

Chemistry 323/423: Medicinal Chemistry
CHEM 323-001 (5201) and CHEM 423-001 (5202)

Dr. Daniel P. Becker, Ph.D.

Flanner Hall 217A, Loyola University Chicago, email: dbecke3@luc.edu

<http://www.beckerlabluc.com/daniel-becker/>

<http://www.luc.edu/chemistry/facultystaff/beckerdaniel.shtml>

Spring 2022 Tuesday & Thursdays 10:00 – 11:15 PM Cuneo 311*

*Or Synchronous via Zoom as announced.

- Zoom Invitation Link:
<https://luc.zoom.us/j/96735970860?pwd=NlpBc0xwWUFDemxOM0FITjFSdHZuQT09>
- Zoom Meeting ID: 967 3597 0860 Passcode: 270324
- *All class sessions including Zoom will be recorded and posted in Panopto on Sakai.*

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 supplementary and reference materials including those distributed in class will be posted on Sakai.

Office Hours: Tuesdays 1:30-2:30 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 a mid-term exam 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 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%

Goals of this course include the demonstration of proficiency in understanding the following topics and concepts: the therapeutic index: the risk/benefit aspect of medicines

- pharmacodynamics of drugs 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
- patent process of protecting intellectual property
- ethical aspects of drug development and marketing

Other Selected 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 the Coffee Table or 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* (7.446), *ACS Medicinal Chemistry Letters* (4.345), *Bioorganic & Medicinal Chemistry* (3.641), *Bioorganic & Medicinal Chemistry Letters*

(2.823), *European Journal of Medicinal Chemistry* (6.51), *ChemMedChem* (3.466),
Current Medicinal Chemistry (4.184)

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/>

Cultural Connections: This course will include regular but concise mention of relevant topics and resources more broadly related to science and medicine in society, including short readings and occasional podcast or YouTube assignments. Some of these topics will appear in homework assignments, and will also appear on exams, insofar as covered by the homework questions.

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

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 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. Any student caught cheating will, at the very minimum, receive a grade of "zero" for the item that was submitted. If cheating occurs during a course exam, the incident will be reported to the Chemistry Department Chair and the Office of the CAS Dean. Additional sanctions may be imposed.

Academic Integrity: 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	1/18 Ch. 1: Brief History Drug Discovery	1/20
2	1/25 Ch. 2: Modern Drug Discovery	1/27
3	2/1 Ch. 3: Trip Through the Body	2/3 MOE tutorial TBD
4	2/8 Ch 4: Enzymes as Drug Targets	2/10
5	2/15 Ch. 5: Receptors as Drug Targets	2/17
6	2/22 Ch 6: Oligonucleotide Drug Targets	2/24 Midterm Exam
7	3/1 Ch 7: PK Pharmacokinetics	3/3
8	<i>3/8 Spring Break</i>	<i>3/10 Spring Break</i>
9	3/15 Ch 8: Drug Metabolism	3/17
10	3/22 Ch 9: Mol. Structure & Diversity	3/24
11	3/29 Ch 10: Lead Discovery	3/31 Ch 11: Lead Optimization
12	4/5 Ch 12: Hansch analysis	4/7 Ch 13: Pharmaceutics
13	4/12 Guest Lecture AbbVie	4/14 Med Chem 423 Presentations
14	4/19 ed Chem 423 Presentations	4/21 Med Chem 423 Presentations
15	4/26 Med Chem 423 Presentations	4/28 Med Chem 423 Presentations
16	4/28 Med Chem Final Exam	