COURSE DATA

Data Subject	
Code	34066
Name	Pharmaceutical Chemistry
Cycle	Grade
ECTS Credits	12.0
Academic year	2018 - 2019

Study (s)

Degree	Center	Acad. year	Period
1201 - Degree in Pharmacy	Faculty of Pharmacy and Food Sciences	3	Annual
1211 - D.D. in Pharmacy-Human Nutrition and Dietetics	Faculty of Pharmacy and Food Sciences	3	Annual

Subject-matter

Degree	Subject-matter	Character
1201 - Degree in Pharmacy	6 - Pharmaceutical chemistry	Obligatory
1211 - D.D. in Pharmacy-Human Nutrition and Dietetics	1 - Asignaturas obligatorias del PDG Farmacia-Nutrición Humana y Dietética	Obligatory

Coordination

Name	Department
MEDIO SIMON, MERCEDES	325 - Organic Chemistry

SUMMARY

Pharmaceutical Chemistry (also known as Medicinal Chemistry) is an annual subject taught in the third year of the Degree in Pharmacy and it is worth 12 ECTS credits (including 2.5 credits of laboratory practicals).

The aim of Pharmaceutical Chemistry is to study the chemistry of the active ingredients of drugs in order to determine the relationship between their chemical structure, physicochemical properties, reactivity and biological response, with the ultimate goal of providing the knowledge required for the creation of new drugs.

Since most drugs are organic molecules, Pharmaceutical Chemistry is mainly based on the knowledge of organic chemistry, although it also requires a solid foundation in biochemistry. On the other hand, it also draws on other subjects, such as Pharmacognosy (the study of natural products as a source of new active compounds), Pharmacology (which uses experimental models for the evaluation of new active compounds), and Molecular Pharmacology, which explains the biological effects at molecular level by interpreting the phenomena related to the association between drugs and the biomolecules triggering their action, from the standpoint of both structural and physicochemical properties.

Although the design of drugs – the ultimate objective of Pharmaceutical Chemistry – originally focused mainly on simple chemical modifications of the molecules of natural origin, current design trends are based on the study of the interactions of drugs with their target structures at molecular level. The development experienced by molecular biology and genetic engineering in the last few decades has allowed reaching a detailed knowledge of many target molecules in drug action, such as enzymes, membrane receptors and nucleic acids. Therefore, part of the design of new drugs is currently based on **drug-target interactions**.

The **synthesis** of designed compounds is another aspect to consider in the study of pharmaceutical chemistry.

The content of the theory classes has been organized into three parts. The first one deals with the drugs' origin, development and design, as well as with the study of the factors to be considered as regards their action. The second part focuses on the study of some representative families of drugs, classified by a criterion based on the molecular mechanism rather than on the more traditional pharmacological activity. Finally, a unit dedicated to the characterization of drugs by spectroscopic methods corresponds to the third part of the subject.

These units are supplemented by laboratory practicals. In the lab, students should acquire the basic skills in the experimental techniques and methodology of basic organic synthesis, and also in the isolation and characterization of organic compounds with biological activity.

PREVIOUS KNOWLEDGE

Relationship to other subjects of the same degree

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

Other requirements

Basic knowledge of organic chemistry, both theoretical (chemical structure, reactivity of functional groups and synthetic methodology) and practical (laboratory techniques in organic chemistry) is required. Basic knowledge of structural biochemistry and physiology is also recommended.

OUTCOMES

1201 - Degree in Pharmacy

- To know how interpret, value and communicate relevant data in the different aspects of pharmaceutical activity, making use of information and communication technologies.
- Skill to communicate ideas, analyze problems and solve them with a critical mind, achieving team-working abilities and assuming leadership whenever required.
- Ability to collect and transmit information in English with a level of competence similar to the B1 of the Council of Europe.
- Develop know-hows for their professional career.
- Facility to obtain and analyze information to face scientific problems.
- Ability to pursue continuous training during professional development.
- To develop in students an understanding of the risks associated with the use of chemical substances and laboratory procedures.
- Module: Chemistry - Capability to know the physico-chemical characteristics of the substances used for the manufacture of drugs.
- Ability to design, identify, obtain and analyze drugs and active ingredients.
- Ability to understand the safe use of drugs, taking into account their physical and chemical properties.
- Ability to develop drug synthetic processes using suitable instrumentation and scientific equipment.
- Ability to use spectroscopic techniques for the structural characterization of drugs and active ingredients.

LEARNING OUTCOMES

On successful completion of the course in its twofold approach – theory and practice–, the student should be able to:
- properly use basic scientific terminology related to the subject;
- demonstrate understanding and knowledge of the facts, concepts, principles and basic theories related to the content of the course;
- know how to apply this knowledge to understand and solve problems in daily life;
- properly present scientific works;
- integrate knowledge of pharmaceutical chemistry with knowledge in other fields;
- develop laboratory processes;
- apply laboratory techniques of organic synthesis to the preparation of drugs;
- evaluate and interpret the mode of action and synthesize drugs;
- estimate the risks associated with the use of chemicals and laboratory processes;

- recognise and apply the scientific method;
- understand and interpret scientific papers related to the subject.

