

# Types of solutions

- **Solution of solid in liquid**

Most of true solutions are example of solid in liquid solution.

- **Solubility:**

- The solubility of an agent in a particular solvent indicates the maximum concentration to which a solution may be prepared with that agent and that solvent.

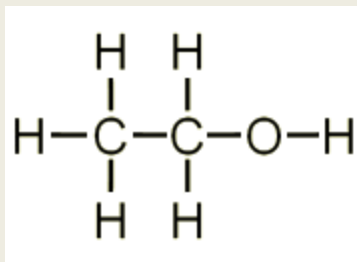
- When excess of solid (solute) is shaken with liquid (solvent) for a period of time a maximum amount of it will be dissolved, the solvent is then saturated by solute resulting in saturated solution at a given temperature.

# Factors affecting solubility of solid in liquid

1. Temperature: the effect of temperature is not always the same, there are three different cases:
  - a. Endothermic system: most chemicals absorb heat when they are dissolved and are said to have a positive heat of solution, resulting in increased solubility with an increase in the temperature.
  - b. Exothermic system: a few chemicals have a negative heat of solution and exhibit a decrease in solubility with a rise in temperature e.g. methyl cellulose, NaOH and  $\text{Ca}(\text{OH})_2$ .
  - c. Neither exothermic nor endothermic system: which means that the solubility of the compound at low temperature is the same when the temperature is high e.g. NaCl.

- ## 2. Effect of molecular structure of solute and solvent (like dissolves like)
- The more nearly solute and solvent are alike molecular structure the greater the solubility of one in the other.
  - In general it may be stated that the polar solvents like water will dissolve salts and other electrolyte readily
  - but they are poor solvents for non polar substances. On other hand, non polar liquids are required for non polar solutes.
  - Polar liquids may act as solvent when solute are capable of H-bond formation with solvent e.g. water and alcohol of low MWt.
  - As the MWt of alcohol increased, resulted in decrease polarity and decrease the solubility in water.

- Polar liquids should be miscible with other polar liquids. Conversely non polar liquids dissolve only slightly in polar solvents, but they dissolve readily in solvents that are non polar.
- Complex organic compounds which have polar and non polar groups in their molecules may dissolve in polar liquids, but their solubility in such solvents tends to decrease in proportion to the number of non polar groups
- Semipolar liquids, such as ethyl alcohol possess some of properties of both polar and nonpolar solvents.



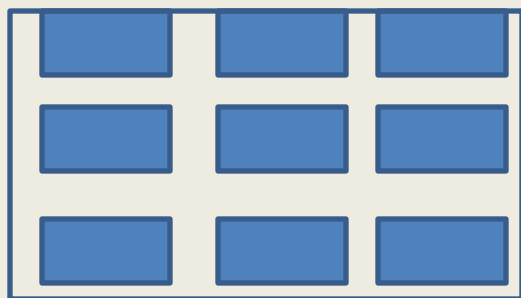
Ethyl alcohol or ethanol have

- 5 non polar carbon–Hydrogen bond
- 1 C-C bond (non polar)
- C-O bond & H-O bond (polar)

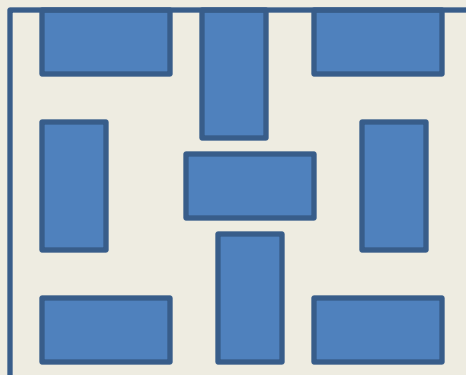
So it is considered as good solvent for some polar and non polar substances due to the presence of distinct polar and non polar regions

3. Effect of nature of solute: the solutes suffer from polymorphism, hydrates, solvates.
- **Polymorphism:** it is a phenomenon that the compound exists in more than one form which has the same chemical structure but different physical properties like melting point, solubility, absorption and therapeutic activity.
  - Some polymorph is inactive, so pharmacist should aware about this phenomenon.

