CLINICAL PHARMACOKINETICS

Syllabus: CLINICAL PHARMACOKINETICS

Code number: 79

Cycle: Undergraduate

Semester: 8th

Course type

	Background/General knowledge
X	Scientific area (pharmacy)

Credit Units (ECTS): 5

Lectures (hours/week): 3 hours per week

Tutorial (hours/week):

Laboratory work (hours/week): 1 hour per week

Course coordinator:
Ioannis S. Vizirianakis, Associate Professor of Molecular Pharmacology and Pharmacogenomics

Tutors:
Ioannis S. Vizirianakis, Associate Professor of Molecular Pharmacology and Pharmacogenomics

Assisting personnel:
George A. Mystridis, MSc Candidate in Pharmacology and Therapeutics

Aims of the course:

Lectures/tutorials:

The lectures and tutorials aim to assist pharmacy students in developing their skills to understand and assess clinically relevant drug interactions in a way to finally contribute for minimizing adverse drug interactions (ADRs) in healthcare. To this end, the predictive as well as the assessment capabilities of students for drug interactions and ADRs will be clearly strengthen and an overall benefit for both pharmaceutical care environment and drug delivery outcomes will be achieved. As a matter of fact, students are expected to acquire knowledge and practical skills as practitioners in order to improve drug efficacy and safety profiles in clinical practice.

In order for these targets to be achieved, specific teaching methodologies are applied:

a) lectures focusing on selected pharmacokinetics, pharmacodynamics, pharmacogenomics and personalized medicine concepts;

b) b) discussions of specific clinical drug interaction case studies within the frame of evidence-based medicine; and

c) c) tutorials for specific drug dosage scheme data evaluation by implementing the "Simcyp-Population Based Pharmacokinetic Modelling and Simulation» platform (academic license agreement since 2009).

Skills: Students assessment capability for drug interactions and ADRs

Teaching methods: Presentations, PowerPoint slides, books, drug case-studies discussion

Contents of the course:

Lectures content

Protein binding of drugs, Intestine drug metabolism, Hepatic drug metabolism, Assessment of drug interactions mechanisms, Drug-drug drug-food and drug-herb interactions, Mechanisms involved in the emergence of adverse drug interactions, Pharmacogenomics and adjustment of drug dosage delivery, PK-based drug prescription principles, Pharmacoeconomy issues in drug delivery, Clinical relevance of drug metabolizing enzymes and transporters genetic polymorphism, Individualizing drug delivery dosage schemes in clinical practice, Environmental toxicants and drug delivery. Examples of pharmacokinetic case studies discussed: a) cerivastatin market removal, b) removal of rofecoxib from the market/clinical practice, c) drug-induced QT-elongation and drug cardiotoxicity and d) PK-based methodological improvements applied upon indinavir new drug development.

Tutorials content

Exercises and tutorials to understand the concepts covered in the lectures so that students acquire skills for the use and application of pharmacokinetic data in drug regimens in clinical practice. At the same time, the "Simcyp- Population Based Pharmacokinetic Modeling and Simulation" tool is utilized with specific clinical data for prediction and adaptation of dosage regimens in the context of a population pharmacokinetic approach titled *"Analysis of Pharmacological Results in Different Population Groups: Monotherapy and Drug Administration".*

Referred Books - Handouts - Slides:

1. Ioannis S. Vizirianakis (In Greek). «Clinical Pharmacokinetics: Basic Principles of Pharmaceutical Care in Clinical Practice", 2016; Stavros Sartinas Publishing: Thessaloniki, Greece.

2. Ioannis S. Vizirianakis. (In Greek). Course handouts referring to slides/presentations available to students for download in the University e-Class Platform of AUTh (slides in total 299) and also the material related to the population pharmacokinetics lessons by the application of "Simcyp- Population Based Pharmacokinetic Modelling and Simulation» (academic license agreement since 2009).

a) Lectures

N° / duration	Title	Tutorσ
1st/ 3 hours	Basic principles of clinical pharmacokinetics: Drug uptake, assessment and clinical utility	Ioannis S. Vizirianakis
2nd / 3 hours	Basic principles of clinical pharmacokinetics: Drug distribution, assessment and clinical utility	Ioannis S. Vizirianakis
3rd / 3 hours	Basic principles of clinical pharmacokinetics: Drug elimination, assessment and clinical utility	Ioannis S. Vizirianakis
4th / 3 hours	Basic principles of clinical pharmacokinetics: Drug metabolism, assessment and clinical utility	Ioannis S. Vizirianakis

