Unit-1

Physical Pharmaceutics

UNIT-I

- **Solubility of drugs:** Solubility expressions, mechanisms of solute solvent interactions,ideal solubility parameters, solvation & association, quantitative approach to the factors influencing solubility of drugs, diffusion principles in biological systems. Solubility of gas in liquids, solubility of liquids in liquids, (Binary solutions, ideal solutions) Raoult's law, real solutions. Partially miscible liquids, Critical solution temperature and applications. Distribution law, its limitations and applications

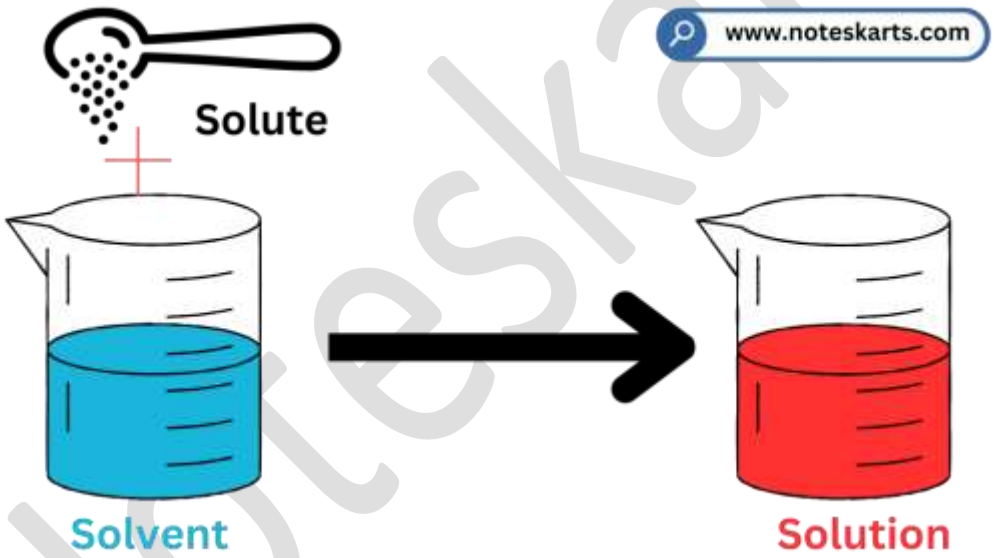
Solubility of drugs:

- Solubility may be defined as the maximum concentration of a substance that may be completely dissolved in a given solvent at a given temperature and pressure.
- The USP/NF generally expresses the solubility in terms of the volume of solvent required to dissolve 1 gram of the drug at a specified temperature (eg. 1 g ASA in 300 ml H2O, 5 ml ethanol at 25°C).

Solution: When solutes are completely dissolve in solvent and remain present at the level of molecular size.

Solute: It is the substance which dissolved in solvent. Solvent are always less abundant while solvents are more abundant part of the solution.

Solvent: It is a component in which solute is dissolved.



Solubility expressions:

S.No.	Terms	Part Of Solvent Required Of One Part Of Solute
1.	Very soluble	Less than 1 part.
2.	Freely soluble	1 to 10 parts
3.	Soluble	10 to 30 parts.
4.	Sparingly Soluble	30 to 100 parts.
5.	Slightly Soluble	100 to 1000 parts.
6.	Very slightly soluble	1000 to 10000 parts.
7.	Practically insoluble	More than 10000 parts.

Types of Solution:

- **Saturated solution**: The solution containing maximum number of solute at a constant temperature is called saturated solution.
- **Super saturated solution**: A solution that contains more of the dissolved material then could be dissolved by the solvent under normal circumstances.
- **Unsaturated Solution** A solution where the solute concentration is lower than its equilibrium solubility.

Mechanisms of solute solvent interactions:

- The dissolution of solute into solvent is depends upon different solute solvent interaction mechanism.
- When solvent molecules aggregate then they must from is cavity in which the solute molecules is entered.
- Solute solvent interaction is based on the mechanism like dissolve like it means the nature of solute and solvent should be similar.
- If salute is polar then solvent should also be polar and if salute is nonpolar then solvent should be non-polar.
- Between salute and solvent molecule also type of attraction force.

