PHA5127 – Dose Optimization I
Homework 1
Fall 2013

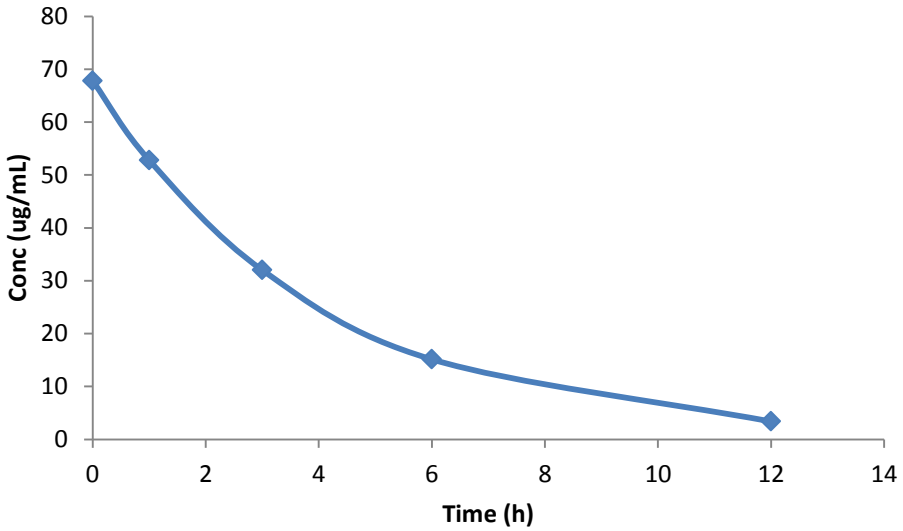
Note: make sure to show units in your work

Question 1

Drug X was administered to a patient via IV bolus administration at a dose of 400 mg. The plasma concentration-time profile is presented in the table below:

Time (h)	Conc (µg/mL)
0	67.8
1	52.8
3	32.02
6	15.13
12	3.38

(1) Plot the concentration versus time in both linear and semi-log scales and determine the order of the elimination process **(1.5 points)**



Concentration vs. time in linear scale

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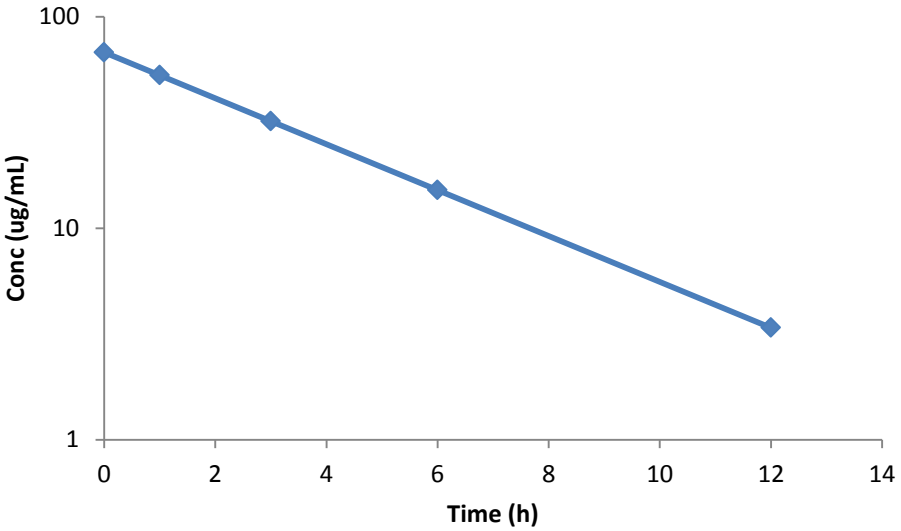

Concentration vs time in log scale

The elimination process is a first-order process since the semi-log plot is linear.

(2) Determine the elimination rate constant and the half-life of the drug **(1 point)**

$$k_e = \frac{\Delta logC}{\Delta t} = \frac{\ln(67.8) - \ln(32.02)}{3 - 0\ h} = 0.25\ h^{-1}$$

$$t_{1/2} = \frac{\ln(2)}{0.25\ h^{-1}} = 2.77\ h$$

(3) Determine the clearance and volume of distribution **(1 point)**

$$V_d = \frac{Dose}{C_0} = \frac{500\ mg}{67.8\ mg/L} = 5.9\ L$$

$$CL = V_d \times k_e = 5.9\ L \times 0.25\ h^{-1} = 1.475\ L/h$$

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(4) Calculate $AUC_{0\text{-last}}$ and $AUC_{0\text{-infinity}}$ (use the trapezoidal rule) **(1 point)**

Time (h)	Conc (µg/mL)	Partial AUC (µg.h/mL)
0	67.8	
1	52.8	60.3
3	32.02	84.82
6	15.13	70.725
12	3.38	55.53
	sum	271.375

The sum of the partial areas from 0 to 12 is AUC0-12 = 271.375 µg.h/mL

$$AUC_{0-\infty} = AUC_{0-12} + \frac{C_{last}}{k_e} = 271.375 + \frac{3.38}{0.25} = 284.895\ \mu g.h/mL$$

(5) Determine the drug concentration at 14 hour **(0.5 point)**

Since the drug follows a first-order elimination process, we can use the following equation:

$$C(t) = C_0 \exp(-k_e t) = 67.8 \exp(-0.25 * 14) = 2.05\ \mu g/mL$$

Question 2

Explain how highly perfused organs differ in drug distribution to fat tissue and bone. **(2 points)**

The rate of delivery for most drugs from the circulation to the particular organ or tissue depends on the blood flow through that organ. Drugs tend to distribute rapidly to areas of high blood flow. Highly perfused organs such as heart lungs and kidneys will have higher drug distribution than poorly perfused organs such as fat tissues and bones.

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True/False **(3 points)**

(1) For a first-order elimination process, the change in drug concentration with respect to time is a constant and is independent of the remaining drug in the system.

F

(2) Therapeutic drug monitoring is only required for drugs with slow clearance.

F

(3) The serum is the supernatant portion of the whole blood that is collected in heparin tube and then centrifuged.

F