

Pharmaceutical Chemistry
CHMD71H3
LECTURE OUTLINE

This document contains important course information and should be kept in a safe place where you can refer to it throughout the semester

Welcome to CHMD71H: Pharmaceutical Chemistry

Welcome to CHMD71! This course is going to require some hard work, but we hope to make it worth your while by exposing you to some of the exciting aspects of medicinal chemistry and how drugs you encounter in your everyday lives and in the news are developed and function in physiological conditions. Before we get started, please take a few minutes to read through this document. It contains important information which will help ensure you have all the tools you'll need to succeed in this course.

Description: The course focuses on the important concepts in the design and synthesis of drugs. Rational basis for drug design including synthetic and medicinal concepts will be discussed. Topics include structure-activity relationships, synthesis and reaction mechanisms, and case studies of drugs. Pharmacology and pharmacokinetics of the various drug classes in biological systems will be discussed as well as protein/enzyme interactions with the different classes of drugs.

Background: Development of a modern drug is a complicated process that demands improved methods for selective transformations of organic molecules. Typically, medicinal chemistry efforts during the discovery stage focus on generating valuable structure/activity relationships for the compounds that are being screened for activity. At this stage, the main synthetic challenges pertain to the selective transformations of available building blocks into diversely functionalized derivatives. At the next stage, process chemists take over the project and face completely different issues that relate to finding the shortest and most efficient route to the candidate identified during the medicinal chemistry part of the campaign. The present course provides an overview of reactions that are being used at different stages of the drug development process. Using representative examples from the literature, we will concentrate on various classes of drugs and their syntheses.

Prerequisites: BGYC13H Biochemistry I: Proteins and Enzymes and II: Bioenergetics and Metabolism, CHMC47H Bio-organic Chemistry and CHMC41H Organic Reaction Mechanisms and CHMC42H Organic Synthesis. **It is imperative that you have these prerequisites in order to succeed in the course and if you have enrolled in the course without having these prerequisites, it is your responsibility to discuss your situation with the instructors.**

otherwise we cannot accept any responsibility for your performance and outcome in the course.

Lectures:

Mondays 3-5 pm AA 205

Lecturers: Dr. Kagan Kerman (SW-533) 1st 6 weeks of lectures (Jan 10th to Feb 14th inclusive)
Dr. Shadi Dalili (SW-651) 2nd 6 weeks of lectures (Feb 28th to Apr 4th inclusive)

Emails: kkerman@utsc.utoronto.ca sdalili@utsc.utoronto.ca

Office Hours: Tues 2:30-3:30pm (Dr. Dalili in SW-651)

Mon 1:00-2:30 pm (Dr. Kerman in SW-533)

Course Website: CHMD71 maintains a Blackboard web space which archives a variety of course-related information including: class announcements, lecture slides and notes if provided, contact information and links to some useful outside resources. In addition, class emails will regularly be sent via Blackboard. ***In order for you to receive these emails, you must have a valid "utoronto.ca" email account registered with ROSI.***

To login, go to: <https://portal.utoronto.ca/webapps/portal/frameset.jsp>. Click on "log-in to the portal" at the top left. Login using your UTORid username and password (same as what's used for your UTOReil). Under the "My Courses" box (top right), click on the CHMD71 link.

Discussion Board:

An online discussion board will be maintained through Blackboard. This online space will provide you with a place to post and answer questions related to the course material. You may post anonymously, or as yourself. The forums will be monitored by both lecturers to ensure that all questions are answered accurately. In addition, frequently asked questions (with their answers) may also be posted here so be sure to check in periodically.

Please note: Posts which contain answers/solutions homework assignments are not permitted and will be removed promptly.

E-mail policy:

- Use UTSC account
- If Yahoo or Hotmail used follow instructions below to prevent email ending up in junk mail:
 - put CHMD71 in the subject line followed by the reason for the email
 - use a greeting of some kind - NOT "Hey"
 - sign your first and last name

- please include your student number after your name
- Student emails will be replied to within 24 hours (M-F) provided that the above protocol is used.

A note on email content: Please, do not email questions regarding the lecture material/assigned reading/suggested problems. These should be posted on the discussion board so that others can benefit from the responses provided.

