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UNIVERSITY OF RUHUNA – FACULTY OF ALLIED HEALTH SCIENCES
DEPARTMENT OF PHARMACY
FOURTH BPHARM PART II EXAMINATION – OCTOBER 2021
PH 4242 BIOPHARMACEUTICS (SEQ)

TIME: TWO HOURS

INSTRUCTIONS

- There are **four (04)** questions in Part **A** and Part **B** of SEQ paper.
- Answer all questions.
- No paper should be removed from the examination hall.
- Do not use any correction fluid.
- Use illustrations where necessary.

PART A

1. A new trial medicine is given in a single IV bolus of 4 mg/kg to five healthy male adults who are at 23 to 38 years (average weight 75 kg) of age. The pharmacokinetics of the plasma drug concentration–time curve for this drug is best fits to a one-compartment model. The equation of the curve that best fits is,

$$C_p = 78e^{-0.46t}$$

1.1. Determine the following (assume units of µg/mL for C_p and hour for t):

1.1.1. Elimination half-life t ½ (***10 marks***)

1.1.2. Volume of distribution V_D (***10 marks***)

1.1.3. Plasma level of the drug after 4 hours (***10 marks***)

1.1.4. Amount of drug left in the body after 4 hours (***10 marks***)

1.1.5. Assuming the drug is no longer effective when levels decline to less than 2 µg/mL, when should you administer the next dose? (***10 marks***)

1.2. A female patient (35 years old, 65 kg) with normal renal function is to be given a drug by IV infusion. According to the literature, the elimination half-life of this drug is 7 hours and the apparent V_D is 23.1% of body weight. The pharmacokinetics of this drug assumes a first-order process. The desired steady-state plasma level for this antibiotic is 10 µg/mL.

1.2.1. Assuming no loading dose was given, how long after the start of the IV infusion would it take to reach 95% of the C_{SS}? (***05 marks***)

1.2.2. What is the loading dose for this antibiotic? (***05 marks***)

1.2.3. What is the infusion rate for this drug? (***10 marks***)

1.2.4. What is the total body clearance? (***10 marks***)

1.2.5. If the patient suddenly develops partial renal failure, how long would it take for a new steady-state plasma level to be established (Assume that 95% of the C_{SS} is a reasonable approximation)? (***10 marks***)

1.2.6. If the total body clearance declined 50% due to partial renal failure, what new infusion rate would you recommend to maintain the desired steady-state plasma level of 10 µg/mL? (***10 marks***)

2. A pharmacist dissolved a few milligrams of new antibiotic drug in to exactly 10 mL of distilled water and placed the solution in a refrigerator (5°C). During various time intervals, the pharmacist removed 10 mL aliquot from the solution and measured the amount drug contained in each aliquot. Following table represent the data

Antibiotic concentration (µg/ml)	**Time (hr)**
84.5	0.5
81.2	1
74.5	2
61	4
48	6
35	8
8.7	12

2.1. What is the order of rate of decomposition of the drug composition (Zero order or First Order)? (***25 marks***)

2.2. What is the rate of decomposition of this anti-biotic? (***25 marks***)

2.3. How many milligrams of antibiotics were in the original solution prepare by the pharmacist (concentration at t=0)? (***25 marks***)

2.4. Write the equation for the line that best fits the experimental data. (***25 marks***)

PART B

3.

3.1. Define the term drug excretion? (***05 marks***)

3.2. List five factors that affect the excretion of a drug. (***10 marks***)

3.3. Briefly describe the characteristics of a drug that follows the first order kinetics of elimination. (***25 marks***)

3.4. The drug P is an oral antiepileptic agent. Pharmacokinetic parameters of P are given in the below table.

Pharmacokinetic Parameters of P	**Value**
Absorption	100%
Protein binding	64%
Apparent volume of distribution (V_{app})	30L
First order elimination half life	12 hours

3.4.1. If 250 mg daily dose of this medicine is given to a patient (75 kg body weight), calculate the fraction of P bound to tissues at the steady state. Consider plasma volume and tissue volume of P is equal is 20% and 50% of V_{app} respectively. (***25 marks***)

3.4.2. Calculate the total clearance of the medicine P (***15 marks***)

3.4.3. If the renal clearance of medicine P is 0.9 L h^{-1}, calculate the fraction of drug metabolized by liver (Assume the drug is metabolized by liver and excreted via kidneys). (***20 marks***)

4.

4.1. The medicine X is an antipyretic. Below table shows urinary excretion data of the medicine X. Calculate the percentage relative bioavailability of the oral tablet compared to the oral solution? (***15 marks***)

Dosage form of X	Dose (mg/kg)	Cumulative urinary drug excretion (D^{∞}_{u}) during 0-72h (mg)
Oral tablet	10	395
Oral capsule	8	420
Oral solution	4	458
IV solution	0.8	22

4.2. Briefly discuss the importance of bioavailability studies in drug designing. (***20 marks***)

4.3. Determination of plasma drug concentration is a direct method use to assess the bioavailability of a medicine. Explain the statement. (***40 marks***)

4.4. Briefly describe 'non-replicated parallel study design' use in bioequivalence studies. (***25 marks***)

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