÷ Unit-1 ÷ Solubility of drug.

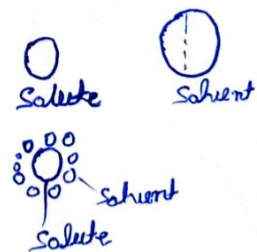**Solubility :-** The mixture of salute and salvent is called solution.

→ Salute are those component of solution which are present in less amount and salvent which are present in large amount; And when salute particle completely dissolve in salvent then it is called solution.

→ The maximum amount of salute which can be dissolve in 100g of salvent is called solubility of the drug.

→ The solubility of drug is depends upon the nature of salute and salvent, particle size, surface area and temprature etc.

Solubility Expression :- For dissolving any salute into salvent different no of salvent particle are required to dissolve one particle of salute and . on the basis of ratio solubility can be expressed as following -

i) Very Soluble. — Less than 1 part.

ii) Freely Soluble — 1 — 10

iii) Soluble — 10 — 30

iv) Sparingly Soluble — 30 — 100

v) Slightly Soluble — 100 — 1000

vi) Very insoluble — 1000 — 10000

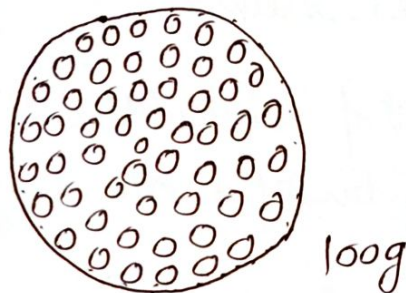vii) Insoluble — More than 10000

:- Types of Solution :- On the basis of

i) Saturated Solution :-
In a 100g solvent at room temp. the maximum amount of solute which can be dissolve is called saturated solution.
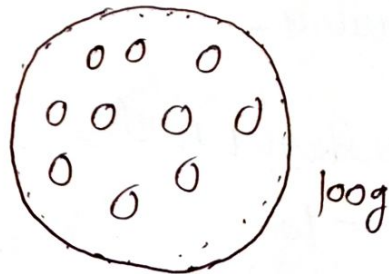
⇒ In a saturated solution at same temp no any Extra particle of solute can be dissolve.

100g

II) Unsaturated Solution :-
In a 100g solvent few amount of solute less than saturated solution is dissolve then it is called unsaturated solution.

→ In unsaturated solution few mole amount of solute can be dissolve.

100g

III) Super Saturated Solution :-
In a 100g solvent in maxi. amount of solute can dissolve after heating is called super satured solution.

⇒ When Tem is Tes then the surface area of solvent is

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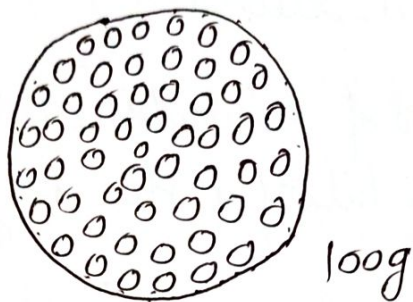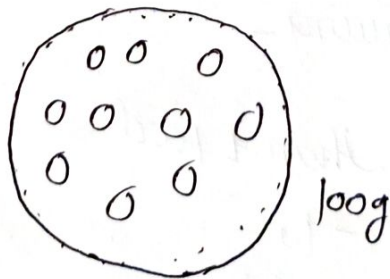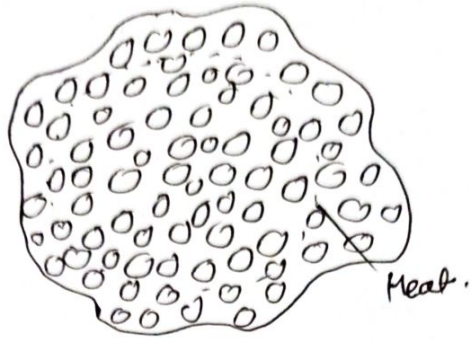In a 100g solvent in maxi. amount of solute can dissolve after heating is called super satured solution.

⇒ When Tem is Tes then the surface area of solvent is

increase. so some more amount of solute can be dissolve than saturated solution.

→ After reaching supersaturated condition no any solute particle can be dissolve.

Heat.

Mechanism of Solute and Solvent Intraction :-

The dissalution of solute into solvent is depends upon diff. solute solvent intraction mechanism.

→ When solvent molecules aggrigate then they must form are cavity. in which the solute molecule is entered.

