

Homework # 5
(PHA 5127)
Fall 2007

SET I: (4 points)

Drug-X is mainly eliminated by liver and kidney. Renal elimination is only by glomerula filtration. C. M was given 70mg of this drug via IV bolus. Two plasma concentrations at 4 hours and 8 hours after dose were 3.22mg/L and 1.61mg/L, respectively. Calculate plasma protein binding of drug-X? (Use 125ml/min for glomerula filtration rate).

$$k_e = -\log(1.61/3.22)/4 = 0.173 \text{ hr}^{-1}$$

$$t_{1/2} = 0.693/0.173 = 4 \text{ hr}$$

OR: 3.22mg/L \rightarrow 1.61mg/L \rightarrow one half-life: 4 hr

$$C_0 = 3.22 * \exp(0.173 * 4) = 6.44 \text{ mg/L}$$

OR: 3.22mg/L \leftarrow 6.44mg/L one half-life: 4hr

$$V_d = \text{Dose}/C_0 = 70/6.44 = 10.87 \text{ L}$$

$$Cl = k_e * V_d = 0.173 * 10.87 = 1.88 \text{ L/hr}$$

$$Cl_{fil} = GFR * f_u = 125 * 60 * f_u / 1000 = 1.88 \text{ L/hr} \rightarrow f_u = 25\% \rightarrow f_b = 75\%$$

SET II: (3 points)

True or False (0.5 point each)

T F 1: Half-life of any drug is only dependent on the elimination rate constant, neither on clearance, nor on volume of distribution. (**F**)

T F 2: For linear pharmacokinetics, there is no any saturation process involved. (**T**)

T F 3: Total drug amount eliminated via urine is always less than the dose administrated. (**F**)

$$\underline{D \geq U_{\infty}}$$

T F 4: AUC_{∞} depends on both dose and volume of distribution. (**F**)

$$\underline{AUC_{\infty} = \frac{Dose}{CL}}$$

T F 5: In a linear one-compartmental model, initial drug concentration and half-life of drug can determine AUC_{∞} after IV bolus. (**T**)

$$\underline{AUC_{\infty} = \frac{C_0}{k_e}}$$

T F 6: Total clearance is always larger than hepatic clearance. (**F**)

$$\underline{CL_{tot} = CL_{ren} + CL_{bil} + CL_{met}}$$

SET III (3 points)

Drug-W, a novel aminoglycoside, has a clearance equal to creatinine clearance. In order to treat pneumonia, a female patient, 5'10", 60 year old, 70 kg, received 200mg of Drug-W via IV bolus. The volume of distribution for Drug-W is 1.114L/kg*(TBW). $C_{p_{creat}}$ in this patient is 0.588mg/dL. What is the drug concentration at 5hr after dose?

$$\underline{Vd = 70kg \cdot 1.114L / kg = 78L}$$

$$\underline{IBW = 45.5 \text{ kg} + 2.3 \text{ kg for each inch over 5 ft in height}} \\ \underline{= 45.5 + 2.3 \cdot 11 = 70.8 \text{ kg} \rightarrow TBW < 1.2 \cdot IBW}$$

$$\underline{CL_{creat} (female) = \frac{(140 - age) \cdot weight}{85 \cdot Cp_{creat}} = \frac{(140 - 60) \cdot 70}{85 \cdot 0.588} = 112 \text{ ml / min} = CL_{Drug-W}}$$

$$\underline{k_e = \frac{Cl}{Vd} = 112 \cdot 60 / 1000 / 78 = 0.086 \text{ hr}^{-1}}$$

$$\underline{C(0) = DOSE / Vd = 200 \text{ mg} / 78 \text{ L} = 2.56 \text{ mg/L}}$$

$$\underline{Cp = C(0) \cdot EXP(-k_e \cdot t) = 2.56 \cdot EXP(-0.086 \cdot 5) = 1.66 \text{ mg/L}}$$