Dispersion System -

It is defined as a heterogeneous two phase system in which internal phase is distributed or dispersed throughout the external phase.

Internal phase is also termed as dispersed phase while external phase is known as continuous phase or dispersion medium.

- The internal and external phase may be solids, liquids, and gases.

- The particles of dispersed phase may range in size from particles of atomic and molecular dimensions to particles whose size is measured in millimeters.
Classification of Dispersed Systems

General Characteristics

Dispersion System

- Based on size of dispersed particles (3 types)

Molecular Dispersion
- Particle size less than 1 nm
- Particles are invisible to naked eyes
- Not seen by electron-microscope
- Particles can pass through filter paper and semi-permeable membrane
- Particles undergo rapid diffusion
- Particles do not settle down (Examples: Sugar in water, nacal in water, oxygen in water)

Colloidal Dispersion
- Particle size between 1 nm - 0.5 µm
- Particles not detected by ordinary microscope
- Particles can be seen by electron or ultra-microscope
- Particles can pass through filter paper
- Particles cannot pass through semi-permeable membrane
- Particles diffuse very slowly
- Particles settle down under high centrifugation (Examples: Colloidal gold, protein, insulin, cheese, milk paint)

Coarse Dispersion
- Particle size greater than 0.5 µm
- Particles are visible under ordinary and also under electron or ultra-microscope
- Particles cannot pass through ordinary filter paper
- Particles do not dialyze through semi-permeable membrane
- Particles do not diffuse
- Particles settle down due to gravity
(Examples: Sand in water, emulsions, suspensions, red blood cells)
Colloidal dispersion is a heterogeneous system which is made up of dispersed phase and dispersion medium.

The particle size of dispersed phase ranges from 1mm - 1000nm.

Dispersed phase can be defined as the very fine particles dispersed in the solution, while dispersion medium can be defined as the solution in which the substances fine particles are uniformly dispersed.

In case of dust, solid particles are dispersed in air as dispersion medium.

Types of Colloidal Dispersions:

On the basis of physical state of dispersed phase and dispersion medium, colloidal dispersions are classified as follows - (8 different types)

1. Foam
2. Solid foam
3. Liquid Aerosol
4. Emulsions
5. Gels
6. Solid Aerosol
7. Sal (Colloidal Suspension)
8. Solid Sal (Solid Suspension)
<table>
<thead>
<tr>
<th>S.No</th>
<th>Dispersed phase</th>
<th>Dispersion medium</th>
<th>Type of Colloidal Dispersion</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Solid</td>
<td>Solid</td>
<td>Solid Sal</td>
<td>Pearls, Gemstones, Pigments, Plastics</td>
</tr>
<tr>
<td>2</td>
<td>Solid</td>
<td>Liquid</td>
<td>Sal</td>
<td>Paste, Ink, Paint, Gold Sal, Foundation</td>
</tr>
<tr>
<td>3</td>
<td>Solid</td>
<td>Gas</td>
<td>Solid Aerosol</td>
<td>Smoke, Dust</td>
</tr>
<tr>
<td>4</td>
<td>Liquid</td>
<td>Solid</td>
<td>Gel</td>
<td>Butter, Cheese, Jellies</td>
</tr>
<tr>
<td>5</td>
<td>Liquid</td>
<td>Liquid</td>
<td>Emulsion</td>
<td>Milk, Rubber, Cream, Lotion</td>
</tr>
<tr>
<td>6</td>
<td>Liquid</td>
<td>Gas</td>
<td>Liquid Aerosol</td>
<td>Mist, Fog, Dust, Hair, Spray</td>
</tr>
<tr>
<td>7</td>
<td>Gas</td>
<td>Solid</td>
<td>Solid foam</td>
<td>Pumice Stone, Sponge, Silica Gel</td>
</tr>
<tr>
<td>8</td>
<td>Gas</td>
<td>Liquid</td>
<td>Foam</td>
<td>Soap, Beer, Lemonade, Whipped Cream, Frost</td>
</tr>
<tr>
<td>9</td>
<td>Gas</td>
<td>Gas</td>
<td>Does not exist i.e. gases are completely miscible into each other, does not form colloidal system</td>
<td></td>
</tr>
</tbody>
</table>

**Note:** When the dispersion medium is liquid, the colloidal dispersion is known as Sal.

**Types of Sol:** depending upon the liquid used

1. **Aerosol** or **Hydrosol**
   - when water is used as dispersion medium
2. **Benzosal**
   - when benzene is used as dispersion medium
3. **Allosal**
   - when alcohol is used as dispersion medium
4. **Organosal**
   - when any organic compound is used as dispersion medium.

