

Phar 6762: Medicinal Chemistry and Neuropharmacology

Fall 2020 2.8 cr.

Tuesdays 8:00-9:55

Wednesdays: 8:00-9:55

Course Director (Medicinal Chemistry)

Elizabeth Ambrose, Ph.D., Office: 417, 717 Delaware, Phone: 612-626-2387

Email: ambrose@umn.edu

Co-Course Director (Neuropharmacology)

Carolyn Fairbanks, Ph.D., Office: 7-101 WDH, Phone: 612-625-2945

Email: carfair@umn.edu

Duluth Course Director

Amanda Klein, Ph.D., Office: 115 Life Sciences, Phone: (218) 726-6037

Email: ahklein@d.umn.edu

Course Faculty Members

Susan Marino, Ph.D., Office: 7-115A WDH, Phone: 612-624-2964

Email: marin007@umn.edu

Angela Birnbaum, Ph.D., Office Hours: Upon Request, Phone: 612-624-3158

Email: birnb002@umn.edu

Todd Doran, Ph.D., Office Hours: Upon Request, Phone: 612-625-9335

Email: doran@umn.edu

Cristina Peterson, Ph.D., Office Hours: Upon Request, Phone: 612-625-1106

Email: pete6187@umn.edu

Benjamin Clements Office Hours: Upon Request, Phone: 6-4073

Email: cleme481@umn.edu

Teaching Assistants:

Minneapolis Campus:

Vrishhali Salian

Email: salia006@umn.edu

Laura Hirsch

Email: hirsch331@umn.edu

Duluth Campus:

Michael Williams

Email: will2086@d.umn.edu

Recommended Reading

Foye's Principles of Medicinal Chemistry: Seventh Edition, 2012 by David A. Williams

Molecular Neuropharmacology: A Foundation for Clinical Neuroscience, Third Edition 2015
by Eric Nestler, Steven Hyman, and Robert Malenka.

In the Moodle site, students may also find resource materials. The course faculty may make documents available in Moodle or assign review articles at their discretion. When possible, review articles will be linked to the Biomed library electronic holdings.

Course Objectives

1. **Major CNS Therapeutic Targets to Restore Neurological Function.** Many neurological disorders are caused by specific dysfunction in synaptic physiology resulting an imbalance of excitatory and inhibitory input. Alterations in basal expression of a variety of proteins or other mediators contribute to this imbalance. Restoring or managing balance is often a focus of pharmacological treatment. Students should, therefore, acquire an understanding of specific mechanisms that result in synaptic and systems level inhibition and excitation. Such an understanding will enable each student to recognize how the pharmacology of the primary classes of neuroactive drugs serves to restore or manage neurological function.

2. **Mechanisms of Action of Neurotherapeutics.** Students should acquire a fundamental knowledge of the current pharmacological agents used to treat neurological disorders. They should understand the respective mechanisms of action of each drug class from receptor binding level through to signal transduction and impact on the respective neurological systems for which they are used. Such knowledge will also include an understanding of off-site and off-target effects resulting in potential central nervous system side effects will also be important to retain.

3. **Limitations of Current Neurotherapeutics and Emerging Therapeutics** Students should develop a familiarity with the current limitations of existing neuropharmacological agents and the ongoing development horizon for each class. Such familiarity will facilitate the integration of ongoing newly introduced pharmacological agents into their overall knowledge of neuropharmacology.

Grading Policy

A student's grade will be based by the following weighting procedure:

Study Guide (Online weekly):	15%
In class questions/assignments*	10 %
Exam I:	15 %
Exam II:	20%
Exam III:	20 %
Final Exam:	20 %

On selected days there will be in-class graded questions and/or graded assignments. These days are marked on the schedule with an asterisk: ""

The following standard cutoffs will be used to assign letter grades for transcript purposes.

