Medicinal Chemistry (MDCH) 5210
Organic Medicinal Chemistry I
Fall Semester 2003, Second Professional Year
10:45-11:40 MW, Skaggs Hall 316

Exam 1 (12 September 2002) Study Guide:

Exam 1 is scheduled for 8:00am (1 hour) in Skaggs Auditorium

Comments, help, concerns?

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Helpful readings:

(1) Class notes!
(2) WebCT or http://www.chpc.utah.edu/~cheatham/courses.html
(3) *Foye*; Principles of Medicinal Chemistry
    a. Introduction, Chapter 1,2,4,5
(4) *Goodman and Gilman*; The Pharmacological Basis of Therapeutics

Exam #1 will cover basics up to and including the review material presented on Weds 10 Sept:

- Basic principles + receptors (4-5 lectures)

Emphasis will be on basic principles (solubility, hydrogen bonding, mechanisms of drug actions, receptor binding, bioisosteres, …)

NOTE: this study guide is not inclusive and is only intended as a guide; in addition to using this guide, please look over the notes… Do not memorize the notes but instead focus on the basic principles…

The WWW page has old exams that have questions on basic principles (and also show the general format used). Go to http://www.chpc.utah.edu/~cheatham/courses.html or WebCT and look for the Spring 2002 and 2001 Organic Medicinal Chemistry II links. Same password and username. (steroid, steroid). I am still looking for last year's exam ☹

Basic principles:

(1) Briefly read over the sections on the drug development process in the notes. Is it expensive to develop a new drug? What are new technologies / discoveries that have enabled the drug development process? How can structure activity relationships aid in the drug discovery process?

(2) What are different mechanisms by which a drug may act? What are examples? [Think of a few examples *beyond* specific receptor or protein binding!]

(3) What can affect drug potency and efficacy? ADMET (absorption, distribution, metabolism, elimination, toxicology). Think about genetic polymorphisms, environmental influences (like grapefruit juice or smoking or alcohol), … We discussed the example of inhibition/induction of cytochrome P450's (metabolism) and p-glycoproteins (transporters on the MDR gene).

(4) Why does a drug's pH matter with respect to oral delivery and absorption?

(5) What is a covalent bond (and how strong is it?). What is an ionic bond? What is a hydrogen bond? What is a dispersion-attraction or Lennard-Jones interaction?

(6) What is the hydrophobic effect? Why do micelles form and/or water and oil separate? Remember that, despite having dipoles, halogen substitutions tend to increase the lipophilicity.

(7) What are the common configurations (bonding patterns) for carbon, nitrogen, oxygen, phosphorous and sulfur?

(8) What are the names and structures/configurations for common functional groups. Are these groups likely to be acidic or basic? You should be able to for sure already identify a carboxylic acid, amine, ammonium, phenol, aryl, alkyl, alcohol, ester, ketone and ether groups… Learning what a sulfonamide, sulfonic acid, sulfone, and a guanidinium group is wouldn't hurt. Concentrate on identification rather than drawing each and every one of them.

(9) What are isosteres and bioisosteres. Given a drug, how might we substitute it to retain the general properties (focusing more on shape, hydrogen bonding and ionic interactions than on reproducing all properties)? Remember, the bioisosteric substitutions are not rock solid rules. There are no hard and fast rules. These are simply guidelines and possibilities. The reason for spending 2+ lectures talking about interactions and chemistry was to reinforce this point; it's the chemistry that is important…

(10) What are the main determinants of water solubility?

(11) Which atoms have the best potential to hydrogen bond?

(12) How might we increase the lifetime (duration) of a given drug? [Think about bioavailability *and* metabolism]

(13) What are stereoisomers? What is the difference between an enantiomer and a diasteromer? Does the chirality of a drug matter? Can a nitrogen or a sulfur ever be a stereochemical site?

(14) What groups are normally charged or ionizable? What are groups are lipophilic? What groups are polar? What groups are electron donating or electron withdrawing?

(15) What is the relative acidity of benzoic acid compared para-methyl and para-chloro substituted benzoic acid. Ortho-nitro substituted benzoic acid is very acidic. What are the influences that lead to the increased acidity? Go look at the modified lecture on the WWW and this will be clearer now…

(16) What is K_D? Most drugs have K_D's in what range?

(17) What is an agonist, partial agonist, competitive antagonist, non-competitive antagonist?

(18) Give an example of how binding a cell-surface receptor can lead to a cascade of biochemical reactions/interactions that amplifies the signal? For example, how can the binding of NE at a β_1 adrenergic receptor cause the heart to increase its force and rate? [OK, I admit, this one is a little trickier to answer since we didn't discuss this.]

(19) How might we amplify a response, for example, to a ligand binding to a receptor?