Types of solutions and factors affecting solubility

Dr. Shashi Kiran Misra

UNSATURATED SOLUTION

more solute dissolves

SATURATED SOLUTION

no more solute dissolves

SUPERSATURATED SOLUTION

becomes unstable, crystals form

Types of solutions

Solutions of pharmaceutical importance include:

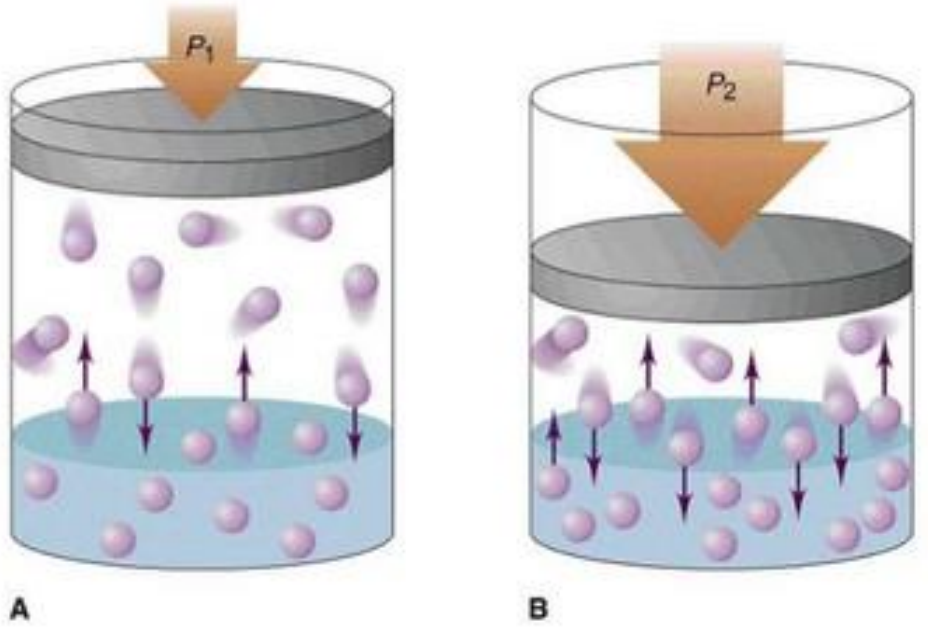
- Gases in liquids
- Liquids in liquids
- Solids in liquids

Solute	Solvent	Solution is called as	Example
Gas	Liquid	Foam	Whipped cream
Liquid	Liquid	Emulsion	Mayonnaise
Liquid	Solid	Gel	Gelatin
Solid	Solid	Solid sol	Cranberry glass
Solid	Gas	Solid aerosol	Smoke

Solubility of gases in liquids

When the pressure above the solution is released (decreases), the solubility of the gas decreases

