SEP 0 6 2017

Mark Scored:

KATHMANDU UNIVERSITY
End of Semester Examination
August/September, 2017

Level : B. Pharm. | Course : PHAR 315
Year : III | Semester : II
Exam Roll No. : | Time: 30 min | F. M. : 20
Registration No.: | Date : SEP 0 6 2017

SECTION "A"
[20 Q × 1 = 20 marks]

Select the correct answer.

1. Which of the following statements best describes pharmacokinetics?
   a. The study of how drugs reach their target in the body and how the levels of a drug in the blood are affected by various factors.
   b. The study of how drugs can be designed using molecular modelling based on a drug's pharmacophore.
   c. The study of how a drug interacts with its target binding site at the molecular level.
   d. The study of which functional groups are important in binding a drug to its target binding site and the identification of a pharmacophore.

2. Drug infusion is usually modeled as a _____order rate constant:
   a. First b. Zero c. Second d. zero and first

3. Cpss is reached when:
   a. The infusion is stopped
   b. The rate of infusion equals the rate of elimination
   c. Two hours after the infusion is started
   d. The rate of infusion is faster than the rate of elimination

4. If kel = 0.2 hr^{-1} and V = 32 L the infusion rate required to maintain a concentration of 12 mg/L is:
   a. 1331 mg/hr b. 76.8 mg/hr c. 6.4 mg/L d. 1920 mg/hr

5. A 100 mg/hr infusion is given for 2 hours and two samples are collected at 2 hr and 8 hr after the infusion was stopped. These values were 7.6 mg/L and 2.4 mg/L. What is the value of kel in this patient?
   a. 0.867 hr^{-1} b. 0.254 hr^{-1} c. 0.192 hr^{-1} d. 1.92 hr^{-1}

6. Enteral routes of administration do not include:
   a. Oral b. Subcutaneous c. Buccal d. Rectal

7. The first pass effect refers to:
   a. the loss of drug by rapid elimination
   b. the loss of drug by metabolism in the liver
   c. the loss of by drug distribution to peripheral tissues
   d. the loss of drug by excretion

8. What is the half life of a drug with a volume of distribution of 100ℓ/70kg and a clearance of 7ℓ/hr/70kg?
   a. 5 hours b. 10 hours c. 12.5 hours d. 15 hours

9. In Biopharmaceutical Classification System (BCS), Class II drug means the drug has _____
   a. High permeability; high solubility
   b. Low permeability; low solubility
   c. High permeability; low solubility
   d. Low permeability; high solubility

10. Volume of distribution equals _____
   a. Dose given/plasma concentration
   b. Total amount of drug in the body/plasma concentration
   c. Urine drug concentration/plasma concentration
   d. Dose given/urine concentration

11. A single compartment model means that_____
   a. One exponential term describes the decreasing plasma concentration of the drug
   b. A single exponential term describes the rise in plasma concentration following oral administration
   c. The drug does not penetrate tissues
   d. The drug is restricted to the ECF

12. (Multiple Answer) Roots of administration that avoid "first-pass" hepatic effects:
   a. sublingual
   b. oral
   c. lower rectal suppositories
   d. inhalation

13. Nonlinear pharmacokinetics means_____
   a. drug serum concentrations decrease in a straight line when plotted on a concentration-time graph
   b. drug serum concentrations decrease in a straight line when plotted on a log concentration-time graph
   c. steady-state drug serum concentrations change proportionally to dose
   d. steady-state drug serum concentrations change non proportionally to dose

14. Volume of distribution determines:
   a. the time to reach steady state
   b. the loading dose required to achieve the desired steady-state concentration
   c. the maintenance dose required to achieve the desired steady-state concentration
   d. the dosage interval

15. Linear pharmacokinetics means :
   a. drug serum concentrations decrease in a straight line when plotted on a concentration-time graph
   b. drug serum concentrations decrease in a straight line when plotted on a log concentration-time graph
   c. steady-state drug serum concentrations change proportionally to dose
   d. steady-state drug serum concentrations change non proportionally to dose

16. The half-life is_____
   a. dependent on the value of volume of distribution.
   b. dependent on the value of clearance.
   c. a function of the physiologic volume of blood and tissues and how the drug binds in blood and tissues.
   d. a and b.

17. Pharmacokinetic models are useful to :
    a. describe concentration-time data sets.
    b. predict drug serum concentrations after several doses or after different routes of administration.
    c. calculate pharmacokinetic constants (clearance, volume of distribution, half-life).
    d. a, b and c

18. Clinicians should begin considering dosage adjustment of renally eliminated drugs at what creatinine clearance value?
    a. 90 mL/min b. 60 mL/min c. 30 mL/min d. 15 mL/min

19. which of the following undergoes acetylation in the liver (phase II biotransformation):
    a. isoniazid b. acetaminophen c. salicylic acid d. diazepam

20. The time of peak concentration after an oral administration depends on:
    a. ka and kel b. ka and kel and F
    c. kel and F d. kel, ka, V, and F

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SECTION "B"
[5 Q. × 3 = 15 marks]

Note: Check (√) the number of each question you have answered in the front page of main answer book (of Sections B, C and D). Use normal and semi-log graph paper provided by the invigilators only.

