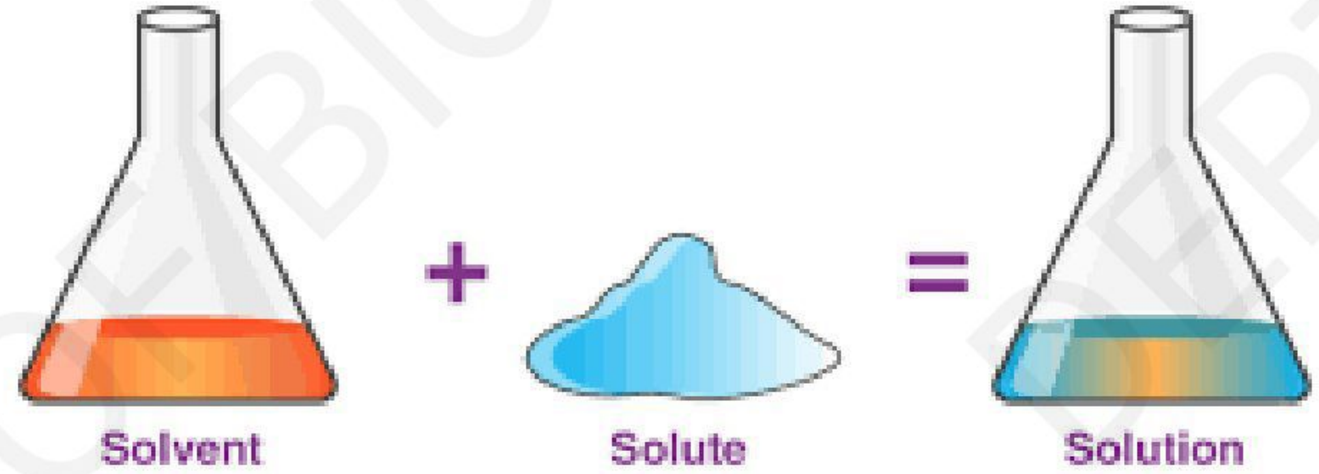
UNIT-1
SOLUBILITY OF DRUGS

SOLUTION- a solute is a substance dissolved in another substance, known as a solvent.

SOLUBILITY-

The maximum concentration of a substance that can be completely dissolved in a given solvent



• SOLUBILITY EXPRESSION

Descriptive terms	Relative amounts of solvents to dissolve 1 part of solute
Very soluble	Less than 1
Freely soluble	From 1-10
Soluble	From 10-30
Sparingly soluble	From 30-100
Slightly soluble	From 100-1000
Very slightly soluble	From 1000-10,000
Insoluble or practically insoluble	More than 10,000

i. Easily dissolve – quick
ii. Freely soluble – dissolve [DEPTH OF BIOLOGY]
iii. Soluble- dissolve by stirring
iv. Sparingly soluble- dissolve by heating
v. Slightly insoluble- by heating or stirring
vi. Very insoluble- only a small amount of solute is dissolved by maximum efforts [DEPTH OF BIOLOGY]
vii. Insoluble- do not dissolve at all

TYPES OF SOLUTION

I) SATURATED

II) UNSATURATED

III) SUPER-SATURATED

1.SATURATED SOLUTION- a solution that contains the maximum amount of solute that can be dissolved (no more solute can be dissolved) under the condition at which the solution exists i.e constant temperature

2.UNSATURATED SOLUTION- condition where more solute can be added to the solvent

3.SUPER-SATURATED SOLUTION- no more solute can be dissolved even after heating or changing the normal condition

