Pharmaceutical Technology for 3rd year students
Lec; 6

By:

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Dispersed Systems

Objective:

After reading this lecture, the student will be able to:

1 . Differentiate between a suspension, an emulsion, a gel, and a magma

2 . Compare and contrast the different disperse systems, and list advantages and disadvantages of each system

3 . Compare and contrast the following emulsification theories: surface tension, oriented-wedge, and interfacial film

4 . Define and differentiate the following terms from one another: lyophobic, lyophilic, hydrophobic, hydrophilic, amphiphilic, imbibition, swelling, syneresis, thixotropy, and xerogel

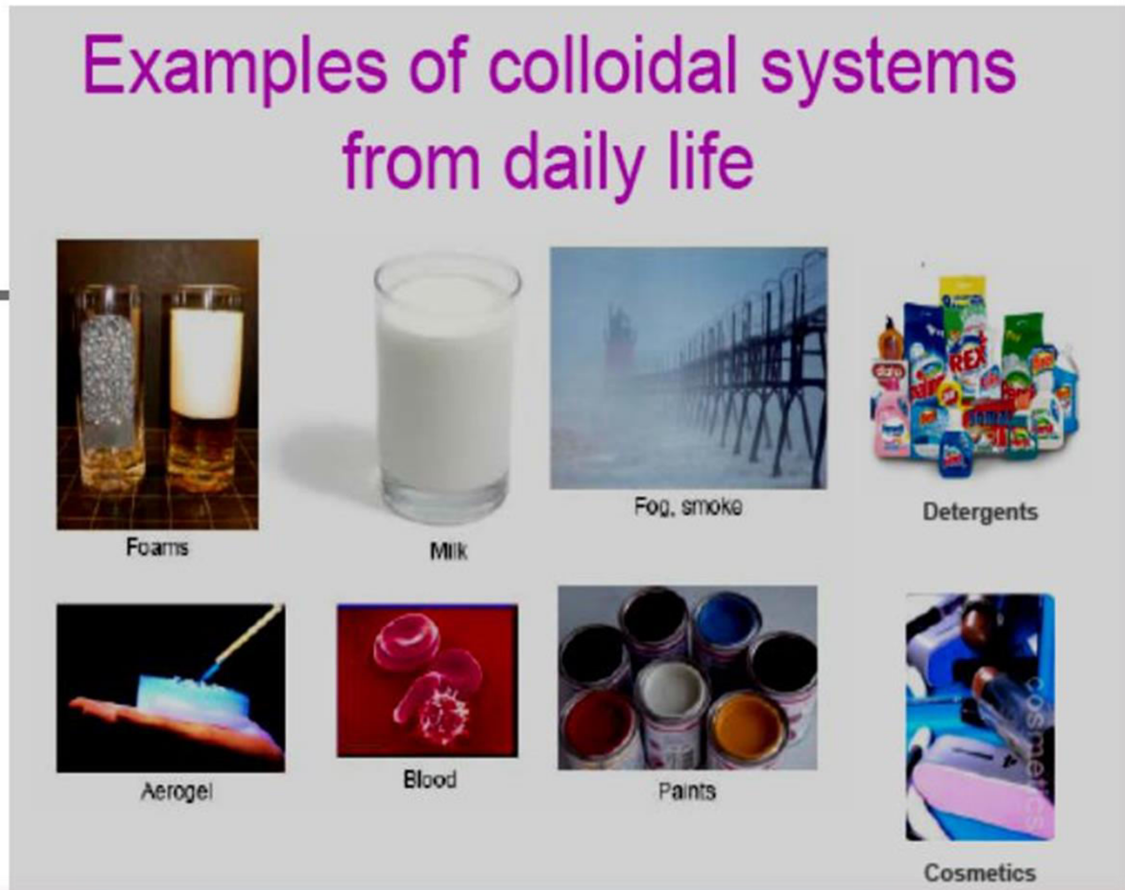
5 . Evaluate and select a proper disperse system and delivery method for a given purpose, patient population, and/or patient circumstance.

- ✓ types of liquid preparations containing **undissolved** or **immiscible** drug distributed throughout a vehicle.

- ✓ ***the dispersed phase***
- ✓ ***dispersing phase*** or ***dispersion medium.***

- Colloid from the ***Greek*** word, ***Kolla***, meaning glue. *Thomas Graham,* one of the early physical chemists, introduced the concept of Colloids.

COLLOIDS


Examples of colloidal systems from daily life
Foams
Milk
Fog, smoke
Detergents
Aerogel
Blood
Paints
Cosmetics

- The particles of the dispersed phase vary widely in size, from large particles visible to the naked eye down to particles of colloidal dimension, falling between 1.0 nm and 0.5 μm.

Classification Of Disperse Systems

Colloids can be classified according to three criteria;

1- Particle diameter of the Dispersed Materials

2- The nature of interaction between the disperse phase & dispersion medium.

3- Physical States of the of the disperse phase & dispersion medium.

1- Particle diameter of the Dispersed Materials

MOLECULAR DISPERSION	COLLOIDAL DISPERSION	COARSE DISPERSION
- Less than 1 um - Particles undergo rapid diffusion e.g. O2 & glucose	- 1 um to 500 um - Very slow diffusion e.g. colloidal silver sol.	- Greater than 500 um - Don't diffuse e.g. suspension & emulsion

Particle diameter of the Dispersed Materials

MOLECULAR DISPERSION	COLLOIDAL DISPERSION	COARSE DISPERSION
-Particles invisible in electron microscope. -Pass through semipermeable membranes and filter paper.	-Particles resolved by electron microscope. - Pass through filter paper but not pass through semipermeable membrane.	-Particles are visible under ordinary microscope. - Do not pass through filter paper or semipermeable membrane.

- ✓ Most solids in dispersion tend to settle to the bottom of the container because of their greater density than the dispersion medium,

- ✓ Complete and uniform redistribution of the dispersed phase is essential to the accurate administration of uniform doses. How?

