Unit - I

Solubility of drugs

Ideal Solution and Raoult's law:

- ✓ 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.
- ✓ No shrinkage or expansion occurs when the substances are mixed.
- ✓ The constitutive properties, for example, the vapor pressure, refractive index, surface tension, and viscosity of the solution, are the weighted averages of the properties of the pure individual constituents.
- ✓ Mixing substances with similar properties forms ideal solutions.
- ✓ When 100 ml of methanol is mixed with 100 ml of ethanol, the final volume of the solution is 200 ml, and no heat is evolved or absorbed. The solution is nearly ideal.
- ✓ When 100 ml of sulfuric acid is combined with 100 ml of water, the volume of the solution is about 180 ml at room temperature, and the mixing is attended by a considerable evolution of heat; the solution is said to be nonideal, or real.

In an ideal solution of two volatile liquids, the partial vapor pressure of each volatile constituent is equal to the vapor pressure of the pure constituent multiplied by its mole fraction in the solution.

Thus, for two constituents A and B:

$$P_A = P_A^O X_A$$

$$P_B = P_B^O X_B$$

where

P_A and P_B are the partial vapor pressures of the constituents over the solution when the mole fraction concentrations are X_A and X_B.

$P_A°$ and $P_B°$ are the vapor pressures of the pure components.

The total vapor pressure = P_A+P_B

For example, if the vapor pressure of ethylene chloride in the pure state is 236 mmHg at 50°C, then in a solution consisting of a mole fraction of 0.4 ethylene chloride and 0.6 benzene, the partial vapor pressure of ethylene chloride is 40% of 236 mm, or 94.4 mm.

The vapor pressure – composition curve for the binary system benzene and ethylene chloride at 50°C is shown in Figure 1 below. The three lines represent the partial pressure of ethylene chloride, the partial pressure of benzene, and the total pressure of the solution as a function of the mole fraction of the constituents.

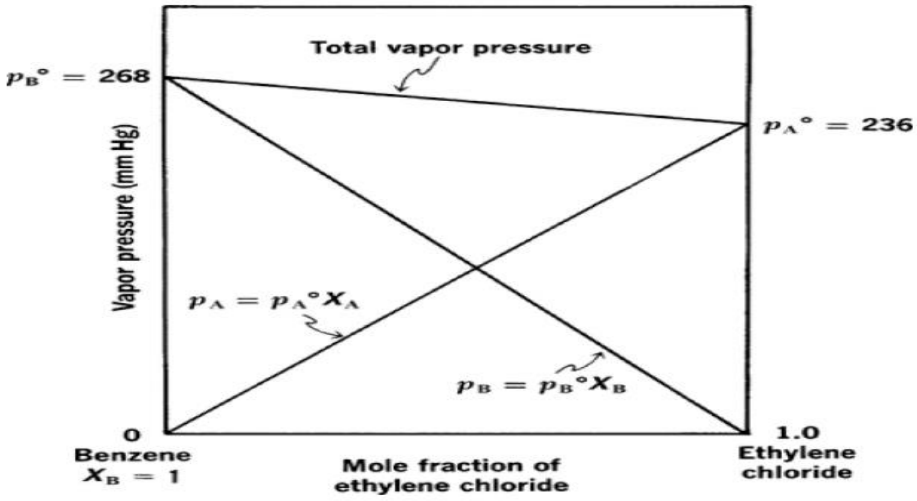


Fig 1: Vapor pressure – composition curve for an ideal binary system.

Real or nonideal solution:

- ✓ 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.

Negative deviation:

- ✓ When the "adhesive" attractions between molecules of different species exceed the "cohesive" attractions between like molecules, the vapor pressure of the solution is less than that expected from Raoult's ideal solution law, and negative deviation occurs. If the deviation is sufficiently great, the total vapor pressure curve shows a minimum, as observed in Figure 2, where A is chloroform and B is acetone.
- ✓ Chloroform and acetone manifest such an attraction for one another through the formation of a hydrogen bond, thus further reducing the escaping tendency of each constituent. This pair forms a weak compound, $[Cl_3C\text{-}H...O=C(CH_3)_2]$ that can be isolated and identified.
- ✓ Reactions between dipolar molecules, or between a dipolar and a nonpolar molecule, may also lead to negative deviations. The interaction in these cases, however, is usually so weak that no definite compound can be isolated.

