FALL 2013 PHA 5127 – Case Study 3

First Order and Zero Order Processes

1. Given below are the plasma concentration time profiles of Drugs A and B after a 600ng I.V. bolus dose in tables A and B correspondingly. Both drugs follow a one compartment body model with respect to distribution (Instantaneous distribution). The elimination however of one drug is a zero order process while that of the other is a first order process. Please answer the following questions:

Table A	
Time(hr)	Conc (ng/ml)
0	6.00
1	4.72
2	3.71
3	2.92
4	2.30
5	1.81
6	1.42
7	1.12

Table B	
Time(hr)	Conc (ng/ml)
0	16
1	14
2	12
3	10
4	8
5	6
6	4
7	2

a) Identify the drug that follows first order elimination process?

b) Calculate the elimination rate constant (**ke**) for drug A and drug B. Clearly state the units in each case.

c) Calculate the area under the curve from time 0 to infinity ($\mathbf{AUC_{0\text{-}inf}}$) for both drugs A and B.

Protein Binding

1) Lipophilic and unionized drug Phenytoin has a volume of distribution of 100L. Valproic acid displaces phenytoin from albumin binding sites (plasma) making a two-fold change in the fraction unbound in plasma. Predict the change in volume of distribution of phenytoin when co-administered with valproic acid.

2) Drug A and drug B are both lipophilic drugs. The plasma protein binding for drug A is 95% and for drug B is 5%, both drug A and drug B have tissue binding 75%. The same doses (200mg) of the two drugs are given to a healthy volunteer through I.V bolus at two different times (2 weeks of wash out period in between), assume Vp = 3L, VT = 38L for both drugs.

    a. Calculate the volume of distribution and initial free drug concentration of drug A and drug B

    b. Suppose the healthy volunteer got liver disease which results in a twofold decrease in plasma protein binding (halved) for both drug A and drug B (assume tissue binding remains the same), recalculate the volume of distribution and initial free drug concentration of drug A and drug B. What conclusions could you make?

True or False

Since $CL = ke * Vd$, a change in clearance will result in a change in volume of distribution.