PHA 5127 Dose Optimization I Homework 5, 2013

Please provide all answers with their appropriate units. 0.5 points will be deducted for each missing or inappropriate unit. Please show how you found your answers. If you do not show your work and your answer differs from the right solution, no points will be given.

1) **A 55-year male patient (78 kg, 6'1'' height) was given a 1000mg IV bolus dose of drug X. His serum creatinine level was 1.6 mg/dL. The volume of distribution of drug X is 40 L. (4 pt)**
   a) **Please compute the patient's creatinine clearance. (1 pt)**

IBW = 50kg + 2.3 kg for each inch over 5 ft in height
= 50 kg + 2.3 kg × 13
= 79.9 kg
≈ 80 kg

TBW = 78 kg < IBW × 120% = 80 kg × 120% = 96 kg

Based on his TBW and height, the patient is not considered obese. As a result, TBW is used for the computation of creatinine clearance.

CrCL = $\frac{(140-age)\times TBW}{72\times SerumCreatinine} = \frac{(140-55)\times 78kg}{72\times 1.6mg/dL} = 57.55\ mL/min$ **(1pt)**

   b) **Assume that the drug is solely eliminated via the kidneys. Please calculate the half-life, AUC $_{0\text{-inf}}$ and C_{max} (3 pt)**

CL = CrCL = 57.55 mL/min = $57.55 \times \frac{\frac{1}{1000}L}{\frac{1}{60}hr} = 3.45\ L/hr$

ke = $\frac{CL}{Vd} = \frac{3.45\ L/hr}{40\ L} = 0.086/hr$

$t_{1/2} = \frac{0.693}{0.086/\text{hr}} = 8.03\ \text{hr}$ **(1pt)**

$\text{AUC}_{0-\text{inf}} = \frac{\text{DOSE}}{\text{CL}} = \frac{1000\ \text{mg}}{3.45\ \text{L/hr}} = 289.86\ \text{mg} * \text{hr/L}$ **(1pt)**

$C_{\text{max}} = \frac{\text{Dose}}{\text{Vd}} = \frac{1000\ \text{mg}}{40\ \text{L}} = 25\ \text{mg/L}$ **(1pt)**

2) **Identify the Pharmacokinetic metrics: Dose, Volume of Distribution or the Clearance (only pick one per scenario), whose changes would determine the differences observed in the following concentration time profiles. (eg: The structure of the answer would look like – The changes in the profiles of Fig A would be because of ____ parameter) (4pt)**

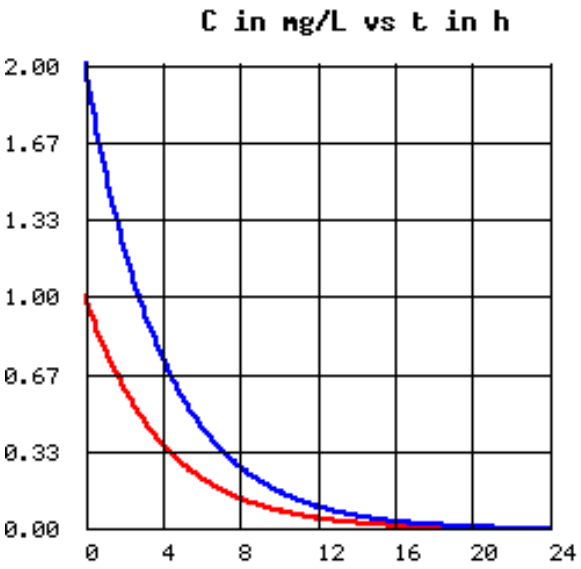

Fig A

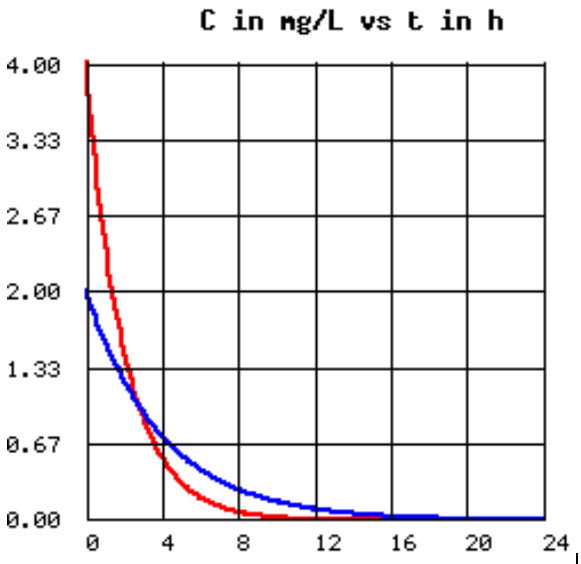

Fig B

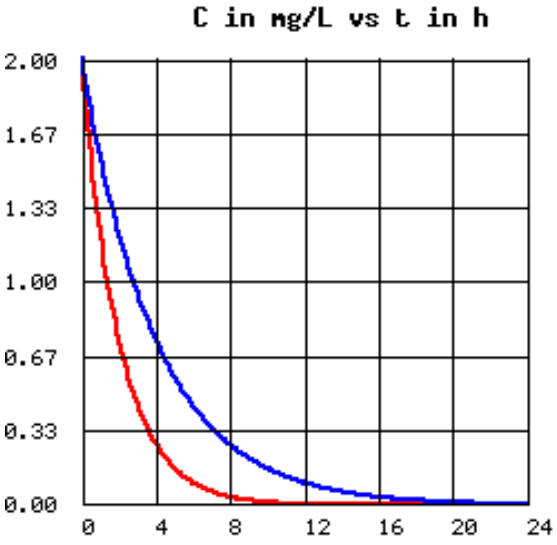

Fig C

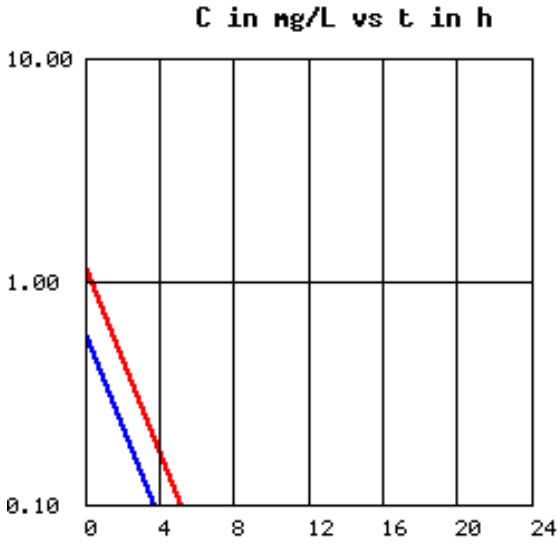

Fig D

Ans) Fig A – Dose; Fig B – Vd; Fig C – Clearance; Fig D – Dose

3) True or False (2pt)

(1) If the half-life of a drug is 2h, it means that from any time point it takes 2h for concentration to drop by half **(0.5pt)**. (T)

(2) If the elimination of drug follows a first order process, the rate of elimination is affected by the amount of drug in the body **(0.5pt)**. (T)

(3) In a linear one-compartmental model, initial drug concentration and half-life of the drug can determine AUC∞ after IV bolus **(0.5pt)**. (T)

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

(4) Since Phenobarbital is a weak acidic drug, the renal clearance will decrease in alkalized urine **(0.5pt)**. (F)