Unique number: 57800

Class time and location: W 9:00 -10:50 A.M. PHR Room # 2.110

Coordinator and instructor:
Zhengrong Cui, Ph.D.

Teaching Assistants:
TBA

Required textbook(s):
Pre-reading materials (and lecture handouts) for each lecture will be available on Canvas prior to each class for printing. There is not a required textbook. However, the Applied Biopharmaceutics & Pharmacokinetics (6th edition) by Leon Shargel, Susanna Wu-Pong, Andrew B.C. Yu is available as an eBook in the University of Texas at Austin library, and you may find some chapters useful. http://accesspharmacy.mhmedical.com/book.aspx?bookId=513 or http://www.lib.utexas.edu/lsl/clinic/search.html

Grading scheme for PHR 252C:

- Eleven (11) pre-reading quizzes will count as 20% of the final grade.
- Two (2) midterm exams will count towards 65% of the final grade.
- A final exam will count towards 15% of the final grade.

Examination schedule for PHR 252C:

- Midterm 1: Thursday, October 15, 2015, room and time to be announced
- Midterm 2: Thursday, November 19, 2015, Room and time to be announced
- Final examination: Time and location to be announced

Course grading:

Semester average = 0.20 X Pre-reading quizzes + 0.35 X Midterm 1 + 0.30 X Midterm 2 + 0.15 X Final exam
Course grades based on semester average:

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<th>Score Range</th>
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<tr>
<td>A-</td>
<td>90-92</td>
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<tr>
<td>B+</td>
<td>87-89</td>
</tr>
<tr>
<td>B</td>
<td>83-86</td>
</tr>
<tr>
<td>C+</td>
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<tr>
<td>C-</td>
<td>70-72</td>
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<tr>
<td>D</td>
<td>60-69</td>
</tr>
<tr>
<td>F</td>
<td>&lt; 60</td>
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**Examination policy for PHR 252C:**

Students must arrive on time for the quizzes and examinations. All instructions and corrections will be made at the beginning of the examination period and will not be repeated. Students arriving after any students have completed the exam and left the room may not be allowed to sit for the exam, and may receive a score of zero for the exam.

No allowances will be made for an exam being missed, other than documented illness or emergency. The student must contact the course instructor for confirmation prior to the exam. If permission is granted to delay the exam or to take the exam earlier, it is the student’s responsibility to complete the College Form titled "Student Request for Alternate Exam Time" for final consideration and final approval by the faculty member. In this event, the nature of the make-up will be at the discretion of the course instructor (oral, written, increased weighting on the final, etc.). An unexcused absence from an exam may result in a grade of "zero" for that exam or quiz.

**Service to students with disabilities:**

“Any student with a documented disability (physical or cognitive) who requires academic accommodations should contact the Services for Students with Disabilities are of the Office of the Dean of Students at 471-6259 (voice) or 471-4641 (TTY for users who are deaf or hard of hearing) as soon as possible to request an official letter outlining authorized accommodations.”

**Scholastic dishonesty:**

The "Statement on Scholastic Integrity of the College of Pharmacy" reads as follows: "Pharmacy practitioners enjoy a special trust and authority based upon the profession's commitment to a code of ethical behavior in its management of client affairs. The inculcation of a sense of responsible professional behavior is a critical component of professional education, and high standards of ethical conduct are expected of pharmacy students. Students who violate University rules on scholastic dishonesty are subject to disciplinary penalties, including failure of the course involved and dismissal from the college and/or the University. Since dishonesty harms the individual, fellow students, and the integrity of the University and the College of pharmacy, policies of scholastic dishonesty will be strictly enforced in this class”.

Students are expected to work independently on all examinations. Any student caught cheating will be given a "zero" on the exam (minimum). Any student suspected of dishonesty will be reported to the Dean of the College of Pharmacy and to the Dean of
Students, as per University regulations. Students are expected to have read and understood the current issue of the General Information Catalog published by the Registrar's Office for information about procedures and about what constitutes scholastic dishonesty.

