KATHMANDU UNIVERSITY
End Semester Examination
August, 2018

Marks scored:

Level : B. Pharm.
Year : III

Course : PHAR 315
Semester : II

Exam Roll No. :

Time: 30 mins.

F. M. : 20

Registration No.:

Date AUG 19 2018

SECTION "A"
[20 Q × 1 = 20 marks]

**I. Encircle the correct answer of the following multiple choice questions:**

1. A medicine that instantly distributed through out the body follows ..... compartment model.
   a. One b. Two c. Three d. Four

2. ..... express the extent of drug absorption.
   a. AUC b. $C_{max}$ c. $T_{max}$ d. $V_d$

3. Analysis of drug in urine data is useful because.....
   a. blood samples may not be convenient
   b. a large apparent volume of distribution mean concentration might be too low
   c. it allows the study of drug metabolism
   d. All of the above

4. If Active pharmaceutical ingredient (API) is aqueous soluble at targeted concentration and stable in that solubility condition. You prefer ..... dosage form of that API.
   a. Ready to use oral liquid b. powder for reconstitution
   c. Suspension d. Emulsion

5. For patients who are infants and less than 5 years of age the preferred dosage form is
   a. Orally disintegrating tablets (ODTs) b. Chewable tablets
   c. Injectables d. oral liquids

6. According to pH partition Hypothesis, Weakly acidic drugs are better absorbed from .....
   a. Duodenum b. Jejunum c. colon d. Stomach

7. If not pure, the substance will exhibit a ..... of its melting point as compared with the pure substance.
   a. Depression b. Elevation c. No change d. a and b

8. Drug disposition means.....
   a. Absorption and distribution
   b. absorption and excretion
   c. Absorption, distribution and elimination
   d. Absorption, distribution and excretion

9. ..... is not the function of TDM service.
   a. Select drug. b. Design dosage regimen.
   c. Evaluate patient response. d. Diagnosis of patient.

10. For Bioequivalence study, ..... are compared.
    a. AUC b. $C_{max}$ c. $T_{max}$ d. All of the above

11. The reaction rate constant may be defined as the rate of the reaction when the concentration of each reactant is.....
    a. Zero b. Unity
    c. Doubled the initial concentration d. Infinite

12. Half life of first order reaction is .....
    a. Greater b. lesser c. high d. constant

13. Successive half-lives which decrease with the passage of time follow
    a. first order b. second order c. zero order d. unit order

14. 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

15. ..... will not alter the volume of distribution of a drug?
    a. Cardiac failure b. Clearance c. Age d. Burns

16. Potential outcomes of pharmacogenetic research include all the following *except*
    a. lower incidence of adverse drug effects b. new drug development.
    c. higher health care costs. d. improved treatment outcomes.

17. The most commonly occurring variant in the human genome is.....
    a. Single Nucleotide polymorphism b. Tandem repeat polymorphism
    c. Nucleotide base deletion d. Nucleotide base insertion

18. Concerning the effect of pH on the urinary excretion of drugs, it can be correctly stated that
    a. urinary acidification accelerates excretion of weak acids and bases
    b. urinary alkalization accelerates excretion of weak acids and bases
    c. urinary acidification accelerates excretion of weak acids
    d. urinary alkalization accelerates excretion of weak acids

19. Clearance 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.

20. 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.

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Level : B. Pharm.
Year : III
Time : 2 hrs. 30 mins.

Course : PHAR 315
Semester: II
F. M. : 55

**Note: Check (√) the number of each question you have answered in the front page of main answer book (of Sections B, C and D).**

SECTION "B"
[5 Q. × 3 = 15 marks]

II. Answer any ***FIVE*** questions:

1. Define the followings:
   a. Bioavailability b. Clearance c. drug Elimination

2. When and why urine samples are essential for pharmacokinetic study of drug?

3. What is the significance of the plasma level–time curve? How does the curve relate to the pharmacologic activity of a drug?

4. What is the difference between a rate and a rate constant? How is clearance related to the volume of distribution and $k$?

5. A 50-kg woman was given a single IV dose of an antibacterial drug at a dose level of 6 mg/kg. Blood samples were taken at various time intervals. The concentration of the drug ($C_p$) was determined in the plasma fraction of each blood sample and the following data were obtained:

| $t$ (hr) | $C_p$ (g/mL) |
|---|---|
| 0.25 | 8.21 |
| 0.50 | 7.87 |
| 1.00 | 7.23 |
| 3.00 | 5.15 |
| 6.00 | 3.09 |
| 12.0 | 1.11 |
| 18.0 | 0.40 |

What are the values for volume of distribution, elimination rate constant and half-life for this drug?

6. What are the main differences in pharmacokinetic parameters between a drug that follows linear and a drug that follows nonlinear pharmacokinetic?