I. Cohesive force: Attraction force b/w solvent molecules
II. Adhesive force: : Attraction force b/w solute and solvent molecules

- If the adhesive force is more than cohesive force then solubility occur.
- If the cohesive force is more than adhesive force then solubility is not occur.

Ideal Solubility Parameters,

The ideal solubility of drug is depends upon the following equation:

$$S = \left(\frac{\Delta \cup}{V}\right) V_2 = \left(\frac{\Delta H - RT}{V}\right) {}^1/_2$$

Where:

S= Solubility

$\Delta \cup =$ Latice energy

V= Volume

$\Delta H = Change\ in$ Enthalpy

R= Rydberg Constant

T= Temperature

As per this equation the solubility is directly proportional to the temp. and Volume.

Solvation:

An interaction that occurs between a solvent and a solute molecule that uses weak bonds is known as solvation.

Association:

- It is a chemical reaction where by ions of opposite electrical change come together in solution to form a distinct chemical entity.
- The forces involved in the attraction of opposite electric charge are electrostatic force.
- Ion associate have been characterized by means of vibration spectroscopy. The most important factor to determine the extent of ion association is dielectric constant of the solvent.
- Ion association are classified according to the number of ion that associate with each other such as

(A)ion pairs, (B) ion triplets etc.

(A)Ion pairs: Ion pairs are formed when a cation and anion come together.

$A_{n+} + B_{m-} \leftrightarrow AB(n\text{-}m)^{-}{}_{+}$

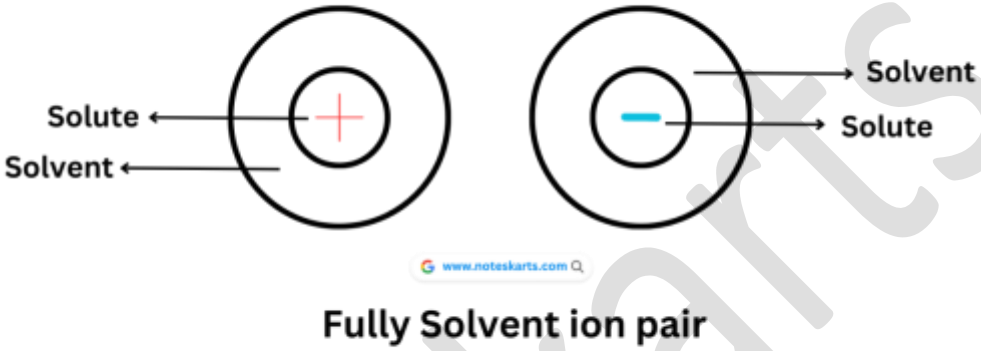
Types of ionpair :

1. Fully solvent
2. Solvent shared or Solvent separated

3. Contact ion pair.

1) Fully Solvent ion pair :—

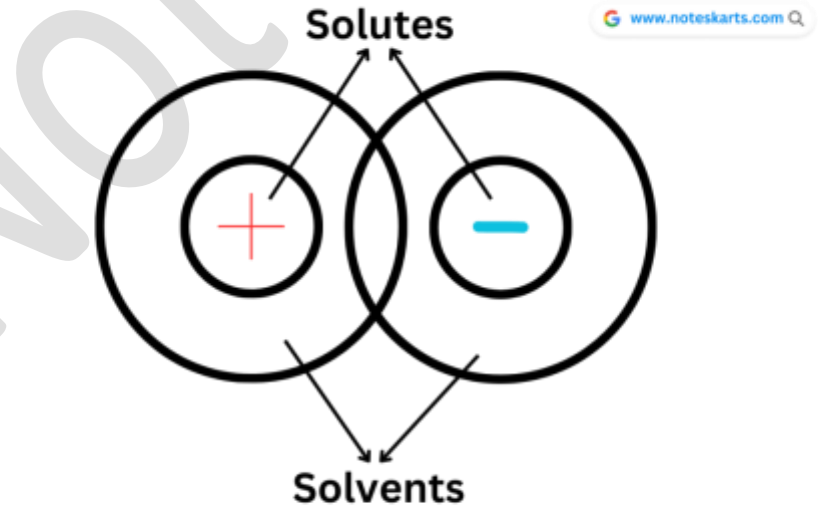
When both ions have a complete primary solvation sphere then the ion pair is known as fully solvated ion pair.



