



# **Physical pharmacy II**

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# Colloidal dispersions

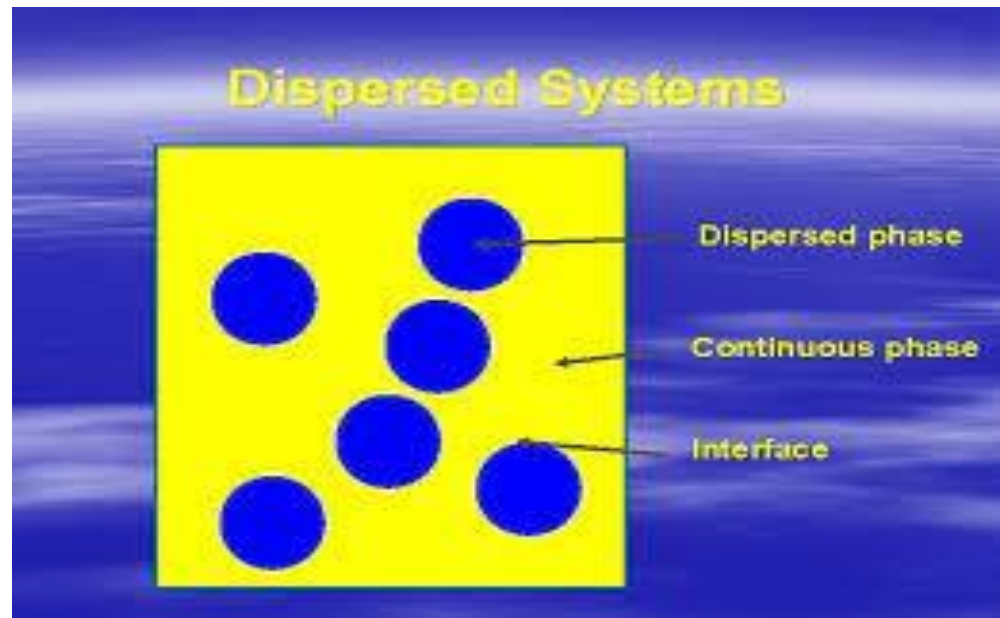
## objectives

- 1-Differentiate between different types of colloidal systems and their main characteristics.
- 2- Understand the main optical properties of colloids and applications of these properties for the analysis of colloids.
- 3- Know the main types of microscopic systems used for analysis of colloids.
- 4- Appreciate the major kinetic properties of colloids.
- 5- Understand the main electrical properties of colloids and their application for the stability, sensitization, and protective action of colloids.
- 6- Recognize the benefits of solubilization by colloids.
- 7- Understand the benefits and know the main types of modern colloidal drug delivery systems

# Dispersed Systems

Dispersed systems consist of particulate matter, known as the **dispersed phase**, distributed throughout a continuous or **dispersion medium**. The dispersed material may range in size from particles of atomic and molecular dimensions to particles whose size is measured in millimeters. Accordingly, a convenient means of classifying dispersed systems is on the basis of the mean particle diameter of the dispersed material. Based on the size of the dispersed phase, three types of dispersed systems are generally considered:

- (a) molecular dispersions,
- (b) colloidal dispersions , and
- (c) coarse dispersions.

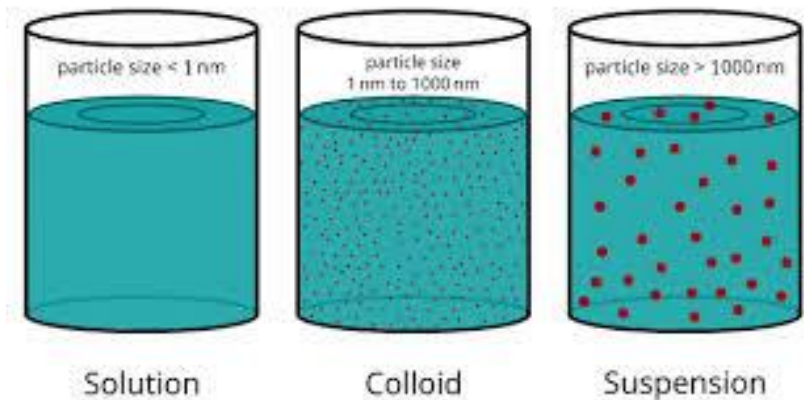


# Classification of dispersed systems based on particle size

- Dispersed systems consist of particulate matter (dispersed phase), distributed throughout a continuous phase (dispersion medium).
- They are classified according to the particle diameter of the dispersed material:

## 1-Molecular dispersion (Less than 1 nm)

- Particles invisible in electron microscope
- Pass through semipermeable membranes and ultrafilter paper
- Particles do not settle down on standing
- Undergo rapid diffusion
- E.g. ordinary ions, glucose , Oxygen molecule



