USC Mann

Alfred E. Mann School of Pharmacy
and Pharmaceutical Sciences

BPSI 403: Biopharmaceutics II

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Office hours: by appointment

Course Weight: 4 Units (two weekly 1.5-hour sessions; computer simulations lab with three assignments combined as a final report to be submitted on the day of the final exam)

Catalogue description: Comprehensive overview of late-stage drug discovery and early-stage medicinal product development; introduction to the biopharmaceutical classification system, *in vitro* and *in vivo* assays through *in silico* simulations and modeling, drug delivery and safety sciences & technology

Day/Time/Location: M/W, 12:30-1:50pm, DMC 211

Introduction and Purpose

This introductory course will provide students with a comprehensive overview of early drug and medicinal product development *in vitro* and *in vivo* assays simulations and modeling, biopharmaceutical classification system, and drug delivery and safety sciences & technology. Biopharmaceutical modeling has become integral to the design and development of new medical products. Influencing key aspects of the development process, including drug substance design, formulation design, and toxicological exposure assessment, biopharmaceutical modeling is now seen as the linchpin to any new medicinal products' future success. Biopharmaceutics II is a multidisciplinary course encompassing areas of study that employ basics of general chemistry, biology (biosystems), and mathematics (calculus), addressing formulation and delivery of drugs using modeling and simulations computer software.

By applying concepts of Pharmacology and Pharmaceutical Sciences to various dosage forms, routs of administration, and their interchangeability students will be introduced to concepts in bioavailability and bioequivalence. Applied chemistry, biology, mathematics, physics, and chemical engineering concepts as they relate to medicinal products will be used to exemplify approaches in building physiologically based pharmacokinetic simulation models. Topics in this course will include principals of pharmacokinetics, physical pharmacy, drug product design and development, as well as pharmaceutical biotechnology. Mathematical calculation of drug concentrations over time will be introduced (computer lab) to study absorption, distribution, metabolism, and elimination of drugs.

Virtual '*healthy volunteers*' and '*preclinical animal species*' will be used in computer simulations, focusing on visualizing kinetic processes describing rates of Absorption, Distribution, Metabolism and Excretion (ADME). A bridge between dosage form characteristics (i.e., type solid vs liquid – pills and injections; route of administration – enteral and parenteral) with potential systemic exposure outcomes will be constructed to understand importance of matching specifications of 'blood concentration vs time' profiles. Students will have the opportunity of learning with literature data (using Gastroplus® software) and generating in vitro solubility/permeability and in vivo pharmacokinetic parameters applying information to absolute drug-dose determination and adjustment. Concepts of translation of these parameters will also be introduced. Students' understanding of basic biopharmaceutics and pharmacokinetic principles will be reinforced preparing them to apply knowledge gained in the design, implementation, and management of pharmacotherapy in a variety of real-world settings.

Principles introduced in this course will familiarize students with biopharmaceutical classification and formulation sciences terminology, including key concepts related to the processes of equivalence (generics and biosimilars) and will help set the stage for future, more sophisticated course work necessary for the student to gain a level of competency to be successful in the biopharmaceutical drug discovery and development setting. Beginning with a focus on the oral absorption of drugs, BPSI 403 discusses the central dogma of oral drug absorption (the interplay of dissolution, solubility, and permeability of a drug), which forms the basis of the biopharmaceutical classification system (BCS), using in silico tools, i.e. virtual computer-software based, that are widely adapted by progressive drug development companies and global regulatory agencies (e.g. US FDA).

To help prepare the student for the ever-changing environment, this course will present foundational and newly advancing modeling and simulation technologies to provide knowledge regarding critical aspects of medicinal product development. Additionally, the course coordinator will try to invite guest lecturers from biotech/pharma industry to speak about their jobs and career opportunities/trajectories.