5th / 3 hours	Pharmacokinetic models, dosage regimens, depiction and application of clinical pharmacokinetic data in clinical practice	Ioannis S. Vizirianakis
6th / 2 hours	The role of clinical pharmacokinetics in modern therapeutics towards improving new drug development era as well as efficacy and safety profiles in clinical practice	Ioannis S. Vizirianakis
7th / 2 hours	Protein binding and drug distribution: Consequences for drug bioavailability and clinically relevant interactions	Ioannis S. Vizirianakis
8th / 3 hours	Hepatic function and drug distribution	Ioannis S. Vizirianakis
9th / 5 hours	Drug metabolizing enzymes and transporters: Function, tissue distribution, pharmacokinetics- pharmacogenomics evaluation and pharmacological assessment	Ioannis S. Vizirianakis
10th / 2 hours	Drug-food interactions: Mechanisms and clinical relevance	Ioannis S. Vizirianakis
11th / 2 hours	Drug-herb interactions: Mechanisms and clinical relevance	Ioannis S. Vizirianakis
12th / 2 hours	Drug-drug interactions: Mechanisms and clinical relevance	Ioannis S. Vizirianakis
13th / 5 hours	Prediction of clinically relevant drug interactions: Pharmacogenomics and pharmacoeconomic evaluation and clinical relevance	Ioannis S. Vizirianakis
14th / 1 hour	Environmental toxicants and drug distribution: clinical evaluation	Ioannis S. Vizirianakis
15th / 2 hours	Pharmacological and pharmacogenomics approaches to improve drug delivery clinical outcomes: Implementation of personalized medicine concepts in drug delivery	Ioannis S. Vizirianakis

b) Tutorials/Exercises

Tutor: Ioannis S. Vizirianakis, Associate Professor of Molecular Pharmacology and Pharmacogenomics
Assistant: George A. Mystridis, MSc Candidate in Pharmacology and Therapeutics

N°	Title	Tutors
1st	Absorption: • Drug Dissolution, • Membrane permeability, • Routes of administration, • Bioavailability • Drug Interactions on absorption **Exercises and examples**	Ioannis S. Vizirianakis, George Mystridis

2nd	Distribution: • Apparent volume of distribution • Protein binding • Unbound fraction of drug • Drug interactions on distribution **Exercises and examples**	Ioannis S. Vizirianakis, George Mystridis
3rd	Renal Elimination: • Mechanisms of renal elimination • Rate of elimination • Drug remaining to be excreted • Drug interactions in renal excretion **Exercises and examples**	Ioannis S. Vizirianakis, George Mystridis
4th	Hepatic Elimination: • Effect of hepatic blood flow • Effect of protein binding • Effect of intrinsic clearance • Drug interactions on hepatic elimination • First pass effect and bioavailability • Differences between low and high extraction drugs **Exercises and examples**	Ioannis S. Vizirianakis, George Mystridis
5th	Orders of drug elimination • 0-order kinetics • 1st order kinetics • Elements of enzyme kinetics • Saturation of enzyme processes **AUC calculation methods**	Ioannis S. Vizirianakis, George Mystridis
6th	Introduction to Compartmental Models: • Link of previously taught to pharmacokinetic models • Summary of different models	Ioannis S. Vizirianakis, George Mystridis
7th	One Compartment IV Bolus: • Equation of plasma drug concentration • Half-life • Clearance • Volume of distribution • Fixed rate of elimination (excretion) • Calculation of plasma concentration and volume of distribution • Estimation of parameters from plasma concentration values. **Exercises and examples in the "IV Bolus Model"**	Ioannis S. Vizirianakis, George Mystridis
8th	One compartment intravenous infusion model: • Plasma concentration equation • Steady States and factors influencing it. • Time to get to Steady State. • Estimation of parameters from plasma concentration values. • Predicted plasma levels based on dosage • Calculation of loading dose • Calculation of rate of administration. **Exercises and examples in the "IV Infusion Model"**	Ioannis S. Vizirianakis, George Mystridis

9th	One compartment per os model (1st order absorption): • Kinetics of absorption • Extent and rate of absorption • Estimation of Absorption Parameters – Curve stripping • Influence of absorption changes on plasma drug concentration • Bioavailability calculation • Time concentration equation **Exercises and examples in the Model**	Ioannis S. Vizirianakis, George Mystridis
10th	Multiple dosing kinetics (Iv and per os) • Concentration at steady state • Maximum and minimum concentrations • Rate of administration • Delivery interval • Dosage scheme design **Exercises and examples**	Ioannis S. Vizirianakis, George Mystridis
11th	Applying population pharmacokinetic models to predict and analyze interactions of drugs of clinical interest • Introduction to Simcyp Platform • Modeling based on physiology (PBPK Modeling and Simulation) **Exercises and examples**	Ioannis S. Vizirianakis, George Mystridis