- **Aerosol** when gas is used as dispersion medium, the solution is called Aerosol.
**Particle size**

The colours of colloidal dispersions is affected by the size of the particles present.

\[ \text{eg} - (a) \text{ If the particles in a red gold sol are large in size} \]

then, the dispersion occurs, shows blue colour

\[ (b) \text{ Antimony and arsenic triphosphides (red colour)} \]

On decreasing particle size

\[ \Rightarrow \text{ becomes yellow in colour} \]

* Based on the size of the dispersed phase, there are three types of dispersions -
  
  a) Molecular dispersions (particle size < 1nm)
  
  b) Colloidal dispersions (1nm - 1000nm)
  
  c) Coarse dispersions (> 1000nm)

* In a solution, the size of a colloidal particle can be calculated by two methods -

  I) Calculating the volume of the particle in a given number with the help of an ultra- microscope.

  II) by analyzing the dispersed phase concentration.
If 'm' is the total amount of dispersed phase then, the density of dispersed phase then, the volume of a single particle can be calculated as:

\[ V = \frac{m}{nd} \]

If particles are assumed to be:

(a) Cube-shaped

\[ V = l^3 \quad (l = \text{length of one side of cube}) \]

or,

\[ l^3 = \frac{m}{nd} \]

\[ l = \left( \frac{m}{nd} \right)^{\frac{1}{3}} \]

(b) Spherical shaped

\[ V = \frac{4}{3} \pi r^3 \quad (r = \text{radius of particle}) \]

or,

\[ \frac{4}{3} \pi r^3 = \frac{m}{nd} \]

\[ r^3 = \frac{3m}{4\pi nd} \]

Hence, the radius of particle can be calculated as:

\[ r = \left( \frac{3m}{4\pi nd} \right)^{\frac{1}{3}} \]

Because of their size, colloidal particles may be separated from large particles by technique of separation called dialysis.
* Particle Shape -

The shape of colloidal particles is also important. It depends on the preparation methods and particle affinity to the dispersion medium.

- The dispersion colour is also influenced by the shape of colloidal particles.
  - e.g. Gold particles
    - Spherical
    - Disc-shaped
      - Red colour
      - Blue colour

- Particle shape is also related to pharmacological actions.

- Importance of colloidal shape -
  - The more extended particles, the greater its specific surface and the greater opportunity for attractive forces to be develop between particles of dispersed phase and dispersion medium.

- Shape of colloidal particles may affect -
  a) flow of particles
  b) Sedimentation rate
  c) Osmotic pressure
Shapes of Some Colloidal Particles:

A) Spheres and Globules
   - Surfactants, Polymers

B) Short rods and prolate-ellipsoids
   - Serum albumin, Microcrystalline Cellulose

C) Oblate ellipsoids and flakes
   - Bentonite, Kaolin

D) Long rods and threads
   - Tobacco mosaic virus

E) Loosely coiled threads

F) Branched threads
   - Cellulose, Abestos
Classification of Colloids

- Depending upon the nature of the interaction between the dispersion medium and the dispersed phase, colloids can be classified as follows:

A) Lyophilic colloids
B) Lyophobic colloids
C) Association colloids

*A) Lyophilic Colloids* - Also called *Intrinsic Colloid*

Lyophilic means – ‘Loving’

- If the dispersed phase interact to a great extent with the dispersion medium, then colloid is called *lyophilic colloid*. e.g. Starch, rubber, protein

→ Types:

  a) Hydrophilic Colloid - If dispersion medium is water, then they are called *hydrophilic colloids*. e.g. acacia in water, insulin in water

  b) Lipophilic Colloid - If dispersion medium is non-aqueous organic solvent, then they are called *lipophilic colloids*. e.g. rubber in non-aqueous solvent (benzene)

→ Preparation - Affinity of lyophilic substances for dispersion medium leads to spontaneous formation of colloidal dispersion. e.g. Acacia, tragacanth, methyl cellulose readily dispersed
- Reversible in nature i.e. readily reconstituted by simple mixing.
- Viscosity increases on addition of dispersed phase.

(B) Lyophobic Colloids - Also called extrinsic colloid.

