※ 注意：請於試卷上依序作答，並應註明作答之大題及其題號。

請詳述解題過程

1. The pharmacokinetic properties of propranolol are:
   F = 26%
   fu = 13%
   elimination half-life t1/2 = 3.9 hours
   Vd = 4.3 L/kg
   a. Calculate **hepatic** extraction ratio for propranolol **(5 points)**
   b. Explain how a change in (1) hepatic blood flow, (2) intrinsic clearance, or (3) plasma protein binding would affect hepatic clearance of propranolol. **(9 points)**

2. phenytoin was administered to a patient at dosing rates of 150 and 300 mg/day, respectively. The steady-state plasma drug concentrations were 8.6 and 25.1 mg/L, respectively.
   a. Find the Km and Vm of this patient. **(5 points)**
   b. What dose is needed to achieve a steady-state concentration of 11.3 mg/L? **(5 points)**
   c. Please suggest two factors that may influence the pharmacokinetic properties of phenytoin. **(4 points)**

3. The pharmacokinetics of amrinone after single IV bolus injection (75 mg) in adult male volunteers follows a two-compartmental open model and fit the following equation:

$$Cp = A e^{-\alpha t} + B e^{-\beta t}$$

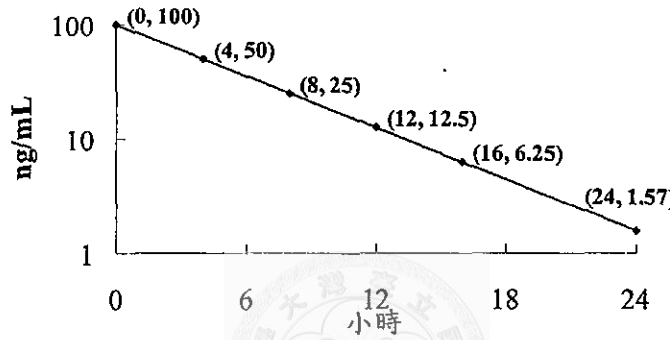
   A = 4.6 μg/ml
   B = 0.6 μg/ml
   $\alpha = 9\ hr^{-1}$
   $\beta = 0.2\ hr^{-1}$
   a. calculate the volume of the central compartment **(4 points)**
   b. explain the meanings of A, B, α and β **(8 points)**

4. For bioequivalence studies,
   a. Why are the parameters t_{max}, C_{max} and AUC acceptable for proving that two drug products are bioequivalent. **(6 points)**.
   b. Is it necessary to use a pharmacokinetic model to completely describe the plasma drug concentration-time curve for the determination of t_{max}, C_{max} and AUC? (please explain the reasons) **(4 points)**

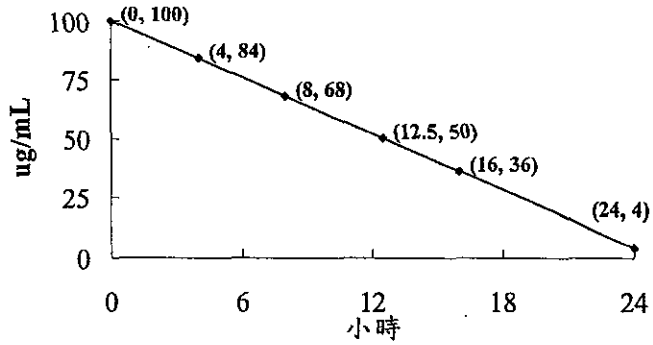
見背面

5. A 藥及 B 藥為新一代降血壓藥品，分別在七十公斤健康男性經靜脈注射給藥，24 小時藥品血中濃度變化如圖 A 及圖 B，圖中資料標籤(x,y)分別表示不同時間點 x，對應之血中濃度值 y，並請留意 A 圖及 B 圖縱座標單位大小及血中濃度單位不同，請回答下列問題。(提示 1 mg = 10^3 ug = 10^6 ng)

圖A
A藥 100 mg 靜脈注射血中濃度變化圖



圖B
B藥 2000 mg 靜脈注射血中濃度變化圖



a. 利用以上資料，請以一數學方程式描述 A 藥於血中之變化。其半衰期為何？分布體積為何？(註明單位) (10%)

b. 利用以上資料，請以一數學方程式描述 B 藥於血中之變化。其半衰期為何？分布體積為何？(註明單位) (10%)

c. 若某病人因腎臟衰竭接受腹膜透析，若 A 藥與 B 藥分子量皆是 1000 Dalton 以下，請問 A 藥與 B 藥相比，哪一藥品比較不容易被透析排出？請簡單說明理由？(5%)

接次頁

6. X 藥為一口服的降血糖新藥，其口服 100 mg 之絕對生體可用率為 80%。今欲瞭解 100 mg X 藥與另二個口服抗生素 Y 及 Z 的藥品交互作用，併用 Y 藥及 Z 藥時，X 藥的血中濃度分別如圖 1 及圖 2。請回答下列問題。

圖 1

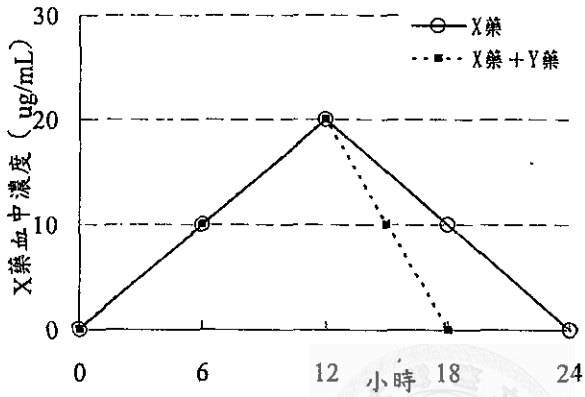
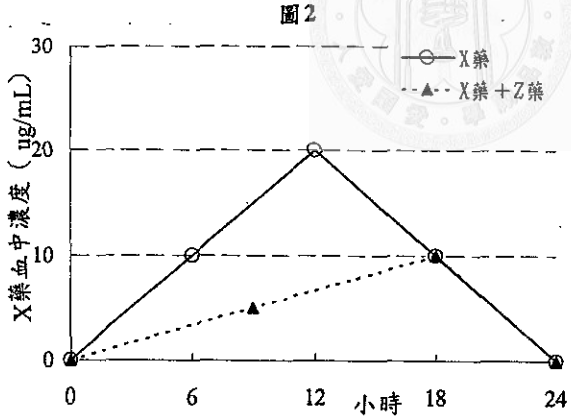


圖 2



a. 請估計併用 Y 藥時，X 藥之絕對生體可用率為何？你推測 Y 藥改變 X 藥生體可用率的可能機轉為何？並簡單說明理由。(10%)

b. 請估計併用 Z 藥時，X 藥之絕對生體可用率為何？你推測 Z 藥改變 X 藥生體可用率的可能機轉為何？並簡單說明理由。(10%)

c. 若 X 藥改為靜脈注射，則口服抗生素 Y 及 Z 分別與 X 藥併用時，是否仍會影響 X 藥的生體可用率？(5%)

試題隨卷繳回