Strathmore UNIVERSITY

STRATHMORE INSTITUTE OF MATHEMATICAL SCIENCES (SIMS)

MASTER OF SCIENCE IN BIOMATHEMATICS

END OF SEMESTER EXAMINATION

BMA 8301-BIOMEDICAL MATHEMATICS

Date: December 19, 2018 Duration: $2\frac{1}{2}$ Hours

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

Question I (20 marks)

1. (a) Define pharmacology and hence differentiate between pharmacokinetics and pharmacodynamics.(**3 Marks**)

   (b) What is an enzyme in chemical reaction and what do you understand by enzyme kinetics (**4 Marks**)

   (c) Assume that a particular enzyme-catalyzed reaction follows Michaelis-Menten kinetics with a K_m for the substrate of $1 * 10^{-6}M$. If the reaction rate is $1 * 10^{-7}$ mol per minute at a substrate concentration of 0.1 M, what would the reaction rate be at substrate concentrations of 0.01 M? (**4 Marks**)

   (d) Discuss the difference between law of mass action and law of mass conservation in modeling. (**4 marks**)

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

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

   Use the law of mass action to formulate the ODEs representing the reaction. (**5 Marks**)

Question 2 (20 marks)

2. Consider a chemical reaction representing metabolism of a certain drug which is denoted by the following chemical notation:

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

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

(i) Show that the rate of drug metabolism v is given by: (**10 Marks**)

$$v = \frac{V_{max} C_P}{K_m + C_p}$$

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

(iii) What does K_m represent in the model in (i) above? . (**2 marks**)

(iv) Discuss V_{max} in relation to the process above (**2 marks**)

(v) Plot the equation in (i). (**2 marks**)

(vi) Given an enzyme with K_M of 0.5 mM. at what drug concentration will the rate of metabolism reach $\frac{1}{4}$ of the V_{max} given $V_{max} = 200$ mol per second ? (**2 marks**)

Question 3 (20 marks)

3. (a) why is the study of enzyme kinetics of interest to molecular biologists? (**2 marks**)

(b) What is the significance of michaelis menten equation? (**2 marks**)

(c) In a particular enzyme-catalyzed reaction, $V_{max} = 0.2$ mol/sec and $K_m = 5$ mM. Assume the enzyme shows standard Michaelis-Menten kinetics.

(i) What is the rate of the reaction when the concentration of the substrate, $[S] = 10$ mM?. (**4 marks**)

(ii) Draw a Michaelis-Menten plot of the reaction kinetics, labeling the axes and giving values for the two points where you know V (from above). (**4 marks**)

(d) If $V_{max} = 100$ mol/sec and $K_m = 2$ mM, what is the velocity of an enzyme-catalyzed reaction when $[S] = 20$ mM? (**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? (**4 marks**)

Question 4 (20 marks)

4. (a) Why is the study of pharmacokinetics important? (**2 marks**)

(b) When a drug is orally administered, it dissolves and releases the medications into the gastrointestinal tract. The medications diffuse from there into the blood and the bloodstream takes medications to the site where it has therapeutic effect. The flow of drugs within the

body is modelled by treating the different parts of the body as compartments and then tracking the medication as it enters and leaves each compartment. Figure 2 below shows the flow of a drug administered orally.

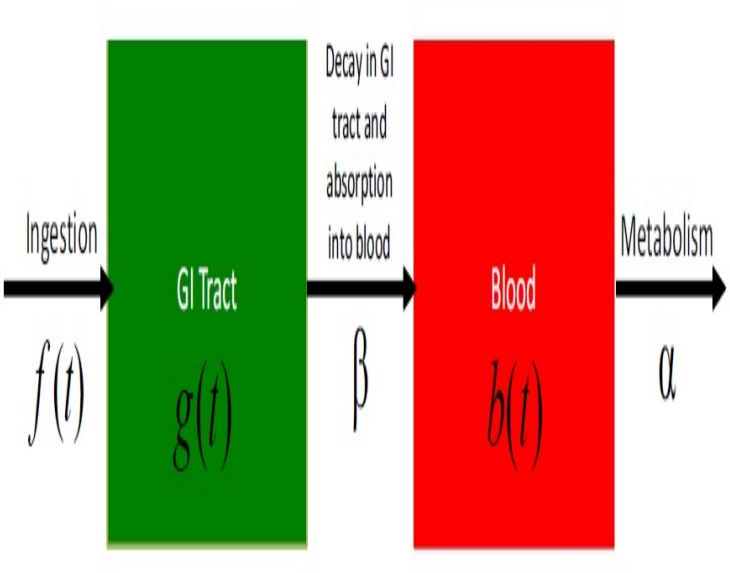

Figure 1: Chemical reaction kinetics

Where $g(t)$ and $b(t)$ denote the concentration of drug in stomach or GI tract and blood stream compartments respectively. Let $g_0 = g(0) = f(t)$ be the initial concentration of drug dosage in the stomach. Also let β and α be the rates of drug absorption and drug metabolism respectively.

(i) Formulate the mathematical models describing the the rate of change of drug concentration in the stomach and blood plasma respectively assuming $b_0 = b(0) = 0$. (**4 marks**)

(ii) Using the initial condition, show that the solution to the model formulated in (i) above is given by: ((**9 marks**)

$$\begin{aligned} g(t) &= g_0 e^{-\beta t} \\ b(t) &= \frac{g_0 \beta}{\beta - \alpha}(e^{-\alpha t} - e^{-\beta t}); \qquad \beta \neq \alpha \end{aligned}$$

(iii) Why is half-life of a drug important? Express the concentration of the drug in the stomach $b(t)$ in terms of half-life of the drug. ((**5 marks**)