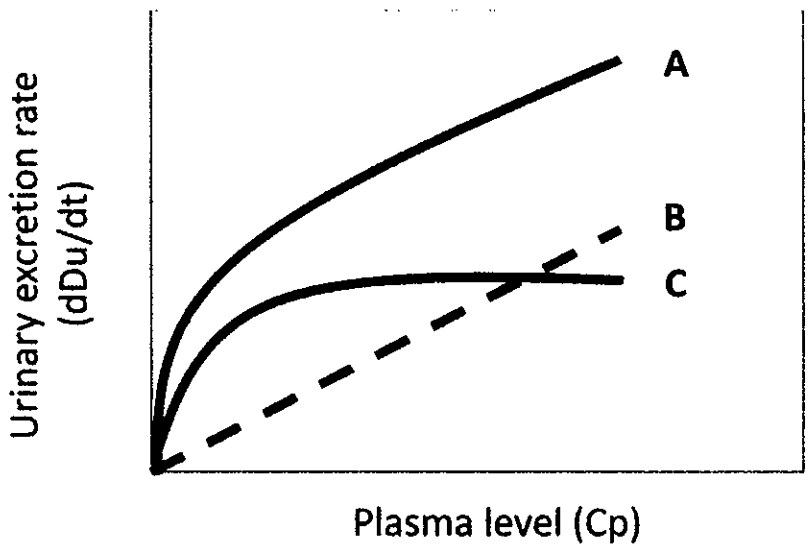
1. 請寫出影響藥物分佈常數 k_d (first-order distribution constant)的三個主要因素及與 k_d 的關係式，並詳細說明之。(15 分)

2. 請回答下列關於藥物與蛋白結合之相關問題：
   (1) 請寫出蛋白結合對擬似分佈體積(V_D)影響之關係式，並標示出各個參數之名稱。(5 分)
   (2) 請說明增加 serum binding (%)對藥物的 half-life、renal clearance、urinary recovery (%)的一般影響。(9 分)
   (3) 請說明 dirithromycin 具有 Large V_D (504-1041 L)及 Long $t_{1/2}$ (16-65 h)之藥動特性的主要原因。(6 分)

3. In evaluating different dosage forms of procainamide obtained the following AUC and cumulative urine excretion data listed in the following Table.
   (1) 請分別定義"absolute availability" 和 "relative availability"。(4 分)
   (2) Calculate both the absolute and relative availabilities of formulation 2 from plasma data. (5 分)
   (3) The half-life of procainamide found in this study is 2.7 hours. Is the urine collected over a long enough time interval to obtain a good estimate of the cumulative amount excreted at infinite time? Why? (6 分)

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

4. The followings are the excretion rate vs. plasma level curves for compound-11. Curve-A represent the total excretion rate vs. the plasma levels.
   (a) Explain the properties of the renal clearance of this compound (**6 分**)
   (b) Explain the meanings of each curve (**9 分**)



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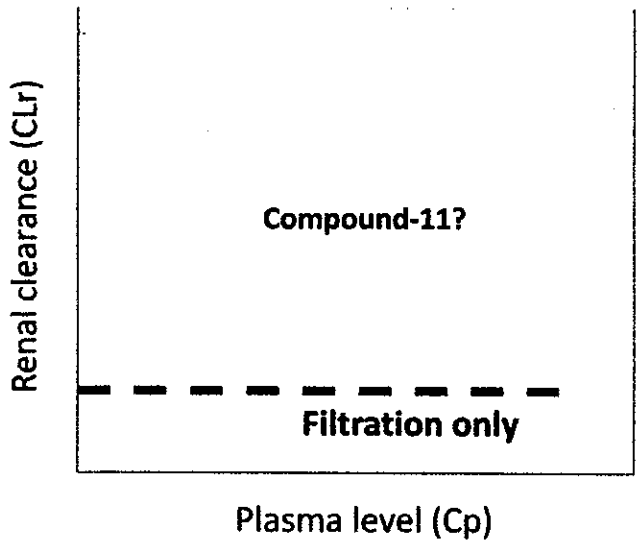
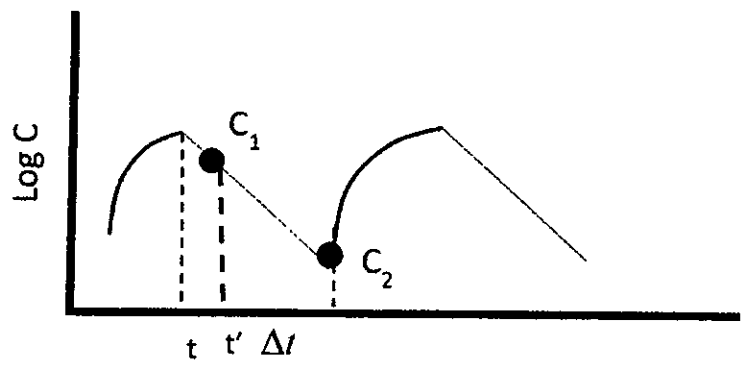
5. Based on the properties of compound-11 described in the above question, draw a figure to describe the relationship between renal clearance (Y-axis) and plasma drug concentration (Cp) of compound-11. (5 分)
(必須在答案卷上作圖回答，否則不計分)



6. For a drug given by intravenous infusion (see the figure), concentrations C1 and C2 were measured. Show an equation to estimate volume of distribution (Vd) of this drug (10 分). (infusion time = t; C_1 at t')



7. A drug that works on central nervous system was given to a patient by oral administration. Following therapeutic drug monitoring, blood samples were measured and drug concentrations were within the therapeutic range. However, clinical response of this patient was far from expectation.
(a) What are the major considerations in therapeutic drug monitoring? (5 分)
(b) Explain why blood concentrations did not reflect clinical outcomes? (5 分)

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8. The followings are the pharmacokinetic properties of drug-B.

Fraction of absorption > 95%

F = 5 %

fu = 3 %

Vd = 2.5 L/kg

Metabolic enzymes: CYP2D6, CYP3A4, CYP2C19

Active metabolite = 5-hydroxy-drug-B

fe = 0.65

Total CL = 1000-1300 ml/min

What should be considered in conducting a clinical study of this drug? (**10 分**)

試題隨卷繳回