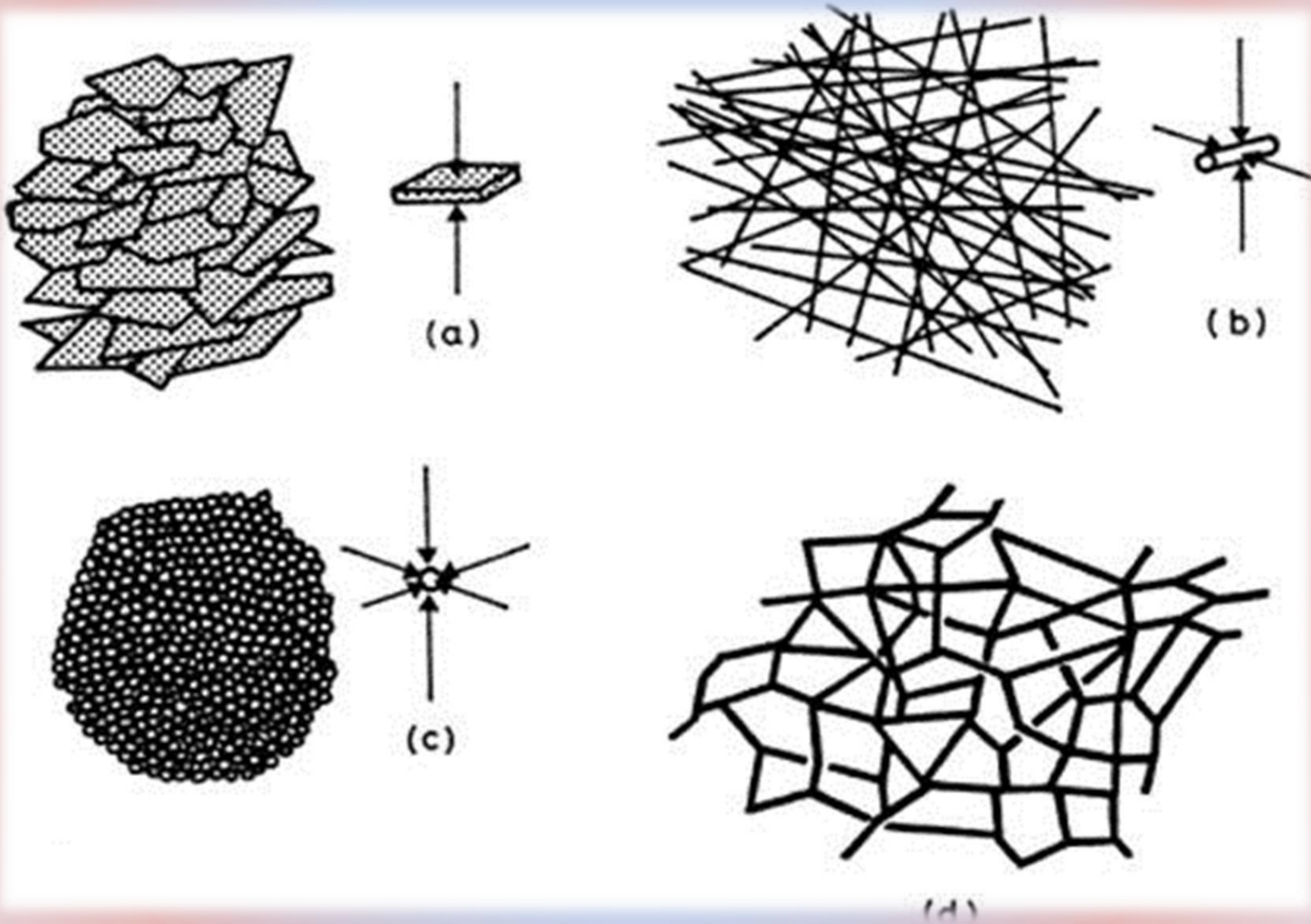
Size and shape of colloids

- ***Specific surface:*** the surface area per unit weight or volume of material.

Problem;

Calculate the specific surface area, in m^2/g of serum albumin in aqueous solution, given that each molecule is a compact sphere of density $d=1.34$ g/cm^3. and the diameter $D= 18Å= 18 \times 10^{-8}$?

- ✓ 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)
(d)

2-The nature of interaction between dispersed phase and dispersion medium

A- Lyophilic colloids (solvent attracting) (solvent loving); The particles have a great affinity for the solvent (great attraction between the disperse phase & dispersion medium).

- the sols are quite stable as the solute particle surrounded by two stability factors:

a- negative or positive charge

b- layer of solvent.

- 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 & dispersion in the solvent.

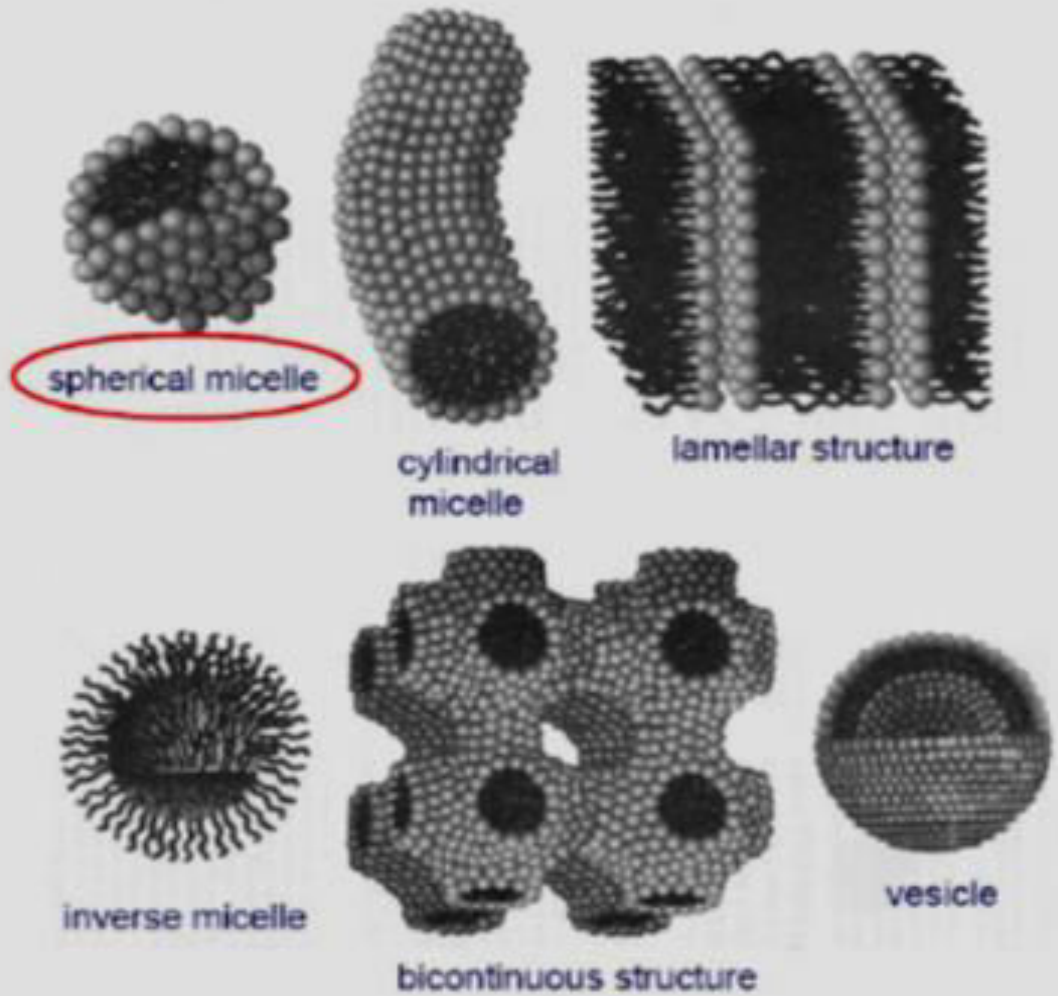
- ✓ Examples of lyophobic sols include sols of metals & their insoluble compounds like sulphides and oxides. e.g. gold in water

