

Name: _____

SS#: _____

PHA 4120

First Exam Fall 1996

On my honor, I have neither given or received unauthorized aid in doing this assignment.

Name

Question/Points

1. _____/5

2. _____/12

3. _____/5

4. _____/4

5. _____/4

6. _____/10

7. _____/10

8. _____/10

9. _____/10

10. _____/10

TOTAL _____/80 x 1.25 = _____

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

- T F The oral bioavailability of this drug is likely to be low.
- T F The volume of distribution is large.
- T F Increase in liver blood flow will decrease the extraction ratio E.
- T F Increase in liver blood flow will decrease clearance.
- T F Increase in plasma protein binding will decrease clearance.

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

Property	Drug A	Drug B	Drug C	Drug D
Molecular weight	85,000	273	315	378
pKa	-	base pKa=2	neutral	acid pKa=11
Polarity of unionized form	Protein	non-polar	non-polar	extremely polar
f_u	0	0.01	1.0	0
f_{uT}	0	0.01	0.1	0
E(liver)	no metabolism	0.01	0.95	no metabolism

- 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. Liver clearance of drug(s) _____ will be depend on liver blood flow.
- D. Liver clearance of drug(s) _____ will depend on plasma protein binding.
- E. Drug(s) _____ show the highest volume of distribution.
- F. Drug (s) _____ show a volume of distribution of about 40L liters.

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3. 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 Drugs with a high K_p value have a large volume of distribution (assume drug is able to cross membranes).
- 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 relatively 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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4. Complete the following statements (4 points)
- A. The maximum value which hepatic clearance can approach that of the
.....
- B. The smallest possible volume of distribution of a drug is that of
.....
- C. The larger the elimination rate constant of a drug the
.....the half-life.
- D. A neutral, lipophilic drug is likely to be absorbed faster
in the
than in the
(Fill in which section of the GI tract)
- E. The higher the hepatic extraction ratio of a drug, the the
oral bioavailability
5. Increasing the following parameters will result in a decrease in the rate of
active transport of a drug (4 points)
- T F decrease in transporter molecules
- T F reduction in ATP
- T F increase in the partition coefficient of the drug between lipid and water.
- T F more efficient removal of the drug from the drug stream close to the site
of absorption

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6. Explain the term volume of distribution in your own words (no equations). Do not use more than 30 words. (10 points)

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7. What might be the rationale for a drug company to develop an insulin aerosol? (10 points)

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8. You are a research pharmacist involved with animal studies for new drugs. You are provided the following data from a recent in vitro study of two Drugs A and B (i.e. conducted in a test tube) which shows the half-life for the metabolism of two different drugs by one enzyme (10 points) .

Drug A		Drug B	
Initial Concentration (mg/L)	half-life (hr.)	Concentration (mg/L)	half-life (hr.)
50	2.5	50	3
100	5	100	3
200	10	200	3

- a) Which drug is exhibiting zero order metabolism and why?

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b) What is the rate constant (K_m) of the metabolic reaction for drug A? To receive complete credit the units of K_m must be correct.

c) What is the rate constant (K_m) of the metabolic reaction for Drug B? To receive complete credit the units of K_m must be correct.

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9. A drug is given as an I.V. bolus injection. The rate of change of the plasma concentration follows zero order kinetics. (10 points)

Give the differential equation describing the above situation.

Solve the differential equation to obtain an expression for C in terms of t.

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10. Patient JA is a asthmatic patient receiving theophylline. After having received an i.v. bolus dose of theophylline JA's theophylline plasma concentrations are determined to be 11.5 and 4.5 mg/ml 1 and 6 hours after administration of the dose. Calculate the elimination rate constant and the half-life of theophylline in this patient (10 points).

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Equation Sheet for First Exam

Rules of differentiation

1. $y = a \cdot x^n \rightarrow \frac{dy}{dx} = n \cdot a \cdot x^{n-1}$
2. $y = n \cdot e^{a \cdot x} \rightarrow \frac{dy}{dx} = a \cdot n \cdot e^{a \cdot x}$
3. $y = \ln x \rightarrow \frac{dy}{dx} = \frac{1}{x}$

Rules for integration

Integration is the reverse of differentiation

for $n \neq -1$

$$y = m \cdot x^n \rightarrow \int (m \cdot x^n) dx = \frac{m}{n+1} x^{n+1}$$

$$y = n \cdot e^{k \cdot x} \rightarrow \int n \cdot e^{k \cdot x} \cdot dx = \frac{n}{k} \cdot e^{k \cdot x}$$

$$y = \frac{1}{x} \rightarrow \int \frac{1}{x} dx = \ln x$$

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Diffusion

$$-\frac{dC_0}{dt} = D \frac{A}{h} \cdot k(C_0 - C_i)$$

Volume of Distribution

$$V = V_P + V_T \cdot K_P$$

$$V = V_P + V_T \cdot \frac{f_u}{f_{uT}}$$

Metabolic and Renal Clearance

$$E_H = \frac{Cl_{int} \cdot f_{u_b}}{Q_H + Cl_{int} \cdot f_{u_b}}$$

$$Cl_H = E_H \cdot Q_H = \frac{Q_H \cdot Cl_{int} \cdot f_{u_b}}{Q_H + Cl_{int} \cdot f_{u_b}}$$

$$F_H = \frac{Q_H}{Q_H + Cl_{int} \cdot f_{u_b}}$$

$$Cl_{ren} = RBF \cdot E = RBF \cdot \frac{C_{in} - C_{out}}{C_{in}}$$

$$Cl_{ren} = \frac{\text{rate of excretion}}{\text{plasma concentration}}$$

$$Cl_{ren} = f_u \cdot GFR + \left[\frac{\text{Rate of secretion}}{\text{Plasma concentration}} \right]$$

$$Cl_{ren} = \frac{\text{Urine flow} \cdot \text{urine concentration}}{\text{Plasma concentration}}$$