

MCH 401 - Principles of Medicinal Chemistry

University at Buffalo

Fall Semester 2007

<i>Lecturers</i>	<i>Location</i>	<i>Time</i>	<i>Days</i>
Michael Detty 627 NSC 645-6800, x2200 e-mail: mdetty@buffalo.edu Office Hours: 11:00 AM – noon, Tuesday and Thursday	115 Talbert	9:30 – 10:50 AM	T, R

Text:

R. B. Silverman, "The Organic Chemistry of Drug Design and Action, 2nd Edition," Elsevier, New York, 2004.

Online References:

Burger's Medicinal Chemistry & Drug Discovery, 6th Edition, D. J. Abraham, Ed., Wiley-Interscience, 2003 (electronically available from UB Libraries Full-Text Databases)

UB Libraries electronic journals

Outline for MCH 401/501 (First Part of Course)

Review: Amino Acids and Their Properties.

- 1. Molecular Basis of Drug Action and Drug Design**
 - 1.1 Molecular properties, geometries, stereochemistry, conformation, energetics
- 2. Drug Discovery, Design and Development**
 - 2.1 Discovery without leads
 - 2.2 Lead discovery strategies
 - 2.3 Combinatorial chemistry: high throughput screening
 - 2.4 Principles of rational drug design
- 3. Lead Modification**
 - 3.1 Pharmacophores
 - 3.2 Functional group modification
 - 3.3 Bioisosterism, structure modification: homologation, chain branching, ...
 - 3.4 SAR
 - 3.5 QSAR: Electronics, hydrophobicity, sterics
- 4. Receptor Targets**
 - 4.1 Forces in Drug/Receptor complex
 - 4.2 Drug receptor theories: occupancy, rate, induced-fit, macromolecular perturbation, activation-aggregation
 - 4.3. Stereochemical consideration: Chirality, geometric isomers, conformational isomers, ring topology
- 5. Enzyme Targets**
 - 5.1 Enzyme catalysis: Approximation, covalent catalysis, general acid/base, electrostatic, desolvation, strain/distortion
 - 5.2 Coenzymes and prosthetic groups: PLP, THF, Flavin, Heme, ATP, CoA
- 6. Enzyme Inhibition and Inactivation**
 - 6.1 Reversible enzyme inhibitors: slow tight binding inhibitors, transition state analogues, multisubstrate analogues

- 6.2 Irreversible enzyme inhibitors: affinity labeling agents, mechanism based enzyme inactivators
- 6.3 Drug resistance
- 6.4 Drug synergism

7. DNA-Interactive Agents

About the Course:

Lecture:

Students should be registered and should attend all lectures. Students are expected read the text in advance of lecture to familiarize themselves with the material. Students are responsible for assigned materials and all materials presented in class whether they attend or not. It is your responsibility to get class notes from a classmate if you are absent. There will be four midterm exams of which the best 3 of 4 will count toward the final grade. A comprehensive final will be based on the content of the entire course.

Grading: MCH 401

Midterm Exams

Best 3 of 4 75%

Final Exam

Comprehensive 25%

The final course grade (A – F, including +/-) will be determined solely on the basis of total points accumulated. Students missing a midterm examination will receive a grade of “0” for that examination. There will be no makeup at anytime for unexcused absences. No makeup examination will be given for the first excused absence. Students may receive an excused absence by providing a valid, written excuse prior to or within 48 h of the examination.

Students who are unavoidably absent from the final must present a valid, written excuse prior to or within 48 h of the final examination. Students should be prepared to document the absence if requested to do so.

Students with a documented, scheduling conflict for the final exam may schedule an alternative time for the final in advance. Students missing the final exam with an unexcused absence will be given a grade of “0” for the final examination. Students who present a valid written excuse prior to or within 48 h of missing the final examination will be given a grade of “I” (incomplete) provided they have a passing average. Students with failing averages are not eligible for incompletes and will be given a grade of “F” if they miss the final exam. The default grade for an incomplete will be computed with the final examination counting as zero points. Incompletes can be removed according to University guidelines.

NOTE: During examinations, students may not use cell phones and cell phones must be kept out of sight. Violation of these rules will result in a grade of “0” for the examination.

Tentative Exam Schedule:

Midterm 1: Tuesday, September 25, 2007

Midterm 2: Tuesday, October 23, 2007

Midterm 3: Tuesday, November 20, 2007

Midterm 4: Best 6 quizzes at 25 pts each.