C- Association / amphiphilic colloids

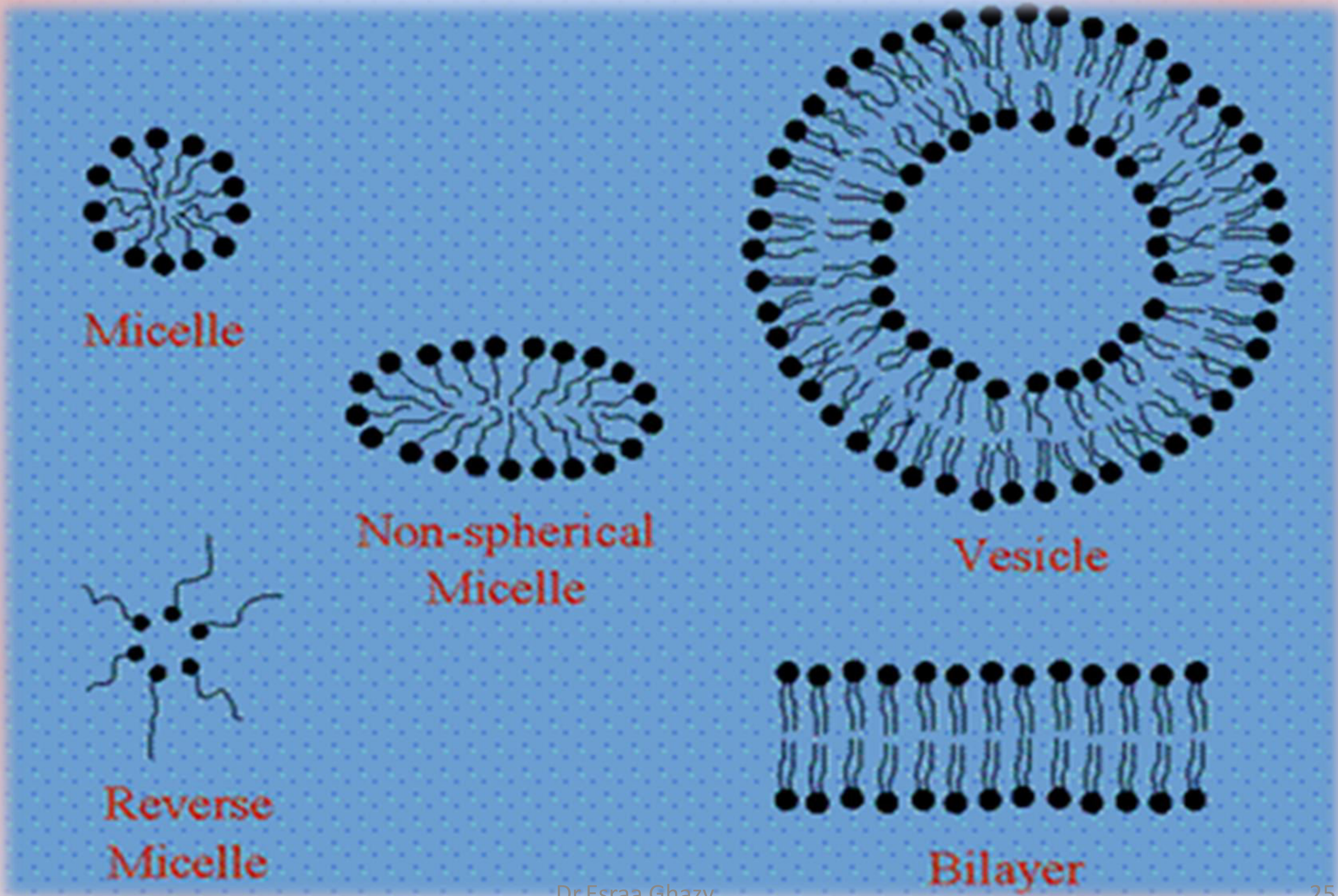
Certain molecules termed amphiphiles or surface active agents, characterized by two regions of opposing solution affinities (lipophilic & hydrophilic) within the same molecule.

- ✓ In water: the hydrocarbon chains face inwards into the micelle forming hydrocarbon core and surrounded by the polar portions of the amphiphile associated with water molecules.

