

046: 138
Pharmacokinetics and Biopharmaceutics
College of Pharmacy

Fall 2006
Credit hours: **3**



Class meeting schedule: **10:30A-11:20A MWTh 100B PHAR**

Course Coordinator: Lee Kirsch, Ph.D.

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Office hours: **arrange**

Course Instructor: Craig Svensson, Pharm.D., Ph.D.

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Office hours: **Wednesdays, 11:30 AM—12:15PM**

Teaching Assistant: Chih-Wei (Charlie) Lin

Office location: **S227**
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Office hours: **arrange**

Role of teaching assistant in this course: **Web site manager, handout preparation, grading, classroom assistant**

Drs. Kirsch or Svensson would like to hear from anyone who has a disability that may require some modification of the seating, testing or other class requirements. Please notify us during the first week of class so that we may work with the Office of Student Disability Services to make appropriate arrangements. The Office of Student Disability Services is located in 3100 Burge Hall and the phone number is 335-1462.

Brief course description:

Qualitative and quantitative description of kinetics of drug absorption, distribution, and elimination, including physiological factors that influence each process; adjustment of dosing regimens for optimizing therapeutic drug levels in the body

Prerequisites:

046:123 and 046:124



Course goals:

The primary goal of this pharmacokinetics section of the course is to provide a conceptual and quantitative background in pharmacokinetic theory and applications needed to pursue advanced studies in clinical pharmacokinetics and biopharmaceutics as applied to drug delivery system design and pharmacokinetic theory.



Learning objectives:

The learning objectives for Dr. Svensson's lectures in the course are as follows.

Determinants of Pharmacologic Effect

- 1. Describe the primary means used to characterize pharmacologic effect.**
- 2. Define and differentiate the terms pharmacokinetics and pharmacodynamics.**
- 3. Identify the potential sources of variability in disposition of a xenobiotic after various routes of administration.**
- 4. Describe the importance of variation in the concentration-effect relationship in determining the pharmacologic effect that is observed.**

Passage of Xenobiotics Across Biological Membranes

- 1. Differentiate between passive diffusion, facilitated diffusion, and active transport.**
- 2. Identify how various physicochemical characteristics of xenobiotics influence their biotransport.**
- 3. Identify and describe the primary mechanisms of intestinal drug absorption.**
- 4. Characterize the impact of efflux proteins at various anatomical sites (i.e., intestinal, placental, and blood-brain barrier) on the concentration and pharmacologic effect achieved.**

Effect of Route of Administration on Drug Disposition and Action

- 1. Compare and contrast the effects of various routes of xenobiotic administration on the onset, intensity, and duration of pharmacologic effect.**
- 2. Compare and contrast the advantages and disadvantages of various routes of xenobiotic administration.**
- 3. Describe the significance and impact of the first-pass effect after oral administration.**
- 4. Describe how formulation characteristics influence the disposition and action of drugs after various routes of administration (especially via the pulmonary and ophthalmic routes).**

Distribution of Xenobiotics

- 1. Identify the 4 factors that determine the extent of xenobiotic distribution in the body.**
- 2. Define the terms distribution and apparent volume of distribution.**

3. Identify 4 mechanisms by which xenobiotics may gain access to the central nervous system.
4. Based on knowledge of the molecular weight and polarity, identify the likelihood that a xenobiotic will significantly accumulate in fetal blood/tissue.

Routes of Elimination of Xenobiotics

1. Identify 4 factors that influence the degree by which a xenobiotic is eliminated via the renal route.
2. Determine the impact of enterohepatic recirculation on the elimination of xenobiotics.
3. Identify the primary contributors to variability in drug concentration and, as a consequence, pharmacologic effect.
4. Describe the relationship between molecular weight and the fraction of a drug eliminated via biliary excretion.

Pharmacogenetics

1. Define the term pharmacogenetics.
2. Differentiate between genotype and phenotype.
3. Identify the major xenobiotic metabolizing enzymes that display genetic polymorphism.
4. Describe mechanisms by which allelic variation in xenobiotic metabolizing enzymes may result in altered metabolism of xenobiotics.
5. Determine the pharmacologic consequences of a genetic polymorphism in the enzyme responsible for metabolizing a drug (i.e., will pharmacologic effect increase, decrease, or remain unchanged?).

