

**DEPARTMENT OF MEDICINAL CHEMISTRY
SCHOOL OF PHARMACY**

Advanced Medicinal Chemistry
Dr. Umesh R. Desai

MEDC 603
September 29, 2006

KEY

STUDENT NAME

HONOR PLEDGE

1. Of the three types of searches for drug discovery (random, rational and combinatorial), choose one that you believe is most effective and justify your answer in less than 10 sentences. (6 pts)

Random Search: is not very effective.

Rational Search is effective because it is expected to be most direct. If enough information has been collected about the system (either receptor, ligand or mechanism), then one can theoretically design a drug much rapidly because millions of compounds are not needed. Few compounds have to be screened, which should be more cost and time effective.

Combinatorial search is effective because it rapidly screens a large number of compounds and generates leads very rapidly. Thus the initial lead derivation is not very expensive in terms of time and perhaps cost.

2. Write an expression for K_I in terms of the concentration of inhibitor $[I]$. (4 pts)

$$K_I \equiv \frac{[I][E]}{[EI]}$$

3. Define competitive inhibition of an enzyme. You may use a figure or diagram to support your answer. (4 pts). Name a drug that inhibits an enzyme competitively. (4 pts)

Competitive inhibition of an enzyme is defined as a process of occupying the same site of binding as the substrate by the inhibitor resulting in reduction of the enzymatic activity.

Statins
Argatroban

[please check an unusual name written here against literature report. If unsuccessful, deduct four points and write clarify with Dr. Desai]

4. An example of a drug that inhibits an enzyme non-competitively is hirudin. (2 pts) The name of this enzyme is thrombin. (2 pts) The clinical use of this drug is as an anticoagulant. (1 pts)

NOTE: [please check an unusual name written here against literature report. If unsuccessful, deduct points and write clarify with Dr. Desai]

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5. Several drugs continue to be used in the clinic today as discovered from nature. Name two drugs in use today that fall in this category, i.e, essentially unmodified from the natural structure, and identify their clinical usage. (4 pts)

<u>Drug</u>	<u>Used in the Clinic As</u>
Heparin	anticoagulant
Digitoxin	cardiac failure
Quinine	anti-malarial
Quinidine	anti-arrhythmic
Reserpine	anti-hypertensive
Statins	anti-hyperlipidemic
Warfarin	anticoagulant

6. Natural products have been the main source of drugs for man todate. List three advantages and three disadvantages these molecules carry in their use as clinically useful agents. (6 pts)

Advantages

- a) _structural diversity_____
- b) _apparently unlimited supply_____
- c) _high potency_____
- d) high specificity

Disadvantages

- e) _synthesis is difficult
 - f) isolation may be difficult
 - g) identification may not be easy
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