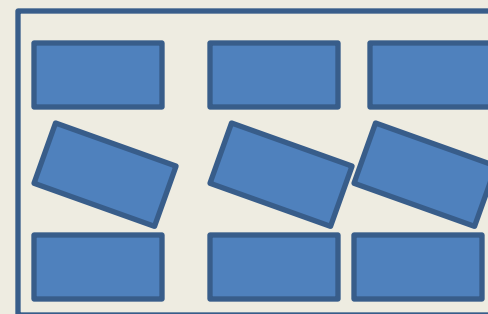
- Q. why solute suffers from polymorphism?
- polymorphism takes place because different arrangement of molecules in crystal.



Polymorph 1



Polymorph 2



Polymorph 3

- Example of drug shows polymorphism chloramphenicol, it exists in more than one polymorph; one active and other not active.
- Various techniques are used in determining crystal properties, the most widely used methods are hot stage microscopy, thermal analysis, infrared spectroscopy and X-ray diffraction.



- **Hydrates**: compounds contain water in their crystals.
- **Solvates**: compounds contain other solvent than water in their crystals.
- The anhydrous form of the compound is more soluble than hydrate form of the same compound, while the solvate of the same compound is more soluble than non-solvate form in water.
- Hydrate may be monohydrate, dihydrate and trihydrate.
- Example of hydrate: Ampicillin trihydrate it contains three molecules of water.

Q. Why the anhydrous form of the same drug is more soluble than the hydrous form?

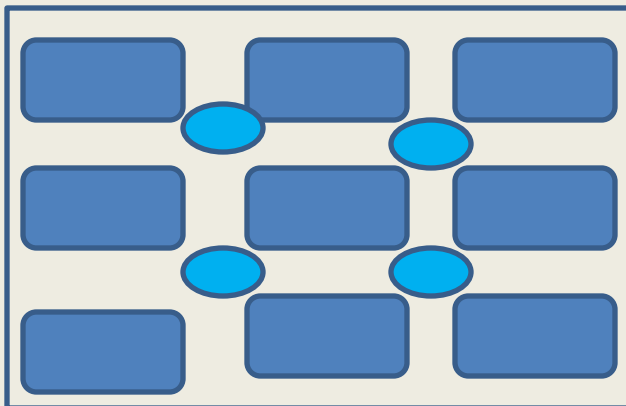
Answer: due to the presence of water within the crystal, so the hydrous form will be busy with its own water of crystallization to form hydrogen bond. While anhydrous is not busy so it can form hydrogen-bond with the external phase (solvent) e.g. the water.

Q. Anhydrous form has a faster dissolution rate than the hydrate.

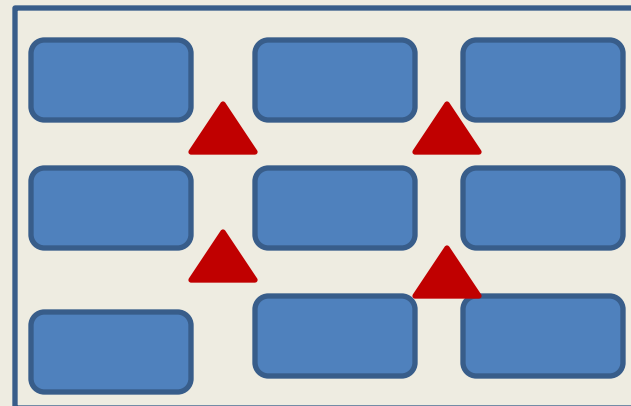
Answer: In hydrate, water could bond between two drug molecules via hydrogen bond and tie the lattice and hence slow down its dissolution rate.

Q. why the solvate form of the same drug is more soluble than non-solvate form in water?

Answer: This is because the compound contains solvent such as ethanol, which has a tendency to interact with the external water, so as a result, it make crystals more soluble.



