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UNIVERSITY OF RUHUNA – FACULTY OF ALLIED HEALTH SCIENCES

DEPARTMENT OF PHARMACY

FOURTH BPHARM PART II EXAMINATION – DECEMBER 2018

PH 4242 BIOPHARMACEUTICS (SEQ)

TIME: TWO HOURS

INSTRUCTIONS

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

PART A

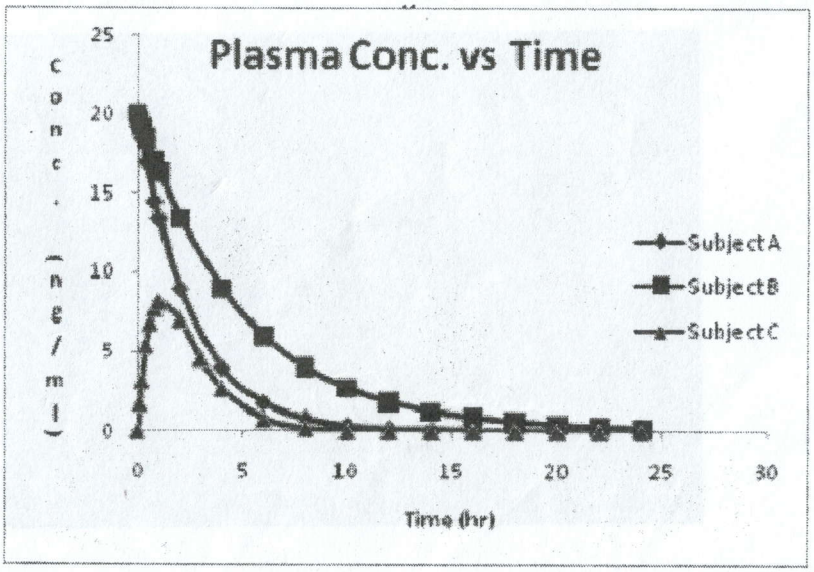
1.

1.1. List **five** physicochemical and **five** physiological factors which affect the drug absorption. (***20 marks***)

1.2. Discuss **one** factor from each listed in 1.1. (***20 marks***)

1.3. Briefly describe characteristic physical properties that determines the rate of passive diffusion and how these properties explain the anatomical characteristics of the intestine which is critical for drug absorption. (***20 marks***)

1.4. **Figure** given below shows the plasma concentration versus time profiles of three subjects (A, B and C) after the administration of the similar amount of **mg** as dose of a drug X.



1.4.1. From the plasma concentration versus time profiles, what is a possible route of drug administration for each of the subject? Give reasons for your answer. ***(10 marks)***

1.4.2. In which subject the drug X is eliminated faster? ***(10 marks)***

1.5. Write short notes on following.

1.5.1. pH partition hypothesis ***(10 marks)***

1.5.2. Hydrostatic pressure ***(10 marks)***

2.

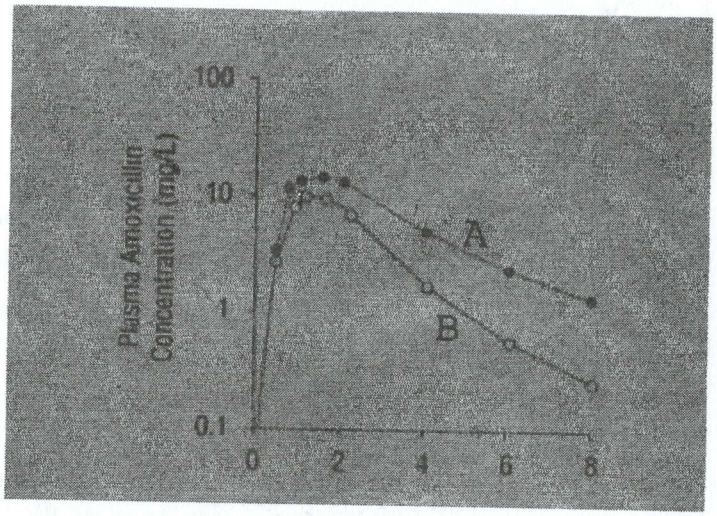
2.1. Drug A and drug B are both lipophilic and low molecular weight drugs. The plasma protein binding for drug A is 95% and for drug B is 5%. Both drug A and drug B have 75% tissue binding. The same doses (200 mg) of the two drugs are given to a healthy volunteer through IV bolus at two different times (2 weeks of wash out period in between). Assume the values for V_p = 3 L and V_T =38 L for both drugs.