7. How do excipients in a drug product that are physically inert, chemically inert, and nontoxic change the bioavailability of the active drug substance?

SECTION "C"

[5 Q. × 5 = 25 marks]

III. Answer any ***FIVE*** questions:

8. If a drug is administered orally as a solution, does it mean that all of the drug will be systemically absorbed? What is the biggest biological factor that contributes to delay in drug absorption? Why are some drugs absorbed better with food and others are retarded by food? What is an "absorption window"?

9. What physical or chemical properties of a drug substance are important in designing a drug for (a) oral administration or (b) parenteral administration?

10. A dose of **50 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) | 0 | 0.5 | 1 | 2 | 4 | 6 | 8 | 10 |
|---|---|---|---|---|---|---|---|---|
| Cp (mg/L) | | 2.44 | 2.37 | 2 | 1.7 | 1.35 | 1.03 | 0.78 |

The table above provides a set of data for you to analyze. Use these data with the trapezoidal rule and calculate each AUC segment including the last segment. Add the area for the last segment to get the total area under the curve.

11. Given the data in Table 1 collected after a 500 mg i.v. bolus dose, calculate kel, $Cp_0$, V, $t_{1/2}$, and AUC (using the trapezoidal rule). Verify that the drug follows linear one compartment pharmacokinetics!

Table 1

| **Time (hr)** | **Concentration (mg/L)** |
|---|---|
| 1 | 30 |
| 2 | 20 |
| 6 | 3.8 |
| 12 | 0.26 |

12. An IV Bolus dose of **150 mg** 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.

| Time (hr) | 0.25 | 0.5 | 0.75 | 1 | 1.25 | 1.5 | 2 | 4 | 6 | 9 | 12 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Cp (mg/L) | 3.03 | 2.47 | 2.14 | 1.93 | 1.8 | 1.7 | 1.55 | 1.14 | 0.85 | 0.54 | 0.35 |

Estimate A, B, α and β. Does the ratio of α to β satisfy the requirement of the method of residuals?

13. A potent drug is to be given by multiple IV bolus injections. On consideration of the patient's clinical condition it is decided that the $Cp_{max}$ and $Cp_{min}$ drug concentrations should be maintained **close to but below** 12 and 0.5 mg/L, respectively. Assume a one compartment linear model applies to this drug in this concentration range. The half-life and V for this drug in this patient (55.3 kg) are 3.8 hr and 0.44 L/kg, respectively. Calculate the dosing interval that will exactly achieve this concentration requirement. Round this dosing interval to the nearest, appropriate multiple of 4 hour. Recalculate the fraction remaining at the end of the dosing interval (R') and estimate an appropriate loading and maintenance dose (rounding to the nearest appropriate 10 mg). Finally, check your answer by estimating Cpmax and Cpmin.

14. A drug was administered by IV infusion of **75 mg/hr** for 5 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. Estimate kel, $t_{1/2}$, V, and Cl.

| Time (hr) | 2 | 3 | 4 | 6 | 8 | 10 | 12 |
|---|---|---|---|---|---|---|---|
| Cp (mg/L) | 0.058 | 0.042 | 0.03 | 0.015 | 0.007 | 0.004 | 0.002 |

SECTION "D"
[2 Q. × 7.5 = 15 marks]

IV. Answer any ***TWO*** questions:

15. A patient is started on a drug at an oral dose of 1000 mg every 8 hours. Calculate the drug concentration at a few of time points during the first three dosing interval. Graph these data on semi-log graph paper (The graph is not required for this homework exercise). 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. For this dosage form and patient the bioavailability is 1 and the absorption rate constant is 1.17 $hr^{-1}$. The kel and V for this drug in this patient are 0.335 $hr^{-1}$ and 31.9 L, respectively.

16. A drug is to be given by multiple oral doses every 8 hr. After consideration of the patient's clinical condition it is decided that the average drug concentrations should be maintained at 5 mg/L. Assume a one compartment linear model applies to this drug in this concentration range. For this dosage form and patient the bioavailability is 0.76 and the absorption rate constant is 0.67 $hr^{-1}$. The half-life and V for this drug in this patient are 3.2 hr and 34.3 L, respectively. Calculate the dose that will achieve this average concentration of 5 mg/L.

17. At the clinic you have a new patient (K.L.), age 27 years and weight 45 kg. An initial dose of 225 mg/day was recommended. The patient was instructed to take this dose each day for a few weeks and return for a plasma sample. This plasma sample was found to contain 7.5 mg/L phenytoin. This was somewhat low so you need to calculate a new dose per day with the aim of achieving an average plasma concentration of 15 mg/L. For this calculation you can assume that the patient has a Km value of 4 mg/L (a population average value).
Enter your estimate for the second dose.....mg/day.

PHAR. 515 - Table

AUG 19 2018

Four Cycle Semi-Log