Fully Solvent ion pair

2) Solvent shared:—-

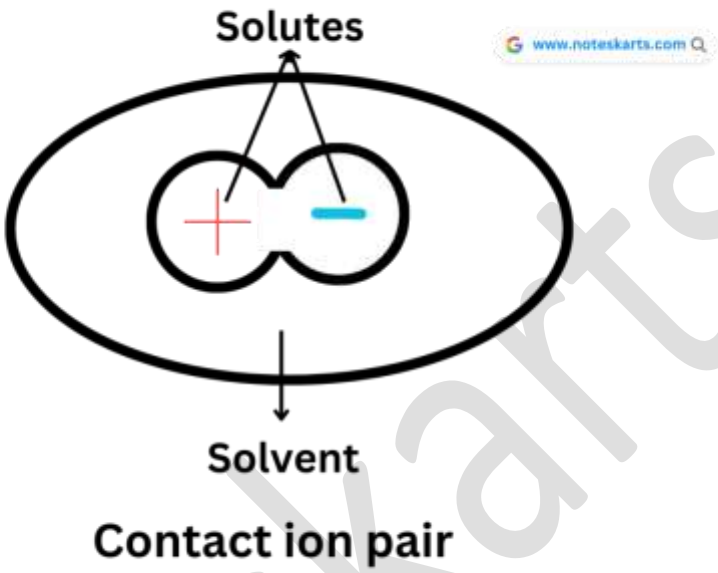
When there is about one solvent molecule between the cation and anion then the ion pair is called as solvent shared or solvent separated ion pair.



Solvent shared

3) Contact ion pair :—-

When the ions are in contact with each other the ion pair is termed as Contact ion pair .



(B)Ion triplet: The association constant of 3 ions is called as ion triplet.

Factors influencing solubility of drugs:

Those Factor which affect the solubility of solution.

1. **Solubility of Solid In Liquid**
2. **Solubility of Gas In Liquid**
3. **Solubility of Liquid In Liquid**

1.. Solubility of Solid In Liquid

- When solute is in solid form and solvent is in liquid from and then solid dissolve in liquid.

Factors:

- Nature: If nature is some then solubility is good.
- Surface Area: If Surface area is more solubility increase

2.. Solubility of Gas In Liquid:

- When solute is in gas from and solvent is in liquid from

a. Temperature :-

- Increase the temperature so, Increase the solubility of gas in liquid because the tendency of gas to expand in the temperature .

b. Presence of Salt (Salting out) :--

- The liberation of dissolved gases from solution with the addition of an electrolyte like Nacl or non electrolyte such as sucrose is called Salting out.
- Presence of salting out increases the solubility of gases in liquid.

c. Surface Area:

- If surface area is directly proportional to solubility.

3.. Solubility of Liquid In Liquid (When both solute and solvent is in liquid form)

It is required to prepare pharmaceutical solution .

Ex :-- H2o is added to alcohol results in the formation of hydroalcoholic solution.

