Strathmore UNIVERSITY

STRATHMORE INSTITUTE OF MATHEMATICAL SCIENCES (SIMS)

MASTER OF SCIENCE IN BIOMATHEMATICS

END OF SEMESTER EXAMINATION

BMA 8204: BIOMEDICAL MATHEMATICS

Date: 8th December, 2023 Duration: $2\frac{1}{2}$ Hours

Answer **Question ONE** and any other **two** questions.

Question I (20 marks)

1. (a) Explain why Pharmacology is an essential field in healthcare and medicine and subsequently outline the distinctions between pharmacokinetics and pharmacodynamics.(**3 Marks**)

   (b) How can you quantify drug potency based on the concentration required to produce a specific effect? What is the significance of the EC50 (half-maximal effective concentration) in pharmacology? (**3 Marks**)

   (c) How does the route of administration affect the absorption of a drug into the bloodstream? (**3 Marks**)

   (d) Can a drug be considered effective if it has high efficacy but low potency, or vice versa? Use graphical illustration to explain. (**4 Marks**)

   (e) An enzyme with a K_m value of 5 mM has a reaction rate of 200 mol per minute at a substrate concentration of 0.5 mM. What is the maximum reaction rate that this enzyme can achieve when it is saturated with substrate? (**3 marks**)

(f) consider the chemical reaction represented by the following chemical notation:

$$D + E \rightleftharpoons_{k_2}^{k_1} C \longrightarrow^{k_3} P + E$$

Use the law of mass action to formulate the ODEs representing the reaction represented by the chemical notation above. (**4 Marks**)

Question 2 (20 marks)

2. (a) Explain the four main principles of pharmacokinetics (ADME) and their significance in drug therapy.(**4 marks**)

(b) When a drug is administered via the oral route, it undergoes dissolution and releases the medication within the gastrointestinal tract. Subsequently, the medications diffuse from there into the bloodstream, which then transports them to the specific site where their therapeutic effects are exerted. The movement of drugs within the body is conceptualized by treating various body regions as compartments and monitoring the drug's progression as it enters and exits each of these compartments. Figure 1 below shows the flow of a drug administered orally.

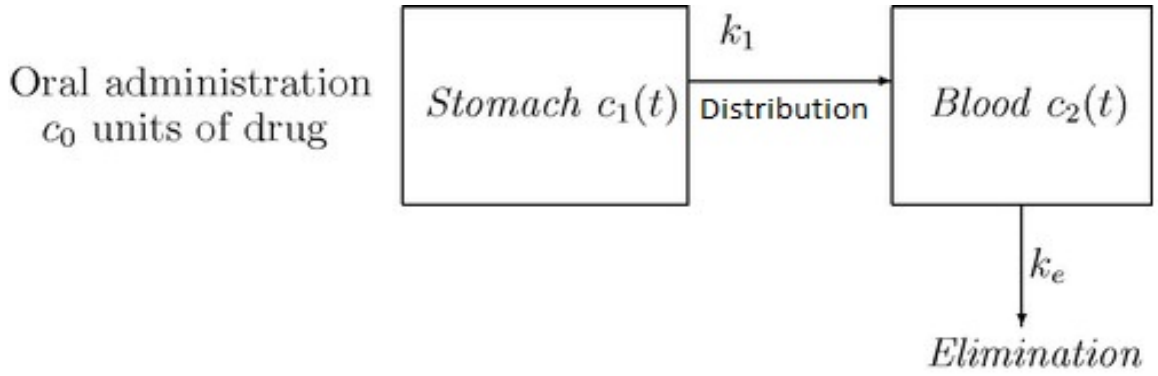

Figure 1: Simple process of drug administration through stomach and blood.

Where $c_1(t)$ and $c_2(t)$ denote the concentration of drug in stomach or GI tract and blood stream compartments respectively. Let $c_0 = c_1(0)$ be the initial concentration of drug dosage. Also let k_1 and k_e be the rates of drug distribution and drug elimination respectively.

(i) Formulate the mathematical models describing the the rate of change of drug concentration in the stomach and blood plasma respectively assuming $c_2(0) = 0$. (**2 marks**)

(ii) Using the initial condition, show that the solution to the model formulated in (i) above is given by: ((**8 marks**)

$$\begin{aligned} c_1(t) &= c_0 e^{-k_1 t} \\ c_2(t) &= \frac{c_0 k_1}{k_1 - k_e}(e^{-k_e t} - e^{-k_1 t}); \qquad k_1 \neq K_e \end{aligned}$$

(iii) What is the definition of drug half-life, and how is it calculated? Express the concentration of the drug in the stomach $c_2(t)$ in terms of half-life of the drug. (**6 marks**)

Question 3 (20 marks)

3. (a) Consider the following chemical notation denoting metabolism of a certain drug.

$$C_d + E \rightleftharpoons_{k_2}^{k_1} C \longrightarrow^{k_3} P + E$$

Where, S represents drug concentration in plasma, E is the drug binding enzyme, C is the bound complex compound and P is the product.

