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UNIVERSITY OF RUHUNA – FACULTY OF ALLIED HEALTH SCIENCES
DEPARTMENT OF PHARMACY
FOURTH BPHARM PART II EXAMINATION – JUNE/AUGUST 2020
PH 4242 BIOPHARMACEUTICS (SEQ)

TIME: TWO HOURS

INSTRUCTIONS

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

PART A

1.

1.1 Briefly explain **three** factors that would affect the protein binding of the drugs. (***15 marks***)

1.2 Mr. A (60-year-old, 70 Kg body weight) was prescribed with drug X and drug Y, for the treatment of a wound in his leg. The details related to the doses are given below.

Drug X – 600 mg daily tab orally

Drug Y – 400 mg daily tab orally

If the plasma protein binding of drug Y is 40%, calculate the fraction of the drug bound to tissues. Write any assumptions you would make in this calculation. Consider the drug Y has 100% absorption.

Plasma volume is 5L

Tissue volume is 12L.

Apparent volume of distribution is 25 L.

(***20 marks***)

1.3 Explain the term 'total body clearance'. (***05 marks***)

1.4 The apparent volume of distribution (V_D) of the drug X is 23% of the body weight. The elimination half-life of the drug X is 4 hours and the oral bioavailability is 85% of the dose. If the creatinine clearance of this patient is 98 mL/min and the excretion rate of the drug in the urine (unchanged) is 77% of the absorbed dose, answer the following,

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1.4.1 What is the total body clearance of drug X? (*15 marks*)

1.4.2 What is the renal clearance of drug X ? (*15 marks*)

1.4.3 Briefly explain the possible mechanism for renal clearance of the drug X. (*15 marks*)

1.4.4 "Clearance" is a better measurement of drug elimination than "the excretion rate" of the drug. Do you agree with this statement? Justify your answer. (*15 marks*)

2.

2.1.

2.1.1 Briefly describe what is a phase II metabolic reaction. (*15 marks*)

2.1.2 "Paediatric and geriatric patients are special categories in prescribing". Explain the statement considering the metabolism of drugs. (*20 marks*)

2.2

2.2.1 What is absolute bioavailability and relative bioavailability? (*10 marks*)

2.2.2 Four different dosage forms containing the same antibiotic (AB) were given to 18 volunteer adult males (20-30 year-old, average weight 68kg) in a four-way crossover design study. Volunteers were fasted for 12 hours prior to the administration of the drug product. Urine samples were collected during 72 hours after the administration of the drug.

Dosage form of the antibiotic AB	Dose (mg/kg)	Cumulative urinary drug excretion (D^{∞}_u) during 0-72h (mg)
Oral tablet	5	355
Oral capsule	5	370
Oral solution	5	397
IV solution	0.4	18

2.2.2.1 Calculate the absolute bioavailability of the drug from the tablet.

2.2.2.2 What is the relative bioavailability of the capsule compared to the oral solution? (*25 marks*)

2.3 Write short notes on following.

2.3.1 Non-replicate, parallel study design

2.3.2 Clinical endpoint bioequivalence study (*30 marks*)

PART B

3. Answer all parts.

3.1. List **five** advantages of using intravenous infusions. ***(10 marks)***

3.2. Explain "Zero order reaction" using a graph. Give **two** appropriate examples. ***(15 marks)***

3.3. A woman weighted 55 kg, was given a single intravenous dose of an antibacterial drug at a dose of 8 mg/kg. Blood samples were taken at different time intervals and the concentration of the drug in the plasma (C_p) was determined. The plasma drug concentrations corresponding to the time are given below.

T (hours)	Cp (µg/mL)
0.25	8.21
0.5	7.87
1	7.23
3	5.15
6	3.09
12	1.11
18	0.40

3.3.1. Calculate the following pharmacokinetic parameters of the above drug.

3.3.1.1. Elimination rate constant (k_e) ***(25 marks)***

3.3.1.2. Volume of distribution (V_D) ***(15 marks)***

3.3.1.3. Elimination half-life ($t_{½}$) ***(05 marks)***

3.3.2. Calculate the time taken to eliminate 99.9% of this drug. ***(10 marks)***

3.3.3. Assuming that the antibacterial agent become ineffective at a plasma concentration less than 2 µg/ml, calculate the followings.

3.3.3.1. The duration of activity of this drug. ***(10 marks)***

3.3.3.2. The increased duration of activity, if the dose of the antibiotic is doubled. ***(10 marks)***

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4.

4.1. A 43- year-old adult male patient (80 kg) is to be given an antibiotic by intravenous infusion. According to the literature, the antibiotic has an elimination half-life ($t_{1/2}$) of 2 hrs and apparent volume of distribution (V_D) of 1.25 L/kg. The antibiotic is effective at a plasma drug concentration of 14 mg/L. If the drug is supplied in 5 mL ampules containing 150 mg/mL of the antibiotic.

4.1.1. Calculate the initial infusion rate that you recommend for this patient in milliliter per hour? ***(15 marks)***

4.1.2. Blood samples were taken from the patient at 12, 16, and 24 hours after starting the infusion. Using the data of the plasma drug concentrations shown below.

t (hours)	**C_p (mg/L)**
12	16.1
16	16.3
24	16.5

Calculate the total body clearance (Cl_T) and the elimination half-life of the antibiotic for this patient. ***(30 marks)***

4.2. "After reviewing pharmacokinetics data of a drug for a particular patient, the clinical pharmacist will have to adjust the infusion rate which is calculated using the data from literature." Explain this statement. ***(10 marks)***

4.3. The drug A, has an elimination half-life ($t_{½}$) of 8 hours, follows first order elimination kinetics. The apparent volume of distribution (V_D) is 400 mL/kg. If a single 600 mg dose is given to a 70 kg body weight female patient by rapid intravenous injection, calculate the expected plasma drug concentration after 24 hours of the dose. ***(20 marks)***

4.4. Describe "Human physiologic factors" that affects the absorption of a drug. **(25 marks)**

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