Shapes of surfactant aggregates



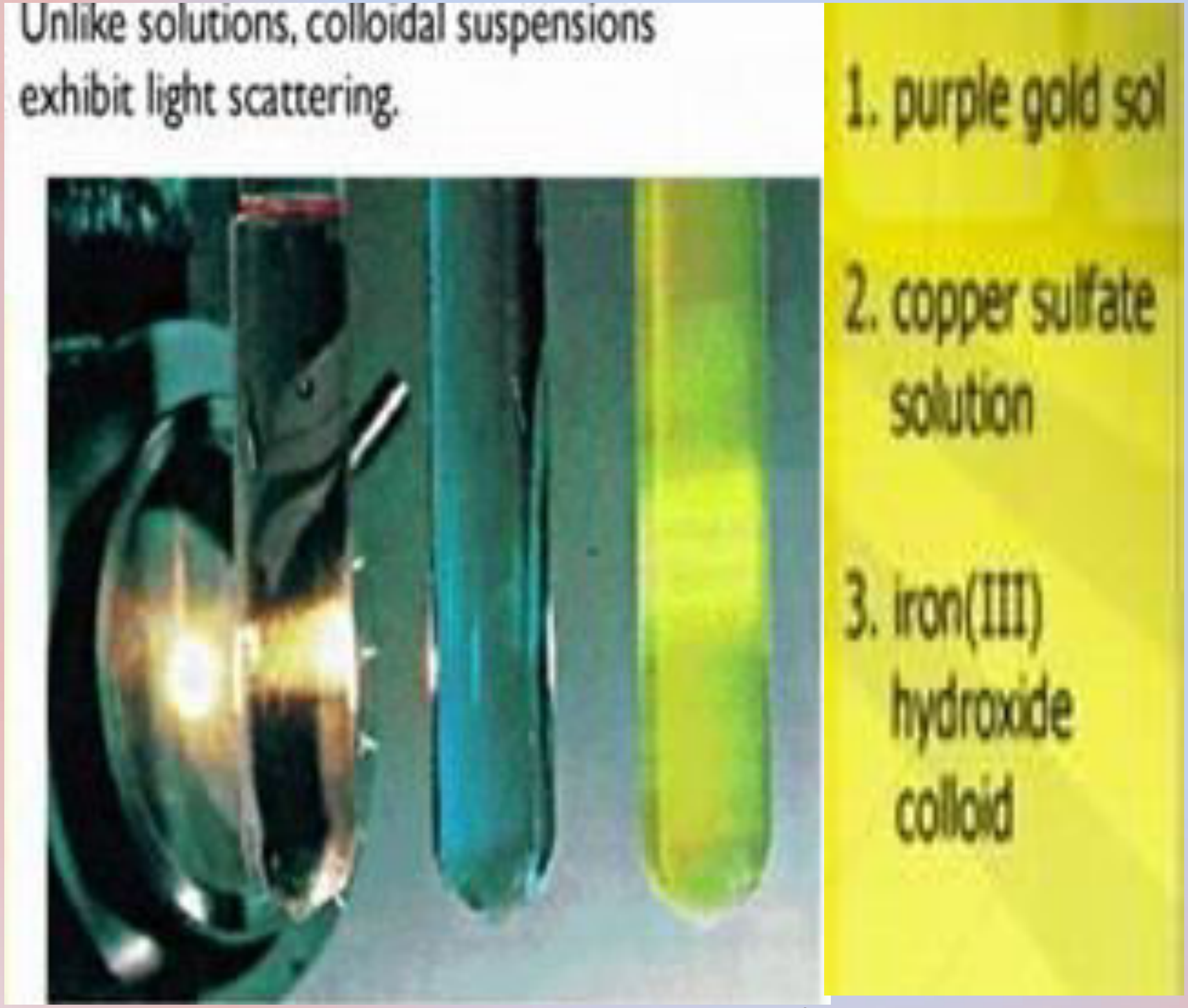
Different types of association colloids



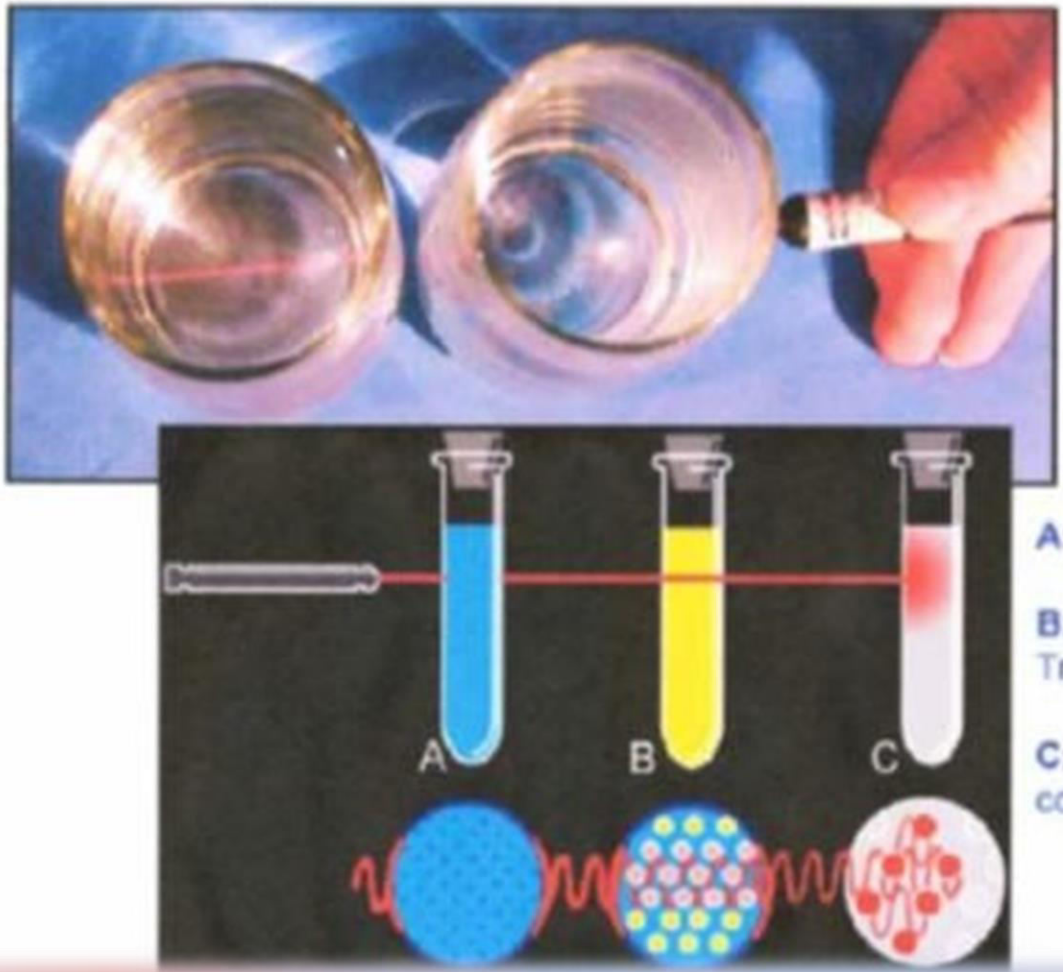
Optical Properties of Colloids

1-Faraday-Tyndall effect; when a strong beam of light is passed through a colloidal sol, the path of light is illuminated (a visible cone formed).

Faraday-Tyndall effect



The Faraday-Tyndall effect



Tyndall Effect: Laser Pointer traveling through a solution (right) and through a colloidal suspension (left).

A: Solution

B: Colloidal Suspension Transparent

C: Colloidal Suspension completely absorbing light

2- Electron microscope;

- ✓ Electron microscope has high resolving power, as its radiation source is a beam of high energy electrons, while that of optical microscope is visible light.

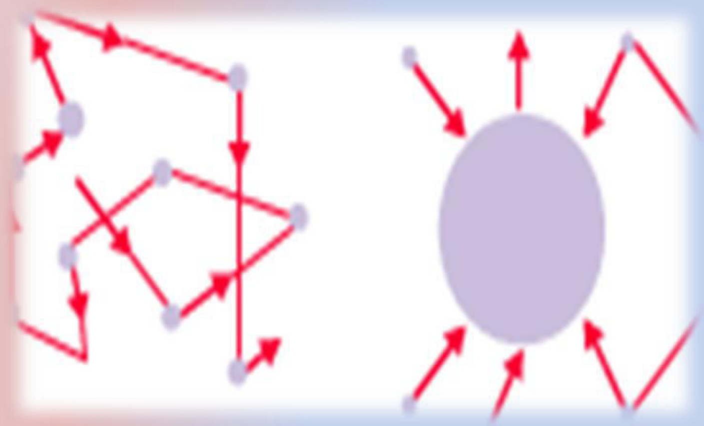
- ***3- Light Scattering - depend on tyndall effect;*** used to give information about particle size and shape and for determination of molecular weight of colloids.

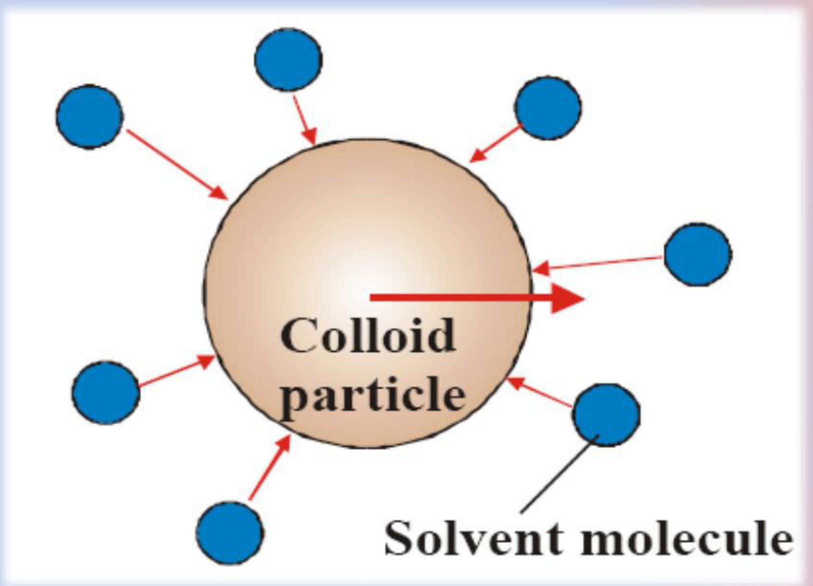
$$Hc / T = 1/M + 2Bc$$

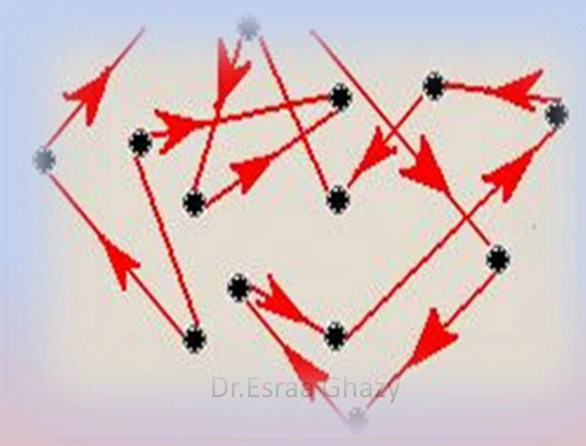
Comparison of Colloidal sol.

Kinetic Properties of Colloids

1-Brownian motion- Brownian motion describes the random movement of colloidal particles.







The zig-zag movement of colloidal particles continuously and randomly. This brownian motion arises due to ??

- Brownian movement was more rapid for smaller particles.
- It decrease with increase the viscosity of the medium.

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 in time dt across a plane of area A is directly proportional to the change of concentration dc with distance traveled

$$dq = -DA\,(dc / dx)\,dt$$

- ✓ D is the diffusion coefficient which is the amount of the material diffused per unit time across a unit area when dc/dx (conc. gradient) is unity.
- ✓ The measured diffusion coeffecient can be used to determine the radius of particles or molecular weight.

3- Osmotic pressure;

van 't hoff equation: $\Pi = cRT$

4- Sedimentation

$$\frac{dx}{dt} = \frac{d2\ (pi - pe)g}{18\eta}$$

Dx/dt= rate of sedimentation (settling),

d= diameter of particles, ρ_i = density of internal phase and Pe= density of external phase, g=gravitational constant, η = viscosity of medium

5- Viscosity: It is the resistance to flow of system under an applied stress.