Objectives

This course a continuation of BPSI 402, Biopharmaceutics I. In BPSI 403, students will learn applications of physicochemical properties of drugs as they impact medicinal product development. Characteristics including solubility and dissolution kinetics, permeability, and the influence of dose-formulation will be systematically evaluated in solid or liquid drug dosage forms administered via common routes to a virtual/simulated body. Modulation of dissolution kinetics will be studied in parallel to biological membrane diffusion/permeability to exemplify

the effect these biopharmaceutical properties have on pharmacokinetics of drug products. Content presented in this course will enable students to acquire a strong understanding of the step-by-step processes involved in the role and importance of solid-state and ionizable/reactive drug functional group properties on the dosing, efficiency, and delivery of pharmaceutical products. Translational aspects of biopharmaceutical developability will be introduced to facilitate understanding interspecies relationships in safety, efficacy, and allometric dose scaling. Importance of gastrointestinal physiological effects (fasted vs fed state) and physicochemical factors (solubility and permeability) that influence the availability of a drug from different dosage forms (immediate vs modified release), and the subsequent disposition of the drug in the body will be introduced. Chapters from required textbooks will be supplemented with a variety of source materials, including articles from scientific journals and public websites. Case studies will be critically reviewed, and emerging "hot" topics discussed.

Upon successful completion of this course, the student should be able to:

- Understand physicochemical property descriptors of composite values of drug solubility and permeability.
- Understand principles of solubility, dissolution, and diffusion.
- Explain the differences between absolute bioavailability, relative bioavailability, and criteria of pharmaceutical bioequivalence.
- List reasons for incorporation of drugs into various dosage forms and describe the essentials of compounding practices by categorizing common excipients.
- Understand and be able to exemplify solid vs liquid dosage forms, and key biopharmaceutical blueprint attributes for oral vs intravenous administration of medicinal products.
- Define and comprehend basic pharmacokinetic principles modulated by dose, route of administration, and formulation of a medicinal product.
- Describe mechanisms of drug degradation and provide examples in vitro/in vivo settings of each.
- Describe various types of drug absorption from a pharmaceutical dosage form.
- Describe the physical and chemical characteristics of a drug that affect its dissolution from various dosage forms and explain how drug dissolution affects drug absorption.
- Perform pharmacokinetic analysis of given plasma drug concentration data and define the concept of oral bioavailability and bioequivalence.
- Compare and contrast advantages and disadvantages of the various types of tablet dosage forms.
- Define solubilization, list major factors affecting solubility, and perform calculations to determine appropriate parameters to establish maximum solubility.
- List physical and chemical characteristics of drugs that make them candidates for an extended-release, comparing/contrasting properties of common modified-release dosage forms.
- Explain the physical-chemical properties of drugs which determine their suitability to be incorporated into common dosage forms and differentiate between the various types of systems used for oral vs. intravenous delivery.
- Identify and explain physiologic factors which influence the drug absorption from oral administration and identify key rate limiting physicochemical factors.

Assignments and Grading:

Table 1 Grading Breakdown

Class participation:	60 pts.	(24 %)
*Up to 10 unannounced quizzes		
Midterm Exam (first 8 weeks):	45 pts.	(18 %)
GastroPlus+ Case Study Report:	45 pts.	(18 %)
MS Word format		
Final Exam (only material covered after midterm):	100 pts.	(40 %)
Total:	250 pts.	

Participation in class is compulsory,* ***there is no makeup for missed quizzes**, since these are not graded (credit/no-credit). Number of Kahoot!'s is subject to vary and pts/quiz value will be adjusted accordingly is <10 or >10. Only if a particular quiz is missed due to an excused absence, alternative assignment will be given for completion outside of class* ***and will be graded*** *on a typical letter grade (e.g. A-through-D) grading scale.*

Table 2 Course Grading Scale (example does not consider possibility of curving the grades)

Letter grade	Corresponding numerical point range
A	95-100
A-	90-94
B+	87-89
B	83-86
B-	80-82
C+	77-79
C	73-76
C-	70-72
D+	67-69
D	63-66
D-	60-62
F	59 and below

Class Participation and Attendance (60 pts): On a scale indicating no participation to full participation. You can therefore increase the probability of getting a higher mark by being proactive in terms of asking (relevant) questions in class and/or contributing to discussions. Must log an identifiable ID/Avatar/Nickname in Kahoot! Participation also includes asking and answering questions and being actively involved in discussions. It is expected that students read assigned papers prior to lecture and prepare to discuss background, current understanding, treatments, and gaps in knowledge for the topic in each lecture.