Lyo means - 'Liquid'
phobic means - 'hating'

- If the dispersed phase has little or no affinity to interact with dispersion medium, then colloid is called lyophobic colloid. eg - dispersion of oil droplets in water
  - dispersion of water droplets in oil
  - inorganic particles sols - gold, silver, iodide, sulphur
  - sols of metallic hydroxides
- They are thermodynamically unstable, requires stabilizing agents for their preservation.
- Irreversible in nature i.e. their reconstitution is difficult.
- Viscosity does not increase on addition of dispersed phase.

Preparation - They require some special methods to prepare.
(i) Dispersion Methods

Principle → Breakdown of coarse material to colloidal size range is achieved by:

(a) Colloidal Mill - by shearing coarse materials between two rapidly rotating plates (set close together) of colloidal mill.

(b) Electromagnetic waves - depend on the passage of ultrasonic waves (at frequency more than 20,000 cycle/second) through dispersion medium so lead to breakdown of coarse particles dispersed in liquid.

(c) Electric arc - by production of an electric arc within a liquid. Due to heat generated by the arc, some of the metal of the electrodes is dispersed as vapour, which condenses to form colloidal particles.

(d) Milling and grinding processes can be used. But their efficiency is low.

(e) Peptization - it is the process in which aggregates break into colloidal size particle in the presence of peptizing agent, which may be liquid electrolytes and non-electrolytes.

(ii) Condensation Methods

Principle → Aggregation of subcolloidal size (molecular size) into particles within colloidal size.
- Involve rapid production of supersaturated solution of colloidal material.
- Under certain conditions, colloidal materials deposited as colloidal particles in the dispersion medium.
- So, supersaturated occur by solvent change.
  
  e.g. sulfur is dissolved in ethanol then by adding water give colloidal sulfur.

(b) **Chemical reactions**

↓

Reduction, oxidation, hydrolysis and double decomposition

- Colloidal silver iodide
  - Obtained by reaction between solution of silver nitrate ($\text{AgNO}_3$) and potassium iodide ($\text{KI}$).

  $\text{KI} + \text{AgNO}_3 \rightarrow \text{AgI} + \text{KNO}_3$

- Colloidal sulfur
  - Obtained from reaction between solution of sodium thiosulfate and HCl solution.

- Colloidal hydrated ferric oxide
  - Obtained from boiling ferric chloride with excess water

* (c) **Association Colloids** (e.g. Soaps & Synthetic detergents)

- Considered as *amphiphilic colloids*.

- Association colloids = Micelle formation

- When surfactant molecules present at low concentration in liquid medium, the amphiphiles exist separately.
Forming micelles.

- Micelle contain 50 or more monomers
- Diameter of each micelle = 50 Å (5nm)
- So they are within size range of colloids.

* Critical Micelle Concentration (CMC) *

The concentration at which micelles begin to form is called CMC.

Amphiphilic molecule

Below CMC →

At CMC →

Above CMC →

Micelle formation

Free energy of system is reduced.

In Non-polar liquid

In polar liquid
<table>
<thead>
<tr>
<th>S. No.</th>
<th>Properties</th>
<th>Lyophilic Colloids</th>
<th>Lyophobic Colloids</th>
<th>Association Colloids</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Dispersed phase</td>
<td>Mostly organic</td>
<td>Largely inorganic</td>
<td>Aggregation of</td>
</tr>
<tr>
<td></td>
<td></td>
<td>molecules</td>
<td>molecules</td>
<td>surface active agents</td>
</tr>
<tr>
<td>2.</td>
<td>Nature of Interaction</td>
<td>Stronger</td>
<td>Little</td>
<td>Aggregates are</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>solvated</td>
</tr>
<tr>
<td>3.</td>
<td>Presence of Charge</td>
<td>Less charged</td>
<td>Highly charged</td>
<td>Charged micelles,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>, Solvated</td>
<td></td>
<td>solvated</td>
</tr>
<tr>
<td>4.</td>
<td>Method of Preparation</td>
<td>Readily form</td>
<td>Special methods</td>
<td>Readily form when</td>
</tr>
<tr>
<td></td>
<td></td>
<td>salt</td>
<td>are required</td>
<td>CMC</td>
</tr>
<tr>
<td>5.</td>
<td>Viscosity of</td>
<td>Higher than that</td>
<td>Nearly same as</td>
<td>viscosity increases,</td>
</tr>
<tr>
<td></td>
<td>Dispersion</td>
<td>of medium alone</td>
<td>the dispersion</td>
<td>but not appreciably</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>medium.</td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>Reversibility</td>
<td>Reversible</td>
<td>Irreversible</td>
<td>Reversible</td>
</tr>
<tr>
<td>7.</td>
<td>Presence of</td>
<td>Stable</td>
<td>Stable</td>
<td>Stable</td>
</tr>
<tr>
<td></td>
<td>electrolytes -</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) At low Conc</td>
<td>Stable</td>
<td>Unstable</td>
<td>Precipitates</td>
<td></td>
</tr>
<tr>
<td>b) A high Conc</td>
<td>Coacervation*</td>
<td>Coagulation</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Coacervation - When two opposite charged hydrophilic colloids are mixed, then there will be separation of colloid rich layer, known as coacervate and the phenomenon is called coacervation.
Physical Pharmaceutics - II

