Reg. No.										

MANIPAL INSTITUTE OF TECHNOLOGY

MANIPAL

(A constituent unit of MAHE, Manipal)

VI SEMESTER B.TECH. EXTERNAL EXAMINATIONS APRIL 2019

SUBJECT: Biopharmaceutical Engineering [BIO 4010]

Date of Exam: **30/04/2019** Time of Exam: **2.00 PM – 5.00 PM** Max. Marks: **50**

Instructions to Candidates:

- Answer ALL the questions & missing data may be suitable assumed

<table>
<tr><td>1A.</td><td>Explain briefly one compartment and two compartment model with neat diagram.</td><td>2</td></tr>
<tr><td>1B.</td><td>The following data for decomposition of two drugs, A and B are given in the table below:
<table>
<tr><td>Time (h)</td><td>0.5</td><td>1</td><td>1.5</td><td>2</td><td>3</td><td>4</td><td>6</td><td>8</td></tr>
<tr><td>Drug A (mg)</td><td>379</td><td>358</td><td>337</td><td>316</td><td>274</td><td>232</td><td>148</td><td>64</td></tr>
<tr><td>Drug B (mg)</td><td>181.2</td><td>164</td><td>148.6</td><td>134.6</td><td>110.4</td><td>90.6</td><td>61</td><td>41</td></tr>
</table>
a. What is their half-lifes?
b. What were the original amounts of drug before decomposition?
c. If the original quantities of drug taken were 800 mg for A and 400 mg for B then what will be there half-lives?
d. Write equations for the line that best fits the experimental data for both the drugs.</td><td>8</td></tr>
<tr><td>2A.</td><td>If drug is eliminated by first order, what % drug eliminated after 2 half lifes of a drug</td><td>2</td></tr>
<tr><td>2B.</td><td>Penicillin has a Cl_T of 15 mL/min. Calculate the elimination rate for penicillin in one compartment model when the plasma drug concentration, C p, is 2 µg/mL</td><td>2</td></tr>
<tr><td>2C.</td><td>Discuss the similarities and differences between passive and facilitated diffusion?</td><td>3</td></tr>
<tr><td>2D.</td><td>A dose of 500 mg was administered to a healthy volunteer. Total urine samples were collected after 2, 4, 6, 8, 10, 12, 18 and 24 hours. Samples were well mixed and analyzed for drug concentration. The volume of each sample was also recorded. The collected data are shown in the table below.
<table>
<tr><td>Time (hr)</td><td>0</td><td>2</td><td>4</td><td>6</td><td>8</td><td>10</td><td>12</td><td>18</td><td>24</td></tr>
<tr><td>Urine Volume (ml)</td><td></td><td>48</td><td>47</td><td>57</td><td>48</td><td>46</td><td>42</td><td>174</td><td>151</td></tr>
<tr><td>Drug (mg/ml)</td><td></td><td>2.074</td><td>1.331</td><td>0.69</td><td>0.516</td><td>0.338</td><td>0.233</td><td>0.072</td><td>0.02</td></tr>
</table>
Determine k, k_e and k_m using sigma minus method.</td><td>3</td></tr>
<tr><td>3A.</td><td>A 400 mg I.V. bolus of theophylline was given (as a form of aminophylline) to a patient, the AUC was 120 mg.hr/L. What will be the rate of I.V. infusion (mg/hr) of aminophylline should be administered to reach a plasma concentration of 15 mg/L? (each 100 mg aminophylline contains 85 mg theophylline).</td><td>3</td></tr>
</table>

3B.	Studied the pharmacokinetics of amrinone after a single IV bolus injection (75 mg) in 14 healthy adult male volunteers. The pharmacokinetics of this drug followed a two-compartment open model and fit the following equation: C_p (mg/L) = $4.62e^{(-8.94t)}$ + $0.64e^{(-0.19t)}$ From these data, calculate: (a) The volume of the central compartment (b) The volume of distribution at steady state (c) The extrapolated volume of distribution (d) The volume of distribution by area	4
3C.	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 weight 75 kg). The pharmacokinetics of the plasma drug concentration–time curve for this drug fits a one-compartment model. The equation of the curve that best fits the data is $C_p=78e^{(-0.46t)}$ Determine the following (assume units of µg/mL for C_p and hr for t): a. How much drug is left in the body after 4 hours? b. Predict what body water compartment this drug might occupy and explain why you made this prediction. c. Assuming the drug is no longer effective when levels decline to less than 2 µg/mL, when should you administer the next dose?	3
4A.	According to the manufacturer, a steady-state serum concentration of 17 µg/mL was measured when the antibiotic cephradine (Velosef, Bristol-Meyers, Squibb) was given by IV infusion to 9 adult male volunteers (average weight, 71.7 kg) at a rate of 5.3 mg/kg hr for 4 hours. a. When the IV infusion was discontinued after 4 hours, the cephradine serum concentration decreased exponentially, declining to 1.5 µg/mL at 6.5 hours after the start of the infusion. Calculate the elimination half-life. b. From the information above, calculate the apparent volume of distribution.	2
4B.	An antibiotic was infused with a 40-mg IV dose over 2 hours. Eight hours later, a second dose of 40 mg was infused, again over 2 hours. What is the plasma drug concentration 1 hours after the second dose infusion was started? Assume k = 0.2 hr^{-1}, V_D = 10 L for the antibiotic.	2
4C.	Develop the mathematical expression to calculate drug concentration after nth dose when the drug is given by multiple IV injections to a patient?	3
4D.	An antibiotic is given by IV bolus injection at a dose of 500 mg. The apparent volume of distribution was 21 L and the elimination half-life was 6 hours. Urine was collected for 48 hours, and 400 mg of unchanged drug was recovered. What is the fraction of the dose excreted unchanged in the urine? Calculate Cl_T and Cl_h.	3
5A.	List out the advantages & disadvantages of the following route of administration of drug a. Buccal & Sublingual b. Intravenous	4
5B.	Write a short note on process validation	2
5C.	Briefly explain the different factors effecting the reabsorption of molecules in the kidney	3
5D.	Write the mathematic expression to calculate renal clearance using AUC	1