

# 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 OR 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 3-5pm BV260

**Lecturers:** Dr. Kagan Kerman (SW533): 1<sup>st</sup> 6 weeks of lectures (Jan 6<sup>th</sup> to Feb 10<sup>th</sup> inclusive)  
Dr. Shadi Dalili (SW636): 2<sup>nd</sup> 5 weeks of lectures (Mar 3<sup>rd</sup> to March 31<sup>st</sup> inclusive)  
*Reading Week-no classes* Feb 18<sup>th</sup> to Feb 21<sup>st</sup>

**Emails:** [kagan.kerman@utoronto.ca](mailto:kagan.kerman@utoronto.ca) & [sdalili@utsc.utoronto.ca](mailto:sdalili@utsc.utoronto.ca)

**Office Hours:** Dr. Kerman: Mon 1:00---2:30pm (SW533)

Dr. Dalili: Mon 1:00-2:30pm (SW-636) starting Mon Feb 24<sup>th</sup>; by appointment  
between Jan 6<sup>th</sup> and Feb 24<sup>th</sup>

**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 UTORmail). Under the “My Courses” box (top right), click on the CHMD71 link.

**E-mail policy:**

- Use University 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 48 hours (M-F) provided that the above protocol is used.

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

<b>Mid-term Test</b>	<b>25%</b>	Mid-term test will be in class on February 24 <sup>th</sup> , 2014.
<b>Final Exam</b>	<b>35%</b>	Entire course work, including assignment/quiz questions, reports and oral presentations
<b>Weekly in-class quizzes</b>	<b>10%</b>	10 minute closed-book quizzes reviewing material from lectures
<b>Assignment-1</b>	<b>10%</b>	Proposal and essay on an approved pharmaceutical agent, discussing the pharmacokinetics, dynamics and effects of the drug under physiological conditions. Each student must present a different drug and must have their drug of choice approved by the instructor. More details to be given in lectures
<b>Final Term Assignment (10%) and Oral Presentation (10%)</b>	<b>20%</b>	Proposal and essay on the approved pharmaceutical agent, discussing/analyzing synthetic routes to the drug in laboratory and industrial settings. Students will prepare a 15 minute oral presentation on their approved pharmaceutical agent encompassing both term assignments. More details to be given in lectures.

**Turnitin.com:** Students will be required to submit their papers to Turnitin.com for review of textual similarity and to access the site, please login to [www.turnitin.com](http://www.turnitin.com) and in order to access the course, you will need a course ID and password provided below:

**Course ID:** 4677809

**Course password:** pharma

**Statement about Turnitin.com:** *"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 Blackboard Gradebook 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 Dr. 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. The exact date of the **mid-term test is February 24<sup>th</sup>, 2014**. Students who miss the term test will be assigned a mark of zero for the test, unless they can document a compelling reason for missing it. 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) Golan, Tashjian, Armstrong, and Armstrong, **Principles of Pharmacology: The pathophysiologic basis of drug therapy**, Lippincott, Williams & Wilkins Publisher, (There is now a 3<sup>rd</sup> edition of the textbook, but the 1<sup>st</sup> edition should be OK!, 2007).
- 2) Block, J.; Delgado, J. N., **Wilson and Gisvold's Textbook of Organic Medicinal and Pharmaceutical Chemistry**, 11th Edition. (9780781734813, Lippincott, Williams and Wilkins, 2004)
- 3) Thomas, G. **Medicinal Chemistry: An Introduction**, 2nd Edition. (978-0-470-02597-0, Wiley, 2008).
- 4) Miller, A. D.; Tanner, J., Editors. **Essentials of Chemical Biology: Structure and Dynamics of Biological Macromolecules**. (978-0-470-84530-1, Wiley, 2008).
- 5) Corey, E. J.; Czako, B.; Kurti, L., Editors. **Molecules and Medicine** (978-0-470-26096-8, Wiley, 2008).
- 6) Holtje, H.-D.; Sippl, W.; Rognan, D.; Folkers, G. **Molecular Modeling: Basic Principles and Applications**, 3rd Edition. (978-3-527-31568-0, Wiley, 2008)
- 8) Schneider, G.; Baringhaus, K.-H.; Kubinyi, **Molecular Design: Concepts and Applications** (978-3-527-31432-4, Wiley, 2008)
- 9) 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).

10) Johnson, D. S.; Li, J. J., Editors. **The Art of Drug Design** (978-0-471-75215-8, Wiley, 2007)  
*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.*

**Topics:**

- 1) **Drug-Receptor interactions-1:** Introduction to Important Functional Groups in Medicinal 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) **Topic 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 (ssnr) for depression; gabaa 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 us 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](mailto: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, 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 instructor in advance at the beginning of the session, and excuse yourself from class to receive the call.

**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 Center for Teaching and Learning, which can be reached at: [http://www.utsc.utoronto.ca/~ctl/Student\\_Support/index.html](http://www.utsc.utoronto.ca/~ctl/Student_Support/index.html)

**Research Help: University of Toronto Scarborough Library:** Staff at the University of Toronto Scarborough Library will be happy to help you find the resources you need for your assignments, and learn the research skills you will need for success at university.

Research help is available by phone, e-mail, chat, or in-person in the Library. For more information, please see the Library's Research Help page [http://guides.library.utoronto.ca/utsc\\_help](http://guides.library.utoronto.ca/utsc_help)

Need in-depth assistance? Contact your Subject Librarian, Sarah Forbes-  
<http://guides.library.utoronto.ca/profile/sforbes>

**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:** Honesty and fairness are considered fundamental to the University's mission, and, as a result, all those who violate those principles are dealt with as if they were damaging the integrity of the University itself. When students are suspected of cheating or a similar academic offence, they are typically surprised at how formally and seriously the matter is dealt with - and how severe the consequences can be if it is determined that cheating did occur. The University of Toronto treats cases of cheating and plagiarism very seriously.

Examples of offences for which you will be penalized include (but are not limited to):

- Using any unauthorized aids on an exam or test (e.g., "cheat sheets")
- Representing someone else's work or words as your own - plagiarism (see web document "How not to plagiarize" available online at <http://www.utoronto.ca/writing/plagsep.html>)
- Falsifying documents or grades
- Purchasing an essay
- Submitting someone else's work as your own
- Submitting the same essay or report in more than one course (without permission)
- Looking at someone else's answers during an exam or test
- Impersonating another person at an exam or test or having someone else impersonate you
- Making up sources or facts for an essay or report.

As a student it is your responsibility to ensure the integrity of your work and to understand what constitutes an academic offence. If you have any concerns that you may be crossing the line, please, read from the website <http://www.utoronto.ca/academicintegrity/resourcesforstudents.html> and always consult your instructor. Your instructor can explain, for example, the nuances of plagiarism and how to use secondary sources appropriately; he or she will also tell you what kinds of aids - calculators, dictionaries, etc. - are permitted in a test or exam. Ignorance of the rules does not excuse cheating or plagiarism. Students agree that by taking this course all required papers may be subject to submission for textual similarity review to **Turnitin.com** for the detection of plagiarism. All submitted papers will be included as source documents in the **Turnitin.com** reference database solely for the purpose of detecting plagiarism of such papers. The terms that apply to the University's use of the **Turnitin.com** service are described on the **Turnitin.com** web site.

This information is taken from the brochure, "*Academic Integrity*" and website, part of a series of UT publications to help students understand the University's rules and decision making structures. For copies, visit the Office of the Registrar at UTSC. All of the policies and procedures surrounding academic offences are dealt with in one policy: "*The Code of Behaviour on Academic Matters*". The full text is located in the back of the UTSC Calendar.