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. ______/15 pts

TOTAL ______/100 pts
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
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.
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)

<table>
<thead>
<tr>
<th>Physiological change</th>
<th>Effect on kinetics</th>
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</thead>
<tbody>
<tr>
<td>1.) Increase in metabolic enzymes__________</td>
<td>a. $Cl_{REN} \downarrow$</td>
</tr>
<tr>
<td>2.) Decrease in urine flow_______</td>
<td>b. $Cl_{HEP} \downarrow$</td>
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<tr>
<td>3.) Increase in liver blood flow_____</td>
<td>c. oral bioavailability $\downarrow$</td>
</tr>
<tr>
<td>4.) Decrease in number of fat cells_______</td>
<td>d. $V_{D} \uparrow$</td>
</tr>
<tr>
<td>5.) Decrease in creatinine clearance_______</td>
<td>e. oral bioavailability $F \uparrow$</td>
</tr>
<tr>
<td></td>
<td>f. $V_{D} \downarrow$</td>
</tr>
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<td></td>
<td>g. none of the above</td>
</tr>
</tbody>
</table>
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 \( f_u = 0.02 \) and \( \text{Cl}_{\text{REN}} = 20 \) mL min\(^{-1}\) is _______________________
- A drug with \( f_u = 0.40 \) and \( \text{Cl}_{\text{REN}} = 52 \) mL min\(^{-1}\) is _______________________
- A drug with \( f_u = 0.30 \) and \( \text{Cl}_{\text{REN}} = 0.45 \) mL min\(^{-1}\) is _______________________

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