Assignment Submission Policy

There will be up to 10 quizzes (*if less quizzes are given, 60pts will be normalized over fewer number of attempts >weight on each Kahoot!, vs more than <weight; i.e. 10 Kahoot!'s will be worth 6 points each, 8 will factor 7.5pts/game, and 12 games will factor 5pts per Kahoot!*) over

the course of the semester that will primarily be based on questions pulled from reading assignments and lectures. Quizzes are rolled up into the class participation, and they are credit/no-credit based (live polls and games with immediate feedback in the classroom).

The midterm (45 points) is intended to be a midpoint exam that tests cumulative understanding of first half of the semester. It will be an in-person exam, closed book/notes, administered on lockdown browser via Brightspace. Questions will be in multiple choice, true/false, and matching style. No fill-ins written answer type.

A maximum 5-page double-spaced essay (pg. count refers to written text only) based on a G+ simulation case study (deliverable) will be due by **11:59pm PST on the day of the final exam** via posting on Brightspace (45 points). The report should focus on an applied pragmatic biopharmaceutical risk analysis of your medicinal product. The written report must be formally submitted through Brightspace option (e.g. Turn It In); it must contain < 15% similarity score. Late submissions may not be accepted, regardless. In special exceptions, i.e. on a case-by-case basis excused rationale for late submission, maximum possible score will be a C (automatic 34/45pts).

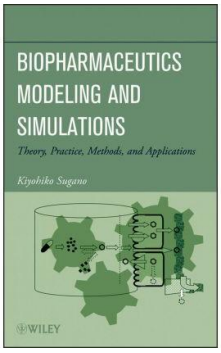
The final exam (100 points) is intended to test cumulative understanding of secand half of the semester; specifically all concepts covered after the midterm. It will be an in-person exam during finals week, closed book/notes, administered on lockdown browser via Brightspace. Questions will be in multiple choice, true/false, and matching style. No fill-ins written answer type.

Additional details will be presented during class and included in templates/rubrics slides/documents. Cell phones or any other aids are not allowed during quizzes or exams.

Students are requested to complete an anonymous critical evaluation of the course at its completion.

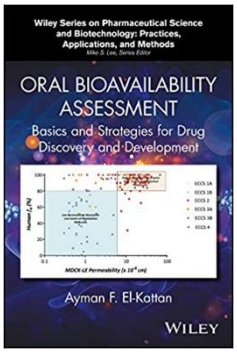
Course Readings

Required Readings



Biopharmaceutics Modeling and Simulations: Theory, Practice, Methods, and Applications. 1st Edition. Kiyohiko Sugano. ISBN-13: 978-1118028681

Additional text that students may find helpful:



Oral Bioavailability Assessment: Basics and Strategies for Drug Discovery and Development (Wiley Series on Pharmaceutical Science and Biotechnology: Practices, Applications and Methods) 1st Edition. Ayman F. El-Kattan (Author), Mike S. Lee (Series Editor). ISBN-13: 978-1118916698

Additional textbooks are not mandatory, however students interested in drug discovery process should consider their purchase to expand comprehension on BCS and drug delivery principles. The students will be able to use identified chapters in the text to support their learning process throughout the semester.

Other course materials including but not limited to the syllabus, supplemental reading assignments and additional handouts will be posted on http://brightspace.usc.edu/. The students will also be encouraged to use the online discussions among students via Brightspace.

Recommended Supplemental Readings

User manual to GastroPlus® (current version) (SimulationsPlus, Inc., Lancaster, CA)

Academic Integrity

The University of Southern California is foremost a learning community committed to fostering successful scholars and researchers dedicated to the pursuit of knowledge and the transmission of ideas. Academic misconduct is in contrast to the university's mission to educate students through a broad array of first-rank academic, professional, and extracurricular programs and includes any act of dishonesty in the submission of academic work (either in draft or final form).

