

Chemistry 323/423: Medicinal Chemistry
CHEM 323-001 (4327) and CHEM 423-001 (4328)

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Spring 2021 Tue & Thur 9:45 – 11:00 AM Synchronous via Zoom

Prerequisite: Organic Chemistry 221/222 or Chem 223/224. This course is open to both undergraduate students (as CHEM 323) and graduate students (as CHEM 423). *One semester of Biochemistry is strongly recommended.*

Required Text: Medicinal Chemistry: The Modern Drug Discovery Process by Erland Stevens, Pearson Press 2014. ISBN 978-0-321-71048-2, ISBN 0-321-71048-7.

Sakai: All materials that are given out in class will be posted on Sakai.

Office Hours: Tuesdays and Thursdays 11:00 a.m. – 12:00 p.m. or by appointment

Course Description: This course will provide an in-depth look at how pharmacologically active molecules are designed to treat human diseases. We will use the text by Erland Stevens, and additional examples and applications will be drawn from the published literature. Selected case histories throughout the course will serve to illustrate the concepts. The course will include guest lecturers including industrial medicinal chemists.

Readings and problems will be assigned, and homework will be collected regularly. Late homework will lose 10% per class period after the due date. There will be two mid-term exams plus a cumulative final examination during our scheduled final exam slot. Graduate students enrolled in Chem 423 will give a presentation to the class. This course is didactic only; there is no lab associated with this course, although some hands-on experience in making drugs would probably be very popular and would provide highly marketable skills.

We are pleased to have a license enabling our class to have hand-on experience with the **Chemical Computing Group Inc.'s** computational suite **Molecular Operating Environment (MOE)**, a state-of-the-art computational ensemble which has capabilities for structure-based design, fragment-based design, pharmacophore discovery, molecular modeling simulations including molecular mechanics, molecular dynamics, and QSAR. To check out just how cool this is, see https://www.chemcomp.com/MOE-Molecular_Operating_Environment.htm

Course Evaluation

	CHEM 323		CHEM 423
Midterm I	25	Midterm I	20
Midterm II	25	Midterm II	20
Homework	25	Homework	20
...	...	Presentation	20
Cumulative Final	25	Cumulative Final	20
Total	100%	Total	100%

Other Medicinal Chemistry Textbooks

- *An Introduction to Medicinal Chemistry*, 5th Ed., by Graham L. Patrick, Oxford University Press, 2013. ISBN-10: 0199697396; ISBN-13: 978-0199697397
- *The Organic Chemistry of Drug Design and Drug Action*, by Richard B. Silverman, 2nd Ed. Elsevier Academic Press, 2004, ISBN 0-12-643732-7.
- *Foye's Principles of Medicinal Chemistry*, 7th Ed., by David A. Williams and Thomas L. Lemke, Lippincott Williams & Wilkins, 2012.
- *Medicinal Chemistry: A Molecular and Biochemical Approach*, 3rd Ed., by Thomas Nogrady and Donald F. Weaver, 2005.
- *Medicinal Chemistry, An Introduction*, 2nd Ed., Gareth Thomas, Wiley & Sons, 2008.
- *The Practice of Medicinal Chemistry*, 3rd Ed., Camille Wemuth, Academic Press, 1996.

Medicinal Chemistry Books Suitable for Gifts or Coffee Table or for Actually Reading

- *Molecules that Changed the World* by K.C. Nicolaou and T. Montagnon, 2008, Wiley-VCH. A lovely coffee table book and gift for the new medicinal chemist in the family.
- *Molecules and Medicine* by E. J. Corey, László Kürti and Barbara Czako, 2007, Wiley. A remarkable little paperback describing the structures and mechanisms of action of over one hundred key pharmaceuticals organized by therapeutic area.

Selected Peer-Reviewed Medicinal Chemistry Journals (I.F. = impact factor)

- *Journal of Medicinal Chemistry* (6.259), *ACS Medicinal Chemistry Letters* (3.746; starting in 2010), *Bioorganic & Medicinal Chemistry* (2.793), *Bioorganic & Medicinal Chemistry Letters* (2.42), *European Journal of Medicinal Chemistry* (4.519), *ChemMedChem* (3.225), *Current Medicinal Chemistry* (3.853)

Additional Resources

- Structure searchable database drugs all stages of development <http://www.drugbank.ca/>
- *Annual Reports in Medicinal Chemistry*
- U.S. Patent and Trademark Office at <http://www.uspto.gov>
- Issued U.S. Patents : <http://www.freepatentsonline.com/>

1. *Course Description*: This 3 credit hour lecture course that provides an overview of the fundamentals of medicinal chemistry from lead identification to market.

