

**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 is halved			
$\tau$ 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 $\mu\text{g/mL}$

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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 bioavailability 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.  $C_{p_{max}}$  and  $t_{max}$  are sufficient to assess bioequivalency.

**Question 5.** Fill in the blanks

1. If  $k_a \ll k_e$  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.