UNSATURATED SOLUTION

more solute dissolves

SATURATED SOLUTION

no more solute dissolves

SUPERSATURATED SOLUTION

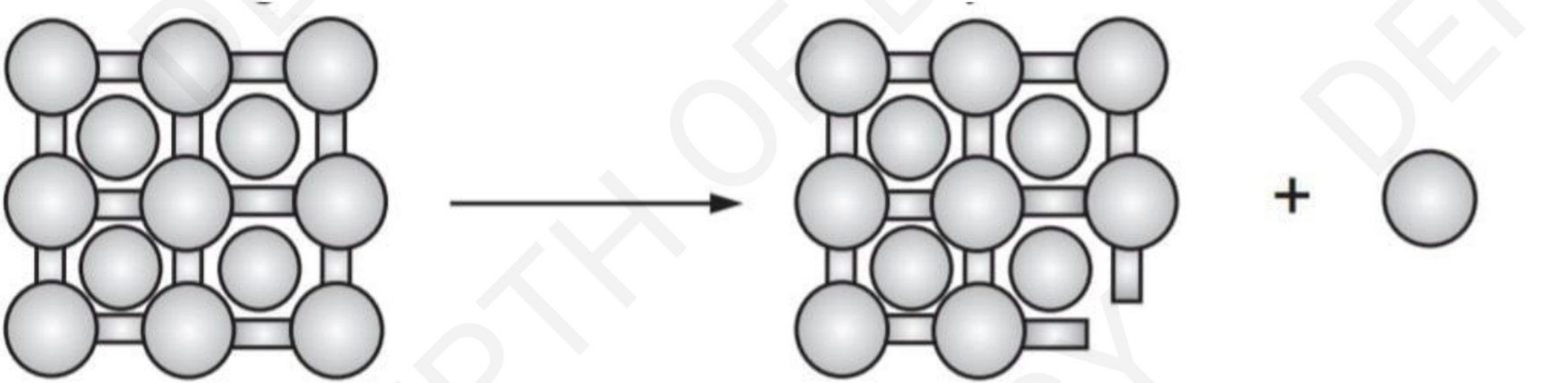
becomes unstable, crystals form

MECHANISM OF SOLUTE-SOLVENT INTERACTION

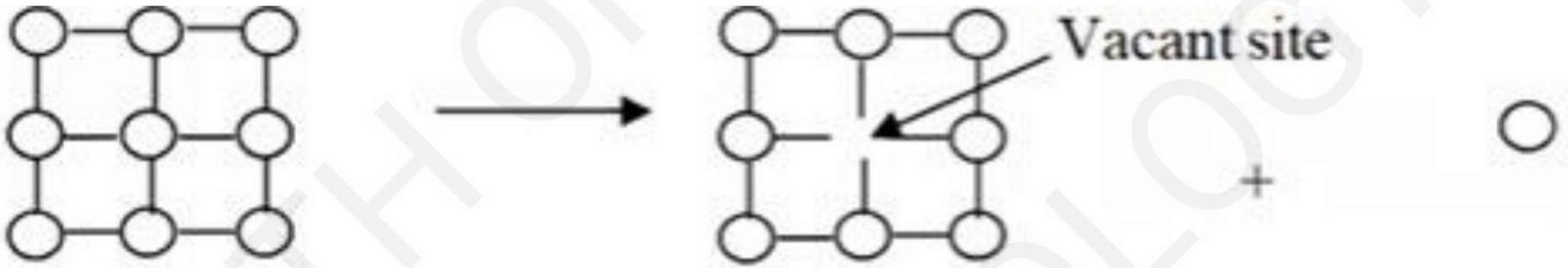
[DEPTH OF BIOLOGY]

A solute dissolves in a solvent when it forms favorable interactions with the solvent.

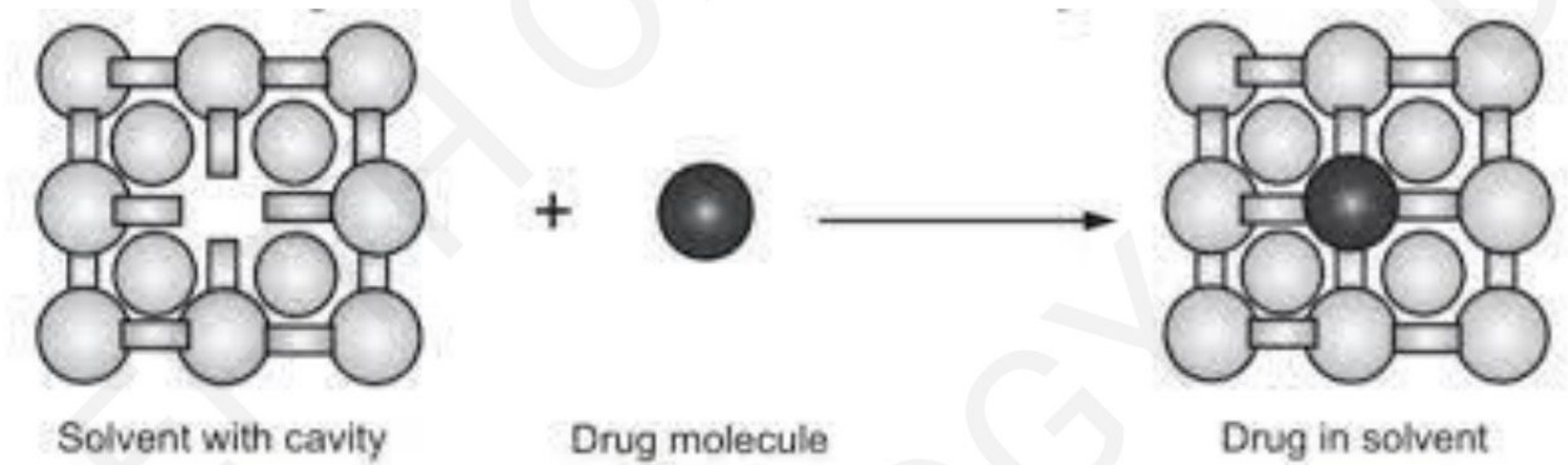
1. DETACHMENT OF SOLUTE FROM BULK FORM-



2. FORMATION OF VACANT SITE IN SOLVENT



3. INSERTION OF DETACHED SOLUTE PARTICLE INTO SOLVENT-



MECHANISM FOR DIFFERENT SOLVENT

1. ***POLAR SOLVENT*** - increase dielectric constant which reduces force of attraction

