PHA 5127

Homework #1

Question #1

100mg drug A was administered to a patient as a single I.V bolus dose. The plasma drug concentration was measured t_1 hours after the drug was administered, and it turned out to be C_1 mg/L, t_2 hours after t_1, the plasma drug concentration was observed to be C_2 mg/L ($C_2<C_1$). Suppose the drug follows one compartment body model with first order elimination, calculate the following PK parameters. (Your answer should only include t_1, t_2, C_1, C_2 and the units of the parameters)

1.1. Calculate the elimination rate constant K_e and half-life ($t_{1/2}$). [1pt]

$$K_e = -\frac{\ln C_2 - \ln C_1}{t_2} \ \mathrm{h}^{-1} \quad \text{[.5pt]}$$

$$t_{1/2} = \frac{0.693}{K_e} = -\frac{0.693 \cdot t_2}{\ln C_2 - \ln C_1} \ \mathrm{h} \quad \text{[.5pt]}$$

1.2. Calculate the initial plasma drug concentration C_0. [1pt]

$$Conc = C_0 \cdot e^{-k_e t} \Rightarrow C_0 = \frac{Conc}{e^{-k_e t}} = \frac{C_1}{e^{\frac{\ln C_2 - \ln C_1}{t_2} \cdot t_1}} \ \mathrm{mg/L}$$

or

$$Conc = C_0 \cdot e^{-k_e t} \Rightarrow C_0 = \frac{Conc}{e^{-k_e t}} = \frac{C_2}{e^{\frac{\ln C_2 - \ln C_1}{t_2} \cdot (t_1 + t_2)}} \ \mathrm{mg/L}$$

1.3. Calculate the volume of distribution V_d. [1pt]

$$V_d = \frac{Dose}{C_0} = \frac{100}{\frac{C_1}{e^{\frac{\ln C_2 - \ln C_1}{t_2} \cdot t_1}}} = \frac{100 \cdot e^{\frac{\ln C_2 - \ln C_1}{t_2} \cdot t_1}}{C_1} \ \mathrm{L}$$

or

$$V_d = \frac{Dose}{C_0} = \frac{100}{\frac{C_2}{e^{\frac{\ln C_2 - \ln C_1}{t_2} \cdot (t_1 + t_2)}}} = \frac{100 \cdot e^{\frac{\ln C_2 - \ln C_1}{t_2} \cdot (t_1 + t_2)}}{C_2} \ \mathrm{L}$$

1.4. Use trapezoidal rule to calculate the area under the curve $AUC_{0\to\infty}$ [2pt]

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

$$AUC_{last\to\infty} = \frac{C_{last}}{K_e} = \frac{C_2}{-\frac{\ln C_2 - \ln C_1}{t_2}} = -\frac{C_2 \cdot t_2}{\ln C_2 - \ln C_1} \ \text{mg}\cdot\text{h/L} \quad [1\text{pt}]$$

$$AUC_{0\to last} = \frac{(C_0 + C_1)\times(t_1 - 0)}{2} + \frac{(C_1 + C_2)\times t_2}{2} = \frac{e^{\left(\frac{C_1}{\frac{\ln C_2 - \ln C_1}{t_2}\cdot t_1} + C_1\right)\times t_1}}{2} + \frac{(C_1 + C_2)\times t_2}{2} \ \text{mg}\cdot\text{h/L}$$

$$AUC_{0\to\infty} = \frac{e^{\left(\frac{C_1}{\frac{\ln C_2 - \ln C_1}{t_2}\cdot t_1} + C_1\right)\times t_1}}{2} + \frac{(C_1 + C_2)\times t_2}{2} - \frac{C_2 \cdot t_2}{\ln C_2 - \ln C_1} \ \text{mg}\cdot\text{h/L} \quad [1\text{pt}]$$

or

$$AUC_{0\to last} = \frac{(C_0 + C_1)\times(t_1 - 0)}{2} + \frac{(C_1 + C_2)\times t_2}{2} = \frac{e^{\left(\frac{C_2}{\frac{\ln C_2 - \ln C_1}{t_2}\cdot(t_1+t_2)} + C_1\right)\times t_1}}{2} + \frac{(C_1 + C_2)\times t_2}{2} \ \text{mg}\cdot\text{h/L}$$

$$AUC_{0\to\infty} = \frac{e^{\left(\frac{C_2}{\frac{\ln C_2 - \ln C_1}{t_2}\cdot(t_1+t_2)} + C_1\right)\times t_1}}{2} + \frac{(C_1 + C_2)\times t_2}{2} - \frac{C_2 \cdot t_2}{\ln C_2 - \ln C_1} \ \text{mg}\cdot\text{h/L}$$

1.5. What's the elimination rate constant Ke and half-life ($t_{1/2}$) if the doctor double the original dose? [1pt]

Remain the same because Ke and $t_{1/2}$ do not change with dose

Question #2

The one compartment body model is frequently used in clinical practice. In the analysis of one compartment model with single I.V bolus dose, what are the assumptions we make to depict the body as a kinetically homogenous unit?

1. Immediate distribution and equilibrium of the drug throughout the body. [1pt]

2. The elimination process is first order. [1pt]

Question #3

3.1. **T** F Blood serum is blood plasma without fibrinogen or other clotting factors. [.5pt]

3.2. **T** F The AUC is of particular use in estimating bioavailability of drugs, and in estimating total clearance of drugs. [.5pt]

3.3. T **F** The amount of drug in the body affects the change in amount of drug in the body, therefore, the elimination rate constant K_e also depends on the amount of drug in the body. [.5pt]

3.4. T **F** For a zero-order elimination process, the amount of drug eliminated per time unit is changing. [.5pt]