## 2- Colloidal dispersions (1 nm - 0.5 $\mu\text{m}$ )

- Particles not determined by ordinary microscope, can be detected by electron microscope.
- Pass through filter paper but not pass through semipermeable membrane.
- Particles made to settle by centrifugation
- Diffuse very slowly
- E.g. colloidal silver sols, butter, paint, jelly, cheese, natural and synthetic polymers

## 3- Coarse dispersions ( $> 0.5 \mu\text{m}$ )

- Particles are visible under ordinary microscope
- Do not pass through filter paper or semipermeable membrane(dialysis).
- Particles settle down under gravity
- Do not diffuse
- E.g. emulsions, suspensions, red blood cells

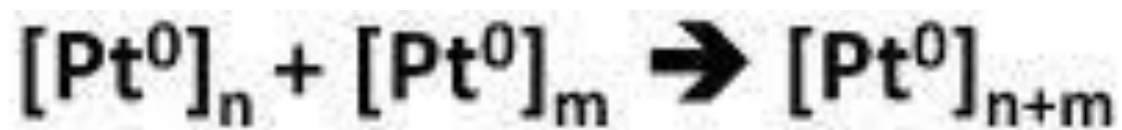
## Size and shape of colloids:

Particles lying in the colloidal size have large surface area when compared with the surface area of an equal volume of larger particles.

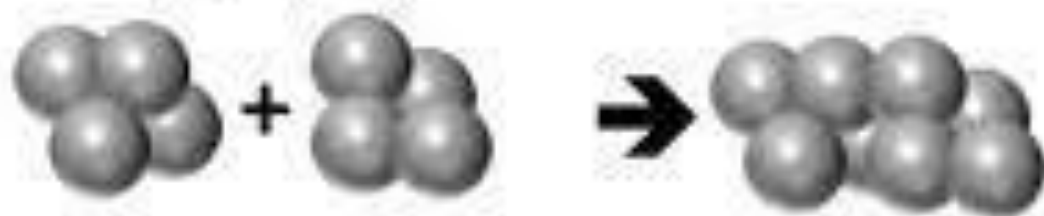
**Specific surface:** the surface area per unit weight or volume of material. The possession of large specific surface results in:

- 1- platinum is effective as catalyst only when found in colloidal form due to large surface area which adsorb reactant on their surface.
- 2- The colour of colloidal dispersion is related to the size of the particles e.g. red gold sol takes a blue colour when the particles increase in size

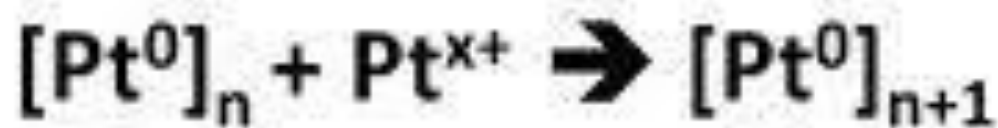
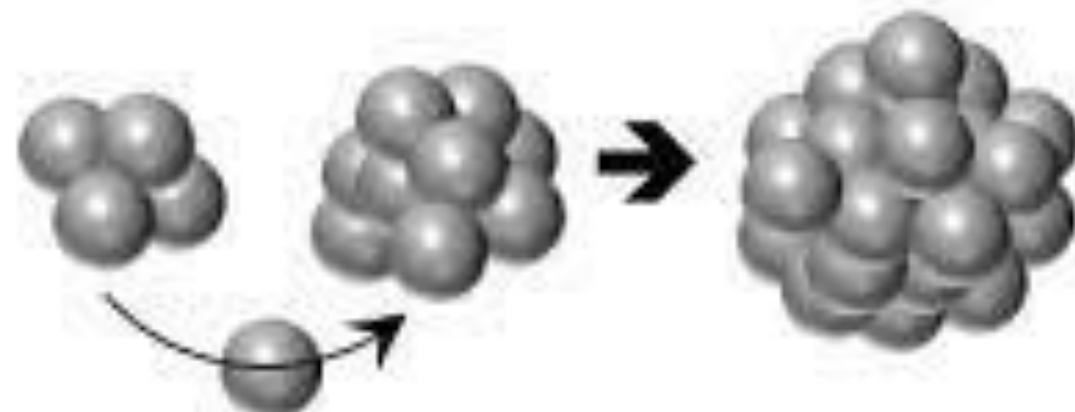
The **shape of colloidal particles** in dispersion is important: The more extended the particle the greater its specific surface the greater the attractive force between the particles of the dispersed phase and the dispersion medium. Flow, sedimentation and osmotic pressure of the colloidal system affected by the shape of colloidal particles. Particle shape may also influence the pharmacologic action.



a)



