PHA 5127 - Homework 1

ANSWER KEY

Please show all work to receive full credit.

Fall 2014

1. Table 1 shows the serum concentration profiles of a certain drug in patient X.

   a. Calculate AUC 0-t_{last} and $AUC_{0\text{-}inf}$ by trapezoidal rule.

   b. Calculate the concentration of the drug X in serum at time 5 hr.

Table 1

Time (hr)	Conc (ng/mL)
0	20
1	16.37
1.5	14.82
2	13.41
4	8.99
6	6.02
8	4.04
10	2.71
12	1.81

ANSWER:

1.a)

Time (hr)	Conc (ng/mL)	AUC partial (ng*hr/mL)
0	20	
1	16.37	18.19
1.5	14.82	7.8
2	13.41	7.06
4	8.99	22.39
6	6.02	15.01
8	4.04	10.06
10	2.71	6.74
12	1.81	4.52
sum(partial AUCs)		**91.77**

$$\text{AUC}_{\text{partial}} = \frac{C2+C1}{2} * (t_2 - t_1)$$

$\text{AUC}_{\text{0-tlast}} =$ 91.77 ng*hr/ml

$$ke = \frac{\ln(C1) - \ln(C2)}{(t2 - t1)} = \frac{\ln(20) - \ln(1.81)}{(12hr - 0hr)} = 0.2\ h^{-1}$$

$$AUC_{\text{tlast-Inf}} = \frac{C_{12}}{ke} = \frac{1.81 ng/mL}{0.2\ h - 1} = 9.05\ ng*hr/ml$$

$$AUC_{\text{0-Inf}} = AUC_{\text{0-tlast}} + AUC_{\text{tlast-Inf}} = 91.77 + (1.81/0.2) = 100.82\ ng*hr/ml$$

1.b)

$$c(t) = c_0 * e^{-ke*t}$$

$$c(5h) = 20 \frac{ng}{mL} * e^{-0.2*5} = 7.358\ ng/mL$$

2. 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 16.37 mg/L. Four hours later the plasma concentration was observed to be 10.98 mg/L. Assume the drug follows first order elimination and a one compartment body model.
    a. Calculate the initial concentration.
    b. Calculate the value of the first order elimination rate constant and half-life.
    c. Calculate the Volume of distribution if the dose given is 500 mg.

ANSWER

a) Calculate the initial concentration C_0:

$$c(t) = c_0 * e^{-ke*t} \Rightarrow c_0 = \frac{c(t)}{e^{-ke*t}} = \frac{16.37\ mg/L}{e^{-0.1*2}} = 20\ mg/L$$

$$(ke = \frac{\ln(C1) - \ln(C2)}{(t2 - t1)} = \frac{\ln(16.37) - \ln(10.98)}{(6hr - 2hr)} = 0.1 hr^{-1})$$

b) Calculate ke and $t_{1/2}$:

$$ke = \frac{\ln(C1) - \ln(C2)}{(t2 - t1)} = \frac{\ln(16.37) - \ln(10.98)}{(6hr - 2hr)} = 0.1 hr^{-1} \Rightarrow t_{1/2} = \frac{ln2}{ke} = \frac{ln2}{0.1 hr^{-1}} = 6.93\ hr$$

c) Calculate the volume of distribution (Dose = 500mg):

$$Vd = \frac{Dose}{c_0} = \frac{500mg}{20mg/L} = 25L$$

3. (T/**F**) When whole blood is collected in a heparinized test tube and then centrifuged, the supernatant that is obtained is serum.
   False: the supernatant obtained is plasma.
4. (T/**F**) The fraction of the drug being eliminated per hour is increasing in a first order process.
   False: the fraction of a drug eliminated remains constant in a first order process.
5. (**T**/F) The $t_{1/2}$ of a zero order process can be determined.
   True: It can be determined, but it is NOT a constant! It depends upon the initial concentration!