1. WEEK

SOLUBILITY

WAHT IS THE SOLUBILITY?

"Solubility" or "Saturation Concentration" is the maximum amount an active substance can dissolve in a unit volume under normal conditions and at a certain temperature.

Unit of the solubility is gram/ml.

WHAT IS THE INTRINSIC SOLUBILITY?

- The solubility of a weakly acidic substance in a strong basic medium or of a strong acidic or weakly basic substance is called "Intrinsic Solubility" or “Real Solubility".
- That is, the solubility of the active substance is still NONIONIC. Because the active material did not constitute salt. Only the substance itself can be mentioned.

- If the active solubility of an active substance is lower than 10 mg / ml, potential absorption and bioavailability problems are frequently encountered at pH 1-7.

BASIC FACTORS THAT AFFECTED THE SOLUBILITY?

1. Molecular weight
2. Medium pH and pKa value
3. Polimorphism
4. Surface active agent effect
5. Temperature
6. Co-solvent presence
7. Partition coefficient
8. Dielectric constant

- If the solubility of the material in the acidic medium is higher than its solubility in water, the material is weak base. Because weak bases constitute salts in acidic medium and their solubility increases.

- The substance is "amphoteric / zwitterionic" if the substance dissolves both in acidic and basic medium at a higher rate than in water.
- In this case, the substance has two pKa values, one of which is base acid pKa values.

- The absence of any change in solubility suggests that the molecule is a non-ionizing neutral molecule, which does not have a measurable value of pKa.

- The solubility should ideally be measured at 2 temperature values.

a) Should be measured at 4-5° C. Because there is no stability problem at this temperature value.

b) Should be measured 37^0C. This temperature value is important for biopharmaceutical evaluations. Can be used at 25^0C or 32^0C instead of 37^0C.

The relation between solubility and pKa value is expressed by Henderson-Hasselbalch Equation.

For weak bases:

$$pH = pK_a + \log \frac{C_{non\text{-}ionise}}{C_{ionise}}$$

C_{ionise}: Ionized drug concentration

$C_{non\text{-}ionise}$: Non-ionized drug concentration

For weak bases:

$$pH = pK_a + \log \frac{C_{ionise}}{C_{non\text{-}ionise}}$$

C_{ionise}: Ionized drug concentration

$C_{non\text{-}ionise}$: Non-ionized drug concentration

- Using this equation, the pKa value can be calculated from the changes in the solubility value or the solubility value of the active substance at any pH can be calculated.