國立臺灣大學 105 學年度碩士班招生考試試題

1. The followings are the pharmacokinetic properties of drug-A.

Fraction of absorption > 95%

F = 5%

f_u = 3-15%

Vd = 2.5 L/kg

Metabolic enzymes: CYP2D6, CYP3A4, CYP1A2

Elimination half-life $t_{1/2}$ = 6.5 hrs (2-32 hrs)

Active metabolite = 5-hydroxy-drug-A

fe < 1%

Total CL = 1000-1300 ml/min

(a) Describe these properties in terms of each process in ADME (20 分)

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

2. Simvastatin is a HMG-CoA reductase inhibitor used to lower blood cholesterol levels. It is known that simvastatin is mainly metabolized by CYP3A4 and is a substrate of OATPs. Patients receiving simvastatin have been reported to have incidence of muscle pain or myalgia. Describe and explain the pharmacokinetic factors that may lead to the occurrence of adverse effects caused by simvastatin. (10 分)

3. Digoxin is a P-glycoprotein (P-gp) substrate and quinidine is a P-gp inhibitor.

(a) Describe the influence of canalicular and sinusoidal sites of hepatocytes, respectively, on the plasma levels of digoxin after oral administration. (10 分)

(b) What changes in AUC and Cmax would you expect for digoxin when co-administered with quinidine? (5 分)

4. Explain why ka is often greater than k with normal drugs? (5 分)

5. A single oral dose (100 mg) of an antibiotic was given to an adult male patient (43 years, 72 kg) with an oral bioavailability of 80%. The pharmacokinetics of this drug fits a one-compartment open model. The equation that best fits the pharmacokinetics of the drug is $Cp = 45(e^{-0.17t} - e^{-1.5t})$ Cp is in μg/mL and the first-rate constants are h^{-1}. From the equation above, calculate (a) half-life ($t_{1/2}$) (5 分) and (b) Volume of distribution (Vd) (10 分).

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6. An antibiotic drug is to be given to an adult male patient (75 kg, 58 years old) by IV infusion. The drug is supplied in sterile vials containing 30 mL of the antibiotic solution at a concentration of 125 mg/mL. Assume this drug follows the pharmacokinetics of a one-compartment open model; the apparent volume of distribution of this drug is 0.5 L/kg and the elimination half-life is 3 hours.
(a) What rate in milliliters per hour would you infuse this patient to obtain a steady-state concentration of 20 μg/mL? (5 分)
(b) How long should it take to reach the steady-state concentration? (5 分)

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? (10 分)
(b) Explain why blood concentrations did not reflect clinical outcomes? (5 分)

試題隨卷繳回