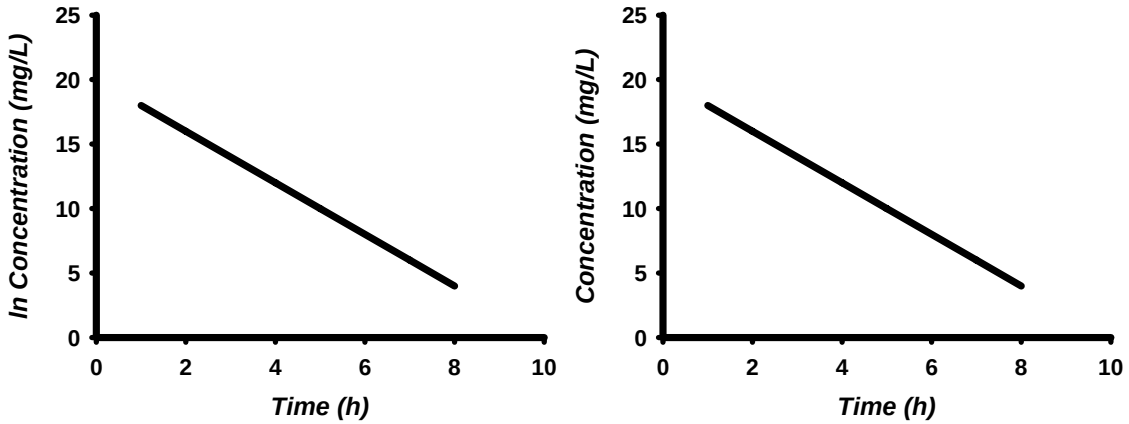
PHA 5127 – Fall 2006
Homework #1

1. Identify which of the graphs below exhibit zero-order and first order kinetics. For which elimination is the half-life ($t_{1/2}$) dependent on the concentration? Write the equations and give explanations. ***(total points = 3)***



Answer:

The plot on the left shows first-order kinetics because it is plotted on a semi-log scale that results in a straight line. **(0.5 points)**

$$C = C_0 * e^{-k_e t} \quad C = \frac{C_0}{2} \; at \; t = t_{1/2}$$

$$\frac{C_0}{2} = C_0 * e^{-k * t_{1/2}}$$

$$\frac{1}{2} = e^{-k * t_{1/2}}$$

$$\ln 2 = k * t_{1/2}$$

$$t_{1/2} = \frac{\ln 2}{k} \quad \therefore half - life \; is \; independent \; on \; concentration.$$

(1 point)

The plot on the right shows zero-order kinetics because the plot on a linear scale results in a straight line. **(0.5points)**

$$C - C_0 = -k * t$$

$$C = C_0 - k * t \quad C = \frac{C_0}{2} \; at \; t = t_{1/2}$$

$$\frac{C_0}{2} = C_0 - k * t_{1/2}$$

$$t_{1/2} = (C_0 - \frac{C_0}{2}) / k$$

$$t_{1/2} = \frac{C_0}{2 * k} \quad \therefore half - life \; is \; dependent \; on \; concentration.$$

(1 point)

2. Fractions and amounts of drugs eliminated through zero and first order kinetics

2a. Do fraction and amount of a drug eliminated through zero order kinetics change? Please, mark the right answer. ***(total points = 2)***

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

(1 point)

2b. Do fraction and amount of a drug eliminated through first order kinetics change? Please, mark the right answer.

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

(1 point)

3. Drug A is given to Mr. Guinea Pig as an i.v. bolus and distributes very rapidly throughout his entire body, resulting in the following concentration-time profile. Please determine the half-life ($t_{1/2}$) and the area under the concentration-time curve from time zero to infinity ($AUC_{0\rightarrow\infty}$) of that particular drug. Hint: Use the trapezoidal rule for the AUC calculation. ***(total points =3)***

Time (h)	***Conc. (mg/L)***
0	99.9
1	51.3
2	25.7
3	13.1
5	3.3

Answer:

$$ke = \frac{\ln\left(\frac{C1}{C2}\right)}{(t2 - t1)} = \frac{\ln\left(\frac{99.9}{51.3}\right)}{1 - 0} = 0.67\,h^{-1}$$ **(0.5 points)**

$$t_{1/2} = \frac{0.693}{ke} = 1h$$ **(0.5 points)**

$$AUC_{t1 \to t2} = \frac{C_2 + C_1}{2} \bullet (t_2 - t_1)$$

$$AUC_{0 \to \infty} = AUC_{0 \to t_x} + AUC_{t_x \to \infty}$$

$$AUC_{t_x \to \infty} = C_x / k_e$$

$$AUC_{0 \to \infty} = 75.6 + 38.5 + 19.4 + 16.4 + 4.9 =$$

$$= 154.8 \frac{mg * h}{L}$$ **(2 points)**

4. Additionally Mr. Guinea Pig receives drug B that is also given as an iv. bolus. It is known that drug B slows the elimination process of drug A down. How will the elimination rate constant (ke) and half-life ($t_{1/2}$) of drug A change? Answer briefly! ***(total points = 2)***

Answer:
When drug A is eliminated slower, its half-life will increase. **(1 point)**

Since $t_{1/2} = \frac{0.693}{ke} = 1h$, ke will decrease. **(1 point)**

Total points for homework #1:
Question #1: 3
Question #2: 2
Question #3: 3
Question #4: 2
Total: 10