ECP/PHAR 5620: Drug Metabolism and Disposition

Course Syllabus Spring 2019
3.0 Credits

This course adheres to the items listed in the College of Pharmacy Central Syllabus:
https://docs.google.com/a/umn.edu/document/d/1artQ5e1rbzxe8lEtWo7BE8k8snZAEgMMz_QcW8yJ-II/edit?pli=1

Course Web Site: http://moodle.umn.edu
Term: Spring 2017

Meeting Times & Locations

Day	Time	Duluth Room	Twin Cities Room
Monday	8:00-8:50	Heller Hall 302	WDH 7-193
Wednesday	8:00-8:50	Heller Hall 302	WDH 7-193
Friday	8:00-8:50	Heller Hall 302	WDH 7-193

Technology Help, Duluth: 218-726-8847 itsshelp@d.umn.edu
Technology Help, Twin Cities: 612-301-4357 help@umn.edu

Course Instructional Team

All faculty have an open door policy for students to meet and discuss the course material. Students should feel free to drop by or call their offices any time, or contact the faculty member to schedule an appointment.

Name	Office Location	Phone	Email
L'Aurelle Johnson *(Course Director: Twin Cities)*	WDH 7-115C	612-624-5430	joh02745@umn.edu
Rory Remmel, Ph.D.	3-120 Weaver-Densford Hall	612-624-0472	remme001@umn.edu
William Elmquist, Ph.D.	9-127D Weaver-Densford Hall	612-625-0097	elmqu011@umn.edu
Linda von Weymarn, PhD	720 Cancer Center Research Building	612-626-5029	vonw0010@umn.edu

Teaching Assistants: See course Canvas Site for roster and contact information

Overview of the course

Course content

This course is designed to provide students with an understanding of advanced principles of drug metabolism and disposition. This course will emphasize how to 1) predict the oxidative (Phase I), conjugative (Phase II) enzymes and transporters (Phase III) systems responsible for xenobiotics metabolism, 2) design experimental strategies to examine drug metabolism and disposition concepts and to 3) translate in vitro results to pre-clinical study development.

Course Description

Drug Metabolism and Disposition will be a lecture/discussion based course. Ten to Fifteen percent of in total class time will consist of active or problem based learning. All lectures will be delivered live in class. Advance topics in drug metabolism and disposition comprise the major portion of the course and serves as a forum to apply basic drug metabolism foundational knowledge to examine and design experiments that would be able to address challenging topics in this field. Students will be assigned topic specific review articles and engage in in class case studies to guide advanced preparation. In this way, the class sessions will be able to offer more in-depth content, and there may be greater opportunity for class discussion, in-class problem solving and team-based learning. Assessments will include individual and group problem sets, individual presentations, and 3 exams.

Prerequisites

Students should be familiar with standard prerequisite material including: organic chemistry, general biology, integrated biochemical sciences (Phar 6702), principles of medicinal chemistry (Phar 6722) and principles in pharmacology, (6726) human anatomy and physiology. In addition, Drug Metabolism and Disposition will build upon topics covered in Integrated Biochemical Sciences (Phar 6702), Principles of Pharmacology (Phar 6726) and Principles of Medicinal Chemistry (Phar 6722) and provide a better understanding of experimental methodologies and application.

Course Materials

Required:

- Handouts and lecture slides, available through the course Canvas Site
- eReserve packet of readings

Recommended/Optional:

- Handbook of Drug Metabolism, Thomas F. Woolf, Marcel Dekker, Inc., 1999. ISBN: 0-8247-0229-8

We expect students to actively take notes during class. The course handouts are a framework for the classes, and are not meant to be a complete, authoritative text. For a discussion about course handouts, note taking, and active learning, see: Brazeau, G. A. Handouts in the Classroom: Is Note Taking a Lost Skill? *Am. J. Pharm. Ed.* **2006**, *70*, Article 38.

Computer/Technology Requirements

The University of Minnesota computer requirements are listed here:

- Moodle: This course will use Moodle to distribute resources and host course activities (quizzes, resources). See Moodle setup requirements at http://www1.umn.edu/moodle/start/technical.html.
- E-Textbooks: Some textbooks will be provided as E-Texts. You will access these through the course Moodle site.
- E-Mail: Course instructors will communicate through email about course administrative issues. We suggest that you check your U of M email daily.
- Internet-enabled device capable of accessing Moodle (computer, tablet, etc.)

