USC Mann

Alfred E. Mann School of Pharmacy
and Pharmaceutical Sciences

BPSI 402: Biopharmaceutics I

Coordinator: Hovhannes J. Gukasyan, PhD
Associate Professor, Department of Pharmacology and Pharmaceutical Sciences
University of Southern California
Email: gukasyan@usc.edu
Office Phone: (323) 442-1362
Office Location: @HSC PSC 716, @UPC STO 312
Office Hours: Weekly, Fridays 4-5:30pm

Instructors: Daryl L. Davies, PhD
Professor, Department of Clinical Pharmacy
University of Southern California
Office: HSC campus PSC 506
Email: ddavies@usc.edu
Office Phone: (323) 442-1427
Office hours: by appointment

Course Weight: 4 Units (two weekly 1.5-hour sessions; plus computer simulations lab ad libitum complete drug discovery practice assignment and case study report)

Catalogue description: Comprehensive overview of industrial approaches to drug discovery; *in vitro* and *in vivo* assays and *in silico* simulations/modeling, exploratory biopharmaceutics.

Day/Time/Location: T/Th, 2:00-3:20pm, KAP 159

Introduction and Purpose

Biopharmaceutics I is a multidisciplinary course encompassing areas of study that employ basics of general chemistry, biology, and biochemistry addressing identification and refinement of early molecular substrate to an optimized candidate worthy of clinical trials. This introductory course – and a precursor to BPSI 403/Biopharmaceutics II - will provide students with a comprehensive overview of industrial approaches to drug discovery. It will focus on all modalities (small molecules, biologics, and other complex non-biological systems). Full spectrum of the course covers the classical division of pharmaceutical research into four phases, commencing with target identification and ending with preclinical testing.

Applied biochemistry and biology concepts will be used to exemplify approaches in discovery of new drugs in a pragmatic, bio-pharmaceutical industrial context. We will build an understanding on how *in vitro* and *in vivo* assays are used to identify and validate drug targets and apply progressive modeling and simulation tools to improve molecular pharmacology of compounds. Modeling, computational methods and quantitative structure activity relationships (in chem-/bio-informatics) have become integral to the design and development of new drugs. Influencing key aspects of the discovery process, including molecular design, pharmacological and toxicological

biochemistry assessment, comprise the linchpins to any new drug molecule and its future chances of becoming a medicinal product.

Case studies demonstrating principals of drug design and pharmacology are discussed. Students will utilize computer aided virtual "blind" docking to protein-targets important in disease (i.e., computer lab in course outline refers to this) to study potency and selectivity of newly designed molecules. Concepts of translation of discovery-centric molecular parameters from virtual pre-clinical research to higher species will be introduced. Students' understanding of basic pharmacology and toxicology principles will be reinforced preparing them to apply knowledge gained in the design, implementation, and management of drug discovery in a variety medical product settings.

"Drug Discovery in the Modern Age: How We Got Here and What Does It Mean?" will be introduced, with case-study driven historical background, and current status of drug discovery. Students will be able to understand the basic concepts and tenets underlying modern drug discovery, how they have evolved, and various approaches and strategies to modern drug discovery. Beginning with a focus on TARGET SELECTION, then VALIDATION, discovery of drugs in BPSI 402 discusses the central dogma of industrial approaches to drug discovery. To help prepare the student for the ever-changing environment, this course uses modeling and simulation technologies to provide and reinforce knowledge regarding critical aspects of medicinal product development related to pharmacology and toxicology.

Objectives

BPSI 402, Biopharmaceutics I, is a recommended prerequisite of BPSI 403, Biopharmaceutics II. In Biopharmaceutics I, students will learn industrial, semi-automation, and digital approaches in drug discovery, question the productivity of each strategy, i.e., high-throughput technologies for screening millions of compounds against the large numbers of new targets from genomics, use of CADD in the same, and drug repositioning. Translational aspects will be introduced to facilitate understanding interspecies relationships in safety and efficacy. (1) Target identification, by which the hypothesis of the involvement of a particular molecular target is postulated; (2) lead identification, delivery of several chemical lead series that show a demonstrable effect on the disease target of interest; (3) bearing on the optimization of the structure-activity relationships (SARs) around specific pharmacophore classes; and finally, (4) optimized lead compounds to enter preclinical/clinical testing where their overall potency and selectivity/specificity profiles are assessed as a precursor – will be covered.

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

- Drug targets: what are they, where they come from, how are they related to disease?
- Understand principles of drug target discovery or identification.
- Criteria for drug target validation. Is there a difference in drug discovery when it comes to validation of a drug target, as opposed to clinical treatment of a disease condition?
- What are different modalities of drugs in a discovery setting?

