COURSE GUIDE

BIOPHARMACEUTICS AND PHARMACOKINETICS

(JULIO 2015)

Degree in PHARMACY
University of Alcalá
Academic year 2015/16
**Title:** Biopharmaceutics and Pharmacokinetics  
**Code:** 570014  
**Degree:** PHARMACY  
**Department:** Biomedical Sciences  
**Field of Knowledge:** Pharmacy and Pharmaceutical Technology  
**Type:** Compulsory  
**ECTS credits:** 6 (4.5 ECTS Theory + 1.5 ECTS Experimental Work)  
**Year:** Third / first season  
**Teacher:** Dr. Jesús Molpeceres García del Pozo  
**Coordinator:** Dr. Jesús Molpeceres García del Pozo  
**Schedule for tutorials:** appointment with the teacher  
**Language:** English

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**1. INTRODUCTION**

This subject is focused to characterize from a qualitative and quantitative standpoint all the processes and factors affecting a drug once it has been given by a particular administration route in a pharmaceutical dosage form, in order to optimize its bioavailability. Biopharmaceutics and Pharmacokinetics are complementary disciplines, being the former focused to study the interaction between the dosage form and the biological substrate and the second more oriented to evaluate drug and metabolites kinetics through the analysis of concentration/time curves in biological fluids.

The learning outcomes pursued with this course can be summarized in the following items:

1. To know the mechanisms for drug passage through biological barriers.
2. To know basic procedures for the study of drug transfer kinetics in the body.
3. To understand the relevance of pharmacokinetic parameters.
4. To understand the influence of physiological, pathological, environmental, etc… factors on drug transit within the body.
5. To identify the influence of the dosage form design on both, the drug incorporation step into the systemic circulation and the therapeutic effect.
6. To understand drug bioavailability and bioequivalence as related to drug product safety.
7. To know and to implement the basis for the establishment of drug dosing regimens.

**Prerequisites y Recommendations**

It is highly recommended that the students have previously passed the courses on Mathematics, and principles of Physics, Biophysics and Physical Chemistry.
2. COMPETENCES AND ABILITIES

Generic competences (Orden CIN/2137/2008, 3 de julio) contributed by this course:

1. Knowledge of the ADME process and the factors influencing drug absorption and disposition as related to each administration route.

2. Knowledge of the physical-chemical and biopharmaceutical properties of drugs and excipients and their potential relationships.

3. Drug dosing and drug dosing adjustment by using pharmacokinetic parameters.


Specific competences:

1. Analyze the passage of drugs through the body: LADME.
2. Knowing the biopharmaceutical factors associated to each administration route.
3. Evaluation and estimation of drug changes in the body by using pharmacokinetic models.
4. Know and estimate drug clearance.
5. Analyze the influence of dosage form design and formulation on drug release and absorption.
6. Know how to evaluate drug bioavailability and bioequivalence.
7. Analyze the pharmacokinetic parameters influencing drug dosing.

3. CONTENTS

Lectures:

I. INTRODUCTION TO BIOPHARMACEUTICS and PHARMACOKINETICS

- Chapter 1.- INTRODUCTION.- Concepts and relevance of biopharmaceutics and pharmacokinetics. Sources of information. The passage of drugs through the body. The LADME process: Overview and basic concepts of drug release, absorption, distribution, metabolism and excretion.

- Chapter 2.- PHARMACOKINETICS.- Data for the study of LADME. Drug plasma level curves and urinary excretion curves. Kinetics of the LADME steps: Zero order, first order and Michaelis-Menten kinetics. Usual kinetics in LADME.

II. KINETIC STUDIES OF DRUG CHANGES WITHIN THE BODY


- Chapter 4.- ONE-COMPARTMENT OPEN MODEL.- Intravenous bolus administration.- Interpretation of plasma concentration/time profiles. Elimination phase: concept and determination of the elimination rate constant. Elimination half-life, area under the curve,

- **Chapter 5.** Extra-vascular administration with first order absorption. Overview and interpretation of plasma concentration/time profiles. Lag time and its determination. Determination of area under the curve, \( C_{\text{max}} \) and \( t_{\text{max}} \). Estimation of the absorption rate constant by using direct and indirect methodologies: method of residuals, cumulative absorption method (Wagner-Nelson), The Dost method.