- Ability of breaking covalent bond
- Formation of hydrogen bond

EX: water, ethanol

2. ***NON-POLAR SOLVENT-*** only non polar solutes are dissolved induced by dipole interaction

EX: fats, oils etc

3. SEMI- POLAR SOLVENTS: only semi polar solutes dissolved by dipole moment

EX: acetone

"LIKE DISSOLVES LIKE" this method is followed by all these parts.

Hence, solute-solvent interaction $\propto$ solubility

IDEAL SOLUBILITY PARAMETERS-

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

S= solubility
Δ V= lattice energy
V= volume
ΔH =enthalpy
R=Rydberg constant
T= temperature

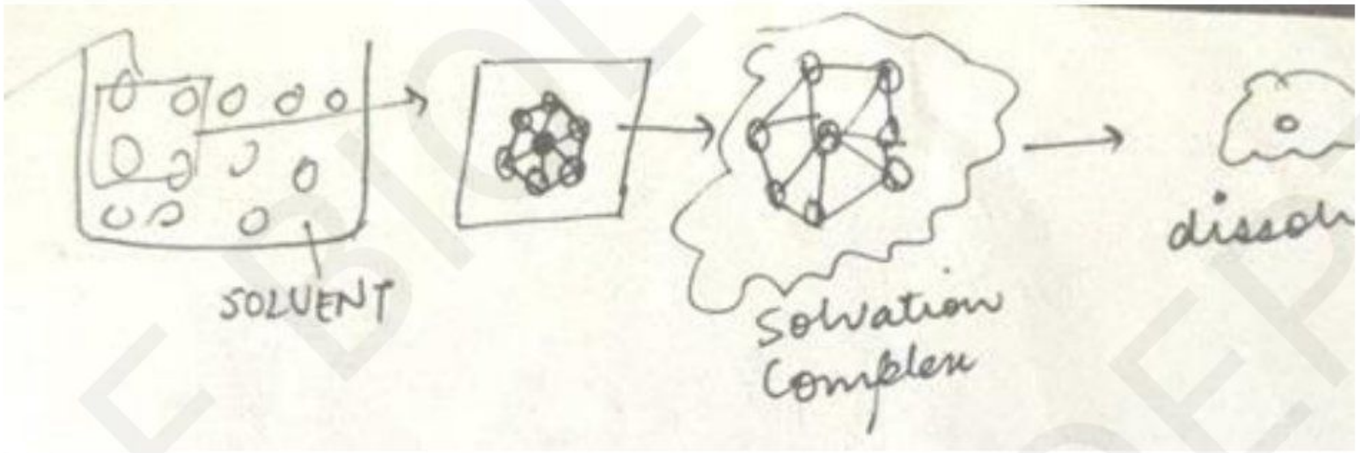
SOLVATION

- Solvation describes the interaction of solvent with dissolved molecules.
- It involves

i. bond formation.

ii. hydrogen bonding.

iii. van der Waals forces.



[DEPTH OF BIOLOGY]

SOLVENT

- **AQUEOUS [H_2O]-hydration**
- **NON-AQUEOUS** [other than water like **OH]-solvation**

ASSOCIATION

[DEPTH OF BIOLOGY]

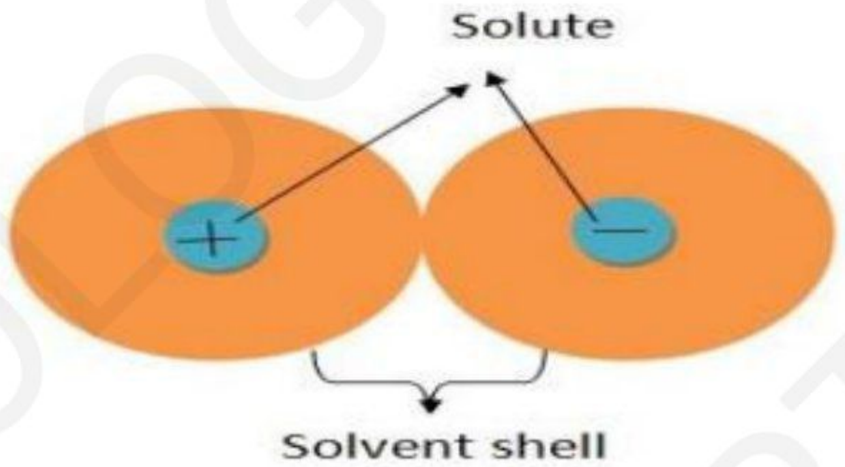
- Phenomenon in which oppositely charged ions come together in a solution & form separate chemical entity.
- So, solvation of ionic solute is known as association