As the temperature increases the solubility of gases decreases



Solubility of liquids in liquids

- Preparation of pharmaceutical solutions involves mixing of 2 or more liquids

✓ Alcohol & water to form hydroalcoholic solutions

✓ volatile oils & water to form aromatic waters

✓ volatile oils & alcohols to form spirits , elixirs

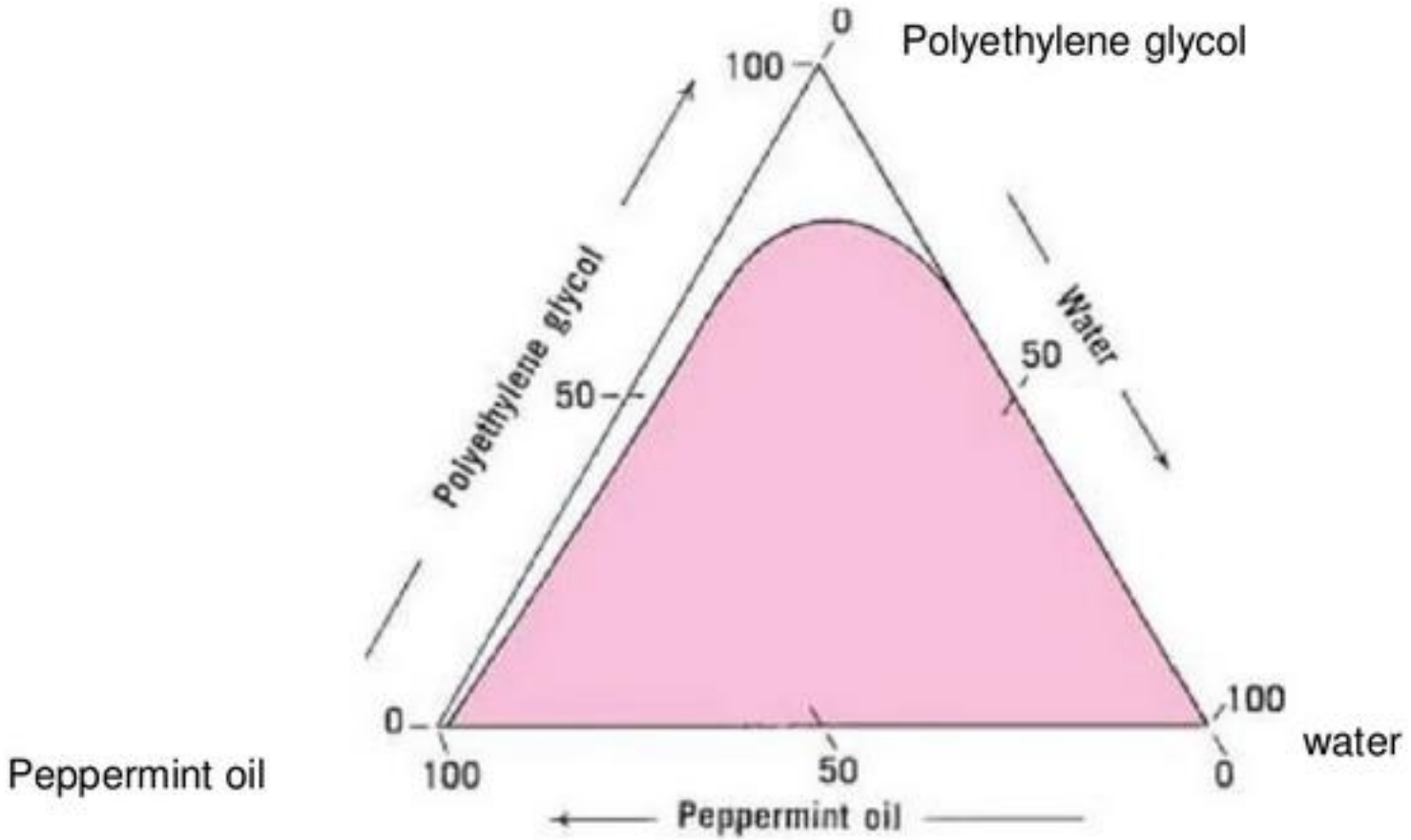
Liquid-liquid systems may be divided into 2 categories:

1. Systems showing *complete miscibility* such as alcohol & water, glycerin & alcohol, benzene & carbon tetrachloride.

2. Systems showing *Partial miscibility* as phenol and water; two liquid layers are formed each containing some of the other liquid in the dissolved state.

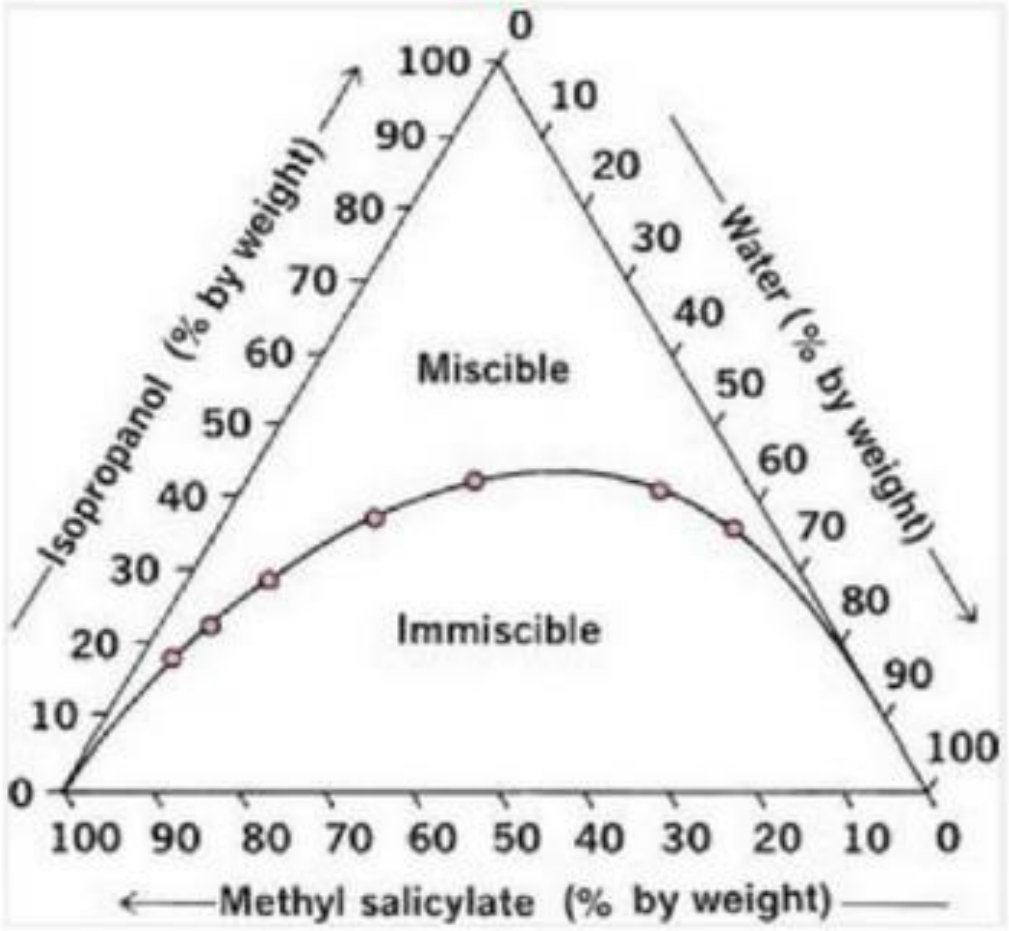
The term miscibility refers to the mutual solubility of the components in liquid-liquid systems.