- **Chapter 7.** TWO-COMPARTMENT OPEN MODEL.- Bolus intravenous dosing.- why this model? Central and peripheral compartments. Overview and interpretation of drug plasma concentration/time curves. Model equations. Determination of hybrid (macro-constants) and individual disposition rate constants (micro-constants), area under the curve and volumes of distribution. Relationships between disposition and elimination rate constants. Mass balance: drug amounts in the body and eliminated.

- **Chapter 8.** Extra-vascular administration with first order absorption. Pharmacokinetic model and equations. Characteristics of the drug plasma concentration/time curves. Calculation of \( C_{\text{max}}, t_{\text{max}} \) and area under the curve. Estimation of the absorption rate constant by different methodologies: Residuals or retro-projection method. The Loo-Riegelman method. Lag phase. Mass balance: drug amounts in the body, eliminated or in the absorption site.


- **Chapter 10.** URINARY EXCRETION CURVES.- Drug plasma concentrations and excretion rates in urine. Distributive and cumulative curves. Determination of pharmacokinetic rate constants in the one- and two-compartment open models. Pros and cons of urinary excretion curves.


- **Chapter 14.** MULTIPLE DOSE KINETICS.- Overview and basic parameters. Calculation of steady-state concentrations. Cumulative index. Cumulative factor. One and two-compartment open models.

**III. DRUG INCORPORATION AND DISPOSITION INTO THE BODY**


IV. BIOAVAILABILITY AND BIOEQUIVALENCE

- Chapter 28.- Bioavailability and Bioequivalence studies.- Goals, experimental design and ethical issues. Methodology, pharmacokinetic analysis and significant parameters to compare.

V. DRUG DOSING


- Chapter 30.- Therapeutic drug monitoring. Concept, methodology and pharmacokinetic significance.


- Chapter 32.- DRUG DOSING IN NEONATOLOGY AND PEDIATRICS. Factors affecting drug absorption, distribution and elimination. Dose adjustment on a weight basis or a body surface basis. Drug dosing in the elderly.


Laboratory:

- “In vitro” simulation of the one-compartment open model by means of a hydraulic device. Pharmacokinetic analysis of simulated blood and urine data.

Exercise 1.- Single dose bolus IV administration.

Exercise 2.- Single dose EV administration.

Exercise 3.- Multiple dose bolus IV administration.

Exercise 4.- Constant rate IV administration.

- Influence of the physical chemical characteristics of a drug and the dosage form on the ADME process.

Exercise 5.- Drug dissolution testing in accordance to the RFE. Influence of the dosage form and kinetic analysis.


Exercise 7.- Protein binding drug displacement interaction study.

Other activities: Seminars

Seminars 1, 2, 5 and 6.- One-compartment open model.

Seminars 3 and 4.- Two-compartment open model.

Seminar 7.- Non-compartmental pharmacokinetics.

Seminar 8.- Bioavailability and bioequivalence.

Seminar 9.- Dissolution studies.

Seminar 10.- Drug dosing.
### 3.1. Distribution of contents

<table>
<thead>
<tr>
<th>Thematic Units</th>
<th>Chapters</th>
<th>Time</th>
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<tbody>
<tr>
<td>Introduction</td>
<td>1 and 2</td>
<td>2h L,</td>
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<tr>
<td>Kinetic study of drug changes within the body</td>
<td>3 to 14</td>
<td>10h L, 5h S, 10h Lab</td>
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<tr>
<td>Drug incorporation and disposition</td>
<td>15 to 26</td>
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<tr>
<td>Bioavailability and Bioequivalence</td>
<td>27 and 28</td>
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</tr>
<tr>
<td>Drug dosing</td>
<td>29 to 33</td>
<td>3h L, 1h S,</td>
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### 4. Teaching-Learning Methodologies. Activities

#### 4.1. Distribution of ECTS credits (specify in hours)

**Classroom:**
- Lecture hours: 28 h
- Seminars: 8 h
- Laboratory work: 18 h
4.2. Materials, methodological strategies and teaching resources

**In the classroom or laboratory**

- Lectures will be based on presentations made by the teacher and discussions about the main items included in each chapter. In some cases, computer programs or videos will be used for comprehensive purposes.

- Seminars will be focused to problem solving and discussion of topics. Group activities can be designed in order to facilitate the active participation of students.