- Non polar -------- Chloroform, C6H6
- Semipolar-------- Alcohol
- Polar -------- Water

Volatile oil + Water ------ > Aromatic water

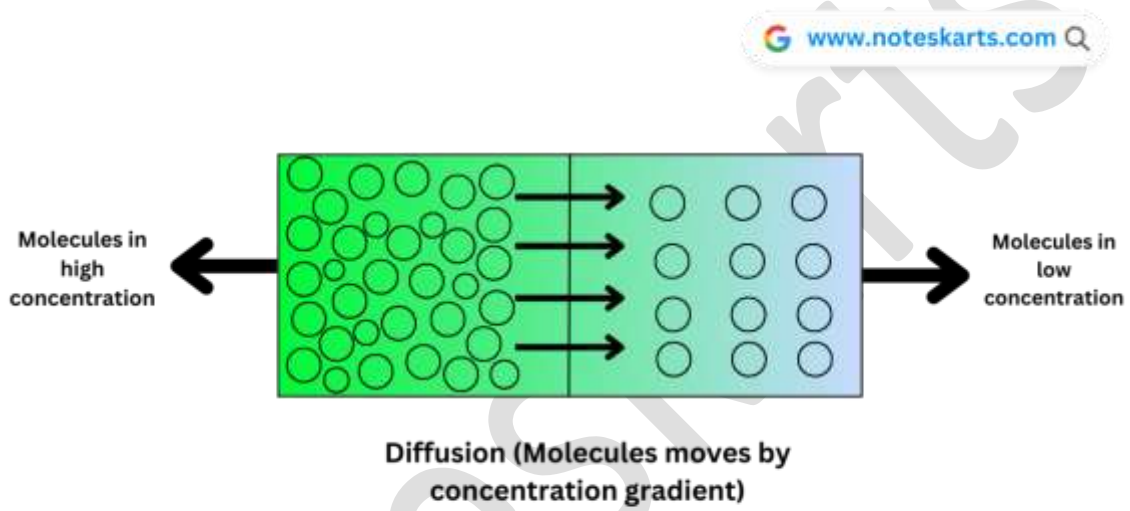
Volatile oil + alcohol ------ > Sprit

Diffusion principles in biological systems:

The process in which the substance moves in to or out of the cell through the membrane is called Diffusion.

Or

Diffusion is the movement of molecules from a higher concentration to a lower concentration. It is a passive process that does not require energy from the cell.



Diffusion (Molecules moves by concentration gradient)

Fick's First Law:

Movement of solute from higher concentration to lower concentration across a concentration gradient.

$$J = -D\frac{d\varphi}{dx}$$

Where,

J: diffusion flux

D: diffusivity

φ: concentration

x: position

Fick's Second Law:

Prediction of change in concentration along with time due to diffusion.

$$\frac{dc}{dt} = D.\frac{d^2C}{dx^2}$$

Where,

D: diffusivity

t: time

x: position

C: concentration

Application:

- Fick's law is applicable for two miscible liquids when they are brought in contact and diffusion takes place at a macroscopic level.
- Fabrication of semiconductor: Diffusion equations from Fick's law are used to fabricate integrated circuits.
- Pharmaceutical application
- Applications in food industries.

Binary solutions:

If a solution contains two components, then it is called a binary solution.

Example: The salt solution containing common salt in water is a binary solution.

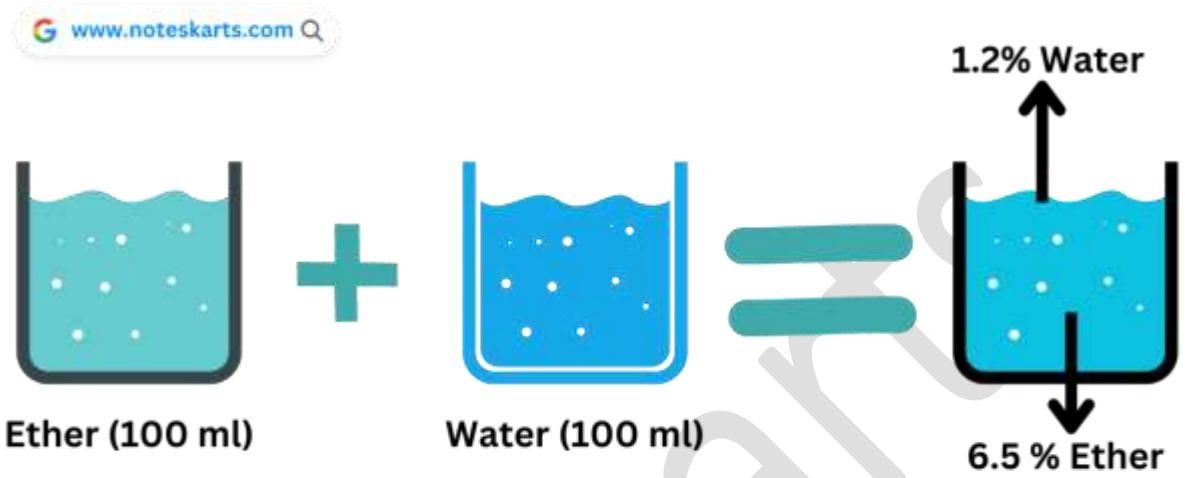
- Completely miscible (Alcohol+Water)
- Partially miscible (Ether+Water)
- Immiscible (Oil+Water)