Class decorum:

- In order to maximize both your learning experience and my teaching efforts, it would be advantageous, not to mention respectful, to follow the following recommendations given in the chronicle of higher education.
- It is your responsibility to attend class and conduct yourself in a manner respectful to both faculty AND your fellow classmates in the classroom.
- If you miss a class for any reason, you will be held responsible for the material covered and announcements made in your absence.
- Due to the new “active learning” approach introduced in this class starting this year, lecture attendance is necessary in order to achieve the best learning experience. Therefore lecture attendance is highly encouraged and it is student’s responsibility to be on time to take pre-reading quizzes during each lecture.
- A professional atmosphere will be maintained. Social visits, talking on cell phones, surfing the web for materials unrelated to the course, or playing games during the lectures are not permitted.

College policy on rescheduling assignments and/or examinations:

I would like to discourage you from trying to re-schedule an examination or an assignment. However, I understand that there are occasions where rescheduling is justifiable. In the event that you must have to reschedule an exam or an assignment please complete a “Student Request for Alternate Examination Time” available in the Student Affairs Office of the College of Pharmacy. This form asks you to justify the reason(s) for your request. I will then review you request, and will decide if your request merits rescheduling of the assignment and/or the examination.

Posting student scores:

Students can access their exam scores via the Canvas page of this course. This can be accessed by logging on to UT Canvas using your UTEID.

Post-exam remarks and reconsideration requests:

If a student believes that an error has been made in grading an exam question, the student will be required to provide a written justification to the course instructor within one week of the exam return date. This will allow the error to be corrected in a timely manner. After the one week period for corrections, NO ADDITIONAL CHANGES will be made to exam grades. However, any errors in score calculation will always be corrected.
Calculators and computers:

You will need a programmable calculator that can perform linear regression. Do not buy a calculator without an instruction manual. Please learn how to use your calculator for the first workshop session. In addition, it will be to your advantage to learn how to use Excel or any other spreadsheet and presentation software. This software packages are available for your use in the College's Computer Laboratories and other laboratories throughout the University.

Other electronic devices:

As a courtesy, please ensure that all cell phones are deactivated or muted prior to attending class. Use of wireless devices is strictly prohibited during periods that contribute to individual assessment (i.e. quizzes, midterms, and final exam).

Accommodation for religious holidays:

By UT-Austin policy, you must notify the instructor of your pending absence at least fourteen days prior to the date of observance of a religious holy day. If you must miss a class or an examination in order to observe a religious holy day, you will be given an opportunity to complete the missed work within a reasonable time after the absence.

Emergency evacuation:

PHR 252C Biopharmaceutics

I. COURSE DESCRIPTION:

Biopharmaceutics (PHR252C) introduces first-year PharmD students at the University of Texas at Austin to the concepts of pharmaceutics and biopharmaceutics. Topics including introduction to pharmaceutics, routes of drug administration, drug absorption and distribution, introduction to pharmacokinetics and pharmacodynamics, dose-response relationship, and bioequivalence are discussed with the purpose of improving the evaluation of drug delivery systems and the therapeutic management of patients. Additionally, the US Food and Drug Administration (FDA) new drug approval process and radioisotopes and their applications in biopharmaceutics and nuclear pharmacy are introduced.

II. COURSE OBJECTIVES:

Drug regulation in the USA

- To know the history of the US FDA
- To understand the role of FDA in drug approval
- The drug approval process
  - To understand the US FDA drug approval process including INDs, NDAs, ANDAs, etc.

Kinetics of drug action, dose-effect relationships, therapeutic index, margin of safety

- To identify factors involved in dose-effect relationships.
- To qualitatively and quantitatively describe the dose-effect relationship.
- To describe how the dose-effect relationship is used to establish a therapeutic index, and safety margins.

Dose-Response Relationships

- To obtain an understanding of direct pharmacokinetics/pharmacodynamics (PK/PD) response relationships
- To understand reasons for indirect dose-response relationships

Transport of drugs across biological membranes

- To discuss the principal transport mechanisms underlying movement across biological membranes (e.g. passive diffusion, active transport, facilitated diffusion, vesicular transport, solvent drag, ion pair formation, and lymphatic absorption).
- To describe a biological membrane and its composition
• To qualitatively and quantitatively describe Fick's First Law of diffusion and its application to drug absorption and the design of transdermal and ocular drug delivery systems.
• To discuss the pH-partition theory and Brodie's experiments.
• To discuss the use of an in vivo model to study membrane transport.
• To describe transporters and discuss the role of intestinal transporters in drug absorption.