2.1.1. Calculate volume of distribution for each drug. ***(10 marks)***

2.1.2. Calculate initial concentration for each drug. ***(10 marks)***

2.1.3. Suppose that the healthy volunteer got liver disease, which results in a two-fold decrease in plasma protein binding for both drug A and drug B (assume tissue binding remains the same), recalculate the volume of distribution and initial free drug concentration of drug A and drug B. What conclusions could you make? ***(20 marks)***

2.2. The image given below shows concentration-time profile when administering amoxicillin with and without Probenecid.



Assuming that amoxicillin is eliminated solely via the kidneys and Probenecid inhibits its active renal secretion.

Identify the curve that corresponds to amoxicillin when administrated alone or in combination with Probenecid. Justify your answer by comparing the pharmacokinetic parameters, such as the peak plasma concentration (Cmax), half-life (t1/2), renal clearance (CLR) and total clearance between the two scenarios. ***(20 marks)***

2.3. Write short notes on following.

2.3.1. Functions of bio-transformation ***(20 marks)***

2.3.2. Relative bio availability ***(20 marks)***

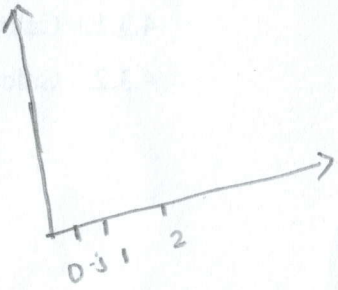
PART B

3.

3.1. Compare and contrast zero-order and first-order kinetic reactions. ***(25 marks)***

3.2. A 60 kg woman was given a single intravenous dose of an antibacterial drug. Drug was administered at the dose level of 5 mg/kg. Blood samples were taken at different time intervals and the concentration of drug in the plasma (C_p) was determined. The plasma drug concentration corresponding to the time are given below.

Time (hours)	C_p (µg/mL)
0.5	7.87
1	7.23
2	6.1
4	4.34
8	2.19
11	1.32
18	0.4



3.2.1. Calculate the following pharmacokinetic parameters of above drug,

3.2.1.1. Elimination rate constant (k) ***(15 marks)***

3.2.1.2. Volume of distribution (V_D) ***(20 marks)***

3.2.1.3. Elimination half-life ($t_{1/2}$) ***(05 marks)***

3.2.2. Predict the body water compartment that this drug might occupy and state the reasons for the prediction. ***(15 marks)***

3.2.3. If this antibacterial agent is not effective when the plasma concentration is less than 1.5 µg/mL, calculate the duration of activity. ***(10 marks)***

3.2.4. Calculate the time taken for 99% of this drug to be eliminated. ***(10 marks)***

4.

4.1. A steady state serum concentration of 18 mg/L was measured when the antibiotic (drug A) was given by intravenous infusion for an adult male at a rate of 5.5 mg/kg per hour for 4 hours. The body weight of the adult is 72 kg.

4.1.1. Calculate the total body clearance (CL_T) for the drug A. (***10 marks***)

4.1.2. Sketch a plasma drug concentration-time curve for above drug A starting from time zero. Your answer should indicate reduction pattern of the plasma drug concentration after the infusion was stopped. (***10 marks***)

4.1.3. When the IV infusion was discontinued after 4 hours, the drug A concentration decreased to a level of 2 mg/mL at 6 hours after the start (initiation) of infusion. Calculate the elimination half-life of the drug A. (***20 marks***)

4.1.4. Calculate the apparent volume of distribution (V_D) for drug A. (***10 marks***)

4.2. Briefly describe the distribution a drug in two-compartment open model related to intravenous bolus administration. (Note: Draw appropriate plasma level-time curve).

(***25 marks***)

4.3. A 55 years-old male patient receives 1.5 g of an antibiotic every 8 hours by repetitive IV injection. The elimination half-life of the drug is 6 hours. Assume the drug distribution follows one-compartment model and the volume of distribution is 25 L.

4.3.1. Calculate the maximum and minimum amounts of drug in the body. (***15 marks***)

4.3.2. Calculate the minimum and maximum plasma concentrations of the drug.

(***10 marks***)

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