Electric Properties Of Colloids

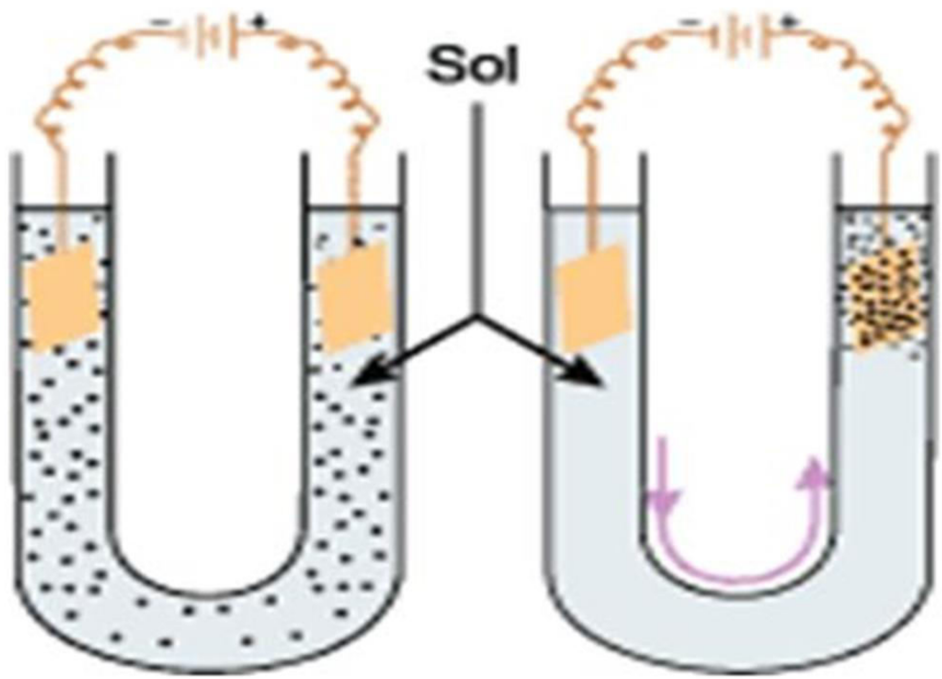
The properties of colloids that depend on, or are affected by, the presence of a charge on the surface of a particle.

The **colloidal particles** constituting the dispersal phase carry an **electric charge** probably due to the preferential **adsorption of** ions in the dispersion medium.

✓

Electrophoresis

Movement of colloidal particles under influence of electric field.



Electrophoresis Is the most known electrokinetic phenomena.

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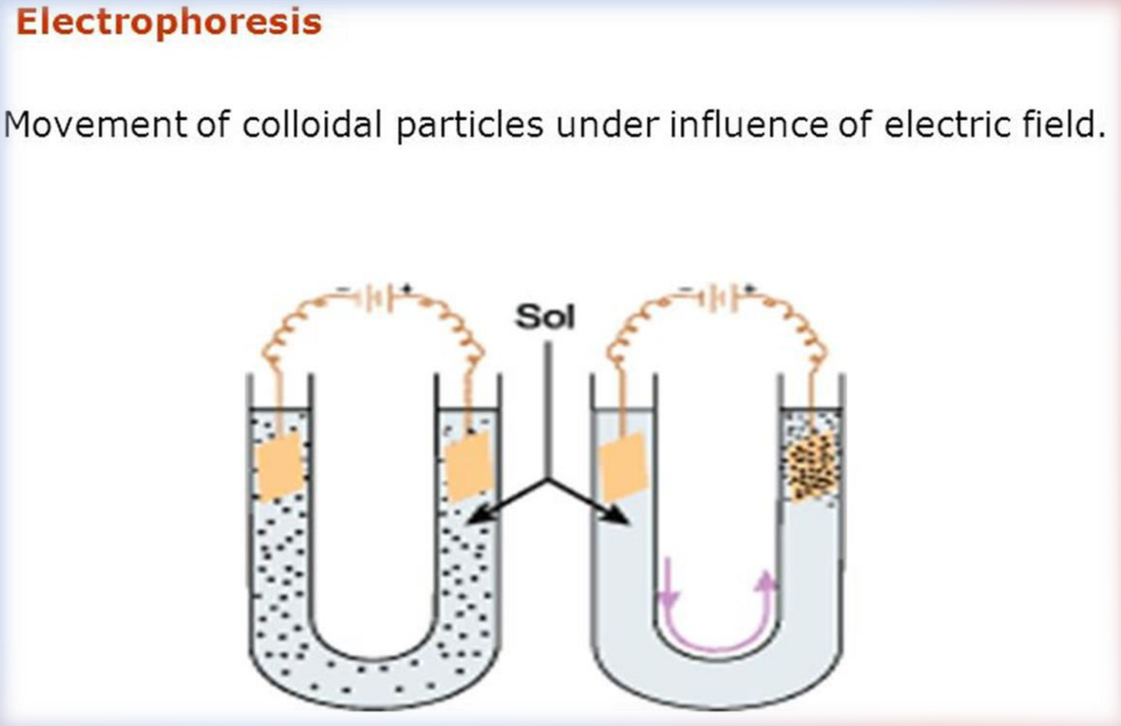
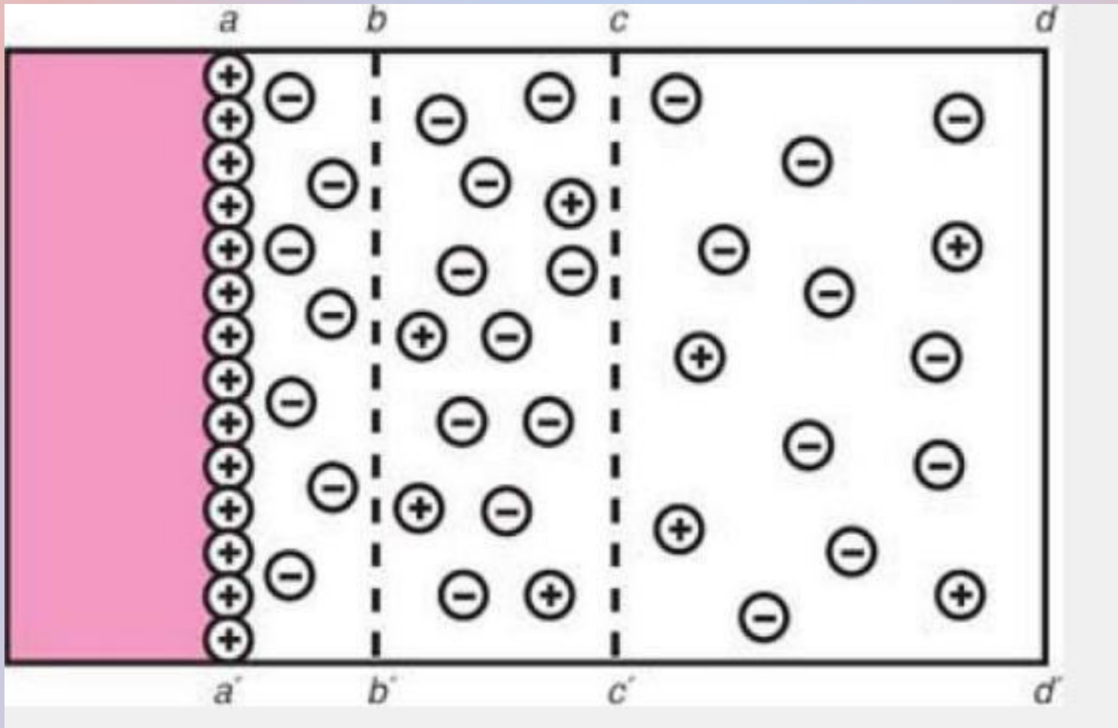


- ✓ Because the shear plane of the particle is located at the periphery of the tightly bound layer, the rate-determining potential is the **zeta potential.**

- ✓ In addition to these electric forces, thermal motion tends to produce an equal distribution of all the ions in solution.