→ Solute Solvent Intraction is based on the mechanism like dissolve like it means the nature of solute and solvent should be similar i.e if solute is palar then solvent should also be palar and if solute is nonpalar then solvent should be non palar.
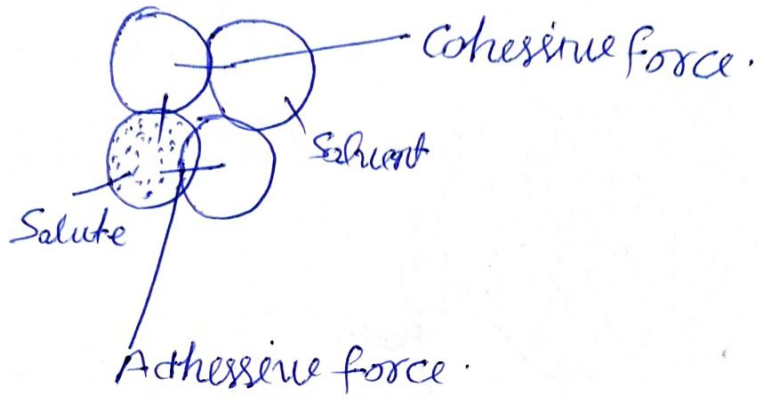
→ Between solute and solvent molecule two type of Attracts force.

i) Cohessive force :- Attraction force b/w solvent 2 molecule.

ii) Adhessive force :- Attraction b/w solute and solvent molecule.

If the Adhessive force is more than cohessive force then solubility occur.

→ If the cohessive force is more than Adhessive force then solubility is not occur.

Cohessive force.

Solvent

Salute

Adhessive force.

Ideal Solubility Parameters:

→ The ideal solubility of drug is depends upon the following equation :-

$$S = \left(\frac{\Delta U}{V}\right)^{1/2} = \left(\frac{\Delta H - RT}{V}\right)^{1/2}$$

Where :-

S = Solubility

ΔU = Lattice energy.

V = Volume.

ΔH = Change in Enthalpy

R = Rydberg gas constant.

T = Temprature.

→ As per this equation the solubility is directly proportional to the Temp. and Volume.
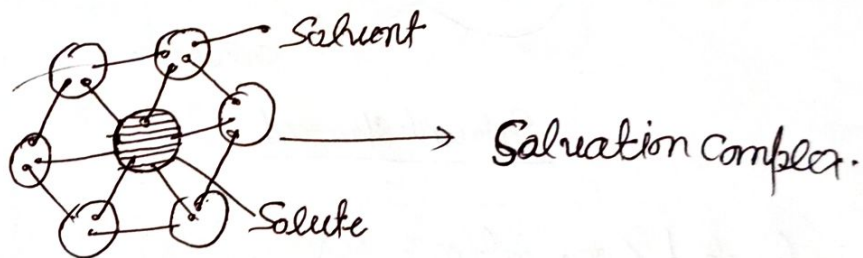
Solvation:

Before dissolution when solute molecules comes in contact with solvent molecule. then they form an Interaction. and it is a kinetic process.

→ When solute molecule is surrounded by the solvent molecule then they form a complex. by different bond. and forces. such as hydrogen bond; dipole moment, cohessive force, Adhessive force. and vander vall force of Attraction; This is called salvation complex and the formation of salvation complex is called salvation.

→ The rate of salvation formation determines the rate of solubility.

→ If solvent is water. then salvation is also K/a Hydration

Association:

Association is a method of solvation when solute is combined with solvent.
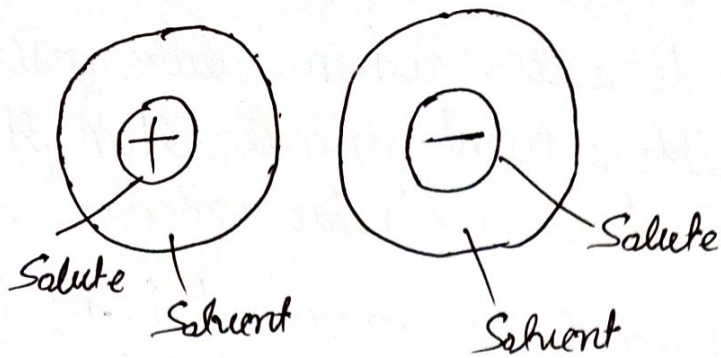
→ Generally association is seen in ionic solute.

→ On the basis of solvation association is of three type.

i) **Fully Solvated Association:**
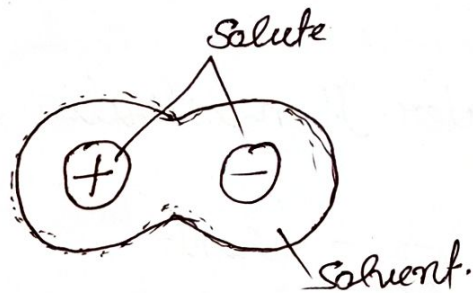
This is generally seen in weak electrolytes.

→ In this association the salvation is make separately for cations and Anions.

Fully Salvated.

