

PHA 5127 (Fall, 2008)

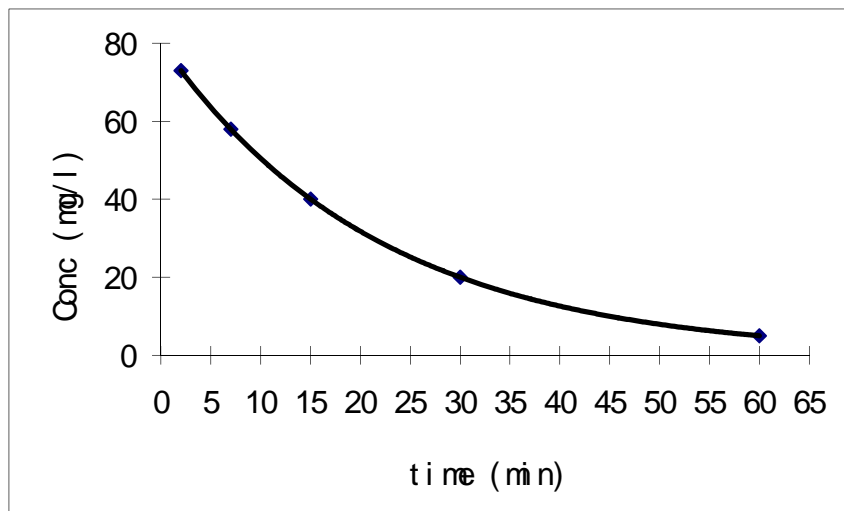
Case Study #1

Answers

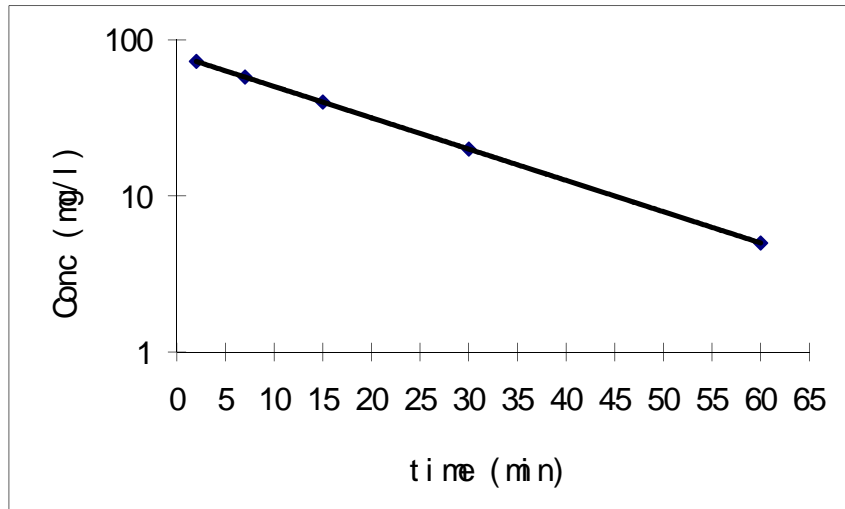
Q1. 800 mg of drug X was administered to a patient through i.v. bolus. The drug plasma concentrations monitored after injection are listed in the table below.

Time (min)	Conc. (mg/l)
2	72.9
7	57.9
15	40
30	20
60	5

a) Please state whether the drug follows a zero- or a first-order elimination process.



Zero-order elimination process has a constant drug elimination rate. If you plot the drug concentration vs. time on an ordinary scale, you should see a straight line. This is not the case here.



If you plot data points on a semi-log scale, you can see they almost perfectly line up on straight line. Therefore, the elimination process is first-order kinetics.

- b) Estimate the elimination rate constant (k_e) and half-life ($T_{1/2}$).

If you study the data carefully, you should be able to see the concentration decreases to half after 15 mins (from 40 mg/l at 15 min to 20 mg/l at 30 min)

$$\text{So: } T_{1/2} = 15 \text{ min} \Rightarrow k_e = 0.693/15 = 0.0462 / \text{min}$$

$$\text{Or: } k_e = (\ln(40) - \ln(20)) / (30 - 15) = 0.0462 / \text{min}$$

$$\Rightarrow T_{1/2} = 0.693 / 0.0462 = 15 \text{ min}$$

- c) Estimate the initial plasma drug concentration (C_0) and volume of distribution (V_d).

$$C_0 = 72.9 * \exp(0.0462 * 2) = 80 \text{ mg/l}$$

$$\text{Or: } C_{15} = 40 \text{ mg/l and } T_{1/2} = 15 \text{ min} \Rightarrow C_0 = 2 * C_{15} = 80 \text{ mg/l}$$

$$\text{And } V_d = D / C_0 = 800 / 80 = 10 \text{ L}$$

- d) Estimate the initial plasma drug concentration (C_0) and $AUC_{0-\text{inf}}$.