DESCRIPTION OF CONTENTS

1. Introduction

Definitions: pharmaceutical chemistry, drug and medicine. Relationship between pharmaceutical chemistry and other sciences. Drug classification criteria. Drug nomenclature. The pharmaceutical industry.

2. Drug targets

Concept of drug target. Drug-target interactions. Chemical nature of the targets: proteins (enzymes and receptors), lipids, nucleic acids and carbohydrates. Examples of drugs that interact with them.

3. Basic concepts in the drug action

Membranes. Physicochemical models that explain the transport across membranes. Physicochemical properties and pharmacological activity: solubility in water, ionization degree, lipid solubility and partition coefficient. Molecular topology and biological activity. Concept of structure, constitution, configuration and conformation: implications in pharmacological activity. Stereoselectivity in drug activity and pharmacokinetics.

4. Drug metabolism

Phase I: Transformation reactions (oxidation, reduction and hydrolysis reactions). Phase II: Conjugation reactions. Bioreversible derivatives: Prodrugs and bioprecursors. "Soft" drugs and "hard" drugs.

5. Design and development of new drugs

Evolution of research and drug discovery methods. Current methods for discovering lead compounds. Qualitative relationships chemical structure-biological activity. Concept of pharmacophore and auxophoric group. Pharmacomodulation: objectives. Pharmacomodulation techniques. Modulative variations: homology, vinylogy, introduction of multiple bonds, bulky groups, opening and closing rings, bioisosterism. Disjunctive variations. Conjunctive variations. Siamese compounds. Examples. Rational strategies in drug design: receptor activation and/or deactivation. Enzyme inhibition. Enzyme inhibitors by structural analogy with the substrate: antimetabolites. Active-site-directed irreversible inhibitors. Suicide inhibitors. Examples. Drug design based on molecular modelling.

6. Quantitative structure-biological activity relationships(QSAR)

Physicochemical parameters. Hammett equation (electronic effects). Taft equation (steric factors). QSAR Hansch equation. Examples. Methods used to correlate physical and chemical parameters with biological activity. Examples.

7. Introduction to drug synthesis

General strategies for C-C and C-heteroatom bond formation. Synthesis and reactivity of simple heterocycles. Fundamentals of asymmetric synthesis.

8. Antibacterial drugs that act by inhibiting enzymes

Inhibitors of the synthesis of tetrahydrofolic acid. Sulfonamides. Inhibitors of bacterial cell wall biosynthesis: penicillins. Production of penicillins. Modifications of penicillins. Semisynthetic penicillins. Production of 6-aminopenicillanic acid. Penicillins resistant to acids: ampicillin and amoxicillin. Penicillins resistant to b-lactamases. Prodrugs of penicillins.
Cephalosporins. Structure. Structure-activity relationship.7-Aminocephalosporanic acid synthesis. Pharmacomodulation of cephalosporins. Synthesis from 7-ACA and from penicillins. Inhibitors of b-lactamase: clavulanic acid. Sulbactam. Others: phosphomicyn. Inhibitors of replication and transcription of nucleic acids: quinolones and fluoroquinolones.

9. Acetylcholine modulating drugs

Cholinergic synapses. Acetylcholine: structure, biosynthesis, metabolism. Cholinergic receptors. Design and synthesis of acetylcholine agonists. Design and synthesis of muscarinic and nicotinic antagonists. Design and synthesis of acetylcholinesterase inhibitors.

10. Norepinephrine modulating drugs

Adrenergic synapse. Noradrenaline and adrenaline: structure, biosynthesis and catecholamine metabolism. Pre-and post-synaptic adrenergic receptors.
Adrenergic agonists: Arylethanolamines: design and synthesis of representative drugs. Indirect adrenergic agonists. Arylethylamines: design and synthesis of representative drugs. Adrenergic antagonists. b-blockers. Aryloxypropanolamines: design and synthesis. Other drugs that affect adrenergic transmission. Inhibitors of the synthesis of NA. Inhibitors of storage release and reuptake of NA.

11. Modulating drugs neurotransmitter in the CNS

Presynaptic and postsynaptic modulators of the g-aminobutyric acid (GABA).
Benzodiazepines and barbiturates. MAO Inhibitors. Selective biogenic amines reuptake inhibitors.

12. Modulating drugs of enkephalins and opioid receptors

Morphine. Structure and properties. Development and semisynthesis of morphine analogues. Modulative variations: drug extension and variation of substituents on N atom, rigidification. Disjunctive variations: morphinans, benzomorphans, phenylpiperidines, phenylpropylamines. Endogenous opioid peptides: endorphins and enkephalins.

13. Introduction to spectroscopic analysis

General principles. Spectroscopic applications for determining organic structures: UV-visible spectroscopy, infrared spectroscopy, nuclear magnetic resonance spectroscopy, mass spectrometry.

14. Laboratory Practices

Drug synthesis and structural characterization. Use of protecting groups in synthesis. Sequential synthesis. Separation of the active ingredients in medicines.