This course will follow the expectations for academic integrity as stated in the USC Student Handbook. All students are expected to submit assignments that are original work and prepared specifically for the course/section in this academic term. You may not submit work written by others or "recycle" work prepared for other courses without obtaining written permission from the instructor(s). Students suspected of engaging in academic misconduct will be reported to the Office of Academic Integrity.

Other violations of academic misconduct include, but are not limited to, cheating, plagiarism, fabrication (e.g., falsifying data), knowingly assisting others in acts of academic dishonesty, and any act that gains or is intended to gain an unfair academic advantage.

The impact of academic dishonesty is far-reaching and is considered a serious offense against the university and could result in outcomes such as failure on the assignment, failure in the course, suspension, or even expulsion from the university.

For more information about academic integrity see the student handbook or the Office of Academic Integrity's website, and university policies on Research and Scholarship Misconduct.

Policy for the use of AI Generators

Since creating, analytical, and critical thinking skills are part of the learning outcomes of this course, all assignments should be prepared by the student working individually or in groups. Students may not have another person or entity complete any substantive portion of the assignment. Developing strong competencies in these areas will prepare you for a competitive workplace. Therefore, using AI-generated tools is prohibited in this course, will be identified as plagiarism, and will be reported to the Office of Academic Integrity.

Course Outline

This course will be in the format of a directed seminar/lecture under the guidance of the instructor for the specific session. During each weekly session the instructor will engage the students with questions and draw comments or interpretations primarily based on the assigned reading. Students are expected to ask questions and participate in an interactive fashion. Course coordinator reserves the option to invite one or more biopharmaceutical industry executives for guest lectures.

Week & Date	Speakers	Subtopics to be Included	Assigned and Supplemental Reading
Introduction and Background			
Week 1 Jan 13, 15	Gukasyan, HJ	Introduction: expectations and goals of this class Career prospects in biopharmaceutics industry vs. regulatory agencies	Syllabus Sugano, Ch.9 and El-Kattan Ch.1
Week 2 Jan 22	Gukasyan, HJ	General overview of drug bioequivalence History of the BCS. Bioequivalence and biowaivers Illustrative description of oral drug absorption: the whole story	Sugano, Ch.1 and El-Kattan Ch.1 Suppl. Amidon GL, et al. Pharm Res. 1995 Mar;12(3):413-20.
Physicochemical Properties and Biophysics			
Week 3 Jan 27, 28	Gukasyan, HJ	Solubility: concentration, acid/base/salt, thermodynamics, polymorphs, and solid form characterization	Sugano Ch. 2, 7.5, 7.6 and El-Kattan Ch. 4
Week 4 Feb 3, 5	Gukasyan, HJ	Dissolution: particules, diffusion layer, 'nucléation'	Sugano Ch. 3, 7.7, 7.8 and El-Kattan Ch. 4
Week 5 Feb 10, 12	Gukasyan, HJ	Permeability: Fick's Law, mechanisms, unstirred layer, relationship physicochemical properties vs. fraction of a dose that is absorbed	Sugano Ch.4, 7.9 and El-Kattan Ch. 4, 9, 10
During Weeks 3-5	Computer labwork	Identify software input modules for solubility, dissolution, and permeability parameters for 3 different published drug molecules	GastroPlus® manual
Advanced Gastrointestinal Absorption and Transit			
Week 6 Feb 19	Gukasyan, HJ	Gastrointestinal transit: ACAT® model, compartments, integration	Sugano Ch. 5 and El Kattan Ch. 2
Week 7 Feb 24, 26	Gukasyan, HJ	Approximate fraction of a dose absorbed (analytical solutions to Fa% estimation, interpretations of Fa equations)	Sugano Ch. 5 and El Kattan Ch. 1, 2
Week 8 March 3, 5	Gukasyan, HJ	In vivo Fa from pharmacokinetic data, PKPlus® IV dose deconvolution: absolute bioavailability, relative bioavailability (solid vs liquid dose, high vs low dose)	Sugano Ch. 5, 7.10 and El Kattan Ch. 1, 2, 4, 11
Week 9 March 10, 12	Gukasyan, HJ	Physiology of the gastrointestinal tract: stomach, intestines, pH, bile acids/food effect	Sugano Ch. 6 and El-Kattan Ch. 1, 2
Spring Recess Sunday, March 16, 2025 to Sunday, March 23, 2025			
*Week 10 March 24, 26	*Gukasyan, HJ	Physiology of the gastrointestinal tract: transporters (efflux vs uptake)	Sugano Ch. 6, 14 and El-Kattan Ch. 6, 7
Week 9, Wed 12th March 2025, Midterm Exam			
*Week 11 March 31, Apr 2nd	*Gukasyan, HJ	Drug Parameters: pKa, logP/D, micelles, size and shape distributions	Sugano Ch. 7 and El-Kattan Ch. 5
During Weeks 6-11	Computer labwork	Identify software input modules for dose, dosage form, route of administration, drug physicochemical characteristics of logP and pH vs solubility relationship, efflux pump effect, and perform a Fa calculation at 3 doses for talinolol	GastroPlus® manual Bolger, M.B. et al. AAPS J. 2009 Jun; 11(2): 353–363.
Applied Drug Delivery: BCS/Bioequivalence			
*Week 12 Apr 14, 16	*Gukasyan, HJ	Validation and reliability of mechanistic absorption models: case studies *(option to have it asynchronous in case of biopharmaceutical industry guest lecture)* Permeability limited vs solubility limited (Caco-2, PAMPA, IVIVC) *(option to have it asynchronous in case of biopharmaceutical industry guest lecture)* Salts?*(option to have it asynchronous in case of biopharmaceutical industry guest lecture)*	Sugano Ch.8 and El-Kattan Ch. 4, 5
*Week 13 Apr 21, 23	*Gukasyan, HJ	BCS and bioequivalence: case studies *(option to have it asynchronous in case of biopharmaceutical industry guest lecture)*	Sugano Ch. 9 and El-Kattan Ch. 8, 13
*Week 14	*Gukasyan, HJ	Changing drug dose and particle size	Sugano Ch. 10

