

أقله من solvent المذيب

- ① ethanol
- ② alcohol
- ③ glycerol

Experiment No. 4

Part 1 (Solubility : Effect of cosolvent)

cosolvent ← مادة للمذيب المبدأ (primary solvent) بكميات قليلة
 Solvent power ← قابلية المواد بالذوبان

Cosolvency

Cosolvent is a second solvent added in small quantities to enhance the solvent power of the primary solvent. The solubility of a weak electrolyte or non-polar compound in water can often be improved by altering the polarity of the solvent. This can be achieved by the addition of another solvent that is both miscible with water and in which the compound is also soluble. Often the solubility in this mixed system is greater than can be predicted from the material's solubility in each individual solvent.

miscible
 miscible
 قابل للامتزاج

The choice of suitable cosolvents is somewhat limited for pharmaceutical use because of possible toxicity and irritancy, particularly if required for oral or parenteral use. Ideally, suitable blends should possess values of dielectric constant between 25 and 80. The most widely used system that will cover this range is a water/ethanol blend. Other suitable solvents for use with water include sorbitol, glycerol, propylene glycol and syrup. For example, a blend of propylene glycol and water is used to improve the solubility of co-trimoxazole, and paracetamol is formulated as an elixir by the use of alcohol, propylene glycol and syrup. For external application to the scalp, betamethasone valerate is available dissolved in a water/isopropyl alcohol mixture.

Prediction of solubility Force of attraction Between solute and solvent
 قابلية الذوبان ← قوة التجاذب بين المذيب والمذاب

Speculation on what is likely to be a good solvent is usually based on the 'like dissolves like' principle, that is, a solute dissolves best in a solvent with similar chemical properties. The concept traditionally follows two rules:

1. Polar solutes dissolve in polar solvents.
2. Non-polar solutes dissolve in non-polar solvents.

~~Dissolve~~ A → Solvent A-A = Force of attraction Between solvent
 B → solute B-B = Force of attraction Between solute
 A-B = Force of attraction Between solute + solvent

To rationalize the above rules, consider the forces of attraction between solute and solvent molecules. If the solvent is A and the solute B and the forces of attraction are represented by A-A, B-B and A-B, one of three conditions will arise:

المادة يكون
 فراغية
 مع بعضها
 وما يتكون
 البنزين
 يدخل بين
 الجزيئات
 الموجودة
 عند بين
 ضعف الروابط
 الموجودة

1. If $A-A \gg A-B$, i.e. the affinity of a solvent molecule for its own kind is markedly greater than its affinity for a solute molecule, the solvent molecules will be attracted to each other and form aggregations from which the solute is excluded. As an example, benzene is almost completely insoluble in water. Attraction between water molecules is very strong, so that water exists as aggregates, which have a similar form to ice, floating in a matrix of free molecules. It may be visualized as 'icebergs' floating in a 'sea' of free water molecules. Molecules are continually moving from sea to icebergs and from icebergs to sea. The attraction between benzene molecules arises from weak van der Waals forces, so that although very little energy is required to disperse discrete benzene molecules, discrete benzene molecules are unable to penetrate the closely bound water aggregates.

2. If $B-B \gg A-A$, the solvent will not be able to break the binding forces between solute molecules and disperse them. This situation would apply if you tried to dissolve sodium chloride in benzene. The sodium chloride crystal is held together by strong electrovalent forces which cannot be broken by benzene. A conducting solvent, such as water, would be required to overcome the attraction between solute molecules.

3. If $A-B > A-A$ or $B-B$, or the three forces are of the same order, the solute will disperse and form a solution.

The attractive forces exerted between polar molecules are much stronger, however, than those that exist between polar and non-polar molecules, or between non-polar molecules themselves. Consequently, a polar solute will dissolve to a greater extent in a polar solvent, where the strength of the solute—solvent interaction will be comparable to that between solute molecules, than in a non-polar solvent, where the solute—solvent interaction will be relatively weak. In addition, the forces of attraction between the molecules of a polar solvent will be too great to facilitate the separation of these molecules by the insertion of a non-polar solute between them, because the solute—solvent forces will again be relatively weak. Thus, solvents for non-polar solutes tend to be restricted to non-polar liquids. The above considerations are often expressed very generally as 'like dissolves like', i.e. a polar substance will dissolve in a polar solvent and a non-polar substance will dissolve in a non-polar solvent. Such a generalization should be treated with caution, because the intermolecular forces involved in the process

سواء كانت الروابط بين solute أقوى من الروابط بين solvent
 أو بين solvent أقوى من الروابط بين solute