(i) Represent the process using chemical reaction flow diagram (**2 Marks**)

(ii) Discuss k_1,k_2 and k_3 in relation to drug metabolism process above. (**2 marks**)

(iii) Show that the rate of drug metabolism v is given by: (**6 Marks**)

$$v = \frac{V_{max}S}{K_m + S}$$

(iv) Discuss K_m and V_{max} as represented in the model in (iii) above? . (**2 marks**)

(b) Explain the significance of Km in enzyme kinetics. How does the value of Km relate to the affinity of an enzyme for its substrate?. (**2 marks**)

(c) Discuss the behavior of an enzyme-catalyzed reaction when $[S] << Km$ and when $[S] >> Km$. How do these conditions relate to the rate of the reaction? (**3 marks**)

(d) Assume that the reaction catalyzed by an enzyme follows Michaelis-Menten kinetics. The substrate concentration (K_m, Michaelis constant) needed to reach 50% of the maximum reaction velocity (V_{max}) is $25\mu M$. What substrate concentration is required to obtain at least 95% of the maximum reaction velocity? (**3 marks**)

Question 4 (20 marks)

4. (a) How does the concept of drug half-life relate to the rate of drug elimination from the body? Can you explain the difference between a drug with a short half-life and a drug with a long half-life? (**4 marks**)

   (b) Explain the importance of considering efficacy when choosing medications for different medical conditions. What factors might influence this decision? (**4 marks**)

   (c) Consider the graph in Figure 2 showing drug dose-response relationship.

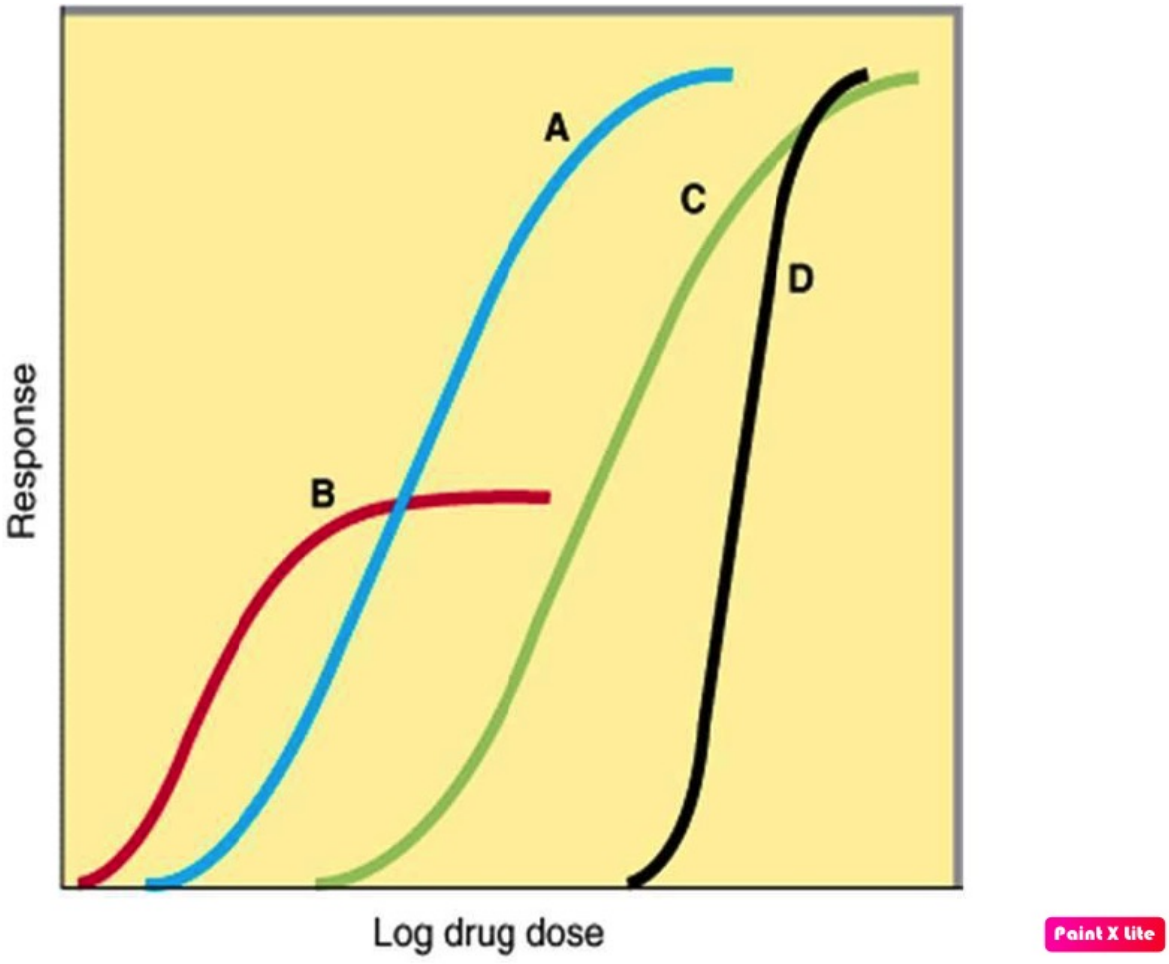

Figure 2: Drug Potency and Efficacy

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   (i) Use Figure 3 to discuss the potency and efficacious of drugs A, B, C and D. (**4 marks**)

   (ii) Why is drug potency important and what determines drug potency? (**4 marks**)

   (d) How does the concept of the therapeutic index (TI) relate to drug potency and safety? (**4 marks**)