Homework 6

Bio pharmaceutics & Pharmacokinetics/PHAR434

Instructor Abdullah Rabba

Student name and I.D Muhammad Musleh /1162595

- **An adult male patient (46 years old, 81 kg) was given orally 250 mg of tetracycline hydrochloride every 8 hours for 2 weeks. From the literature, tetracycline hydrochloride is about 75% bioavailable and has an apparent volume of distribution of 1.5 L/kg. The elimination half-life is about 10 hours. The absorption rate constant is 0.9 hr^{-1}. From this information, calculate:**

    a) **C_{max} after the first dose.**

    b) **C_{min} after the first dose.**

    c) **Plasma drug concentration C_p at 4 hours after the 7th dose.**

    d) **Maximum plasma drug concentration at steady-state $C^{\infty}_{max.}$**

    e) **Minimum plasma drug concentration at steady-state $C^{\infty}_{min.}$**

    f) **Average plasma drug concentration at steady-state C^{∞}_{av}.**

Answers Below

Muhammad Musleh

HomeWork. 6

Answers

1

- Info:-
  - → Male, 46 years
  - → 81 kg
  - → 250 mg / 8 hours → for 2 weeks
  - → $V_D = 1.5\ L/kg$, (75 % bioavailable) = F
  - → $t_{\frac{1}{2}} = 10$ hours
  - → $K_a = 0.4\ hr^{-1}$

$V_D = 121.5\ L$ (1.5 * 81 kg)

ⓐ Cmax after 1st dose.

$$Cp_{max} = \frac{F * K_a * D_o}{V_D (K_a - K)} * \left(e^{-K t_{max}} - e^{-K_a t_{max}}\right)$$

$$t_{max} = \frac{2.3}{K_a - K} \log \frac{K_a}{K}, \quad K = \frac{0.693}{t_{\frac{1}{2}}} \rightarrow \frac{0.693}{10} \Rightarrow 0.07\ h^{-1}$$

$$= \frac{2.3}{0.4 - 0.07} \log \frac{0.4}{0.07}$$

$t_{max} = 3.07h$

$$= 2.7711 * 1.11 \Rightarrow 3.07\ h$$

$$Cp_{max} = \frac{0.75 * 0.4 * 250}{121.5 * (0.4 - 0.07)} * \left(e^{-0.07 * 3.07} - e^{-0.4 * 3.07}\right)$$

$$= 1.6734 * (0.8066 - 0.0631)$$

$Cp_{max} = 1.25\ mg/L$

b) Cmin after 1st dose (At t = 8 h) - Before 2nd dose

$$C_{min} = \frac{F * K_a * D_o}{V_D (K_a - K)} * \left(e^{-Kt} - e^{-K_a t}\right)$$

$$= \frac{0.75 * 0.9 * 250}{121.5 * (0.9 - 0.07)} * \left(e^{-0.07*8} - e^{-0.9*8}\right)$$

2

$$= 1.67336 * (0.5712 - 0.0007466)$$

$$\boxed{C_{p_{min}} = 0.954 \text{ mg/L}}$$

(c) C_p^4 (After 7th dose) :-

$$C_p = \frac{F\, k_a\, D_0}{V_D\,(k_a - k)} \cdot \left[\left[\frac{1 - e^{-nk\tau}}{1 - e^{-k\tau}}\right] e^{-kt} - \left[\frac{1 - e^{-nk_a\tau}}{1 - e^{-k_a\tau}}\right] e^{-k_a t}\right]$$

$$= \frac{0.75 * 0.9 * 250}{121.5 * (0.9 - 0.07)} \cdot \left[\left[\frac{1 - e^{-7*0.07*8}}{1 - e^{-0.07*8}}\right] e^{-0.07 \cdot 4} - \left[\frac{1 - e^{-7*0.9*8}}{1 - e^{-0.9*8}}\right] e^{-0.9*4}\right]$$

$$= 1.67336 * \left[\left(\frac{0.9801}{0.4287} * 0.7558\right) - \left(\frac{1}{0.99925} * 0.0273\right)\right]$$

$$= 1.67336 * 1.7006$$

$$\boxed{C_p^4 = 2.8457 \approx \boxed{2.846 \text{ mg/L}}}$$

(d) C_{max}^{ss} at S.S

$$t_p(S.S) = \frac{1}{k_a - k} * \ln \frac{k_a(1 - e^{-k\tau})}{k(1 - e^{-k_a\tau})}$$

$$= \frac{1}{0.9 - 0.07} * \left(\ln \frac{0.9 * (1 - e^{-0.07*8})}{0.07 * (1 - e^{-0.9*8})}\right)$$

$$= 1.2048 * \left(\ln \frac{0.38591}{0.069947}\right)$$

$$\boxed{t_p = 2.05 \text{ hr}}$$

3

$$C_{max}^{\infty} = \frac{F * D_0}{V_D} * \left(\frac{1}{1-e^{-k\tau}}\right) * e^{-kt_p}$$

$$= \frac{0.75 * 250}{121.5} * \left(\frac{1}{1-e^{-0.07*8}}\right) * e^{-0.07*2.05}$$

$$= 1.543209 * \left(\frac{1}{0.42879} * 0.8663208\right)$$

$$\boxed{C_{max}^{\infty} = 3.12 \text{ mg/L}}$$

(e) C_{min}^{∞} at S.S

$$= \frac{k_a * F * D_0}{V_D (k_a - k)} * \left(\frac{1}{1-e^{-k\tau}}\right) \cdot e^{-k\tau}$$

$$= \frac{0.9 * 0.75 * 250}{121.5 (0.9 - 0.07)} * \left(\frac{1}{1-e^{-0.07*8}}\right) \cdot e^{-0.07*8}$$

$$= 1.67336 * \left(\frac{1}{0.42879}\right) \cdot 0.571209$$

$$\boxed{C_{min}^{\infty} = 2.23 \text{ mg/L}}$$

(f)

$$C_{av}^{\infty} = \frac{F * D_0}{V_D * k * \tau}$$

$$= \frac{0.75 * 250}{121.5 * 0.07 * 8} \Rightarrow \frac{187.5}{68.04}$$

$$\boxed{C_{av}^{\infty} = 2.756 \text{ mg/L}}$$