Solubility of Gas in Liquid

The solubility of gases in liquids depends on:

1. The mass of gas molecules
2. Pressure
3. Temperature
4. Presence of salt
5. Chemical reactions with solvent

Solubility of Gas in Liquid

The Mass of Gas Molecules

- The solubility of gas molecules typically increases with increasing mass of the gas molecules.
- The larger the mass of gas molecules, the stronger London and Debye forces is between gas and solvent molecules.

Solubility of Gas in Liquid

Pressure

- Gases increase in solubility with an increase in pressure.
- Increasing the pressure results in more collisions of the gas molecules with the surface of the solvent (more **solvation**); and hence greater solubility.

Henry's law

- The effect of the pressure on the solubility of a gas is expressed by *Henry's law*
- *Henry's law states,* “In a very dilute solution at constant temperature, the concentration of dissolved gas is proportional to the partial pressure of the gas above the solution at equilibrium”
- The partial pressure of the gas is obtained by subtracting the vapor pressure of the solvent from the total pressure above the solution.
- *If* C_2 is the concentration of the dissolved gas in grams per liter of solvent and p is the partial pressure in millimeters of the undissolved gas above the solution,
- Henry's relationship may be written as $C_2 = \sigma p$
- *σ=1/k solubility coefficient*

Solubility of Gas in Liquid

Temperature

- Gases decrease in solubility with an increase in temperature.
- Increasing temperature causes an increase in kinetic energy of gas molecules which leads to breakdown of intermolecular bonds and gas escaping from solution.
- E.g. Carbon dioxide gases escape faster from a carbonated drink as the temperature increases.

Solubility of Gas in Liquid

Presence of Salts

- Dissolved gases are often liberated from solutions by the introduction of an electrolyte (e.g. NaCl) and sometimes by a non electrolyte (e.g. sucrose)
- This phenomenon is known as **SALTING OUT**.

Solubility of Solid in Liquid

pH

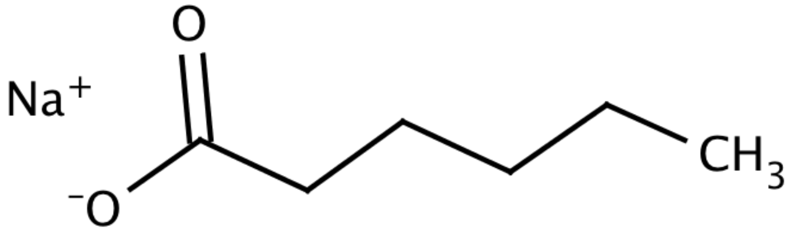
- Systems of solids in liquids include the most frequent and important type of pharmaceutical solutions.
- Most drugs belong to the class of weak acids and bases. They react with strong acids or bases to form water soluble salts.
- Acidic drugs (e.g. NSAIDs), are more soluble in solutions where the ionized form is the predominant.

- Basic drugs(e.g. ranitidine), are more soluble in acidic solutions where the ionized form of the drug is predominant.

Solubility of Solid in Liquid

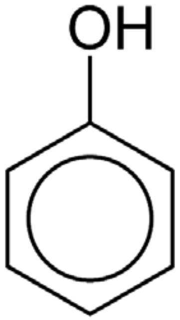
pH

Carboxylic acids containing more than 5 carbons are relatively insoluble in water; however, they react with dilute NaOH, carbonates, and bicarbonates to form soluble salts.



The fatty acids (> 10 carbon) form soluble soaps with the alkali metals and insoluble soaps with other metal ions.

Phenol is weakly acidic and only slightly soluble in water but is quite soluble in dilute sodium hydroxide.



Solubility of Solid in Liquid

pH

- Drug (HP) is weak electrolyte (salt of weak acid), and dissociate
- $HP + H_2O \Leftrightarrow H_3O^+ + P^-$
- $\log (S-S_0) = \log K_a + \log S_0 - \log [H_3O^+]$
- $$pH_p = pK_a + \log \frac{S-S_0}{S_0}$$
- Where,
- pH_p is the pH below which drug separate
- S= Total solubility of drug (Dissociated + undissociated)
- S_0= molar solubility (of un dissociated form of drug) is constant

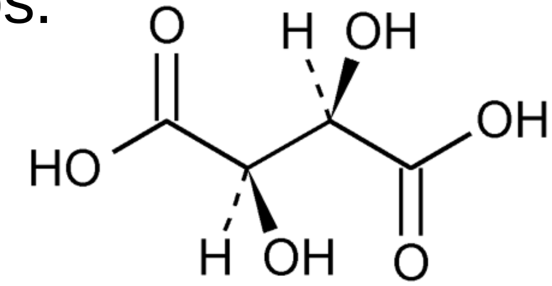
Solubility of Solid in Liquid

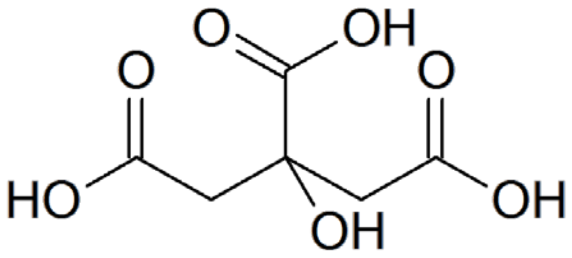
Substituents

Substituents can influence solubility by affecting the solute molecular cohesion and its interaction with water molecules.

