JRG College of Pharmacy

JRG COLLEGE OF PHARMACY

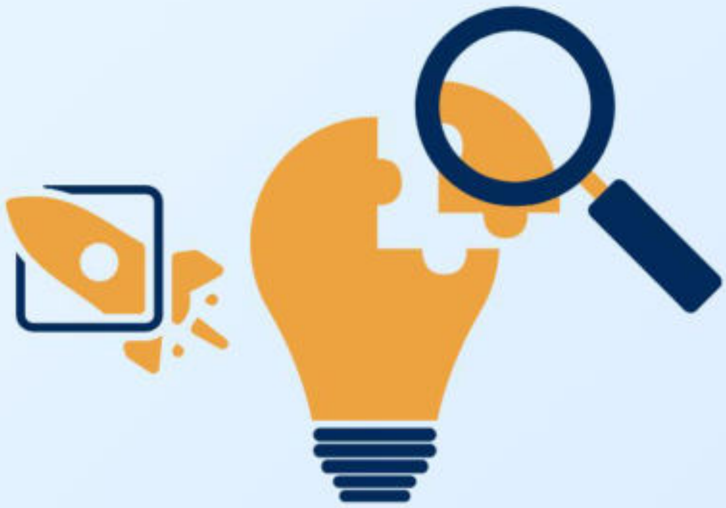
UNIVERSITY SOLVED QUESTION WITH ANSWER

Year : 2019-2020

Subject : Physical Pharmaceutics - I

Subject Code : BP302T

Subject In-Charge : Ms. Monali Padhi



Registration No:

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B.Pharm
BP302T

3rd Semester Regular/Back Examination 2019-20
PHYSICALPHARMACEUTICS-I
BRANCH : B.Pharma
Max Marks: 75
Time : 3 Hours
Q.CODE : HRB592

Answer Question No.1 (Part-A) and 02 (Part-B) which are compulsory and any TWO from Part-C.
The figures in the right hand margin indicate marks.

Part-A

Q1 Only Short Answer Type Questions (Answer All-10) **(2 x 10)**

- **a)** What do you mean by thermodynamic solubility of drugs?
- **b)** Differentiate between real and ideal solution.
- **c)** Define CST and miscibility temperature.
- **d)** What is aerosol? List two applications.
- **e)** What is dipole moment? How is it related to aqueous solubility?
- **f)** State Henderson-Hasselbalch equation for weak acid and weak base.
- **g)** How does drug-protein binding affect the absorption and metabolism of drugs?
- **h)** What are Chelates? How is it useful in pharmacy?
- **i)** What do you mean by buffer capacity?
- **j)** Define isotonic and hypotonic solution.

Part-B

Q2 Only Focused-Short Answer Type Questions- (Answer Any SEVEN out of NINE) **(5 x 7)**

- **a)** Write down the factors affecting the solubility of gas in liquid.
- **b)** State and explain Raoult's law.
- **c)** Discuss eutectic mixtures and its importance in formulations.
- **d)** Write a short note on 'glassy state'.
- **e)** Explain spreading co-efficient with suitable equation.
- **f)** What is HLB? What are its applications in pharmacy?
- **g)** Briefly explain about Langmuir isotherm with its derivation.
- **h)** Define Sorensen's pH scale. Write down different methods of determination of pH.
- **i)** Write down the capillary rise method for determining surface tension.

Part-C

Only Long Answer Type Questions (Answer Any TWO out of FOUR)

Q3 State and explain distribution law. Write down its limitations and applications. **(10)**

Q4 Discuss in brief about the measurement and applications of refractive index. **(10)**

Q5 State buffer solutions. Derive buffer equation and write its application in pharmacy. **(10)**

Q6 Define complexation. Briefly explain about inclusion complex. **(10)**

PHYSICAL PHARMACEUTICS - I

3rd Semester 2019 - 2020

Part - 'A'

1-

(a) What do you mean by thermodynamic solubility of drugs ?

Ans:- Thermodynamic Solubility of drug means the maximum amount of drug that can dissolve in a solvent under equilibrium condn at a given tempr and pressure.

