CH 7: pharmacokinetic of oral absorption:

Learning Questions

1. Plasma samples from a patient were collected after an oral bolus dose of 10 mg of a new benzodiazepine solution as follows:

Time (hr)	**Concentration (ng/mL)**
0.25	2.85
0.50	5.43
0.75	7.75
1.00	9.84
2.00	16.20
4.00	22.15
6.00	23.01
10.00	19.09
14.00	13.90
20.00	7.97

From the data above:
a. Determine the elimination constant of the drug.
b. Determine k_a by feathering.
c. Determine the equation that describes the plasma drug concentration of the new benzodiazepine.

2. Assuming that the drug in Question 1 is 80% absorbed, find **(a)** the absorption constant, k_a; **(b)** the elimination half-life, $t_{1/2}$; **(c)** the t_{max}, or time of peak drug concentration; and **(d)** the volume of distribution of the patient.

3. Contrast the percent of drug-unabsorbed methods for the determination of rate constant for absorption, k_a, in terms of **(a)** pharmacokinetic model, **(b)** route of drug administration, and **(c)** possible sources of error.

4. What is the error inherent in the measurement of k_a for an orally administered drug that follows a two-compartment model when a one-compartment model is assumed in the calculation?

5. What are the main pharmacokinetic parameters that influence **(a)** time for peak drug concentration and **(b)** peak drug concentration?

6. Name a method of drug administration that will provide a zero-order input.

7. A single oral dose (100 mg) of an antibiotic was given to an adult male patient (43 years, 72 kg). From the literature, the pharmacokinetics of this drug fit a one-compartment open model. The equation that best fits the pharmacokinetics of the drug is

From the equation above, calculate **(a)**t_{max}, **(b)**C_{max}, and **(c)**$t_{1/2}$ for the drug in this patient.

Assume C_p is in g/mL and the first-order rate constants are in hours^{-1}.

8. Two drugs, A and B, have the following pharmacokinetic parameters after a single oral dose of 500 mg:

Drug	k_a **(hr^{-1})**	k **(hr^{-1})**	V_D **(mL)**
A	1.0	0.2	10,000
B	0.2	1.0	20,000

Both drugs follow a one-compartment pharmacokinetic model and are 100% bioavailable.

a. Calculate the t_{max} for each drug.

b. Calculate the C_{max} for each drug.

9. The bioavailability of phenylpropanolamine hydrochloride was studied in 24 adult male subjects. The following data represent the mean blood phenylpropanolamine hydrochloride concentrations (ng/mL) after the oral administration of a single 25-mg dose of phenylpropanolamine hydrochloride solution.

Time (hr)	**Concentration (ng/mL)**	**Time (hr)**	**Concentration (ng/mL)**
0	0	3	62.98
0.25	51.33	4	52.32
0.5	74.05	6	36.08
0.75	82.91	8	24.88
1.0	85.11	12	11.83
1.5	81.76	18	3.88
2	75.51	24	1.27

a. From the data, obtain the rate constant for absorption, k_a, and the rate constant for elimination, k, by the method of residuals.

b. Is it reasonable to assume that $k_a > k$ for a drug in a solution? How would you determine unequivocally which rate constant represents the elimination constant k?

c. From the data, which method, Wagner–Nelson or Loo–Riegelman, would be more appropriate to determine the order of the rate constant for absorption?

d. From your values, calculate the theoretical t_{max}. How does your value relate to the observed t_{max} obtained from the subjects?

e. Would you consider the pharmacokinetics of phenylpropanolamine HCl to follow a one-compartment model? Why?