biological function.

The skills referred to above involve the following general objectives:

a) To relate the concepts of the molecular structure of organic compounds (acquired in Basic Sciences II) with relevant properties such as ionization state, solubility in water/lipids, transmembrane movement, etc.

b) To be able to interpret the effect that substituents or other modifications may have on the molecular properties of a drug.

c) To understand the basic workings and applications of HPLC and gas chromatography. To be able to interpret chromatograms of simple separations.

d) To understand the basic workings and applications of proton NMR and mass spectrometry. To be able to interpret, by using the relevant tables, the ^{1}H NMR spectra of drugs with a simple

molecular structure. To know how to interpret mass spectra (using electronic impact or MALDI-TOF equipment).

e) To understand the basic stages in drug design and development processes.

f) To understand the principal strategies for the molecular modification of drugs, in particular those which aid the metabolism and pharmacokinetics. To be able to identify and interpret them for the development of specific drugs.

g) To be acquainted with the main techniques currently available for drug design using computational methods (2D- and 3D-QSAR, CoMFA, etc.).

h) To identify and interpret the main contents (in terms of design and results analysis) of a typical product of modern pharmaceutical chemistry.

i) To perfect the experimental skills acquired in Basic Sciences II, particularly in relation to separation techniques, both manual and instrumental.

3. Contents

The topics will be taught in the theoretical classes and seminars, and the problems and presentations during the course revolve around the following aspects:

• Review of concepts of organic chemistry relevant to analytical pharmaceutical chemistry: electron structure, acid/base equilibrium, effects of substituents, stereochemistry, reaction mechanisms.

• Analytical techniques (separation, identification) applied to medicines: HPLC, GC, ^{1}H NMR, mass spectrometry.

• Pharmaceutical Chemistry: discovery, development and validation of prototypes.

• Qualitative (conventional SAR) and quantitative (2D- and 3D-QSAR) approaches to the design and modification of drugs.

• Pharmacokinetic aspects of the design and development of drugs.

Topics to be taught during lectures (24 hours)

Lesson 1. Review of the concepts of organic chemistry. Bonding, functional groups, Lewis structures, resonance.

Lesson 2. Acidity and basicity of organic compounds. Solubility and hydrophobicity. Effects of substituents.

Lesson 3. Resonance in benzene and conjugated systems. Effect of substituents on the acidity of phenols, carboxylic acids, etc.

Lesson 4. Stereochemistry (I). Constitution. Conformation. Configuration.

Lesson 5. Stereochemistry (II). Optical isomers. Enantiomers. Diastereomers.

Lesson 6. Stereochemistry (III). Stereochemistry and molecular recognition.

Lesson 7. Separation techniques: chromatography, general concepts. HPLC and GC.

Lesson 8. Analytical techniques: mass spectrometry; instrumental aspects.

Lesson 9. Interpretation of mass spectra for simple drugs.

Lesson 10. Nuclear magnetic resonance. Magnetic properties of nuclei. Chemical shift.

Lesson 11. Factors which influence chemical displacement. Spin-spin coupling.

Lesson 12. Analysis of elementary spin systems and of the spectra of simple drugs.

Lesson 13. Medicinal Chemistry: definition, objectives, terminology. Relationship with other disciplines. Principal types of therapeutic targets.

Lesson 14. Drug-receptor interaction: types of bonding involved: Structural analysis of drug-target interactions.

Lesson 15. Drug solubilty and distribution: pharmacokinetic implications. Concept of drug-likeness. Lipinski's rule of five. Stereochemical aspects of drug action. Chiral switch.

Lesson 16. Research and discovery of prototypes. Stages and strategies in the development of drugs. Systematic screening of natural and synthetic products.

Lesson 17. Structure-activity relationships (I). Structural manipulation of pharmacophores. Disjunctive approaches. Pharmacophore concept.

Lesson 18. Structure-activity relationships (II). Modulative approaches: ring manipulation, homology, isomerization.

Lesson 19. Structure-activity relationships (III). Modulative approaches: vinilogy, isosteric replacement. Peptidomimetics. Conjunctive approaches: twin drugs.

Lesson 20. Structure-activity relationships (IV). QSAR methods.

Lesson 21. Structure-activity relationships (V). QSAR-3D methods.

Lesson 22. General aspects of drug metabolism: review of the main phase I and II reactions. Chemo- and stereoselectivity of metabolic reactions.

Lesson 23. Drug design based on pharmacokinetic criteria (I). Structural manipulation for pharmacokinetic purposes: solubility, permeability, toxicity and metabolic stability modelling. Hard drugs and soft drugs.

Lesson 24. Drug design based on pharmacokinetic criteria (II). Concept of prodrugs and strategies for their design. Other aspects: targeting, synergism, administration and formulation.

Seminars (13 hours)

Seminar 1 (1 h). Computer tools for molecular representation.

Seminar 2 (2 h). Review of organic chemistry concepts: bonding and molecular properties.

Seminar 3 (2 h). Review of organic chemistry concepts: stereochemistry.

