

Name: _____

SS#: _____

PHA 4120

First Exam Fall 1997

On my honor, I have neither given nor received unauthorized aid in doing this assignment.

Name

Question/Points

1. _____/5

2. _____/12

3. _____/5

4. _____/4

5. _____/5

6. _____/10

7. _____/10

8. _____/10

9. _____/8

10. _____/9

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1. The volume of distribution of a drug X is 40,000 L. Indicate which **one** of the following statements is (are) consistent with this observation (5 pts)
 - A ____ plasma protein binding is more pronounced than tissue binding
 - B ____ highly metabolized in the tissue
 - C ____ the drug does not leave the plasma
 - D ____ not at all bound to plasma proteins
 - E ____ drug is able to cross membranes

2. For each fluid below give the approximate volume you would expect in an adult person (12 pts)
 - Extracellular fluid

 - Total body water

 - plasma

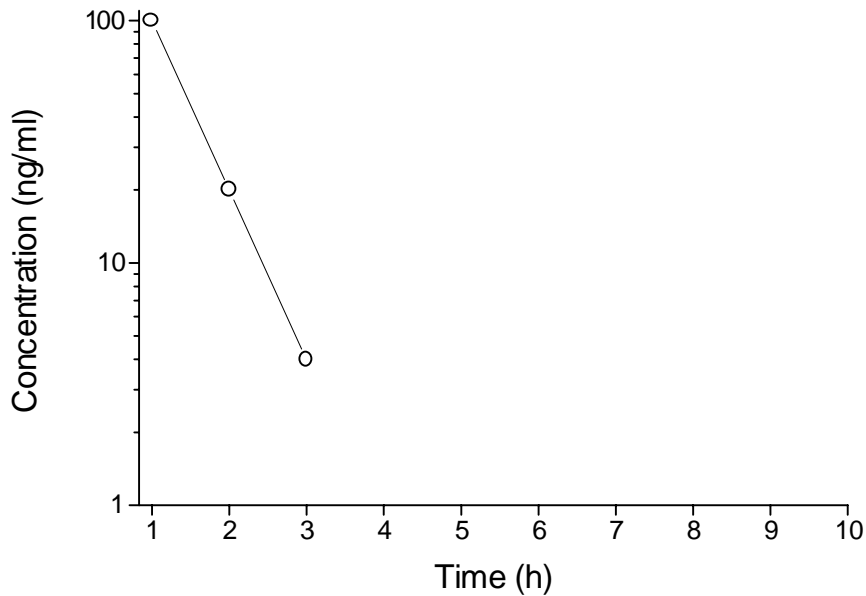
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3. For a typical 70-kg person, the volume of distribution of drug X is about 35 L. We assume that the plasma volume is 5 L, and the tissue volume is 30 L. Generally the unbound fraction in plasma and tissue is about 0.2. Plasma protein binding of drug X is reduced in patients with hypoalbuminemia. (5pts)

a) If the plasma protein binding decreases to 60% ($f_u=0.4$) what is the expected volume of distribution.

b) Assume that this drug can be modeled after an i.v. bolus injection with a one compartment body model. The following plasma concentration time profile was observed in a typical patient. Indicate on the graph what concentration time profile would be expected in a patient with hypoalbuminemia. Consider also resulting changes in k_e .



4. The distribution of two drugs A & B into the brain is driven by permeability limitations. The distribution of drug B into the brain is driven by perfusion

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limitations. **Which** of the two drugs will enter the brain faster (short explanation) (4 pts)

5. Mark whether the following statements are True or False (5 pts)
- | | | |
|---|---|--|
| T | F | Drugs which are very lipophilic tend to distribute well into body tissues. |
| T | F | Lipophilic drugs with a high K_p value have a large volume of distribution. |
| T | F | The volume of distribution depends on the ability of the drug to pass membranes and the degree of plasma and tissue binding. |
| T | F | The extraction ratio for a high extraction drug is independent of the <i>plasma</i> protein binding. |
| T | F | The extraction ratio for a low extraction drug is independent of the <i>tissue</i> protein binding. |
6. Explain the term clearance in your own words (no equations). Do not use more than 30 words. (10 points)

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7. You have a lipophilic, protein bound, low extraction drug. Indicate what pharmacokinetic parameter will **be changed** by the following physiological changes. Mark also whether the selected parameters will increase or decrease. List only one parameter per item (8 points)

increase in plasma protein binding.....

increase in liver blood flow.....

increase in the “number of fat cells”

increase in the number of metabolizing enzymes.....

8. A drug is given as an IV bolus injection. The initial plasma concentration was 80 $\mu\text{g/ml}$. 3 hours later the plasma concentration was 40 $\mu\text{g/ml}$. What is the plasma concentration 6 hours after dosing if (10 pts)

a) the elimination is first order?

b) the elimination is zero-order?

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9. Drug A is given by i.v. bolus injection. The dose is known. Two plasma samples were taken one and 3 hours after dosing. Having only the above information, give the equations or describe the procedure **by** which you would determine the (8 pts)

- elimination rate

- the half-life

- C_{po}

- the volume of distribution

- the AUC

- the clearance