Polar groups such as –OH are capable of hydrogen bonding (high solubility).

E.g. Hydroxy acids, such as tartaric and citric acids, are quite soluble in water because they are solvated through their hydroxyl groups.



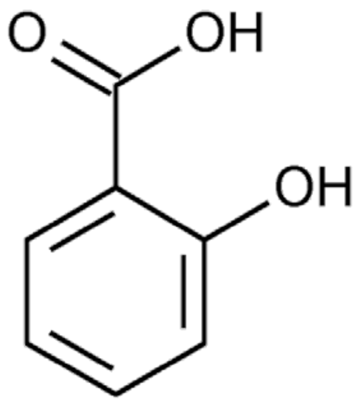


Non-polar groups such as $–CH_3$ and –Cl are hydrophobic (low solubility).

Solubility of Solid in Liquid

Substituents

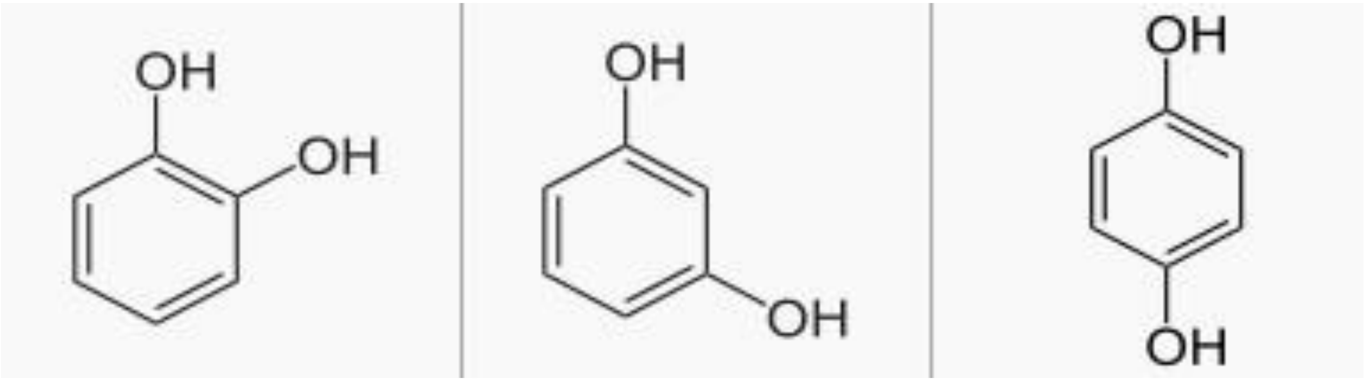
- The position of the substituent on the molecule can affect the solute molecular cohesion and its interaction with water molecules, and hence its solubility.
- E.g. the OH group of salicyclic acid cannot contribute to the solubility because it is involved in an intramolecular hydrogen bond.



Solubility of Solid in Liquid

Substituents

E.g. the aqueous solubility of o-, m- and p-dihydroxybenzenes are 4, 9 and 0.6 mol/L, respectively.



Symmetric particles (p-dihydroxybenzenes) can be less soluble than asymmetric ones (m-dihydroxybenzenes) because they form a compact crystals (which require more work to separate the particles), while the asymmetric particles pack less efficiently in crystals.

Solubility of Solid in Liquid

Solvent

- Frequently solute is more soluble in mixture of solvents than in single solvent.
- The solvent, which in combination with the main solvent increases solubility is known as **cosolvent**.

Solubility of Solid in Liquid

Crystal Characteristics

- Different crystalline forms of the same substance (known as **polymorphs**) possess different lattice energies.
- The polymorphic form with the lowest free energy will be the most stable.
- Less stable (**metastable**) forms with the highest energy will be the most soluble one. They tend to transform into the most stable form over time.
- The solubility of a crystalline material and its rate of dissolution can be increased by using a metastable polymorph.
- Many drugs exhibit polymorphism, e.g. steroids, barbiturates and sulphonamides.

Solubility of Solid in Liquid

Crystal Characteristics

- Incorporation of solvent molecules into the lattice structure of crystalline material during crystallization will result in solids that are called **solvates**. If water is the solvating molecule, the solids are called **hydrate**.
- The interaction between the substance and water that occurs in the crystal phase reduces the amount of energy liberated when the solid interact with the solvent (water).
- Therefore **unsolvated crystals will dissolve faster**.

Solubility of Solid in Liquid

Complexation

- Complexation can increase or decrease the solubility of drugs depending whether the formed complex is water soluble or insoluble.
- e.g. Cyclodextrin can form water soluble complexes with most drugs, thus increasing their water solubility.
- e.g. Tetracycline can form water insoluble complexes with various metal cations. Therefore tetracycline solubility is decreased in the presence of those metals.

Solubility of Solid in Liquid

Boiling and Melting Point

- In general, aqueous solubility decreases with increasing boiling and melting point.
- This is because the higher the boiling point of liquids and melting point of solids, the stronger the interactions between the molecules in the pure liquid or the solid state.

Particle Size

- Solubility increases with decreasing particle size, due to the increased particle surface area; meaning more of the solid is in contact with the solvent.