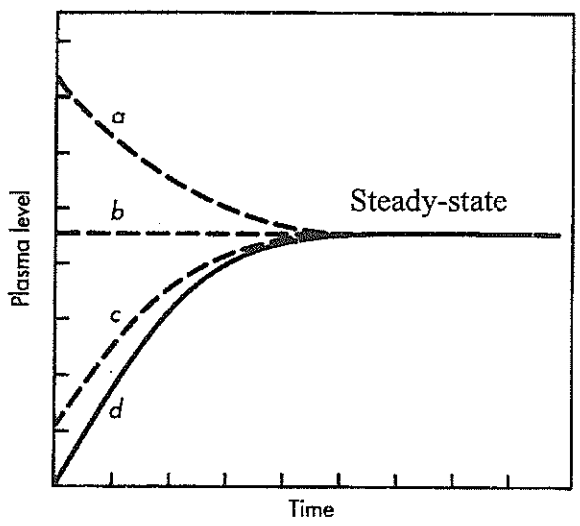
1. If the disposition of drug after iv bolus administration of 200 mg dose in a newborn infant follows one compartment pharmacokinetics, where the plasma drug concentration can be described by $C_P = 100e^{-0.0231t}$. $C_P$ (μg/mL) is the plasma drug concentration, and $t$ (hour) represents the time.
   (1) Estimate the half-life of the drug. (3 分)
   (2) Calculate the apparent volume of distribution. (3 分)
   (3) Estimate the total clearance. (2 分)
   (4) Estimate the total area under the plasma drug concentration-time curve. (2 分)

2. You are assigned to conduct a bioequivalence study of a generic drug product and a brand name product. A randomized two-way crossover design with a proper washout period is performed between two treatments. The subjects are randomly assigned to receive a single dose of each product orally. The blood and urine samples are collected at specific time points. Please answer the following questions in detail.
   (1) How do you decide the total sampling time period for blood samples and what is your reason? (3 分)
   (2) How do you decide the total sampling time period for urine samples and what is your reason? (3 分)
   (3) What are the pharmacokinetic parameters which can be used for assessing bioequivalence if plasma samples are collected? (4 分)

3. There are four plasma drug concentration-time curves shown in the following figure. **Curve *d*** represents a plasma drug concentration-time curve following intravenous infusion at a constant infusion rate $R$ until a steady-state concentration is reached
   (1) Please explain under what circumstance curve $b$ will be achieved where the concentration desired at steady state is obtained immediately. (5 分)
   (2) Write down the concentration-time equation for curve $b$. (5 分)




4. Fill in the blanks in the following Table. (↓: decrease；↑: increase；↔: no change) (每個空格 2 分，共 10 分)

| ***ka*** | ***k*** | ***tmax*** | ***Cmax*** | ***AUC*** |
|---|---|---|---|---|
| ↑ | ↔ | | | |
| ↔ | ↑ | ↓ | | |

見背面

5. Four different drug products containing the same antibiotic were given to 12 volunteer adult males in a four-way crossover design. The volunteers were fasted for 12 hours prior to taking the drug product. Urine samples were collected up to 72 hours after the administration of the drug to obtain the maximum urinary drug excretion. The data are presented in the Table.

| Drug Product | Dose (mg/kg) | Cumulative urinary drug excretion 0-72 hr (mg) |
|---|---|---|
| IV solution | 0.2 | 20 |
| Oral solution | 3 | 300 |
| Oral tablet | 4 | 320 |
| Oral capsule | 4 | 360 |

(1) What is the absolute bioavailability of the drug from the tablet? (5 分)

(2) What is the relative bioavailability of the capsule compared to the oral solution? (5 分)

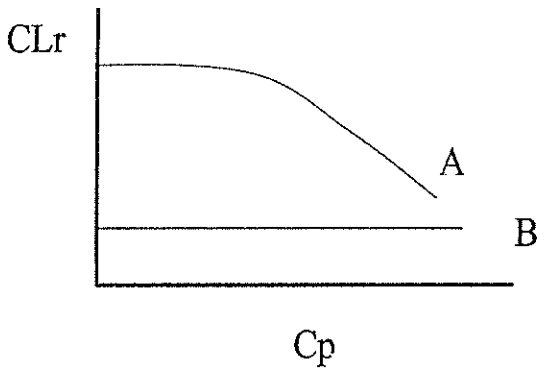
接次頁

本部分試題共 50 分，請詳細解釋作答。

6. 藥動或藥效之性質可作為評估是否需要進行銜接性試驗〈bridging study〉的重要參考。
A 何謂銜接性試驗，其目的為何？〈6 分〉
B 請解釋以下表格所列各項資料之意義及重要性。(24 分)

| Less Sensitive | More sensitive |
|---|---|
| Linear PK | Non-linear |
| Flat concentration-response | Steep |
| Wide therapeutic range | Narrow |
| Minimal metabolism | High metabolism |
| or multiple pathways | Single (polymorphic) |
| High bioavailability | Low |
| Low protein binding | High |
| Low potential for interactions | High |
| Non-systemic action | |

7. 下圖為 Drug-A 與 Drug-B 之腎清除率 (renal clearance; CLr) 與其血中濃度 (plasma concentrations; Cp) 之關係圖。請分別描述 Drug-A 與 Drug-B 之藥動特性，以及在臨床給藥時需要注意之處。請解釋原因。〈10 分〉




8. 對於具有高抽提率 (high extraction ratio) 的藥品，以口服方式 (oral administration) 或以 靜脈注射 (intravenous administration) 投藥後，何者具有較大的個體差 (inter-individual difference)？請以公式解釋原因。〈10 分〉

試題隨卷繳回