Apr 28, 30		Guidance in the Setting of Drug Particle Size Specifications to Minimize Variability in Absorption Food Effect: physiological and pharmacokinetic changes, predicting and applying to BCS, impact of medicinal product formulation	Suppl. Kevin C. Johnson & Archie C. Swindell Pharm Res v13, pgs 1795–1798 (1996) Sugano Ch. 12, 13 and El-Kattan Ch. 1, 2
During Weeks 12-14	Computer labwork	Physiologically Based Absorption Modeling to Explore the Impact of Food and Gastric pH Changes on the Pharmacokinetics of Alectinib	GastroPlus® manual Parrott, N.J. AAPS J. 2016 Nov;18(6):1464-1474.
Friday May 9th 2025, 11am-1pm, DMC 211 Final Exam. Simulation Term Paper/Report is due by 11:59 pm PST.			
****line item weekdays *marked* are to-be-determined, shown/planned topic may be replaced by an invited guest lecture from biotech or pharma industry (zoom/remote or in person)***			

Statement on Academic Conduct and Support Systems

Academic Integrity:
The University of Southern California is a learning community committed to developing successful scholars and researchers dedicated to the pursuit of knowledge and the dissemination of ideas. Academic misconduct, which includes any act of dishonesty in the production or submission of academic work, compromises the integrity of the person who commits the act and can impugn the perceived integrity of the entire university community. It stands in opposition to the university's mission to research, educate, and contribute productively to our community and the world.

All students are expected to submit assignments that represent their own original work, and that have been prepared specifically for the course or section for which they have been submitted. You may not submit work written by others or "recycle" work prepared for other courses without obtaining written permission from the instructor(s).

Other violations of academic integrity include, but are not limited to, cheating, plagiarism, fabrication (e.g., falsifying data), collusion, knowingly assisting others in acts of academic dishonesty, and any act that gains or is intended to gain an unfair academic advantage.

