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UNIVERSITY OF RUHUNA – FACULTY OF MEDICINE

ALLIED HEALTH SCIENCES DEGREE PROGRAMME

FOURTH BPHARM PART II EXAMINATION – JUNE 2017

PH 4242 BIOPHARMACEUTICS (SEQ)

TIME: TWO HOURS

INSTRUCTIONS

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

1. Answer **all** parts.

1.1. Define the term pharmacokinetics. (***10 marks***)

1.2. State the relationship between the rate and the concentration in first order reactions in relation to one compartment model. (***05 marks***)

1.3.

1.3.1. Define the term half-life of a drug.

1.3.2. Using $C = C_0 \, e^{-kt}$, derive an equation for the half-life.

(***15 marks***)

1.4.

1.4.1. What is volume of distribution? (***10 marks***)

1.4.2. Define the term clearance. (***10 marks***)

1.4.3. Define the terms of an equation used to calculate clearance. (***10 marks***)

1.5. Drug X was given as an IV bolus and plasma concentration had been measured at different time intervals after administration.

Time (Hours)	C_p (mg/L)
1	243
2	200
3	165
4	135
5	110

1.5.1. Plot plasma concentration over time graph in a semi-log paper and calculate the elimination rate constant (Ke). (***20 marks***)

1.5.2. Calculate the half-life using;

1.5.2.1. Graphdrawn in 1.5.1. (***05 marks***)

1.5.2.2. Elimination rate constant (Ke). (***05 marks***)

1.5.3. If the volume of distribution is 8 L, Using the graph, calculate the dose to be injected.

(***10 marks***)

2. Answer **all** parts.

2.1. Define 'high solubility and permeability' as per Food and Drug Administration (FDA)? ***(20 marks)***

2.2. Define dissolution and disintegration in relation to oral dosage forms. ***(15 marks)***

2.3. Briefly explain **two** rate limiting factors for permeation of drugs. ***(15 marks)***

2.4. Mention **two** ways of increasing permeability of drugs. ***(15 marks)***

2.5. Mention **three** factors to be considered in designing an IV dosage form. ***(15 marks)***

2.6. Oral bioavailability of drug X is 80%. It is assumed that total amount of bioavailable dose is distributed evenly in plasma without any loss due to distribution, metabolism or excretion in first 2 hours. 10 mg of drug molecules are absorbed in to the blood stream in every 10 minutes irrespective of the amount remaining to be absorbed in gastric juice during first two hours. ***(20 marks)***

Calculate the followings,

2.6.1. The order of absorption kinetics.

2.6.2. The total amount of drugs in plasma at 2 hours.

2.6.3. The total dose administered.

3.

3.1. Following table shows some pharmacokinetic data regarding drug absorption following an oral intake of a new synthetic antibiotic drug.

Condition	C_{max} (ng/ml)	$AUC_{0\text{-}24\ hrs}$ (ng. h/ml)	t_{max} (minutes)
Fasting	811±317	417±135	14±8
With antacid	689±315	349±108	20±14
With high fat diet	303±176	373±111	64±79

3.1.1. What do you understand by bioavailability of a drug? ***(10 marks)***

3.1.2. What additional data you can gain from relative bioavailability data which you cannot gain from absolute bioavailability data? ***(15 marks)***

3.1.3. What is the effect of antacid and high fat diet on the bioavailability of this new drug? ***(20 marks)***

3.1.4. Comment on how this food and concurrent administration of an antacid affects on rate and extent of absorption of the new drug. ***(02 marks)***

3.2. Consider following data for a newly developed oral tablet formulation.

Tested drug product	Dose (mg)	AUC (ug.hr/ml)	Standard deviation
Oral Tablet	200	89.5	19.7
Oral Solution	200	86.1	18.1
IV/Bolus injection	50	37.8	5.7

3.2.1. Calculate relative bioavailability and absolute bioavailability using above data. (***18 marks***)

3.2.2. Give reasons to observe relative bioavailability data greater than 100% in some instances. (***10 marks***)

3.2.3. Give reasons not to achieve 100% bioavailability with oral drugs compared to IV bolus drugs. (***10 marks***)

3.2.4. What is meant by two sequence, cross over, open labeled, two period bioequivalence study? (***10 marks***)

3.2.5. What can you say about the clinical response of two pharmaceutical equivalents that are not bioequivalent? (***05 marks***)

4.

4.1. Briefly outline the nomenclature of cytochrome P450 enzymes and its subtypes. (***15 marks***)

4.2. Cytochrome P450 shows variant genes in some individuals. Describe the effect of these variant genes in relation to drug metabolism in the liver. (***15 marks***)

4.3. After a drug is absorbed systemically from the site of administration, the drug molecules are distributed throughout the body by the systemic circulation.

4.3.1. How does partition coefficient of a drug affects on drug distribution? (***05 marks***)

4.3.2. State reason(s) for rapid uptake of drugs into some tissues, and slower uptake to other tissues. (***10 marks***)

4.3.3. Are all rapidly absorbed drugs into tissues accumulate in the tissues? (***05 marks***)

4.3.4. What physical and chemical characteristics of a drug that would increase or decrease the uptake of the drug into the brain or cerebral spinal fluid? (***05 marks***)

4.4. A new drug has been screened to find the metabolic pathway of the drug. Most of the drug metabolites are conjugates which are found in the urine. What are metabolic pathways that this drug can undergo? Briefly describe using appropriate examples. (***20 marks***)

4.5. Liver extraction ratio is defined as the ratio of the hepatic clearance of a drug to the hepatic blood flow.

4.5.1. Why does a drug with high hepatic extraction ratio (eg: Propranolol) show higher bioavailability in conditions such as congestive heart failure? ***(10 marks)***

4.5.2. Why does a drug with high extraction ratio demonstrate greater differences between individuals after oral administration than that after intravenous administration? ***(15 marks)***

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