KATHMANDU UNIVERSITY
End Semester Examination
July/August, 2024

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

30 JUL 2024

Course : PHAR 223
Semester : II
F. M. : 55

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

SECTION "B"

[5 Q. × 3 = 15 marks]

Attempt *ANY FIVE* questions.

1. Write short notes on:
   a. Biopharmaceutics
   b. Presystemic metabolism

2. How does polymorphism affect the drug solubility?

3. Differentiate between Linear and non-linear kinetics.

4. How can you estimate Cpmax and Cpmin for multiple IV bolus dosage regimen?

5. How you quantitatively express followings?
   a. Extent of absorption
   b. Drug elimination from body
   c. Rate of absorption

6. Draw the plasma drug concentration vs. time for intravenous (IV single dose) bolus, intravenous infusion and extravascular single dose following one compartment model.

7. A dose of 300 mg was administered to healthy volunteers. 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	α
Cp (mg/L)		8.94	8.01	6.85	5.1	3.8	2.67	2.01	

Estimate area from 0 to infinity using trapezoid rule.

SECTION "C"

[5 Q. × 5 = 25 marks]

Attempt *ANY FIVE* questions.

8. Define Biopharmaceutical classification system (BCS). Explain the techniques that can improve the drug permeability.

9. Define K_m and V_{max} in non-linear Pharmacokinetics. How can we determine them?

P.T.O.

10. Mention the acceptance criteria for the two products be bioequivalence. Give your opinion on Biowaiver study.

11. 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 20 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 0.69 and the absorption rate constant is 2.12 hr-1. The half-life and Vd for this drug in this patient (72.2 kg) are 2.6 hr and 0.46 L/kg, respectively. Calculate the dose that will achieve this average concentration of 20 mg/L.

12. A dose of 50 mg was administered to a healthy volunteer as a IV bolus. Seven blood samples were collected at 1, 2, 3, 4, 6, 10, and 12 hours. Plasma was separated from each blood sample and analyzed for drug concentration. The collected data are shown in the table below.

Time (hr)	1	2	3	4	6	10	12
Cp (mg/L)	3.26	2.8	2.55	2.26	1.71	1.04	0.76

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

13. A drug was administered by IV infusion of 200 mg/hr for 45 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)	2	3	4	6	8	10	12
Cp (mg/L)	2.951	2.343	1.877	1.208	0.782	0.507	0.317

Estimate kel, t1/2, V, and Cl.

14. Assuming a one compartment linear pharmacokinetic model, with kel = 0.14 hr-1; ka = 1.1 hr-1; F = 0.95; and V = 21.8 L, calculate the plasma concentration 2, 4, 6, 9, and 12 hours after a 250 mg oral dose.

SECTION "D"

[2 Q. × 7.5 = 15 marks]

Attempt *ANY TWO* questions.

15. Define crossover design and its importance for Bioavailability and Bioequivalence (BA&BE) study. Give your opinion on In-vitro In-vivo correlation (IVIVC) concept.

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16. Explain stereoisomerism and its effect on drug absorption. Explain how the various biological factors influence the bioavailability of drug.

17. An IV Bolus dose of 250 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)	1.8	1.52	1.42	1.37	1.34	1.32	1.28	1.15	1.03	0.87	0.73

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

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F. M. :20
Registration No.:
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SECTION "A"
[20 Q. × 1 = 20 marks]

Choose and encircle the most appropriate option.

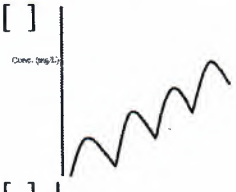
1. If the absorption rate of the procainamide drug is Slow but shows complete absorption, then we can obtain:
[ ] long Tmax, high Cmax, high AUC [ ] long Tmax, low Cmax, low AUC
[ ] short Tmax, high Cmax, high AUC [ ] short Tmax, low Cmax, low AUC

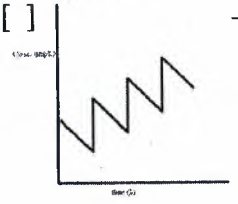
2. According to the "rule of Five", the number of H-bond acceptors for permeability of drug across intestinal epithelium is:
[ ] 1 [ ] 5 [ ] 10 [ ] 50

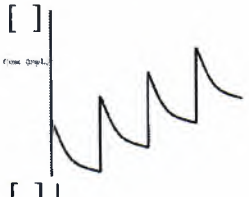
3. Which of the following statements regarding facilitated transport is incorrect?
[ ] It is a carrier mediated transport system.
[ ] It can transport a substance against a concentration gradient of that substance.
[ ] It does not require energy input.
[ ] It has a very minor role in terms of drug absorption

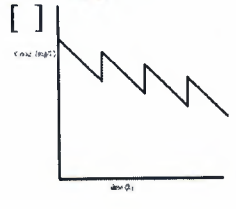
4. Normally, transit time of orally administered pharmaceuticals in small intestine is expected to be between.....
[ ] 1 to 2 h. [ ] 3 to 6 h. [ ] 6 to 12 h. [ ] Less than 1 h.

