Name: _____

SS#: _____

PHA 5127

First Exam
Fall 2002

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

Name

Question/Points

1. _____/15 pts
2. _____/15 pts
3. _____/15 pts
4. _____/15 pts
5. _____/25 pts
6. _____/15pts

TOTAL _____/100 pts

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1. True or False The oral bioavailability of a drug whose clearance is close to the liver blood flow (15 points)

T F will be small

T F will depend on liver blood flow

T F will depend on plasma protein binding

T F will be close to 100%.

T F will be affected by the GFR

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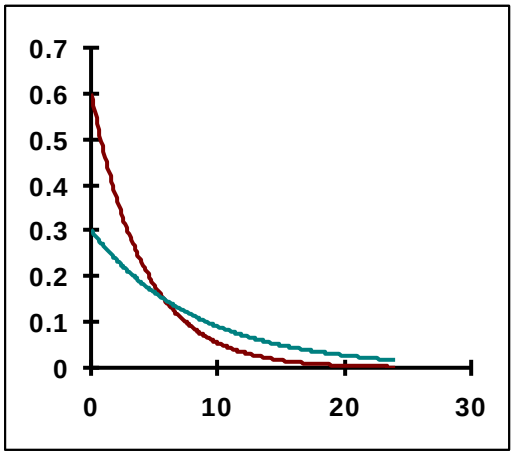
2. Compare the following two concentration time profiles (15 points).



The 2 graphs differ in either

Dose,
Vd
Clearance

Give the reasons for your decision.

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3. 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.)	Increase in 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.)	Decrease in creatinine clearance_____	e. oral bioavailability $F\uparrow$
		f. $V_D \downarrow$
		g. none of the above

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4. 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 = 0.02and a Cl_{REN} = 20 mL min^{-1} is _____
   - A drug with f_u = 0.40 and a Cl_{REN} = 52 mL min^{-1} is _____
   - A drug with f_u = 0.30 and a Cl_{REN} = 0.45 mL min^{-1} is _____

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5. A drug is eliminated through glomerular filtration and hepatic metabolism (no other clearance mechanisms are observed). **It does not bind to plasma proteins**. Glomerular filtration rate is normal (**130 ml/min**). 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)

5a. What is k_e?

5b. What is the total clearance of the drug.

5c. What is the renal clearance of the drug?

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5c. What is the hepatic clearance of the drug?

5d. After 10 doses of this drug (given once a day) the concentration two hours after the last dose is 3.67 mg/L. What will be the concentration 10 hours later (12 hours after the last injection)

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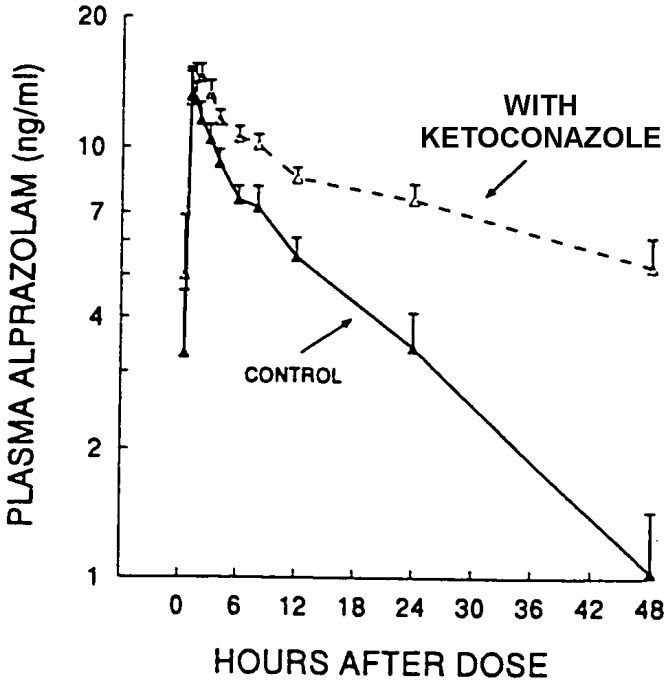
6. The same dose of Alprazolam was given either alone or with ketocozanole. Explain what is going on. (15 points)



Greenblatt, 26 September 1998