**PHRM 240 Molecules & Medicine – Principles of Drug Design**

**Fall Semester 2021**

**Dr. Wolfgang Dostmann, Professor of Pharmacology, Larner College of Medicine**

## Syllabus

This 3-credit course conveys the molecular mechanisms by which drugs act in the body and the principles drug design. It highlights the importance of medicinal chemistry as it overlaps with the disciplines of chemistry, biochemistry, microbiology, cell biology, and pharmacology.

Most lectures are split into two parts. Part 1 lasts 40-45 minutes and loosely follows the flow of the textbook. Following a short questions/answers break, Part 2 will be more relaxing, and we will take a trip back in time and review an example of the "*Most important drugs in history".* These are world changing, famous compounds that have had a significant impact on civilization.

## Prerequisites

Organic Chemistry and Background in Biology or Biochemistry or Permission

## Course Director

Wolfgang Dostmann, Department of Pharmacology, Given B303B
wdostman@uvm.edu

## Time and Place

Tuesdays and Thursdays 11:40 am – 12:55 pm, Stafford Hall 101

## Office Hours

By appointment only

## Format

All lectures will be in-person in Stafford 101 and also available remotely through Windows Teams. All lecture materials (recorded lectures, ppt files, handouts, etc.) will be made available through Blackboard.
Note: attendance during lectures and live streaming is not mandatory (you can watch the lectures later, should you have time conflicts).

## Required Textbook

An Introduction to Medicinal Chemistry (6th Ed), Graham L. Patrick, Oxford Press, 2017. **This textbook is required for the class**. The course is tightly structured along this awesome book, which is not just a great read but also a valuable resource. You can buy it easily online, and you should do so now. You will be asked to prepare certain chapter(s) before each lecture.

**Handouts**
I will post handouts before each lecture. The handouts are detailed and usually contain learning objectives, when appropriate background information not in your textbook, web links and, chemical structures to memorize. Most importantly, the handouts contain lots and lots of study questions including detailed answers to the study questions.

**Examination Format**
Throughout the course students will be taking **four, 60-minute** exams. All exams are essentially cumulative.
All exam questions will be multiple choice and strictly follow the format from the study questions.

**Extra Credit**
All Students who wish to obtain extra credit can do so by submitting up to **two papers** on a subject **approved by the course director**. Each paper is approximately worth an **additional 5-7%** of any of your exams (equivalent of a full letter grade bump).

Graduate Students taking the course for graduate school credit will have to submit an additional term paper on a drug considered to be one of the most important drugs in history. Students will be graded (pass/fail) on the thoroughness and quality of their paper.

**Extra Credit Format**
All Students
- Undergraduate and graduate students who wish to obtain extra credit can do so by submitting up to two papers on a drug approved by me (submit your choice by email).
- Students will be graded 1-10 points on the thoroughness and quality of their paper.
- Points will be added to the lowest scored exam (a paper scoring 10 points would be worth the equivalent of a full letter grade bump up).
- If possible, the paper(s) should include the drug's discovery, structure, chemical properties, synthesis, SAR, biological effects, and historical significance.
- Here are the specifics: 6-8 pages, 1-inch margins, 1.5 space, 11 font.
- Figures do not count towards the page limit.
- References at the end; they are not counted towards the page limitation.
- Figures are welcome.
- The structure of the drug is required.
- Papers are due at midnight at the day of the final exam.
- For every day past the due date, a point will be subtracted.
- Submit your paper as pdf to wdostman@uvm.edu

Graduate Students
Students taking the course for graduate school credit are required to submit an additional term paper on a drug approved by me.
- Format and specifics same as above.
-Students will be graded (pass/fail) on the thoroughness and quality of their paper.

**Course Schedule**

**Part I: Drug Targets**

08/31 Lecture 1: Dostmann
Introduction
Intermolecular bonding forces
*Most important drugs in history: Salvarsan*

09/02 Lecture 2: Dostmann
Proteins: Structure/Function
Enzymes: Structure/Function
*Most important drugs in history: Penicillin*

09/07 Lecture 3: Dostmann
Receptors: Structure/Function
Receptors: Signal Transduction
*Most important drugs in history: 6-Mercaptopurine*

09/09 Lecture 4: Dostmann
Nucleic acids: structure and function
*Most important drugs in history: Thalidomide*

09/14 Lecture 5: Dostmann
Enzymes and Receptors as drug targets

09/16 **EXAMINATION 1**

09/21 Lecture 6: Dostmann
Nucleic acids as drug targets
*Most important drugs in history: Ivermectin*

09/23 Lecture 7: Dostmann
Pharmacokinetics I
*Most important drugs in history: Hydrocortisone*

09/28 Lecture 8: Dostmann
Pharmacokinetics II
*Most important drugs in history: Librium*

**Part II: Drug discovery, design and development**

09/30 Lecture 9: Dostmann
Drug discovery: finding a lead I
*Most important drugs in history: AZT*

10/05 Lecture 10: Dostmann
Drug discovery: finding a lead II
*Most important drugs in history: Cyclosporine*

10/07 Lecture 11: Dostmann
Rational Approaches to Lead Discovery I
*Most important drugs in history: Thorazine*

10/12 Lecture 12: Dostmann
Rational Approaches to Lead Discovery II

10/14 **EXAMINATION 2**

10/19 Lecture 13: Dostmann
Drug design: optimizing target interactions
*Most important drugs in history: Sumatriptan I*

10/21 Lecture 14: Dostmann
Drug design: optimizing access to the target I
*Most important drugs in history: Sumatriptan II*

10/26 Lecture 15: Dostmann
Drug design: optimizing access to the target II
*Most important drugs in history: Quinine I*

10/28 Lecture 16: Dostmann
Drug Design: Novel design strategies
*Most important drugs in history: Quinine II*

**Part III: Selected topics in medicinal chemistry**

11/02 Lecture 17: Dostmann
Anti-ulcer agents I
*Most important drugs in history: Cimetidine*

11/04 Lecture 18: Dostmann
Anti-ulcer agents II
*Most important drugs in history: Omeprazole*

11/09 **EXAMINATION 3**

11/11 Lecture 19: Osborne
The challenges of getting a drug to the market I

11/16 Lecture 20: Osborne
The challenges of getting a drug to the market II

11/18 Lecture 21: Dostmann
Antibiotics I
*Most important drugs in history: Sofosbuvir*

11/23 ***No Class - Thanksgiving Recess***

11/25 ***No Class - Thanksgiving Recess***

11/30 Lecture 22: Dostmann
Antibiotics I
*Most important drugs in history: Artemisinin*

12/07 Lecture 23: Dostmann
Opioid analgesics I
*Most important drugs in history: Methadone*

12/09 Lecture 24: Dostmann
Opioid analgesics II
*Most important drugs in history: Fentanyl*

12/14 **EXAMINATION 4 1:30pm – 4:15pm**