Seminar 4 (2 h). Mass spectrometry.

Seminar 5 (2 h). ^{1}H NMR.

Seminar 6 (2 h). Development and modification of drugs (I).

Seminar 7 (2 h). Development and modification of drugs (II).

Presentations by students

Students will give 50-min **presentations** on topics related to medicinal chemistry proposed by the lecturers. Each presentation will be prepared by a group of 5-6 students, as described below.

Practical laboratory sessions (24 hours in total)

Practical Session 1. Determination of paracetamol in plasma through HPLC.

Practical Session 2. Determination of paracetamol, acetylsalicylic acid and caffeine in a drug through liquid chromatography.

Practical Session 3. Separation of the components of a mixture of drugs through liquid-liquid extraction.

Practical Session 4. Spectrophotometric determination of thiocyanate in saliva as an indicator of tobacco consumption.

4. Assessment

Methods

Assessment will be in the form of multiple-choice tests (following Faculty criteria), written essay exams, problem solving, an individual presentation, a group presentation and a laboratory log-book.

Type and number of assessments

1. During the course, problem-solving seminars will be held, during which students will be individually assessed.

2. During the course there will be a group presentation subject to assessment.

3. Midawy through the term a formative assessment test will be conducted, which will include the topics studied so far, and will have a positive affect on the final marks of students who pass the test (marks ≥ 5).

4. With regard to the practical sessions, attitude and behaviour in the laboratory, completion of the log book and interpretation of the results obtained will be evaluated.

5. At the end of the course there will be the final tests, which will consist of ten multiple-choice questions (10% of the total mark) and a small number of questions involving data analysis, conceptual preparation and problem solving, including a possible question about the laboratory practical sessions. Greater priority is given to capacity of analysis than to the memorization of data or concepts (60% of the total mark).

Effect of the different types of assessment on the final mark

Final assessment:

Multiple-Choice Test 10% Essay 55%

Assessment during the course:

Practical work 15%

Individual problems 10%

Presentations 10%

Passing of the formative assessment test (with a mark ≥ 5) will lead to an increase of 5% of this mark, applied to the final summative mark.

Pass criteria

In order to pass the subject, students are required to:

a) Participate in the planned activities. Specifically, there will be ***obligatory attendance checks*** covering the seminar activities, student presentations and laboratory practical sessions.

b)Hand in their laboratory log-books within the specified time-limit.

c) Obtain a minimum mark of 4 in the final assessment test.

Please note: Any form of copying or cheating will lead to the student failing the subject.

Bibliography and teaching resources

5.1. Basic bibliography

Vollhardt, K. P. C.; Schore, N. E. *Química orgánica*. 5a ed. Barcelona: Ediciones Omega, 2007. ISBN 978-8428214315. Avendaño, M. C. (coord.). *Introducción a la química farmacéutica*. 2a. ed. Madrid: McGraw-Hill-Interamericana de España, 2001. ISBN 8448603613. Skoog, D. A.; West, D. M. *Principles of Instrumental Analysis*. 5a. ed. Belmont, CA: Brooks Cole, 2006. ISBN 978-0030012297. Rubinson, K. A.; Rubinson, J. F. *Análisis instrumental*. Madrid: Prentice Hall, 2001. ISBN 8420529885.

5.2. Supplementary bibliography

Wermuth, C. G. (ed.). *The Practice of Medicinal Chemistry*. 3a. ed. Amsterdam: Elsevier-Academic Press, 2008. ISBN 978-0123741943.

6. Methodology

Lectures

The theoretical content will be taught in 24 sessions of one hour each.

Seminars

The seminars are of two types: (i) Seminar 1 (one hour), dealing with the use of computer tools for molecular representation (ChemSketch, Rasmol), and (ii) six seminars (2-7) dealing with problem solving. Attendance to all seminars is obligatory. Seminars will be conducted in groups of ten. At the start of the course, for each of the seminars (2-7) all students will be assigned a problem for which they will be required to find a solution and to be prepared to present this ***individually, on the blackboard, as an assessable activity*** during the relevant seminar.

Students' presentations

Presentations will be conducted in groups of six students, on a topic relating to pharmacological chemistry as assigned by the lecturers and prepared by the group with a lecturer advising as tutor. Each student will have two hours of tutorial so as to prepare the presentation. The latter will last for approximately 40-50 minutes and ***attendance is obligatory***.

Laboratory practical sessions

Practical sessions will be conducted in groups consisting of a quarter of the students on the course. It will be emphasised that students must take a responsible and serious attitude in the laboratory, acting with initiative, independence and a critical spirit, over and above the mere following of an experimental plan. ***Attendance is obligatory***.

Students will, ***during the period of the practical sessions,*** keep a laboratory log book which records in a sufficiently detailed and comprehensible way the different operations performed during the practice session, together with the results obtained and the conclusions arrived at.

Individual study

Students are required to dedicate 78 hours of individual study to solving questions relating to the content of the course.

7. Activities schedule

The schedule for the course activities can be collected during the official Faculty working hours.