國立臺灣大學96學年度碩士班招生考試試題

請詳述解題過程

1. A new antibiotic drug was given in a multiple intravenous bolus of 1 mg/kg every 8 hours to five healthy male adults ranging in age from 23 to 38 years (average weight 75 kg). The pharmacokinetics of the plasma drug concentration-time curve for this drug fits a one-compartment model. The fe and fu of this drug are 0.9 and 0.7, respectively. The equation of the curve that best fits the data is
   $Cp = 58 \times e^{-0.46 \times t}$ (assuming units of μg/ml for Cp and hour for time)

   (a) What is the renal clearance? **(5 points)**
   (b) What is the area under the curve (AUC)? **(5 points)**

2. An adult female patient (52 yrs, 56 kg) whose serum creatinine is 2.6 mg/dL is to be given the antibiotics described above (i.e, question-1). Please calculate the appropriate dosage regimen for this patient if we intend to prolong the dosing interval **(10 points)**

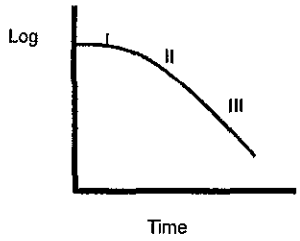
3. Part of pharmacokinetic properties of drug-A and drug-B are listed in the following table. Concomitant use of phenobarbital can induce the metabolic enzymes for drug-A and drug-B. If a patient needs to take drug-A or drug-B with phenobarbital, please predict possible effects of phenobarbital on AUC, F, and CL of oral drug-A and drug-B based on pharmacokinetic equations. **(10 points)**

	Drug-A	Drug-B
F	0.2-0.35	0.7-1
fu	0.1	0.07-0.12

4. Gentamicin sulfate was given to an adult male patient (57 yrs, 70kg) by intermittent IV infusions. One-hour IV infusion of 90 mg of gentamicin was given at 8-hour intervals. Gentamicin clearance is about 7.2 L/hr and the elimination half-life was 3 hours.
   (a) How many hours will it take to reach steady state in plasma concentrations? **(2 points)**
   (b) Please calculate Cmax and Cmin concentrations at steady state. **(5 points)**

5. The following plasma concentration-time curves represent I.V. bolus dose of drug-A.
   (a) Please describe the possible reasons in the area I, II and III **(5 points)**

見背面



(b) Drug-B is known to interact with drug-A in terms of hepatic metabolism. To study drug-drug interaction, please use a linear method (用作圖法) to estimate the whether the interaction is competitive or noncompetitive. Please also indicate the way to estimate the Km and Vm values. **(8 points)**

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6. Drug A is a new antibiotic. The blood concentrations of drug A after intravenous injection of 100 mg to a 70-kg healthy male are shown in the following table. A two-compartment model can describe the change of concentrations (25%).

時間 （小時）	血漿濃度 （ng/mL）
0.25	43
0.5	32
1.0	20
1.5	14
2.0	11
4.0	6.5
8.0	2.8
12.0	1.2
16.0	0.52

a. 請於半對數紙上，畫出藥品濃度與時間之變化圖。(5%) ＊ 請作答於試卷內半對數紙上。
b. 利用上圖，請以一數學方程式描述 A 藥於血中之變化。(5%)
c. 請問其分布半衰期及代謝半衰期為何？(5%)
d. 請問其 volume of the central compartment 為何？(5%)
e. 若該病人因腎臟衰竭接受血液透析，請問 A 藥是否可被透析排出，並請說明理由？(5%)

7. a. 請設計一實驗以比較原廠藥錠劑（Tablet A）與他廠藥錠劑 (Tablet B)、及膠囊 (Capsule C) 之生體相等性（bioequivalence），包括實驗設計及統計分析。(10%)
   b. 若實驗結果如下表，以 AUC_{0-24} 來看，請算出 Tablet B 及 Capsule C 相對於 Tablet A 之生體可用率。(5%)
   c. 請說明在比較生體相等性時，為何需比較 C_{max} 、T_{max}、AUC_{0-24}？(5%)
   d. 請就下表實驗結果及統計分析，說明 Tablet B 及 Capsule C 相較於 Tablet A 是否具有生體相等性？(5%)

Dosage	C_{max}	T_{max}	AUC_{0-24}	Bioavailability relative to the Tablet A	90% confidence interval for AUC
Tablet A	16.1 ± 2.5	1.5 ± 0.85	1835 ± 235	--	--
Tablet B	13.7 ± 4.1	2.1 ± 0.98	1707 ± 317		88-98 %
Capsule C	10.5 ± 3.2	2.5 ± 1.0	1523 ± 381		74-90 %

試題隨卷繳回