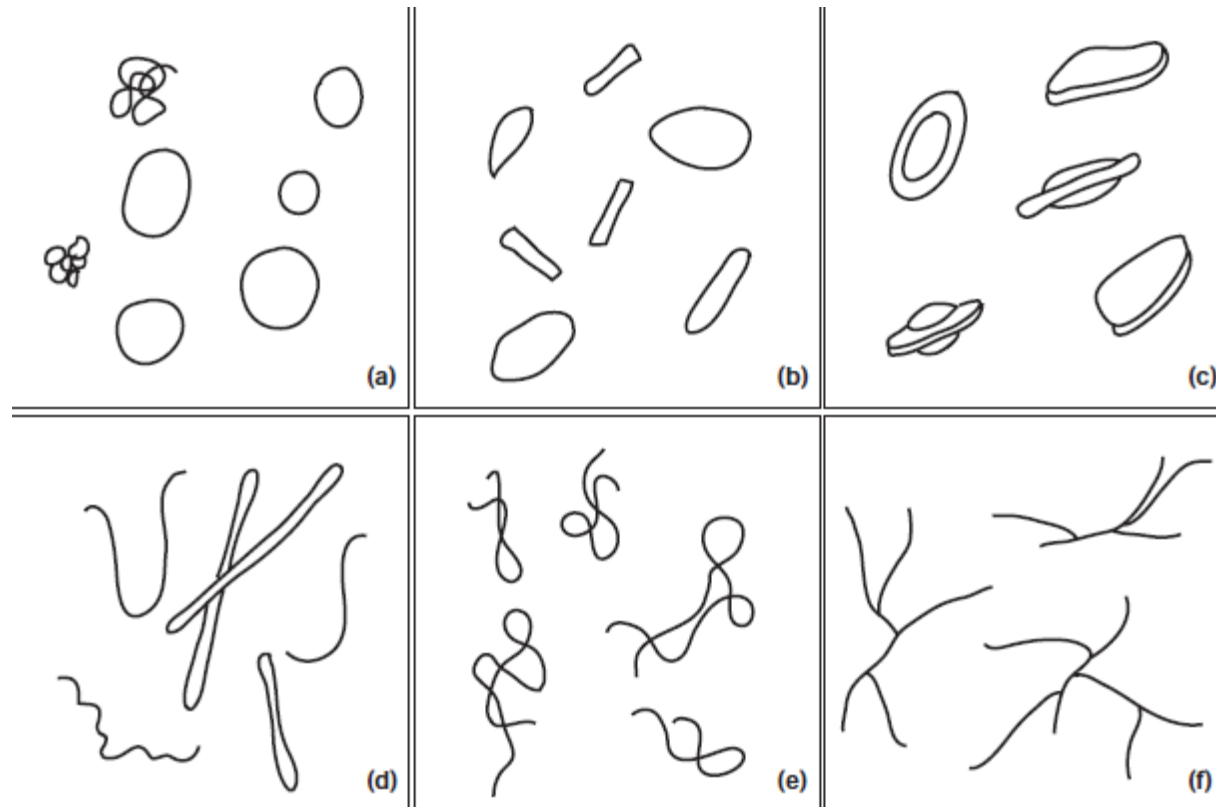
b)



c)







Some shapes that can be assumed by colloidal particles: (a) spheres and globules, (b) short rods and prolate ellipsoids, (c) oblate ellipsoids and flakes, (d) long rods and threads, (e) loosely coiled threads, and (f) branched threads.

# Types of colloidal systems

Colloidal systems are best classified into three groups lyophilic, lyophobic, and association on the basis of the interaction of the particles, molecules, or ions of the dispersed phase with the molecules of the dispersion medium (Association / amphiphilic colloids).

1-The nature of interaction between dispersed phase and dispersion medium.

**A-Lyophilic colloids** (solvent attracting) (solvent loving)

The particles in a lyophilic system have a great affinity for the solvent.

- If water is the dispersing medium, it is often known as a hydrosol or hydrophilic.
- readily solvated (combined chemically or physically, with the solvent) and dispersed, even at high concentrations.
- More viscid