Grade	A	A-	B+	B	B-	C+	C	C-	D	F
%	100-93	92-90	89-87	86-84	83-80	79-77	76-74	73-70	69-60	59-0

<https://policy.umn.edu/education/gradingtranscripts>

Exams:

- Examination questions may pertain to information presented in class, recommended readings, or handout materials. Examination questions may include the following types: multiple choice, matching, true-false, short answer, and calculations.
- In the case of online study guide, as in a take home exam, students may access any available written information but may not seek the assistance from another student or any other person
- If a student cannot take an exam due to illness or other emergency the instructor must be notified as soon as possible.
- If a student wishes to have an examination re-graded, requests must be submitted in writing by the second class period following posting of the exam.

Excused/Unexcused Absences

A student will receive excused absences for acceptable emergencies (as defined by University Policy, e.g. illness or serious family emergencies) provided written documentation is given to the instructor within two class periods after returning to class. It is the student's responsibility to make up the missed in class questions, problem sets, and/or exams. Absence without an acceptable excuse will result in receiving zero points for any missed requirements.

The College of Pharmacy also provides students an excused absence for sponsored functions (e.g. students representing the College at state or national meetings, immunization clinics, and certain service activities). It is our position that every effort should be made to avoid scheduling these extracurricular activities during class time. Students must themselves directly inform faculty of these events as soon as possible. Students are not excused from the required work that they miss, and it is the faculty's prerogative to determine the form of the make up work.

Class representative communications to faculty do not substitute for expected communication from the students to the course directors. Each student is expected to directly communicate information regarding potential absences to the course directors.

Honor Code

Each student is bound by the following specific provisions as part of the Honor Code. Academic misconduct is any unauthorized act which may give a student an unfair advantage over other students, including but not limited to: falsification, plagiarism, misuse of test materials, receiving unauthorized assistance and giving unauthorized assistance. Each student will be asked to sign a sheet that reaffirms the honor code as it applies to this course.

Disability Accommodations

Any student with a documented disability (e.g. physical learning, psychiatry, vision, hearing etc.) who needs to arrange reasonable accommodations must contact the Course Director and Disability services (626-1333) at the beginning of the semester. All discussions will be confidential.

University of Minnesota Educational Policies

Students are required to know and abide by all University and College of Pharmacy Policies. Please contact the Course Director for information.

[Grade definitions from the Administrative Policy: Grading and Transcripts](#)

[Scholastic Dishonesty](#)

[Teaching and Learning: Instructor and Unit Responsibilities](#)

[Makeup Work for Legitimate Absences \(Administrative Policy\)](#)

[Use of Personal Electronic Devices in the Classroom \(Administrative Policy\)](#)

[Appropriate Student Use of Class Notes and Course Materials \(Administrative Policy\)](#)

[Student Conduct Code](#)

[Board of Regents Sexual Harassment Policy](#)

[Board of Regents Equity, Diversity, Equal Employment Opportunity, an Affirmative Action Policy](#)

Statement about the availability of mental health services

[Academic Freedom and Responsibility Statement](#)

College of Pharmacy Educational Policies

[Attendance Policy](#)

Course meeting time and place for both campuses as applicable

[ITV Recording of Required Courses](#)

This course will be recorded. Access to the course recordings, per College of Pharmacy policy, will be restricted to students enrolled in the course, course instructors and instructional staff, and appropriate College of Pharmacy support staff.

[Participation and Communication Between Campuses via ITV](#)

Course Schedule

Below is a schedule for the course. Every effort will be made to meet this timeline; however, the course faculty reserves the right to make changes at any time as needed.

