VNIVERSITAT DE VALÈNCIA

Course Guide
34081 Biopharmacy and Pharmacokinetics

COURSE DATA

Data Subject	
Code	34081
Name	Biopharmacy and Pharmacokinetics
Cycle	Grade
ECTS Credits	10.5
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	15 - Biopharmaceutics and pharmacokinetics	Obligatory
1211 - D.D. in Pharmacy-Human Nutrition and Dietetics	1 - Asignaturas obligatorias del PDG Farmacia-Nutrición Humana y Dietética	Obligatory

Coordination

Name	Department
PERIS RIBERA, JOSE ESTEBAN	134 - Pharmacy and Pharmaceutical Technology

SUMMARY

Pharmacokinetics deals with the changes of drug concentration in the drug product and changes of concentration of a drug and/or its metabolite (s) in the human or animal body following administration, i.e., the changes of drug concentration in the different body fluids and tissues in the dynamic system of liberation, absorption, distribution, body storage, binding, metabolism, and excretion. Is interrelated with biopharmaceutics, pharmacology and therapeutics

Biopharmaceutics deals with the physical and chemical properties of the drug substance, the dosage form, and the body and the biological effectiveness, of a drug and/or drug product upon administration, i.e., the drug availability to the human or animal body from a given dosage form, considered as a drug delivery system. The time course of the drug in the body and the quantifying of the drug concentration pattern are explained by pharmacokinetics.

The application of pharmacokinetics focuses on two areas: the development of new drugs and the optimization of dosing regimens of drug treatments, both objectives are complemented by the Pharmaceutical Technology and Clinical Pharmacy, respectively.

PREVIOUS KNOWLEDGE

Relationship to other subjects of the same degree

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

Other requirements

It is recommended to have knowledge of mathematics, statistics, physical chemistry, physiology and anatomy.

OUTCOMES

1201 - Degree in Pharmacy

- To possess and to understand the knowledge in the different areas of study included in the formation of the pharmacist.
- To apply this knowledge to the professional world, contributing to the development of Human Rights, democratic principles, principles of equality between women and men, solidarity, protection of the environment and promotion of a culture of peace with Gender perspective.
- 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.
- Development of skills to update their knowledge and undertake further studies, including pharmaceutical specialization, scientific research and technological development, and teaching.
- Ability to collect and transmit information in English with a level of competence similar to the B1 of the Council of Europe.
- To develop communication and information skills, both oral and written, to deal with patients and other health professionals in the center where they carry out their professional activity. To promote the capacity of work and collaboration in multidisciplinary teams and those related to other health professionals.

- Module: Pharmacy and Pharmaceutical Technology - Program and correct the dosage of drugs based on their pharmacokinetic parameters.
- Module: Pharmacy and Pharmaceutical Technology - Determination of bioavailability, evaluation of bioequivalence and factors that determine them.
- To know the processes of release, absorption, distribution, metabolism and excretion of the drugs.
- To be able to identify the factors that influence the absorption and disposition of drugs depending on their route of administration
- To know the biopharmaceutical properties of the active principles and excipients as well as the possible interactions between both.

LEARNING OUTCOMES

1. To acquire knowledge of liberation, absorption, distribution, metabolism and excretion of drugs when are administered by any route of administration.

2. To develop the skills to describe and quantify the aforementioned processes using the compartment approach.

3. To acquire knowledge of physical, chemical, biological and technological factors involved in the dosage form of drugs which modulate the bioavailability when are administered by any route of administration.

4. To acquire skills to design, implement and interpret the bioequivalence studies.

5. To acquire knowledge of pharmacokinetic factors those determine the dosage regimens.

6. To develop the skills to establish and modify dosage regimens in patients.

7. To acquire knowledge to interpret the data sheet of the drugs and use the pharmacokinetics in clinical situations.

DESCRIPTION OF CONTENTS

1. Introduction

Biopharmaceutics and pharmacokinetics. Concept, objectives and scope of the discipline Transit of drug in the body: Liberation, Absorption, Distribution, Metabolism, Excretion and Response (LADMER). Equivalence of drugs. Equivalents chemical, biological and therapeutic. Bioavailability. One order, zero-order and mixed order kinetics. Usual kinetics of ADMER processes. Linear kinetics. Limiting factors. Data for the study of LADME. Compartmental analysis and simplifications.