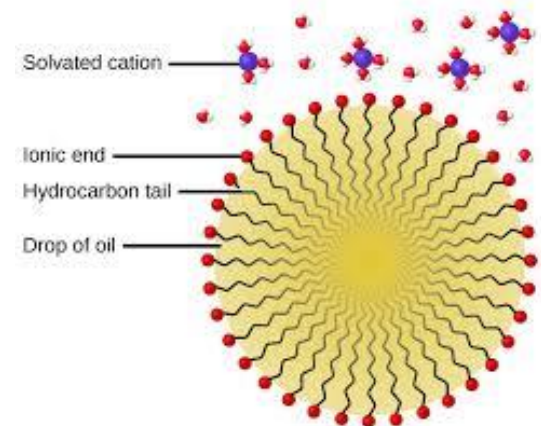
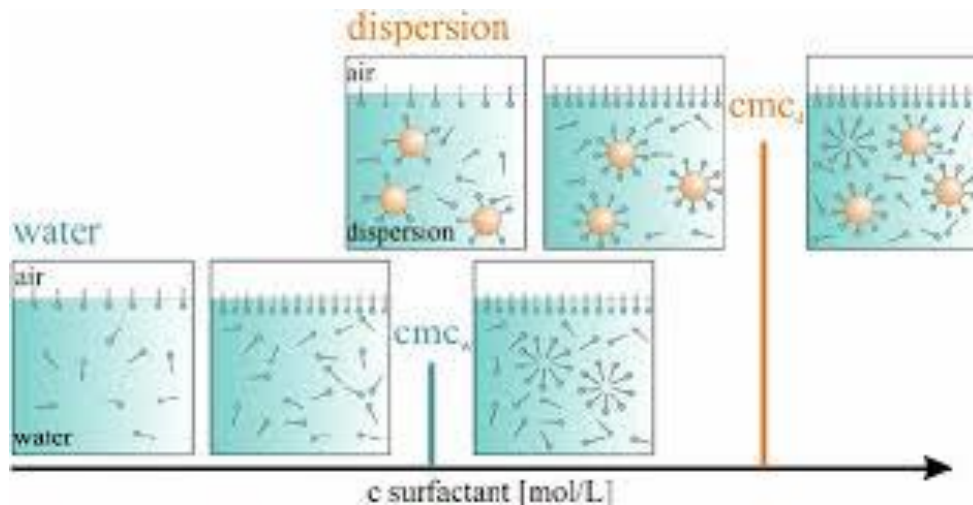
- Examples of lyophilic sols include sols of gum, gelatin, starch, proteins and certain polymers (rubber) in organic solvents.
- the dispersed phase does not precipitate easily
- the sols are **quite stable** as the solute particle surrounded by two stability factors:
  - a- negative or positive charge
  - b- layer of solvent
- If the dispersion medium is separated from the dispersed phase, the sol can be reconstituted by simply **remixing** with the dispersion medium. Hence, these sols are called **reversible sols**.
- Prepared simply by dissolving the material in the solvent being used e.g. dissolution of acacia in water

**B-lyophobic** (solvent repelling) (solvent hating) - The particles resist solvation and dispersion in the solvent.

- The concentration of particles is usually relatively low.
- Less viscid
- Less stable as the particles surrounded only with a layer of positive or negative charge
- Once precipitated, it is **not easy to reconstitute** the sol by simple mixing with the dispersion medium. Hence, these sols are called **irreversible sols**.
- Examples of lyophobic sols include sols of metals and their insoluble compounds like sulphides and oxides. e.g. gold in water charge

## C-Association / amphiphilic colloids

- Certain molecules termed amphiphiles or surface active agents, characterized by two regions of opposing solution affinities within the same molecule .
- At low concentration: amphiphiles exist separately (subcolloidal size)
- At high concentration: form aggregates or micelles (50 or more monomers) (colloidal size)



## 2-The original states of their constituent parts

### TYPES OF COLLOIDAL DISPERSIONS\*

Dispersion Medium	Dispersed Phase	Colloid Type	Examples
Solid	Solid	Solid sol	Pearls, opals
Solid	Liquid	Solid emulsion	Cheese, butter
Solid	Gas	Solid foam	Pumice, marshmallow
Liquid	Solid	Sol, gel	Jelly, paint
Liquid	Liquid	Emulsion	Milk, mayonnaise
Liquid	Gas	Foam	Whipped cream, shaving cream
Gas	Solid	Solid aerosols	Smoke, dust
Gas	Liquid	Liquid aerosols	Clouds, mist, fog

\* A gas in a gas always produces a solution.

# Kinetic Properties of Colloids

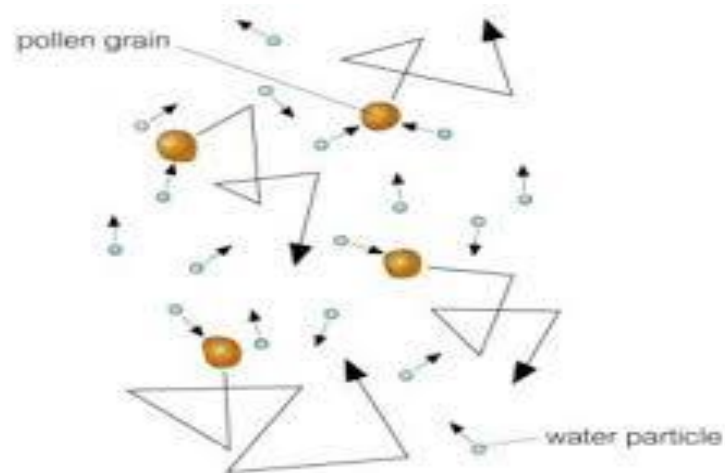
## 1-Brownian motion

- The zig-zag movement of colloidal particles continuously and randomly .
- This brownian motion arises due to the uneven distribution of the collisions between colloid particle and the solvent molecules.
- Brownian movement was more rapid for smaller particles.
- It decrease with increase the viscosity of the medium.