- Are all modalities equal when it comes to drug discovery?
- Are all targets "druggable"?
- What are hits? What are leads? What are candidates?
- What are druggable attributes in drug discovery?
- What is the mode of action or mechanism of action and how is it different from efficacy?
- What is potency as opposed to selectivity?
- What is pharmacology as opposed to toxicology?
- Use of:
    - Databased such as PubMed, PubChem, PDB, and Clinicaltrials.gov
    - Software such as Autodock Veena® and CB-Dock® for molecular docking; ChemDraw®/ChemSketch®/Marvin Sketch®/Online etc. for molecular editing.
- Interpret drugs bound to targets and mode of binding / cavity location detection / size

Assignments and Grading:

Class participation:	10 pts	(~3.3 %)
10 quizzes @ 10 pts each:	100 pts	(~33.3%)
Drug discovery project report:	90 pts	(30 %)
Cumulative final exam:	100 pts	(~33.3 %)
Total:	300 pts.	

Class Participation and Attendance (10 pts): Attendance, in person, at all classes is expected unless otherwise announced (there may be situations when a industry guest teaches over Zoom videoconferencing if they are located in a different time zone). Participation will include asking and answering questions and being actively involved in the discussion. It is expected that the students read the assigned papers prior to the lecture and be prepared to discuss background, current understanding, treatments, and gaps in knowledge for the topic in each lecture.

There will be 10 (or more) quizzes over the course of the semester that will primarily be based testing students' understanding of key concepts (10pts for class attendance/participation will be derived from quiz attempts; e.g. if 10 quizzes are given and student attempts 9-out-10, 9pts will be proportionally awarded for class participation). There will be no makeup for quizzes. The final exam, cumulative (100 points) will include multiple choice questions and/or T/F questions centered around all the quizzes taken over the course of 15 weeks. Notes, books, calculators, electronic dictionaries, regular dictionaries, cell phones or any other aids are not allowed during exams.

Double-spaced report, not more than 5 pages including figures and references, based on drug discovery case study (deliverable) will be due by **5pm PST on the day of the final** via posting on Blackboard or via email to gukasyan@usc.edu. The report will focus on designing a new drug against a specific target, with rationale on target selection, validation, and quantitative structure activity vina score (Vina. An empirical scoring function calculates the affinity, or fitness, of protein-ligand binding by summing up the contributions of several individual terms)

improvement demonstration.

Additional details will be presented during week one of the class and included in the Week 1 PPT slides.

Students will be asked to complete an anonymous critical evaluation of the course at its completion.

Course Readings

Required Readings

Handen, P.D.,.J.S. (Ed.). (2005). Industrialization of Drug Discovery: From Target Selection Through Lead Optimization (1st ed.). CRC Press. https://doi-org.libproxy2.usc.edu/10.1201/9781420028072

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.

Additional text that students may find helpful:

1. Drug Design: Principles and Applications, Grover, A. ISBN 9789811051876, https://books.google.com/books?id=n2AwDwAAQBAJ, 2017, Springer Singapore
2. Smith and Williams' Introduction to the Principles of Drug Design and Action. Smith, H.J., Williams, H. ISBN 9781135299750, https://books.google.com/books?id=4XmmDwAAQBAJ, CRC Press, 2005.

Additional textbooks are not mandatory, however students interested in drug discovery process should consider purchasing them to expand comprehension related 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://blackboard.usc.edu/. The students will also be encouraged to use the online discussions among students via Blackboard.

Recommended Supplemental Readings

Additional readings are found in the respective column of the course outline.

USC Mann

Alfred E. Mann School of Pharmacy and Pharmaceutical Sciences

Course Outline

Week & Date	Speakers	Subtopics to be Included	Assigned and Supplemental Reading
Week 1 Tues. Aug. 22 Thur. Aug. 24	Gukasyan, HJ	▪ Welcome Orientation ▪ "Druggable" Property Space: Desired properties and qualities of an ideal candidate? Safety, Efficacy, Delivery	Syllabus, PowerPoint Slides
Week 2 Tues. Aug. 29 Thur. Aug. 31	Gukasyan, HJ	▪ Drug Discovery in the Modern Age: How We Got Here and What Does It Mean? ▪ The Regulatory Age	Handen Ch.1, 2
Labor Day, University Holiday, Monday September 4, 2023			
Week 3 Tues. Sept. 5 Thur. Sept. 7	Gukasyan, HJ	▪ Drug Discovery in the Modern Age: How We Got Here and What Does It Mean? ▪ The Regulatory Age	Handen Ch.1, 2
Week 4 Tues. Sept. 12 Thur. Sept. 14	Gukasyan, HJ	Industrialisation, Not Automation Applications of Computer-Aided Drug Design	Handen Ch. 3 Abhinav Ch. 9
Week 5 Tues. Sept. 19 Thur. Sept. 21	Gukasyan, HJ	Compound Management Applications of Computer-Aided Drug Design	Handen Ch. 4 Abhinav Ch. 9
Weeks ~3-5	Computer lab work	Setting up drug files and protein target files, create a workflow for modification of templates, create a workflow for tracking Vina scores	Liu Y, et al. **CB-Dock: a web server for cavity detection-guided protein-ligand blind docking.** Acta Pharmacol Sin. 2020;41(1):138-144. 1. DDT • Volume 11, Number 3/4 • February 2006 2. Current Pharmaceutical Design, 2002, 8, 2269-2278 3. Cancer Treatment Reviews 84 (2020) 101966

