SOLUBILITY OF DRUGS

by

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Solubility

Solubility is

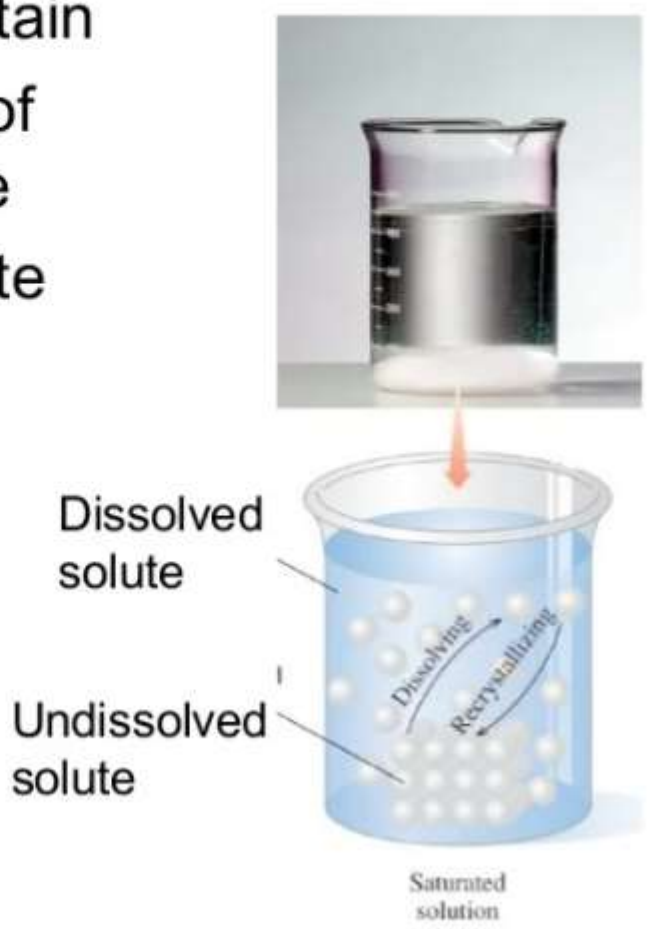
- the maximum amount of solute that dissolves in a specific amount of solvent
- expressed as grams of solute in 100 grams of solvent (usually water):

$$\frac{\text{g of solute}}{100\text{ g water}}$$

Saturated Solutions

Saturated solutions contain

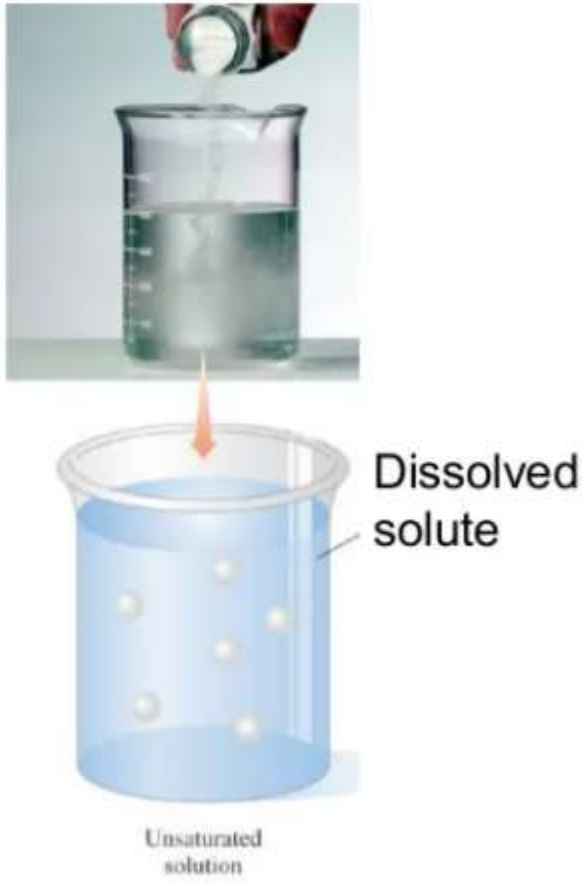
- the maximum amount of solute that can dissolve
- some undissolved solute at the bottom of the container