✓ **Temperature**

✓ **Viscosity**

✓ **Particle size**



## 2- Diffusion

- Particles diffuse spontaneously from a region of higher conc. to one of lower conc. until the conc. of the system is uniform throughout.
- Diffusion is a direct result of Brownian motion.
- Fick's first law used to describe the diffusion: (The amount of  $Dq$  of substance diffusing (**diffusion quantity**) in time  $dt$  across a plane of area  $A$  is directly proportional to the change of concentration  $dc$  with distance traveled' Fick's law is written as

$$dq = -DS \frac{dc}{dx} dt$$

$D$  is the ***diffusion coefficient (not constant)***, the amount of material diffusing per unit time across a unit area when  $dc/dx$ , called the ***concentration gradient***, is unity.  $D$  thus has the dimensions of area per unit time. The coefficient can be obtained in colloidal chemistry by diffusion experiments in which the material is allowed to pass through a porous disk, and samples are removed and analyzed periodically.



$$dq = -DS \frac{dc}{dx} dt$$

- $dq$  = change in amount of substance,  $dt$  = change in time,  $D$  = diffusion coefficient,  $S$  = area of a defined plane,  $dc/dx$  is the concentration gradient
- The law basically states that the amount of substance diffusing in time across a plane of area  $S$  is directly proportional to the change in concentration with distance traveled.

### 3-Osmotic Pressure

The osmotic pressure,  $\pi$ , of a dilute colloidal solution is described by the van't Hoff equation:

$$\pi = cRT$$

where  $c$  is molar concentration of solute. This equation can be used to calculate the molecular weight of a colloid in a dilute solution.

Replacing  $c$  with  $c g/M$  in equation in which  $c g$  is the grams of solute per liter of solution and  $M$  is the molecular weight, we obtain

$$\pi = \frac{c_g}{M} RT$$

$\pi$  = osmotic pressure

R = molar gas constant

## 4- Sedimentation

- The velocity of sedimentation is given by Stokes' Law:

$$v = d^2 (\rho_i - \rho_e)g / 18\eta$$

V = rate of sedimentation

d = diameter of particles(radius)

$\rho$  = density of internal phase and external phase

g = gravitational constant

$\eta$  = viscosity of medium

Sedimentation occur due to gravity .ex centrifuge .Factor effect on sed.

- ✓ Particle size
- ✓ Radius
- ✓ Density
- ✓ Gravity
- ✓ Viscosity (adding thicken agent)

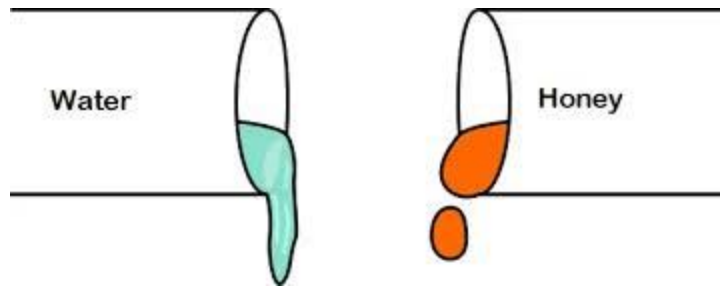
## 5- Viscosity:

It is the resistance to flow of system under an applied stress. The more viscous a liquid, the greater the applied force required to make it flow at a particular rate.

The viscosity of colloidal dispersion is affected by the **shape of particles** of the disperse phase:

- ❑ Spherocolloids dispersions of low viscosity
- ❑ Linear particles more viscous dispersions

**Molecular weight** also effect on viscosity e.g poly ethylene glycol



# Electric Properties Of Colloids

Particles dispersed in liquid media may become charged mainly in one of two ways :

**The first** involve selective adsorption of a particular ionic species present in solution. This may be an ion added to the solution or, in the case of pure water, it may be the hydronium or hydroxyl ion. The majority of particles dispersed in water acquire a negative charge due to preferential adsorption of the hydroxyl ion.