Noncompartmental Pharmacokinetics

1. Define the terms clearance, extraction ratio, systemic clearance, mean residence time, mean transit time, mean absorption time.
2. Given drug concentration versus time data, calculate the AUC and AUMC for a drug.
3. Given the AUC and AUMC for a drug, determine the clearance, volume of distribution at steady-state, and the mean residence time.
4. Calculate and compare the mean absorption time for two drug products made by different manufacturers.

Hepatic Clearance

1. Identify the three independent determinants of hepatic clearance.
2. Given hepatic clearance and hepatic blood flow data, determine whether a drug is perfusion-rate limited or exhibits restrictive hepatic clearance.
3. Describe and contrast the effect of changes in enzyme activity or hepatic blood flow on the blood concentration versus time curve and key pharmacokinetic parameters after oral and intravenous administration for low and high intrinsic clearance drugs.
4. Describe and contrast the effect of changes in plasma protein binding on the steady-state free and total concentrations of both low and high hepatic clearance drugs.
5. Provided data on total clearance, hepatic blood flow, and urinary excretion, determine the contribution of the liver to overall drug elimination.

Metabolite Kinetics

1. Compare and contrast the pharmacokinetic and pharmacologic consequences of formation rate-limited and elimination rate-limited metabolite disposition.

2. Describe the pharmacokinetic and pharmacologic impact of metabolic interconversion.

The learning objectives for Dr. Kirsch's sections on pharmacokinetics are as follows:
The specific learning objectives for the pharmacokinetics section of this course include the following:

1. Students will be able to estimate pharmacokinetic parameters used in clinical pharmacokinetics and biopharmaceutics using plasma and urine drug level data.
2. Students will be able to predict the effects of various physicochemical, biochemical, physiological and pathological processes on the kinetics and extent of drug absorption, distribution, and elimination.
3. Students will be able to use empirical pharmacokinetic models to devise and optimize dosage regimens.
4. Students will be able to relate the effects of dosage form design and routes of drug administration on therapeutic drug levels optimization.

Methods of instruction:

Class meetings will be three lecture sessions weekly. Additional problem-solving session may be scheduled on an ad hoc basis. Periodic problem sets will be assigned.

Instructional materials:

- Recommended texts:
 - **Malcolm Rowland and Thomas N. Tozer, Clinical Pharmacokinetics: Concepts and Applications, Williams & Wilkins, Baltimore, 1995 (3rd).**
 - **Physiologic Pharmaceutics: Barriers to Drug Absorption (2nd Ed). N. Washington, C. Washington, and C. Wilson**
 - **Ronald D. Schoenwald, Pharmacokinetic Principles of Dosing Adjustment, Technomic Publishing Co. Lancaster, 2001.**
- WebCT course site access: Class notes, problem sets, background information
- Svensson's course site:
http://www.uiowa.edu/~c046138/KINETICS_HOMEPAGE.htm



Why this course is an important component of the Doctor of Pharmacy curriculum:

This course is the first in a series of courses that train pharmacists in clinical pharmacokinetics. This course provides students with the mathematical and conceptual framework to develop their skills in dosage adjustment and dosage regimen optimization.



What you can do to improve your learning in this course:

In additional to traditional mastery of didactic materials presented in lecture formats, students should be prepared to become facile with performing the computations that are essential to dosage adjustments and optimization. Mastery of these techniques requires mathematical aptitude and skills which are best obtained by training and practice. Students are provided numerous problems sets to develop their skills and are strongly advised to complete all of the problems, even if they seem repetitious.

