DATE: 27th FEBRUARY 2019 TIME: 01.30 P.M. – 04.30 P.M.

01.

1.1 A patient was given an IV infusion of drug X. It achieves its steady state (ss) concentration (10 mg/mL) 10 min after starting the infusion. 30 min after reaching ss, the infusion pump was removed. Within 20 min the drug was completely eliminated from the body. Draw the graph which represent these data. (05 marks)

1.2 What are drug plasma level time curves? (02 marks)

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1.3 Write three (03) applications of pharmacokinetic models. (03 marks)

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II.....

III.....

02.

2.1 What is "drug clearance"? (02 marks)

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2.2 Write the typical equation which can be used to calculate plasma drug concentration at any time point in two compartment model. Define its terms. (04 marks)

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2.3 Write four (04) advantages of IV infusions. (04 marks)

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II.....

III.....

IV.....

**Part C (60 marks)**

01. Answer **All** parts.

1.1 What is the meaning of "Rate of a reaction"? (01 marks)

1.2 Write four (04) assumptions which are needed to be taken when one compartment open model is used. (02 marks)

1.3 State the importance of the volume of distribution. (02 marks)

1.4 A 50 kg woman was given a single IV dose of an antibiotic at a dose of 6 mg/kg. Blood samples were collected at various time intervals and the plasma drug concentration was determined and following data was obtained.

| Time (hours) | $C_p$ (µg/mL) |
|---|---|
| 0.25 | 8.21 |
| 0.5 | 7.87 |
| 1 | 7.23 |
| 3 | 5.15 |
| 6 | 3.09 |
| 12 | 1.11 |
| 18 | 0.40 |

a. Draw the graph to represent above data by using suitable graph paper. (05 marks)

b. What are the values for $V_d$, k and $t_{1/2}$? (03 marks)

c. This antibiotic is not effective if the $C_p$ is less than 2 µg/mL. Therefore what is the duration of action? (02 marks)

02. Answer **All** parts.

2.1 Drug X is administered orally as its HCl salt (S = 0.95). It undergoes degradation through stomach pH and liver enzymes. Therefore 75% of the drug is unable to reach the systemic circulation. What will be the effective dose for a 5 mg tablet? (03 marks)

2.2 Write the typical equation for renal clearance and define its terms. (03 marks)

2.3 The drug disolvprazole is almost completely eliminated by renal excretion. A 10 mg dose was administered intravenously to a healthy subject. Urine samples were collected over various periods and the plasma drug concentration was measured at the midpoint of each collection period. The data are given in following table.

| Urine data | | | Plasma data | |
|---|---|---|---|---|
| Collection Period (h) | Volume of urine (mL) | Urine drug concentration (µg/mL) | Time (h) (Midpoint of urine collection Period) | Cp (µg/mL) |
| 0-1 | 200 | 15 | 0.5 | 240 |
| 1-3 | 180 | 19.4 | 2 | 142 |
| 3-5 | 140 | 12.8 | 4 | 71 |
| 5-10 | 400 | 3.5 | 7.5 | 21 |

a. Draw the graph using suitable graph paper. (06 marks)

b. Determine the renal clearance of the drug. (03 marks)

03. Answer **All** parts.

An old female patient was given a 500 mg of co-amoxicillin drug as IV bolus. Her blood samples were collected at various time intervals and analyzed for plasma drug concentration and results were tabulated as below.

| **Time(h)** | **Concentration(mg/L)** |
|---|---|
| 0.5 | 20.60 |
| 1 | 13.40 |
| 2 | 7.30 |
| 3 | 5.00 |
| 4 | 3.70 |
| 6 | 2.20 |
| 8 | 1.40 |
| 10 | 0.82 |
| 12 | 0.50 |

3.1 Draw the graph in a suitable graph paper. (04 marks)

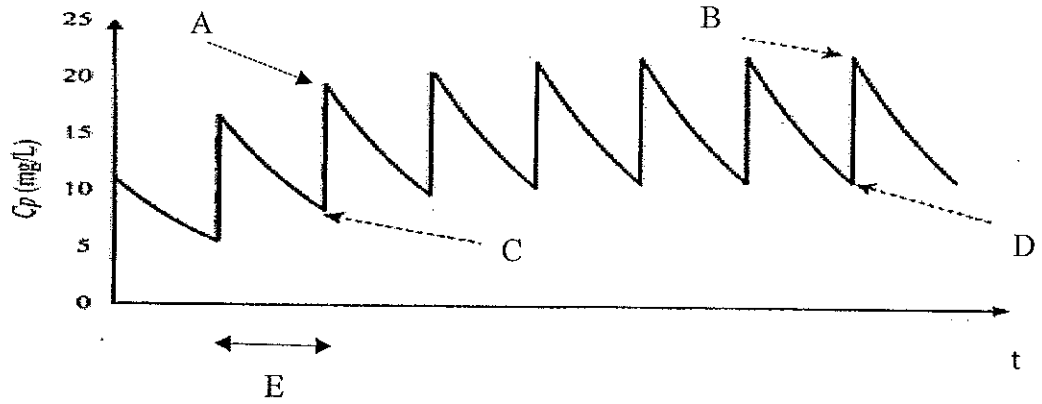
3.2 Based on the graph how many compartments are there? (01 mark)

3.3 Give the equation which can be used to find plasma drug concentration at any time point. Show your all calculations clearly. (07 marks)

3.4 Calculate the plasma drug concentration when the time equals 4 hour using the obtained equation in 3.3 and comment on the obtained equation. (03 marks)

04. Answer **All** parts.

4.1 What type of therapy is represented from the following time vs plasma drug concentration graph? What is the compartment model? (02 marks)




4.2 Label A to E in the above given graph (in 4.1). (03 marks)

4.3 A developing drug has a very narrow therapeutic range; 12 – 25 mg/L. The goal is to design a dosing regimen that will result in a steady state peak and trough of 20 and 14 mg/L respectively. The drug's elimination rate constant showed a population average value of $0.043h^{-}$.

a. What dosing interval is needed to provide the desired steady state peaks and troughs? (02 marks)

b. What will be the dosing interval if the drug is designed to work in its therapeutic range? (02 marks)

4.4 What is the meaning of absolute bioavailability? (02 mark)

4.5 Write four (04) FDA regulatory recommendations for bioequivalence studies. (04 marks)

Following are useful equations and their terms have usual meanings.

$a+b = k_{12} + k_{21} + k$

$ab = k_{21} * k$

$C_p = A\, e^{-at} + B\, e^{-bt}$

$A = Do\,(a - k_{21}) / \{ V_p\,(a-b)\}$

$B = Do\,(k_{21} - b) / \{ V_p\,(a-b)\}$

$k = ab\,(A+B) / \{ Ab+Ba \}$

$k_{12} = AB\,(b-a)^2 / \{(A+B)\,(Ab+Ba)\}$

$k_{21} = (Ab+Ba) / (A+B)$

$C_{pss} = C_{pmax.ss}\, e^{-kt}$

$C_{pmin.ss} = C_{pmax.ss}\, e^{-k\,\tau}$