Unsaturated Solutions

Unsaturated solutions

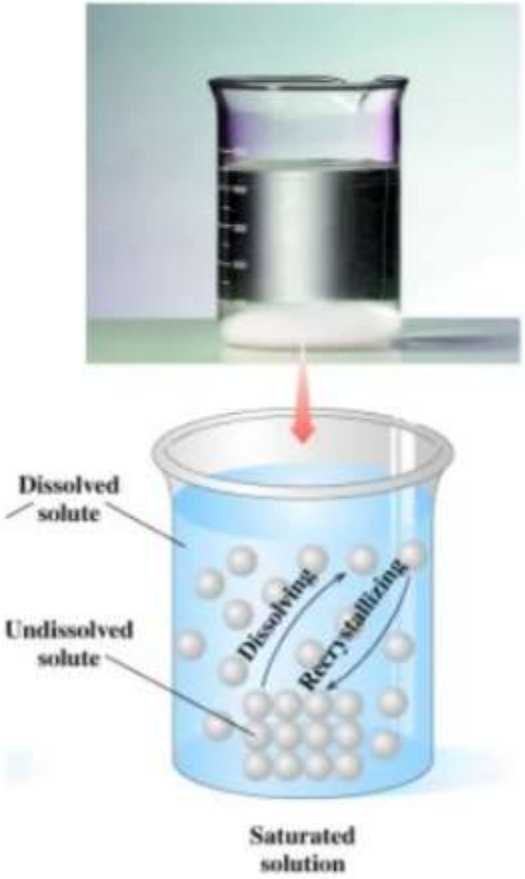
- contain less than the maximum amount of solute
- can dissolve more solute



Supersaturated Solutions

Supersaturated solutions

- An unstable solution that contains an amount of solute greater than the solute solubility.
- Also has undissolved solute at the bottom of the container.



Learning Check

At 40 °C, the solubility of KBr is 80 g/100 g of H_2O.

Identify the following solutions as either (S) saturated or (U) unsaturated. Explain.

A. 60 g KBr added to 100 g of water at 40 °C.

B. 200 g KBr added to 200 g of water at 40 °C.

C. 25 g KBr added to 50 g of water at 40 °C.

Solution

A. U 60 g of KBr/100 g of water is less than the solubility of 80 g of KBr/100 g of water.

B. S 200 g KBr added to 200 g of water at 40 °C. This is the same as 100 g of KBr in 100 g of water, which is more than the solubility of 80 g of KBr/100 g of water at 40 °C.

C. U 25 g KBr added to 50 g of water at 40 °C. This is the same as 50 g of KBr in 100 g of water, which is less than the solubility of 80 g of KBr/100 g of water at 40 °C.

Solubility expressions

- The USP lists the solubility of drugs as: the number of ml of solvent in which 1g of solute will dissolve.
- E.g. 1g of boric acid dissolves in 18 mL of water, and in 4 mL of glycerin.
- Substances whose solubility values are not known are described by the following terms:

Term	Parts of solvent required for 1 part of solute
Very soluble	Less than 1 part
Freely soluble	1 to 10 parts
Soluble	10 to 30 parts
Sparingly soluble	30 to 100 parts
Slightly soluble	100 to 1000 parts
Very slightly soluble	1000 to 10 000 parts
Practically insoluble	More than 10 000 parts

Solubility expressions

Expression	Symbol	Definition
Molarity	M, c	Moles (gram molecular weights) of solute in 1 liter (1000 ml) of solution.
Molality	m	Moles of solute in 1000 gm of solvent.
Normality	N	Gram equivalent weights of solute in 1 liter of solution
Mole Fraction	x	Ration of moles of solute to total moles of solute+ solvent
Percentage by Weight	% w/w	gm of solute in 100 gm of solution
Percentage by Volume	%v/v	ml of solute in 100 ml of solution
Percentage Weight in Volume	% w/v	gm of solute in 100 ml of solution

