1.計算題 (15 分)

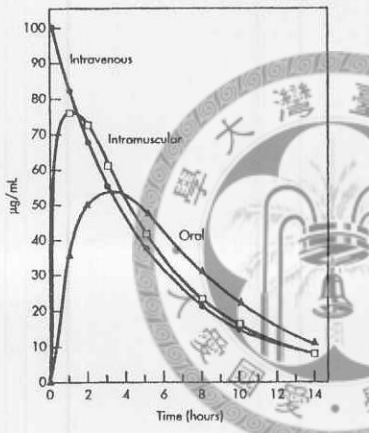
(1)一藥物以定速連續靜脈輸注方式投予，而該藥物的半衰期是 4 小時，請問應該連續輸注多久才能使藥物血中濃度到達穩定濃度的 87.5%？

(2)一藥物以 500 mg 的劑量靜脈注射至人體內，其血中濃度變化以 $C_P = 16e^{-0.8t} + 5e^{-0.05t}$ 表示，C_p 是指時間 t 小時之藥物血中濃度(μg/mL)，試問該藥物的濃度-時間曲線下面積(AUC)是多少？

(3)在一多次口服投藥控制中，每次投予 500 mg 的藥物至一體重 50 kg 的受試者體內，預期的穩定狀態平均血中濃度(C_{av}^{∞})是 100 μg/mL，已知該藥物之排除速率常數為 0.025 hr^{-1}，V/F 值為 0.2 L/kg。請問每次投藥間隔應為幾個小時？

2. Is it reasonable to assume that $k_a > k$ for a drug in a solution? How would you determine unequivocally which rate constant represents the elimination constant k from the concentration-time curve? (10 分)

3. Please write down what you see or what you get from this figure based on your biopharmaceutical concept ? (15 分)



4. Explain in detail about why the disposition of some drugs follow one-compartment model, and some drugs follow two-compartment or multi-compartment model. In addition, how do you distinguish them according to the concentration-time curve obtained following administration of a drug? (10 分)

接背面

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(1) The following pharmacokinetic parameters for drug M were reported in Micromedex. Please calculate **(a)** total body clearance **(b)** renal clearance **(c)** hepatic clearance and describe the assumption needed to claim these values. (5 points each; Total **15** points)

F = 0.9

fe = 0.25

fu = 0.96

Volume of distribution = 6.54 L/kg

Elimination half-life = 8 hr

(2) The bioavailability and fu values of verapamil and phenytoin are listed in the following table. Warfarin is known to be a low extraction ratio drug and its protein binding degree is high (about 99%). If patient-A needs to take verapamil or phenytoin with warfarin, please predict possible effects of warfarin on **(a)** AUC **(b)** F, and **(c)** CL of verapamil and phenytoin based on suitable equations. (5 points each; Total **15** points)

	Verapamil	Phenytoin
F	0.2-0.35	0.7-1
fu	0.1	0.07-0.12

(3) An adult female patient (52 yrs, 56 kg) whose serum creatinine is 2.6 mg/dL is to be given gentamicin sulfate for a confirmed Gram-negative infection. The usual dose of gentamicin in adult patients with normal renal function is 1 mg/kg every 8 hours by multiple IV bolus injections. The fe value of gentamicin is about 0.98. Please calculate **(a)** the creatinine clearance in this patient by the Cockcroft and Gault method and **(b)** the appropriate dosage regimen of gentamicin sulfate for this patient if we intend to prolong the dosing interval (5 points each; Total **10** points)

(4) 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 mg/L and 25.1 mg/L, respectively. **(a)** Find the Km and Vm of this patient. **(b)** What dose is needed to achieve a steady-state concentration of 11.3 mg/L? (5 points each; Total **10** points)

試題隨卷繳回