Three-Component Systems



Three-Component Systems

IPA



Methyl salicylate

water

Solubility of solids in liquids
Factors influencing solubility

$$\log \frac{S}{S_0} = \frac{2\ \gamma\ V}{2.303\ R\ T\ r}$$

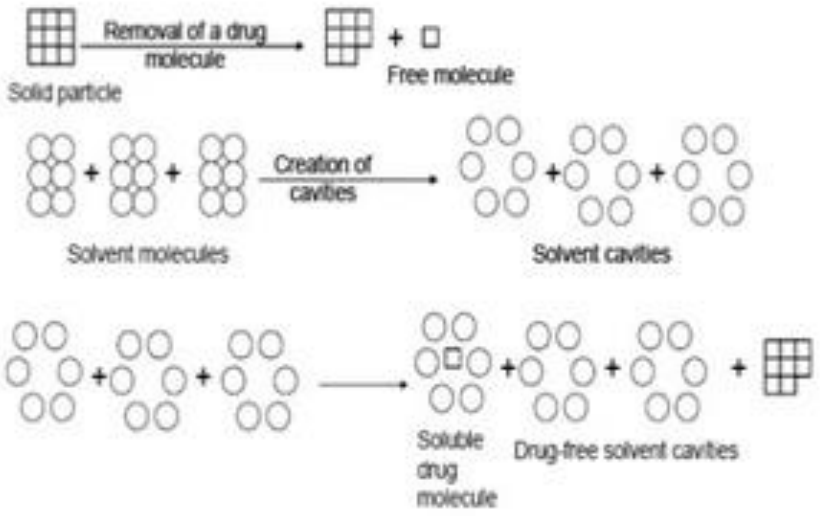
- S_o is the solubility of large particles
- **S** is the solubility of fine particles
- ***γ*** is the surface tension of the particles
- **V** is molar volume
- ***T*** is the absolute temperature
- **r** is the radius of the fine particle
- ***R*** is the gas constant

Solubility of solids in liquids
Factors influencing solubility

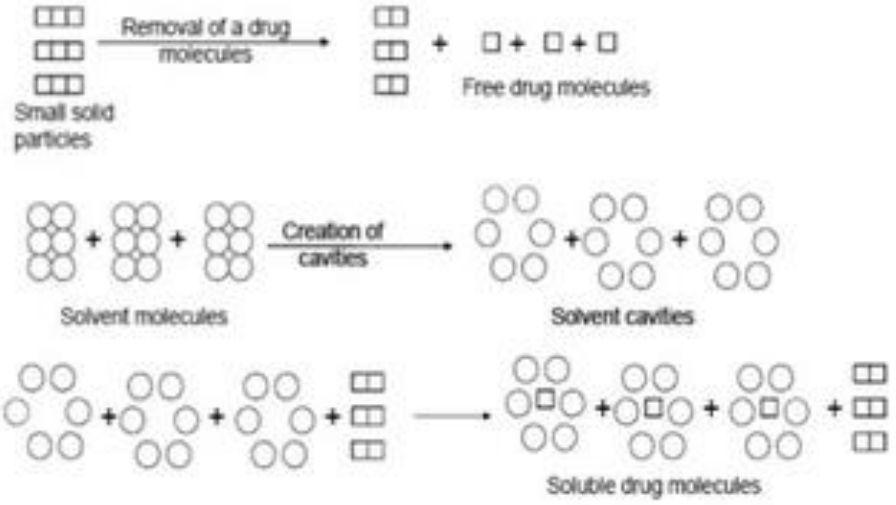
1- Particle size (surface area) of drug particles

