Unit - I

Solubility of drugs

Partially miscible liquids:

In cases of partial miscibility Degree of miscibility may be dependent on the temperature

1. Solubility ↑ with ↑ in temperature (water-phenol)
2. Solubility ↓ with ↑ in temperature (water- triethylamine)
3. Solubility ↑ with ↓ and ↑ in temperature (water- nicotine)
4. Solubility not affected by temperature.

In case of three component system the third liquid may influence the degree of solubility of the 2 liquid systems.

Effect of temperature variation on the degree of miscibility in these systems is described by means of phase diagrams.

Phase diagrams = graphs of temperature versus composition at constant P.

Systems showing an increase in miscibility with rise in temperature:

- A +ve deviation from Raoult's law due to difference in the cohesive forces that exist between the molecules of each component in a liquid mixture.
- Each phase consists of a saturated solution of one component in the other liquid.
- Such saturated solutions are known as conjugate solutions

Phenol and water system phase diagram:

Temperature fixed at 50 °C:

❖ Point a, system containing 100% pure water. Addition of phenol to water will result in the formation of a single liquid phase until the point b is reached.

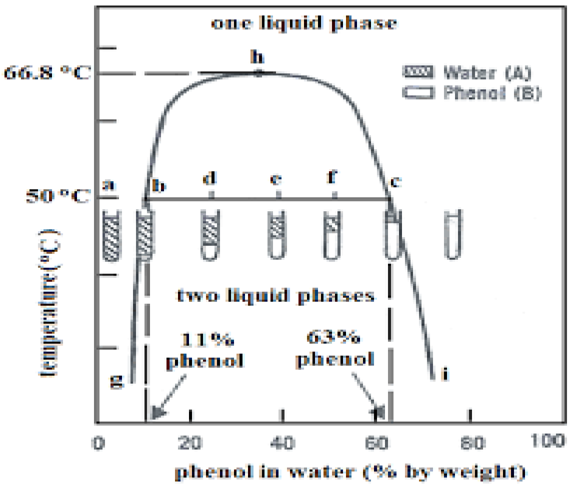
❖ At point b, appears a second phase.

Phase A: water rich phase containing 11% phenol

Phase B: phenol rich phase containing 63% phenol

❖ Increasing quantities of phenol, i.e., as we proceed across the diagram from point b to point c, we form systems in which the amount of the phenol-rich phase (B) continually increases.

❖ At the same time the amount of the water-rich phase (A) decreases. Once the total conc. of phenol exceeds 63 % at 50 0C a single phenol-rich liquid phase is formed.



At 50°C

Aqueous phase saturated with phenol:

contains 11% phenol (point b)

Phenolic phase saturated with water:

contains 63% phenol (point c)

- The line be drawn across the region containing two phases is termed a tie line; it is always parallel to the base line in two component systems.
- All systems prepared on a tie line at 50° C will separate into phases of constant composition whose composition is b and c. These phases are termed conjugate phases.
- All combinations of phenol and water above this temperature are completely miscible and yield one-phase liquid systems.

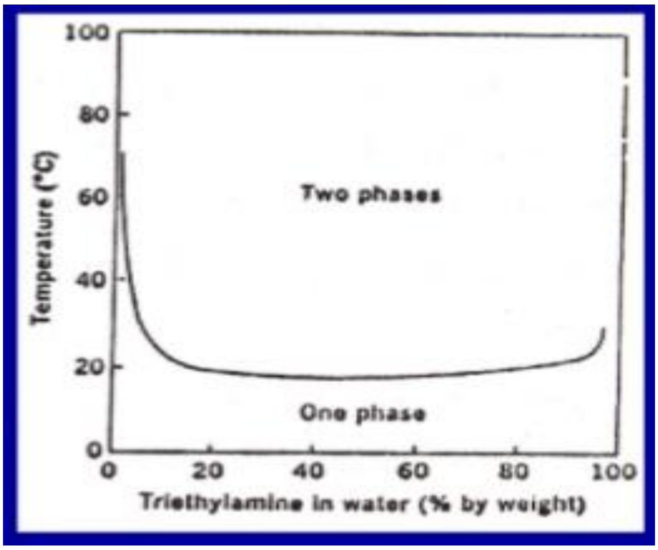
The critical solution temperature (upper consolute temperature): It is the maximum temperature at which the two phase region exists. In the case of the phenol-water system this is 66.8° (point h in Figure).

- All combinations of phenol and water above this temperature are completely miscible and yield one- phase liquid systems..

