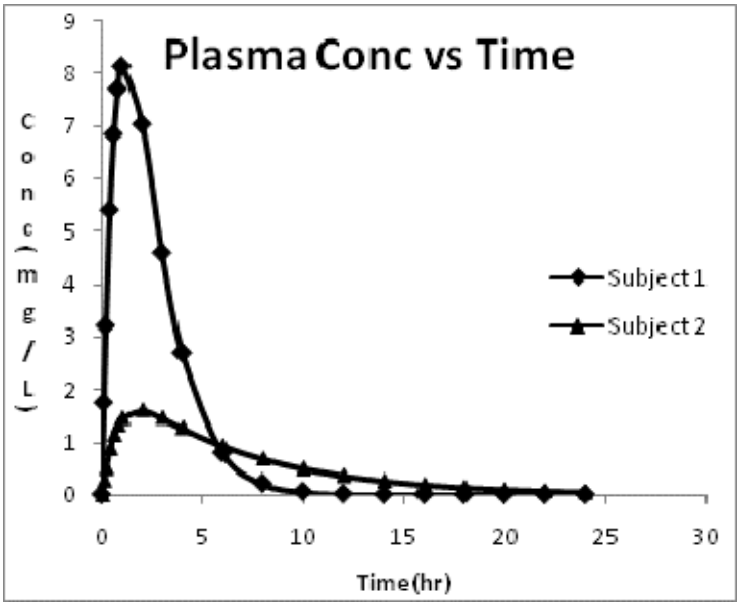
PHA 5127 Homework-1 Due Date:

1) Two formulations of a hydrophilic drug X exist on the market. One formulation is a solution of the drug in water and the other formulation is a suspension of the drug in oil. The two formulations of the drug having the same dose are administered intra muscularly (i.m.), one formulation at random to subject 1 and the other formulation to subject2. From the fig1 match the appropriate formulation with the subject. Give logical reasoning for your answer? [2pt]

Fig 1



Ans) From the profile it is clear that subject 1 received the formulation of the drug solution in water and subject 2 received the oil suspension of the drug.

For the drug solution in water, the drug being hydrophilic, it is in solution form and is readily absorbed into the systemic circulation, hence the initial high concentrations and a short life of the drug in the blood before it is eliminated. On the other hand for the oil suspension, it takes a lot of time for the drug to dissolve in an aqueous medium and hence the liberation of the drug from the

dosage form is slower resulting in lower initial concentrations but prolonged life of the drug in plasma.

2) $Conc = \left(\frac{Dose}{Vd}\right) * \exp(-ke * t)$. Transform this equation into a logarithmic form. Use both natural log (ln) and a log to base 10 (log). [2pt]

Ans $\ln conc = \ln\left(\frac{Dose}{vd}\right) - Ke * t$

$\log conc = \log\left(\frac{dose}{vd}\right) - (Ke * t)/2.303$

3) A single dose of a drug X was administered as an IV bolus to a patient. The plasma concentration was determined 2 hrs after the drug was administered and it came out to be 16.37mg/L. 4hr later the plasma concentration was observed to be 10.98mg/L. Assume the drug follows first order elimination and a one compartment body model.

a) Calculate the initial concentration (zero time)? [1pt]

b) Calculate the value of Ke (first order elimination rate constant) and $t_{1/2}$? [2M]

c) Calculate the $AUC_{0\text{-}inf}$ if the dose given is 500mg? (Use the relation clearance = ke * Vd). [1.5M]

Ans) $\ln 16.37 = lnCo - ke * 2$

$\ln 10.98 = \ln Co - Ke * 6$

Solving the simultaneous equations we get

a) Co = 20mg/L
b) Ke = 0.1 hr^{-1} , $t_{1/2}$ = 6.93hr
c) Vd = 25L (Vd = dose/Co), Clearance = 2.5L/hr, AUC = 200mg*hr/L (AUC = dose/Clearance)

True or False:

1) When whole blood is collected in a heparinized test tube and then centrifuged, the supernatant that is obtained is serum. (False)[0.5M]
2) The fraction of the drug being eliminated per hour is increasing in a first order process. (False) [0.5pt]
3) The $t_{1/2}$ of a zero order process can be determined. (True)[0.5pt] (The t1/2 of a zero order process can be calculated, but it is not a constant)