2) **Salvent Shared or Salvent Separated Association:-**
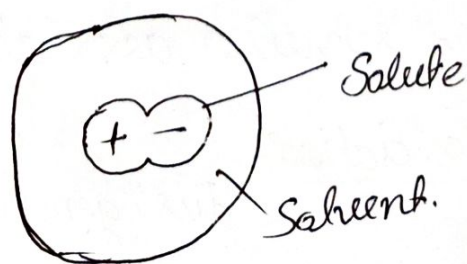
In this association cations and anions comes together. and someth particle of salvent is shared to make salvation complex for both

Salvent Shared

3) **Contacted Association:**

This association is seen in strong electrolyte when both cation and anion combines to form an associa complex and the salvent completely makes salvation with complex.

Contacted Association

∴ **Factor Affecting Solubility:-** The study of solubility and their factor affecting can be categories into three category

can be categories into three category.

i)

Solubility of
- Solid in liquid.
- Gas in liquid.
- Liquid in liquid.

i) **Solubility of Solid in liquid:**

A) **Nature of Solute and solvent :-**
It depends upon the principle like dissolve like it means polar solute will dissolve in polar solvent and non polar solute will dissolve in non polar solvent.

B) **Surface Area**
If the surface area of solvent is large then more solute particle will absorb and solubility increase.

Solubility $\propto$ Surface Area.

B) **Temprature :**
The solubility of salid solute two types of rxn invalue.

If rxn is Endothermic then on increasing temp solubility is increase.

And for Exothermic rxn when temp is increase then solubility is decrease.

2) **Solubility of Gas in liquid:**

i) **Surface Area.**

ii) **Temprature:** When temp is increase then the solute gas expend and moves upward. So solute can not intract with soluent and solubility decrease.

$$Solubility \propto \frac{1}{Temp.}$$

iii) **Pressure:** - The solubility of gas in liquid is depends upon the henary law.

$$- S \propto P$$

$$- \boxed{S = K_h P}$$

Where - S = Solubility
K_h = Henary Constant
P = Pressure.

When pressure is increas by applying piston then solute molecule comes closer to the soluent and solubility increase.

3) **Solubility of liquid in liquid:-**

i) **Nature:-** like dissolve like.

ii) **Temp:-** Solubility is directly proportional to the temp.

iii) **Pressure:-** - Solubility is directly proportional to the pressure.

iv) **Surface Area:-** Solubility is directly proportional to the surface Area.

v) **PH value of buffer:-** If the solvent is buffer solution then it works on a specific pH value.
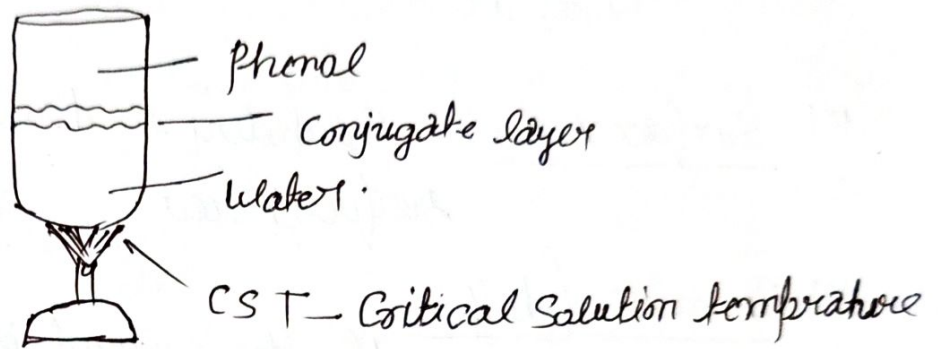
Binary Solution:-

- Binary solution is the mixture of two diff. solvent in any satn.

- The binary satn is may be of three types.

i) When both solvent are completely miscible
   Ex Alcohal and water.

ii) When both solvent are partialy miscible-
   Ex- Phenol and water.

iii) When both solvent are imiscible.
   Ex- Oil & water.

In partialy miscible binary soln. both solvent are seprated with a conjugate liquid layer.

→ As well as temp is ↑es both solvent mixed together and conjugate layer is disappear.

→ That temp. at which bath solvent are mixed together. is called critical solution temp.

— Phenol
— Conjugate layer
— Water.

CS T— Critical Solution temperature

◦ Ideal and Real Solution ◦ (Non Ideal)

Those solutions which fallow the fallowing gaseous law of solution is called ideal solution.

→ Roult's law.

→ Henry law

→ Dalton 's law

- Charls law

- Bayl's law

→ Avagadro law.