Course Goals and Learning Objectives

Course goals and objectives are based on ACPE Accreditation standards and the expertise of our faculty body, who have identified specific learning Domains and Scientific Objectives, which are available by clicking the links below:
Domains: https://docs.google.com/a/d.umn.edu/document/d/1n1lqsjUBzIr_ZCzXJ5UW7N6FrsGdskgYfzn6K98kkPU/edit
Scientific Foundations: https://docs.google.com/a/d.umn.edu/document/d/1Zyf4QpHakxB1yubUImbOAL-18uNqzejfurx3tv1F38I/edit

Drug Metabolism and Disposition builds upon the foundational material from integrated biomedical sciences and principles of medicinal chemistry and principles in pharmacology to further explore the ADME of xenobiotics. This class will provide methodologies that can experimentally address inquiries in the drug metabolism and disposition field as it pertains to drug development.

Course goals

1. Predict the oxidative (Phase I), conjugative (Phase II) enzymes and transporters (Phase III) systems involved in human drug metabolism and disposition of chemical entities.

1. Describe 4 oxidative and 6 conjugative enzymes and 5 transporter families that are important in drug metabolism.
2. Identify 2 selective substrates and inhibitors for oxidative enzymes, conjugative enzymes and transporters families.
3. Interpret and explain the clinical impact pharmacogenomics data of drug metabolism enzymes
4. Predict potential sites of metabolism of drugs and new chemical entities.

2. Design experimental strategies to examine the effect of drug metabolism on drug disposition.

1. Explain 6 in vitro model systems used to evaluate the metabolism of a drug or new chemical entity and understand the pros and cons of each model system
2. Design in vivo drug metabolism studies and lists the strengths and limitations of these studies
3. Develop a presentation, using an example from the literature, describing a model study of human drug metabolism
4. Interpret 5 kinetic models used in drug metabolism studies

3. Predict in vivo drug disposition from in vitro experimental data.

1. Interpret in vitro experimental data to predict in vivo response
2. Formulate initial first in human dosing strategies based in pre-clinical studies

Assessments and Grading

Course Score: Details about the structure and format of all graded assessments are described below. The course score will be determined by applying the following percentage (weight) to each assessed activity:

Exam 1	125 pts (25%)
Exam 2	125 pts (25%)
Exam 3	125 pts (25%)
3 problem sets	30 pts (6%) 10 pts each
2 Case Study	40 pts (8%) 20 pts each
1 class presentation	55 pts (11%)
Total	500 pts(100%)

A letter grade will assigned using the course score according to the following grading scale:

Grade	**A**	**A-**	**B+**	**B**	**B-**	**C+**	**C**	**C-**	**D**	**F**
%	100-93	92- 90	89-87	86-83	82-80	79-77	76-73	72-70	69-60	59-0

Student Assessment: Three take home exams consisting of short answer/essay questions. Exams will each be worth 100 points (25% of the final grade). One presentation worth 50 points (12.5% of final grade) will be required and will consist of a short (~20 minute) presentation describing a model study from the primary literature that demonstrates usage of a method or concept covered previously in the semester (instructor will OK papers to be presented). There will be a total of 4 individual problem sets worth 7.5pts each (7.5% of final grade) and 2 group in class case studies worth 10pts each (5% of final grade) One hour of "release time" will be given for each exam and the exams will be due at the beginning of the next class period follow the respective "release days". In order for the exam turn in time to be changed, a 100% positive vote by students in the class will be required.

Exams: During the course there will be 3-non-cumulative exams. The exams will be take home, open book, consisting of short answer type exam questions. The exams will be based on the course content listed under "Detailed Course Outline & Schedule". Collectively all exams will represent 75% of your final course grade.

Problem sets: During each unit there will be a molecule of the week. Students are expected to work through the major and minor pathways and determine enzymes responsible for metabolism. These problem sets will be worth 7.5% of total grade.

Learning Activities Case Study: Students will have opportunities in class to ask and answer questions related to the current topics including instructor lead question and answer/discussion. Students will be expected to spend significant time with the lecture material and text readings outside of class to actively participate in class. They will be given multiple opportunities to self-assess with low stakes problem sets and have opportunities to work in groups in class and outside of class to reinforce concepts and further engage with the material. In class small group engagement between campuses will be facilitated through the use of mobile device video chatting technologies (i.e. facetime, google chat, etc.). Students will also be asked to individually actively research and deliver in class presentations on current topic in drug metabolism and disposition.

