BIRLA INSTITUTE OF TECHNOLOGY & SCIENCE, PILANI
DEPARTMENT OF PHARMACY
Comprehensive Examination
Pharmacokinetics and Clinical Pharmacy PHA G612 (Closed Book)
Weightage: 35% (total marks 35) Duration: 180 Min Date: 20/12/2023

Instructions:

- ✓ **Write correct and precise answers.**
- ✓ **No marks will be awarded if the final answer is correct "by chance" unless a proper conceptual solution is provided in the answer booklet.**
- ✓ **Marks will only be given to correct and well-explained answers and not to partial answers.**
- ✓ **Write in clear and legible handwriting.**
- ✓ **Answer the questions in exact sequence. Answer the following question from the fresh page.**
- ✓ **Important formulae are written on the last page**

Q1 Clarify the concept of pharmaceutical alternatives and examine their interchangeability when a prescribed pharmaceutical is unavailable. **(2M)**

Q2 Define the Orange Book, identify its publisher and its official name, and elucidate the significance of the code "AB" within its context. **(0.5+0.5+0.5+0.5M)**

Q3 Calculate the relationship between the amount of drug administered and eliminated during the steady state of a multiple-dosing regimen of IV bolus for a drug following the first-order elimination kinetics. **(2M)**

Q4 Identify and resolve the problems in the given statements. **(0.5+0.5+0.5+0.5M)**

a) R= 2 suggests that the average plasma concentration at steady state will be twice the minimum plasma concentration for the first dose.
b) The lowest value for drug accumulation cannot be lower than 0.5
c) The fluctuation in plasma concentration is influenced only by the amount of drug administered in every dose
d) At steady state, the difference between peak and trough concentrations is equal to the double of initial plasma concentration following the administration of the first dose of iv bolus.

Q5 What do you understand by saturable and non-saturable kinetics? Explain how pharmacokinetics determine the therapeutic index of a drug. What elimination kinetics follow phenytoin, gentamicin, and ethyl alcohol?? **(3M)**

Q6 Generate a representative graph on semi-logarithmic paper for the given equation, and incorporate the calculation and depiction of the half-life within the graph. **(3M)**

$$C = 0.8e^{-0.231t}$$

Where C in mg/mL and t in hours

Q7 Check if the following equation is correct in multiple dosing oral administration at steady state; assume the drug follows one compartment, first-order elimination kinetics. **(3M)**

$$\frac{K_a e^{-K_a tmax}}{1 - e^{-K_a \tau}} = \frac{K_e e^{-K_e tmax}}{1 - e^{-K_e \tau}}$$

Q8 The following table gives the plasma concentrations (Cp) obtained after the intravenous infusion of 13mg $min^{-1}$of a drug, which is eliminated exclusively by urinary excretion. The infusion was terminated at 2 h. **(6M)**
Plot the data and, using the plot, determine the following.

a. The elimination half-life (t1/2).
b. The elimination rate constant (K).
c. The apparent volume of distribution (V).
d. The true steady-state plasma concentration, (Cp)ss.
e. The 'practical' steady-state plasma concentration and time it takes to reach the 'practical' steady-state condition.

Time (h)	Con (µg/ml)
0.5	37.50
1.0	56.30
1.5	65.60
2.0	70.30
2.5	35.20
3.0	17.70
3.5	8.70
4.0	4.40
5.0	1.10

Q9 The physician has decided to administer a drug with multiple dosing intervals. The therapeutic plasma range for this drug is between 0.5 and 12 mg/L. Assuming a one-compartment linear model for this drug in this concentration range, the ke and Vd for this patient are 0.168 hr-1 and 44.2 L, respectively. To achieve this concentration requirement, calculate the maximum dosing interval that will work best. The physician has also decided to modify the dosing interval for the convenience of the nursing staff, with options such as once a day, twice a day, or four times a day. The dose will be rounded off to a multiple of 10 mg for ease of administration and to reduce the chances of dosing errors. Calculate the loading dose and maintenance dose, as well as the dosing interval in this scenario, and check your answer by estimating Cpmax and Cpmin. **(6M)**

Q10 Your organization is testing a new drug. According to pharmacological data, the average plasma concentration required to achieve therapeutic effects is 10mg/L. The pharmacokinetic scientist team has obtained the following plasma concentration-time profile after administering 50mg of the drug. Your task is to determine the dosing schedule every 12 hours and $t_{1/2}$ based on the information provided. Assume the drug follows first-order elimination kinetics. **(6M)**

Time (h)	Con (µg/ml)
0	0
1.0	2.3
2	4.7
4	5.2
8	4.0
12	2.8
24	0.6
36	0.03

Important formulas

IV Bolus Single dose

$$Cp = C_0 e^{-K_e t}$$

Extravascular Single dose

$$Cp = \frac{FK_a X_0}{V(K_a - K_e)}(e^{-K_e t} - e^{-K_a t})$$

Continuous IV infusion

$$Cp = \frac{Q}{VK}(1 - e^{-K_e t})$$

Dost Ratio

$$r = \frac{(1 - e^{-nK_e \tau})}{(1 - e^{-K_e \tau})}$$