



Unit - I

Solubility of drugs

Nernst's Distribution Law:

Nernst gave a generalization governing the distribution of a solute between two non-miscible solvents.

This is called Nernst's Distribution law or Nernst's Partition law or simply Distribution law or Partition law.

Statement of Nernst's distribution law: If a solute X distributes itself between two immiscible solvents A and B at constant temperature and X is in the same molecular condition in both solvents.

$$\text{Thus, } \frac{\text{Concentration of X in A}}{\text{Concentration of X in B}} = KD$$

(Or)

$$C_1 / C_2 = KD$$

Where, C_1 & C_2 denotes the concentration of the solute in solvent A and B respectively.

Explanation:

If we take two immiscible solvents A and B in a beaker, they form separate layers. When a solute X which is soluble in both solvents is added, it gets distributed or partitioned between them. Molecules of X pass from solvent A to B and from solvent B to A.

Finally a dynamic equilibrium is set up. At equilibrium, the rate, at which molecules of X pass from one solvent to the other is balanced.

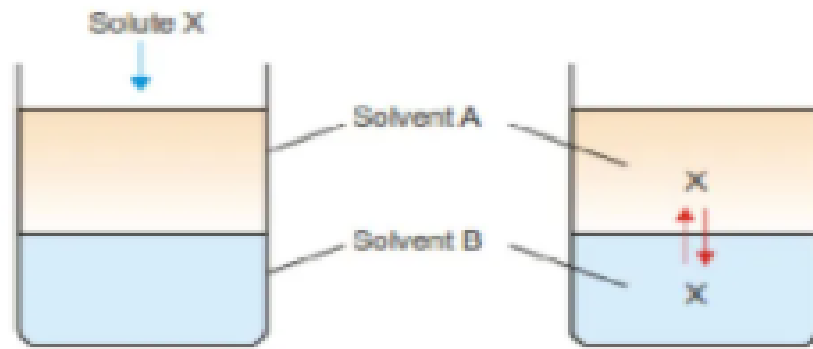


Figure: Distribution of solute X between solvent A and B.

Now according to Nernst's distribution law the distribution of solute x between solvent A and B = a constant

Solubilities and distribution law:

When a solute is shaken with two non-miscible solvents, at equilibrium both the solvents are saturated with the solute.

Since the solubility also represents concentration, we can write the distribution law as

$$C_1/C_2 = S_1/S_2 = K_D$$

Where

S₁ and S₂ are the solubilities of the solute in the two solvents.

Hence knowing the value of the Distribution coefficient (K_D) and the solubility of solute in one of the solvents, the solubility of solute in the second solvent can be calculated.

Application of distribution law:

There are numerous applications of distribution law in the laboratory as well as in industry

Solvent Extraction:

This is the process used for the separation of organic substances from aqueous solutions.

The aqueous solution is shaken with an immiscible organic solvent such as ether (or benzene) in a separatory funnel.

The distribution ratio being in favour of ether, most of the organic substance passes into the ethereal layer.

The ethereal layer is separated and ether distilled off.

Organic substance is left behind.

Partition Chromatography:

A paste of the mixture is applied at the top of a column of silica soaked in water. Another immiscible solvent (hexane) is allowed to flow down the column.

Each component of the mixture is partitioned between the stationary liquid phase (water) and the mobile liquid phase (hexane).

The various components of the mixture are extracted by hexane in order of their distribution coefficients.

Desilverization of Lead (Parke's Process):

When molten zinc is added to molten lead containing silver (argentiferous lead), zinc and lead form immiscible layers and silver is distributed between them.

Since the distribution ratio is about 300 in favour of zinc at 800° C, most of silver passes into the zinc layer.

On cooling the zinc layer, an alloy of silver and zinc separates. The Ag-Zn alloy is distilled in a retort when zinc passes over leaving silver behind.

The lead layer still contains unextracted silver. This is treated with fresh quantities of molten zinc to recover most of the silver.

Confirmatory Test for Bromide and Iodide:

The salt solution is treated with chlorine water. Small quantity of bromine or iodine is thus liberated.

The solution is then shaken with chloroform.

On standing chloroform forms the lower layer.

The free bromine or iodine being more soluble in chloroform concentrates into the lower layer, making it red for bromine and violet for iodine.

Determination of Association:

When a substance is associated (or polymerized) in solvent A and exists as simple molecules in solvent B, the Distribution law is modified as

$$n\sqrt[n]{C_a / C_b} = k$$

When n is the number of molecules which combine to form an associated molecule.

Determination of Dissociation:

Suppose a substance X is dissociated in aqueous layer and exists as single molecules in ether. If x is the degree of dissociation (or ionisation), the distribution law is modified as

$$C_1 / C_2 (1-x) = K$$

where

C₁ = concentration of X in benzene

C₂ = concentration of X in aqueous layer.

The value of x can be determined from conductivity measurements, while C_1 and C_2 are found experimentally. Thus the value of K can be calculated. Using this value of K , the value of x for any other concentrations of X can be determined.

Determination of Solubility:

Suppose the solubility of iodine in benzene is to be determined. Iodine is shaken with water and benzene.

At equilibrium concentrations of iodine in benzene (C_b) and water (C_w) are found experimentally and the value of distribution coefficient calculated.

$$C_b / C_w = K_d$$

$$S_b / S_w = K_d$$

Where

S_b = solubility in benzene

S_w = solubility in water.

Limitations of Distribution Law:

- ❖ The selected solvent liquid pair must immiscible with each other. Any mutual solubility must not affect distribution of solute if left aside for enough time to separate.
- ❖ The experimental temperature must be maintained constant. As temperature has effect on solubility of solute, any change in temperature during determinations may change the findings.
- ❖ The solute in question should be in same molecular state in both the solvents. If any chemical change is observed the concentration of species common to both solvents only should be considered.
- ❖ Solute must present in both the solvent at low concentrations. At high concentrations of solutes Nernst's distribution law does not hold good.

❖ Samples should be withdrawn for analysis only after achievement of equilibrium. Early equilibrium attainment can be possible by vigorous shaking.