請詳列解題過程

1. According to the data given in Table 1,
(a) Explain how doses affect the linear/nonlinear pharmacokinetic properties **(8 分)**
(b) Explain the impact of doses on the values of MRT. **(8 分)**

Table 1. Pharmacokinetic parameters of drug-A in humans following a single intravenous dose. (Data are presented as the mean values, given low variations)

Dose (mg)	AUC_{inf} (mg×hr/L)	Cmax (mg/L)	$T_{1/2}$ (hr)	Vss (L)
200	6.7	2.56	10.6	127
400	14.5	6	12.1	102
600	21.6	8	11.7	108
800	42.7	13.3	15.3	106
1000	66.5	20.2	17.1	90

2. To estimate the renal clearance of a drug in a patient, a 4-hour postdose urine sample was collected and found to contain 200 mg of drug. Drug concentrations in the plasma at 1 hour and 2 hour postdose were 1.0 and 2.5 mg/dL, respectively. Explain probable mechanisms for renal clearance of this drug in this patient **(10 分)**

3. The risk of myopathy during treatment with HMG-CoA reductase inhibitors is increased with concurrent therapy with erythromycin, cyclosporine, or fibrate. Pravastatin (F = 0.17) is HMG-CoA reductase inhibitor and is a substrate of OATPs and MRP2. Explain the impacts of
(a) Changes in the OATP1B1 activity on the therapeutic efficacy and myopathy of pravastatin, respectively. **(8 分)**
(b) Changes in the MRP2 activity on the therapeutic efficacy and myopathy of pravastatin, respectively. **(8 分)**

4. For a drug (half-life = 2 hrs) given by multiple intravenous infusion (infusion time = 1 hr) every 8 hours, a concentration C1 was measured at 0.5 hr post-infusion and another concentration C2 was measured prior to the start of next infusion. Show an equation to estimate volume of distribution (Vd) of this drug. **(8 分)**

見背面

5. A drug is administered intravenously. Its therapeutic range is 4-10 μg/mL. In healthy subjects, the elimination half-life is 6.93 h, the apparent volume of distribution is 2 L/kg. It is necessary to administer this drug as an intravenous infusion in a patient (60 kg) admitted into a hospital.
   (1) Determine the infusion rate of drug required to attain the true steady-state plasma drug concentration of 6 μg/mL. (3 分)
   (2) Determine the rate of elimination of drug at true steady-state condition. (3 分)
   (3) Because the patient is responding poorly to the therapy, the physician wants to increase the plasma drug concentration in the patient to 8 μg/mL. What dosage recommendation would you give the physician? Would you recommend the loading dose? (4 分)
   (4) In a patient with cardiac failure, shock, and renal impairment, the apparent volume of distribution and the elimination half-life are reported to be 1.5 L/kg and 33 h, respectively. Determine the loading dose and infusion rate of drug necessary to attain and then maintain the steady-state plasma drug concentration of 6 μg/mL. (4 分)

6. When a 750 mg dose of drug A is administered intravenously to a healthy subject (70 kg), the following information is obtained:
   - the elimination half-life is 3 h
   - the apparent volume of distribution is 2 L/kg
   - 65% of drug is excreted in urine

   When a tablet containing 250 mg of drug A is administered orally to the same healthy subject, the following information is obtained further:
   - absorption rate constant is 2.8 h^{-1}
   - intercept of the plasma drug concentration-time profile is 1.665 μg/mL

   Assuming the relationship between the peak drug concentration and the dose administered is directly proportional (linear pharmacokinetics).
   (1) Determine the systemic clearance and renal clearance in the healthy subject. (4 分)
   (2) Determine the absolute bioavailability of drug from tablet dosage form in this healthy subject. (4 分)
   (3) Is the absolute bioavailability of the drug influenced by the dose administered? What is your rationale? (4 分)
   (4) Is the absolute bioavailability of the drug influenced by renal impairment? What is your rationale? (4 分)

7. When a 750 mg dose of drug B is administered intravenously to a healthy subject (65 kg), the following information is obtained:
   - the elimination rate constant is 0.3 h^{-1}
   - the apparent volume of distribution is 2 L/kg

   When a tablet containing 250 mg of drug B is administered orally to the same healthy subject, the following information is obtained:
   - The absorption rate constant is 3 h^{-1}
   - intercept of the plasma drug concentration-time profile is 1.28 μg/mL
   - the absolute bioavailability is 60%

   Assuming the relationship between the peak drug concentration and the dose administered is directly proportional (linear pharmacokinetics).
   (1) Determine the peak time and peak drug concentration following oral administration of a 250 mg tablet. (4 分)
   (2) Are the peak time and peak drug concentration influenced by the oral dose administered? What is your rationale? (4 分)
   (3) Determine the absorbable amount of drug remaining at the site of administration and the amount of drug in the body at a time when the rate of absorption is equal to the rate of elimination for orally administered dose of 250 mg via tablet. (4 分)
   (4) Determine the rate of absorption and the rate of elimination at peak time following the administration of a 500 mg tablet. (4 分)
   (5) What will the peak time in the renal impaired patient following the oral administration of a 500 mg tablet? If the elimination half-life is reported to be 9 h in a patient with renal impairment. (4 分)

試題隨卷繳回