Imp in Pharmaceuticals:-

→ Helps in understanding drug absorption & bioavailability.

→ useful in formulation design.

→ Provides a reference value for comparing other solubility types (like apparent solubility, Kinetic solubility)

(b) Differentiate between real and ideal solution?

Ans:-

Real Solution	Ideal Solution
→ A soln that doesn't obey Raoult's law over the entire conc. range.	→ A soln that obey Raoult's law at all conc. and tempr.
→ Intermolecular forces betn solute & solvent are not equal to those in pure components.	→ Intermolecular forces betn solute-solute, solvent-solvent & solute-solvent are equal.
→ Enthalpy change (ΔH_{mix}) is not zero.	→ Enthalpy change (ΔH_{mix}) is zero
→ Volume change (ΔV_{mix}) is not zero	→ Volume change (ΔV_{mix}) is zero

(c) Define CST and miscibility tempr?

Ans:- CST (critical solution Tempr):-

→ The soln is partially mix & form a conjugate layer betn them when heat is applied the conjugated layer slowly disappear when the conjugate layer completely disappear is called CST.

→ It is also called consolute Tempr.

Miscibility Tempr:-

→ The specific tempr at which two partially miscible liquids just become completely miscible in all proportions.

→ Miscibility tempⁿ is another term for CST.

(d) What is aerosol? List two applications?

Ans:- An aerosol is a suspension of very fine solid particles or liquid droplets dispersed in a gas medium.

Applications of Aerosol:-

(1) Pharmaceutical / Medical use:-

→ Inhalers for Asthma & COPD → deliver bronchodilators or Corticosteroids directly to the lungs.

→ Ex:- Salbutamol inhaler.

(2) Topical Appⁿ:-

→ Used for applying drugs to skin wounds, burns & infections in the form of sprays.

→ Ex:- Local anesthetic or antiseptic sprays.

(e) What is dipole moment? How is it related to aqueous solubility?

Ans:- Dipole moment: (μ)

→ It is the measure of the separation of positive and negative charge in a molecule.

→ It is a vector quantity. → unit = Debye (D)

$$\boxed{\mu = q \times d}$$ where, q = magnitude of charge
d = distance betⁿ charges.

Related to Aqueous Solubility:-

→ Water is highly polar (dipole moment ≈ 1.85D).

→ Molecules with higher dipole moments interact strongly with water molecules.

→ Molecules with low or zero dipole moment are non-polar.

(f) State Henderson-Hasselbalch Eqⁿ for weak acid & weak base?

Ans:- Weak acid buffer:-

$$pH = pKa + \log \frac{[Salt]}{[Acid]}$$

Weak base buffer:-

$$pH = 14 - \left(pK_b + \log \frac{[Salt]}{[Base]}\right)$$

(g) How does drug-protein binding affect the absorption & metabolism of drugs?

Ans:- When a drug-protein binding bloodstream, part of it binds reversibly to plasma proteins.

→ Bound drug → pharmacologically inactive.

→ Free drug → pharmacologically active, available for absorption, distribution, metabolism & excretion.

Affect on absorption:-

→ Protein binding mainly occurs after the drug enters circulation.

→ High binding may maintain a conc. gradient bet^n blood & GI tract.

Affect on Metabolism:-

→ High protein binding → Less free drug → slower metabolism

→ Low protein binding → more free drug → faster metabolism

(h) What are chelates? How is it useful in pharmacy?

Ans:- A chelate is a complex formed when a metal ion binds with a ligand that has two or more donor groups capable of attaching to the same metal ion, forming a ring. etc.

Ex:- EDTA

Useful in Pharmacy:-

→ It is used to reduce blood & tissue levels of injurious heavy metals

→ It is used in chelation therapy to remove toxic heavy metals

(i) What do you mean by buffer capacity?

Ans:- Buffer capacity is the ability of a buffer sol^n to resist changes in pH when small amount of acid or base are added.

$\beta = \frac{dB}{d(pH)}$ where, dB = small amount of strong base or acid added in mol/L

d(pH) = resulting change in pH.

(j) Define isotonic and hypotonic solution?