- ✓ As a result, 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.


a
b
c
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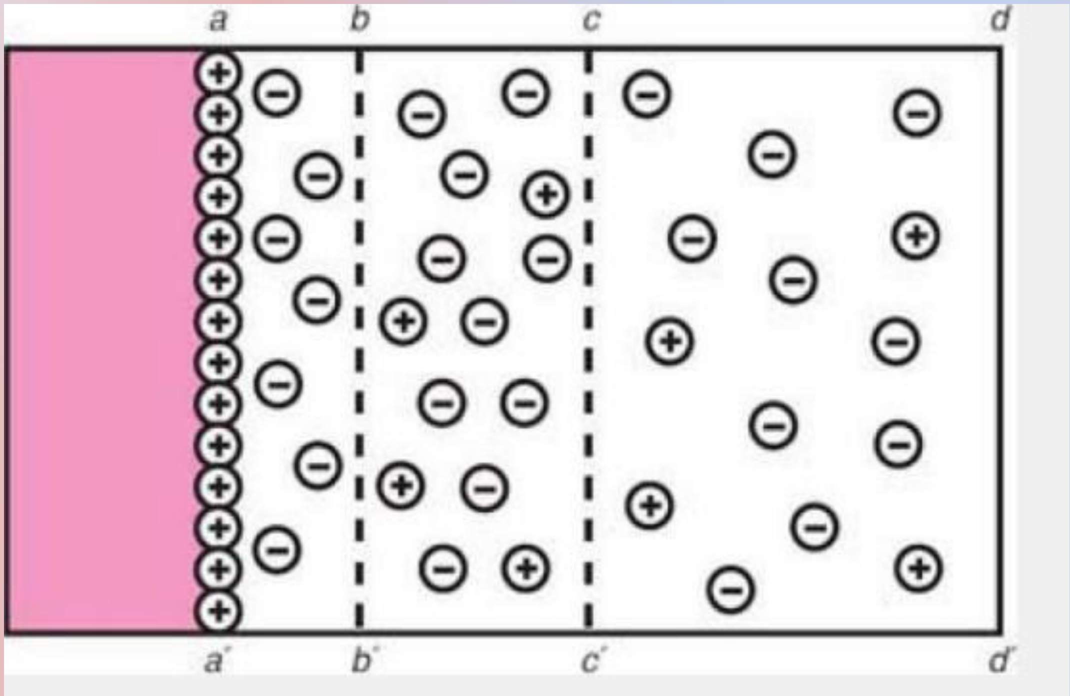


A figure illustrate :

The electric double layer at the surface of separation between two phases, showing distribution of ions.

The system as a whole is electrically neutral.

- ✓ The potential located at the shear plane bb′is known as the electrokinetic, or zeta, potential, δ.

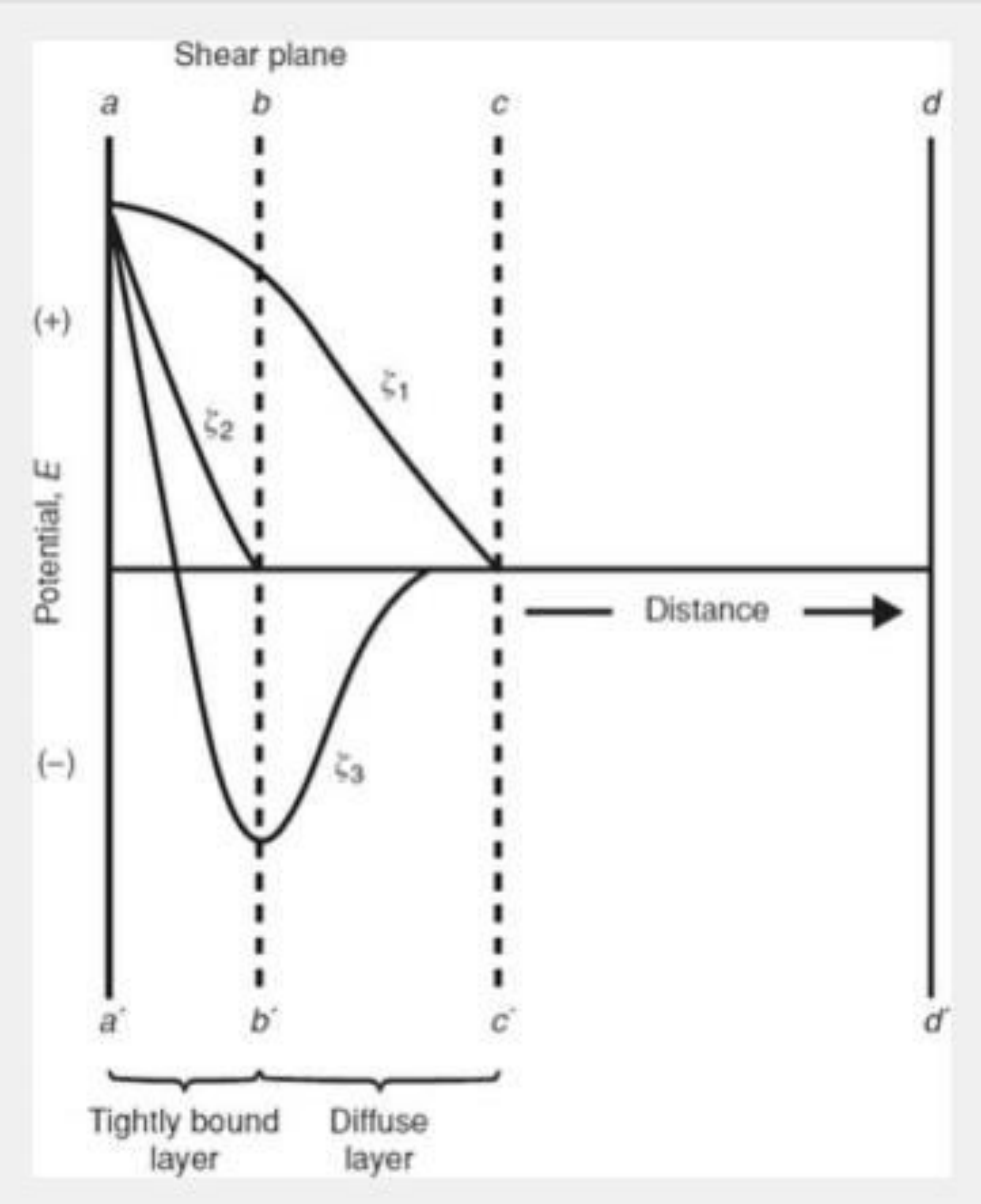


Figure illustrate Electrokinetic potential, E, at solid–liquid boundaries.

- ✓ 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 .

$$\zeta = \frac{v}{E} \times \frac{4\pi\eta}{\varepsilon} \times (9 \times 10^4)$$

The relevant equation, which yields the zeta potential, ζ, in volts, requires a knowledge of

-the velocity of migration, v, of the sol in cm/sec in an electrophoresis tube of a definite length in cm,

-the viscosity of the medium, η, in poises (dynes sec/cm2),

-the dielectric constant of the medium, ε,

-and the potential gradient, E, in volts/cm.

-The term v/E is known as the mobility.

Example;

The velocity of migration of an aqueous ferric hydroxide sol was determined at 20°C was found to be 16.5 × 10-4cm/sec. The distance between the electrodes in the cell was 20 cm, and the applied emf was 110 volts.

What is (a) the zeta potential of the sol and (b) the sign of the charge on the particles?

Electro-osmosis;

- It is the opposite in principal to that of electrophoresis.

- The reverse of electro osmosis is called streaming potential. Which Differs from electro-osmosis in that the ***potential is created by forcing a liquid to flow through a bed or plug of particles.***

- ✓ Electro-osmosis is essentially opposite in principle to electrophoresis.

- ✓ Electro-osmosis provides another method for obtaining the zeta potential by determining the rate of flow of liquid through the plug under standard conditions

- ✓ **Sedimentation potential,** the reverse of electrophoresis, is the creation of a potential when particles undergo sedimentation.