DATES	DAY	FAC	TOPIC	SUGGESTED READING ASSIGNMENTS/NOTES
Week 1				
Aug 25	T 8:00-8:50	CF	Course Orientation	Recommended Chapter 1 of <i>Nestler: Molecular Neuropharmacology (Mol-Neuropharm)</i>
	T 9:05-9:55	CF	CNS and PNS; Gross anatomy	
Aug 26	W 8:00-8:50	AK	Neurotransmission and Synaptic Physiology	<i>Nestler: Chapter 2 and 3</i>
	W 9:05-9:55	AK	Peripheral Nervous System	<i>Nestler: Chapter 11</i>
Week 2				
Aug 31			Study Guide 1 Due 11:59 pm	
Sept 1	T 8:00-8:50	CF	Ligand-Gated Ion Chan NMDA-NOS Cascade	
	T 9:05-9:55	CF	Neuroplasticity; Neuroadaptation	<i>Nestler: Chapter 5: Excitatory and Inhibitory Amino Acids, Chapter 8: Atypical Neurotransmitters</i> Review Article: Peltoniemi MA; Hagelberg NM; Oikkola KT; Saari TI. <u>Ketamine: A Review of Clinical Pharmacokinetics and Pharmacodynamics in Anesthesia and Pain Therapy.</u> <i>Clinical Pharmacokinetics</i> 55(9):1059-1077, 2016.
Sept 2	W 8:00-8:50	CF/ AK	Exam I Review	
	W 9:05-9:55	CF	Analgesic Ladder: NSAIDs	
Week 3	Study Guide 2 Due Friday Sept 4th 11:59 pm (Note this due date differs from other study guides)			
Sept 7			EXAM I: Opens Midnight Sept 4, Due Mon Sept 7 at 11:59 pm	
Sept 8*	T 8:00-8:50	CF	Opioid Receptors	<i>Nestler: Chapter 7: Neuropeptides</i>
	T 9:05-9:55	CF	Opioid Receptors	<i>Nestler: Chapter 11: Pain, Chapter 16: Reinforcement and Addictive Disorders</i> Review Article: Walter C; Knothe C; Lotsch J. Abuse-Deterrent Opioid Formulations: Pharmacokinetic and Pharmacodynamic Considerations <i>Clinical Pharmacokinetics</i> 2016 Jul;55(7):751-767.
Sept 9*	W 8:00-8:50	CF	Opioid Receptors	<i>Nestler: Chapter 7: Neuropeptides</i>
	W 9:05-9:55	AK	Voltage Gated Channels (Na ⁺ , Ca ²⁺ , K ⁺)	
Week 4				
Sept 14			Study Guide 3 Due 11:59 pm	
Sept 15	T 8:00-8:50	EA	Intro to the Med Chem Section; Cation Channel Blocking Agents	Foye, Chapter 17
	T 9:05-9:55	EA	NMDA Receptor Agents	Foye, Chapters 12, 13 and 16

Sept 16	W 8:00-8:50	EA	Opioids/Strong Analgesics	Foye, Chapter 20
	W 9:05-9:55	EA	Opioids/Strong Analgesics	Foye, Chapter 20
Week 5				
Sept 21 Study Guide 4 Due 11:59 pm				
Sept 22	T 8:00-8:50	EA	Non-Narcotic Analgesics	
	d 9:05-9:55	EA	Non-Narcotic Analgesics	
Sept 23*	W 8:00-8:50	CF	Non-Opioid GPCR Analgesics: Adrenergic, Cannabinoids	
	W 9:05-9:55	CF	Non-Opioid GPCR Analgesics: Adrenergic, Cannabinoids	
Week 6				
Sept 28 Study Guide 5 Due 11:59 pm				
Sept 29*	T 8:00-8:50	EA	Cannabis sativa and the cannabinoid receptors; medical marijuana; THC and its variants	Foye, Chapters 19 and 20
	T 9:05-9:55	EA	Cannabis etc., continued	Foye, Chapters 19 and 20 In-Class Exercise
Sept 30	W 8:00-8:50	CF	Triptans: 5HT1B/1D receptors	Chapter 20: Stroke and Migraine
	W 9:05-9:55	EA	Triptans: 5HT1B/1D agonists	Foye, Chapter 11
Week 7				
Oct 5 Study Guide 6 Due 11:59 pm				
Oct 6*	T 8:00-8:50	AK	TRP channels	Discussion: In class assignment
	T 9:05-9:55	AK	TNF-alpha inhibitors	Discussion: In class assignment
Oct 7	W 8:00-8:50	CF/ AK	IN CLASS Review	REVIEW Covers content Sept 2 through Oct 6
	W 9:05-9:55	CF/ EA	IN CLASS Review	REVIEW Covers content Sept 15 through Oct 6
Week 8				
Oct 12-14 IPPE Week NO CLASS				
Week 9				
Oct 19 No Study Guide Due				
Oct 20	T 8:00-8:50	CF/ AK	EXAM II	Covers Content Sep 2 through Oct 7
Oct 21	W 8:00-8:50	TD	Barbiturates, benzodiazepines, selective benzo site agonists and antagonists	Foye, Chapters 14 and 15
	W 9:05-9:55	AB	GABA-A receptors (barbiturates/benzodiazepines)	Chapter 5 (Excitatory and Inhibitory Amino Acids), Chapter 20: Seizure Disorders
Week 10				
Oct 26 Study Guide 7 Due 11:59 PM				
Oct 27*	T 8:00-8:50	AK	GABA related agents (analogs/prodrugs baclofen, gabapentin, pregabalin)	Discussion: In class assignment
	T 9:05-9:55	EA	GABA analogs, GABA site agonists, GABA transporter inhibitors, GABA transaminase inhibitors	Foye, Chapter 17