Method of Evaluation: The grading scheme for the course is shown in the table below:

Term Test	25%	First 6-7 weeks
Final Exam	35%	Entire course work including the assignment questions and reports and oral presentations.
Weekly in-class quizzes	5%	10 minute closed-book quizzes reviewing material from lectures. There will be no make-up quizzes.
Assignment 1	15%	Students will prepare a report about the pharmacological properties of their choice of drug (Minimum word count: 5000). Each student should get their choice of drug approved by the Instructor to avoid overlap. Each student will present a different drug.
Final Term Assignment and Oral Presentation	20%	Students will prepare an oral presentation for 15 min and a short report about the synthesis and applications of their assigned drug. Each student should get their choice of drug approved by the Instructor to avoid overlap. Each student will present a different drug. More details including the time and place of the oral presentations will be announced after the mid-term exam.

"Normally, students will be required to submit their course essays to Turnitin.com for a review of textual similarity and detection of possible plagiarism. In doing so, students will allow their essays to be included as source documents in the Turnitin.com reference database, where they will be used solely for the purpose of detecting plagiarism. The terms that apply to the University's use of the Turnitin.com service are described on the Turnitin.com web site".

Online Grades:

Individual grades will be posted on the intranet as they become available. Please check these periodically to make sure that the posted grades match your own records. Any discrepancy should be reported immediately to the instructors.

No calculators, models, pagers, cell phones or other aids will be allowed during any quizzes, lecture test or exam, unless announced previously.

Persons who miss a test or exam are expected to contact the S. Dalili or K. Kerman immediately. Documentation, for approval, **must be given within one week** (e.g. Doctor's note - which should say that you were seen on the day in question, and that in the Doctor's opinion you were unable to write a test that day). If the documentation is insufficient, you may be required to obtain further, signed, paperwork. Those presenting a valid, documented reason for absence, in writing, within this time frame, will be allowed to be excused OR to write a deferred exam, AT THE INSTRUCTOR'S DISCRETION.

Please note that if you miss the Final Exam, you must petition the Registrar's Office to write a make-up exam in the next formal exam period. Check the UTSC Calendar for instructions and deadlines.

There is no individual textbook assigned for the course and students should rely on course notes, literature articles, and lectures for the material covered. The following is a list of suggested texts you may use for extra reading on covered topics:

Recommended textbooks:

- 1) Block, J.; Delgado, J. N., **Wilson and Gisvold's Textbook of Organic Medicinal and Pharmaceutical Chemistry**, 11th Edition. (9780781734813, Lippincot, Williams and Wilkins, 2004)
- 2) Thomas, G. **Medicinal Chemistry: An Introduction**, 2nd Edition. (978-0-470-02597-0, Wiley, 2008).
- 2) Miller, A. D.; Tanner, J., Editors. **Essentials of Chemical Biology: Structure and Dynamics of Biological Macromolecules**. (978-0-470-84530-1, Wiley, 2008).
- 3) Corey, E. J.; Czako, B.; Kurti, L., Editors. **Molecules and Medicine** (978-0-470-26096-8, Wiley, 2008).
- 4) Holtje, H.-D.; Sippl, W.; Rognan, D.; Folkers, G. **Molecular Modeling: Basic Principles and Applications**, 3rd Edition. (978-3-527-31568-0, Wiley, 2008)
- 5) Schneider, G.; Baringhaus, K.-H.; Kubinyi, **Molecular Design: Concepts and Applications** (978-3-527-31432-4, Wiley, 2008)
- 6) Schreiber, S. L.; Kapoor, T. M.; Wess, G.; Editors. **Chemical Biology: From small molecules to Systems Biology and Drug Design**, 3 Vol. (978-3-527-31150-7, Wiley, 2007).

- 7) Johnson, D. S.; Li, J. J., Editors. **The Art of Drug Design** (978-0-471-75215-8, Wiley, 2007).
8) Golan, D. E.; Tashjian, A. H.; Armstrong, E. J.; Armstrong, A. W. **Principals of Pharmacology**, 2nd Edition, (978-0781746786, Lippincot, Williams and Wilkins, 2008).

These textbooks are available in the UTSC Library or in Gerstein Science Library.

The following is a tentative list of topics that will be covered throughout the semester. The topics may change, so students should refer to lecture notes provided for content of the course.

