1. (本題組共 25 分)

A 50-kg woman was given a single intravenous (I.V.) dose of a drug at a dose level of 2 mg/kg. The pharmacokinetics of the plasma drug concentration-time curve for this drug fits a one-compartment model. The equation of the curve that best fits the data is $C_p = 78e^{-0.46t}$.

Determine the following (assume units of μg/ml for Cp and hour for t):

(a) What is the half-life ($t_{1/2}$)? (5 分)

(b) What is the total clearance (CL)? (5 分)

(c) How long would it take for 90% of this drug to be eliminated? (5 分)

(d) If this patient was given an intravenous (IV) infusion for 6 hours of this drug at a rate of 2 mg/hr. What is the concentration of the drug in the body 2 hours after cessation of the infusion? (5 分) ($e^{-0.92} = 0.4$; $e^{-1.5} = 0.223$; $e^{-3} = 0.05$)

(e) If this patient was given by IV multiple dosing; 100 mg was injected every 6 hours for 6 doses. What was the plasma drug concentration 4 hours after the 6th dose (i.e., 40 hours later)? (5 分) ($e^{-2.76} = 0.063$; $e^{-1.84} = 0.159$)

2. (本題組共 20 分)

According to the literature, the oral bioavailability of drug-A is 90% and its elimination half-life is 1 hour. When this drug is given 100 mg orally, the total amount of unchanged drug recovered in the urine is 60 mg and the total amount of metabolite recovered in the urine is 30 mg.

Drug-A was given to a male patient (50 kg) by intravenous infusion at a rate of 300 mg/hr. At 7 hours after infusion, the plasma drug concentration was 11 μg/ml.

(a) What is the total body clearance for this drug? (5 分)

(b) What is the renal clearance for this drug? (5 分)

(c) What is the volume of distribution of this drug? (5 分)

(d) What is the probable mechanism for renal clearance of this drug? (5 分)

3. (本題 5 分)

Proton pump inhibitors (PPIs) such as omeprazole are frequently used in the treatment of *Helicobacter pylori* (幽門螺旋桿菌) infection. The major purpose of using PPIs in this treatment is to elevate intragastric pH to maintain the stability of antibiotics. It is known that most PPIs are metabolized by CYP2C19. Explain the impact of CYP2C19 polymorphism on the treatment of *Helicobacter pylori* infection.

見背面

4. (本題組共 20 分)
Membrane transporters play important roles in pharmacokinetics (i.e., ADME properties) of drugs. Describe the roles of at least one membrane transporter on the followings:
(a) Intestinal absorption of drugs (5 分)
(b) brain distribution of drugs (5 分)
(c) hepatic metabolism of drugs (5 分)
(d) renal excretion of drugs (5 分)

5. (本題組共 10 分)
Explain the followings about the population pharmacokinetics.
(a) What is NONMEM? (5 分)
(b) Describe the applications of population pharmacokinetics in drug development. (5 分)

6. (本題組共 15 分)
Define nonlinear pharmacokinetics.
(a) Describe the rate of change in the plasma drug concentration with respect to time, $\frac{dC_p}{dt}$, under linear and nonlinear conditions. (10 分)
(b) When a drug is given by intravenous bolus, draw a plasma concentration-time profile if this drug is eliminated nonlinearly? (use log scale in the Y-axis). (5 分)

7. (本題 5 分)
Explain "effect compartment" and its applications in PK/PD modeling.

試題隨卷繳回