Unit - II

Colloidal Dispersions

* Properties of Colloids -

(A) Optical Properties

1. Tyndall Effect
2. Ultramicroscopy
3. Electron-microscopy
4. Light Scattering

(B) Kinetic Properties

1. Brownian Movement
2. Diffusion
3. Osmotic Pressure
4. Viscosity
5. Sedimentation

(C) Electrical Properties

1. Electrophoresis
2. Electro-Osmosis
3. Donnan Membrane Effect
4. Electrical Double Layer Effect

(A) Optical Properties -

(i) Tyndall Effect -
- It was first observed by John Tyndall in 1869.
- When a beam of light is pass through a colloidal solution, the path of light gets illuminated and this illuminated path is called Tyndall Cone.
- The intensity of the scattered light is related to the difference between the refractive indices of the dispersed phase and the dispersion medium.

- True solutions do not show Tyndall effect because the solute molecules or ions are so small.

  \[ \downarrow \]

  \[ \therefore \text{ do not show scattering of light.} \]

Hence, a true solution and colloidal solution can be distinguished on the basis of Tyndall effect.

For example → a) Twinkling of stars
b) Blue colour of the sea and sky
c) Tails of comets
- Also known as Dark Field Microscopy
- When a cell containing colloidal dispersion is viewed through a ultramicroscope against dark background at slight angles to an intense beam of incident light

The particles will appear as the bright spots against the dark background, can be observed and counted.

Ultra-microscope is used in micro-electrophoresis technique for the measurement of particle charge.

(iii) Electron-Microscopy -
- Main feature, is its high resolving power.
- The electron microscope is useful to get pictures of actual particles.
- It helps in the study of size, shape and structure of colloidal particles.

(iv) Light Scattering -
- When a beam of light is passed through a colloidal dispersion, some light gets absorbed, scattered and remaining is transmitted.
- Absorbed light imparts colour to some colloids.
  - Gold chloride particles absorb deep red colour lights.
  - Silver particles absorb brown colour lights.
  - Silver iodide particles absorb yellow colour lights.
- Scattered light results in turbidity of the colloidal dispersion which can be calculated from intensity of scattered light.
The turbidity of colloidal dispersion can be determined by -

\[ I = I_0 e^{-2l} \]

where,
\[ I = \text{Intensity of transmitted light} \]
\[ I_0 = \text{Intensity of the incident beam} \]
\[ l = \text{Length of the sample tube} \]
\[ T = \text{Turbidity} \]

- Turbidity is also used to determine the molecular weight of the colloid by using the following equation:

\[ \frac{Hc}{T} = \frac{1}{M} + 2BC \]

where,
\[ H = \text{Optical constant for a particular system} \]
\[ C = \text{Concentration of solute in g/cm}^3 \text{ of solution} \]
\[ T = \text{Turbidity} \]
\[ M = \text{Molecular weight} \]
\[ B = \text{Interaction constant} \]

- Measuring the scattering light:
  - helps in estimation of the particle size, shape and interaction of dissolved macromolecules.
  - is useful in determining the size of association colloids and the no. of surfactants molecules forming them.
  - also studies the nature of proteins, natural and synthetic polymers.

\* Instruments used for the measurement of turbidity are -
- Spectrophotometer
- Nephelometer
(i) Brownian Movement
- It was first observed by Robert Brown in 1827 with pollen grains suspended in water.
- There are continuous collisions between the colloidal particles and the molecules of dispersion medium which are in constant motion and transfer kinetic energy to colloidal particles by striking it from all sides.