Ans:- Isotonic sol^n:-

→ A sol^n that has the same osmotic pressure as body fluids. (Ex:- blood plasma, tears)

→ Ex:- 0.9% Sodium chloride; 5% glucose sol^n.

Hypotonic Solution:-

→ A sol^n that has lower osmotic pressure than body fluids.

→ Ex:- 0.45% sodium chloride solution.

2. **Part - 'B'**

(a) Write down the factors affecting the solubility of gas in liquid ?

Ans- The solubility of gases in Liquids is influenced by several physicochemical factors.

1 - Nature of the gas and Liquid :-

polar gases like CO_2, SO_2 and NH_3 dissolve better in polar solvent like water due to dipole-dipole intractions and hydrogen bonding.

→ Non-polar gases such as O_2, N_2 are more soluble in non-polar solvent.

2- Temperature :-

Solubility of most gases decreases with rise in temperature.

3- Pressure :-

According to Henry's Law, the solubility of a gas in a liquid is directly proportional to the partial pressure of the gas above the solution. $C = KP$.
This principle is used in carbonation of soft drinks.

4- Presence of salts or solutes :-

Electrolytes often reduce the solubility of gases, a phenomenon called salting out.

Ex:- CO_2 solubility decreases in saline water compared to pure water.

5. PH of solution :-

For ionizable gases (e.g. CO_2, NH_3) solubility is strongly affected by PH. In acidic medium CO_2 forms H_2CO_3, increasing solubility, where as NH_3 dissolves better in acidic solution due to formation of NH_4^+ ions.

(b) State and explain Raoult's Law ?

Ans- Raoult's Law provides a fundamental relationship between vapour pressure and composition in liquid mixtures.

→ In 1887, Francois marie Raoult develops this relationship.

→ According to this law for a solution of volatile liquid, the partial VP of each component of a solution is proportional to the mole fraction of the component present in the solution.

$$P_{solution} = X_{solvent} \cdot P^{\circ}_{solvent}$$

Mathematical Expression :-

For a binary solution of components A & B.

- partial vapour pressure of component A :

$$P_A = X_A \cdot P^{\circ}_A$$

- Partial vapour pressure of component B :

$$P_B = X_B \cdot P^{\circ}_B$$

Where,

P_B & P_A = partial vapour pressure of A & B.

X_A & X_B = Mole fraction of A and B in the solution.

P°_B & P°_A = Vapor pressure of pure components A & B.

Total vapour pressure of the solution :

$$P_{total} = P_A + P_B$$

$$P_{total} = X_A \cdot P^{\circ}_A + X_B \cdot P^{\circ}_B$$

(C) Discus eutectic mixture and it's importance in formulations ?

Ans- A eutectic mixture is a homogeneous mixture of two or more substance that solidifies at a lower temperature than the melting point of any of its individual components.

→ The eutectic point is the lowest temperature at which the mixture remains in the liquid state.

→ At this composition, the mixture has a sharp melting point (Like a pure substance) even though it contains multiple components.

Importance in formulations :-

1 - Improved solubility & Dissolution :-

Eutectic mixture often have better solubility than individual drugs, leading to improved bioavailability.

2- Lower Melting point for processing :-

Allows drugs to be processed at lower temp: useful for heat-sensitive APIs (Active pharmaceutical Ingredients).

3. Topical preparations :-

Lidocaine + prilocaine eutectic → Forms an oily liquid at room temperature, enhancing skin penetration and providing effective local anesthesia.

4- Taste Masking :-

Eutectic Formation can reduce unpleasant taste of drugs.

5- Controlled Release systems :-

Used in solid dispension and lipid-based drug delivery for sustained release.

(d) Write a short note on "Glassy state"?

Ans- The glassy state refers to an amorphous, non-crystaline solid form of a drug that exists below its glass-transition temperature (Tg). Unlike crystalline solids which have long-range order, glassy materials have a random, disordered molecular arrangement but are rigid and brittle.

Characteristics:-

→ No definite melting point, instead shows a glass transition temperature.

→ Hard, brittle, & transparent.

Examples:-

Common glass, Some polymers, sugar glasses.

Applications:-

widely used in making windows, optical lenses, containers, pharmaceutical formulations & in electronics.

