JRG College of Pharmacy

JRG COLLEGE OF PHARMACY

UNIVERSITY SOLVED QUESTION WITH ANSWER

Year : 2022-2023

Subject : Physical Pharmaceutics - I

Subject Code : BP302T

Subject In-Charge : Ms. Monali Padhi

Registration No : | | | | | | | | | | |

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Course: B.Pharm
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3rd Semester Regular/Back Examination: 2022-23
SUBJECT: Physical Pharmaceutics-I
BRANCH(S): Pharmacy
Time : 3 Hour
Max Marks : 75
Q.Code : L698

Answer Question No.1 (Part-1) which is compulsory, any eight from Part-II and any two from Part-III.

The figures in the right hand margin indicate marks.

Part-I

Q1 **Answer the following questions :** **(2 x 10)**

a) Define the term solubility.
b) Differentiate between ideal and real solution.
c) State polymorphism and its application.
d) Write down the Henderson-Hasselbalch equation for weak acid and weak base.
e) What is HLB? Write any two importance of HLB.
f) Define surface active agents with suitable example.
g) Explain about sublimation.
h) What is Sorensen's pH scale?
i) Mention the physicochemical properties of the drug molecules.
j) Differentiate between surface and interfacial tension.

Part-II

Q2 **Focused-Short Answer Type Questions- (Answer Any Seven)** **(5 × 7)**

a) Write notes on "Liquid Crystal" and glassy state.
b) Write a detailed note on spreading coefficient.
c) What is buffer? Write about the determination of buffer capacity.
d) Describe the diffusion principles in biological systems
e) What is BET equation? Write different types of isotherms.
f) Narrate basic principle of aerosol.
g) Define refractive index. Explain any one procedure to determine it.
h) What are Chelates? write its usefulness in pharmacy
i) Classify the drug Complexation

Part-III

Long Answer Type Questions (Answer Any Two)

Q3 Discuss in detail of Raoult's low and its deviations. **(10)**

Q4 What is universal gas law, derive it. **(10)**

Q5 Enlist the methods used to measure the surface and interfacial tensions. Explain any one in detail. **(10)**

Q6 Explain the kinetic of drug-protein binding. Write down its significance. **(10)**

b) Solubility:-

- The mixture of Solute and Solvent is called Solution. Solute are phase component and Solution which are present in low amount and Solvent which are present in large amount and when Solute particles completely dissolve in Solvent it is called Solution.
- The maximum amount of Solute which can be dissolve in 100gm of Solvent is called Solubility of drug.

b) Ideal Solution

→ The Solution which obeys Raoult's law at all concentration over whole range of temp.

→ No heat is absorbed or evolved.

→ No change in property.

Real Solution

→ The Solution which doesn't obey Raoult's law or shows deviation.

→ Heat may be evolved or adsorbed.

→ Change in properties in real Solution.

c) Polymorphism is the ability of a substance to exist in multiple crystaline form each with distinct physical and chemical properties.

Application:-

→ Helps to control crystallization process and product quality.

→ Controlling and understanding polymorphism is critical in pharmacy for ensuring a drug's safety, efficacy and consistency.

d) The Henderson Hasselbalch equation is

$$pH = pKa + \log_{10}[A^-]/[HA]$$

for weak acid and weak base buffer Solution.

e) it is a numerical scale that indicates the balance between the water-loving (hydrophilic) and oil-loving (lipophilic) portions of a surfactant.

Importance:-

- HLB value helps decide whether a surfactant will form an oil-in-water (O/W) emulsion or water in oil (W/O) emulsion.
- Correct HLB ensures optimum stability of emulsions, creams, lotions and other dosage forms by preventing phase separation.

f) Surface active agents:-

compounds that reduce surface/interfacial tension and improve stability, solubility and dispersion in pharmaceutical formulations.