The impact of academic dishonesty is far-reaching and is considered a serious offense against the university. All incidences of academic misconduct will be reported to the Office of Academic Integrity and could result in outcomes such as failure on the assignment, failure in the course, suspension, or even expulsion from the university.

For more information about academic integrity see the student handbook or the Office of Academic Integrity's website, and university policies on Research and Scholarship Misconduct.

Please ask your instructor if you are unsure what constitutes unauthorized assistance on an exam or assignment, or what information requires citation and/or attribution.

Students and Disability Accommodations:

USC welcomes students with disabilities into all of the University's educational programs. The Office of Student Accessibility Services (OSAS) is responsible for the determination of appropriate accommodations for students who encounter disability-related barriers. Once a student has completed the OSAS process (registration, initial appointment, and submitted documentation) and

accommodations are determined to be reasonable and appropriate, a Letter of Accommodation (LOA) will be available to generate for each course. The LOA must be given to each course instructor by the student and followed up with a discussion. This should be done as early in the semester as possible as accommodations are not retroactive. More information can be found at osas.usc.edu. You may contact OSAS at (213) 740-0776 or via email at osasfrontdesk@usc.edu.

Support Systems:

Counseling and Mental Health - (213) 740-9355 – 24/7 on call
Free and confidential mental health treatment for students, including short-term psychotherapy, group counseling, stress fitness workshops, and crisis intervention.

988 Suicide and Crisis Lifeline - 988 for both calls and text messages – 24/7 on call
The 988 Suicide and Crisis Lifeline (formerly known as the National Suicide Prevention Lifeline) provides free and confidential emotional support to people in suicidal crisis or emotional distress 24 hours a day, 7 days a week, across the United States. The Lifeline is comprised of a national network of over 200 local crisis centers, combining custom local care and resources with national standards and best practices. The new, shorter phone number makes it easier for people to remember and access mental health crisis services (though the previous 1 (800) 273-8255 number will continue to function indefinitely) and represents a continued commitment to those in crisis.

Relationship and Sexual Violence Prevention Services (RSVP) - (213) 740-9355(WELL) – 24/7 on call
Free and confidential therapy services, workshops, and training for situations related to gender- and power-based harm (including sexual assault, intimate partner violence, and stalking).

Office for Equity, Equal Opportunity, and Title IX (EEO-TIX) - (213) 740-5086
Information about how to get help or help someone affected by harassment or discrimination, rights of protected classes, reporting options, and additional resources for students, faculty, staff, visitors, and applicants.

Reporting Incidents of Bias or Harassment - (213) 740-5086 or (213) 821-8298
Avenue to report incidents of bias, hate crimes, and microaggressions to the Office for Equity, Equal Opportunity, and Title for appropriate investigation, supportive measures, and response.

The Office of Student Accessibility Services (OSAS) - (213) 740-0776
OSAS ensures equal access for students with disabilities through providing academic accommodations and auxiliary aids in accordance with federal laws and university policy.

USC Campus Support and Intervention - (213) 740-0411
Assists students and families in resolving complex personal, financial, and academic issues adversely affecting their success as a student.

Diversity, Equity and Inclusion - (213) 740-2101
Information on events, programs and training, the Provost's Diversity and Inclusion Council, Diversity Liaisons for each academic school, chronology, participation, and various resources for students.

USC Emergency - UPC: (213) 740-4321, HSC: (323) 442-1000 – 24/7 on call
Emergency assistance and avenue to report a crime. Latest updates regarding safety, including ways in

which instruction will be continued if an officially declared emergency makes travel to campus infeasible.

USC Department of Public Safety - UPC: (213) 740-6000, HSC: (323) 442-1200 – 24/7 on call
Non-emergency assistance or information.

Office of the Ombuds - (213) 821-9556 (UPC) / (323-442-0382 (HSC)
A safe and confidential place to share your USC-related issues with a University Ombuds who will work with you to explore options or paths to manage your concern.

Occupational Therapy Faculty Practice - (323) 442-2850 or otfp@med.usc.edu
Confidential Lifestyle Redesign services for USC students to support health promoting habits and routines that enhance quality of life and academic performance.