

Name: _____

SS#: _____

PHA 5127

**First Exam
Fall 2001**

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

Name

Question/Points

1. _____/ 10 pts

2. _____/10 pts

3. _____/10 pts

4. _____/15 pts

5. _____/15 pts

6. _____/15 pts

7. _____/25 pts

TOTAL _____/100 pts

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1. Complete the following statements for a low molecular weight drug which does not bind to plasma proteins....
(10 points)

A. The maximum value which renal clearance can approach that of

.....

B. If this drug is hydrophilic and not interacting with transporters the largest possible renal clearance is that of

.....

C. If this drug is lipophilic, neutral drug and not interacting with transporters the smallest possible renal clearance is that of

.....

D. Assuming that the lipophilic drug is a base, renal clearance can be reduced by...

.....

.....

2. Consider the two drugs A and B. Drug A shows perfusion limited distribution into the brain. Drug B is entering the brain characterized by permeability limited distribution. List the statements in agreement with this observation (10 points).

- a) Drug A might be more lipophilic than drug B.
- b) Drug A will enter the brain faster than drug B.
- c) Drug A might be a stronger base than drug B.
- d) Drug B might be a stronger base than drug A.
- e) Drug B will enter the brain faster if blood flow through the brain is increased.
- f) Drug A will enter the brain faster if blood flow through the brain is increased.

List correct statement(s):

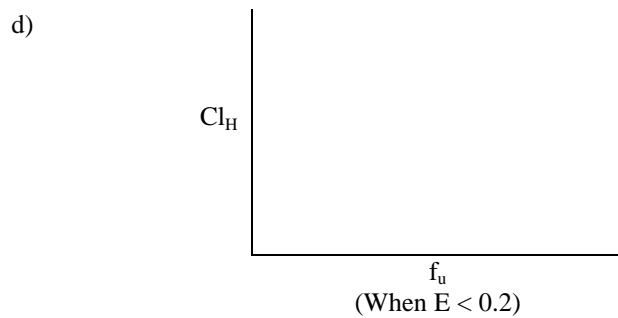
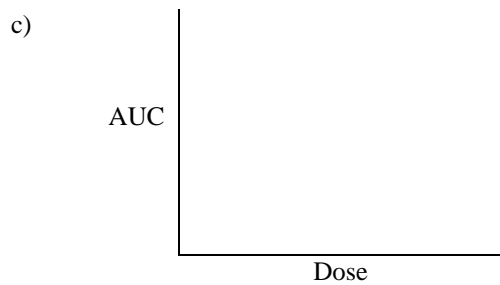
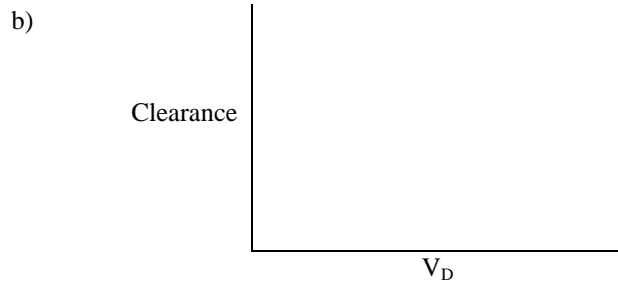
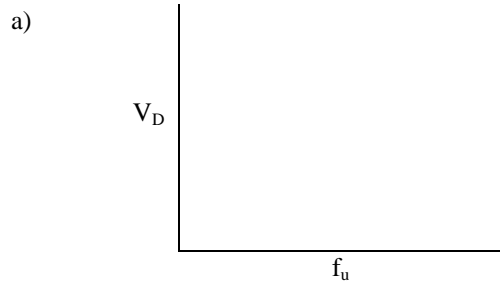
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3. Choose whether the following statements for a **high extraction drug** are True or False (10 points)

- T or F The volume of distribution has to be small
- T or F A decrease in liver blood flow will increase oral bioavailability
- T or F An increase in intrinsic clearance, due to enzyme induction will increase hepatic clearance
- T or F An increase in plasma protein binding will decrease clearance
- T or F Oral bioavailability is increased with increased liver blood flow

4. For the following relationships, draw a line that best describes the relationship between the two parameters. If no relationship exists, write "N/R". (15 points)



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5. For the physiological changes listed below, select the induced changes on the pharmacokinetic parameters for a lipophilic, unionizable (no acid or basic group in the molecule), protein bound drug that shows **extensive liver** metabolism ($E=1$) and renal elimination. (some answers may be used more than once). (15 points)

Physiological change	Effect on kinetics
1.) Decrease metabolic enzymes _____	a. $Cl_{REN} \downarrow$
2.) Decrease in urine flow _____	b. $Cl_{HEP} \downarrow$
3.) Increase in liver blood flow _____	c. oral bioavailability \downarrow
4.) Decrease in number of fat cells _____	d. $V_D \uparrow$
5.) Increase in creatinine clearance _____	e. oral bioavailability \uparrow
	f. $V_D \downarrow$
	g. none of the above

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6. For the following situations, indicate whether the drug is *filtered, reabsorbed or actively secreted* (Assume GFR is 130 mL min^{-1} , urine flow is 1.5 ml min^{-1}) (15 points)
- A drug with $f_u = 0.01$ and a $\text{Cl}_{\text{REN}} = 20 \text{ mL min}^{-1}$ is _____
 - A drug with $f_u = 0.50$ and a $\text{Cl}_{\text{REN}} = 65 \text{ mL min}^{-1}$ is _____
 - A drug with $f_u = 0.20$ and a $\text{Cl}_{\text{REN}} = 0.3 \text{ mL min}^{-1}$ is _____
7. A drug is eliminated through glomerular filtration and hepatic metabolism. It does not bind to plasma proteins. Glomerular filtration rate is normal. No active renal secretion and passive or active reabsorption after renal filtration is observed. The volume of distribution is 50 L. When given as an i.v. bolus, plasma concentrations one hour after administration were 5.2 mg/L. 3 hours after administration the concentration was 2.6 mg/L. (25 pts)
- a. What is the plasma concentration 8 hours after administration of the drug?

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7b. What is the hepatic clearance?