Ex:- Anionic- Sodium lauryl sulfate.
Cationic- cetyltrimethylammonium bromide.
Non-ionic- tween 80.
Amphoteric- lecithin.

g) Sublimation:-

It is the process in which a substance changes directly from solid to vapour state without passing through the liquid state.

Ex:- used in preparation of porous tablets.

h) It was introduced by SPL. Sorensen (1909) to express the hydrogen ion concentration of a solution on a logarithmic scale.

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

1) physicochemical properties of drug molecules:
→ physical state, particle size, polymorphism.
→ solubility, partition co-efficient, pKa
→ stability (chemical / physical), hygroscopicity.

2) Surface tension

→ force per unit length acting at the interface between a liquid and air.

→ ex: drop formulation in water.

Interfacial tension:

→ force per unit length acting at the interface between two immiscible liquids.

→ ex: oil - water interface in emulsions

2a) Liquid crystals :-

-> Three states of matter gas, liquid and Solid, have been discussed.

-> The fourth state of matter is the liquid crystal state or mesophase.

-> The liquid crystal state is the distinct state of matter observed between the crystalline Solid and liquid states.

-> In the crystalline Solid state, arrangement of molecules is regular.

-> The molecules are held in fixed positions by intermolecular forces.

Glassy State :-

-> The glassy state of materials refers to non-equilibrium, Solid state, such as is typical of inorganic glasses, synthetic non-crystalline polymers and food components.

-> Characteristics of glassy state include transparency, Solid appearance and brittleness.

-> In such systems, molecule have no ordered structure and volume of the system is larger than that of crystalline systems with the same composition.

-> These systems are often referred to as amourphous

6) Spreading co-efficient :-

→ The concept of work of cohesion and work of adhesion help to understand the spreading of one liquid on another and predict whether it should spread spontaneously or not.

→ There exists a mathmatical relationship, which can be used to forecast the outcome of the situation called as spreading co-efficient, denoted by S.

→ there are two possibilities, first, the liquid can be spread over the surface of sublayer liquid or second, the added liquid determining net loss in free energy.

→ if a force is applied on a liquid tube to separate into two parts, then the work done is called the work of cohesion.

→ if a force is applied ~~on this~~ to cause the liquid to separate, we have done three things and the work done is called work of adhesion (W_a).

→ The spreading of liquid is controlled by surface tensions of pure immisable liquids and interfacial tension between them.

c) Buffer :-

-> Buffer are defined as a compound or a mixture of compounds that resists the pH upon the addition of small quantities of acid or alkali.

Buffer capacity :-

-> Buffer counteracts the change in pH of a solution upon the addition of a strong acid, a strong base, or other agents that tend to alter the hydrogen ion concentration.

-> The magnitude of the resistance of a buffer to pH change is referred to as the buffer capacity (β).

-> It is also known as buffer efficiency, buffer index, and buffer value.

-> Koppel and Spiro and Van Slyke introduced the concept of buffer capacity.

$$\beta = \frac{\Delta B}{\Delta pH} \quad \text{---------- (1.)}$$

-> According to equation -(1), the buffer capacity has a value of 1 when 1 gram equivalent of strong base is added to 1L of buffer solution, if the change in pH is 1 unit.

-> The buffer capacity has its greater capacity, when salt/acid is equal to 1. therefore Henderson Hasselbalch equation may be written as $pH = pK_a$.

-> The buffer capacity decreases appreciably as the pH deviate more than 1 unit on each side of the pK_a value.

→ buffer capacity is not a fixed value for a given buffer system, but depends on the amount of base added.

Q) Diffusion principles of biological systems.

- **Blood:-**

→ Blood consist of primary and secondary buffer erythrocytes system contributing the PH 7.4.

→ when the PH of the blood below 7.0 or above ... ary . the PH of blood in diabetic ... as 6.8 ...

2) d) Diffusion is defined as the process of mass transfer of individual molecules of a substance caused by random molecular motion and associated with a concentration gradient.

→ The rate of diffusions depends on temperature, size of the particles, and the size of the concentration gradient.