- Laboratory work will consist on the development and setting of different experimental approaches to mimic compartmental models and real systems to identify basic concepts exposed during the lectures.

- Materials and teaching resources will be blackboard, powerpoint presentations, printed material provided by the teacher, a laboratory notebook and web resources.

**Independent work**

- Students will analyze and assimilate the information provided in classroom and laboratory activities on their own. They can use all available information such as books and literature search tools to complete this information.

- Use of ICTs to facilitate the contact between the students and the teacher during independent work outside of the classroom.

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5. EVALUATION: Procedures, criteria and rating

Every academic year the student has two calls for assessment, regular and extraordinary. The regular call can be undertaken in two different formats, continuous assessment or final evaluation. Continuous assessment is strongly recommended but there are a few exceptional cases considered in UAH (Art. 8.3) regulatory documents allowing the students to do a final exam. The student can leave this course and join the corresponding spanish version within the first two weeks.

**REGULAR CALL**

**Continuous assessment:**
Continuous assessment is the default option associated to the regular call. Attendance to all classroom activities is mandatory. In accordance to UAH¹ regulations (Art. 9) students will have two formal tests to evaluate their progress with regards to their knowledge of the subject including theoretical concepts and problem solving abilities. The first one will take place at the middle of the teaching period and the second one at the end. The assessment of those skills and knowledge acquired through laboratory work will also be carried out with a formal examination. Students who have not performed the laboratory work and passed the exam will not pass the subject in this call.

Students must show a minimum level in the achievement of the corresponding competences for the gathering of partial marks to obtain the global score.

Students that do not pass the subject in a regular call will follow a second final evaluation as extraordinary call within the same academic year.

**Final examination:**
It will evaluate theoretical concepts and problem solving abilities focused to assess the acquisition of specific competences detailed previously. The assessment of those skills and knowledge acquired through laboratory work will also be carried out with a formal examination.

**EXTRAORDINARY CALL**
It will evaluate theoretical concepts and problem solving abilities focused to assess the acquisition of specific competences detailed previously. Students who have completed the laboratory work but failed must pass a specific exam.

**Assessment criteria:**
- Assimilation and understanding of course’s contents.
- Attendance and participation in seminars.
- Ability to apply acquired knowledge.
- Interpretation of results and resolution of numerical problems or questions.
- Critical and coherent thinking.
- Compliance with laboratory safety rules.
- Skills for laboratory work.
- Integration and communication of knowledge.

**Rating criteria:**
As the subject holds a high experimental degree, laboratory work is mandatory and it must be passed by doing the corresponding exam, regardless of the course assessment format selected by the student.

**REGULAR CALL**

**Continuous assessment:**
- Laboratory work: 15%.
- First exam: 15%.
- Problem solving 30%
- Final exam: 40%

**Final Examination:**
This assessment will be based on a test including questions, problems and exercises focused to assess the acquisition of specific competences detailed previously. In order to
pass the course, a score higher than or equal to 5 is needed. Students who have completed
the laboratory work but failed must pass a specific exam with scores higher than or equal to
5. Laboratory work will contribute 15% to the final score.

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This assessment will be based on a test including questions, problems and exercises
focused to assess the acquisition of specific competences detailed previously. In order to
pass the course, a score higher than or equal to 5 is needed. Students who have completed
the laboratory work but failed must pass a specific exam with scores higher than or equal to
5. Laboratory work will contribute 15% to the final score.

### 6. BIBLIOGRAPHY

[1] Ritschel, W, Kearns G. "Handbook of basic pharmacokinetics including clinical

[2] Rosenbaum, S. "Basic pharmacokinetics & pharmacodynamics an integrated


International Inc., 2004. (Reference: BAF615.03SHA)

and applications”. Ed. Lippincott & Wilkins,2011. (Reference: BAF615.03ROW)

solubility, permeability, absorption and bioavailability". Wiley-Vch 2005. (Reference: BAF615-032WAT)

[7] Software available at the computer classroom in the Faculty of Pharmacy :
   a. Biofarmacia Moderna. Amidon G.M. Ed. TSRL. Inc. 5.04.
   c. Introductory Pharmacokinetics Workshop.University of Bath. COACS. Ed.
PCCAL,1999.