

Medicinal Chemistry (MDCH) 5210
Organic Medicinal Chemistry I
Fall Semester 2002, Second Professional Year
10:45-11:40 MW, Skaggs Hall 316

Exam 1 (23 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) <http://www.chpc.utah.edu/~cheatham/courses.html>
- (3) *Foye; Principles of Medicinal Chemistry*
 - a. Introduction, Chapter 1,2,4,5
 - b. Chapter 10, drugs effecting cholinergic neurotransmission
 - c. Chapter 11, drugs effecting adrenergic neurotransmission
- (4) *Goodman and Gilman; The Pharmacological Basis of Therapeutics*
[neurotransmission]

Exam #2 will cover material up through class on Weds 18 Sept:

- Basic principles + receptors (2 lectures)
- Cholinergic neurotransmission and drugs (2.5 lectures)
- Adrenergic neurotransmission and drugs (2.5 lectures)

Emphasis will be on basic principles, common/obvious structure-activity relationships, MOA (mechanism of action) where known, and well-known, well used, and important drugs in each class. May also go over basic principles (solubility, hydrogen bonding, mechanisms of drug action—physical, receptor binding, ...)

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... Well known and Top200 drugs are worthwhile to recognize (and name).

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> and look for the Spring 2002 and 2001 Organic Medicinal Chemistry II links. Same password and username. (steroid, steroid).

Basic principles:

- (1) What are different mechanisms by which a drug may act? What are examples? [Think of examples beyond specific receptor or protein binding]
- (2) What are the main determinants of water solubility?
- (3) What is polarity / hydrophobicity / hydrophilicity / lipophilicity
- (4) What is a hydrogen bond and which atoms have the best hydrogen bonding potential.
- (5) Does solubility decrease with increasing size?
- (6) How might we increase the lifetime (duration) of a given drug? [Think about bioavailability *and* metabolism]
- (7) What is efficacy and potency?
- (8) What are stereoisomers? What is the difference between an enantiomer and a diastereomer? Does chirality of drugs matter?
- (9) What groups are normally charged or ionizable? What are groups are lipophilic? What groups are polar? What groups are electron donating or electron withdrawing?
- (10) 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?
- (11) What are bioisosteres? Know the common bioisosteric substitutions possible for various groups (i.e. ring equivalents, tetravalent substitutions, ...)
- (12) What is K_D ? Most drugs have K_D 's in what range?
- (13) What is an agonist, indirect agonist, competitive antagonist, non-competitive antagonist?
- (14) 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?

Drugs affecting cholinergic & adrenergic neurotransmission

- (1) Know what effects the sympathetic and parasympathetic divisions of the autonomic nervous system are on various organs.
- (2) Know and be able to draw the basic cholinergic and adrenergic neurotransmitters (ACh, NE, epinephrine). Know the classic antagonists for ACh (muscarine, nicotine).
- (3) How is ACh made? How is it deactivated?
- (4) Know the basic SAR for ACh (i.e. stereochemistry, rule of five, quaternary amine, trans geometry, ...). Think about each part of the molecule and what changes are possible to retain activity (or affinity). How can we increase its duration of action? [Think hydrolysis and carbachol/bethanechol]
- (5) Why is AChE a target for cholinergic drugs? How might we irreversibly inhibit AChE? How might we reversibly inhibit AChE? [Tacrine, Donepezil].
- (6) Why do various chemical warfare agents target AChE? What is aging (in the context of AChEI's)? How chemical features would make a good (irreversible) inhibitor for this enzyme? What compound may serve as an antidote to insecticides or chemical warfare agents targeting AChE? Give an example of an antidote. Is this antidote effective against Sarin?
- (7) Know the prototypical antagonists for muscarinic receptors (atropine, scopolamine). What is the basic SAR for a muscarinic antagonist?
- (8) Know the prototypical antagonists for nicotinic receptors (hexamethonium vs. curare/decamethonium). With nicotinic receptors, what is the difference between a non-depolarizing and depolarizing antagonist?
- (9) Considering the biochemical processes occurring in neurons, what might be targets for drug action? [i.e. that Goodman & Gilman table from Monday's adrenergic lecture & the pictures of neurons and biochemical pathways in the notes]. Think of example drugs that modulate these processes at various stages.
- (10) What is a catecholamine? What are the primary effects of α_1 , β_1 and β_2 adrenergic receptor agonism and antagonism?
- (11) Know examples of indirect agonists of the adrenergic neurons; what is the basic SAR?
- (12) Know examples of direct agonists; what is the basic SAR? (Know examples in each of the main receptor classes: α_1 , β_1 and β_2).
- (13) Albuterol vs. salmeterol vs. terbutaline? Antagonists for α_1 , β_1 and β_2 ?