→ The Glassy state is often described as a "frozen liquid", where molecular mobility is highly restricted but structural disorder remains.

→ In this state, the material appears solid but lacks the long-range periodic arrangement of atoms or molecules found in crystals.

(e) Explain spreading co-efficient with suitable equation ?

Ans- The spreading co-efficient is a thermodynamic parameter that determines the ability of one liquid to spread over another liquid or over a solid surface.

→ It is used to predict whether a liquid will wet the surface and form a continuous film or bead up and form droplets.

Equation :-

$$S = \gamma_S - (\gamma_L + \gamma_{SL})$$

where,

S = spreading co-efficient

γ_S = Surface tension of the substrate.

γ_L = surface tension of the spreading liquid.

γ_{SL} = Interfacial tension between substrate and spreading liquid

Interpretation :-

value of S	meaning	Resulting Action
$S > 0$ →	Favorable spreading →	Liquid spread completely.
$S < 0$ →	unfavorable spreading →	Liquid forms droplets
$S = 0$ →	Neutral condition →	may form a partial film

Example :-

Suppose a liquid (e.g. oil) is placed on a water surface.

If,

Surface tension of water (γ_S) = 72.8 mN/m

Surface tension of oil (γ_L) = 30.0 mN/m

Interfacial tension between oil and water (γ_{SL}) = 35.0 mN/m

Then :

$S = 72.8 - (30.0 + 35.0)$

$= 7.8$ mN/m

$S > 0$, so oil will spread over water.

(f) What is HLB? What are its application in pharmacy?

Ans:- The Hydrophilic - Lipophilic Balance (HLB) is a numerical scale that expresses the relative degree of hydrophilicity (water-loving) and lipophilicity (oil-loving) of a surfactant.

→ It was 1st discovered by Griffin in 1949 (1948 - 1949).

→ HLB has 3 generation.

- 1-40 → 1-20, 20-40
- 1-20 → 1-10, 10-20
- 1-16 (latest generation) → 1-8, 8-16

→ HLB values range from 0 to 20.

HLB Value	Function
1 - 3	Antifoaming agent
3 - 6	water-in-oil (w/o) emulsifiers
7 - 9	wetting and spreading agent
8 - 16	Oil-in-water (o/w) emulsifiers
13 - 18	Solubilizing agent

Application in pharmacy :-

1- Emulsion formulation :-
The required HLB value of an oil phase determines which surfactant should be selected.

2- Solubilization :-
Surfactant with HLB values around 15-18 help in solubilizing poorly soluble drugs.

3- Wetting agents :-
Surfactant of intermediate HLB (7-9) improve wetting of powders in suspensions.

4- Detergents and cleaning agent :-

High HLB surfactants are used in pharmaceutical cleaning.

5- Stabilizers in creams and lotions :-

proper selection of surfactant based on HLB improves texture and shelf life.

(9) Briefly explain about Langmuir isotherm with it's derivation ?

Ans- The Langmuir adsorption isotherm is a theoretical model that describes the adsorption of a gas or solute onto a solid surface, forming a monolayer. It assumes that adsorption occurs on a homogeneous surface with a fixed number of identical site and no interaction between adsorbed molecules.

Derivation :-

The isotherm is mathematically expressed as :

$$\theta = KP / 1 + KP$$

where,

θ = Fraction of surface sites occupied

K = Langmuir adsorption constant (related to affinity)

P = partial pressure (for gases) or concentration (For sol)

Alternate form (For amount adsorbed) :-

$$X/m = abc/1 + bc$$

where,

X/m = amount of adsorbate per unit mass of adsorbent

C = concentration of adsorbate

a, b = Langmuir constants

Application :-

1- Catalysis :-
Used to design heterogeneous catalysts, where gases adsorb onto metal surface

2. Gas mask Design :-
Models how activated charcoal adsorbs toxic gases - crucial in protective respirators.

3- moisture Adsorption :-
Help study how excipients or packing material absorb water vapour.

4- Chromatography :-
Explain how adsorption onto stationary phase impacts separation efficiency.

Limitations :-

→ Not applicable to multilayer adsorption

→ Assumes ideal behavior - real surface may be heterogeneous.