This results into zig-zag movement of colloidal particles.

It is known as Brownian movement.

- In Brownian Movement, particles move from region of higher concentration to lower concentration.
- The velocity of particles increases with being particle size and viscosity.
- To increase the viscosity of dispersion medium (by adding glycerine), they then stop Brownian motion.

*Significance*
- It helps in imparting stability to the colloidal solution by enabling them to remain dispersed in the medium and not allowing them to settle down.
It is a natural and spontaneous process of the transport of ionic, atomic, or molecular species, across the concentration gradient.

Brownian Motion results in the diffusion of colloidal particles. However, the rate of diffusion becomes slower due to large size of particles and their slow movement.

Diffusion can be described with the help of Fick’s 1st Law -

Fick’s 1st Law -

It states that, “the particles diffuse from a region of higher concentration to lower concentration until the concentration of the system is uniform throughout.

Molecular weight of spherical molecules of polymer, can be calculated by the following equation -

\[ D = \frac{RT}{6\pi\eta N} \sqrt{\frac{4\pi N}{3\nu^2}} \]

where,

- \( M \) = Molecular Weight
- \( \nu \) = Partial Specific Volume
- \( R \) = Molar Gas Constant
- \( N \) = Avogadro No.
- \( \nu \) = radius of spherical particle
- \( T \) = Absolute Temperature
- \( \eta \) = Viscosity
The osmotic pressure, \( \pi \), of a dilute colloidal solution is described by the Van't Hoff equation:

\[
\pi = \frac{C_g RT}{M}
\]

Where,

- \( \pi \) = Osmotic Pressure
- \( C_g \) = grams of solute per liter of solution
- \( M \) = Molecular Weight
- \( T \) = Absolute Temperature
- \( R \) = Molar gas constant.

This equation is used to calculate the molecular weight of a colloid in a dilute solution.

(IV) Viscosity

Viscosity is the resistance to fluid to flow under an applied stress. Einstein derived an equation of flow to dilute colloidal dispersions of spherical particles.

\[
\eta = \eta_0 (1 + 2.5\phi)
\]

where,

- \( \eta_0 \) = Viscosity of the dispersion medium.
- \( \eta \) = Viscosity of the dispersion when the volume fraction of colloidal particles present is \( \phi \).

According to the Mark-Houwink equation, intrinsic viscosity \( [\eta] \) is used to calculate the molecular weight of polymers:

\[
[\eta] = K M^a
\]

where,

- \( [\eta] \) = Intrinsic Viscosity
- \( M \) = Molecular Weight of Polymer
- \( K \) and \( a \) = Constants of particular polymer-solvent system.
as follows:

- Shape of the dispersed particles
- Affinity of particles to the medium
- Type of colloids
- Molecular weight of the particle

(V) Sedimentation - (Brownian motion tends to disturb sedimentation)

The rate of sedimentation is given by Stokes' law:

\[ v = \frac{2\pi r^2 (\rho - \rho_0) g}{9\eta_0} \]

where:
- \( g \) = acceleration due to gravity
- \( v \) = velocity
- \( \rho \) = density of spherical particle
- \( \rho_0 \) = density of medium
- \( \eta_0 \) = viscosity.

When the particles settle on the basis of their molecular weight, the following equation is used to determine the mol. wt.

\[ M = \frac{RT_s}{D(1 - \gamma'\rho_0)} \]

where:
- \( T_s \) = Absolute temperature
- \( R \) = Molar gas constant
- \( D \) = Diffusion coefficient
- \( \rho_0 \) = Density of medium
- \( \gamma' \) = Partial specific volume

* Ultra-centrifuge is used for studying sedimentation.
Properties of colloidal particles to carry charges on their surface either by ionisation or by adsorption.

(d) Electrophoresis:
- The movement of colloidal particles under the influence of electric field is called Electrophoresis.
- When an electric field is applied across the colloidal solution, the colloidal particles migrate to oppositely charged electrode where they get neutralised. This phenomenon is known as electrophoresis.
- The rate of migration of particles is observed by Ultramicroscope.
- The rate of movement of single colloidal particle is directly related to zeta potential.
- The sign and magnitude of the zeta potential in a colloidal system is expressed by the following equation:

\[ \zeta = \frac{v \eta}{E} \times (9 \times 10^{-4}) \]

where, 
- \( \zeta \) = Zeta potential
- \( v \) = Velocity of migration in electrophoresis tube of definite length in cm.
- \( \eta \) = Viscosity of the medium
- \( E \) = Dielectric constant of medium
- \( E \) = Potential gradient (Vols/cm).

