Name : .....

Roll No. : .....

Invigilator's Signature : .....

CS/B.PHARM (NEW)/SEM-6/PT-611/2013

2013

PHARMACEUTICS (BIOPHARMACEUTICS & PHARMACOKINETICS)

Time Allotted : 3 Hours Full Marks : 70

The figures in the margin indicate full marks.

Candidates are required to give their answers in their own words as far as practicable.

GROUP – A

(Multiple Choice Type Questions)

1. Choose the correct alternatives for any *ten* of the following : $10 \times 1 = 10$

   i) When hepatic extraction ratio of a drug is one, its clearance is said to be

      a) intrinsic capacity limited

      b) perfusion rate limited

      c) hepatic blood flow independent

      d) none of these.

ii) In curve stripping technique, flip-flop kinetics refers to the case where

a) Ka/Ke > 3·0 b) Ka/Ke < 0·3

c) 0·3 < Ka/Ke < 3·0 d) Ke/Ka < 0·3.

iii) Which of the following mechanisms is responsible for GI absorption of Vitamin B1 and B2 ?

a) Passive diffusion b) Active Transport

c) Facilitated diffusion d) Pore transport.

iv) The total number of micro-constants that can be calculated for a n-compartment model is

a) $2n$ b) $2n - 1$

c) $2n + 1$ d) $n - 1$.

v) The slope of a log (% unabsorbed) versus time plot is – 0·4. Find out the first order absorption rate constant (K_a) .

a) 0·9212 hr^{-1} b) 1·1515 hr^{-1}

c) 0·8212 hr^{-1} d) 1·1212 hr^{-1}.

vi) Which of the following drugs shows rapid and pH independent absorption ?

a) Oxazepam b) Aspirin

c) Imipramine b) Chloroquine.

vii) Which of the following lubricants promotes dissolution ?

a) Magnesium stearate

b) Purified talc

c) Sodium lauryl sulphate

d) Finely divided talc.

viii) Facillated Diffusion is

a) Downhill process where energy is not required

b) Downhill process where energy is required

c) Uphil process where energy is not required

d) Uphill process where energy is required.

ix) Orally administered Sabin Polio Vaccine and Large Protein Molecules are absorbed by

a) Phagocytosis

b) Pinocytosis

c) Ion Pair Transport

d) None of these.

x) Formula used for calculating Mean Residence Time (MRT) is

a) $\dfrac{\int_0^{\infty} C\,dt}{\int_0^{\infty} Ct\,dt}$ b) $\dfrac{\int_0^{t} C\,dt}{\int_0^{t} Ct\,dt}$

c) $\dfrac{\int_0^{\infty} Ct\,dt}{\int_0^{\infty} C\,dt}$ d) $\dfrac{\int_0^{t} Ct\,dt}{\int_0^{t} C\,dt}$.

xi) If a drug has a very small volume of distribution (V_d), it is likely that this drug

a) has short biological half life

b) does not accumulate in various tissues and organs

c) not bioavailable

d) will not be effective.

xii) If the pKa value of a weakly basic drug is 8·4, then its percentage ionization in intestine (intestinal pH = 7·4) is

a) 90·99 b) 90·09

c) 90·19 d) 90·91.

GROUP – B

(Short Answer Type Questions)

Answer any *three* of the following. 3 × 5 = 15

2. Explain why *in vivo* drug dissolution is always faster than *in vitro* drug dissolution.

3. After intravenous infusion of a drug it requires 6·6 biological half lives for the plasma concentration (C) to reach 99% of the steady state concentration (C_{ss}). Prove the statement mathematically.

4. What is the influence of change in plasma pH on distribution pattern of a drug ? Based on pKa values, which drugs are most affected and which will be least affected by a change in plasma pH ? Phenobarbital and salicylic acid have almost the same $K_{o/w}$ but the former shows extensive distribution. Why. $1\frac{1}{2} + 1\frac{1}{2} + 2$

5. Why the volume of distribution is apparent ? Can a drug have a value larger than total body water volume ? How ?

6. The amount of drug excreted in urine after an *i.v.* bolus dose of 250 mg of amoxicillin was as follows :

Time (t) in hr.	X_u in mg	dX_u	dt	t^*	dX_u/dt	Log (dX_u/dt)
0	0					
0–2	40					
2–4	60					

After completing the table determine the first order elimination rate constant (K_E) and excretion rate constant (K_e) of the drug using rate of excretion method.

GROUP – C

(Long Answer Type Questions)

Answer any *three* of the following. 3 × 15 = 45

7. a) Name the parameters examined in urinary excretion data to determine bioavailability. Differentiate between bioavailability and bioequivalence.

b) The three pharmacokinetic parameters from urinary excretion data of a drug given as 50 mg oral formulations of two different companies, of which *A* is the innovator's product, are as follows :

Parameters	*Formulation*	
	A	*B*
$(dX_u/dt)_{max}$ (mg/hr)	6·0	8·0
$(t_u)_{max}$ (hour)	2·0	1·0
X_u^{∞} (mg)	39·1	35·9

i) What is the relative availability of formulation *B* against *A* ?

ii) Are the two formulations bioequivalent ?

iii) If the drug is meant for treatment of an acute condition, which one of the two formulations is better ?

c) Enlist the elements of a bioequivalence study protocol.

6 + 6 + 3

8. a) Enumerate the Loo-Riegelman method for estimation of absorption rate constant (K_a) in case of drugs that exhibit two compartment characteristics. 8

b) The plasma concentration obtained after 4 and 8 hours are 10 and 16 µg/ml respectively after *i.v.* infusion of cefoperazone. If the apparent volume of distribution is 50 litres, then find out the following :

i) Elimination rate constant (K_E)

ii) Steady state concentration (C_{ss})

iii) Infusion rate (R_0) to achieve the desired steady state

iv) Loading dose to obtain C_{ss} rapidly. 3 + 2 + 1 + 1

9. a) In compartment modeling what does the term 'open' means ?

b) Disposition of a drug that follows one compartment kinetics is a mono exponential process. Explain.

c) The half life of propanolol in a 60 kg patient is 4 hr and V_d is 5·5 ltr/kg.

i) Determine the total systemic clearance of the drug in ml/min.

ii) What will be its renal clearance (ml/min) if fraction excreted unchanged in urine is 0·047 ?

iii) If the drug is eliminated only by hepatic and renal routes, then what will be the hepatic extraction ratio if blood flow to the liver is 1·5 ltr/min ?

iv) If the blood flow rate to the liver is reduced to 0·8 ltr/min what will be the new hepatic and total systemic clearance values (ml/min) ?

v) What is the % decrease in the overall clearance of the drug ? 1 + 6 + 2 + 2 + 2 + 1 + 1

10. a) Define the term 'dissolution' and 'dissolution rate'. Discuss the three theories of dissolution with their mathematical equations. 1 + 1 + 5 + 2 + 2

b) If a tablet follows Hixson and Crowell's cubic root law of dissolution having original drug content 343 mg. After 6 hours of dissolution amount of drug released was 279 mg, then calculate the dissolution rate constant. 4

11. a) Based on pH-partition theory, predict the degree of ionization and absorption of weak acidic drug salicylic acid (pKa 3) in stomach (pH 1·2) and blood (pH 7·4).

b) Define displacement interaction. What characteristics of the displacer and the displaced drug are important for displacement interactions to be clinically significant ?

c) Displacement of a drug with a large Vd from its plasma protein binding site may not produce significant toxic reaction, why ?

d) How is the Scatchard plot useful in determining the number of binding sites and association constants ?

5 + 5 + 3 + 2