

**PHA 4120**

**Biopharmaceutics and Pharmacokinetics**

**First Exam**

**Fall 1995**

Name: \_\_\_\_\_

SS#: \_\_\_\_\_

**Total Points**

1. \_\_\_\_\_/5pts
2. \_\_\_\_\_/5pts
3. \_\_\_\_\_/5pts
4. \_\_\_\_\_/5pts
5. \_\_\_\_\_/6pts
6. \_\_\_\_\_/4pts
7. \_\_\_\_\_/12pts
8. \_\_\_\_\_/6pts
9. \_\_\_\_\_/6pts
10. \_\_\_\_\_/6pts
11. \_\_\_\_\_/6pts
12. \_\_\_\_\_/6pts
13. \_\_\_\_\_/6pts
14. \_\_\_\_\_/8pts

TOTAL \_\_\_\_\_X 1.163 pts

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First Exam**

1. Mark whether the following statements for a **high extraction drug** are True or False (5 pts)

T F The oral bioavailability will depend on the liver blood flow.  
T F Clearance will increase significantly after induction of the relevant enzyme.  
T F Increase in plasma protein binding will decrease the extraction ratio E.  
T F The hepatocyte membranes do not represent a barrier.  
T F If the hepatic blood flow is reduced, the clearance will be decreased.

2. Mark whether the following statements concerning the partitioning of a drug into erythrocytes and the erythrocyte partition coefficient (D) for a particular drug are True or False (5 pts)

T F D varies from patient to patient, depending on their hematocrit.  
T F With increasing D, but constant protein binding the ratio of drug concentration in plasma and plasma water will change  
T F Can be determined experimentally in a suspension of erythrocytes in **plasma water**.  
T F Is analogous to an oil/water partition coefficient.  
T F For whole blood, the drug concentration in erythrocytes decreases with increased protein binding

3. Mark whether the following statements concerning phase I metabolic reactions are True or False (5 pts)

T F Might be responsible for the formation of active drug.  
T F Might be responsible for the formation of inactive metabolites.  
T F Often involve condensation of a drug with glucuronic acid.  
T F The corresponding metabolic clearance cannot be increased by other drugs.  
T F Is independent of genetic influences.

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4. Mark whether the following statements are True or False. (5 pts)

- T F For two drugs which are given as solution to the same administration site, the drug whose absorption from the administration site into the blood is permeability rate limited will be taken up slower than a drug whose uptake is perfusion rate limited.
- T F The net transport through passive diffusion across a membrane stops when the *free* drug concentrations are the same on both sites of the membrane.
- T F For a drug with a erythrocyte partition coefficient of 10 and no protein binding, the drug concentration in plasma is lower than in whole blood.
- T F Enterohepatic re-circulation might be responsible for the drug staying in the body for a longer period of time.
- T F Drugs are only given to the lung to achieve local effects.

5. Mark whether the following statements are True or False (6 pts)

- T F Drugs which are very lipophilic tend to distribute well into body tissues.
- T F Small hydrophilic molecules do not readily distribute from the muscle tissue into the systemic circulation.
- T F Drugs with a high  $K_p$  value always have a large volume of distribution.
- T F Drugs with a high tissue binding always have a large volume of distribution.
- T F The hepatic extraction ratio for a low extraction drug is independent of the *plasma* protein binding.
- T F The extraction ratio for a low extraction drug is independent of the *tissue* protein binding.

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6. Complete the following statements (4 pts)

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

B. The smallest possible volume of distribution of a drug is that of  
.....

C. Urinary excretion of amphetamine can be increased by  
.....

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7. Listed below are 4 drugs and their physicochemical properties. Choose the drug(s) that most appropriately complete(s) each of the following statements: (12 pts)

Property	Drug A	Drug B	Drug C	Drug D
Molecular weight	85,000	273	315	378
pKa	-	base pKa=11	neutral	quarternary Ammonium
Polarity of unionized form	Protein	nonpolar	non-polar	—
Plasma binding	0	0%	99%	0
Tissue binding	0	90%	1%	0
E(liver)	X	0.01	0.95%	0

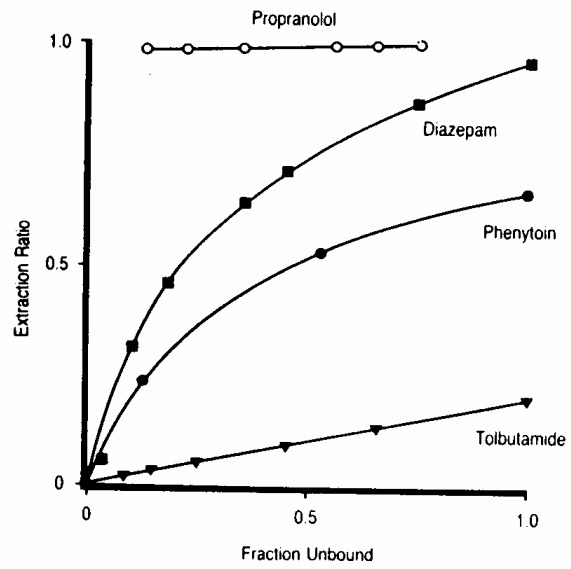
Remarks mainly metabolized in blood

- A. A volume of distribution of 3-7 L is likely to be seen with drug(s)\_\_\_\_\_.
- B. Drug(s)\_\_\_\_\_ are likely to be taken up by the brain.
- C. Renal clearance by glomerular filtration will be smaller than 12.5 ml/min for \_\_\_\_\_.
- D. Clearance will depend on liver blood flow

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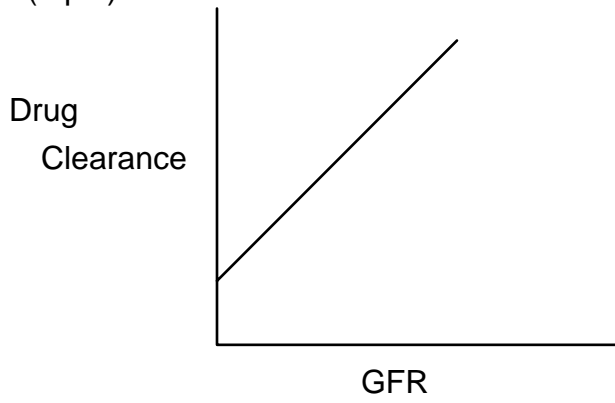
8. (6 points)  
Explain the following diagram



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9. Explain the following diagram  
(6 pts)



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10. The renal clearances and the fractions unbound to plasma proteins of three drugs in a 70 kg man are listed as follows.(6 pts)

	<b><u>Renal Clearance</u></b> <b><u>ml/minute</u></b>	<b><u>Fraction unbound</u></b>
Theophylline	10	0.5
Phenytoin	0.15	0.1
Cefonicid	20	0.02

State the likely contribution of filtration, secretion and reabsorption to the renal handling of each of these drugs. Assume a GFR of 120 ml/min and a urine flow of 1.5ml/min.

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11. A drug is given as an i.v. bolus injection.

a) The rate of change in the plasma concentration is described by

$$-\frac{dC}{dt} = k \cdot C$$

Solve the differential equation

b) Explain why the half-life is constant and does not depend on the concentration in blood.

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12. Explain **briefly** what drug properties are described by the volume of distribution and clearance terms. (6 pts)

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13. Explain why thiopental is taken up by cerebrospinal fluid (CSF) much faster than barbitol. Assume permeability rate limited equilibrium between blood and CSF.

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14. What is the maximum extraction ratio for renal excretion. What is the resulting renal clearance? Explain (8 pts).