* The migration rate is a function of the charge on a particle and related to zeta potential.
When electrophoresis of dispersed particle in a colloidal system is prevented by some suitable means, it is observed that dispersion medium itself begins to move in an electric field.

This phenomenon is known as *electro-osmosis*.

(iii) **Donnan Membrane Effect**

Diffusion of small ions through semi-permeable membrane will be affected by presence of charged macromolecule that can't penetrate the membrane due to its size. and therefore, create uneven electrical charge. This is known as **Donnan Effect**.

**Principle of Donnan Membrane Equilibrium**

Let us suppose, on one side of a semi-permeable membrane, NaCl is placed in solution and on other side of membrane a *negatively* charged colloid together with its counterions R^- Na^+ is placed. The system is in equilibrium and the volumes of solution on the two sides of membrane are considered to be equal.

At equilibrium:

- Outside (o)  
  - Na^+  
  - Cl^−

- Inside (i)  
  - R^-  
  - Na^+  
  - Cl^−

For applying the condition of electro-neutrality, the +ve and −ve charges on either side of membrane should be balanced.

According to this, the equation can be written as —
According to the principle of escaping tendency of the electrolytes, the concentrations of electrolytes on both the sides of the membrane must be same. Then,

\[ [\text{Na}^+]_0 [\text{Cl}^-]_0 = [\text{Na}^+]_i [\text{Cl}^-]_i \quad (iii) \]

Substituting eqn (i) & (ii) in eqn (iii) we get,

\[ [\text{Cl}^-]_0 \times [\text{Cl}^-]_0 = ([\text{R}^-]_0 + [\text{Cl}^-]_0) + [\text{Cl}^-]_0 \]

\[ [\text{Cl}^-]_0^2 = [\text{Cl}^-]_0^2 + ([\text{R}^-]_0 + [\text{Cl}^-]_0) \]

\[ [\text{Cl}^-]_i^2 = [\text{Cl}^-]_i^2 (1 + [\text{R}^-]_0 / [\text{Cl}^-]_0) \]

\[ \frac{[\text{Cl}^-]_0^2}{[\text{Cl}^-]_i^2} = 1 + \frac{[\text{R}^-]_0}{[\text{Cl}^-]_0} \quad (iv) \]

**Applications:**

1. Facilitate adsorption of ionizable drugs from GIT by using same charge macromolecules that penetrate into semipermeable membrane, so, mutual ionic repulsion occurs.

   \[ \downarrow \]

   Retardation of drug absorption occurs, if the drug complexes with the macromolecule.

2. The above eqn (iv), is useful in calculating the ratio of cation of diffusible anion outside & inside the membrane, at equilibrium.
- In this theory, charge is imparted to the particles by placing ions which are adsorbed preferentially at immovable points → first layer.
- Second layer consists of diffused mobile ions.
- The charge present on both the layers is equal.
- This two layer arrangement leads to development of potential called zeta potential or electro-kinetic potential.
- As a result of this potential developed across the particles, under the influence of electric field these particles move.

* There are several theories to describe it -

a) Helmholtz Double Layer Theory -

It states that the surface charge is neutralized by opposite sign counterions placed at distance of \( d \) away from the surface.
b) Gouy - Chapman Double Layer Theory -

Developed diffuse double layer.

- According to this the change in concentration of the counter ions near a charged surface follows the Boltzmann distribution.

C) Stern Modification of the Diffuse double layer -

- This theory states that ions do have finite size so, cannot approach the surface closer than a few nm.
- Stern supposed that it is possible that some of the ions are specifically adsorbed by the layer which is called Stern layer.
Effect of electrolytes:

(1) On lyophobic colloids-

Lyophobic colloids are unstable. DLVO Theory is used to describe the stability of dispersion. The name DLVO Theory is given on the name of 4 scientists - Derjaguin, Landau, Verwey, and Overbeek.

- According to this theory, distance between two colloidal particles affects the behaviour of particle. This theory is also used to measure the amount of electrolyte used to precipitate or stabilize a colloid.

- Suppose we have two magnets or particles.
  a) When attraction between two magnets or particles predominate, then the particles will form aggregate.

  b) When repulsion between two magnets or particles predominate, then the particles will remain individually dispersed.