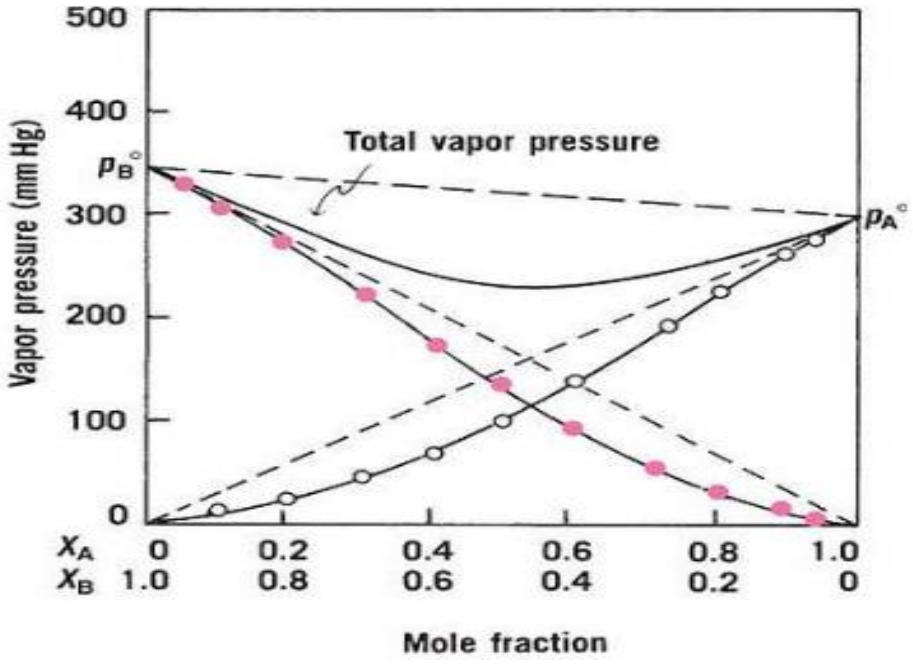


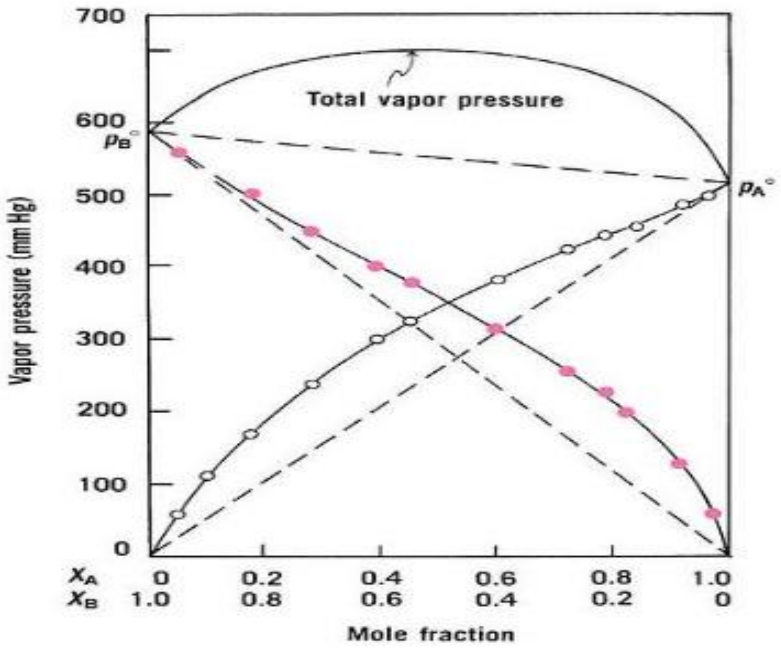
Fig.2. Vapor pressure of a system showing negative deviation from Raoult's law.

Positive deviation:

When the interaction between A and B molecules is less than that between molecules of the pure constituents, the presence of B molecules reduces the interaction of the A molecules, and A molecules correspondingly reduce the B—B interaction.

Accordingly, the dissimilarity of polarities or internal pressures of the constituents results in a greater escaping tendency of both the A and the B molecules. The partial vapor pressure of the constituents is greater than that expected from Raoult's law, and the systemis said to exhibit positive deviation.

The total vapor pressure often shows a a maximum at one particular composition if the deviation is sufficiently large. An example of positive deviation is shown in Figure 3. Liquid pairs that demonstrate positive deviation are benzene and ethyl alcohol, carbon disulfide and acetone, and chloroform and ethyl alcohol.



Raoult's law does not apply over the entire concentration range in a nonideal solution. It describes the behavior of either component of a real liquid pair only when that substance is present in high concentration and thus is considered to be the solvent. Raoult's law can be expressed as

$$P_{solvent} = P^{O}_{solvent}\ X_{solvent}$$