2. *Expected Outcomes*: Understand pharmacodynamics of drug interactions with receptors, enzymes, and oligonucleotides; pharmacokinetics of drug action including ADME (ADMET), metabolism of drugs, and the role of metabolism in PK and drug safety, strategies of lead discovery toward new drugs, strategies of lead optimization to a drug candidate including bioisosterism, synthesis of drug molecules using the reactions of synthetic organic chemistry, structure activity relationships (SAR), relevance of the principles of drug discovery to environmental and dietary exposure, role of molecular modeling to enhance and facilitate the drug discovery process, the patent process of protecting intellectual property, ethical aspects of drug development and marketing.

3. *Syllabus*: The current syllabus is posted on Sakai and is subject to change (dated at the top) during the semester. You are responsible for all changes announced whether or not you are in attendance.

4. *Exams and Grading*: There are three mid-term exams and one 2-hour final exam. This grading standard will be applied: 90 A; 87 A-; 83 B+; 78 B; 74 B-; 68 C+; 60 C; 50 C-; 45 D; <45 F. A further

curve for each individual exam may be applied based on the specific average and standard deviation, and will be provided upon return of each exam, along with exam distribution statistics.

All exams are closed book and closed notes unless otherwise specifically noted. In the case of in-person exams, you must bring a form of photo identification to the exam, which you may be asked to show. When you are finished with your exam, please bring your completed exam to the front, and leave the room quietly without disturbing the other students. For remote exams and assignments, you must scan your completed exam or homework as a single PDF document named Lastname, Firstname.

Exams will be graded and returned as quickly as possible. All grading questions, points of clarification, and grading errors must be brought to the instructor's attention no later than one week after the graded exam is returned.

The University sets the schedule for all final exams and has set the final exam policy. You will have two hours to complete your final exam. Please contact your instructor immediately about any issues (e.g. poor internet connection, defective equipment) that arise before or during the exam. Instructors may not reschedule final exams for a class for another day and/or time during the final exam period. There can be no divergence from the posted schedule of dates for final exams. Individual students who have four (4) final examinations scheduled for the same date may request to have one of those exams rescheduled. If a student reports having four final examinations scheduled for the same date, students should be directed to e-mail a petition to Adam Patricoski, Assistant Dean for Student Academic Affairs, CAS Dean's Office (apatricoski@luc.edu).

5. Cultural Connections: This course will include regular readings of relevant topics more broadly related to science and medicine in society, including possible podcast or YouTube assignments. These topics will appear in homework assignments.

6. Outside Dissemination of Materials: Please note that materials from the course cannot be shared outside the course without the written permission of the instructor.

7. Academic Honesty: For this course, all in-class exams are closed book and closed note. Academic dishonesty includes using notes or books during exams, looking at another student's test during the exam period, or sharing information online during an exam. The consequence of academic dishonesty including plagiarism will result minimally in the instructor's assigning the grade of "F" for the assignment or examination. The instructor may impose a more severe sanction, including failure of the course, and the incident will be reported to the Chemistry Department Chair and the Office of the Dean. Additional sanctions including expulsion from the university may be imposed. The Undergraduate Handbook contains a complete description of the University policy regarding academic dishonesty. Anything you submit that is incorporated as part of your grade in this course (quiz, exam, lab report, etc.) must represent your own work, unless collaboration is explicitly permitted.

All students in this course are expected to have read and to abide by the appropriate standard of personal honesty and integrity, drafted by the College of Arts & Sciences that can be viewed online at: <http://www.luc.edu/cas/advising/academicintegritystatement/>

Medicinal Chemistry 323/423 Tentative Schedule Outline (subject to change)

Wk	Tuesday	Thursday
1	1/19 Ch 1: Brief History Drug Discovery	1/21 Brief History Drug Discovery (cont.)
2	1/26 Ch 2: Modern Drug Disco; Lead Opt.	1/28 Drug-receptor interactions & Lead Opt. (cont.)
3	2/2 Ch 3: Trip Through the Body	2/4 Ch 3: (cont.)
4	2/9 Ch 4: Enzymes as Drug Targets	2/11 Ch 4: Enzymes as Drug Targets (cont.)
5	2/16 Case Study - Oseltamivir (Tamiflu ^R)	2/18 Ch 5: Receptors as Drug Targets
6	2/23 Ch 5: Receptors as Drug Targets (cont.)	2/25 Midterm 1
7	3/2 Case Study – Cimetidine/Tagamet	3/4 MOE Instruction
8	3/9 Ch 6: Oligonucleotide Drug Targets	3/11 Ch 7: PK Pharmacokinetics
9	3/16 Ch 8: Drug Metabolism	3/18 Ch 9: Mol. Structure & Diversity
10	3/23 Case: Artemisinin	3/25 Ch 10: Lead Discovery
11	3/30 Ch 11: Lead Optimization	4/1 Midterm 2
12	4/6 Ch 11-12 Captopril & Hansch QSAR	4/8 Ch 13: Pharmaceutics
13	4/13 Guest Speaker	4/15 Guest Speaker
14	4/20 Guest Speaker	4/22 Chem 423 Presentations
15	4/27 Chem 423 Presentations	4/29 Chem 423 Presentations
16	5/4 TO CONFIRM Med Chem Final Exam	