- Let us explain this theory with the help of diagram of potential energy vs interparticle distance.
Potential Energy vs Interparticle Distance

(i) Primary minimum: If the particles are very close to each other then the orbitals on surface overlaps and form strong bond. This causes rapid increase in potential energy.

Effect of electrolyte: In the absence or removal of electrolytes - the interparticle repulsion decreased to such extent that coagulation occurs. The particles deposit at the bottom as hard cake. This behaviour is correspond to primary minimum in DLVO theory.

Lyophobic Colloid

Dialysis

Coagulation, settle at bottom, unstable

(Primary Minimum)

Electrolytes
When distance between the particles are large, particles experience attractive force and aggregates are formed.

* Effect of electrolyte: On addition of excess of electrolyte—floccule formation occur, this behaviour is corresponding to secondary minimum in DLVO theory.

\[ \text{Lysophobic colloids} + \text{Excess of electrolytes} \rightarrow \text{Flocculation, unstable accumulation of electrolytes (Secondary minimum)} \]

(iii) The accumulation of opposite charged ions to lysophobic colloids reduces the zeta potential below its critical value.

The critical potential for finely dispersed oil droplets in water is about 40 millivolts, this high value signifying relatively great instability.

According to Schulze–Hardy rule—

"The precipitating power increases rapidly with the valence or charge of the ions."
Lyophilic colloids are thermodynamically stable, but particles undergo aggregation, coagulation or precipitation. This is due to following reasons:

(i) Addition of excess electrolytes-
When electrolytes are added in higher concentration, hydration of particles is observed. There is no more water for hydration of particle.
As a result, flocculation or salting out of colloidal particles occur.

(ii) Addition of oppositely charged colloids-
The addition of non solvent like alcohol to hydrophilic colloids cause dehydration of particles. When small amount of electrolytes are added it cause flocculation.

\[ \text{Hydrophilic Colloid} \quad \text{Excess Electrolytes} \quad \text{Dehydrated Unstable} \quad \text{Hydrated Ions} \]

\[ \text{Lyophilic Colloid} \quad \text{Stable} \quad \text{Lyophilic Colloid} (\text{W}) \quad \text{Lyophilic Colloid} (\text{W}) \]

\[ \text{Solvant Sheath} \quad \text{Solvant Sheath} \quad \text{Solvant Sheath} \quad \text{Solvant Sheath} \quad \text{Solvant Sheath} \]

\[ \text{Lyophilic colloid (solv) stable} \quad \text{Lyophilic colloid (nsolv) unstable} \quad \text{Colloid Sick} \]

\[ \text{Gelatin (less pH 4.7)} \quad \text{Gelatin} \quad \text{Acacia} \]

\[ \text{Mixture of acacia with gelatin} \rightarrow \text{formation of coacervates} \rightarrow \text{Supersaturated} \quad \text{(solvant)} \]

\[ \text{Colloidal Dick} \quad \text{Coagulation} \quad \text{(Unstable)} \]
Coacervation

When two oppositely charged hydrophilic colloids are mixed, then there will be separation of the colloid-rich layer. The colloid-rich layer is known as coacervate.

This phenomenon is called coacervation.

For example:

- Gelatin and Acacia
- Gelatin at a pH below 4.7 (its isoelectric point) is positively charged while Acacia carries a negative charge. When solutions of these colloids are mixed in a certain proportion, coacervation results.

Peptization

The process of converting a freshly prepared precipitate into colloidal form by the addition of suitable electrolyte is called peptization.

- Cause of peptization is the adsorption of the ions of the electrolyte by the particles of the precipitate.
- The electrolyte used for this purpose is called peptizing agent or stabilizing agent, e.g., sugar, gum, gelatin & electrolytes.

\[
\text{Fe(OH)}_3 + \text{Fe}^{2+} \rightarrow \text{colloidal particles of Fe(OH)}_3
\]

Preparation of colloidal sol by peptization
When large amount of hydrophilic colloids carrying negative charge is combined with positive charged hydrophobic colloids, then they form protective sheath around them. This protective layer prevent particles from precipitation on addition of electrolytes. This phenomenon is called protection. The colloids that are used to stabilize other colloids are called protective colloid.

Hydrophilic colloid

Hydrophobic colloid

Large quantity of hydrophilic colloid

Protective action

Protective colloid

* The protective ability of colloids is measured as Gold number.