↓Particle size → ↑ surface area→ ↑Solubility

(A) Before particle size reduction (Small surface area)



(B) After particle size reduction (i.e. increasing the surface area of drug solute)



Solubility of solids in liquids Factors influencing solubility

2- Molecular size

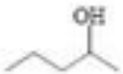
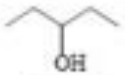
- Molecular size will affect the solubility.
- The larger the molecule or the higher its molecular weight the less soluble the substance.
- Larger molecules are more difficult to surround with solvent molecules in order to solvate the substance.
- In the case of organic compounds the amount of carbon branching will increase the solubility since more branching will reduce the size (or volume) of the molecule and make it easier to solvate the molecules with solvent

Solubility of solids in liquids
Factors influencing solubility

3- The boiling point of liquids and the melting point of solids:

Both reflect the strengths of interactions between the molecules in the pure liquid or the solid state.

In general, aqueous solubility decreases with increasing boiling point and melting point.

		Boiling point (°C)	Solubility (M/l)
n-Pentanol		137.8	0.26
3-methyl-1-butanol		131.2	0.31
2-Pentanol		119	0.53
3-Pentanol		115.3	0.62
2-methyl-2-butanol		102	1.40

	Melting Point	Solubility
Sulfadiazine	253°C	1g in 13 dm^3
Sulfamerazine	236°C	1g in 5 dm^3
Sulfapyridine	192°C	1g in 3.5 dm^3
sulfathiazole	174°C	1g in 1.7 dm^3

Solubility of solids in liquids
Factors influencing solubility

4-The influence of substituents on the solubility of molecules in water can be due to their effect on the properties of the solid or liquid (for example, on its molecular cohesion, or to the effect of the substituent on its interaction with water molecules.

Substituents can be classified as either hydrophobic or hydrophilic, depending on their polarity

Influence of substituents on the solubility

- Polar groups such as –OH capable of hydrogen bonding with water molecules impart high solubility
- Non-polar groups such as $-CH_3$ and –Cl are hydrophobic and impart low solubility.
- Ionization of the substituent increases solubility, e.g. –COOH and $-NH_2$ are slightly hydrophilic whereas –COO– and $-NH_3$ are very hydrophilic.

Substituent	Classification
$-CH_3$	Hydrophobic
$-CH_2-$	Hydrophobic
–Cl, –Br, –F	Hydrophobic
$-N(CH_3)_2$	Hydrophobic
$-SCH_3$	Hydrophobic
$-OCH_2CH_3$	Hydrophobic
$-OCH_3$	Slightly hydrophilic
$-NO_2$	Slightly hydrophilic
–CHO	Hydrophilic
–COOH	Slightly hydrophilic
$-COO^-$	Very hydrophilic
$-NH_2$	Hydrophilic
$-NH_3^+$	Very hydrophilic
$-OH^-$	Very hydrophilic

Solubility of solids in liquids
Factors influencing solubility

5-Temperature

- Temperature will affect solubility. If the solution process absorbs energy then the solubility will be increased as the temperature is increased.
- If the solution process releases energy then the solubility will decrease with increasing temperature.
- Generally, an increase in the temperature of the solution increases the solubility of a solid solute.
- A few solid solutes are less soluble in warm solutions.
- For all gases, solubility decreases as the temperature of the solution increases.

Solubility of solids in liquids
Factors influencing solubility

6-Crystal properties

Polymorphic Crystals, Solvates, Amorphous forms

Polymorphs have the same chemical structure but different physical properties, such as solubility, density, hardness, and compression characteristics

A drug that exists as an amorphous form (non crystalline form) generally dissolves more rapidly than the same drug in crystalline form

Solubility of solids in liquids
Factors influencing solubility

7- PH

- is one of the primary influences on the solubility of most drugs that contain ionizable groups
- Large number of drugs are weak acids or weak base.
- Solubility depends on the degree of ionization.
- Degree of ionization depends on the pH

About 85% of marketed drugs contain functional groups that are ionised to some extent at physiological pH (pH 1.5 – 8).