Oct 28	W 8:00-8:50	SM/ CP	Dopamine receptors	Chapter 20: Schizophrenia and Bipolar Disorder
	W 9:05-9:55	EA	Dopamine biosynthesis and metabolism, augmentation of dopamine biosynthesis, dopamine agonists, typical and atypical antipsychotics, mixed agonists/antagonists	Foye, Chapter 13
Week 11				
Nov 02			Study Guide 8 Due 11:59 PM	
Nov 3*	T 8:00-8:50	CP/ CF	Monoamine Transporters (MET, NAT, DAT) (CNS stimulants), Lithium	Chapter 6: Widely Projecting Systems, Monoamines etc., Chapter 15: Mood and Emotion
	T 9:05-9:55	EA	MAO inhibitors, monoamine transporters, nonselective and SERT-selective tricyclics, 2 nd and 3 rd generation antidepressants, SSRIs, SNRT and NERT inhibitors	Foye, Chapters 11 and 18 In-Class Exercise
Nov 4	W 8:00-8:50	SM/ CP	Serotonin receptor agonists: 5HT1A: Antianxiolytics, 5HT2C	Chapter 15: Mood and Emotion
	W 9:05-9:55	TD	5-HT1A partial agonists, 5-HT2C agonists, 5-HT3 antagonists, 5-HT4 agonists, MT1/MT2 agonists	Foye, Chapters 11, 14, and 18
Week 12				
Nov 9			Study Guide 9 Due 11:59 pm	
Nov 10*	T 8:00-8:50	AK	Nicotinic/muscarinic acetylcholine receptors	Discussion: In class assignment
	T 9:05-9:55	EA	Nicotinic receptor agonists	Foye, Chapter 9
Nov 11*	T 9:05-9:55	AK	Amphetamines/Cocaine	Discussion: In class assignment
	W 9:05-9:55	BC	Alcohol	
Week 13				
Nov 16			No Study Guide Due	
Nov 17	T 8:00-8:50		Review for Exam III	Covers Content Oct 21 through Nov 11
	T 9:05-9:55			
Nov 18	W 8:00-8:50		No Class	
	W 9:05-9:55		No Class	
Week 14				
Nov 23				
Nov 24	T 8:00-8:50		EXAM III	Covers Content Oct 21 through Nov 17
Nov 25	W 8:00-8:50		NO CLASS THANKSGIVING EVE	
Week 15				
Nov 30				
Dec 1	T 8:00-8:50	CF/ AK	Pharmacology Course Summary	
	T 9:05-9:55	CF/ AK		

Dec 2	T 8:00-8:50	EA	Medicinal Chemistry Course Summary	
	T 9:05-9:55	EA	Med Chem Q&A	
Week 16				
Dec 8	T 8:00-8:50		FINAL EXAM	
	T 9:00-9:55		FINAL EXAM	

Lecture Notes/Texts

Powerpoint versions of lectures will be posted online prior to each class. Students are welcome to use the Powerpoint lectures for their review material and can print or review online at their discretion. The course director and faculty may make additions and deletions of material as appropriate up until time of lecture. The course faculty will make every effort to distinguish what information in the lectures will be emphasized in the assessments and what is primarily for the students' reference only. Please be mindful that the organization of the material as a lecture remains the intellectual property of the faculty members as is in accordance with University policy. The slides may be photocopied and used exclusively for this course for review purposes during the Fall 2016. All other use requires written consent of the faculty.

