Unit - I

Solubility of drugs

Solvation and Association:

Solvation:

- ✓ Commonly known as dissolution
- ✓ It is the process of interacting and associating the molecules of a solvent with the molecules or ions of the solute.
- ✓ When solute or ions dissolves in a solvent, then the solute gets surrounded by solvent molecules.This process is known as the solvation complex.
- ✓ Solvation of solute with solvation: The larger the ion, the more solvent molecules can surround it and the more they are solvated.
- ✓ In solvation, if solvent used is water then the process is called Hydration.
- ✓ Solvation is quantified with respect to rate and the measuring unit mole/sec.
- ✓ Solvationn depends upon –
    - Hydrogen bonding
    - Vander wall force.
- ✓ For solvation to occur, enrgy is released from crystal lattice in which they are present.
- ✓ The solvation energy is the amount of energy related with the dissolution of the solvent.
- ✓ If it is positive number, the dissolution process is endothermic.
- ✓ If it is negative number, it is exothermic.

Association

- ✓ Assosiation means joining/ addition.
- ✓ The assosoation is a phenomenon in which opposite electrically charged ions come together in a solution and form a separate/ distinct chemical entity.
- ✓ The process of assosiation is reverse of dissolution.
- ✓ The extent of ionic association depends in the dielectric constant of the solvent.
- ✓ The ions of opposite charge are naturally attracted to in another by electrostatic force.
- ✓ This is described by Coulomb's Law – "The magnetic of Electrostatic Force of attraction between two oppositely electrically charge ions is directly proportional to the product of magnitudes of charges and inversly proportional to the square of distance between them. i.e

$$F = \varepsilon \frac{q_1 q_2}{r^2}$$

Where,

F= Force of attraction.

q_1 and q_2 = magnitude of electric charge.

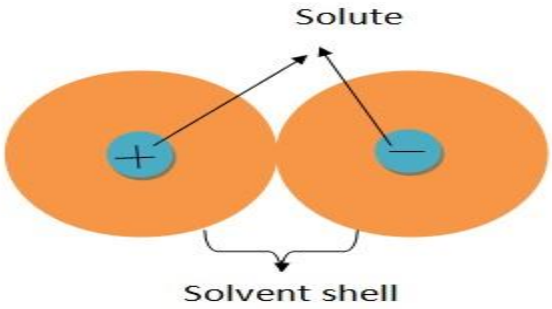
ε = Dielectric constant for medium.

r = Distance between the ions.

Three types of ion pairs are present:

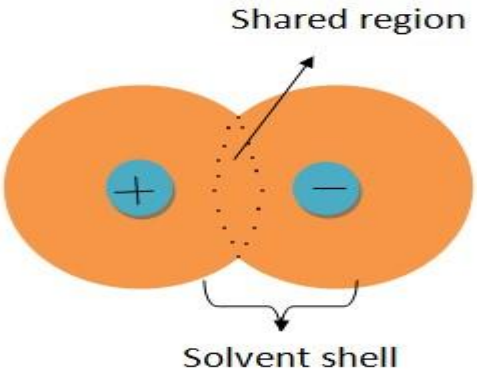
A. Fully solvated:

In this, the solvent shell of opposite electrically charged ions comes in contact with each other.



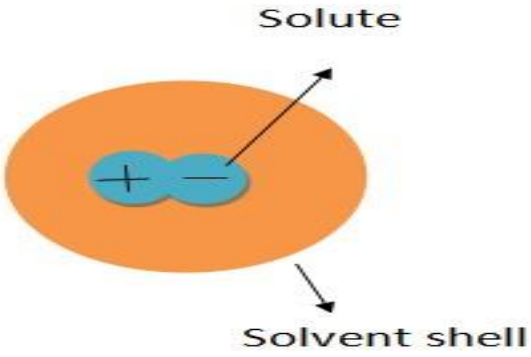
B. Solvent shared:

In this, the opposite electrically charged ions shared their solvent.



C. Contracted:

In this, the solute specie is in contact with another one and is surrounded by solvent species.



Factor affecting assosiation

- ✓ Magnitude of electric charge ∝ Association.
- ✓ Dielectric constant of medium (ε) ∝ 1/ Association.
- ✓ Distance between Ions (r) ∝ 1/ Association.

Factors affecting dissolution

- ✓ Surface area of solute and solvent ∝ Dissolution.
- ✓ Agitation/ Stirring ∝ Dissolution.
- ✓ Heat ∝ Dissolution.

Classification of solvents:

- ❖ Polar solvents.
- ❖ Non Polar solvents
- ❖ Semi Polar solvents

Polar Solvent:

- ✓ The solubility of a drug in large measure is due to the polarity of the solvent i.e to its dipole moment.
- ✓ High Dielectric constant reduces force of attraction.
- ✓ Ability of breaking covalent bond example.
  - ✓ $CH_3COOH + NaOH \rightarrow CH_3COONa + H_2O$
- ✓ Polar solvents dissolve ionic solutes and other polar substances.
- ✓ The ability of the solute to form hydrogen bond is far more significant factor than in the polarity as reflected in a high dipole moment. Eg. water dissolves phenols, alcohols, aldehydes, ketones and amine and other oxygen and nitrogen containing compound that can form hydrogen bonds with water.

- ✓ In addition, the solubility also depends on structural features sec as ratio of polar to the non-polar groups of molecule. i.e increase lenght of a non-polar chain of aliphatic alcohols ∝ 1/solubility of compound in water.
- ✓ Straight chain mono-hydroxy alchohol, aldehyde, ketone and acids with more than 4/ carbons can not enter into hydrogen-bonded structure of water. Hence they are only slightly soluble.
- ✓ Branch of carbon chain reduces non-polar effect and leads to increase water solubility.
- ✓ When additional polar groups are present in the molecule as found in propylene glycol, glycerine and tartaric acid, water solubility increases greatly.
- ✓ Tertiary butyl alcohol is miscible in all proportions with water.
- ✓ n-butyl alchohol dissolves to the extent of about 8g / 100ml of water at 20° C.
- ✓ Hydrogen bonding is an attractive interaction of H-bond with an electronegative atom (N, O etc)
- ✓ Dipole- Dipole forces are electrostatic interactions of permanent dipoles in the molecules.

Non-polar solvents:

- ✓ Non-polar solvents are unable to reduce the attraction between the ions of strong and weak electrolyte, because of the solvent's low dielcetric constants.
- ✓ They cannot break covalent bonds and also not form hydrogen bridges with non-electrolytes.
- ✓ Ionic and polar solutes are slightly soluble in non-polar solvents.
- ✓ Non-polar solvents can dissolve non-polar solutes through weak vander- wall forces.
- ✓ Examples: Benzene, carbon tetra chloride, Diethyl ether, etc.

Semi-polar solvents

- ✓ Semi-polar solvents such as ketones and alcohols can induce a certain degree of polarity in the non-polar solvent molecules.
- ✓ For example, Benzene (readily polarisable) soluble in alcohol.
- ✓ Semi-polar compounds can act as intermediate solvents to bring about miscibility of polar and non- polar liquids.