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PHA 5127

First Exam

Fall 2014

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

ANSWER KEY

Name

Question Set/Points

I.	30 pts
II.	20 pts
III.	15 pts
IV	15 pts
V.	25 pts
VI.	10 pts
VII.	10 pts
VIII.	10 pts
IX.	35 pts

TOTAL: 170 pts

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Question Set I (True or False)

(30 points)

True (A) or False (B). On the bubble sheet mark *A for true* or *B for false. Assume passive diffusion as the driving force for distribution.*

1: T (F) The $t_{1/2}$ of a drug eliminated through a zero order process is a drug specific constant.

2: T (F) A lipophilic drug of low molecular weight, cannot have a volume of distribution that is smaller than V_T.

3: T (F) The fraction of the drug being eliminated per hour is increasing in a first order process.

4: T (F) Two drugs that have similar elimination half-lives will have similar volumes of distributions.

5: (T) F The same dose of a drug is given orally either as a solution or in form of a slow dissolving crystal suspension. The solution will show higher maximum concentrations in plasma.

6: T (F) When heparin is added to blood and the blood is centrifuged, the resulting supernatant is called serum.

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Question Set II (20 points) True (A) or False (B). On the bubble sheet mark *A for true* or *B for false.*

True (A) or False (B). On the bubble sheet mark *A for true* or *B for false. Consider a lipophilic acidic drug A (pka=14, logP=5, If you have difficulties with pKa values: The pKa of HCl is close to zero) and a lipophilic neutral drug B (logP=5). Both do not show any affinity to transporters and show similar tissue and plasma protein binding.*

7: T (F) Drug B will enter the brain faster.

8: T (F) Drug A will be unable to enter the interstitial fluid.

9: T (F) Drug B be is likely to have a larger volume of distribution

10: (T) F The Ke of both drugs will only differ, if CL differs.

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Question Set III

(15 points)

Listed in the Table are two properties of acidic drug molecules:

- the fraction unionized at ph=7.4 and
- the partition coefficient of the unionized form.

DRUG	Fraction Unionized at pH=7.4	Partition Coefficient of Unionized form	Molecular Weight (Dalton)	effective Partition coefficient
1	0.6	3.1	240	1.86
2	0.91	0.1	290	0.091
3	0.074	10	320	0.74
4	0.72	0.005	456	0.0034

11: Select the correct rank order with which drugs 1-4 will enter brain tissue. Assume that the drugs are not subject to transporters at the blood-brain barrier.

A) 1 slower than 2 slower than 3 slower than 4

(B) 4 slower than 2 slower than 3 slower than 1

C) 4 slower than 2 slower than 1 slower than 3

D) 3 slower than 1 slower than 4 slower than 2

E) 1 slower than 3 slower than 2 slower than 4

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Question Set IV (True or False)

(15 points)

True (A) or False (B). On the bubble sheet mark *A for true* or *B for false. Assume no active transport.*

12: T (F) Assume a drug is substrate of a specific transport protein. Transporters only eliminate drugs from the body

13: T (F) The rate with which hydrophilic compounds will move across well-built membranes will depend on the concentration gradient between total drug in plasma and total drug in tissue.

14: T (F) Assuming that a protein drug does not bind to plasma and tissue component, the volume of distribution is likely to be 41 liters.

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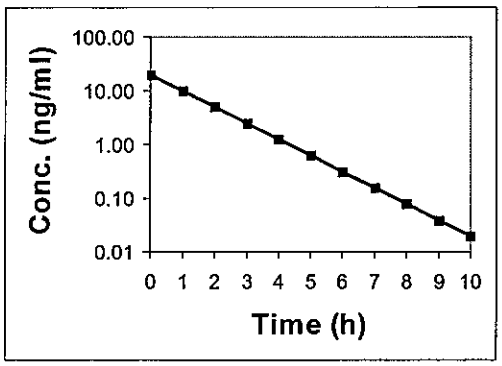
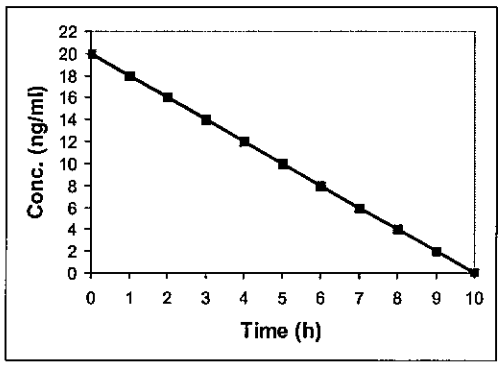
Question Set V (True or False)

(25 points)



Drug A



Drug B

True (A) or False (B). On the bubble sheet mark *A for true* or *B for false*

15: T (F) Drug B's rate of elimination is affected by the amount of drug in the body.