FREQUENTLY ASKED QUESTIONS

Study Guides

“Can the study guides be posted immediately after class on Wednesday?”

The study guides will be posted Thursday weekly and students have the opportunity to complete them up until midnight on Monday evening (11:59 pm to be precise). We cannot post immediately after class because we may need the time on Thursday morning to adjust study guides according to how the class proceeded.

Immunization Clinics and other service oriented activities:

“I have made a commitment to volunteer in a college sponsored service-oriented activity (such as immunization clinics). Will I be awarded points for the “in class questions” regardless of my absence in class since it qualifies as “excused”

We commend all students who choose to volunteer their time in service-oriented activities. As with excused illnesses, our policy is that students volunteering in the occasional service activity, which prevents their attendance in class, may choose to request to complete and submit the alternative assignment for that particular missed lecture. Doing so provides the potential to re-gain their participation points. Such students have a choice to complete or not complete these missed assignments. We will consider these requests on a case-by-case basis. Please note that each student must contact the *Phar 6267* course director directly to make such requests in advance of the service event and not through any other faculty member whether or not the other faculty member has made the arrangements for the service activity. However, participation in those activities is a commendable choice and each student must plan accordingly to either make up the work or to accept reduction in points for that session.

Travel to Professional Meetings

“I am traveling to participate in a professional meeting that is sponsored by the College of Pharmacy Will I be awarded points for the “in class questions” regardless of my absence in class since it qualifies as “excused”

We completely support and encourage all students to take advantage of such career development opportunities. As with excused illnesses, and the immunization clinic services, our policy is that students attending a professional meeting, which prevents their attendance in class, may choose to request to complete and submit the alternative assignment for that particular missed lecture. As with immunization clinics and illnesses, students have a choice to complete or not complete these missed assignments. Please note that each student must contact the course director directly to make a request for a make-up assignment in advance of the professional meeting event and not through any other faculty member or college representative whether or not the other faculty member or college representatives have made the arrangements for the professional meeting. Participation in those activities is a commendable choice and each student must plan accordingly to either make up the work or to accept reduction in points for that session.

“I am traveling to participate in a professional meeting that is sponsored by the College of Pharmacy The meeting conflicts with an Exam Day, What should I do”

We will reschedule Exams for students traveling to ASHP and ACCP and selected other meetings, provided that you arrange your travel to be back to take the makeup exam which will be proctored on the Friday following the missed Exam during a time that there are no other . To qualify for this you must directly inform the Course Directors Drs. Fairbanks or Klein of your plans to attend and they will provide you with the makeup information.

Class Representative

“My class representative indicate that they were providing a list to you regarding my planned absence to attend a professional meeting”

We appreciate the proactive service that the class representatives provide to the PDIII class. However, it is each student’s responsibility to contact the faculty members directly regarding their planned absences. Only those students who do so will be eligible for make-up exams or assignments.

CONCLUDING COMMENTS

Medicinal Chemistry and Neuropharmacology is intentionally designed with multiple assessment approaches to meet diverse learning styles. This is likely to be the only time in your career that you will have dedicated time to think about the scientific principles that underlie pharmacology of CNS and PNS drugs, CNS distribution and how they different brain and spinal cord disorders. Take the time this Fall to consider this information carefully and integrate it with your prior knowledge. All students will do well in the course if you keep on schedule and invest time in the process. For any questions do not hesitate to contact the course directors directly (Dr. Fairbanks, carfair@umn.edu or Dr. Ambrose, ambrose@umn.edu) or the Duluth course director (Dr. Klein, ahklein@umn.edu).