

PGS 383P Unique No (61890)
Advanced Pharmacokinetics
1 - 4 p.m. PHR 3.114B
FALL 2016

SYLLABUS

1. ETHICS

- 1.1.** Protecting Human Research Participants
(<https://phrp.nihtraining.com/users/login.php>) in Pharmacokinetic and Pharmacodynamic Studies.
- 1.2.** Introduction
- 1.3.** History
 - 1.3.1. Nuremberg Code
 - 1.3.2. Declaration of Helsinki
 - 1.3.3. Federal Protections of Human Subjects
- 1.4.** Codes and Regulations
 - 1.4.1. Belmont Report
 - 1.4.2. Common Rule
- 1.5.** Case Studies
- 1.6.** Respect for Persons
- 1.7.** Justice
- 1.8.** Beneficence
- 1.9.** Conclusions

2. COMMENTS ON MATHEMATICAL WORK

- 2.1. Aids to Mathematical Work**
 - 2.1.1. Dimensions
 - 2.1.2. La Place transforms
 - 2.1.3. Proper Arrangements of Graphs
 - 2.1.4. Implications of Fitting a Line to the Points on a Graph
 - 2.1.5. Fitting Experimental Points by an Empirical Equation
 - 2.1.6. What is a good fit?
 - 2.1.7. Constant error during linear transformations
 - 2.1.8. Proper attention to weighing
 - 2.1.9. The method of least squares
 - 2.1.10. Relationship between variables

3. PHILOSOPHY OF MATHEMATICAL MODELING

- 3.1. Models**
 - 3.1.1. What is modeling?
 - 3.1.2. What is the Purpose?
 - 3.1.3. Mathematical Models:
 - 3.1.4. Stochastic Models

- 3.1.5. Parametric Models
- 3.1.6. Nude Models

3.2. Characteristics of a Mathematical Model

- 3.2.1. Validity
- 3.2.2. Generality
- 3.2.3. Prediction ability
- 3.2.4. Computability

3.3. The Fitting of Data to a Model

- 3.3.1. Non Unique Solution
- 3.3.2. Inconsistent Solution
- 3.3.3. Acceptable Solution

3.4. Model Building Strategies

3.5. Kinetic Analysis of Physiological Systems

4. ONE COMPARTMENT MODEL

4.1. Intravenous Injection

- 4.1.1. Blood data
- 4.1.2. Excretion data
- 4.1.3. Sigma minus-method
- 4.1.4. Excretion rate method
- 4.1.5. Renal clearance
- 4.1.6. Total body clearance
- 4.1.7. Metabolite levels in plasma

4.2. Intravenous Infusion

- 4.2.1. Determination of Steady State levels
- 4.2.2. Infusion terminated prior to steady state
- 4.2.3. Infusion terminated at steady state

4.3. First Order Absorption

- 4.3.1. Method of Residuals to get K_a
- 4.3.2. Three possible cases
- 4.3.3. $K_a > K$; $K_a < K$; $K_a = K$
- 4.3.4. Lag Time in absorption
- 4.3.5. Wagner Nelson Method of Obtaining K_a

4.4. Multiple Dosing

- 4.5. Intravenous
- 4.6. Oral

5. THE TWO COMPARTMENT MODEL

- 5.1. Derivation and estimation of rate constants
- 5.2. Estimation of inter-compartmental rate constants

6. PRINCIPLES OF BIOAVAILABILITY AND BIOEQUIVALENCE

- 6.1. Definitions
- 6.2. Biopharmaceutical Consideration of Drug Products
- 6.3. Population Bioequivalence
- 6.4. Individual Bioequivalence
- 6.5. Metabolite Consideration in Bioequivalence
- 6.6. Statistical Considerations

7. PLASMA AND TISSUE BINDING - CONSIDERATIONS IN DRUG ABSORPTION

- 7.1. Background
- 7.2. Equilibrium Considerations
- 7.3. Klotz Analysis
- 7.4. Scatchard Analysis
- 7.5. Probabilistic considerations
- 7.6. Factors affecting drug binding
- 7.7. Nature of binding sites
- 7.8. Effect of protein concentration
- 7.9. Effect of drug concentration
- 7.10. Effect of binding affinity
- 7.11. Variability in drug binding

8. BINDING AND IN VIVO DISPOSITION

- 8.1. Volume of Distribution
- 8.2. Clearance
- 8.3. First Pass Effect
- 8.4. Blood Concentration time profiles
- 8.5. Perspectives

9. HEPATIC DISEASE IN PHARMACOKINETICS

- 9.1. Pharmacokinetic principles
- 9.2. Hepatic Blood Flow
- 9.3. Factors Affecting the Ability of the Liver to Extract a Drug from the Blood
- 9.4. Low and High extraction ratio
- 9.5. Intrinsic Hepatic Clearance
- 9.6. Perfused limited model

9.7. Exponential model

10. NONLINEAR PHARMACOKINETICS

10.1. Michaelis-Menten Kinetics

- 10.1.1. Enzyme Considerations
- 10.1.2. Initial Estimates of Pharmacokinetic Parameters
- 10.1.3. Intravenous Injection
- 10.1.4. Oral Absorption
- 10.1.5. Population pharmacokinetics
- 10.1.6. Empirical Approaches

11. PHARMACOKINETIC AND PHARMACODYNAMIC MODELING OF BIOLOGICS

- 11.1. Understanding New Complexities
- 11.2. PK/PD Modeling & Simulation
- 11.3. Biomarkers in PK/PD Modeling
- 11.4. Model-Based Drug Development
- 11.5. Target Mediated Drug Disposition
- 11.6. Disease induced PK/PD Changes
- 11.7. Drug Induced PK/PD Change

12. DISEASE STATE PHARMACOKINETICS

- 12.1. Pharmacogenomics and Patient Populations
- 12.2. Variability in Dose Response
- 12.3. Drug Development Considerations
- 12.4. Biomarkers

13. DATA ANALYSIS AND INTERPRETATION

- 13.1. Useful Software
- 13.2. WinNonlin-Phoenix
 - 13.2.1. Convolution and Deconvolution
- 13.3. Non-compartmental analysis
- 13.4. Pharmacokinetic modeling
- 13.5. Bioequivalence
- 13.6. Excel
- 13.7. Population Pharmacokinetics - NONMEM

Course Policies

1. Examinations and Assignments

There will be two exams throughout the semester. The first exam is an in class-exam. The second examination is a take-home exam. In addition, there will be several assignments related to the course content, and an individual project with a class presentation.

The final grade will be calculated as follows:

Final Grade = 30% Take-home exam + 20% In-class exam + 30% Assignments + 20% Special Project and class presentation

Course Grade:

A = 100-93

A- = 92-90

B+ = 89-87

B = 86-83

B- = 82-80

C+ = 79-77

C = 76-73

C- = 72-70

D+ = 69-67

D = 66-65

F < 65

2. Academic Dishonesty:

Students are expected to work independently on all examinations. Any student caught cheating will be given a “zero” on the exam (minimum) and a grade of “F” in the course. Any student suspected of dishonesty will be reported to the Dean to the Dean of Students, as per University regulations.

3. Students with Disabilities:

The University of Texas at Austin provides upon request appropriate academic accommodations for qualified students with disabilities. All University rules concerning accommodations must be followed, including the student arranging for special accommodations prior to each examination. In the absence of such prearrangement, the student will be assumed that the student is not requesting special accommodations for that exam, and will be expected to take the exam with the rest of the class at regularly scheduled exam time. For more information, contact the Office of the Dean of Students at 512-471-6259, 512-471-4641 TTY.