Systems showing a decrease in miscibility with rise in temperature:

Triethylamine & water:

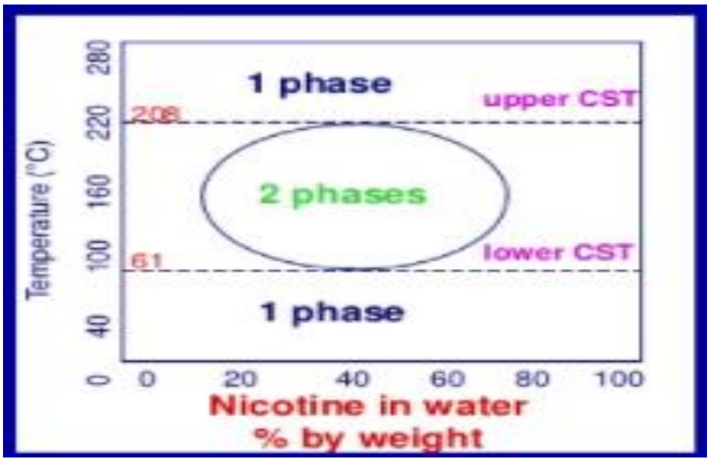
- The solubility of liquid pairs may increase as the temperature is lowered.
- The system will exhibit a lower consolute temp.
- Below which the two members are soluble in all proportions.
- Above which two separate layers are formed.



Systems showing upper and lower consolute temperature:

Nicotine & water:

Mixtures such as nicotine & water show both an upper and a lower consolute temperature with an intermediate temperature region in which the two liquids are only partially miscible.



Systems with no critical solution temperature:

The pair, ethyl ether and water, has neither an upper nor a lower consolute temperature and shows partial miscibility over the entire temperature range at which the mixture exists.

The effect of added substances on critical solution temperatures:

- ❖ Critical solution temperatures are very sensitive to impurities or added substances.
- ❖ The addition of a substance to a binary liquid system produces a ternary system.

A) If the added material is soluble in only 1 of the 2 components or if the solubility in the two liquids are markedly different, the solubility of the liquid pair is decreased due to salting-out.

- ➢ If the original binary mixture has an upper CST, the Temp increases if it has a lower CST, the Temp decrease by the addition of the third component.

Examples:

- ➢ If 0.1 M naphthalene is added to a mixture of phenol and water it dissolves only in the phenol and raises the CST about 20°C
- ➢ If 0.1 M KCl is added to a phenol-water mix, it dissolves only in water and raises the CST approximately 8°.

B) If the added material is soluble in both of the liquids to about the same extent, the solubility of the liquid pair is increased.

- ➢ The increase in solubility of two partially miscible solvents by an additive is referred to as blending. An upper CST is lowered and a lower CST is raised.

Example: The addition of succinic acid or Na oleate to a phenol-water system.

Determination of miscibility temperature:

Phenol - Water system:

- ✓ Weigh out about 5.0 g of phenol in a dry boiling tube.
- ✓ Add 2.0 ml of distilled water. The solution is stirred.
- ✓ Heat the solution in a water bath, with continuous stirring.
- ✓ At a certain temperature, the mixture becomes clear. Note this temperature (t1˚C).
- ✓ Remove the tube from the water bath, and allow the solution to cool down slowly. Note the temperature at which the turbidity 're-appears (t2˚C).
- ✓ Repeat Steps 2 to 6, after each addition of 2 ml of solution, followed by heating and subsequent cooling, note the temperature of disappearance of turbidity, and the temperature of the re- appearance of turbidity.
- ✓ The observation is that the temperature (°C) of complete miscibility rises, reaches a maximum value,and then decreases.
- ✓ Phase diagram is constructed by plotting percent composition on x axis and miscibility temperature on y axis.

Precautions:

1) Temp. of solution should be increased very slowly.
2) Mixture should be continuously and uniformly stirred.
3) Care should be taken while handling phenol.

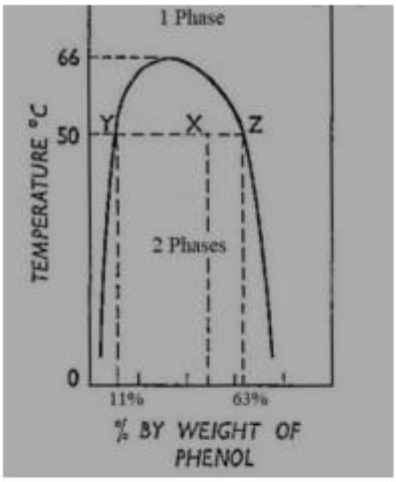
Critical solution temperature:

It is a temperature at which the co-existing liquids are completely miscible with each other and resulting in the formation one phase liquid system. So it is also called as Critical Solution Temperature (C.S.T).

C.S.T is of 2 types:

1. Upper Consolute Temperature
2. Lower Consolute Temperature

1. Upper Consolute Temperature:



The temperature at or above which the component of 2 liquid phase system behave as like a single liquid phase system.

Example: Phenol Water System, .C.S.T --- 66.8 ℃

2. Lower Consolute Temperature:

The minimum temperature lower which 2 liquid phase completely miscible with each other and behaves like a single phase .

Example: Triethylamine water, C.S.T --- 18.5 ℃

Applications:

1. Tie line represented in phenol water system bimodal curve helps to find the composition and the weight of 2 phase.

2. Tie line helps to find the concentration at which both the phase exicts as a single phase.

3. The phase diagram can be used to test the purity of phenol and other substance.

4. Binary phase diagram helps to find out the composition of the partially miscible liquid.