請依題號順序作答

1. An antibiotic was given by IV bolus injection at a dose of 500 mg. The apparent volume of distribution was 21 L and the elimination half-life was 6 hours. Urine was collected for 48 hours and 400 mg of unchanged drug was recovered.
   (1) What is the renal clearance? (5 points).
   (2) Please explain whether there is renal reabsorption or secretion. (5 points)
   (請詳加說明解題過程)

2. The followings are the values of total body clearance of drug-A and drug-B:
   Drug A: 1300 ml/min
   Drug B: 26 ml/min
   Both drugs are mainly metabolized by CYP2C19. Which drug is likely to show the greatest decrease in hepatic clearance in a patient who is a CYP2C19 poor metabolizer?_(請詳加說明解題過程) (5 points)

3. A cephalosporin ($k = 0.2\ hr^{-1}$, $Vd = 10$ L) was administered by IV multiple dosing; 100 mg was injected every 6 hours for 6 doses. What was the plasma drug concentration 4 hours after the 6^{th} dose if the 4^{th} dose was omitted. (5 points)
   (請詳加說明解題過程)

4. Based on the following pharmacokinetic data for drug A, B, and C:
   (1) Which drug takes the longest time to reach steady state?
   (請詳加說明解題過程) (5 points)
   (2) Which drug would achieve the highest steady-state drug concentrations?
   (請詳加說明解題過程) (5 points)

	Drug A	Drug B	Drug C
Rate of infusion (mg/hr)	10	20	15
K (hr^{-1})	0.5	0.1	0.05
CL (L/hr)	5	20	5

見背面

5. One drug is used for the treatment of ventricular tachyarrhythmia, and its therapeutic range is 4-8 mg/L. When a 250 mg tablet is administered orally to a 70 kg normal healthy subject, the following pharmacokinetic parameters are obtained. (21 points)

   The elimination half life ($t_{1/2}$) = 3.0 h
   The apparent volume of distribution (Vd) = 2.0 L/kg
   The absorption rate constant (ka) = 2.8 h^{-1}
   The intercept of the plasma concentration-time profile = 2.0 mg/L
   The fraction of dose absorbed (i.e. reaching the general circulation) = 85%

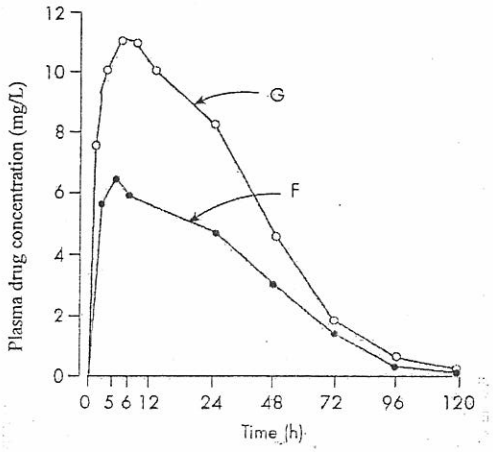
   Answer the following questions based on the above available information and appendix. In addition, a linear and one-compartment pharmacokinetics is followed.
   (1) Determine the peak time (t_{max}) and peak plasma concentration (C_{max}) following the oral administration of a 500 mg tablet.
   (2) How many tablets (250 mg strength) will be required to control arrhythmia?
   (3) Determine the absorbable amount of drug remaining at the site of administration (X_a) after oral administration of a 500 mg tablet.
   (4) Determine the amount of drug in the body and/or blood (X_b) at a time when the rate of absorption is equal to the rate of elimination after oral administration of a 250 mg tablet.

6. It is necessary to administer a drug as an intravenous infusion to achieve therapeutic efficacy in a 100 kg patient admitted into a hospital. The true steady-state plasma drug concentration is determined to be 6 mg/L. The related pharmacokinetic parameters of this drug are provided as follows: (16 points)

   The elimination half life ($t_{1/2}$) = 3.0 h
   The apparent volume of distribution (Vd) = 2 L/kg
   The absorption rate constant (ka) = 2.8 h^{-1}

   (1) Determine the infusion rate of drug required to attain the true steady-state plasma concentration.
   (2) Based on clinical consideration, is it possible to reach the true steady state after intravenous infusion? Provide your detailed rationale.
   (3) Determine the time it will take to attain the desired 95% steady-state condition in this subject.
   (4) Based on the answer of question (3), what is your suggestion if this drug is still considered to administer via an intravenous infusion to this patient?

7. This figure shows two plasma drug concentration-time curves after administration of same dose (i.e. 500 mg) of same active drug to the same subject. The area under the plasma drug concentration versus time curve is 40 and 66 mg・h /L for F and G, respectively. Base on your biopharmaceutical knowledge; please provide five possible reasons which may result in the difference between G and F. The detailed rationale is necessary. (15 points)



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8. 某藥品之體內動態遵循線性一室模式(one compartment open model)，其由胃腸道吸收與從體內排除均為一級動力學 (first-order kinetics)，請依下列各子題之敘述條件，正確地描繪出改變前與改變後的血中濃度(C_p)與時間(t)關係圖之變化；另外所有相關藥動參數的變化亦應清楚說明。(18 points)
   (1) 若靜脈注射給藥劑量不變，但擬似分佈體積變成原來的一半，而半衰期變成原來的兩倍時。
   (2) 若靜脈注射給藥劑量變成原來的兩倍，清除率亦變成原來的兩倍，但擬似分佈體積不變時。
   (3) 已知在相同口服劑量下，與食物併服會使此藥之吸收速率常數變成空腹給藥時的一半，但清除率、擬似分佈體積與生體可用率則維持不變時。

[Appendix]

Ln 0.05 = -3.0	Log 0.077 = -1.11	$e^{-0.077} = 0.93$
Ln 0.231 = -1.47	Log 0.231 = -0.64	$e^{-0.22} = 0.80$
Ln 0.693 = -0.37	Log 0.693 = -0.16	$e^{-0.99} = 0.37$
Ln 2.8 = 1.03	Log 2.8 = 0.45	$e^{-2.72} = 0.07$
Ln 3 = 1.10	Log 3 = 0.48	$e^{-3} = 0.05$
Ln 9 = 2.20	Log 9 = 0.95	$e^{-9} = 1.23*10^{-4}$

試題隨卷繳回