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Science Of Solubility: Introduction, Importance And Factor Of Solubility

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Abstract: Solubility has the important role in the science and it's a physical property of the different type's preparations'. The maximum amount of Solute that can dissolve in a known quantity of solvent at a certain temperature is its Solubility. A Solution is a Homogeneous mixture of one or more Solutes in a Solvent. Sugar cubes added to a cup of tea or coffee is a common example of a Solution. The property which helps sugar molecules to dissolve is known as Solubility. Hence, the term Solubility can be defined as a property of a substance (Solute) to dissolve in a given solvent. A Solute is any constituent which can be either solid or liquid or gas liquefied in a solvent. When we talk about the pharmacy industry, solubility is main factor for the all dosage form like as solid, liquid and semi-solid or semi-liquid dosage form. Solubility very important for the different type's formulation of drugs. The drug bioavlability depends on the solubility. The solubility of a compound depends on its structure and solution conditions. Structure determines the lipophilicity, hydrogen bonding, molecular volume, crystal energy and ignitability, which determine solubility. Solution conditions are affected by pH, co solvents, additives, ionic strength, time and temperature. Poorly soluble compounds can dramatically reduce productivity in drug discovery and development.

A "good compound" must be able to reach its target at effective concentrations. Therefore, the lowest acceptable solubility of a compound is related to its pharmacologic potency and its permeability. Low micro molar aqueous solubility can be acceptable only for extremely potent or permeable compounds.

Keyword: Solubility, Surface tension

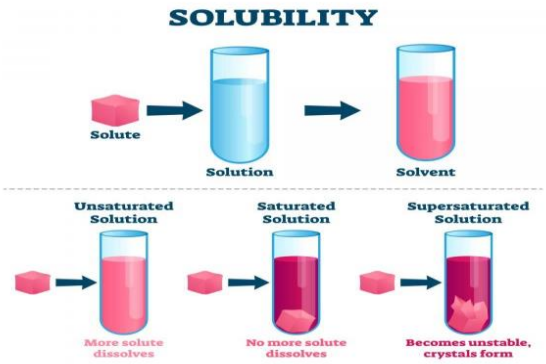

Figure -1

IMPORTANCE OF SOLUBILITY-: Oral ingestion is the most convenient and commonly employed route of drug delivery (easy administration, high patient compliance, cost effectiveness, least sterility constrains and flexibility in the design of dosage form) However, the major challenge with the design of oral dosage forms lies within their poor bioavailability. The cause of low oral bioavailability is the poor solubility and low permeability. Low aqueous solubility is the major problem encountered with formulation development of new chemical entities as well as generic development. Any drug to be absorbed must be present in the form of an aqueous solution at the site of absorption. More than 40% of NCEs developed in the pharmaceutical industry are insoluble in water. For this reason, the problem of solubility is one of the major challenges for formulation chemists.

Solubility also plays a major role for other dosage forms like parenteral formulations as well. Solubility is one of the important parameters to achieve desired concentration of drug in systemic circulation for achieving required pharmacological response. Poorly water soluble drugs often require high doses in order to reach therapeutic plasma concentrations after oral administration. Low aqueous solubility is the major problem encountered with formulation development of new chemical entities as well as generic development. Any drug to be absorbed must be present in the form of an aqueous solution at the site of absorption. Water is the solvent of choice for liquid pharmaceutical formulations. Most of the drugs are either weakly acidic or weakly basic having poor aqueous solubility.

The improvement of drug solubility thereby its oral bio-availability remains one of the most challenging aspects of drug development process especially for oral-drug delivery system. There are numerous approaches available and reported in literature to enhance the solubility of poorly water-soluble drugs. The techniques are chosen on the basis of certain aspects such as properties of drug under consideration, nature of excipients to be selected, and nature of intended dosage form. The poor solubility and low dissolution rate of poorly water soluble drugs in the aqueous gastrointestinal fluids often cause insufficient bioavailability. Especially for class II (low solubility and high permeability) substances according to the BCS, the bioavailability may be enhanced by increasing the solubility and dissolution rate of the drug in the gastro-intestinal fluids. As for BCS class II drugs rate limiting step is drug release from the dosage form and solubility in the gastric fluid and not the absorption, so increasing the solubility in turn increases the bioavailability for BCS class II drugs.

The negative effect of compounds with low solubility include poor absorption and bioavailability, insufficient solubility for IV dosing, development challenges leading to increasing the development cost and time, burden shifted to patient (frequent high-dose administration).

What factors affect solubility? Solubility is affected by 4 factors – temperature, pressure, polarity, and molecular size.

Effect of temperature on solubility-:

Solubility increases with temperature for most solids dissolved in liquid water. This is because higher temperatures increase the vibration or kinetic energy of the solute molecules. Solute molecules are held together by intermolecular attractions. The increased kinetic energy weakens the intermolecular attractions, making it easier for the solvent molecules to break up the solute molecules, causing them to dissolve more readily. Temperature affects gas solubility differently. Solubility of a gas in water decreases with increasing temperature while solubility of a gas in an organic solvent tends to increase with increasing temperature.

Effect of pressure on solubility-:

Solubility of a gas in a solvent increases with increasing temperature, although the increase in solubility based on pressure is not the same for all gasses. The effect of pressure on the solubility of condensed phases - solids and liquids - is negligible.

Effect of polarity on solubility-:

In most cases, polar solute will dissolve in a polar solvent while a nonpolar solute will dissolve a nonpolar solvent. Polar solutes will not dissolve in a nonpolar solvent and vice versa. The reason fat does not dissolve in water is because both are non-polar.

Effect of molecular size on solubility-:

Solubility decreases as the molecular size increases. The larger the size of molecules in a solute, the more difficult it is for solvent molecules to wrap around them in order to dissolve them. On the other hand, solvent molecules wrap around molecules of smaller size more easily, increasing the solubility of the substance. In general, under the same temperature and pressure conditions, solutes with smaller particles are more soluble than solutes with larger particles. Changing the temperature and pressure can change the solubility of the substance.

These are the factor which can affect the solubility of matter. In the drugs formulation solubility is the main part of a manufacturing unit.

Dissolution of the dosage form depend on the solubility because its important for the bioavlability.

Conclusion-: Dissolution of drug is the rate determining step for oral absorption of the poorly water soluble drugs and solubility is the basic requirement for the absorption of the drug from GIT. The various techniques described above alone or in combination can be used to enhance the solubility of the drugs. Proper selection of solubility enhancement method is the key to ensure the goals of a good formulation like good oral bioavailability, reduce frequency of dosing and better patient compliance combined with a low cost of production. Selection of method for solubility enhancement depends upon drug characteristics like solubility, chemical nature, melting point, absorption site, physical nature, pharmacokinetic behavior and so forth, dosage form requirement like tablet or capsule formulation, strength, immediate, or modified release and so forth, and regulatory requirements like maximum daily dose of any excipients and/or drug, approved excipients, analytical accuracy and so forth.

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