- If you are having trouble learning the subject matter of this course
 - **Students requiring training and instruction beyond that provided in lectures are encouraged to schedule individualized help sessions with the course instructors.**

Other useful references and web sites: **Course WebCT and Dr. Svensson's Web site**

Class schedule, topic list, and assigned readings:

Session	Date	Instructor	Topic	Exams
1	8/21	Dr. Svensson	Course Introduction Determinants of Pharmacological Effect	
2	8/22 *8:30*	Dr. Svensson	Determinants of Pharmacologic Effect	
3	8/23	Dr. Svensson	Passage Across Membranes	
4	8/24	Dr. Svensson	Parenteral Administration	
5	8/28	Dr. Svensson	Enteral and Pulmonary Administration	
6	8/29 *8:30*	Dr. Svensson	Topical Administration	
7	8/30	Dr. Svensson	Distribution of Xenobiotics	
8	8/31 9/4	Dr. Svensson	Routes of Elimination University Holiday	
9	9/5 *8:30*	Dr. Svensson	Routes of Elimination	
10	9/6	Dr. Svensson	Pharmacogenetics	
11	9/7	Dr. Svensson	Pharmacogenetics	
12	9/11	Dr. Svensson	Non-compartmental Pharmacokinetics	
13	9/12 *8:30*	Dr. Svensson	Hepatic Clearance Concepts	
14	9/13	Dr. Svensson	Hepatic Clearance Concepts	
15	9/14	Dr. Svensson	Metabolite Kinetics	
16	9/18	Dr. Kirsch	Measuring Pharmacokinetic Disposition	
	9/20		No Lecture	EXAM 1 3:30-5:30 9/20
17-18	9/21- 9/25	Dr. Kirsch	Measuring Pharmacokinetic Disposition	
19-26	9/21- 10/12	Dr. Kirsch	Introduction to Dosage Regimens	
27-29	10/16- 10/19	Dr. Kirsch	Distribution Kinetics	
30-33	10/23- 10/30	Dr. Kirsch	Biopharmaceutics in Drug Development	
	11/1		No Lecture	EXAM 2 3:30-5:30
34	11/2	Dr. Kirsch	Biopharmaceutics in Drug Development	
	11/6		No Class	

35-37	11/8-11/13	Dr. Kirsch	Introduction to Nonlinear Kinetics	
	11/15-11/16		No lecture	
	11/20-11/23		No Class THANKSGIVING BREAK	
38	11/27	Dr. Kirsch	Nonlinear Kinetics	
	11/29		No Class	EXAM 3 3:30-5:30
39	11/30	Dr. Kirsch	Nonlinear Kinetics	
40-41	12/4-12/6	Dr. Kirsch	Principles of Therapeutic Monitoring	
42	12/7			Course evaluation
	12/13			FINAL EXAM 12-2PM

Evaluation of student performance

- How your grade will be determined in this course:
 - **Three evening exams:**
 - **Exam I (9/21) 100 points**
 - **Exam II (11/2) 100 points**
 - **Exam III (11/30) 60 points**
 - **Final exam (comprehensive): 100 points**
 - **Total course: 360 points**

Grading Scale:	A⁺	95-100%	B	80-83%	C⁻	67-69%
	A	90-94%	B⁻	77-79%	D⁺	64-66%
	A⁻	87-89%	C⁺	74-76%	D	60-63%
	B⁺	84-86%	C	70-73%	D⁻	55-59%
					F	54% or less

Expectations and course policies:

- Expectations for attendance and participation: Students are expected to attend lectures
- Missed examinations: If you are ill, or have a family emergency, and cannot be present at the exam, you must contact Dr. Kirsch before the examination. Failure to do so may result in a score of zero on the exam for you. A doctor's excuse or other documentation may be required for you to receive permission to take the exam at a later date. Under no circumstances will exams be administered early.
- What to do in case of illness: See under "Missed Examinations"
- Classroom civility: Students should expect common courtesies from each other and from the instructor.

If a problem or dispute arises in connection with faculty actions in this course, you should take the following actions in order:

1. Contact the faculty member and attempt to resolve the issue directly.
2. If your complaint is not resolved, contact the course coordinator, if applicable**.
3. If your complaint is still not resolved, you may contact the appropriate division head.
4. If your complaint is still not resolved, you may contact the Associate Dean for Academic Affairs.
5. If your complaint is still not resolved, you may contact the Dean of the College of Pharmacy.

A full explanation of the College of Pharmacy and UI procedures for disputes is in the PharmD program Student Handbook on the College of Pharmacy web site.

***If your complaint concerns accommodation for a disability and it is not resolved after contacting the course coordinator, you should then contact the Associate Dean for Academic Affairs.

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