→ ~~For~~ ideal solution the heat of fusion is equals to the heat of solution. and the. total pressure of solution is equals to the. ~~heat of solution~~ and the sum of the pressure of its constituent _

And those solution which do not follow are so deviation from Ideal behaviour is called non ideal or Real solution
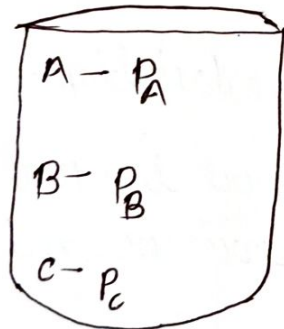
1) Roull's law :

→ According to roull's law in any gaseous mixture the partial pressure of any gas is equal to the multiplication of its vapour pressure and mole fraction.

→ According to dalton's law in any gaseous mixture. the total pressure of gaseous mixture is equal to the sum of partial pressure of all gases.

→ Suppose in any gaseous container gas A, B, C, are present and their partial pressure are P_A, P_B, P_C respectively, And their mole friction is X_A, X_B, X_C.

- Then -

$$\boxed{P = P_A + P_B + P_C} \longrightarrow (i)$$

$A \Big\langle \begin{array}{l} P_A - \text{Vapour Pressure.} \\ X_A - \end{array}$

$B \Big\langle \begin{array}{l} P_B^\circ \\ X_B \end{array}$

$C \Big\langle \begin{array}{l} P_C^\circ \\ \mathbf{X_C} \end{array}$

$$\boxed{P = P_\bullet^o x}$$

Partial Vapour M.f.

$$P_A = P_A^o \cdot X_A$$

$$P_B = P_B^o \cdot X_B$$

$$P_C = P_C^o \cdot X_C.$$

Put those value in equation (i)

$$\boxed{P = P_A^o X_A + P_B^o X_B + P_C^o X_C}$$

Ideal Solution.

$$P < P_A^o X_A + P_B^o X_B + P_C^o X_C$$

(−) Negative deviation.

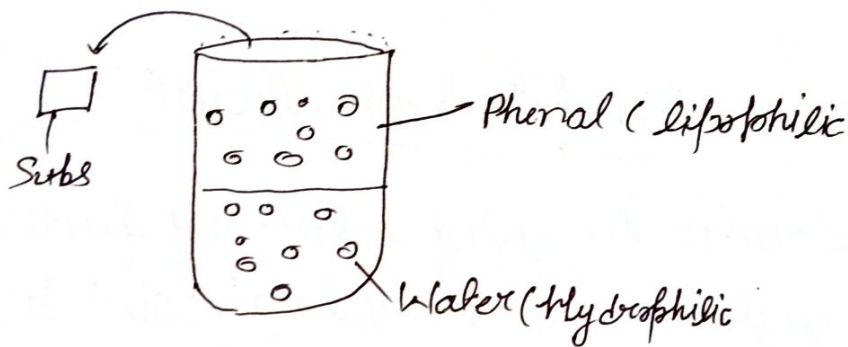$$P > P_A^o X_A + P_B^o X_B + P_C^o X_C$$

(+) Positive deviation.

For Ideal solution the total pressure is equal to the some of the multiplication of vapour pressure and mole friction.

→ If the total pressure is less than the some of all pressure then it called −ve deviation. and if the total pressure is greater than some of all pressure then it is called +ve deviation.

Distribution law : (Partition Cofficent)

In a binary saln of two immiscible liquid when any drug is mixed then some friction of drug is dissolve in oil phase and some friction of drug is dissolve in water phase this is called Distribution law.

The ratio of drug is dissolve in lipophilic medium to the drug dissolve in hydrophilic medium is called distribution cofficent or Partition cofficent.

Substance → Phenal (lipophilic

Water (Hydrophilic

$$\text{Partition Cofficent} = \frac{\text{drug dissolve in oil phase}}{\text{drug dissolve in water phase}}$$

$$\boxed{P = \frac{X_o}{X_w}}$$

if, (P) is more than one (1) then subs is lipophilic in nature.

- (P) is less than one (1) then subs is hydrophilic in nature.

P = Partition Cofficent

X_o = Fraction of drug dissolve in oil.

X_w = Fraction of drug dissolve in water.

→ If the value of partition cofficent is greater than one it means the value of X_o is more so the nature of drug is licophilic.

→ If the value of partition cofficient is less than one then the value of X_w is more and the nature of drug will be hydrophilic. main application of partition cofficent is determine the nature of unknown drug sample

After determination of nature we can choose the suitable solvent.

Method of determination of Partition Cofficient:-

It is determine by using separating funnel apparatus. Add 50 ml water and 50 ml octonal (oil) in separating funnel.

→ Now add the pawder drug mixture in separating funnel and shake vigrously.

→ Left the separating funnel for thirty minute and takes out the oil and water in separate beaker.

→ By using UV spectroscopy or HPLC we can determine the concentration in water and oil.

→ The value of partition cofficent is determine by using formula-

Subs / Separating funnel / water / oil