Biopharmaceutical considerations in drug product design

• To discuss the relationship of the physicochemical properties and in vitro behavior of the drug and drug product on the delivery of the drug to the body.
• To qualitatively and quantitatively describe the Noyes-Whitney equation.
• To discuss in vitro testing of solid dosage forms and in vitro-in vivo correlations.

Drug absorption and availability considerations

• To have an overview of the GI tract
• To understand the regional differences related to drug absorption in the GI tract
• To discuss absolute versus relative bioavailability.

Bioequivalence

• To understand generic equivalence and therapeutic equivalence.
• To understand methods to establish bioequivalence.
• To discuss statistical methods to establish bioequivalence.

Routes of drug administration

• To understand the different routes of drug administration
• To discuss the advantages and disadvantages of difference routes of drug administration

Radioisotopes and nuclear medicine

• To review the concept of nuclides (e.g. isotopes, isobars, and isotones), atomic number, mass number and neutron number.
• To briefly review nuclear equations and define a target nucleus.
• To review radiation from radioactive nuclei (alpha, beta and gamma radiation).
• To review nuclear reactions (fission and fusion).
• To understand the units of radioactivity (e.g. Curie, millicurie, dps, dpm, cpm).
• To discuss the tracer concept, and to discuss sensitivity of tracer methods.
• To understand the rate of radioactive decay (e.g. half-life).
• To discuss several applications of radioisotopes in biopharmaceutics and in nuclear pharmacy.
III. CORE CONCEPTS EXPECTED TO MASTER AFTER COMPLETING BIOPHARMACEUTICS (PHR 252C):

1. Concepts of drug development

   1.1. History of drug regulation in the United States
       1.1.2. Kefauver-Harris Amendments (1962): Efficacy
       1.1.3. Drug Price Competition & Patent Restoration Act
               Waxman-Hatch Act, 1983
       1.1.4. Treatment Use of Investigational New Drugs (1987)
       1.1.5. Prescription Drug User Fee Act, 1987

2. How Drugs are developed

   2.1. Technical development of new drugs
   2.2. Patent considerations
   2.3. New drug development process
       2.3.1 Preclinical studies
       2.3.2 Investigational new drug application
       2.3.3 IND study protocol
       2.3.4 Phase I clinical studies
       2.3.5 Phase II clinical studies
       2.3.6 Phase III clinical studies
       2.3.7 Phase IV drug development studies
   2.4. Institutional review boards
   2.5. Treatment IND and expanded access program
   2.6. Abbreviated NDA (ANDA)

3. The United State Food and Drug Administration (FDA)

   3.1. FDA history
   3.2. FDA Review Process

4. Radioisotopes in biopharmaceutics and nuclear pharmacy

   4.1. Particles and nomenclature
   4.2. Nuclear reactions
       4.2.1. Fusion
       4.2.2. Fission
   4.3. Units of radioactivity
   4.4. Types of radiation
       4.4.1. Alpha
       4.4.2. Beta
       4.4.3. Gamma
4.5. Rate of radioactive decay
   4.5.1 Mathematical development
   4.5.2 Specific activity
4.6. Selected applications of radioisotopes in biopharmaceutics
   4.6.1. Radioisotopes in studying pharmacokinetics
   4.6.2. Gamma camera - scintillation camera
   4.6.3. Nuclear pharmacy - dosage calculation

5. Kinetics of drug action

   5.1. Potency
   5.2. Efficacy
   5.3. Therapeutic index
   5.4. Margin of safety
5.5. Dose optimization based on pharmacokinetic-pharmacodynamic modeling
   5.5.1. Fixed effect model
   5.5.2. Linear model
   5.5.3. Log-linear model
   5.5.4. Emax model
   5.5.5. Sigmoidal Emax model
5.6. Hysteresis loops
   5.6.1. Equilibration delays and links to other compartments

6. Transport of drugs across biological membranes

   6.1. Membrane structure and composition
       6.1.1. Davson-Danieli Model
       6.1.2. Singer-Nicolson Model
       6.1.3. Intrinsic, extrinsic proteins
   6.2. Transport mechanisms
       6.2.1. Fick’s Law and passive diffusion
       6.2.2. Facilitated diffusion
       6.2.3. Active transport
       6.2.4. Vesicular transport
       6.2.5. Solvent drag
       6.2.6. Ion-pair formation
   6.3. Role of intestinal transporters in drug absorption
       6.3.1. Absorption and exsorption
           6.3.1.1. Apical Transporters – Organic anions and cations
           6.3.1.2. The ABC (ATP- binding cassette proteins), Pgp (for lipophilic compounds), MRP2 (for drug conjugates), BCRP
       6.3.2. Transporters in drug distribution