3 types- [DEPTH OF BIOLOGY]

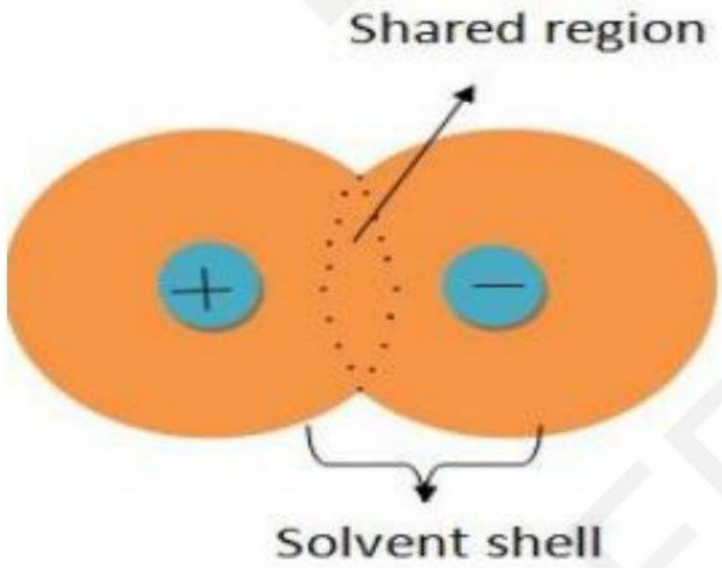
a. Fully solvated
b. Solvent shared
c. contracted

1. **FULLY SOLVATED-** different particle of solvent separately cover anionic & cationic

Particle of solute. [DEPTH OF BIOLOGY]



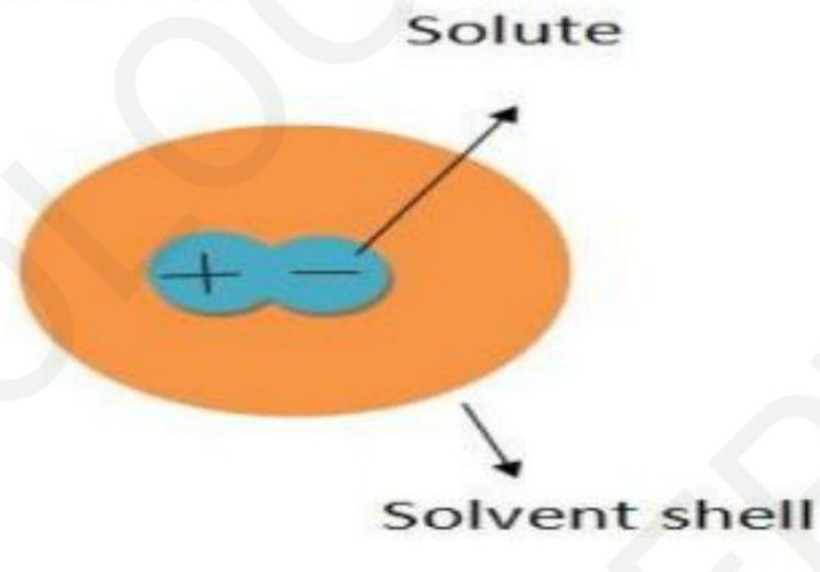
2. SOLVENT SHARED-



[DEPTH OF BIOLOGY]

3. CONTRACTED- works on strong electrolytes

In this, ions maintain contact with each other.



FACTORS AFFECTING SOLUBILITY

SOLUBILITY OF-

1.Solid in liquid.

2.Gas in liquid

3.Liquid in liquid

1.SOLID IN LIQUID- solute= solid & solvent= liquid

FACTORS-

i. **NATURE-** same nature= good solubility,
EXAMPLE- polar solute in polar solvent & non-polar solute in non-polar solvent

ii. **SURFACE AREA** ∝ to solubility

iii. TEMPERATURE- 2 types of reaction occur

EXOTHERMIC	ENDOTHERMIC
Heat released EX; POP in water	Heat absorbed EX; sugar in water
Solubility ∝ 1/ temperature	Solubility ∝ temperature

2.GAS IN LIQUID- solute= gas form & solvent= liquid form

i. **NATURE** cannot affect this because gas is non polar

ii. **SURFACE AREA-** ∝ to solubility

iii. **TEMPERATURE** ∝ 1/ solubility.

