2.1. General Pharmacokinetic Applications

Solutions

1. $\text{Dose} \times e^{-kt} = 1000\text{ mg} \times e^{-\left(\frac{0.693}{t½}\right)(5\ t½s)}$

   1000 mg × 0.0313 = 31.3 mg;

   or 1000 mg × ½ × ½ × ½ × ½ × ½ = 31.3 mg

2. Because the concentration drops from 8 to 4 in 6 (i.e., 9–3) hours, the half-life is 6 hours.

3. Since the concentration drops from 12 to 6, then from 6 to 3, it can be seen that two half-lives occurred in 4 (i.e., 12–8) hours. The half-life is the time between the two concentrations divided by the number of half-lives that have occurred. Thus, the half-life is 4 hours ÷ 2 t½s, or 2 hours.

4. The concentration decreased from 10 to 5 in one t½; from 5 to 2.5 in the second, and a third t½ would have decreased the concentration to 1.25. However, the concentration did not decrease that much in the 8 hours (11–3) between the two concentrations. Hence, it can be said that more than two, but less than three half-lives occurred in the 8-hour time period. Thus, the t½ is between 2.67 (8 hr ÷ 3 t½s) and 4 (8 hr ÷ 2 t½s) hours.

   Because the final concentration of 2 is about halfway between 2.5 and 1.25, you could guess the half-life would be about halfway between 2.67 and 4 hours, perhaps about 3.4 hours. Half-life should be estimated whenever possible to help reduce the likelihood that data resulting from calculator or computer input errors are accepted as valid.

5. Begin by solving for k using **Equation 1**.*

$$k = \frac{\ln\left(\frac{C_i}{C}\right)}{t_\Delta}$$

$$k = \frac{\ln\left(\frac{32\ \text{mcg/mL}}{8\ \text{mcg/mL}}\right)}{(10\ \text{hr} - 3\ \text{hr})}$$

k = 0.198 hours^{-1}

Next, solve for t½

$$t½ = \frac{0.693}{k}$$

$$t½ = \frac{0.693}{0.198\ \text{hr}^{-1}}$$

t½ = **3.5 hours**

Note: This answer could have easily been estimated because two half-lives elapsed (32 to 16 to 8) in 7 hours (10–3).

6. Begin by solving for k using **Equation 1**.

$$k = \frac{\ln\left(\frac{6.8\ \text{mg/L}}{3.5\ \text{mg/L}}\right)}{(11\text{p.m.} - 1\text{p.m.})}$$

k = **0.066 hours^{-1}**

Next, solve for t½ using **Equation 2**.

$$t½ = \frac{0.693}{k}$$

$$t½ = \frac{0.693}{0.066\ \text{hr}^{-1}}$$

t½ = **10.4 hours**

7. $$k = \frac{\ln\left(\frac{22\ \text{mg/L}}{4.5\ \text{mg/L}}\right)}{10.25\ \text{hr}} = 0.155\ \text{hr}^{-1}$$

t½ = 0.693/0.155 hr^{-1}

= **4.5 hours**

Note: Since half of 22 is 11 and half of 11 is 5.5, you could have estimated this to be a bit less than 5.1 hours.

* Equation 1 and other numbered equations used in this chapter can be found in ***Select Pharmacokinetic Equations***, p xix.

8. First, solve for k by revising **Equation 2**.

$$k = \frac{0.693}{t½}$$

$$k = \frac{0.693}{2\ \text{days}}$$

k = **0.347 days^{-1}**

Next, solve for t_Δ using **Equation 1** (altered to isolate t_Δ rather than k).

$$t_\Delta = \frac{\ln\left(\frac{C_i}{C}\right)}{k}$$

$$t_\Delta = \frac{\ln\left(\frac{5\ \text{mcg/L}}{1\ \text{mcg/L}}\right)}{0.347\ \text{d}^{-1}}$$

t_Δ = **4.6 days**

What would your estimate have been based on the half-life?

9. A. $$t½ = \frac{0.693}{k}$$

$$k = \frac{0.693}{8\ \text{hr}}$$

k = 0.087 hours^{-1}

$$t_\Delta = \frac{\ln\left(\frac{C_i}{C}\right)}{k}$$

$$t_\Delta = \frac{\ln\left(\frac{13\ \text{mg/L}}{4\ \text{mg/L}}\right)}{0.087\ \text{hr}^{-1}}$$

t_Δ = **13.5 hours**

B. A logical interval would be 12 hours. Although once daily (every 24 hours) dosing might be attractive in terms of adherence, if it were used for the interval at least one of the concentrations would be above or below the stated therapeutic range and both could be outside the range.