7. Physiological variables in the gastrointestinal (GI) tract relevant to drug absorption
   7.1. pH
7.2. Complexation  
7.3. Transit time  
7.4. Bile components  
7.5. Luminal and brush border enzymes  
7.6. Absorbing capacity of the epithelia

8. Anatomical variables in the GI tract relevant to drug absorption  

8.1. Gastric phase  
8.2. Chemical agents  
8.3. Stomach emptying  
8.4. Functional movements in the GI tract

9. Effect of food and drink on drug absorption  

9.1. Triglycerides, amino acids, carbohydrates  
9.2. Acids  
9.3. Alkali  
9.4. Other factors  
  9.6.1. Viscosity  
  9.6.2. Particle geometry  
  9.6.3. Enterohepatic cycling

10. Lymphatic absorption  

10.1. Lymph formation  
10.2. Chylomicrons

11. Routes of drug administration, bioavailability, advantages and disadvantages  

11.1. Enteral  
  11.1.1. Oral cavity  
  11.1.2. Sublingual  
  11.1.3. Buccal  
  11.1.4. Oral  
  11.1.5. Rectal  
11.2. Parenteral  
  11.2.1. Intravenous and intra-arterial  
  11.2.2. Intramuscular  
  11.2.3. Subcutaneous  
  11.2.4. Intraperitoneal  
  11.2.5. Intradermal  
11.3. Others  
  11.3.1. Nasal  
  11.3.2. Topical
11.3.3. Inhalation
11.3.4. Intrathecal
11.3.5. Ophthalmic

12. Biopharmaceutics considerations in drug product design

12.1. Rate limiting steps in drug absorption
   12.1.1. Pharmacodynamic considerations
      12.1.1.1. Therapeutic objective
      12.1.1.2. Toxic effects
      12.1.1.3. Adverse reactions
   12.1.2. Drug considerations
      12.1.2.1. Chemical and physical properties
   12.1.3. Drug product considerations
      12.1.3.1. Pharmacokinetics of drug
      12.1.3.2. Bioavailability of drug
      12.1.3.3. Route of administration
      12.1.3.4. Desired dosage form
      12.1.3.5. Desired dose of drug
   12.1.4. Patient considerations
      12.1.4.1. Compliance and acceptability of product
      12.1.4.2. Costs
   12.1.5. Manufacturing considerations
      12.1.5.1. Cost
      12.1.5.2. Availability of raw materials
      12.1.5.3. Stability
      12.1.5.4. Quality control

12.2. In vitro disintegration

12.3. In vitro dissolution
   12.3.1. Noyes Whitney equation
      12.3.1.1. Compendial methods of dissolution
      12.3.1.2. Basket method
      12.3.1.3. Paddle method
   12.3.2. In vitro-in vivo correlations

12.4. Bioavailability
   12.4.1. Relative
   12.4.2. Absolute
   12.4.3. Assessment of Bioavailability
      12.4.3.1. From plasma levels after a single dose or at steady state
         12.4.3.1.1. Area calculation
      12.4.3.2. From urine levels after a single dose or at steady state
      12.4.3.3. From pharmacological response

12.5. Bioequivalence
   12.5.1. Sources of variability of bioequivalence studies
      12.5.1.1. Inescapable variation
12.5.1.2. Controllable variation
12.5.1.3. Statistical considerations
    12.5.1.3.1. Design, reference standard, and data evaluation
    12.5.1.3.2. 90% confidence intervals
12.5.4. Therapeutic equivalence
12.5.5. Generic substitution
12.6. Federal and State Regulations
Lecture Schedule:

As a part of active learning experience, during the first lecture, all the topics that will be covered in the semester will be introduced, and the order by which each topic will be presented during the semester will be determined by the class following group discussion. (* Lecture topics may be adjusted during the semester)

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<tr>
<th>Date</th>
<th>Week No.</th>
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<tr>
<td>8/26/2014</td>
<td>Week 1</td>
<td>Syllabus overview, introduction to pharmaceutics and biopharmaceutics</td>
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<tr>
<td>9/2/2014</td>
<td>Week 2</td>
<td>US FDA new drug approval process</td>
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** Tentative