16: T (F) Drug A's elimination rate constant has the unit "ng/ml".

17: T (F) For drug B, the fraction of drug eliminated per hour is constant.

18: T (F) Drug A's concentration-time profile might be explained by saturated metabolic enzymes.

19: (T) F For drug A, the elimination rate constant does not depend on the amount of drug in the body.

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Question Set VI

(10 points)

20: An investigational new drug is eliminated entirely by hepatic metabolism, with a clearance of 1 L/h in healthy subjects. Assume an average liver blood flow of 80 L/h in these healthy subjects. What would be the expected clearance in a congestive heart failure patient with a liver blood flow of 66 L/h? Use the most appropriate relationships

A) 0.83 L/h
B) 1.0 L/h
C) 0.66 L/h
D) 66 L/h
E) None of the above

low extraction drug ; change in liver blood flow does not affect the clearance

$\leftrightarrow CL = Q\downarrow \cdot E\uparrow$

when the liver blood flow decreases the extraction ratio increases

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Question Set VI

21: A drug has an intrinsic clearance of 40,000 L/min. The plasma protein binding and liver blood flow are 60% and 80 L/h, respectively.

Calculate the hepatic clearance.

A) 80 L/h

B) 35 L/h

C) 48 L/h

D) 320 L/h

E) None of the above

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Question Set VII

(10 points)

22: Assume drug A is predominantly cleared through hepatic metabolism. Drug A has an intrinsic clearance of 40,000 L/min. The plasma protein binding and liver blood flow are 60% and 80 L/h, respectively.

How will the increase in both tissue binding and liver blood flow affect the initial concentration (C_0 when given as i.v. bolus), hepatic clearance (CL), bioavailability (F) for tablet, AUC, and half-life ($t_{1/2}$)? (Please note that ↔ means: about the same)

A) $\downarrow C_0, \uparrow CL, \downarrow F, \downarrow AUC, \downarrow t_{1/2}$

B) $\leftrightarrow C_0, \leftrightarrow CL, \uparrow F, \uparrow AUC, \leftrightarrow t_{1/2}$

C) $\downarrow C_0, \leftrightarrow CL, \leftrightarrow F, \leftrightarrow AUC \leftrightarrow, \uparrow t_{1/2}$

D) $\uparrow C_0, \downarrow CL, \leftrightarrow F, \uparrow AUC, \uparrow t_{1/2}$

(E) $\downarrow C_0, \uparrow CL, \uparrow F, \downarrow AUC, \leftrightarrow t_{1/2}$

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Question Set VIII

(10 points)

23. A new analysis technique has enabled you to measure the drug concentration before and after the blood passes the liver. The plasma concentrations before and after the liver was passed were 6.5 and 2.4 mg/mL, respectively.

Calculate the hepatic clearance (assume a liver blood flow of 1450 mL/min).

A) 15 L/h

B) 35 L/h

C) 55 L/h

D) 75 L/h

E) None of above

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Question Set IX

(35 points) **Mark "A" for True or "B" for False**

24: (T) F Free drug concentrations are always the same in plasma and tissues, when the distribution occurs instantaneously.

25: T (F) Enzyme induction affects the hepatic clearance of a low and high extraction drugs

26: (T) F Enzyme induction affects the oral bioavailability of high extraction drugs

27: T (F) A fast absorption might allow less frequent dosing.

28: (T) F A slower absorption might be advantageous for a drug with a narrow therapeutic window.

29: T (F) The Fick's law is: $dQ/dt=D*K*(Cplasma-Ctissue)/h$. The concentration terms (C_{plasma} and C_{tissue})refer to total drug concentrations in either plasma or tissue.

30: (T) F Concentrations in plasma are of relevance for drug therapy as they generally correlate well with concentrations observed at the effect (target) site.