

Chemistry 323/423: Medicinal Chemistry

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Mondays & Wednesdays

7:00-8:20 PM

Cuneo 311

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).

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 4:00-5:00 or by appointment

Course Description: This course will provide an in-depth look at how novel, 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 several industrial medicinal chemists.

Readings and problems will be assigned, both from the text and from the primary literature as handouts. There will be a cumulative final examination during our scheduled final exam slot. Students enrolled in Chem 425 will be required to give a presentation on some aspect of drug discovery, from the recently-published literature, and folks in Chem 323 will submit notes from those presentations. This course is didactic only; there is no lab associated with this course, although some hands-on experience in making drugs would probably be popular and would build 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. See https://www.chemcomp.com/MOE-Molecular_Operating_Environment.htm

Course Evaluation

	% for CHEM 323		% for CHEM 425
Homework/Assignments	65	Homework/Assignments	40
	...	Med Chem Project	25
Cumulative Final	35	Cumulative Final	35
Total	100%	Total	100%

Goals of this course include the demonstration of proficiency in understanding the following topics and concepts:

- risk/benefit aspect of medicines, understanding toxicity and therapeutic index
- 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
- synthesis of drug molecules using the reactions of synthetic organic chemistry
- 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., by Gareth Thomas, John Wiley & Sons, 2008.
- *The Practice of Medicinal Chemistry*, 3rd Ed., ed. Camille Wemuth, Academic Press, 1996.

Fun Med Chem Books Suitable for Gifts or Your Own 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 Czakó, 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* (5.447), *ACS Medicinal Chemistry Letters* (3.120; starting with 2010, Volume 1), *Bioorganic & Medicinal Chemistry* (3.151), *Bioorganic & Medicinal Chemistry Letters* (2.42), *European Journal of Medicinal Chemistry* (3.447), *ChemMedChem* (2.968), *Current Medicinal Chemistry* (3.853)

Additional Resources

- *Annual Reports in Medicinal Chemistry*
- The U.S. Patent and Trademark Office at <http://www.uspto.gov/>
- Free patent pdf files are available at: <http://www.freepatentsonline.com/>

6. *Academic Honesty*: 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/>

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.

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

Wk	Monday	Assignments Due	Wednesday	Assignments Due
1	1/18 <i>Martin Luther King, Jr. Day – Holiday</i>	...	1/20 Ch 1: <i>Intro to Med Chem; History</i>	...
2	1/25 Ch. 2: <i>Modern Drug Discovery</i>	PS-1	1/27 Ch. 2 <i>Cont.; Orgo Review</i>	...
3	2/1 Ch. 3: <i>Trip Through the Body</i>	PS-2	2/3 Ch. 3 <i>Cont.</i>	...
4	2/8 Ch 4: <i>Enzymes as Drug Targets</i>	PS-3	2/10 <i>Case History: Tamiflu</i>	...
5	2/15 Ch. 5: <i>Receptors as Drug Targets</i>	PS-4	2/17 <i>Case History: Cimetidine</i>	...
6	2/22 Ch 6: <i>Oligo-nucleotide Drug Targets</i>	PS-5	2/24 <i>Marlon Lutz: Flow Chemistry</i>	...
7	2/29 Ch 7: <i>PK</i>	PS-6	3/2 Ch 7 <i>PK (cont)</i>	
8	<i>3/7 Spring Break</i>	...	<i>3/9 Spring Break</i>	...
9	3/14 Ch 8: <i>Drug Metabolism</i>	PS-7	3/16 Ch 8: <i>Drug Metabolism (cont.)</i>	...
10	3/21 <i>Cory Reidl: MOE</i>	PS-8	3/23 <i>Tom Penning confirmed</i>	
11	3/28 <i>Hillary Pelltier confirmed</i>	<i>Penning summary</i>	3/30 <i>Cory Reidl: MOE</i>	<i>Hillary Pelltier summary</i>
12	4/4 Ch 9: <i>Mol. Structure & Diversity</i>		4/6 <i>Kathy Mortell</i>	PS-9
13	4/11 Ch 10: <i>Lead Disco</i>	<i>Kathy Mortell sum</i>	4/13 Ch 10 (<i>cont</i>)	PS-10
14	4/18 Ch 11: <i>Lead Optimization</i>		4/20	PS-11
15	4/25 Ch 12: <i>Hansch</i>	PS-11	4/27 Ch 13: <i>Pharmaceutics</i>	<i>Chem 523 Project</i>
16	5/2 <i>Med Chem Final Exam</i>	...	5/4