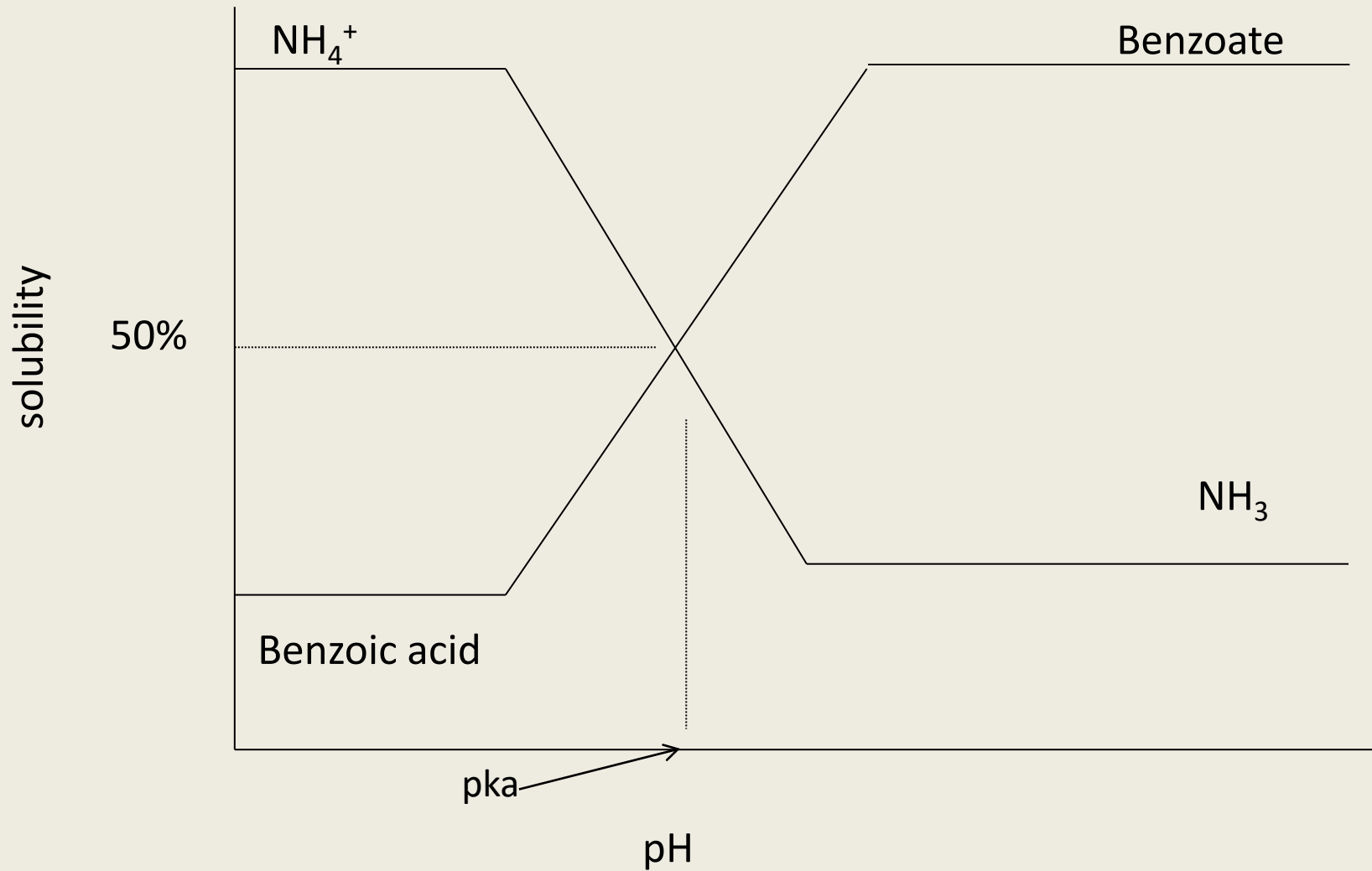
Hydrate



Solvate

## 4. Effect of pH on solubility:

- The pH of medium is important for certain compounds such as weak acid and weak base; it affects the degree of dissociation and the ratio of ionized to unionized form of the compound.
- The ionized form of drug is more soluble than unionized form in water, this affect on absorption and excretion rate.
- There is a curve called pH-solubility profile for weak acid and weak base. At  $\text{pH} = \text{pka}$  the ratio of ionized to unionized = 1, that 50% ionized or soluble in water (Figure 1).



- The solubility in water of weak organic acids such as barbiturates & sulfonamides is increased as the pH increased by addition of base.
- This increase in solubility is due to the formation of water soluble salts. For example solubility of Phenobarbital (free acid) in water at pH 5.5, 25°C is 1.25 g /1000 mL. While, the solubility is increased to 1000 g/1000 mL due to soluble salt formation at pH 9.3, 25°C.
- If the pH of this solution is decrease by addition of strong acid, Phenobarbital (free acid) will precipitate.