2. Linear pharmacokinetic. One compartment open model

Intravenous administration.
Pharmacokinetic parameters: elimination rate constant, half-life and volume of distribution. Clearance. Extraction rate. Equivalences between pharmacokinetic parameters. Plasma concentration-time profiles: intravenous bolus administration and intravenous infusion.
Extravascular administration.
Pharmacokinetic parameters: absorption rate constant, absorption half-life, Cmax, tmax, lag time and bioavailability in magnitude. Plasma concentration-time profiles: single dose and multiple dosage regimens. Determination of absorption rate constants from oral absorption data. Method of residuals. Cumulative absorption method or Wagner-Nelson method. Influence of route of drug administration and dosage form on plasma concentration-time profiles.

3. Linear pharmacokinetic: Two compartment open model

Intravenous administration.
General equation of the plasma concentration-time curve. Pharmacokinetic parameters. First order transfer rate constants from central to peripheral, and from peripheral to central compartment. Apparent volumes of distribution: concept and calculation. Drug clearance: equivalence with pharmacokinetic parameters.
Extravascular administration. Bateman function. Determination of absorption rate constants from oral absorption data. Method of residuals. Cumulative absorption method or Loo-Riegelman method. Collapse of the plasma concentration time curve.

4. NON linear pharmacokinetics

Concept and causes of nonlinear pharmacokinetics. Methods for detection. Nonlinear elimination processes. Pharmacokinetic parameters. One compartmental nonlinear model: general equation of the plasma concentration-time profile after intravenous and extravascular administration. Nonlinear two-compartment model: simplifications. Relationship between pharmacokinetic parameters and dose. Pharmacokinetics of the metabolite. Metabolite plasma concentration-time profile. Linear and Nonlinear kinetics.

5. Pharmacokinetics /pharmacodynamic models

Response models. Direct response. Indirect response. Empirical pharmacodynamic models. Matematical modelling to dose-effect-time data. Linear model, log-linear model, maximum effect. Pharmacokinetic-pharmacodynamic modeling (PK/PD). Link models. Direct link. Indirect link: the effect-compartmental model.

6. Dosage regimen design

Dosage regimen design

Dosage regimens schedules: basic parameters. One compartment model: repetitive intravenous injections, intermittent intravenous infusion and multiple-oral dose regimen. Plasma drug concentration-time curves. Steady-state: maximum and minimum plasma drug concentrations at steady state. Two compartmental model: repetitive intravenous injections. Plasma drug concentration-time curves.
Individualization of drug dosage regimens. Determination of dose. Effect of changing dose and dosing interval on minimum and maximum concentrations at steady-state. Determination of frequency of drug administration. Determination of both dose and dosage interval.
Therapeutic drug monitoring. Nomograms and tabulations in designing dosage regimens. Population Pharmacokinetics: Bayesian approach. Dosing of drugs in specific population groups of patients: infants, pregnant women, elderly, obese, renal impairment and hepatic disease.

7. Non compartmental pharmacokinetics

Concept. Statistical moment theory. Mean residence time (MRT). Area under the curve plasma concentration-time. Volume of distribution. Clearance. Relationships with compartment pharmacokinetic parameters.

8. Bioavailability and bioequivalence

Definitions. Purpose of bioavailability studies. Relative and absolute availability. Methods for assessing bioavailability. Clinical significance of bioavailability studies.
Bioequivalence studies. Design and evaluation of bioequivalence studies. Evaluation of the data. Bioequivalence study submission and drug review process. Clinical significance of bioequivalence studies. Generic substitution.

9. Biopharmaceutical factors of ADME processes

Absorption of drugs. Routes of administration. Circulation and recirculation of drugs in the body, rather than losses. Absorption mechanisms. Passive absorption. Convective transport. Active transport. Facilitated transport. Other absorption mechanisms. Distribution of drugs. Binding of drugs to plasma proteins. Calculation of protein binding.
Pharmacokinetic importance of protein binding. Disease and protein binding. Displacement from protein binding. Uptake of drugs by red blood cells.
Drug biotransformation. Liver Physiology. Biotransformation reactions. Intrinsic clearance. Factors which can influence drug metabolism. Sources of variability in drug biotransformation activity. Drug interactions. Pharmacokinetic and clinical implications. Renal excretion of drugs. Renal excretion mechanisms. Renal clearance: determination. Factors influencing renal clearance. Glomerular filtration of drugs. Passive diffusion. Renal excretion. Other excretion routes: Biliary, salivary, expired air, sweat and mamary.