Tentative Topics:

- 1) **Drug-Receptor interactions:** Introduction to Pharmaceutical Chemistry, Physico-chemical Aspects and Principals of Drug Action
- 2) **Pharmacodynamics:** Drug-dose relationships, actions of agonists and antagonists, efficacy.
- 3) **Pharmacokinetics:** Factors that affect drug adsorption, distribution, metabolism and excretion.
- 4) **Drug Metabolism:** Pathways of drug metabolism
- 5) **Drug Toxicity:** Mechanisms of drug toxicity
- 6) **Topics in rational drug design:** Pharmacophore-based drug design; Functional group modification; Molecular mimicry; Structure modification; Receptor- based drug design; Receptors; Docking and Molecular modeling
- 7) **Structure - activity and quantitative structure relationships**
- 8) **Drug structure and solubility**
- 9) **Fundamentals of drug development and regulation:** The process of drug evaluation and clinical drug development as it pertains to the drug approval process

The following is a tentative list of selected drug molecules that will be discussed according to their pharmacological effects:

- 10) **Antibiotics:** Quinolone antibiotics: levofloxacin (levaquin), moxifloxacin (avelox), gemifloxacin (factive), and garenoxacin (t-3811)
- 11) **Antifungals:** Triazole antifungals: itraconazole (sporanox), fluconazole (diflucan), voriconazole (vfend), and fosfluconazole (prodif)

12) **Neuroactive agents:** Dual selective serotonin and norepinephrine reuptake inhibitors for depression; gaba_a receptor agonists for insomnia: zolpidem (ambien), zaleplon (sonata), eszopiclone (estorra, lunesta), and indiplon

13) **Cholinergic agents:** Adrenergic, dopaminergic and serotenergic agents; neuroactive amino acid analogs: gaba, glutamate and glycine

14) **Cardiovascular agents:** Angiotensin antagonists for hypertension; leading ACE inhibitors for hypertension; dihydropyridine calcium channel blockers

15) **Anti-cancer agents:** Aromatase inhibitors for breast cancer: exemestane (aromasin), anastrozole (arimidex), and letrozole (femara); protein-tyrosine kinase inhibitors

AccessAbility:

Students with diverse learning styles and needs are welcome in this course. In particular, if you have a disability/health consideration that may require accommodations, please feel free to approach me and/or the AccessAbility Services Office as soon as possible. The UTSC AccessAbility Services staff (located in S302) are available by appointment to assess specific needs, provide referrals and arrange appropriate accommodations (416) 287-7560 or ability@utsc.utoronto.ca.

The sooner you let us know your needs the quicker, we can assist you in achieving your learning goals in this course.

Cell Phones:

During lectures and labs please turn off your cell phones to avoid disruption of the class. If circumstances warrant use of your cell phone and you must receive an emergency call, please inform the Course Instructor at the beginning of the session in advance and then excuse yourself from the session to respond to the call outside the lecture.

Academic Calendar:

Further information about academic regulations and course withdrawal deadlines can be found in the UTSC Calendar. You are encouraged to read this material.

Centre for Teaching and Learning:

If you need assistance with effective writing skills, study skills, exam preparation, note taking, or time management, free workshops and advice are available from the Centre for Teaching and Learning, which can be reached at:

http://www.utsc.utoronto.ca/~ctl/Student_Support/index.html

Computer Use:

Ethical use of University computers is expected at the University of Toronto Scarborough. Guidelines are set out in the UTSC Calendar. It is expected that the equipment and/or resources accessed in the UTSC Library and the computer labs are to be used for academic research, assignments, and course activities only.

Academic Integrity:

Academic integrity is one of the cornerstones of the University of Toronto. It is critically important both to maintain our community which honours the values of honesty, trust, respect, fairness and responsibility and to protect you, the students within this community, and the value of the degree towards which you are all working so diligently. According to Section B of the University of Toronto's Code of Behaviour on Academic Matters <http://www.governingcouncil.utoronto.ca/policies/behaveac.htm> which all students are expected to know and respect, it is an offence for students to:

To use someone else's ideas or words in their own work without acknowledging that those ideas/words are not their own with a citation and quotation marks, i.e. to commit plagiarism.

To include false, misleading or concocted citations in their work.

To obtain unauthorized assistance on any assignment.

To provide unauthorized assistance to another student. This includes showing another student completed work.

To submit their own work for credit in more than one course without the permission of the instructor.

To falsify or alter any documentation required by the University. This includes, but is not limited to, doctor's notes.

To use or possess an unauthorized aid in any test or exam.

There are other offences covered under the Code, but these are by far the most common. Please respect these rules and the values which they protect. Offences against academic integrity will be dealt with according to the procedures outlined in the Code of Behaviour on Academic Matters.