UNIVERSITY OF RUHUNA – FACULTY OF ALLIED HEALTH SCIENCES

DEPARTMENT OF PHARMACY

FOURTH BPHARM PART II EXAMINATION – JUNE 2018

PH 4242 BIOPHARMACEUTICS (SEQ)

TIME: TWO HOURS

INSTRUCTIONS

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

01. A new antibiotic drug was given in a single intravenous bolus of 4 mg/kg to five healthy male adults ranging in age from 23 to 38 years (average body weight 75 kg). The equation of the curve that best fits the data for the pharmacokinetics for the drug is,

$$C_p = 78\ e^{-0.46t}$$

Determine the following (Assume units of concentrations in μg/mL for C_p and time in hour for t).

1.1 Calculate the half-life ($t_{1/2}$) and volume of distribution for above drug. (***20 marks***)

1.2 How much drug is left in the body after four hours? (***15 marks***)

1.3 Predict what body water compartment this drug might occupy and explain why you made this prediction. (***15 marks***)

1.4 Assuming the drug is no longer effective when the levels decline to less than 2 μg/mL, when should you administer the next dose? (***10 marks***)

1.5 If the dose of the antibiotic was doubled, what would be the increase in duration of activity? (***15 marks***)

1.6 Briefly describe the drug distribution in two compartment open model using appropriate plasma level-time curve for single IV dose. (***25 marks***)

02.

2.1 An antibiotic is to be given an adult male patient (60 years, 75 kg) by IV infusion. The elimination half-life is 7 hours and the apparent volume of distribution is 1.2 L/kg. The drug is supplied in 60 mL ampules at a drug concentration of 12 mg/mL. The desired steady-state concentration is 20 μg/mL.

2.1.1. What infusion rate in mg/h would you recommend for this patient? (***15 marks***)

2.1.2. What loading dose would you recommend for this patient and by what route of administration would you give the loading dose? (***15 marks***)

2.1.3. Using appropriate plasma concentration-time graph, briefly explain, why a loading dose should be recommended. (***15 marks***)

2.1.4. If the patient suddenly develops impaired renal function, how long would it take to new steady-state plasma level to be established (assume that 95% of C_{ss} is reasonable approximation)? (*15 marks*)

2.2 A patient receives 500 mg of an antibiotic with an elimination half-life of 2 hours, every 8 hours by repetitive IV injection. Assume the drug is distributed according to a one compartment model and the volume of distribution is 25 L. Find the maximum, minimum and average amount of drug in the body. (*25 marks*)

2.3 Differentiate pharmacokinetic and pharmacodynamic drug interactions, giving **one** example for each. (*15 marks*)

03.

3.1 Drug A is a steroid that is used as an immunosuppressant. This drug is eliminated from the body via urine and the main metabolite that is found in urine is a conjugated product.

3.1.1 Discuss different methods that this drug can become the said metabolite. Elaborate your answer with known examples. (*20 marks*)

3.1.2 The usual dose of the drug is 20 mg per day. However in patients with known liver diseases the drug has shown toxicities. What would be the reason for this obervation? (*10 marks*)

3.1.3 Studies have shown that this drug accumulates in high concentrations in adipose tissues of patients. Discuss the reasons for different accumulation patterns of the drugs. (*20 marks*)

3.2 Discuss the differences between pharmaceutical equivalents and pharmaceutical alternatives. (*20 marks*)

3.3 "Generic Substitution" is substitution of a branded drug with the same drug marketed in Generic name. Explain the validity of this statement. (*10 marks*)

3.4 A student has identified **four** different reasons that could affect the absorption of a drug in the presence of food. Some of these reasons will support absorption where as some will act against it.

a) Concentration of surfactant has increased.
b) Increased degree of agitation due to presence of food.
c) Reduced thickness in diffusion layer.
d) Reduce rate of diffusion through diffusion layer.

3.4.1 What are the reasons that will support systemic absorption? Justify your answer. (***10 marks***)

3.4.2 If blood circulation is high immediately after a heavy meal and if the drug is highly metabolized in liver, what can you say about the amount of drug that actually reaches the systemic circulation? (***10 marks***)

04. An investigational new drug is being developed for oral administration. The drug is stable in gastrointestinal fluids and has good water solubility and membrane permeability. The drug is a weak acid and has pKa of 4.2 (stomach pH is 3 and small intestine pH is 6.8).

4.1 Based on pH partition hypothesis where do you expect the drug to be absorbed in the gastrointestinal tract? Explain your answer. (***10 marks***)

4.2 The absolute bioavailability of an orally administered solution of this drug is 20%.

4.2.1 What is absolute bioavailability? (***10 marks***)

4.2.2 Discuss the possible reasons for low oral bioavailability of this drug. (***20 marks***)

4.3 Human studies have shown that the oral bioavailability of a solution form and a suspension form of this drug is almost same.

4.3.1 What advantages can be gained from relative bioavailability studies? (***10 marks***)

4.3.2 What could be the possible reasons for this observed similarity? Clarify your answer. (***20 marks***)

4.4 A weak basic drug is poorly absorbed when it is administered 2 hours after the administration of cimetidine on H_2 blocker.

4.4.1 Describe this phenomenon. (***10 marks***)

4.4.2 Amount of drug excreted via urine is measured in a clinical study. When the urine is slightly acidic, amount of drug in urine is high compared to in alkaline urine.

4.4.2.1 Briefly describe the drug excretion via kidney. (***10 marks***)

4.4.2.2 How would you relate the above mentioned clinical observation with renal drug elimination? (***10 marks***)

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