10. Routes of drug administration

Parenteral administration. Injection sites. Absorption sites: physiological features. Parenteral absorption kinetics from aqueous solutions. Factors influencing the parenteral bioavailability.
Oral administration. Gastrointestinal physiology. Places of oral absorption of drugs. Factors influencing drug absorption. General recommendations for oral drug administration. Biopharmaceutical Classification System.
Other administration routes. Rectally, vaginal, perlingual, buccal, sublingual, nasal, otic and ocular.
Transdermal administration. Routes of exposure: their importance compared. Percutaneous absorption kinetics. Factors influencing the permeability through the skin: biological, physicochemical and dependent on the vehicle. Percutaneous formulations and discussion.

WORKLOAD

ACTIVITY	Hours	% To be attended
Theory classes	66,00	100
Laboratory practices	16,00	100
Seminars	10,00	100
Computer classroom practice	8,00	100
Tutorials	5,00	100
Development of individual work	10,00	0
Study and independent work	60,00	0
Readings supplementary material	20,00	0
Preparation of evaluation activities	10,00	0
Preparing lectures	20,00	0
Preparation of practical classes and problem	10,00	0
Resolution of case studies	17,50	0
Resolution of online questionnaires	10,00	0
TOTAL	**262,50**	

TEACHING METHODOLOGY

1. Lectures.

2. Problems: Discussion and solving problem exercises in pharmacokinetics.

3. Laboratory practice.

4. Computing practice

5. Tutorials

EVALUATION

	Evaluation system	Evaluation criteria	% calification
Theory evaluation	Written exam: Short questions and multiple choice questions related with the contents of the lectures and problem classes	-Precise answers -Clear concepts -Consistent reasoning -Proper presentation	80
Problem evaluation	Written exam: problem solving related with the contents of the lectures and problem classes	Clear concepts -Consistent reasoning -Proper presentation	10
Laboratory and computing evaluation	Written exam: short questions and problem solving Control of assistance	-Teamwork and participative attitude -Skill in laboratory work -Work with order and cleanliness -Proper disposal of waste- -Successful completion of practice -Reflective attitude to the results -Order and clarity in the resolution of the practice -Mandatory attendance at all sessions	8 laboratory 2 computing
Each item has to be need a 50%			

When a student does not submit to the theory exam at the first regular call for the academic year but has been evaluated in any of the rest educational activities (problems, laboratory practice, informatics practices, tutorials) the qualification report will be not attended. However, if in the second call, the student does not attend the theory exam, the qualification report will be failed, and the numerical will be calculated according to the percentages allocated to each of the activities carried out. In summary: in second call not attended will qualify only students who had not attended any of the activities integrating the subject.

If the student pass laboratory or computing practice during the current course, the mark of approved practice is saved for the next course.

REFERENCES

Basic

- Doménech, J., Martínez Lanao, J., Plá Delfina, JM
  Biofarmacia y Farmacocinética. Volumen I: Farmacocinética
  Ed. Síntesis. 1997
  Doménech, J., Martínez Lanao, J., Plá Delfina, JM
  Biofarmacia y Farmacocinética. Volumen II: Biofarmacia.
  Ed. Síntesis. 1998
  Gibaldi, M.
  Biopharmaceutics and Clinical Pharmacokinetics
  Lea and Febiger. Filadelfia, 1991
  Jiménez, NV, Casabó, VG, Sancho, V.
  Manual de procedimientos para la farmacocinética clínica.
  Edita Afaphe, 1997
  Ritschel WA, Kearns GL
  Handbook of basic pharmacokinetics.
  American Pharmacist Association, 2004
  Shargel L, Wu-Pong S.
  Applied biopharmaceutics and pharmacokinetics.
  McGraw-Hill. Medical publishing division. , 2005.
  Hedaya, MA
  Basic Pharmacokinetics
  CRC Press. 2007
  Amidon G, Bermejo M.
  Biofarmacia Moderna versión 6.
  TSRLinc. 2003
  http://www.tsrlinc.com/mbindex.htm
- Doménech-Berrozpe J, Martínez-Lanao JM, Peraire Guitard C.
  Tratado general de Biofarmacia y Farmacocinética. Volumen I. LADME. Análisis farmacocinético. Biodisponibilidad y bioequivalencia.
  Editorial Síntesis, 2013

- Domench-Berrozpe J, Martínez-Lanao JM, Peraire Guitard C.
  Tratado general de Biofarmacia y Farmacocinética. Volumen II. Vías de administración de fármacos: aspectos biofarmacéuticos. Farmacocinética no lineal y clínica.
  Editorial Síntesis, 2013