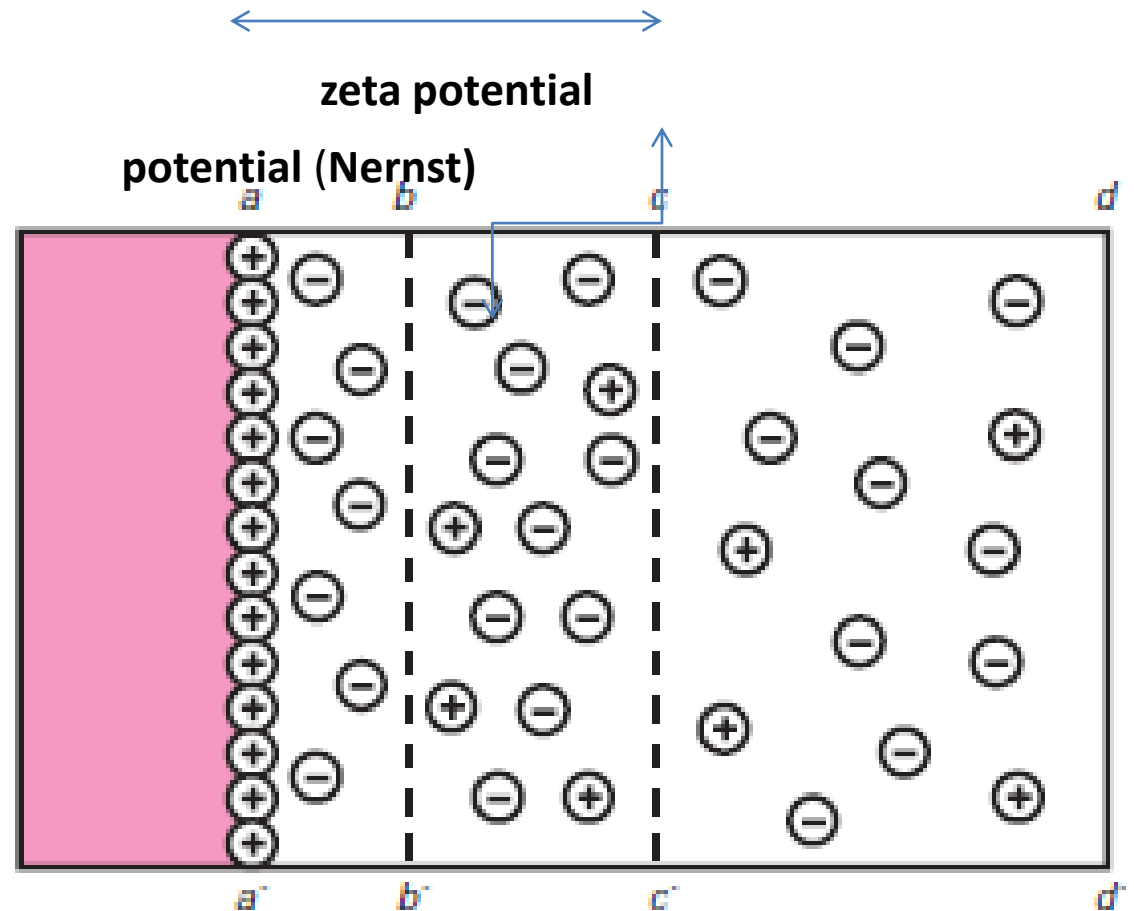
**A Second** : charges on particles arises from ionization of groups (such as COOH) that may be situated at the surface of the particles.

A **third**, less common origin for the charge on a particle surface is thought to arise when there is a difference in dielectric constant between the particle and its dispersion medium.

# The Electric Double Layer

- Consider a **solid surface in contact with a polar solution** containing ions, for example, an aqueous solution of an electrolyte. Furthermore, let us suppose that some of the cations are adsorbed onto the surface, giving it a positive charge.
- Remaining in solution are the rest of the cations plus the total number of anions added. These anions are attracted to the positively charged surface by electric forces.
- In addition to these electric forces, thermal motion tends to produce an equal distribution of all the ions in solution.
- An equilibrium situation is set up in which some of the excess anions approach the surface, whereas the remainder are distributed in decreasing amounts as one proceeds away from the charged surface.
- At a particular distance from the surface, the concentrations of anions and cations are equal, that is, conditions of electric neutrality prevail

aa' is the surface of the solid. The adsorbed ions that give the surface its positive charge are referred to as the potential-determining ions. Immediately adjacent to this surface layer is a region of **tightly bound** solvent molecules, together with some negative ions, also tightly bound to the surface. The limit of this region is given by the line bb'



The electric double layer at the surface of separation between two phases, showing distribution of ions. The system as a whole is electrically neutral

These ions, having a charge opposite to that of the potential-determining ions, are known as **counterions or gegenions**.

The degree of attraction of the solvent molecules and counterions is such that if the surface is moved relative to the liquid, the shear plane is  $bb'$  rather than  $aa'$ .

In the region bounded by the lines  $bb'$  and  $cc'$ , there is an excess of negative ions. The potential at  $bb'$  is still positive because, as previously mentioned, there are fewer anions in the tightly bound layer than cations adsorbed onto the surface of the solid. Beyond  $cc'$ , the distribution of ions is uniform and electric neutrality is obtained.