→ Selectively permeable cell membrane exhibits two forms of diffusion namely:
a) osmosis for the diffusion of water.
b) Dialysis for the diffusion of solutes.

a) Osmosis: It is the passage of solvent across a membrane which is semi-permeable in nature.

2) Dialysis: Separation process based on unequal rates of passage of solutes and solvents through microporous membranes, carried out in batch or continious mode.

Principles:
1) Fick's first law of diffusion.
2) Fick's second law of diffusion.

Rate of diffusion is expressed by equation

$$\frac{dm}{dt} = DSK \frac{(C_1 - C_2)}{h}$$

e) BET equation (Brunauer - Emmett - Teller equation)

-> it explains the adsorption of gas molecules on a solid surface and is widely used to determine the surface area of powders on pharmaceutics.

$$\left[\frac{P}{X(P_0 - P)}\right] = \left[\frac{1}{X_m b}\right] + \left[\frac{(b-1)}{X_m b}\right] \times \left[\frac{P}{P_0}\right]$$

P is the pressure of the adsorbate.

X is mass of vapour per gram of adsorbent.

P_0 is vapour pressure at saturation of adsorbent by adsorbate.

X_m is amount of vapour adsorbed per unit mass of adsorbent.

b is constant.

Types of adsorption isotherms:

-> Type-I (Langmuir isotherm): monolayer adsorption.

-> Type-II: multilayer adsorption on non porous or macroporous solids.

-> Type-III: weak interaction between adsorbate and adsorbent.

-> Type-IV: multilayer adsorption with capillary condensation in mesospores.

-> Type-V: weak adsorbate-adsorbent interaction with capillary condensation.

f) Pharmaceutical aerosols are pressurized dosage forms containing one or more active ingredients that, upon actuation, emit a fine dispersion of liquid and/or solid materials in a gaseous medium.

Principles:

1) Two-phase system: consist of a liquid phase and vapour phase.

2) Pressure principle: The propellant maintains constant pressure inside the container, ensuring uniform dose delivery until nearly empty.

3) Dispersion principle: The drug is dispersed as fine particles or droplets due to rapid vaporization of the propellant.

4) Valve and actuator system: controls the dose, rate, and form of the emitted product.

5) Types of propellants: liquefied gases, compressed gases.

6) Stability principles: The sealed container prevents contamination, oxidation and maintain sterility.

7) Delivery principle: Aerosol allow direct application to skin, mucous membrane, lung.

Application:

-> Inhalation therapy (asthma, COPD).

-> Topical Sprays (antiseptics, anesthetics).

8) Refractive index is defined as the ratio of the velocity of light in vacuum to the velocity of light in a given medium.

$$n = \frac{c}{v} = \frac{\sin i}{\sin r}$$

where, n = refractive index
i = angle of incidence
r = angle of refraction.

Procedure to determine RI (using Abbe refractometer).

1) Principles: Based on measurment of critical angle of total internal reflection when light passes from sample to prism

2) Steps:
-> Place a drop of the sample liquid between the measuring prism and illuminating prism.
-> Allow light to pass through
-> Adjust the compensator to obtain a sharp boundary line between bright and dark field.
-> Read the refractive index from the instrument scale.

Applications:
-> To check purity of drugs, essential oils, and solvents.
-> To identify and characterize crystals and polymorphs of drugs.

h) chelates are complex compounds formed when a metal ion binds with a single ligand at two or more donor sites to form a stable ring-like structure.

Ex:- EDTA

Usefulness of chelates in pharmacy:

-> Stabilization of drug formulations - chelating agents bind trace metals like Fe^{3+} and Cu^{2+} that catalyze oxidation, thus preventing degradation.

-> Antimicrobial preservation: chelating agents enhance the action of preservatives by removing trace metals required for microbial growth.

-> Therapeutic use: Used to remove toxic metals from the body e.g. EDTA for lead poisoning, Desferoxamine for iron poisoning.