Use the trapezoidal rule to calculate the area under the curve from time zero to the last time point (AUC_{0-60}). The general formula to calculate the area of a trapezoid is:

$$AUC_{1 \rightarrow 2} = \frac{C_1 + C_2}{2} * (t_2 - t_1)$$

$$AUC_{0-60} = 1/2 * \{(80+72.9)*2 + (72.9+57.9)*5 + (57.9+40)*8 + (40+20)*15 + (20+5)*30\}$$

$$= 1696.5 \text{ min} * \text{mg/l}$$

In order to calculate the area under the curve from the last time point to infinity ($AUC_{60-\text{inf}}$), we need to divide the last given concentration (C_{60}) by the elimination rate constant (k_e):

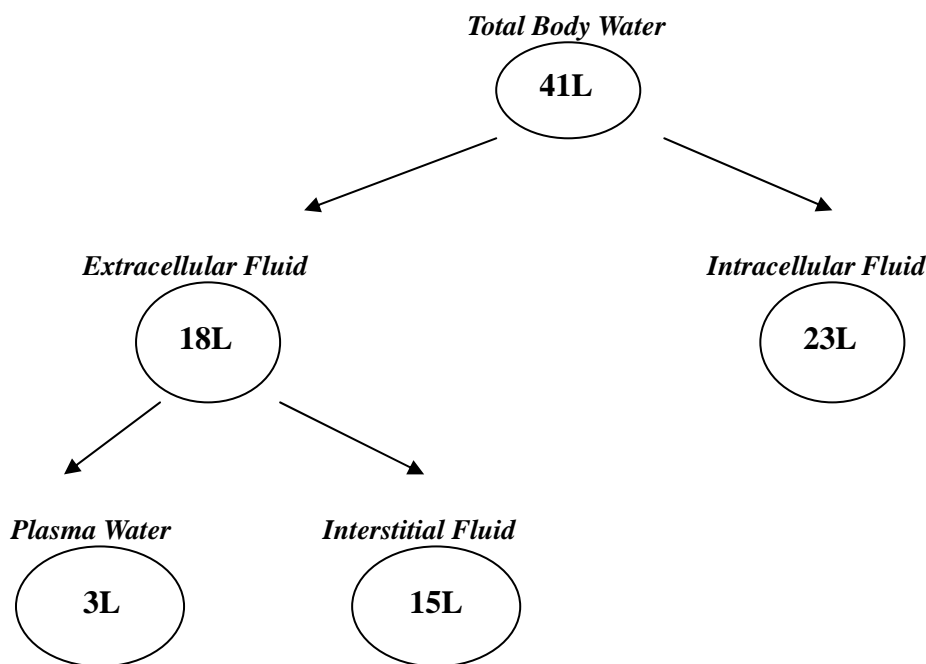
$$AUC_{60-\text{inf}} = 5/0.0462 = 108.2 \text{ min} * \text{mg/l}$$

Therefore, $AUC_{0-\text{inf}} = AUC_{0-60} + AUC_{60-\text{inf}} = 1696.5 + 108.2 = 1804.7 \text{ min} * \text{mg/l}$

e) Predict the drug plasma concentration 2 hrs after the injection (C_{120}).

$$C_{60} = 5 \text{ mg/l and } T_{1/2} = 15 \text{ min} \Rightarrow C_{120} = C_{60} / (2^4) = 5/16 = 0.3 \text{ mg/l}$$

Q2. Please fill in the missing numbers!



Q3. Mark each of the following statements True or False.

T F For a first-order elimination process, the same amount of drug is eliminated during a given time interval.

T F For a zero-order elimination process, the half-life ($t_{1/2}$) depends on the drug concentration.

- T F** In a perfusion limited distribution, tissue membrane represents no barrier for the drug diffusion.
- T F** In a permeability limited distribution, blood flow is not important for rate of uptake.
- T F** Volume of distribution is the real tissue volume that contains the drug.

Q4. Define the term biopharmaceutics and pharmacokinetics.

Biopharmaceutics studies the influence of the dosage form of a drug on its pharmacological effect (or conc.).

Pharmacokinetics studies what the body does to the drug. It describes the time course of drug and metabolite concentrations in the body.