iv. **PRESSURE ∝ solubility** [henry`s law]

3.LIQUID IN LIQUID- solute & solvent = liquid

i. **NATURE** like dissolve like method

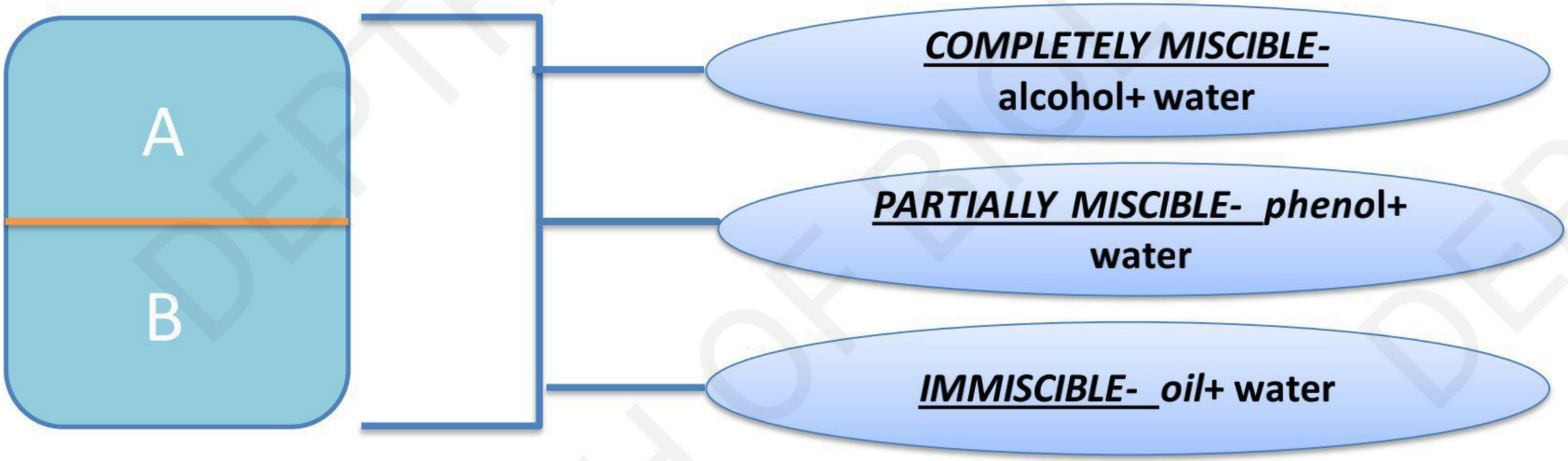
ii. **SURFACE AREA-** ∝ to solubility

iii. **TEMPERATURE** ∝ solubility.

iv. **PRESSURE** ∝ solubility.

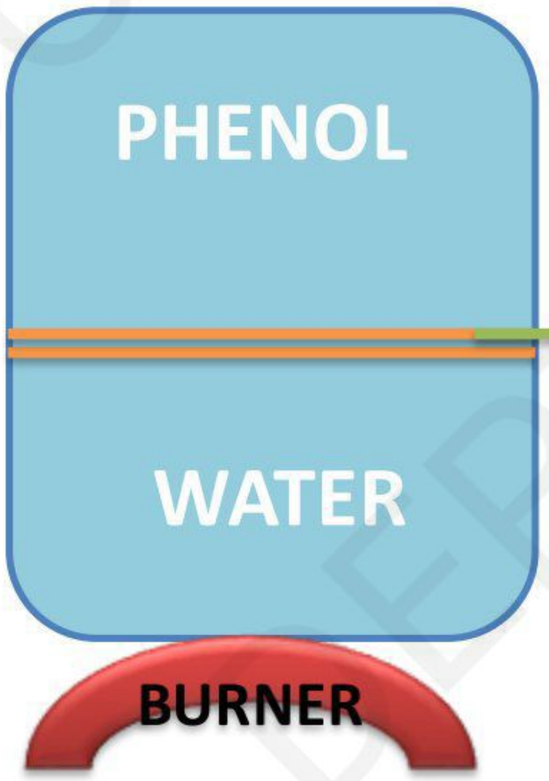
BINARY SOLUTION

When solute is mixed in 2 different solvent then it the solution formed is called binary solution.



[DEPTH OF BIOLOGY]

PARTIALLY MISCIBLE



These solutions partially mix and form a Conjugate layer between them.