-> Improved solubility: Chelates can increase the aqueous solubility of poorly soluble drugs.

-> Enhanced bioavailability: Some chelates facilate drug absorption by improving stability and permeability.

1) Drug complexation is the reversible association between a drug molecule and others molecules to form a stable complex.

Classification of complexes:-

1) Inorganic complexes:-
   formed between metals and ligands
   Ex:- EDTA = metal complexes.

2) Co-ordination complexes:-
   central metal ion bound to molecules/ions via co-ordinate bonds.
   Ex:- cisplatin.

3) Chelates:- complexes where a metal can bind with a ligand at two or more donor sites forming a ring.
   Ex:- Calcium - EDTA complex.

4) Molecular complexes:-
   weak interactions (H-bond, Van der waals, hydrophobic).
   Ex:- caffeine - benzocaine complex.

5) Inclusion complexes:-
   one molecules gets 'trapped' inside the cavity of another.

4) Toxicity :- Binding can affect the drugs toxicity profile.

factors affecting Drug-protein Binding :-

1) Protein concentration :- Changes in protein levels can affect binding.

2) Drug concentration :- High drug concentrations can saturate binding sites.

3) PH and temperature :- Changes in PH or temp. can affect binding affinity.

4) Other Substances :- Other drugs, nutrients, or endogenous compounds can compete for binding sites.

Clinical Implications :-

1) Dose Adjustment :- Understanding Binding kinetics can inform dosing strategies.

2) Drug monitoring :- monitoring Drug levels can help optimize therapy.

3) Drug Development :- understanding binding kinetics can aid in designing new drugs.

6) Drug protein binding kinetics

Drug - protein binding is a reversible interaction between a drug molecules and a protein, such as albumin or globulin, in the blood stream or tissues. This binding affects the drugs distribution, metabolism and elimination.

Kinetics of Drug - protein binding:-

1) Association Rate constant (Kon) :- The rate at which the drug binds to the protein.

2) Dissociation Rate constant (Koff) :- The rate at which the drug dissociates from the prote

3) Binding affinity :- The strength of the interaction between the drug and protein, determined by the ratio of Kon to Koff.

4) Binding Capacity :- The maximum amount of drug that can bind to the protein.

Significance of Drug- protein Binding :-

1) pharmacokinetics :- Binding affects drug distribution metabolism and elimination.

2) pharmacodynamics :- Binding influences drug efficacy and potency.

3) Drug interactions :- Binding can be affected by other drugs or substances, leading to altered pharmacokynetics or pharmacodynamics.

5) methods to measure surface tension and interfacial tension.

→ Du Nouy ring method: measures the force required to pull a ring from the surface of a liquid.

→ Wilhelmy plate method: measures the force exerted on a plate partially submerged in a liquid.

→ pendant drop method: Analyze the shape of a pendant drop to determine surface tension.

→ Sessile drop method: measures the contact angle of a drop on a surface to estimate surface tension.

→ Spinning drop method: measures the deformation of a drop in a rotating tube to determine interfacial tension.

Detailed explanation of the Du Nouy Ring method

The Du Nouy ring method is widely used technique for measuring surface tension. it involves a ring, typically made of platinum or another inert material.

Steps:-

1) Ring preparation: The ring is cleaned and dried before measurement.

2) liquid preparation: The liquid is poured into a container, and the ring is brought into contact with surface.

3) measurement: The force required to pull the ring from the surface is measured using a tensiometer.

4) Calculation: The surface tension is calculated using the formula: $\gamma = F / (2 \times \text{circumference of ring})$.

Advantages :-

1) Accurate :- provides accurate measurement of surface tension.

2) Simple :- Relatively simple to perform and interpret.

3) Versatile :- can be used for a wide range of liquids.

limitations :-

1) Ring calibration :- the ring must be properly calibrated for accurate measurement.

2) liquid properties :- the method may not be suitable for liquids with high viscosity or complex rheology.