PHA 5127

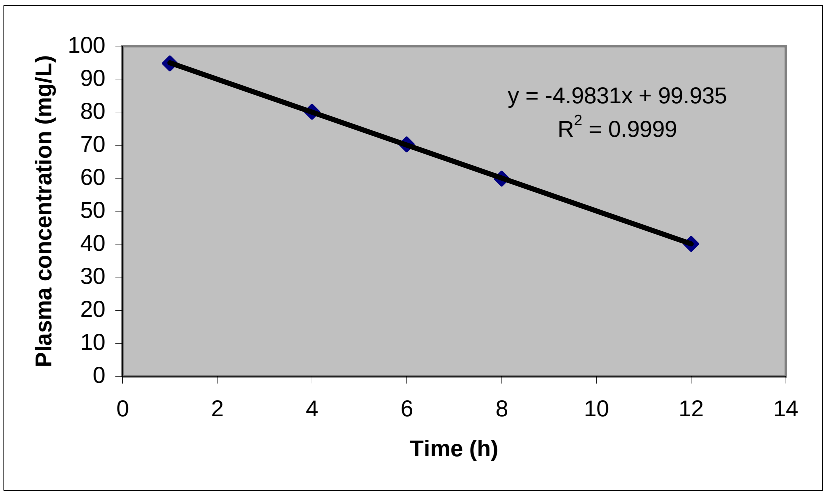
Homework #1

(Total: 10 points)

#1) *Calculate $AUC_{0\rightarrow\infty}$ from the given concentration-time profile.* (3 points)

Time (h)	Plasma concentration (mg/L)
1	94.8
4	80.1
6	70.3
8	59.9
12	40.1

We first need to determine whether the drug is eliminated in a first or a zero-order elimination process. An easy way to approach this question is to graph the data.



Plasma concentration and time show a linear relationship on a normal scale. Therefore, drug is eliminated in a zero-order process. (First-order process would show a linear relationship on a semi-log scale!) → Equal amounts of drug are eliminated per hour. In order to determine $AUC_{0\rightarrow\infty}$ we need to calculate t(0 hours) and the time when the plasma concentration reaches zero. Looking at the data set, we see that the plasma concentration decreases by approximately 5mg/L per hour. Thus, the plasma concentration will be about 100mg/L at time zero and approach zero after about 20 hours.

Now let's calculate the areas of the individual trapezoids according to:

$$\frac{C_2 + C_1}{2} \bullet (t_2 - t_1)$$

Time (h)	Plasma concentration (mg/L)	AUCs (mg*h)/L
0	100	
1	94.8	97.4
4	80.1	262.35
6	70.3	150.4
8	59.9	130.2
12	40.1	200
20	0	160.4
	SUM	**1000.75**

The $AUC_{0\to\infty}$ can be determined by summing up the individual areas which results in a value of about 1000mg*h/L. (Alternatively, you could calculate the area of the triangle formed by the data: 100mg/L*20h/2 = 1000mg*h/L)

#2) *Fractions and amounts of drugs eliminated through zero- and first-order kinetics* (2 points)

#2a) How do fraction and amount of a drug eliminated through first-order kinetics change? Please, mark the right answer. (1 point)

- O Fraction changes, amount stays constant
- O ***Fraction stays constant, amount changes***
- O Fraction changes, amount changes
- O Fraction stays constant, amount stays constant

#2b). How do fraction and amount of a drug eliminated through zero-order kinetics change? Please, mark the right answer. (1 point)

- O ***Fraction changes, amount stays constant***
- O Fraction stays constant, amount changes
- O Fraction changes, amount changes
- O Fraction stays constant, amount stays constant

#3) *Please derive the half-life equation for a first-order elimination process.* (3 points)

$$C_t = C_0 \cdot e^{-k_e \cdot t}$$

$$C(t_{1/2}) = \frac{1}{2} \cdot C_0$$

$$\rightarrow \frac{1}{2} C_0 = C_0 \cdot e^{-k_e \cdot t_{1/2}}$$

$$\rightarrow \frac{1}{2} = e^{-k_e \cdot t_{1/2}}$$

$$\rightarrow \ln \frac{1}{2} = -k_e \cdot t_{1/2}$$

$$\rightarrow -0.963 = -k_e \cdot t_{1/2}$$

$$\rightarrow t_{1/2} = \frac{0.693}{k_e}$$

#4) *What is the difference in distribution of drugs into organs such as the heart and the lung compared to fat tissue and bone? Explain!* (2 points)

Heart, lungs and kidneys are highly perfused organs compared to fat tissue and bone. For most drugs the rate of delivery from the circulation to a particular tissue depends greatly on the blood flow of the respective tissue. Therefore, drugs apparently distribute more rapidly to areas with higher blood flow.

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Total points given for homework 1: **10**

#1) 3
#2) 2
#3) 3
#4) 2