→ Ignores adsorbate - adsorbate interaction

(h) Define Sorensen's pH scale. Write down different method of determination of pH ?

Ans- The pH scale was introduced by Sorensen in 1909 to express the hydrogen ion concentration in a solution.

$$pH = -\log_{10} [H^+]$$

The scale generally ranges from 0 to 14.

$pH < 7$ → Acidic solution

$pH = 7$ → Neutral solution

$pH > 7$ → Basic / alkaline solution

Methods of Determination of pH :-

1 - Indicator method (colorimetric method) :-

Uses acid - base indicators such as methyl orange, phenolphthalein, bromothymol blue or universal indicator.

→ The solution's pH is determined by the color change of the indicator or by comparing with a standard pH color chart.

2. pH paper method :-

Litmus paper or universal pH paper strips are dipped in the solution.

→ The paper changes color, which is compared with a colour scale to estimate pH.

3. Electrometric method (pH meter) :-

• The most accurate method.

→ Uses a glass electrode and a reference electrode connected to pH meter.

→ Widely used in pharmacy, medicine, and industry.

4. Conductometric method :-

Based on the fact that conductance of a solution changes with hydrogen ion concentration.

→ Not as common but useful in very dilute solution.

5. Spectrophotometric method :-

Measures the absorbance or transmittance of light by a solution containing an indicator.

→ The wavelength shift is related to pH.

(i) Write down the capillary rise method for determining surface tension?

Ans. Surface tension :-

Surface tension is defined as the force acting along the surface of a liquid at right angle to any line drawn in the surface, tending to minimize the surface area.

→ It is expressed in N/m or dyne/cm.

Capillary rise method :-

Principle :-

A liquid rises in a capillary tube due to surface tension, forming a concave meniscus.

Formula :- $\gamma = hr\rho g/2$

where,

γ = Surface tension (in N/m)

h = Height of the liquid column in the capillary (in meters)

r = Radius of the capillary tube (in meters)

ρ = Density of the liquid (in kg/m^3)

g = Acceleration due to gravity ($9.8\ m/s^2$).

Application :-

Common method for water and aqueous liquid

Advantages :-

→ Simple experimental method

→ Suitable for liquid that wet the capillary wall.

'Part - C'

3. State & explain distribution law. Write down its limitations & applications.

Ans → The distribution law states that: when a solute is distributed between two immiscible solvents at equilibrium the ratio of its concentrations in the two phases remains constant at a given temp.

Partition co-efficient = $\frac{\text{Drug dissolve in lyophilic}}{\text{Drug dissolve in hydrophilic}}$

$$\boxed{P = \frac{X_o}{X_w}}$$

X_o = drug in oil phase

X_w = drug in water phase.

∴ if $P > 1$ = lyophilic

$P < 1$ = hydrophilic

limitations:-

→ The solute should not undergo dissociation or association in either solvent.

→ The solvents must be immiscible & the solute should not chemically react with them.

→ Temp. must remain constant.

→ Accurate results require equilibrium to be established.

Applications in pharmacy:-

- **Drug absorption:-** Partition co-efficient determine drug distribution between lipid membrane & aqueous body fluids.

→ Lipid-soluble drugs cross biological membrane more easily.

- **Extraction process:-**

Solvent Extraction of drugs & natural products depends on distribution law.

- **Formulation studies:-**

Helps in selection of solvents & vehicles for suspensions, emulsions & injections.

- **Antibacterial action of drugs:-**

Drugs with optimum partition co-efficient penetrate bacterial cells walls effectively.

- **Determination of ionization Constant:- (pKa)**

Partitioning of weak acids & bases in aqueous & organic solvents provides Pka value.

→ The distribution law is an important physiochemical principle in pharmaceutics with applications in drug adsorption, extraction, formulation & studies. though it is limited by assumptions of solute stability & immissibility of solvents.

4. Discuss in brief about the measurement and application of refractive index ?

ANS → It is the ratio of speed of light between any two medium.

$$RI_{A/W} = \frac{\text{speed of light in air}}{\text{speed of light in water}}$$

→ speed of light is different in different medium. So we take ratio of any two medium.

