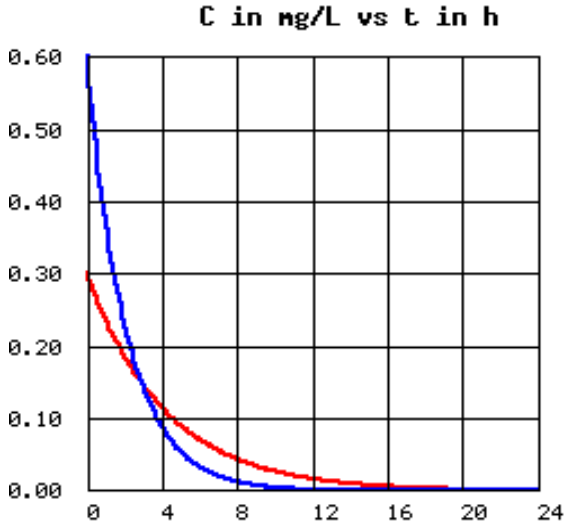
Homework 5 Dose Optimization-I PHA 5127 – Fall 2010

Due Date:

Do not forget the units of the results. 0.1 points will be deducted for each time an answer is provided without the appropriate unit. If you do not show your work and your answer differs from the right solution, no points will be given. Assume that all elimination processes are first-order.

1) The same dose (500 mg) of drug A was administered to two distinct patients via IV-bolus. The following plasma-concentration-time profiles were obtained. The blue line is Subject 1 and the red line is subject 2. Answer the questions below.




True or False: (Mark whether True or False and Explain) [4 points]

a) The clearance of subject 1 is higher to the clearance in subject 2. (T/F)
b) The AUC0-t of the subject 1 is higher to the AUC0-t of subject 2. (T/F)
c) The Vd of the subject 2 is higher to the Vd of subject 1. (T/F)
d) The tissue binding in subject 1 is higher to the tissue binding in patient 2. (T/F)

Explanation:

In the figure above the two subjects receive the same dose of the drug A. But the initial concentrations are the different. The C0 for subject 2 is lower than that of subject 1, hence the subject 2 has higher Vd. At later times the concentration of the subject 2 are higher than that of 1 and hence from the figure we can conclude that the AUC0-t is the same in both

the subjects. Hence clearance is constant in both the subjects. The only Pk metric changing in the two subjects is Vd.

2) The table below shows the concentration time data after IV bolus administration of a 500mg dose of drug X. Assume that there is only renal elimination. Calculate the rate of excretion at time 2hr and 8 hr. Do they differ? If yes, can you conclude that the clearance changes with time? [4 points]

| time(hr) | conc (mg/l) |
|---|---|
| 0 | 14.29 |
| 1 | 12.38 |
| 1.5 | 11.53 |
| 2 | 10.74 |
| 4 | 8.07 |
| 6 | 6.06 |
| 8 | 4.56 |
| 10 | 3.42 |
| 12 | 2.57 |

Ans Ke = 0.142 $hr^{-1}$ (From the slope) [0.5 point]

C0 = Dose/Vd; Vd = Dose/C0 = 500/14.29 = 35L

Vd = 35 L [0.5 point]

Clearance = Ke* Vd; Clearance = 35*0.142 = 4.97 L/hr

Clearance = 4.97 L/hr

Rate of Excretion (ke*X) at time 2hr = 0.142*10.74*35 = 53.37 mg/hr [1point]

Rate of Excretion at time 8hr = 0.142*4.56*35 = 22.66 mg/hr [1 point]

Though the rate of excretion is different, the clearance doesn't change, since the fraction (rate of excretion/plasma concentration) is constant all time points.

[1 point]

True or False: [2 points]

1) Linear Pharmacokinetics assumes that the plot of clearance vs dose is a flat line parallel to the dose axis i.e. the clearance stays constant with change in dose. (T/F)
2) The change is clearance will not necessarily result in a change in Vd. (T/F)