University and College of Pharmacy Policies

For information about College-wide policies, see:

University of Minnesota and College of Pharmacy Policy Reference (Centralized Syllabus)

[includes all required UMN and CoP policies, e.g., Attendance; Academic Freedom; Copyright; Course Evaluations; Disability Accommodations; FERPA, etc.]

Week-by-week schedule

Date	Topic/In-Class Activities Assessed activities are in **bold**.	Assignments Generally, these are to be completed before class	Instructor
MODULE 1: General Principles of Drug Metabolism			
1/23/19	Introduction to Drug Metabolism		JOHNSON
1/25/19	Sites of Drug Metabolism and First-Pass Effects		JOHNSON
MODULE 2: Oxidative and Conjugative Drug Metabolism Enzymes			
1/28/19	Cytochrome P450 Enzymes	**Molecule of the week problem set (Due 2/1/19)**	JOHNSON
1/30/19	Cytochrome P450 Enzymes (Cont)		JOHNSON
2/1/19	Chemical Structures and Reactive Metabolites 1 of 2		REMMEL

2/4/19	Conjugative (Phase II) Enzymes	**Molecule of the week problem set Due (2/11/19)**	REMMEL
2/6/19	Conjugative (Phase II) Enzymes (Cont)		REMMEL
2/8/19	Other Metabolizing Enzymes		REMMEL
2/11/19	Pharmacogenomics of Cytochrome P450		REMMEL
2/13/19	Pharmacogenomics of Other Oxidative enzymes and Conjugative enzymes		REMMEL
2/15/19	Pharmacogenomics (In Class Active Learning Exercise)		REMMEL
2/18/19	Case Study (1)		JOHNSON/REMMEL
MODULE 3: Drug metabolism regulation and transporters			
2/20/19	Regulation of drug metabolism enzymes	**Distribution of take home exam 1 at end of in class case study (Due 2/25/19)**	REMMEL
2/22/19	Release Day (no class work on take home exam)		
2/25/19	Regulation of drug metabolism enzymes (Cont)		REMMEL
2/27/19	Transporters		EMLQUIST
3/1/19	Transporters (Cont)		EMLQUIST
3/4/19	PG Transporters		REMMEL
MODULE 4: In vitro Drug Metabolism experimental strategies			
3/6/19	In Vitro Metabolism Methods Recorded Lecture	NO CLASS	JOHNSON
3/8/19	In Vitro Phenotyping & Kinetics Recorded Lecture	NO CLASS	JOHNSON
3/11/19	In Class Active Learning Exercise through Sertraline Example	**Publication: Obach FS. DMD. 2005. 33:262-270**	REMMEL
3/13/19	Inhibition Kinetics Recorded Lecture	NO CLASS	JOHNSON
3/15/19	Atypical Enzyme Kinetics		REMMEL
3/18-3/22	**NO CLASS SPRING BREAK**		

3/25/19	Mechanism-Based Inhibition		Von WAYMARN
3/27/19	Chemical Structures and Reactive Metabolites 2 of 2	**Distribution of take home exam 2 at end of in class reactive metabolite activity (Due 4/1/19)**	REMMEL
3/29/19	Release Day (no class work on take home exam)		NO CLASS
MODULE 5: In vivo Drug metabolism experimental strategies			
4/1/19	In Vivo Drug Metabolism Studies		JOHNSON
4/3/19	In Vivo Drug Metabolism Studies (Cont)		JOHNSON
4/5/19	Disease Susceptibility through bioconversion by Drug metabolism enzymes	Maybe 2D6 Phenotyping lab activity	REMMEL
4/8/19	In Vitro-In Vivo Correlations		REMMEL
4/10/19	In Vitro-In Vivo Correlations	**Problem set In vitro/ in-vivo homework assignment**	REMMEL
4/12/19	Predicting Drug Disposition & Drug Interactions in Drug Discovery		REMMEL
4/15/19	Case Study (2)		REMMEL
4/17/19	Student Presentations (3)		JOHNSON/REMMEL
4/19/19	Student Presentations (3)		JOHNSON/REMMEL
4/22/19	Student Presentations (3)		JOHNSON/REMMEL
4/24/19	Student Presentations (2)	**Distribution of take home exam 3 at end of in class student presentation (Due 4/29/19)**	JOHNSON/REMMEL
4/26/19	Release Day (no class work on take home exam)		NO CLASS
4/29/19	Test turn in day and class evaluation	Final Exams to be grades to be completed by 5/10/19	JOHNSON/REMMEL