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UNIVERSITY OF RUHUNA – FACULTY OF ALLIED HEALTH SCIENCES

DEPARTMENT OF PHARMACY

FOURTH BPHARM PART II EXAMINATION – OCTOBER/NOVEMBER 2022

PH 4242 BIOPHARMACEUTICS -SEQ PAPER

TIME: TWO HOURS

INSTRUCTIONS

- Answer **all** questions in parts **A** and **B**.
- No paper should be removed from the examination hall.
- Do not use any correction fluid.
- Use illustrations where necessary.

PART A

1.

1.1 Biotransformation reactions of drugs are mainly in two types namely, synthetic and non-synthetic.

1.1.1 List three biochemical reactions belong to each of the types mentioned above. (***12 marks***)

1.1.2 Briefly describe what is meant by synthetic and non-synthetic biotransformation. (***06 marks***)

1.1.3 List three consequences of drug biotransformation. (***06 marks***)

1.2 Hepatic extraction ratio affects the bioavailability of an oral drug. Explain this statement giving appropriate examples. (***36 marks***)

1.3 The drug A is newly developed oral antibiotic. It has an intrinsic clearance of 9000 mL/min when given to a person whose hepatic blood flow is 1.2 L/min. Calculate below parameters for the drug, assuming complete absorption.

1.3.1 Hepatic clearance

1.3.2 Bioavailability factor

1.3.3 If the same patient develops a liver disease that reduces his hepatic blood flow to 0.8 L/min but does not affect intrinsic clearance, what is the hepatic drug clearance in this patient? (***40 marks***)

2.

2.1 A group of researchers are conducting a bioavailability study of a new brand of paracetamol oral formulation (Drug X). They plan to assess the plasma drug concentration of 50 healthy volunteers at selected time intervals after administering 1000 mg of drug X.

2.1.1 Draw the typical graph that the researchers would be able to plot at the end of this study. (***08 marks***)

2.1.2 Label four parameters on the graph that you would be able to determine from the graph drawn in 2.1.1. (***12 marks***)

2.2 The drug X is 70% protein bound and apparent volume of distribution (Vapp) is 40 L. It has a plasma volume (Vp) of 6 L and tissue volume of 15 L in a person with 50 kg body weight.

2.2.1 Briefly describe five factors that influence the binding of drug molecules to plasma proteins. (***15 marks***)

2.2.2 Calculate the fraction of drug X bound to tissues. (***15 marks***)

$$V_{app} = V_p + V_t\left(\frac{f_u}{f_{ut}}\right)$$

f_u= unbound fraction of drug in plasma

f_{ut} = unbound fraction of drug in tissues

2.2.3 If the first order elimination half-life of the drug X is 6 hours and 45% of the drug eliminated unchanged, calculate following parameters. (***50 marks***)

2.2.3.1 Total body clearance (Cl_T)

2.2.3.2 Elimination rate constant (k_e)

2.2.3.3 Renal clearance (Cl_R)

PART B

3.

A 80-kg woman was given a single IV dose of drug Z at a dose level of 6 mg/kg. Blood samples were taken at various time intervals. The concentration of the drug (C_p) was determined in the plasma and the following data were obtained.

T (hours)	C_p (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

3.1 Calculate the Vd, K and T ½ of this drug. (***50 marks***)

3.2 This drug Z is only effective at a plasma concentration greater than or equal to 2 µg/ml. What is the duration of activity of this drug? (***20 marks***)

3.3 How long would it take for 80% of this drug to be eliminated? (***15 marks***)

3.4 Calculate the duration of activity of this drug if dose is doubled. (***15 marks***)

4.

A drug H is to be given to a 65 years old male patient (80 kg) by IV infusion. The elimination half-life is 8 hours and the apparent volume of distribution (Vd) is 1.5 L/kg. Manufacturer provides the drug in 60-ml ampules at a drug concentration of 15 mg/ml. The desired steady-state drug concentration is 20 µg/ml.

4.1 What is the infusion rate that you would recommend for this patient? (***20 marks***)

4.2 What is the loading dose that you would you recommend for this patient? By what route of administration would you give the loading dose? (***20 marks***)

4.3 Why should a loading dose be recommended? (***10 marks***)

4.4 According to the manufacturer, the recommended starting infusion rate is 20 mL/hr. Do you agree with this recommended infusion rate for your patient? Give a reason for your answer. (***10 marks***)

4.5 If you were to monitor the patient's serum drug concentration, when would you request a blood sample? Give a reason for your answer. (***20 marks***)

4.6 The observed serum drug concentration is higher than anticipated. Give two possible reasons based on your understanding of pharmacokinetic principles that would account for this observation. (***20 marks***)

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