Application:-

1. pharmaceuticals → used for drug quality control & solution concentration analysis.
2. food industry → Determines sugar concentrations in juices & beverages.
3. optics → Designing lenses, prisms, & optical instrument.
4. Geology → Identifying minerals & gemstones.
5. Medical field → measuring corneal refractive index in opthalmology.
6. chemical Analysis → Monitoring reaction progress or concentration changes.

Measurement:-

- Refractometer – common in labs & industries.
- Critical angle method – based on total internal reflection.

5 state buffer Solutions. derive buffer equation & Write its application in pharmacy.

ANS → A buffer solution is defined as a solution that resists change in pH upon addition of Small amounts of acid or base.

→ Buffers are made up of weak acid & its conjugate base, or weak base & its conjugate acid.

Types :-

i) **Acidic**:- Acidic buffers are those buffer soln which is used in acidic solution.

Composition :-

weak acid + strong base.

e.g ÷ [CH_3COOH + CH_3COONa] .

ii) **Basic** :- Basic buffers are those which is used in basic solution.

Composition :-

weak base + strong acid.

e.g ÷ [NH_4OH + NH_4Cl]

buffer equation :-

→ It is used to calculate the pH of a buffer solution & the change in pH with the addition of acid / base.

→ Dissociation of weak acid & salt :-

$$HA \rightleftharpoons H^+ + \boxed{A^-}$$

$$BA \longrightarrow B^+ + \boxed{A^-} \rightarrow \text{common ion effect}$$

By applying law of mass action

$$Ka = \frac{[H^+][A^-]}{[HA]}$$

on rearrange,

$$[H^+] = Ka \frac{[HA]}{[A^-]}$$

$$[H^+] = ka \frac{[Acid]}{[salt]}$$

Taking $-\log$ on both sides,

$$-\log[H^+] = -\log\left[Ka\frac{(Acid)}{(Salt)}\right]$$

$$-\log[H^+] = -\log Ka - \log\left[\frac{(Acid)}{(Salt)}\right]$$

$$-\log(H^+) = pH \quad \&$$

$$-\log Ka = pKa$$

$$pH \Rightarrow pKa - \log\frac{[Acid]}{[Salt]}$$

$$pH = pKa + \log\frac{[Salt]}{[Acid]}$$

Application in pharmacy :-

- **Drug stability :-**

  Buffers maintain drug solutions at stable pH to prevent degradation.

- **Biological system :-**

  Blood is buffered by carbonic acid - bicarbonate system.

- **Solubility Control :-**

  Buffers are used to adjust drug Solubility by maintaining ionization equilibrium.

6. Define Complexation. Briefly explain about inclusion complex?

Ans- Complexation :-

Complexation refers to the reversible association between a ligand and a substrate (metal ion, drug or molecule) to form a complex.

→ The interaction may involve covalent, ionic, hydrogen bonding, or vander waals forces.

Types of complexes in pharmacy :-

→ Metal complexes :-
Formed between metal ions and ligand.

→ Organic molecular complexes :-
Non-covalent associations between molecules.

→ Inclusion complexes :-
Host-guest complexes where one molecule entraps another within its lattice or cavity.

Inclusion Complexes :-

An inclusion complex is a type of complex where one molecule gets trapped inside the cavity of another molecule, without forming any true covalent or ionic bond.

→ The association is mainly due to hydrophobic interaction hydrogen bonding or van der waals forces.

→ The host molecule has a cage-like or hollow structure that allows the guest molecules to fit inside.

Example :-

Complexation of hydrophobic drug like nifedipine, itraconazole, indomethacin with cyclodextrins improves dissolution and absorption.

→ Volatile drugs can be stabilized by inclusion to reduce evaporation.

→ Bitter taste of drugs like paracetamol can be masked by cyclodextrin complexation.

Applications :-

1. Drug solubility enhancement
   (Hydrophobic drug become more soluble)
2. Stability improvement
   (protection against oxidation, hydrolysis photodegradation)
3. Taste masking
   (important in pediatric formulations)
4. Controlled release
   (guest molecules released slowly from host structure)