بعض لا يتم يكون قد
 attraction force
 Between A-B B-B أقوى من A-A solvent and solvent بصير عند إذابة كما يكون التراب

Polar substance dissolved in polar solvent
 non polar substance dissolved in non polar solvent

of dissolution are influenced by factors that are not obvious from a consideration of the overall polarity of a molecule. For example, the possibility of intermolecular hydrogen-bond formation between solute and solvent may be more significant than polarity

Solubility determination

A saturated solution is obtained either by stirring excess powdered solute with solvent for several hours at the required temperature until equilibrium has been attained, or by warming the solvent with an excess of the solute and allowing the mixture to cool to the required temperature. It is essential that some undissolved solid should be present at the completion of this stage in order to ensure that the solution is saturated.

A sample of the saturated solution is obtained for analysis by separating it from the undissolved solid.

Filtration is usually used, but precautions should be taken to ensure that:

1. it is carried out at the temperature of the solubility determination, in order to prevent any change in the equilibrium between dissolved and undissolved solute; and

2. loss of a volatile component does not occur.

The amount of solute contained in the sample of saturated solution may be determined by a variety of methods, e.g. gravimetric or volumetric analysis, electrical conductivity measurements, ultraviolet (UV) spectrophotometry and chromatographic methods. The selection of an appropriate method is affected by the natures of the solute and the solvent and by the concentration of the solution.

بوجود کثرت فی سaturated solution وینا analysis
 اول شیوه فیلتراسیون (فیلتر) من ای powder موجوده
 و کثرت با ای طریقہ کلیں

Procedure

1. Prepare five hydroethanolic mixtures with ethanol concentrations of 0, 5, 10, 15 and 20% v/v.
2. Add excess amount of salicylic acid to each hydroethanolic mixture in a stoppered Erlenmeyer flask and shake them using a magnetic stirrer for 24 hours.
3. Remove 10 ml sample of the supersaturated solution and filter it.
4. Determine the concentration by UV spectroscopy at 303 nm after suitable dilution using Quartz Cuvette.

Solubility ↑, concentration of cosolvent ↑

حسابات فی السیرین

dilution Factor (2)
 $= \frac{50}{5} \times \frac{100}{5} = 200$
 يكون ثابت بهر ای بیارن

Solubility = Concentration x d.f

cluster and the hydrophilic portions are exposed to the solvent. Such aggregates are called **micelles**. An example of a spherical micelle is diagrammed above (illustration C).

The proportion of molecules present at the surface or as micelles in the bulk of the liquid depends on the concentration of the amphiphile. **At low concentrations** surfactants will favor arrangement on the surface. As the surface becomes crowded with surfactant more molecules will arrange into micelles. At some concentration the surface becomes completely loaded with surfactant and any further additions must arrange as micelles. This concentration is called the **Critical Micelle Concentration (CMC)**.

Surface-active agents (**surfactants**) form micelles in aqueous solution above a critical concentration called the critical micelle concentration (**CMC**). Since the surfactant molecules would much rather live at an interface than be in either solution alone, when the interface is saturated, the surfactant molecules create more interface by increasing the surface area real estate by creating micelles. In aqueous solution, the micelle has a hydrophobic core and a dielectric gradient towards the surface of the micelle making the micelle surface hydrophilic.

Thus, the micelle can act as a soluble phase for non-polar solutes (**core**), semi-polar solutes (**palisade layers**) and polar solutes (**surface**). As a result, the efficiency of a particular surfactant as a solubilizing agent varies from substance to substance. The process of increasing the water solubility of a solute (**drug**) using a surfactant is called micellar solubilization.

The solubilizing power of water surfactant solutions is of great importance in the preparation of dosage forms containing sparingly soluble drug. The factors affecting micellar solubilization are many and their interrelationship is complex. In general, the degree of solubilization is a function of the physiochemical properties of the surfactant and solubilize .

In this experiment, the effect of surfactant structure on the solubility of undissociated salicylic acid will be investigated. The surfactants used will be nonionic - Tween 60 (polyoxyethelene (20) sorption monostearate) , Tween 40 (شحم حيوانى السوربيت polyoxyethelene (20) sorbitan monopalmitate). Solubility determinations will also be conducted in Tween 60 solutions buffered at higher pH's to determine the effect of solute ionization on solubilization. At the conclusion of this experiment you should be aware of the effect of surfactant structure and solubilize Ionization State on solubilization.

Tween 20 (polyoxyethylene (20) sorbitan monolaurate)