WORKLOAD

ACTIVITY	Hours	% To be attended
Theory classes	58,00	100
Seminars	25,00	100
Laboratory practices	25,00	100
Tutorials	6,00	100
Development of group work	10,00	0
Study and independent work	60,00	0
Readings supplementary material	5,00	0
Preparation of evaluation activities	32,00	0
Preparing lectures	30,00	0
Preparation of practical classes and problem	40,00	0
TOTAL	**291,00**	

TEACHING METHODOLOGY

Theory classes. Students must acquire the basic knowledge included in the list of units through self-study and by attending the lectures. In those lectures, the lecturer will give an overview of the topic under study with special emphasis on the most relevant aspects and on those of particular complexity. In order to encourage the active participation of students, the expositive method (lecture) will alternate with case studies and related problems. For individual work and further preparation of the units, proper references and the necessary supporting material will be provided to the students.

Seminars. The group of students could be divided into subgroups for seminars, so each student must attend 1 session per week. These seminars are aimed at solving problems, exercises and questions related to pharmaceutical chemistry, and at introducing complementary topics. In addition to this type of problem-solving seminar, the lecturer may propose that students, in groups of 4-5 members, prepare and present selected topics on pharmaceutical chemistry to their colleagues. The reduced number of students in these small groups facilitates an active participation in these seminars, aimed to provide information search skills, the ability to schematise, summarise, and to prepare oral presentations, as well as to promote teamwork. Complementary activities may also be carried out (debates, analyses of readings, press releases) on topical issues related to the subject, or they may also delve into some specific aspects of more complex units.

Laboratory. Students must attend a mandatory introductory seminar prior to the practical sessions. In addition, each student has to complete prior tasks before attending the laboratory, involving the understanding of the experiment, the review of the theoretical concepts involved and the preparation of a scheme of the work process. At the beginning of each session, the lecturer will insist on the most relevant aspects of the experimental work and will monitor the student's performance during the session. Once the experiment is completed, the student will analyse the results and will solve the questions posed by the lecturer at the beginning or during the course of the session. All this should be reflected in the lab notebook, which will be systematically reviewed by the lecturer.

Tutorials. Students will attend the tutorial sessions in small groups, according to the timetable set. In these sessions, the lecturer will evaluate their learning process in a globalised manner. To do so, he or she may present the students with specific problems to be solved either individually or collectively and which may be more complex than those presented in seminars, according to the needs of students. Tutorials will also be used to solve the queries raised by students during the lectures and to advise them on the strategies to follow in order to avoid the learning difficulties that they may have.

EVALUATION

The assessment of the student's learning takes into consideration all the elements outlined in the methodology section included in this guide. To pass the course, a minimum score of 5 out of 10 must be achieved.

70% of the mark (7 points out of 10) will be calculated on the basis of the results obtained in the exams corresponding to the contents covered in lectures and problem-based seminars. At the end of the first term, a partial exam will be administered dealing with the contents given up to that moment. At the end of the second term there will be an exam on the contents developed during the 2nd term, including the application of the concepts taught in the first term. The final mark of this section will correspond to the mark of this second exam, except for those students who have a higher mark in the first exam and have a

mark of 4.5 out of 10 or higher in the second one, in which case the final mark will be the average between them. Students who fail this part will have a second opportunity in the same course. The exams will consist of questions related to the subject and questions that require connecting aspects of the subject that appear in different units or that are complemented with other subjects. Written examinations will be held on the dates determined by the faculty.

15% of the mark (1.5 points out of 10) will come from the laboratory practicals. The attendance at the sessions is mandatory. 70% of the mark will be based on the assessment of practical sessions taking into account elements such as the preparation of the laboratory sessions, the updating of the laboratory notebook and the experimental work carried out. The remaining 30% will correspond to the mark obtained by the student in a written exam on questions related to practical issues, which will be done at the same date than the exams corresponding to the theory part. Students who fail will have a second practical and/or written call. The lab mark can be carried forward for the two subsequent academic years although students who repeat the subject have the right to attend lab sessions again, if they wish to do so. To pass the course it is necessary that students pass the laboratory practices.

15% of the mark (1.5 points out of 10) will correspond to a continuous assessment, taking into account different aspects such as participatory class attendance, progress in the use of subject-specific terminology, critical thinking, ability to work with the rest of the group, participation in seminars and tutorials, etc. This mark will be considered only if the student has passed the exams and the laboratory practices with a minimum mark of 4.5 points out of 10.

For the second examination session, the marks obtained in the continuous assessment and in laboratory practicals will be considered, and students will only have to sit the exams again. Students who do not sit the exam in the first examination session, but have been given a mark for the other elements of assessment, will be marked as ABSENT in the first examination session. However, in the second examination session, the marks from the different elements of assessment will be weighted as explained above in this section, so not sitting the exam in this second attempt will imply a mark of FAIL.

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Basic

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  - C. Avendaño. Introducción a la Química Farmacéutica. Ed. Interamericana - McGraw-Hill, 2ª edición 2001.
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- C. Avendaño. Ejercicios de Química Farmacéutica. Ed. Interamericana. Mc. Graw-Hill, 1997.
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