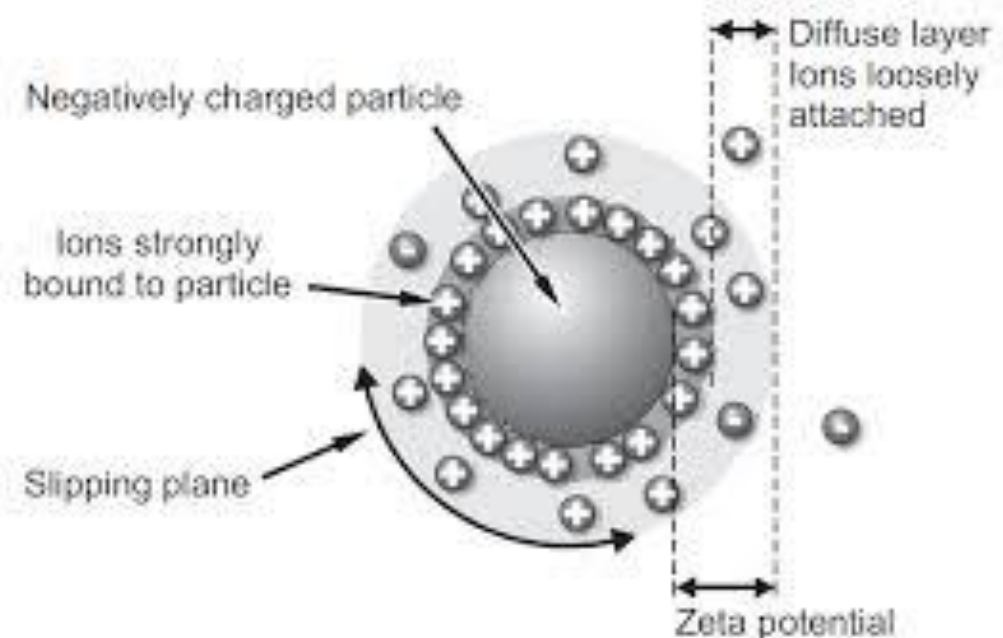
Thus, the electric distribution at the interface is equivalent to a double layer of charge, the first layer (extending from  $aa'$  to  $bb'$ ) **tightly bound** and a second layer (from  $bb'$  to  $cc'$ ) that is more **diffuse**. The so called **diffuse double** layer therefore extends from  $aa'$  to  $cc'$ .



# Nernst and Zeta Potentials

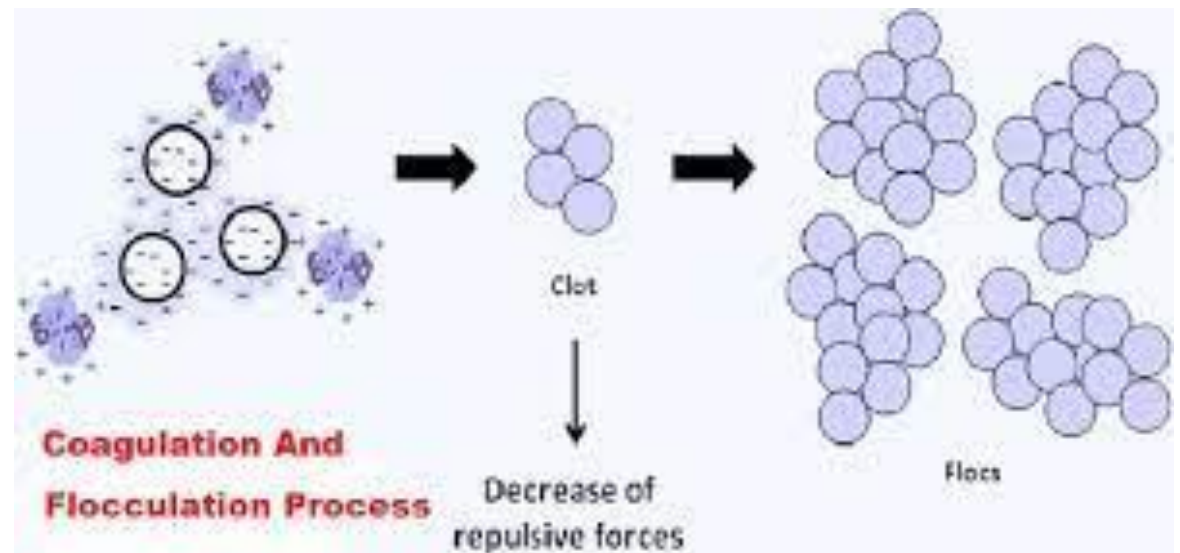
The potential at the solid surface aa' due to the potential-determining ion is the electrothermodynamic (**Nernst**) potential,  $E$ , and is defined as **the difference in potential between the actual surface and the electroneutral region of the solution.**