Week 6 Tues. Sept. 26 Thur. Sept. 28	Gukasyan, HJ	High-Throughput Screening Applications of Computer-Aided Drug Design	Handen Ch. 5 Abhinav Ch. 9
Week 7 Tues. Oct. 3 Thur. Oct. 5	Gukasyan, HJ	Parallel Lead Optimization Applications of Computer-Aided Drug Design	Handen Ch. 6 Abhinav Ch. 9
Week 8 Tues. Oct. 10	Gukasyan, HJ	Knowledge Management Part 1	Handen Ch. 7
Fall Recess, Thursday Oct. 12 to Friday. Oct. 13, 2023			
Week 9 Tues. Oct. 17 Thurs. Oct. 19	Gukasyan, HJ	Knowledge Management Part 2	Handen Ch. 7
Week 10 Tues. Oct. 24 Thurs. Oct. 26	Gukasyan, HJ	Cheminformatics Approaches in Modern Drug Discovery Part 1	Abhinav Ch. 9
Week 11 Tues. Oct. 31 Thurs. Nov. 2	Gukasyan, HJ	Cheminformatics Approaches in Modern Drug Discovery Part 2 Understanding the Value of Research	Abhinav Ch. 9 Handen Ch. 8
Weeks 6-11	Computer lab work	Produce simple two dimensional correlations tracking simple structure modifications vs. Vina score and cavity size location	Yang Liu, et al. **CB-Dock2: improved protein–ligand blind docking by integrating cavity detection, docking and homologous template fitting**. Nucleic Acids Research, 2022, vol. 50, is. W1, p. W159–W164. 1. DDT • Volume 11, Number 3/4 • February 2006 2. Current Pharmaceutical Design, 2002, 8, 2269-2278 3. Cancer Treatment Reviews 84 (2020) 101966
Week 12* Tues. Nov. 7 Thurs. Nov. 9	Gukasyan, HJ	Collaboration in a Virtual and Global Environment	Handen Ch. 9

Week 13* Tues. Nov. 14 Thurs. Nov. 16	Gukasyan, HJ	From Genome to Drug: Ethical Issues	Handen Ch. 10
Week 14* Tues. Nov. 21	Gukasyan, HJ	From Genome to Drug: Ethical Issues ADMET Properties: Overview and Current Topics	Handen Ch. 10 Abhinav Ch. 8
Thanksgiving Holiday, Wednesday, Nov. 22 to Sunday, Nov. 26, 2023			
Week 15 Tues. Nov. 28 Thurs. Nov. 30	Gukasyan, HJ	Pharmacogenetics and Personalized Medicine ADMET Properties: Overview and Current Topics	Abhinav Ch. 10 Abhinav Ch. 8
Weeks 12-15	Computer lab work	Compose a brief report with literature based background on target, disease, drug starting point and individual lead optimization experimental results. Explain final candidate selection in terms of best Vina score, and draggability criteria.	Save final discovered drug candidate molecule and report for BPSI 403 if planning to take second half of Biopharmaceutics (e.g. II). 1. DDT • Volume 11, Number 3/4 • February 2006 2. Current Pharmaceutical Design, 2002, 8, 2269-2278 3. Cancer Treatment Reviews 84 (2020) 101966
Dec 7th-14th	Finals Week	**Final Exam Thursday, December 7 2-4 p.m; reports due by 5pm on day of Final Exam**	
Fri. Dec. 1: Last Day of the Fall Semester			
Saturday, December 2 to Tuesday, December 5, 2023– Study Days			

*Place holder for possible biopharmaceutical industry guest lectures

USC Mann

Alfred E. Mann School of Pharmacy
and Pharmaceutical Sciences

Course Content Distribution and Synchronous Session Recordings Policies

USC has policies that prohibit recording and distribution of any synchronous and asynchronous course content outside of the learning environment. Recording a university class without the express permission of the instructor and announcement to the class, or unless conducted pursuant to an Office of Student Accessibility Services (OSAS) accommodation. Recording can inhibit free discussion in the future, and thus infringe on the academic freedom of other students as well as the instructor. (Living our Unifying Values: The USC Student Handbook, page 13).

Distribution or use of notes, recordings, exams, or other intellectual property, based on university classes or lectures without the express permission of the instructor for purposes other than individual or group study. This includes but is not limited to providing materials for distribution by services publishing course materials. This restriction on unauthorized use also applies to all information, which had been distributed to students or in any way had been displayed for use in relationship to the class, whether obtained in class, via email, on the internet, or via any other media. (Living our Unifying Values: The USC Student Handbook, page 13).

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.

USC Mann

Alfred E. Mann School of Pharmacy
and Pharmaceutical Sciences

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, comprises 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.