But when heat is applied the conjugate layer Slowly disappears

When the conjugate layer completely disappears [the bases completely mix] it is called ***CST (critical solution temperature)***

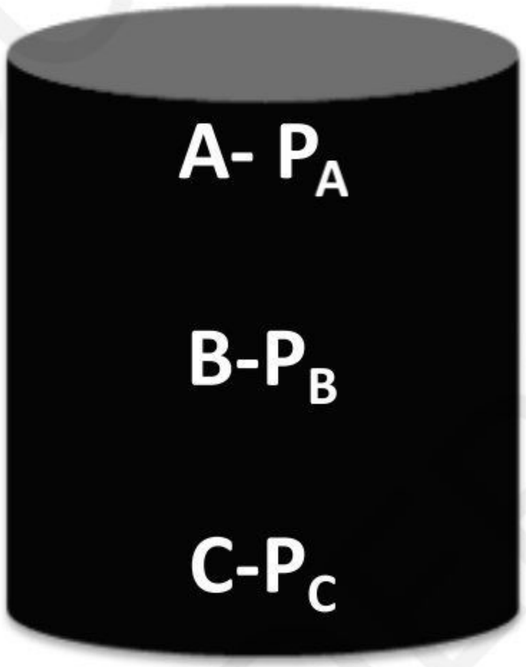
IDEAL & REAL SOLUTION {NON-IDEAL}:

- IDEAL: follows all rule (raoult`s law)- perfect solution.
- NON- IDEAL: does not follows all rule. [DEPTH OF BIOLOGY]

- ❑ RAOULT`S LAW
- ❑ HENRY`S LAW
- ❑ DALTON`S LAW
- ❑ CHARLE`S LAW

[DEPTH OF BIOLOGY]

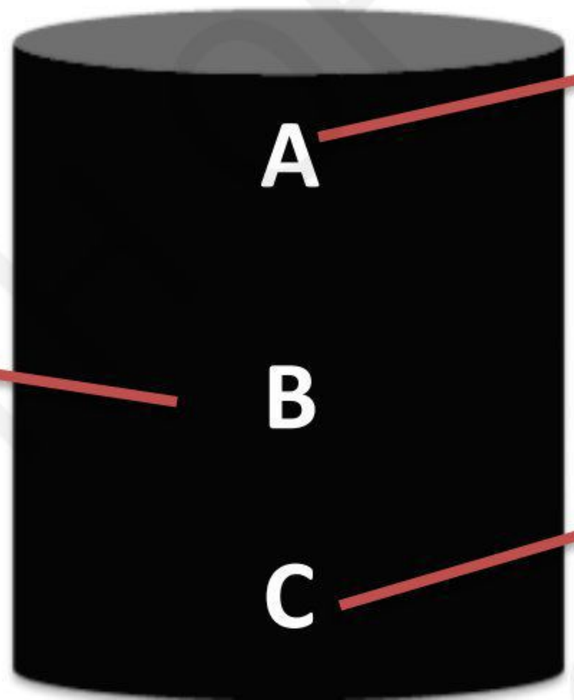
• DALTON`S LAW



total pressure of container

$$P = P_A + P_B + P_C$$

P_A ,P_B & P_C are partial pressure



P^o_A = vapour pressure
X_A= mole fraction

P^o_B = V.P
X_B= m.f.

P^o_C = V.P
X_C= m.f

MOLE FRACTION; $X_A = P_A / P_A + P_B + P_c.$

PARTIAL PRESSURE: $P_A = P°_A . X_A$

$P_B = P°_B . X_B$

$P_C = P°_C . X_C$

[DEPTH OF BIOLOGY]

[DEPTH OF BIOLOGY]

TOTAL PRESSURE: $P = P_A + P_B + P_C$

$P = P°_A X_A + P°_B X_B + P°_C X_C$

Solution which follows raoult`s law is called ideal solution.

If

$$P < P^\circ_A X_A + P^\circ_B X_B + P^\circ_C X_C$$ **negative deviation**

$$P > P^\circ_A X_A + P^\circ_B X_B + P^\circ_C X_C$$ **positive deviation**

[DEPTH OF BIOLOGY]

then, solution is non-ideal or real solution

APPLICATION: [DEPTH OF BIOLOGY]

- determine vapour pressure of components in a solution
- Boiling point of 2 component mixture

LIMITATION:

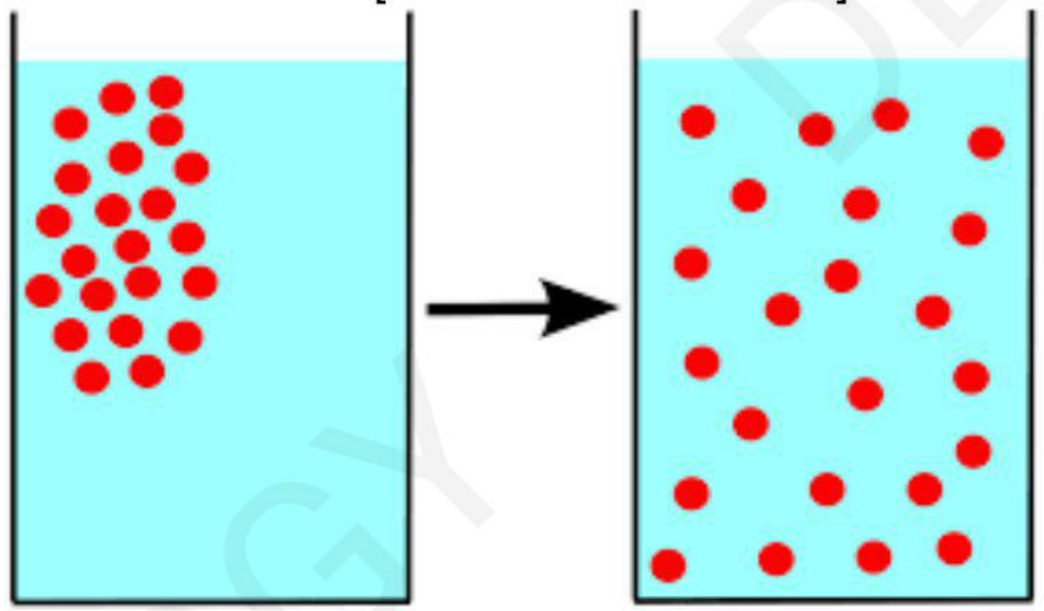
- This applies only to very dilute solution
- Applies to solution containing only a non-volatile solution
- This does not apply to solutes that dissociate or associate within the particular solution

DIFFUSION PRINCIPAL IN BIOLOGICAL SYSTEM

Diffusion:- [DEPTH OF BIOLOGY]

- It is a process of mass pasfer of individual molecules of a substance from a region of high concentration to low concentration (under concentration gradient)

[DEPTH OF BIOLOGY]



- ***•FICK'S FIRST LAW OF DIFFUSION:-***

It states that the rate of diffusion of a solute molecules through a barrier is proportional to the concentration gradient

- J=dm/dt or J= -d dc/dx

Where,

- J= flux of a component(rate of diffusion)
- Dm= amount transport
- Dt= time taken
- D= diffusion constant
- Dc/dx = concentration gradient

- Negative sign indicates that diffusion occurs in the direction opposite to that of high concentration.(high to low concentration)

• FICK'S SECOND LAW OF DIFFUSION:-

- It states that the change in concentration with respect to time at a particular region is proportional to the change in concentration gradient at that point in the system

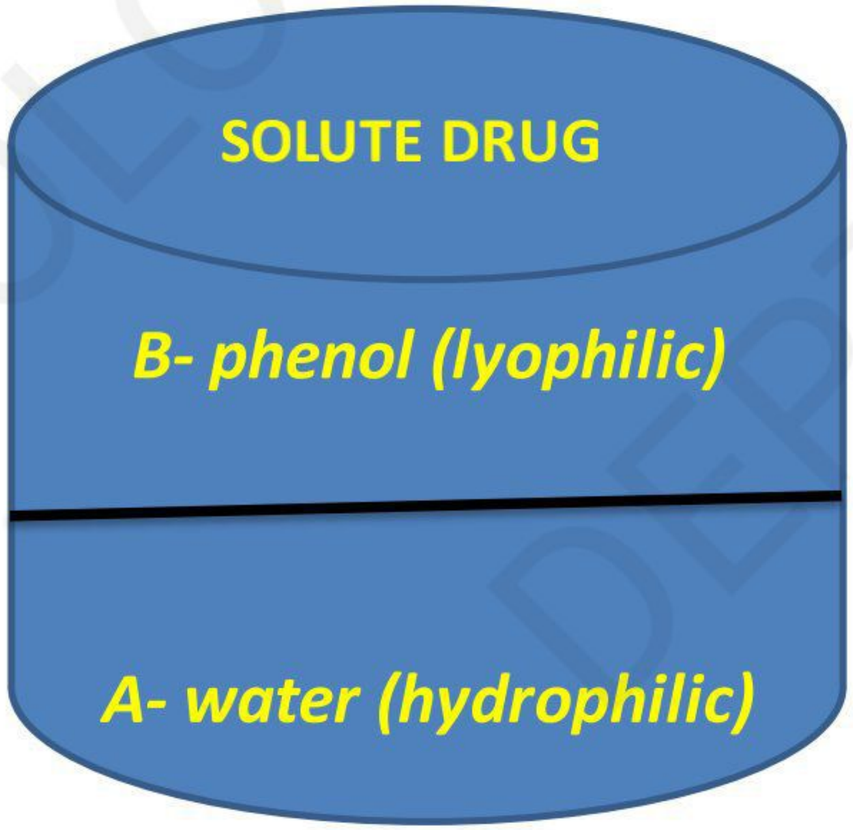
- $Dc/dt = d \bullet d^2c/dx^2$

- Applications in pharmaceutical science

1. Release of drug from dosage form.
2. dispersion of drugs.
3. Prediction of absorption.

Distribution law(Partition coefficient)

- It is used to find out the nature of solute particle (unknown drug) that is drug is lyophilic or hydrophilic.



