UNIVERSITY OF JAFFNA, SRI LANKA

FACULTY OF ALLIED HEALTH SCIENCES

FOURTH YEAR SECOND SEMESTER EXAMINATION IN BPharmHons-2023

PHABP 4212 BIOPHARMACEUTICS & PHARMACOKINETICS

Date: 14.05.2025 **Time: 02 hours**

ANSWER ALL FOUR QUESTIONS

ANSWER PART A, B & C IN SEPARATE ANSWER BOOKS.

PART A

1.

1.1 List the applications of pharmacokinetic models. **(25 Marks)**

1.2 Write a short note on the followings.

1.2.1 Physiological model. **(25 Marks)**

1.2.2 Two-compartment model. **(25 Marks)**

1.2.3 Non-compartmental model. **(25 Marks)**

2.

2.1 Define the following terms.

2.1.1 Apparent volume of distribution. **(10 Marks)**

2.1.2 Elimination half-life. **(10 Marks)**

2.1.3 Steady-state drug concentration. **(10 Marks)**

2.1.4 Bioavailability. **(10 Marks)**

2.2 An antibiotic is to be given to an adult male patient (58 years old, body weight of 75 kg) by IV infusion. The elimination half-life is 8 hours and the apparent volume of distribution is 1.5 L/kg. The drug is supplied in 60 mL ampoules at a drug concentration of 15 mg/mL. The desired steady-state drug concentration is 20 mg/mL.

2.2.1 Calculate the recommended infusion rate in mg/h for this patient? **(15 Marks)**

2.2.2 Why should a loading dose be recommended? **(05 Marks)**

2.2.3 What is the recommended loading dose for this patient? **(10 Marks)**

2.2.4 According to the manufacturer, the recommended starting infusion rate is 15 mL/h. Do you follow this recommended infusion rate for this patient? Explain your answer. **(30 Marks)**

PART B

3.

3.1 Differentiate pharmacokinetics and pharmacodynamics. **(10 Marks)**

3.2 Explain any five (05) routes of drug administration with examples for each. **(40 Marks)**

3.3 What is the role of cytochrome P450 enzymes in drug metabolism? **(10 Marks)**

3.4 Explain the factors that influence the activity of cytochrome P450 enzymes. **(20 Marks**

3.5 Explain the Phase II reactions in drug metabolism. **(20 Marks)**

PART C

4.

4.1 Outline the recommended procedure for conducting a bioequivalence study under fasting conditions. **(30 Marks)**

4.2 A single-dose, randomized, open-label, 3-period crossover study was conducted to compare 2 branded generic products (A and B) and the branded innovator product of valsartan 160 mg immediate-release tablets among 18 healthy volunteers under fasting conditions. Each study period was separated by a 5-days washout period. The results of this study are summarized in Table 1 and Table 2. No treatment, period, or sequence effects were found in the statistical analysis using ANOVA for C_{max}, AUC_0^t and AUC_0^∞.

Table 1 Pharmacokinetic parameters of three brands of single-dose valsartan 160 mg immediate-release tablets in healthy volunteers (n = 18)

Pharmacokinetic Parameters	Mean (± Standard deviation)		
	Brand A	Brand B	Branded innovator (Reference)
C_{max} (μg/mL)	6.11 (2.98)	5.94 (2.04)	5.94 (2.37)
AUC_0^t (μg·h/mL)	33.18 (17.50)	33.87 (13.77)	34.52 (15.74)
AUC_0^∞ (μg·h/mL)	35.32 (17.54)	35.89 (14.09)	36.60 (15.68)
T_{max} (h)	2.71 (0.86)	2.24 (1.07)	2.90 (1.07)
$T_{1/2}$ (h)	4.23 (1.55)	4.25 (1.21)	4.31 (0.99)

Table 2 Summary statistics of log-transformed pharmacokinetic properties of three brands of single-dose valsartan 160 mg immediate-release tablets in healthy volunteers (n = 18)

Pharmacokinetic parameters	90% confidence interval	
	Brand A vs Reference	Brand B vs Reference
C_{max}	96.93 (81.18–115.74)	101.12 (84.69–120.73)
AUC_0^t	91.67 (77.27 –108.75)	99.33 (83.72–117.84)
AUC_0^∞	92.85 (79.32 –108.70)	98.81 (84.40–115.67)

4.2.1 What are meant by sequence, period and washout period in a crossover bioequivalence study? **(15 Marks)**

4.2.2 Based on the results of this study, determine whether the two branded generic products (A and B) are bioequivalent to the branded innovator. **(25 Marks)**

4.2.2 Justify whether a bioequivalence study is necessary for immediate-release valsartan 80 mg tablets manufactured by the pharmaceutical manufacturers of the two branded generics (A and B). **(20 Marks)**

(Valsartan is a Biopharmaceutics Classification System (BCS) category III drug).

4.3 List two (02) instances that require replicated crossover study design for evaluating the bioequivalence. **(10 Marks)**