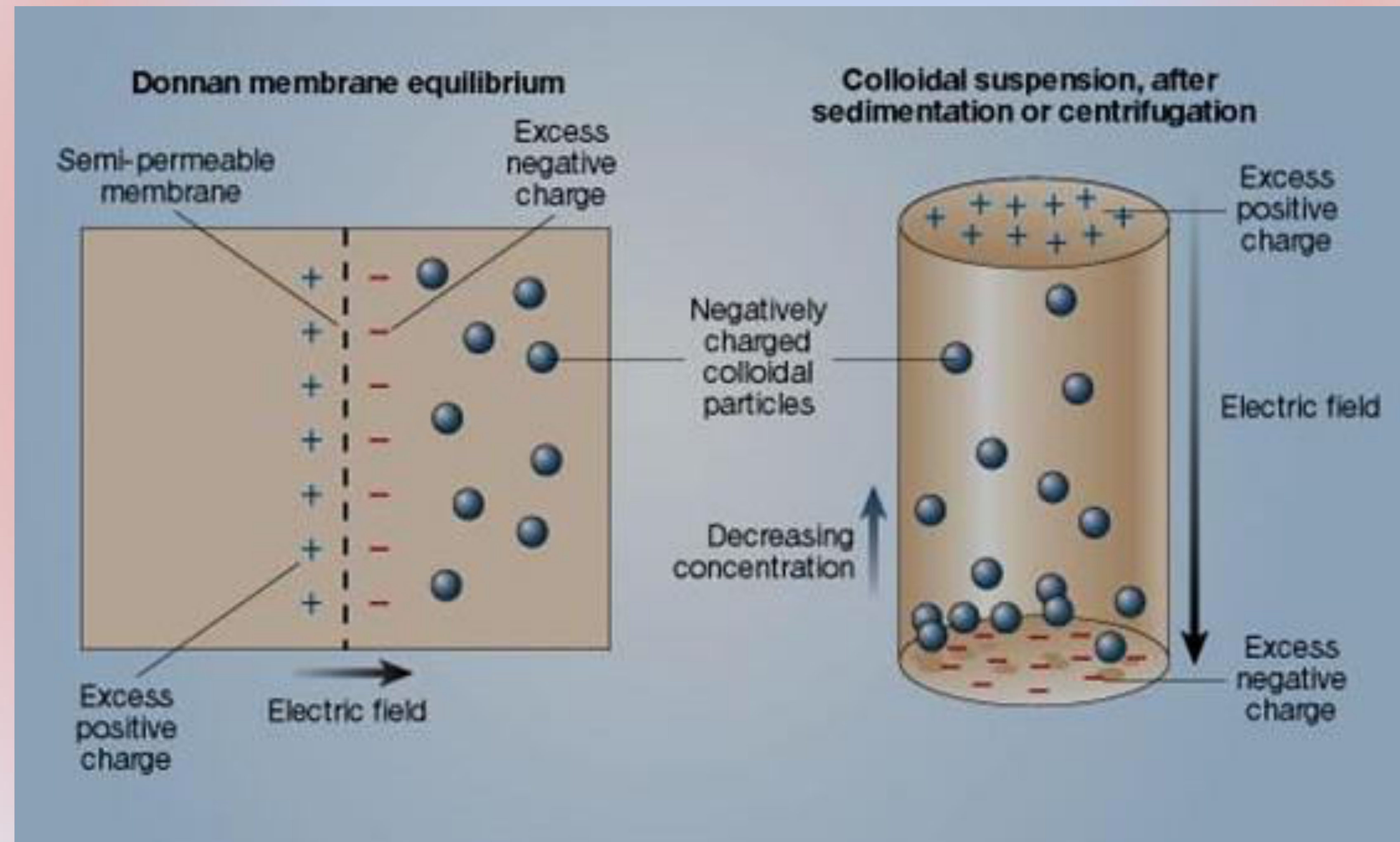
- ✓ The sedimentation potential also called the (Donnan effect).

- ✓ Some species of ions may pass through the barrier while others may not.

- ✓ The solutions may be gels or colloids as well as ionic liquids, and as such the phase boundary between gels or a gel and a liquid can also act as a selective barrier.

Sedimentation Potential

- ✓ Electric potential arises between two solutions is called Donnan potential.
- ✓ It is the potential induced by the fall of a charged particle under an external force field.
- ✓ It is analogous to electrophoresis in the sense that a local electric field is induced as a result of its motion.



Donnan membrane equilibrium
Semi-permeable membrane
Excess negative charge
Excess positive charge
Electric field
Colloidal suspension, after sedimentation or centrifugation
Excess positive charge
Negatively charged colloidal particles
Electric field
Decreasing concentration
Excess negative charge

Gel

- ✓ The word “gel” is derived from “gelatin,” and both“gel” and “jelly” can be traced back to the Latin gelu for “frost” and gelare, meaning “freeze” or “congeal.”

- ✓ A gel rich in liquid (usually water) may be called a jelly

- ✓ **Gels** are defined as semisolid systems aggregation of colloidal sol dispersions. In which the movement of the dispersing medium is restricted by an interlacing three-dimensional network of particles or solvated macromolecules of the dispersed phase

- ✓ The colloidal particles may be dispersed solids, e.g. kaolin, bentonite or, alternatively, dispersed polymers.

- ✓ Xerogel :formed when liquid removed from the gel and only framework remains
- ✓ Example, Sheet gelatin, acacia tears, Tragacanth flakes

(1) dispersed solids (lyophobic sols) small inorganic particles.

(2) hydrophilic polymers (lyophilic sols) large organic molecules enclosing and interpenetrated by a liquid.

Thixotrophy

- ✓ ***Thixotrophy*** : is a reversible sol- gel formation, with no change in volume or temperature , type of non –Newtionian flow.

- **Hydrogels**
- Whereas a gel is a colloid with a liquid as dispersion medium and a solid as a dispersed phase. a hydrogel is a colloidal gel in which water is the dispersion medium.
- Wound gels are excellent for helping create or maintain a moist environment.

- ✓ Because they are loaded with pharmaceutical ingredients, hydrogels provide a sustained release of drugs.

- ✓ Special attention has been given to environmentally sensitive hydrogels. Which have the ability to sense changes in pH, temperature, or the concentration of a specific metabolite and release their load as a result of such a change.

- ✓ Hydrogels that are responsive to specific molecules, such as glucose or antigens, can be used as biosensors as well as drug delivery systems.

- ✓ Light-sensitive, pressure-responsive, and electrosensitive hydrogels also have the potential to be used in drug delivery.

Microparticles

Microparticles are small (0.2–5 μm), loaded microspheres of natural or synthetic polymers.

- ✓ Microparticles were initially developed as carriers for vaccines and anticancer drugs. increase the efficiency of drug delivery and improve release profiles and drug targeting.

- ✓ It was found in this study that after mucosal delivery, microparticles can translocate to tissues in the systemic compartment of the immune system and provoke immunologic reactions.

- ***Emulsions and Microemulsions***

Microemulsions are excellent candidates as potential drug delivery systems because of their improved drug solubilization, long shelf life, and ease of preparation and administration.

- microemulsions are usually formed with more or less homogeneous particles. Microemulsions are used for controlled release and targeted delivery of different pharmaceutic agents. For instance, microemulsions were used to deliver oligonucleotides (small fragments of DNA) specifically to ovarian cancer cells.

- ✓ In contrast to microemulsions, nanoemulsions consist in very fine oil-in-water dispersions, having droplet diameter smaller than 100 nm.

- ***Liposomes***
- Liposomes consist of an outer uni- or multilaminar membrane and an inner liquid core.
- Liposomes can be loaded by pharmaceutical or other ingredients by two principal ways:
- A- lipophilic compounds can be associated with liposomal membrane,
- B- and hydrophilic substances can be dissolved in the inner liquid core of liposomes.

- ✓ Because they are relatively easy to prepare, biodegradable, and nontoxic, liposomes have found numerous applications as drug delivery systems.

- ***Nanoparticles***
- Two technologies can be used to obtain such nanocapsules:

1/ the interfacial polymerization of a monomer or

2/ the interfacial nanodeposition of a preformed polymer.

Solid lipid nanoparticles were developed at the beginning of the 1990s as an alternative carrier system to emulsions, liposomes, and polymeric nanoparticles.

- ✓ They were used, in particular, in topical cosmetic and pharmaceutical formulations.

- ✓ Nanoparticles have also found applications as nonviral gene delivery systems.