- How we used it ?
- -firstly take partially miscible binary solution fig.(phenol + water), then mix unknown drug into that binary solution , then mix it.

- Now we have to check on which solvent (phenol + water) drug dissolve more.

- Partition coefficient = drug dissolve in lyophilic (oil phase)/drug dissolve in hydrophilic (water phase)
- P= xo/xe [DEPTH OF BIOLOGY]

- Where,
- Xo= drug in oil phase/
- Xw = drug dissolve in water phase

- If,

  P>1 = lyophilic

  P<1=hydrophilic [DEPTH OF BIOLOGY]

HOW WE SEPARATE DRUG IN OIL PHASE AND WATER PHASE??

- Firstly put it into separating funnel then add unknown drug mix up to 15 min then stay it or put it for 30 min.

- Now, take one beaker put it into down of stand weight for conjugate layer then take another beaker

- —Now take each sample 5ml and check drug concentration in UV spectroscopy.

- –Now , put the value in partition coefficient formula
- If P>1 then lyophilic or P<1 then hydrophilic.

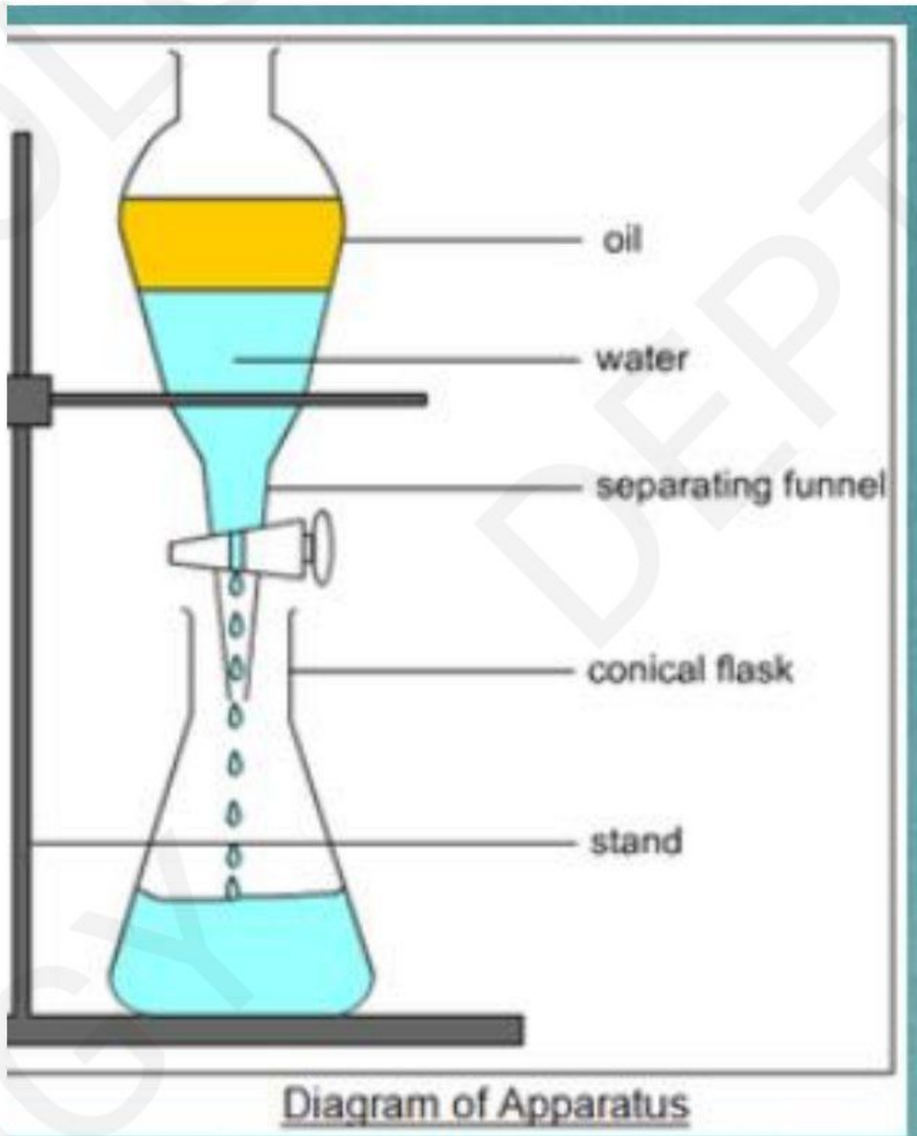


Diagram of Apparatus