

Answer to case study 1

1.

You can use Excel or graph paper to plot the Ln(concentration) vs Time, then add the trendline. The slope of the trendline will be $-K_e$.

Or, you can use any of the two time points to determine K_e by the equation below:

$$K_e = -(\ln C_1 - \ln C_2) / (t_1 - t_2) = 0.004153 \text{ /min}$$

$$C_p(t) = C_p(0) \cdot \exp(-K_e \cdot t)$$

$$C_p(0) = C_p(t) \cdot \exp(K_e \cdot t)$$

$$C_p(0) = C_p(5) \cdot \exp(K_e \cdot 5) = 32.7 \cdot \exp(0.004153 \cdot 5) = 33.39 \text{ mg/L}$$

By trapezoidal rule ,

$$\text{AUC}(0-5) = (C_0 + C_5) \cdot 5 / 2 = 165.25 \text{ mg} \cdot \text{min/L}$$

$$\text{AUC}(5-10) = 161.75 \text{ mg} \cdot \text{min/L}$$

$$\text{AUC}(10-15) = 158.25 \text{ mg} \cdot \text{min/L}$$

$$\text{AUC}(15-25) = 306.5 \text{ mg} \cdot \text{min/L}$$

$$\text{AUC}(25-50) = 713.75 \text{ mg} \cdot \text{min/L}$$

$$\text{AUC}(50-100) = 1227.5 \text{ mg} \cdot \text{min/L}$$

$$\text{AUC}(100-150) = 995 \text{ mg} \cdot \text{min/L}$$

$$\text{AUC}(150-200) = 807.5 \text{ mg} \cdot \text{min/L}$$

$$\text{AUC}(200-250) = 657.5 \text{ mg} \cdot \text{min/L}$$

$$\text{AUC}(250-300) = 533.75 \text{ mg} \cdot \text{min/L}$$

$$\text{AUC}(300-355) = 481.25 \text{ mg} \cdot \text{min/L}$$

$$\text{AUC}(355-400) = 320.625 \text{ mg} \cdot \text{min/L}$$

$$\text{AUC}(400-500) = 522.5 \text{ mg} \cdot \text{min/L}$$

$$\text{AUC}(500-600) = 344.5 \text{ mg} \cdot \text{min/L}$$

$$\text{AUC}(600-800) = 393 \text{ mg} \cdot \text{min/L}$$

$$\text{AUC}(800-1000) = 171 \text{ mg} \cdot \text{min/L}$$

$$\text{AUC}(1000-\text{inf}) = C_{1000} / K_e = 125.2172 \text{ mg} \cdot \text{min/L}$$

$$\text{AUC}(\text{total}) = 8084.84 \text{ mg} \cdot \text{min/}$$

2. Small V_d is due to very large plasma protein binding compared to tissue binding or the inability of a drug to cross membranes. The smallest (theoretical) V_d is 3L, the volume of plasma in the body.

3.

80% of plasma protein binding is used for calculation of V_d of normal people

$$V_d = V_p + V_t \cdot F_u / F_{u,t}$$

$$V_d = 3 + 38 \cdot 0.2 / 0.7 = 13.86 \text{ L (normal patient)}$$

In patients with chronic liver disease,

$$F_u = 1 - 0.8 \cdot 0.8 = 0.36$$

$$V_d = 3 + 38 \cdot 0.36 / 0.7 = 22.54 \text{ L}$$