Applications of colloidal solution/Systems

1- **Therapy;**

2- **Stability;**

3- **Absorption**;

As colloidal dimensions are small enough, they have a huge surface area. Hence, the drug constituted colloidal form is released in large amount. e.g- sulphur colloid gives a large quantity of sulphur and this often leads to sulphur toxicity.

4-Targeted Drug Delivery;

Liposomes are of colloidal dimensions & are preferentially taken up by the liver & spleen.

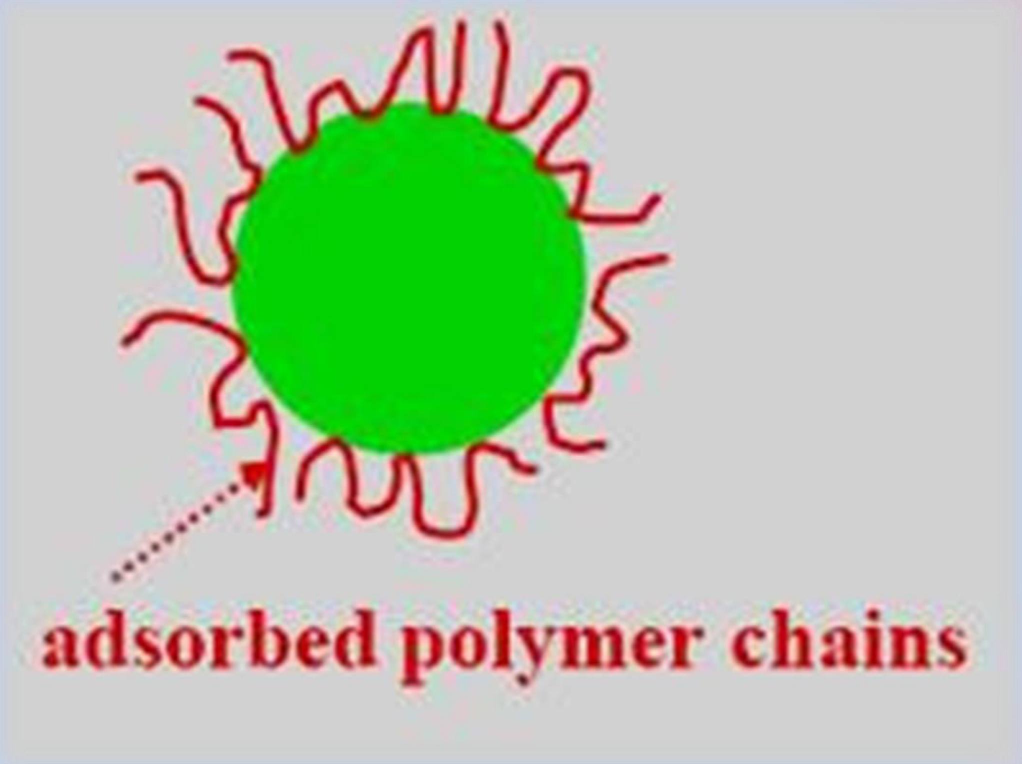
***5-* Photography;** A colloidal solution of silver bromide in gelatine is applied on glass plates or celluloid films to form sensitive plates in photography.

***6-* Clotting of blood;** Blood is a colloidal solution and is negatively charged. -On applying a solution of Fecl3 bleeding stops & blood clotting occurs as Fe +3 ions neutralize the ion charges on the colloidal particles.

Sensitization and protective colloidal action:

- ✓ **Sensitization:**
- ✓ Polymer flocculants can bridge individual colloidal particles by attractive electrostatic interactions. For example, negatively-charged colloidal silica particles can be flocculated by the addition of a positively-charged polymer.

✓Protection:.



Stability of colloids

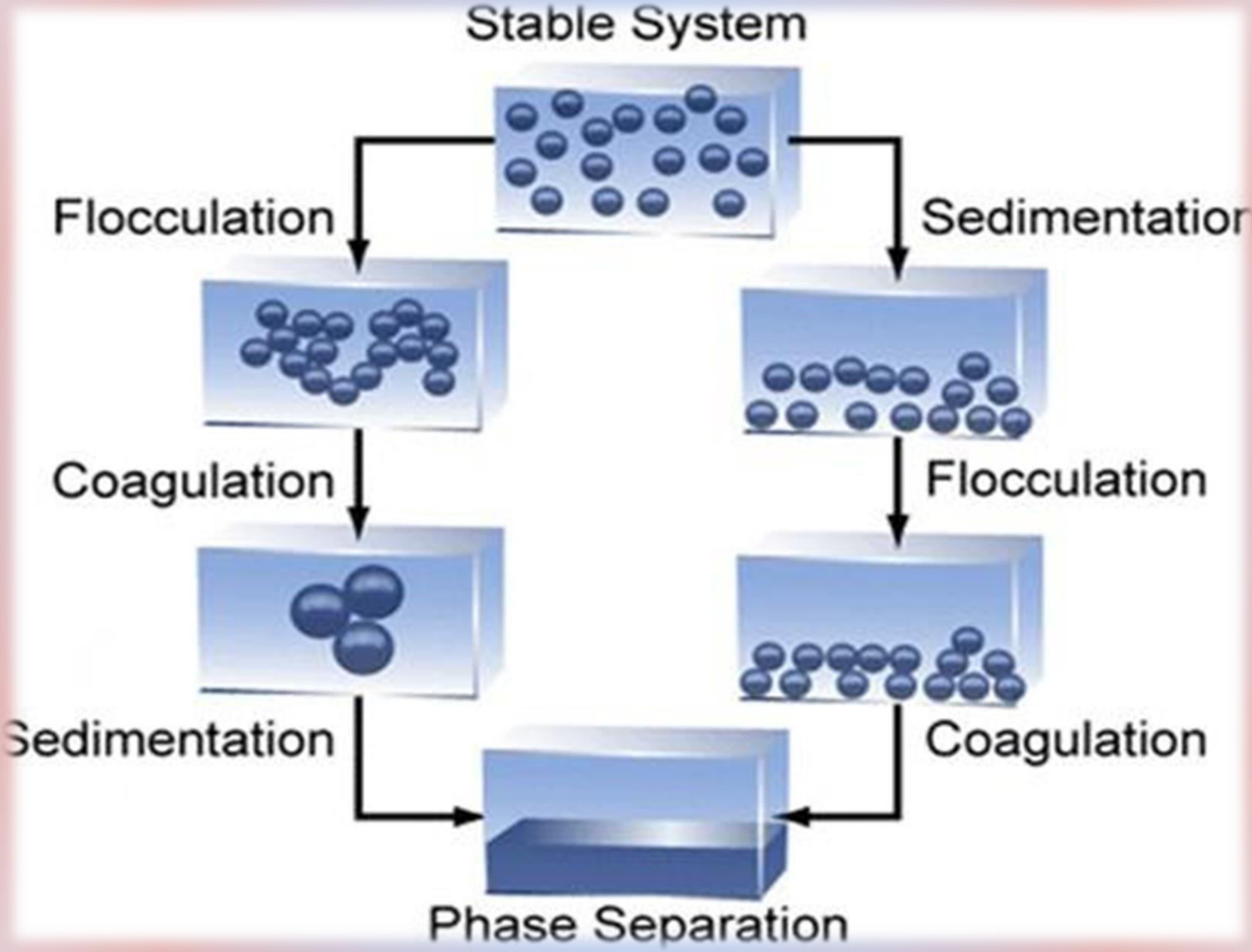
- ✓ Two main mechanisms for colloid stabilization:

  1-Steric stabilization i.e. surrounding each particle with a protective solvent sheath which prevent adherence due to Brownian movement

  2-electrostatic stabilization i.e. providing the particles with electric charge

- ✓ Summary;

Although colloidal dispersion have been important in the pharmaceutical sciences for decades, with the advent of nanotechnology, they are now becoming a driving force behind drug delivery systems and technology.


Stable System
Flocculation
Sedimentatior
Coagulation
Flocculation
Sedimentation
Coagulation
Phase Separation