- The solubility in water of weak organic base (alkaloids and local anesthetic) increase as the pH decrease by addition of acid due to the formation of water soluble salts.

	<b>Temperature</b>	<b>Solubility</b>	<b>pH</b>
<b>Atropine(free base)</b>	25 °C	2.2g/1000 mL	>10
<b>Atropine Sulfate (Salt)</b>	25 °C	2500g/1000 mL	5.4

## 5. Effect of other substances on solubility:

- The solubility of substance is depends on the type and concentration of other substance in the solution.
- In general the solubility of slightly soluble electrolytes is reduced by addition of second salt which contain a common ion for example when NaCl is added to a saturated solution of silver chloride AgCl, some of AgCl is precipitates from the solution due to the presence of common ion (Cl<sup>-</sup>).





- The common ion may form complex with slightly soluble electrolyte may lead to increase the solubility of salts. e.g. Mercuric iodide is insoluble in water yet it dissolved by solution of soluble iodide.

**Q.** How can solubility of a substance in a given solvent be determined?

**A.** By preparing a saturated solution of it at specific temperature and by determining by chemical analysis the amount of chemical dissolved in a given weight of solution. The amount of solvent required to dissolve the amount of solute can be determined by a simple calculation.

- The solubility may then be expressed as grams of solute dissolving in milliliters of solvent; for example "1 g of sodium chloride dissolves in 2.8 ml, of water". When the exact solubility has not been determined, general expressions of relative solubility may be used.
- These terms are defined in the USP and presented in table 1.

Table 1 Relative terms of solubility

Descriptive term	Part of solvent required for 1 part of solute
Very soluble	< 1
Freely soluble	1-10
Soluble	10-30
Sparingly soluble	100-1000
Slightly soluble	1000-10000
Practically insoluble or insoluble	> 10000

- **Solution of liquid in liquid**

1. Two liquids such as water/ alcohol, water/glycerin and water/ acetone. When are mixed, homogenous system is formed irrespective of the proportions in which the two are taken. Such pairs of liquid are said to be miscible.
2. Liquefied phenol/ water or ether /water are formed homogenous system only when mixed in a certain proportion. Such liquids are said to be miscible in certain proportion.
3. Water/mineral oil is in soluble in each other in any proportion so they are immiscible.

- **Solution of gas in liquid**

1. According to Henry's law the solubility of gas by weight in liquid is proportional to the pressure at constant temperature.
2. If there is a chemical interaction between the solute (gas) and the solvent (liquid), this will lead to high solubility as in case of gases  $\text{NH}_3$ ,  $\text{HCl}$ , their solubility will not be affected if the pressure is changed (increased or decreased).
3. Temperature: solubility of gas in liquid decrease as temperature increase, so the gas in solution should be cool down before opening and should be store in cool places.

- Increase the temperature lead to decrease the solubility, e.g.,  $\text{CO}_2$  is twice soluble at  $0^\circ\text{C}$  as it at  $20^\circ\text{C}$ . So the gaseous solutions should be stored at cool place (refrigerator). Containers holding strong ammonia solution should be cooled before they are opening in order to reduce libration and expansion of gas since on cooling the solubility of gas increase.
- **Note:** When a salt is added to a liquid containing dissolved gas, libration of gas occurs due to the decrease solubility. This effect is referred to salting out of the gas.

# Rate of dissolution

- Rate of dissolution: it is the speed at which the solute goes into solution its unit is equal to unit of concentration/ unit of time =  $\Delta C/\Delta t$  = mg/ml/min.
- If the solubility increase, the rate of the dissolution will also increase, but if the rate of dissolution increase, the solubility will not always increase.



# Factors affecting rate of dissolution

1. Particle size of the substance: decreasing the particle size by comminution, the surface area will increase, and the rate of dissolution will increase also.

The finer the powder, the greater the surface area, which comes in contact with the solvent, and the more rapid the dissolving process.

2. Temperature: the rate of dissolution increases when the temperature increased because increasing the collisions between the solvent and the solute.
3. Agitation: the greater the agitation, the more unsaturated solvent pass over the drug and faster the formation of the solution. In other word, increases the interaction between the solute and the solvent.