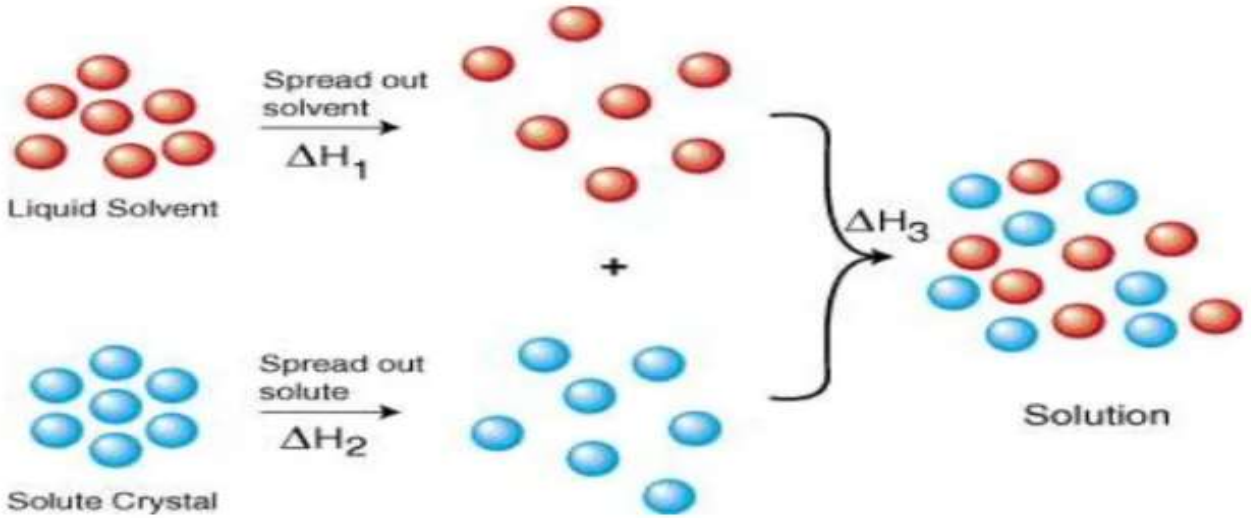
Solubility process

A mechanistic perspective of solubilization process for organic solute in water involves the following steps:

1. Break up of solute-solute intermolecular bonds
2. Break up of solvent-solvent intermolecular bonds
3. Formation of cavity in solvent phase large enough to accommodate solute molecule
4. Transfer of solute into the cavity of solvent phase
5. Formation of solute-solvent intermolecular bonds

Tree types of interaction in the solution process

1. solvent – solvent interaction
2. solute – solute interaction
3. solvent solute interaction



$$\Delta H_{sol} = \Delta H_1 + \Delta H_2 + \Delta H_3$$

- The enthalpy change of solution refers to the overall amount of heat which is released or absorbed during the dissolving process (at constant pressure).

Solvent - Solute Interactions

- In pre - or early formulation, selection of the most suitable **solvent** is based on the principle of

"like dissolves like"

- That is, a solute dissolves best in a solvent with similar chemical properties. Or two substances with similar intermolecular forces are likely to be soluble in each others
- Polar solutes dissolve in polar solvents. E.g **salts & sugar dissolve in water .**
- Non polar solutes dissolve in non polar solvents. Eg**. naphtalene dissolves in benzene.**

MECHANISM OF SOLUTE SOLVENT INTERACTIONS

"LIKE DISSOLVES LIKE"

Sr. No	Nature of Solvent	Mechanism of solubility	Example
1.	Polar	a. High dielectric constant b. H- bond formation c. dipole interactions	Water+ ethanol
2.	Non-polar	weak van der waal's forces	Fats, oils, alkaloidal bases + CCL4, benzene
3.	Semi-polar	induce certain degree of polarity	Acetone increase solubility of ether in water

Solute-Solvent interactions

- If the solvent is **A** & the solute is **B**, and the forces of attraction are represented by **A-A**, **B-B** and **A-B**,

One of the following conditions will occur:

1. If **A-A >> A-B** ⇨ The solvent molecules will be attracted to each other & the solute will be excluded. Example: Benzene & water, where benzene molecules are unable to penetrate the closely bound water aggregates.

2. If **B-B >> A-A** ⇨ The solvent will not be able to break the binding forces between solute molecules. Example NaCl in benzene, where the NaCl crystal is held by strong electrovalent forces which cannot be broken by benzene.

3. If **A-B >> A-A** or **B-B**, or the three forces are equal ⇨ the solute will . form a solution. Example: NaCl in water.