Case Study #2 Answers
PHA5128

Question #1: Salt factor

a) *What does the salt factor stand for?*

It is a correction factor that accounts for the acid/base of the drug in its salt form.

$$S = \frac{acid\ or\ base[mg]}{salt[mg]}$$

b) *When do you use a salt factor?*

Basically, one always uses a salt factor. In order to keep it simple, we assumed it to be 1 so far. However, you need to take it into consideration as soon as a salt factor (S<1) or a difference in weight salt vs. acid/base is given.

Question #2: Bioequivalence

a) *Which parameters are used to determine Bioequivalence?*

C_{max}, AUC_{∞}

b) *Which parameter characterizes the rate and which one the extent of availability?*

rate → t_{max}, (t_{max} is the time to reach C_{max} → parameters are linked)
extent → AUC, (C_{max} → given similar AUCs, a higher C_{max} characterizes a greater extent)

c) *Drug X was administered as an i.v. bolus. Calculate AUC_{∞} from the values given in the table below. Assume a 1-compartment body model and linear pharmacokinetics.*

Time (hrs)	Concentration (mcg/L)
0	110
4	50
8	22
12	10
16	5
20	2

$$AUC_{t_1 \to t_2} = \frac{C_{t_2} + C_{t_1}}{2} \times (t_2 - t_1)$$

$$AUC_{0h \to 4h} = \frac{50\,{}^{mcg}\!/_{L} + 110\,{}^{mcg}\!/_{L}}{2} \times (4hr - 0hr) = 320\,{}^{mcg \cdot hr}\!/_{L}$$

$$AUC_{4h \to 8h} = 144\,{}^{mcg \cdot hr}\!/_{L}$$

$$AUC_{8h \to 12h} = 64\,{}^{mcg \cdot hr}\!/_{L}$$

$$AUC_{12h \to 16h} = 30\,{}^{mcg \cdot hr}\!/_{L}$$

$$AUC_{16h \to 20h} = 14\,{}^{mcg \cdot hr}\!/_{L}$$

$$AUC_{20h \to \infty} = \frac{C_{20h}}{k_e} = \frac{2\,{}^{mcg}\!/_{L}}{0.2hr^{-1}} = 10\,{}^{mcg \cdot hr}\!/_{L}$$

$$AUC_{0 \to \infty} = AUC_{0h \to 4h} + AUC_{4h \to 8h} + AUC_{12h \to 16h} + AUC_{16h \to 20h} + AUC_{20h \to \infty}$$

$$= (320 + 144 + 30 + 14 + 10)\,{}^{mcg \cdot hr}\!/_{L} = 582\,{}^{mcg \cdot hr}\!/_{L}$$

Question #3: Cockroft and Gault

a) *Give the equation(s) used to calculate Cl_{creat}. Are there differences within a patient population?*

Males: $$Cl_{creat} = \frac{(140 - age) \cdot BW}{Cp_{creat} \cdot 72}$$

Females: $$Cl_{creat} = \frac{(140 - age) \cdot BW}{Cp_{creat} \cdot 85}$$

Use IBW up to 120% TBW. If patients TBW exceeds 120%IBW use ABW.

$$ABW = IBW + 0.4(TBW - IBW)$$

IBW_{male} = 50kg+2.3kg for each inch over 5ft in height
IBW_{female} = 45kg+2.3kg for each inch over 5ft in height

b) *Patients A and B receive 1000mg of drug D per day, given as two 500mg tablets. Patient B was diagnosed with impaired renal function (Cl_{creat} = 50mL/min). Laboratory results further indicated that 80% of the drug is excreted into the urine. What would you do? Assume linear pharmacokinetics.*

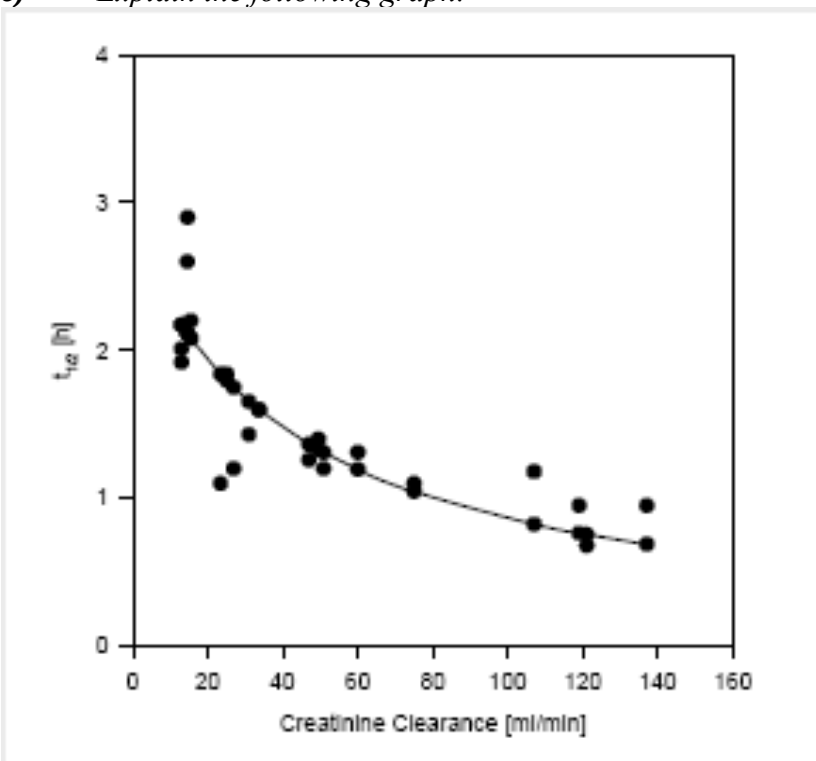
$$D_{pat} = D_{norm} \cdot \left[1 - f_{ren} \cdot (1 - RF)\right]$$

$$RF = \frac{Cl_{creat} actual}{GFR} = \frac{50mL/\min}{125mL/\min} = 0.4$$

$$D_{pat} = 1000mg \cdot \left[1 - 0.8 \cdot (1 - 0.4)\right] = 520mg$$

Give only one tablet to patient B.

c) *Explain the following graph.*



The half-life for this particular drug is approximately 0.9hours for patients with normal renal function. The half-life increases with decreasing renal function.