COLLOIDS

COLLOIDS

Greek – glue like

Colloids are dispersions where in **dispersed particles** are distributed uniformly in the **dispersion medium**.

Dispersed particles size **Small-** less than 0.01µ

Medium- 5-1µ

Large- 10-1000µ

Def:

Colloids systems are defined as those polyphasic systems where at least one dimension of the dispersed phase measures between 10-100A^0 to a few micrometers.

Characteristics of dispersed phase:

1.Particle size:

This influence colour of dispersion.

Wavelength of light absorbed α 1/ Radius

(small wavelength)**VIBGYOR** (large wavelength)

2.Particle shape:

Depends on the preparation method and affinity of dispersion medium

This influence colour of dispersion.

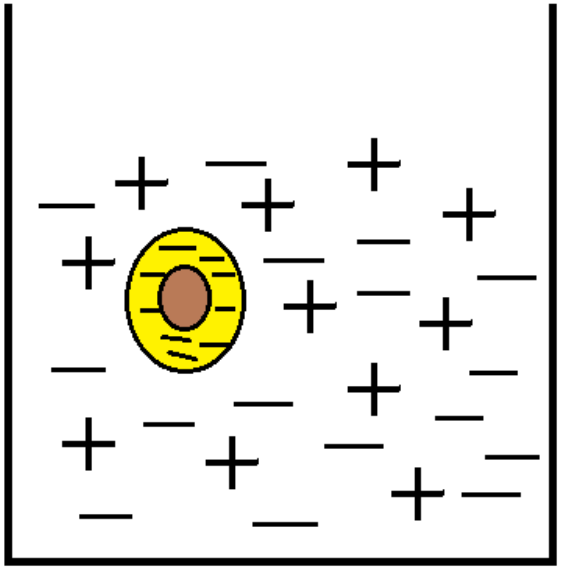
Shapes- spherical, rods, flakes, threads, ellipsoidal.

Gold particles- spherical (red), disc (blue).

3. Surface area:

Particle size small- large surface area

Effective catalyst, enhance solubility.



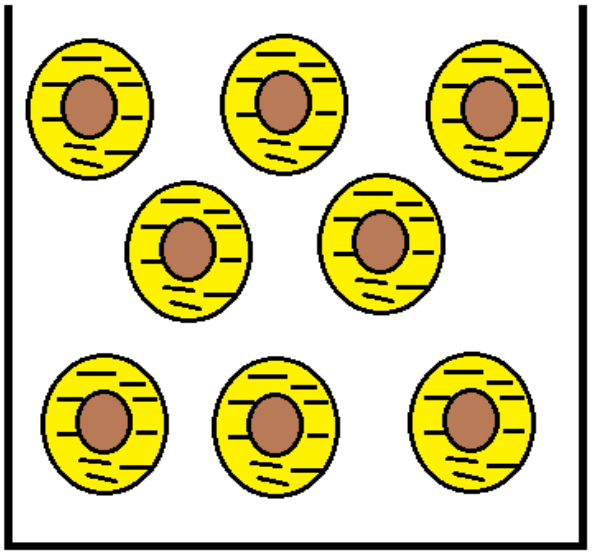
4. Surface charge:

Positive (+)= gelatin, aluminum.

Negative (-) = acacia, tragacanth.

Particle interior neutral, surface charged.

Surface charge leads to stability of colloids because of repulsions.



Pharmaceutical applications:

1. **Therapy**
2. **Absorption & toxicity**
3. **Solubility**
4. **Stability**
5. **Targeting of drug to specific organ.**

1. Therapy:

Small size – good absorption- better action- treatment.
Silver-germicidal
Copper-anticancer Mercury- anti syphilis

2.Absorption & toxicity

Sulfur deficiency treatment
Colloidal sulfur- small size particles- faster absorption- excess sulfur concentration in blood- toxicity

3.Solubility

Insoluble drug ➔ Colloidal system+ Surfactants
(sulfonamides, phenobarbitones) (micellar solublization)

4. Stability:

Colloidal systems are used as pharmaceutical excipients, vehicles, carriers, product components.