It is defined as no. of mg of protective colloid required in 10 ml of red gold sol to prevent the change in colour from red to violet on addition of 1 ml of 10% solution of sodium chloride.

* If the gold no. is less then the protective action will be more.
Gold Numbers of few colloids -

<table>
<thead>
<tr>
<th>Sol</th>
<th>Gold Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin</td>
<td>0.15 - 0.25</td>
</tr>
<tr>
<td>Acacia</td>
<td>0.1 - 0.2</td>
</tr>
<tr>
<td>Tragacanth</td>
<td>2</td>
</tr>
<tr>
<td>Gelatin</td>
<td>0.005 - 0.001</td>
</tr>
<tr>
<td>Potato starch</td>
<td>25</td>
</tr>
<tr>
<td>Haemoglobin</td>
<td>0.03</td>
</tr>
<tr>
<td>Dextrin</td>
<td>6 - 20</td>
</tr>
</tbody>
</table>

Methods for determining gold number:

1. Involves following steps:
   i) A series of test tubes are taken, each containing 10 ml of gold sol.
   ii) A protective colloid in order of rising concn is added to each test tube.
   iii) Now, 1 ml of 10% NaCl soln is added to each test tube.
   iv) The test tubes are left undisturbed and allowed to stand for a certain period of time.
   v) The colour of the gold sol changes from red to violet at lower concn of protective colloid, while at higher concn the colour does not show any change.

Thus, the gold no. of a protective colloid is the minimum quantity of colloid contained in a test tube which prevents the change in colour of the gold sol.
The following techniques are generally used for purification of colloids:

i) Dialysis

ii) Electrodialysis

iii) Ultrafiltration

Dialysis

- The process of separating the particles of colloid from those of crystallloid, by means of diffusion through a suitable membrane.

- Principle: Colloidal particles cannot pass through a cellophane membrane while the ions of the electrolyte can pass through it.

- The impurities slowly diffuse out of the bag leaving behind a pure colloidal solution.

- The distilled water is changed frequently to avoid accumulation of the crystallloids otherwise they may start diffusing back into the bag.

Dialysis can be used for removing HCl from the ferric hydroxide sol.
Ultra filtration is a process of high pressure filtration through a semi-permeable membrane in which colloidal particles are retained while the small sized solutes and the solvent are forced to move across the membrane by hydrostatic pressure forces.

Ultra filtration is a vital process that takes place in the kidneys.

**Electrodialysis**

The process of dialysis is very slow, process is speeded up by application of electrical potential. This is called electrodialysis. By the application of electric potential, impurities present in the form of slow molecular weight electrolytes can be removed from the solution.
* Applications of Colloids in Pharmacy *

1. Therapy:
   Colloidal systems are used as therapeutic agents in different areas.
   - Silver Colloid - Germicidal
   - Copper Colloid - Anti-Cancer
   - Mercury Colloid - Anti-syphilis

2. Absorption & Toxicity:
   As colloidal dimensions are small enough, they have a huge surface area. Hence, the drug constituted colloidal form is released into the vicinity in large amount (surrounding area)
3. Solubility -

By the use of colloidal systems containing surfactants, the solubility of drugs can be improved up to a marked level.

For e.g. Solubilisation of phenobarbitol and sulphonamides are made in micellar solution i.e. association colloid.

4. Stability -

Charges play an important role in determining the stability of a colloidal system.

If lymphotic colloids having like charges on particle surface repel each other and prevent flocculation in suspension.

E.g. Colloidal dispersion of gelatin is used in coating over tablets and granules which upon drying leaves a uniform dry-film over them and protect them from adverse conditions of the atmosphere.

5. Targeted Drug Delivery -

The colloids in the development of drug delivery systems are used in targeting the drugs to a particular organ of the body.
Drug delivery systems forming colloidal delivery systems like liposomes, nanoparticles, and microemulsions are used to target the specific site of tissue organs of the body.

* Drug entrapment by liposomes is specifically taken up only by the spleen and liver.

**Some other applications of colloids -**

1. Food stuffs and medicines
2. Purification of water
3. Sewage disposal
4. Smoke precipitation
5. Artificial rain
6. Rubber industry
7. Leather tanning
8. Cleaning action of soaps
9. Smoke screen
10. Metallurgical operations
11. Preparation of nano-materials
12. Blue colour of sky
13. Formation of delta
14. Building roads