5. A semilog plot of Cp versus time after four equal IV bolus doses of 250 mg given every 6 hours is represented by:

[ ] 

[ ] 

[ ] 

[ ] 

6. Which of the following factors is most like ly to decrease the bioavailability of an orally administered drug?
[ ] High lipid solubility of the drug [ ] Rapid gastric emptying
[ ] Extensive first-pass metabolism [ ] High stability in the GIT

7. Which of the following factors does NOT typically influence drug absorption?
[ ] pH of the gastrointestinal tract [ ] Molecular weight of the drug
[ ] Surface area available for absorption [ ] Blood flow at the site of administration

8. Which of the following is used when bioavailability measurement by pharmacokinetic methods is difficult?
[ ] Acute toxicological study [ ] Acute pharmacologic response
[ ] In vitro dissolution test [ ] Clinical trial

9. Which statistical method is commonly used in bioequivalence studies?
[ ] Regression analysis [ ] T-test
[ ] Chi-square test [ ] ANOVA

10. Acidic drugs administered orally are best absorbed from:
[ ] Oral cavity [ ] Stomach [ ] Intestine [ ] Rectum

11. The half life of a drug following therapeutic doses in human is 4 hours, therefore the elimination rate constant of this drug is_____ hr-1
[ ] 0.17325 [ ] 5.77 [ ] 0.693 [ ] 2.772

12. _____ of the following statements is **CORRECT**.
[ ] All other parameter remaining unchanged, the slower the absorption process, the higher is the peak plasma concentration after a single oral dose
[ ] After a single oral dose, an increase in bioavailability causes the peak time to shorten.
[ ] For a given drug in a subject, AUC is proportional to the amount of drug absorbed.
[ ] Absorption rate constant denote extent of drug absorption.

13. _____ of the following statements is **FALSE**.
[ ] Oral bioavailability increases with increasing body weight.
[ ] Volume of distribution varies in direct proportion to body weight.
[ ] Drug distribution is denoted by apparent volume of distribution
[ ] Drug elimination is denoted clearance

14. The AUC of a drug when administered extravascularly (dose = 500mg) was found to be 278.7 mg.hr/L. So the relative bioavailability of drug in comparison to intravenous administration (AUCiv = 149.2 mg.hr/L, dose 250 mg) will be_____
[ ] 0.934 [ ] 1.86 [ ] 2 [ ] 0.53

15. The bioavailability of drug administered via intravenous route is equal to_____
[ ] 1 [ ] >10 [ ] 10 [ ] 0.1 to 1

16. _____ of the following states of a drug will have better solubility/dissolution.
[ ] Crystalline [ ] Amorphous [ ] Solvates [ ] Acicular

17. An I. V. bolus (Dose = 400mg) which follows one compartment model was given to a patient. The initial plasma drug concentration and elimination half-life of the drug were 2μg/ml and 6 hours respectively. The plasma drug concentration after 4 hours was _____ μg/ml.
[ ] 1.26 [ ] 1.89 [ ] 1.48 [ ] 1.83

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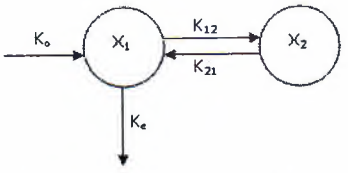
18. Assuming a one compartment linear pharmacokinetic model, with ke = 0.16 hr-1; and Vd = 16.2 L, The plasma concentration at 9 hours after starting a 200 mg/hr I.V. infusion will be _____ µg/ml.

[ ] 58.88 [ ] 325.67 [ ] 5.88 [ ] 32.58

19. _____ is the suitable differential equation for the following schematic diagram with reference to X1.



[ ] $\frac{dx_1}{dt} = K_o - K_{21}X_2 - K_{12}X_1 - K_eX_1$

[ ] $\frac{dx_1}{dt} = K_o + K_{21}X_1 - K_{12}X_2 - K_eX_1$

[ ] $\frac{dx_1}{dt} = K_o - K_{21}X_2 + K_{12}X_1 - K_eX_1$

[ ] $\frac{dx_2}{dt} = K_o + K_{21}X_2 - K_{12}X_1 - K_eX_1$

20. Movement of drug from GI tract to systemic circulation is known as_____

[ ] Absorpption [ ] Distribution [ ] Metabolism [ ] Bioavailability