

※ 考生請注意：本試題不可使用計算機。請於答案卷(卡)作答，於本試題紙上作答者，不予計分。

1. Which of the following is directly proportional to the infusion rate? (6%)

- (A) Systemic clearance
- (B) Number of elimination half-lives required to reach a fraction of steady state
- (C) Steady state plasma concentration
- (D) Time required for reaching steady state

2. The elimination half-life and the apparent volume of distribution of amikacin are reported to be 3 hr and 0.25 L/kg, respectively. Determine the amikacin plasma concentration at 4 hr following the intravenous bolus dose of 6.25 mg/kg. (6%)

- (A) 25  $\mu\text{g/L}$
- (B) 6.25 mg/L
- (C) 9.92 mg/L
- (D) 19.75 mg/L

3. Levofloxacin is reported to be completely eliminated in unchanged form into the urine and its elimination half-life is 7 hr. Determine the *amount* of levofloxacin eliminated *in urine* at 14 hr following the intravenous bolus administration 6.25 mg/kg dose to a subject weighing 80 kg. (6%)

- (A) 125 mg
- (B) 250 mg
- (C) 375 mg
- (D) 500 mg

4. Prazosin is an antihypertensive agent. The systemic clearance and the absolute bioavailability of prazosin are reported to be 0.15 L/hr/kg and 0.6, respectively. If it is desired to attain the "average" steady-state prazosin plasma concentration of 5 ng/mL in a subject weighing 80 kg, determine the prazosin dose to be administered orally once daily. (6%)

- (A) 12  $\mu\text{g/kg}$
- (B) 18  $\mu\text{g/kg}$
- (C) 24  $\mu\text{g/kg}$
- (D) 30  $\mu\text{g/kg}$

5. Which of the following will be observed if the creatinine clearance value in a patient drops below 50 mL/min and the intravenously administered drug is being eliminated by the kidneys? (6%)

- (1) Longer elimination half-life
- (2) Higher elimination rate constant
- (3) Lower systemic clearance
- (4) Higher initial elimination rate

- (A) 1 and 3 only
- (B) 1 and 4 only
- (C) 2 and 3 only
- (D) All of the above

6. Which of the following is applicable following an intravenous administration of an identical dose of a drug, at a dosing interval equal to one half-life of the drug, to a healthy subject? (6%)

- (1) Peak steady state plasma concentration will be twice the initial plasma concentration for the first dose.
- (2) Accumulation will be equal to 2.
- (3) Fluctuation will be equal to 2.
- (4) Difference between peak and trough steady state concentrations is equal to the administered dose.

- (A) 1 and 3 only
- (B) 2 and 4 only
- (C) 1, 2 and 3 only
- (D) All of the above

7. Describe the Biopharmaceutics Classification System and its applications. (14%)

8. Giving the following information, what will be the total solubility of an antibiotic, which is a weak acid, in an aqueous solution of pH 6? If a pharmacist wants to prepare a 3% solution of the antibiotic as an ophthalmic solution, at least what pH should the solution be adjusted to? (10%)

Molecular weight of the antibiotic    285 (salt)    263 (free acid)

Acid form solubility                      3.1 mg/mL

$K_a$                                                $5.86 \times 10^{-6}$

( $\log 2 = 0.301$ ,  $\log 3 = 0.477$ ,  $\log 5 = 0.699$ ,  $\log 7 = 0.845$ )

9. Reduction of particle size of a solid substance to a finer state is used to increase the dissolution rates of a drug and enhance the absorption of drugs. If a powder consists of 10  $\mu\text{m}$  diameter spheres is reduced to particles of 1  $\mu\text{m}$  diameter, how many folds of increase in the dissolution rate of the powder will be produced? Explain using the equation governing the effect of particle size on dissolution rate. (10%)

10. The degradation of a new anticancer drug follows first-order kinetics and has first-order degradation rate constants of 0.0001 per hour at 60°C and 0.0009 at 80°C. What are its  $E_a$  and  $Q_{10}$ ? (10%)

$$(R = 1.987 \text{ cal/deg/mol})$$

11. A pharmaceutical company determines methotrexate content in a batch of tablets using HPLC methods. The average weight of methotrexate tablets is 100 mg/tab. A technician sampled 20 tablets from the batch, and triturated them to fine powders. He then accurately weighed 201.5 mg of the powder and diluted with HPLC mobile phase to a total volume of 100 mL. After centrifugation, 5 mL of the supernatant is further diluted with the mobile phase to 50 mL. Representative data for standard curve from HPLC analysis of methotrexate are as follows:

Concentration ( $\mu\text{g/mL}$ )	0	5	10	15	20
Response (peak height in units)	0	1310	2600	3895	5190

If the sample provides a peak height response of 2550, what is the methotrexate content per tablet? (10%)

12. Describe the characteristics of protein therapeutics that require special consideration in designing their delivery systems. What strategies can be used to deliver these drugs? (10%)