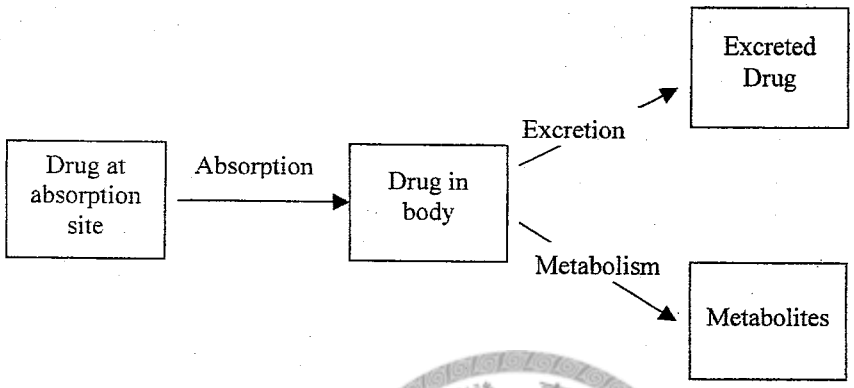
一、

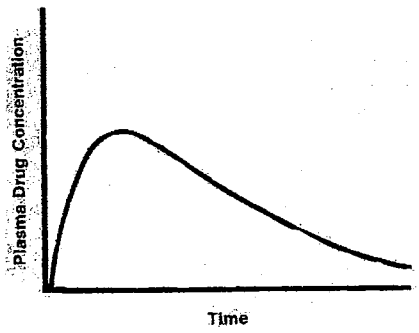
1. Answer each of the following questions based on the basic model for drug absorption, metabolism, and disposition as shown below. (14 分)



(a) What does it indicate if 100% of unchanged drug is recovered in the urine following oral administration?
(b) When does drug in the body reach a peak concentration following administration of an oral dose?
(c) When does the rate of change of drug in the body approach the rate of absorption?
(d) When is the rate of change of drug in the body equal to the rate of drug elimination?

2. If the disposition of drug after iv bolus administration of 184 mg dose in a newborn infant follows one compartment pharmacokinetics, where the plasma drug concentration can be described by $C_P = 140\ e^{-0.025t}$. C_P (μg/mL) is the plasma concentration of drug, and t (hour) represents the time. (12 分)
(a) Estimate the half-life of the drug.
(b) Calculate the volume of distribution.
(c) Estimate the total clearance.
(d) Estimate the total area under the plasma concentration-time curve.

3. The following figure shows the plasma drug concentration in the body with time following oral ingestion of a single dose of drug. Draw a figure identical to that for each question, and then draw another curve that shows the effect of each of the following alternations in pharmacokinetic parameters. In addition, you need to describe in detail how these changes affect the other pharmacokinetic parameters, too. (12 分)



(a) V increased, k decreased
(b) ka increased
(c) CL increased, k increased

接背面

4. In evaluating different dosage forms of procainamide obtained the following AUC and cumulative urine excretion data listed in following table. (12 分)

Route	Dose (mg)	AUC (mg·h/L)	Amount Excreted (0-48 hr) (mg)
i.v.	500	13.1	332
oral			
formulation 1	1000	20.9	586
formulation 2	1000	19.9	554

(a) Estimate both the absolute and relative availabilities of formulation 2 from both plasma and urine data. What are the assumptions made in your calculations?

(b) The half-life of procainamide found in this study was 2.7 hours. Was the urine collected over a long enough time interval to obtain a good estimate of the cumulative amount excreted at infinite time?

(c) Does the renal clearance of procainamide vary much among the three treatments?

接次頁

國立臺灣大學95學年度碩士班招生考試試題

二、

1. A drug follows the kinetics of a one-compartment model and has an elimination half-life of 3 hours. Given the apparent volume of distribution of 7 L, calculate the elimination rate when the plasma drug concentration is 2 μg/ml. **(5 分)**

2. A drug with an elimination constant of 0.693 hr^{-1} was given to a male patient (80 kg) by intravenous infusion at a rate of 300 mg/hr. At 7 hours after infusion, the plasma drug concentration was 11 μg/ml. if the fraction of unchanged drug excreted in urine is 0.8,
   (a) What is the renal clearance of this drug. **(5 分)**
   (b) What is the probably mechanism for the renal excretion of this drug? **(5 分)**

3. The bioavailability of propranolol is 26%. Propranolol is 87% bound to plasma proteins and has an elimination half-life of 3.9 hours. The apparent volume of distribution of propranolol is 4.3 L/kg. Less than 0.5% of the unchanged drug is excreted in the urine. Assuming the hepatic blood flow is 1500 ml/min,
   (a) Estimate the hepatic extraction ratio for propranolol. **(5 分)**
   (b) Provide at least two factors that would affect the clearance of propranolol. **(5 分)**

4. Both drug A and drug B were reported to be metabolized by CYP3A4. The hepatic intrinsic clearance of two drugs are as follows:
   Drug A: 1300 ml/min
   Drug B: 26 ml/min.
   Which drug is likely to be significantly influenced by the concomitant use of grapefruit juice. Why? **(5 分)**

5. The elimination half-life of an antibiotic is 3 hours with an apparent volume of distribution equivalent to 20% of body weight. The usual therapeutic range for this antibiotic is between 5 and 15 μg/ml. Adverse toxicity for this drug is often observed at serum concentrations greater 20 μg/ml. Calculate dosage regimen (multiple IV doses) that will maintain the serum concentration between 5 and 15 μg/ml for a 70-kg man. **(10 分)**

6. Explain why subsequent equal doses of a drug do not produce the same pharmacodynamic effect as the first dose of drug.
   (a) Provide an explanation based on pharmacokinetic considerations. **(5 分)**
   (b) Provide an explanation based on pharmacodynamic considerations. **(5 分)**

試題隨卷繳回