Max marks 75 **Time 3 hours**

Note: All the questions are compulsory

Q.1 Answer the following questions (20)

A. What do you mean by the terms "open" and "closed" in compartmental modelling? (1)

B. Classify sampling methods in pharmacokinetic studies. Which is the most commonly used sampling method and why? (2)

C. What are the advantages of administering drugs to a patient by constant i.v infusion? (2)

D. State the applications and limitations of methods of residuals. (2)

E. Discuss the objectives for conducting bioequivalence studies. (2)

F. The term Css_{av} is not an arithmetic mean of Css_{max} and Css_{min}. Why? (2)

G. Why should volunteers be instructed to completely empty their bladders while giving urine samples for pharmacokinetic determination? (1)

H. Rapidity and completeness of drug absorption is important in drug therapy. Explain. (2)

I. Unless distribution occurs, the drug may not elicit a pharmacological response. Explain. (2)

J. Define the terms: i. Optimal dosage regimen. ii. Therapeutic index (2)

K. What is trapezoidal rule and for which pharmacokinetic parameter is it applicable? (2)

Q.2A. An intravenous bolus dose of 25 mg of a drug following one compartmental kinetics has a volume of distribution of 27,000 litres and a biological half life of 36 hours. Calculate the elimination rate constant, clearance, AUC (zero to infinity) and the amount of drug in the body after 42 hours of drug administration. (4)

Q.2B. State the equation used for determining the kinetics of a saturable process. How can you estimate K_m and V_{max} in saturable kinetic processes? (4)

Q.2C. Describe briefly the rate of excretion method for analysis of urine after an I.V bolus dose of a drug following one compartmental kinetics. (3)

Q.3A. State the equations that indicate the concentration of drug in plasma at any time 't' after the N^{th} dose and at steady state. What are the preconditions for derivation of stated equations? (4)

Q.3B. A patient receives 1000 mg of an antibiotic every 6 hours by repetitive i.v injection. The drug has a volume of distribution of 20 litres and half life of 3 hours. Calculate the plasma concentration at 4 hours after the second dose and the steady state drug concentration at 3 hours after the last dose for this drug. Also calculate the maximum and minimum steady state concentrations of drug in the plasma. (4)

Q.3C. What are drug transporters? State their role in absorption of drugs. (3)

Q.4A. An intravenous continuous administration of a drug given at steady state of R_0 follows one compartmental kinetics. Derive an equation to calculate its rate of elimination, half life and volume of distribution. (4)

Q.4B. Describe the influence of absorption and elimination rate constant on C_{max}, T_{max} and AUC. (3)

Q.4C. The equation that best fits the pharmacokinetics of Tolbutamide (F=0.6) after oral administration of 500 mg drug is given by: (4)

$$C = 2.23 (e^{-0.24t} - e^{-1.6t})$$

Assuming that the concentration is expressed in mcg/L, time in litres and no flip flop kinetics occurs in this case; calculate any four (primary or secondary) pharmacokinetic parameters for Tolbutamide. On the semi log graph paper, plot the calculated concentrations at any eight time points of your choice.

Q.5A. What are pharmacokinetic models? What is the importance and utility of developing such models? Discuss briefly the types of pharmacokinetic models. (4)

Q.5B. Prove mathematically that when an i.v loading dose is followed immediately by a constant rate infusion, the plasma concentration remains steady as long as the infusion is continued. (3)

Q.5C.According to the manufacturer, a steady state serum concentration of 20 mcg/ml was measured when the antibiotic cephradine was given by i.v infusion to 9 adult male volunteers (avg wt: 71.7 kg) at a rate of 5.3 mg/kg for 4 hours. Calculate the total body clearance for this drug. When the i.v infusion was discontinued, the drug serum concentration declined to 1.5 mcg/ml at 6.5 hours after the start of infusion. Calculate the elimination half life. From this information, calculate the apparent volume of distribution. (4)

Q.6A. The following data was obtained from a bioequivalence study of three marketed products A, B, C of diclofenac sodium with an oral doses of 50 mg, 100 mg and 50 mg respectively. Calculate the absolute bioavailability for products B and C, considering A as the standard product. Also calculate the elimination rate constants for all the three products. Calculate the relative bioavailability for product B against C. (4)

Drug product	**AUC (zero to infinity) (mcg.hr/ml)**	**$t_{1/2}$ (hrs)**
A	7.34	1.51
B	7.06	1.68
C	6.35	1.55

Q.6B. Describe various experimental designs for bioavailability and bioequivalence studies. Comment on the selection of volunteers and interpretation of data. (4)

Q.6C. Explain the phenomenon of drug accumulation and time to reach steady state during multiple dosing of a drug. (3)