Partially miscible:

- Two liquids shows limited solubility in each other.

Eg: Ether & Water

- Ether dissolves around 1.2% of water and water dissolves 6.5% of ether, they are Partially miscible due to their limited mutual solubility.



On shaking equal vol. of ether and water, one layer of saturated sol. Of ether in water and second layer of a saturated solution of water in ether is formed.

These two layers are conjugate solution.

Ideal Solution:

- Ideal solution is defined as the one in which there is no change in the properties of the components, other than dilution, when they are mixed to form the solution.
- No heat is evolved or absorbed during the mixing process
- The final volume of the solution represents an additive property of the individual constituents.

Non-Ideal Solution (real solutions):

- Ideality in solutions presupposes complete uniformity of attractive forces.
- Ideal solutions do not adhere to Raoult's law throughout the entire range of composition.
- For the real solutions, two types of deviation from Raoult's law are recognized, negative deviation and positive deviation.

Raoult's law:

It states that the partial pressure (P_A) of each component of an ideal mixture of liquid is equal to the vapour pressure of the pure component of an ideal mixture of liquid is equal to the vapour pressure of the pure component ($P°_A$) multiplied by its mole fraction (X_A) in the mixture.

Equation:

$P_A = P°_A \times X_A$ ..... For Liquid A

$P_B = P°_B \times X_B$ ..... For Liquid B

Where,

P = vapour pressure of the solution
X = mole fraction of the solvent
P^0 = vapour pressure of the pure solvent

Total Vapour Pressure:

P Tatal = $P_A + P_B = (P°_A \times X_A) + (P°_B \times X_B)$

$P_T = P°_A \times X_A + P°_B \times X_B$

Partially miscible liquids:

Partially miscible liquids The dissolved state of each liquid is found to be in two layers when certain amounts of water and ether are mixed. Reminding ourselves that partial miscible are partially soluble at different temperatures will suffice here.

A conjugate phase, such as phenyl and water, will become identical at the critical solution temperature (or upper convolutional temperature) when the mutual solubilities for each increase with temperature. The temperature at which normal phase separation is formed is called the homogeneous temperature.

Critical Solution Temperatures:

The temperature at which complete miscibility is reached as the temperature is raised or in some cases lowered in two liquids that are partially miscible under ordinary conditions is called Critical Solution Temperatures or Consolute temperature.

