Case Study VI Questions
PHA 5127 – Fall 2006

Question 1. A patient is given a 250 mg immediate-release theophylline tablet (Tablet A). A week later, the same patient is given a 250 mg sustained-release theophylline tablet (Tablet B). The tablets follow a one-compartmental model and have a first-order absorption and elimination. The bioavailability is 90% for both tablets. The plasma drug concentration-time profiles for both tablets are as follows:

Time (hrs)	Plasma Drug Conc. (mg/L)	
	Tablet A	Tablet B
0.5	2.52	0.11
1	4.04	0.21
2	5.36	0.39
3	5.56	0.55
6	4.47	0.90
12	2.38	1.23
18	1.26	1.28
24	0.66	1.20
36	0.18	0.93
48		0.68
72		0.34
96		0.16

Determine k_e, k_a, and V_d for both tablets.

Question 2. For a one-compartment, first-order absorption and elimination, multiple oral administration, state whether the follows parameters will increase, decrease, or no change. (Hint: Use simulation files to answer this question)

	$C_{ss,avg}$	Fluctuation, F	t_{max}
CL in halved			
τ is doubled			
F is halved			
k_a is doubled			

Question 3. A patient is to be put on a continuous iv infusion. Devise a dosing regimen (including a loading dose) for the patient. (Assume the drug to follow a one-compartment model and has a first-order elimination). Following are the properties of the drug and the patient:

Patient Weight	130 lbs
Drug's half-life ($t_{1/2}$)	3 hrs
Volume of distribution (V_d)	1.8 L/kg
Desired average steady state concentration (C_{ss})	7.5 µg/mL

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Question 4. True and False

1. The absorption rate constant (k_a) is always larger than the elimination rate constant (k_e).

2. The oral bioavailiability of a very lipophilic, neutral, high extraction drug (showing linear pharmacokinetics) after oral administration of a tablet is significantly affected by the liver blood flow, the plasma protein binding, and the dissolution rate.

3. Cp_{max} and t_{max} are sufficient to assess bioequivalency.

Question 5. Fill in the blanks

1. If $k_a << k_e$ for a drug administered orally (typical of a sustained release formulation), the drug is said to follow "_____" kinetics.

2. The method of residuals, also known as "_____", is means by which k_e and k_a may be separated and calculated when oral data is analyzed.

3. The _____ is the fraction of an oral dose that enters systemic circulation after administration.

4. Once a constant rate infusion is started, the time required to reach steady state levels is dependent on the _____ (multiplied by 5) of the drug.