Answer *ANY FIVE* questions:

1. Define followings:
   a. Bioavailability b. Clearence c. volume of distribution

2. Define followings:
   a. Pharmaceutical equivalent
   b. Bioequivalent
   c. Therapeutic equivalence

3. What are the Physicochemical factors that affect dissolution rate of a drug?

4. A dose of **250 mg** was administered to healthy volunteer. Seven blood samples were collected at 0.5, 1, 2, 4, 6, 8, 10 hours. Plasma was separated from each blood sample and analyzed for drug concentration. The collected data are shown in the table below.

Time (hr)	Cp (mg/L)	Δ (AUC mg.hr/L)	AUC (mg.hr/L)
0			
0.5	35.85		
1	32.1		
2	27.86		
4	21.44		
6	17.49		
8	11.39		
10	9.01		
∞			

The table above provides a set of data for you to analyze. Use these data with the trapezoidal rule to calculate each AUC segment including the last segment.

5. Define the followings:
a. Absolute bioavailability b. Relative bioavailability c. Loading dose

6. What are the parameters to measure drug absorption, Distribution, Metabolism and excretion and what are their units?

7. Calculate the required dose of a drug (K_e = 0.17 hr^{-1} and V_d = 25 L) by rapid IV bolus to achieve a plasma concentration of 2.84 ug/ml (= 2.84 mg/L) at 4 hours.

SECTION "C"

[5 Q. × 5 = 25 marks]

Answer *ANY FIVE* questions:

8. A drug is to be given orally every six hours to achieve an average concentration of 15 mg/L. Calculate the dose (F = 0.90) required if $t_{1/2}$ = 11 hours and V = 23 L. Estimate the peak and trough concentrations after steady state is reached.

9. Describe formulation and Phycochemical factors affecting drug absorption.

10. Describe Biopharmaceutical and drug factors in design of dosage form

11. A drug was administered by IV infusion of 25 mg/hr for 15 min to healthy volunteer. Seven blood samples were collected at 2, 3, 4, 6, 8, 10, and 12 hours after the start of the infusion. Plasma was separated from each blood sample and analyzed for drug concentration. The collected data are shown in the table below.

Time (hr)	Cp (mg/L)
2	0.161
3	0.127
4	0.101
6	0.064
8	0.039
10	0.025
12	0.015

Estimate kel, $t_{1/2}$, V, and Cl.

12. The AUC calculated after an oral tablet (A) of **250 mg** was 73.9 mg.hr/L. The apparent volume of distribution and elimination rate constant estimated after this dose was 23.46 L and 0.1871 hr^{-1}. After an oral capsule dose (B) of **200 mg** the calculated AUC was 82.5 mg.hr/L. The apparent volume of distribution and elimination rate constant estimated after this dose was 25.24 L and 0.1641 hr^{-1}. Calculate the relative bioavailability of the tablet A with respect to the capsule B.

13. A drug was given by multiple oral doses of 150 mg every 3 hr. Assume a one compartment linear model applies to this drug in this concentration range. For this dosage form and patient the bioavailability is 0.88 and the absorption rate constant is 0.96 hr^{-1}. The kel and V for this drug in this patient are 0.218 hr^{-1} and 44.1 L, respectively. Calculate the average drug concentration.

14. Describe therapeutic consideration in dosage form design.

SECTION "D"
[2 Q. × 7.5 = 15 marks]

Answer *ANY TWO* questions:

15. A patient is started on a drug at an IV bolus dose of 10 mg every 6 hours. Calculate the drug concentration at a few of time points during the first three dosing interval. Specifically calculate the concentration three hours after the first dose, two hours after the second dose and one hour after the third dose. Assume a one compartment linear model applies to this drug in this concentration range. The Clearance and V for this drug in this patient (81.6 kg) are 17.8 L/hr and 0.63 L/kg, respectively.

16. A 50 mg oral dose of a drug was administered to a healthy volunteer. Blood samples were collected and plasma was separated from each blood sample and analyzed for drug concentration. The collected data are shown in the table below. Estimate kel, ka and V/F. Does the ratio of ka to kel satisfy the requirement of the method of residuals?

Time (hr)	**Cp (mg/L)**		
0.2	1.219		
0.3	1.542		
0.5	1.892		
0.6	1.964		
0.8	2.004		
0.9	2.019		
1.75	1.814		
3.5	1.339		
5.5	0.9358		
7	0.7281		

17. Describe the Method of assessing bioavailability and bioequivalence study. What are the purposes of Bioequivalence study?

Table — PHAR-315

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Two Cycle Semi-Log