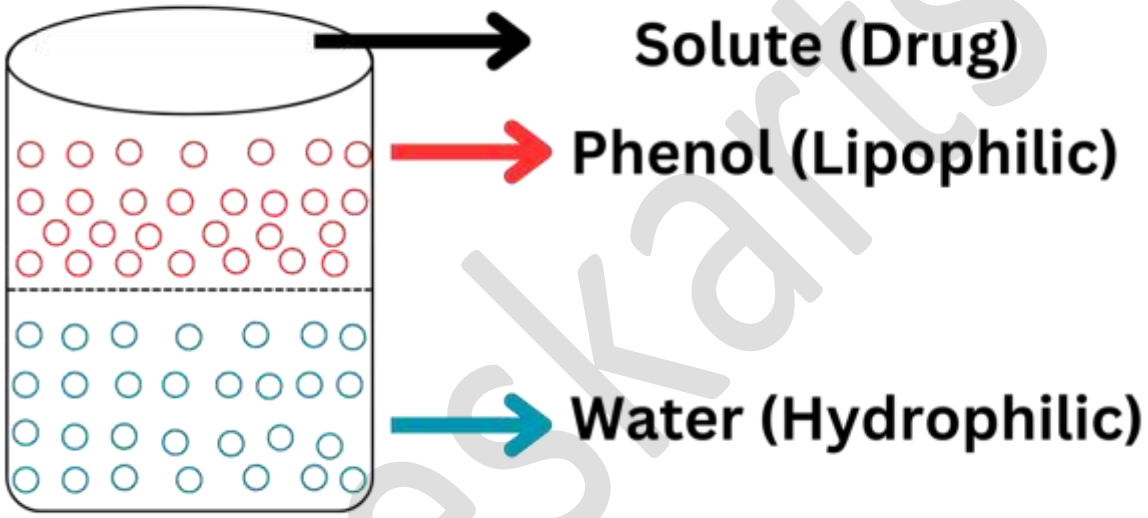
Applications of critical solution temperature:

- CST allows the temperature limits for some reactions to be determined if it requires that two liquids are miscible.
- An important application of the CST is to determine the water content in substances such as methyl and ethyl alcohols.

Distribution Law (Partition Coefficient):

In a binary solution of two immiscible liquid when any drugs is mixed then some friction of drug is dissolve in oil phase and some friction of drugs is dissolve in water phase this is called **Distribution Law.**

The ratio and drug is dissolve in lipophilic medium to the drug dissolve in hydrophilic medium is called distribution coefficient or partition coefficient.



$$Partition\ Coficent = \frac{Drug\ dissolve\ in\ oil\ phase}{Drug\ dissolve\ in\ water\ phase}$$

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

Where,

$X_o = Drug\ dissolve\ in\ oil\ phase$

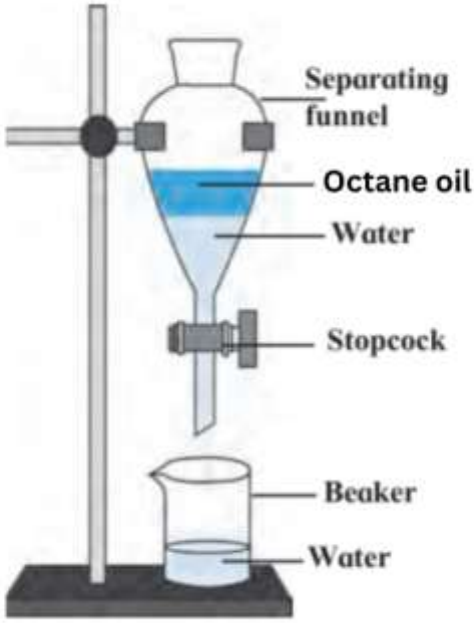
$X_w = Drug\ dissolve\ in\ water\ phase$

If (P) is more than one (1) then solution is lipophilic in nature.

(P) is less than 1 then solution is hydrophilic in nature.

Method of determination of Partition Coefficient:

- It is determine by using the separating funnel apparatus. And 50ml water and 50ml octane oil separating funnel.
- Now add the powder drug mixture in separating funnel and shake vigorously.
- Left the separating funnel for 30 min and takes out the oil and water in separate beaker.
- By using UV spectroscopy or HPLC we can determine the concentration in water and oil.
- The Value of partition cofficent is determine by using formula



Applications of the Distribution Law

- Pharmaceutical solubility in a mixture of solvents and water can be predicted.
- Drug-drug connections can be determined using the Structure-Activity Relationship (SAR).
- From a solution comprising numerous compounds, one component can be extracted.
- Preservation of emulsions and creams.