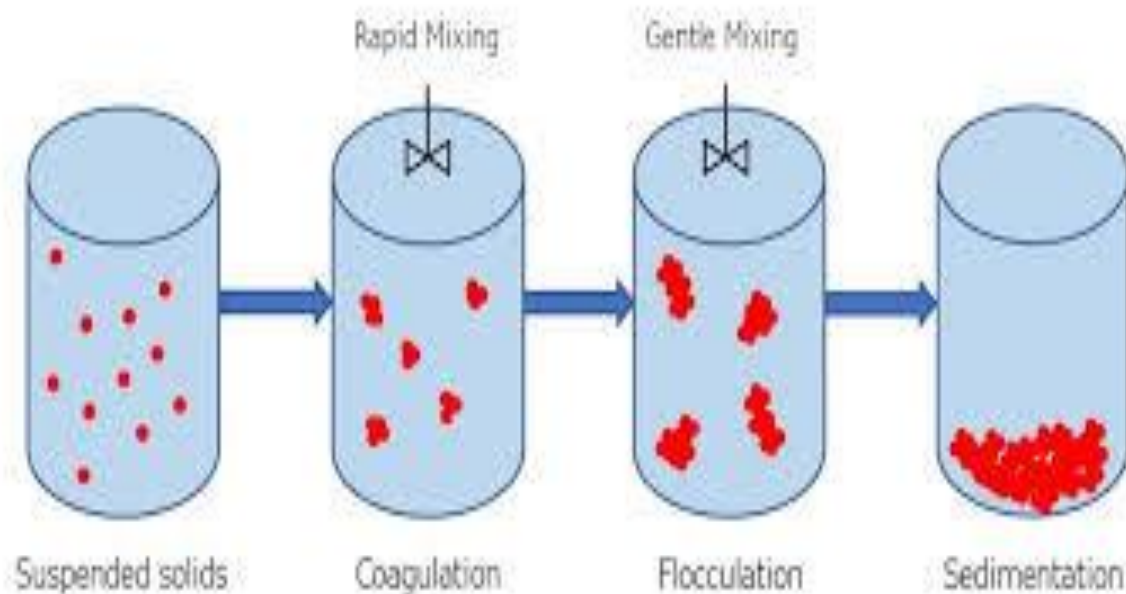
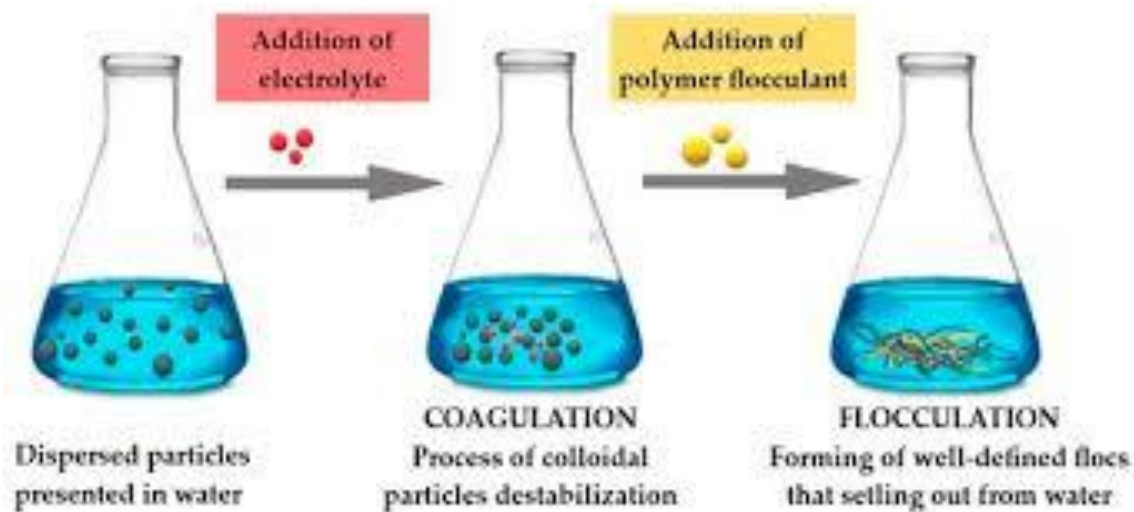
potential located at the shear plane bb' is known as the electrokinetic, or **zeta, potential,  $\delta$** . The zeta potential is defined as the difference in potential between the surface of the tightly bound layer (shear plane) and the electroneutral region of the solution



The zeta potential has practical application in the stability of systems containing dispersed particles because this potential, rather than the Nernst potential, governs the degree of repulsion between adjacent, similarly charged, dispersed particles.

If the zeta potential is reduced below a certain value (which depends on the particular system being used), the **attractive** forces exceed the **repulsive forces**, and the particles come together. This phenomenon is known as **flocculation**.





# Solubilization

An important property of association colloids in solution is the ability of the micelles to increase the solubility of materials that are normally insoluble, or only slightly soluble, in the dispersion medium used. This phenomenon, known as ***solubilization***, The pharmacist must give due attention to several factors when attempting to formulate solubilized systems successfully. It is essential that, at the concentration employed, the **surface-active agent**, if taken internally, be **nontoxic, miscible** with the solvent (usually water), **compatible** with the material to be solubilized, free from disagreeable **odor and taste**, and relatively **nonvolatile**.

**Toxicity** is of paramount (vital) importance, and, for this reason, most solubilized systems are based on **nonionic surfactants**. The amount of surfactant used is important: A large excess is undesirable, from the point of view of both possible toxicity and reduced absorption and activity; an insufficient amount can lead to precipitation of the solubilized material.

Solubilization has been used in pharmacy to bring into solution a wide range of materials, including volatile oils, coal tar and resinous materials, phenobarbital, sulfonamides, vitamins, hormones, and dyes.

# Pharmaceutical applications of colloids

**Colloids** are extensively used for modifying the properties of pharmaceutical agents. The most common property that is affected is the **solubility of a drug**. However, colloidal forms of many drugs exhibit substantially different properties when compared with traditional forms of these drugs. Another important pharmaceutical application of colloids is their use as **drug delivery systems**. The most often-used colloid-type drug delivery systems include hydrogels, microspheres, microemulsions, liposomes, micelles, nanoparticles, and nanocrystals

Thank

you