Dispersion of surfactants ➔ Association colloids – increase stability of drug (liquid dosage form)

Dispersion of macromolecules (gelatin), ➔Tablet Coating synthetic polymers (HPMC)

5. Targeting of drug to specific organ.

Drug entrapped liposomes, niosomes, nanoparticles, microemulsions targeted to liver, spleen**.**

Official preparations;

1. Iron drxtran inj (B.P)- anemia treatment
2. Iron sorbitol inj (B.P)- sorbitol, dextran, citric acid, iron.

Classification of colloidal dispersion:

1.Basing on charge- (+), (-)

2.Basing on state of matter – Solid, Liquid, Gas.

3.Interaction of dispersed particles with dispersion medium- lyophilic, lyophobic, association colloids.

Dispersed particles	Dispersion medium	Example
Solid	Solid	ZnO tooth paste
Solid	Liquid	Bentonite magma sols
Solid	Gas	Solid aerosols
Liquid	Solid	Oil in hydrophilic ointment
Liquid	Liquid	Castor oil-water emulsion
Liquid	Gas	Liquid aerosols
Gas	Solid	Solid foams
Gas	Liquid	Carbonated beverages
Gas	Gas	----------

Based on interactions;

I) Lyophilic colloids: (solvent loving)

Particles have greater affinity to dispersion medium (solvent).

Solvent forms a **sheath** on particle- **thermodynamically stable** dispersion.

Lyophilic colloid preparation and purification is easy.

Lyophilic colloid prepared with/without charge.

Acacia colloid (+) ➔Iso-electric point ➔Neutral charge

Dispersed particles

a)Hydrophilic- acacia, gelatin (water)

b)Lipophilic- rubber, polystyrene (organic solvents)

Dispersion medium

a)Hydrophilic – water

b)Lyophilic- organic solvents (benzene, ethylmethyl ketone)

II) Lyophobic colloids: (solvent hating)

Particles have less affinity to dispersion medium (solvent).

Solvent do not form a sheath on particle- thermodynamically **unstable** dispersion.

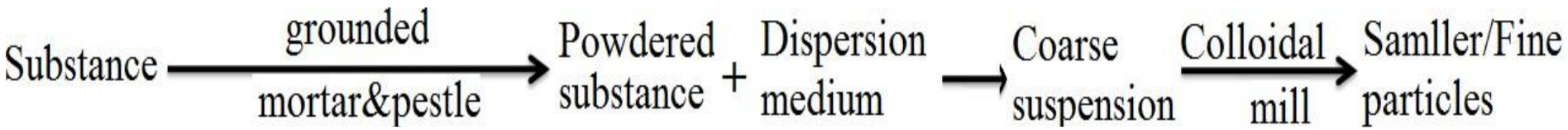
Dispersed particles- same charges- repulsions- uniform distribution.

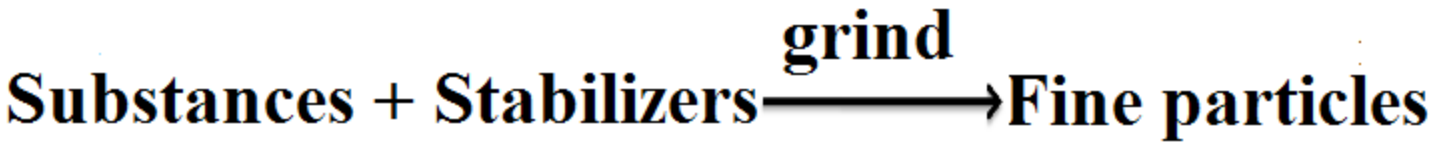
Preparation methods:

1. Dispersion method	2. Condensation method
Milling & grinding process	Addition of non-solvent
Peptization	Chemical methods
Eletric arc method	
Ultrasonic treatment	

1. Dispersion method (size decreasing)

a) Milling & grinding process:





b) Peptization:

Defined as a process of breaking aggregates/ secondary particles in to particles of colloidal size.

Peptizing agent: compound that promotes dispersibility of solids with out entering in to combination with them.

Ex: glycerin, sugar, lactose, citric acid.

Peptization is done by

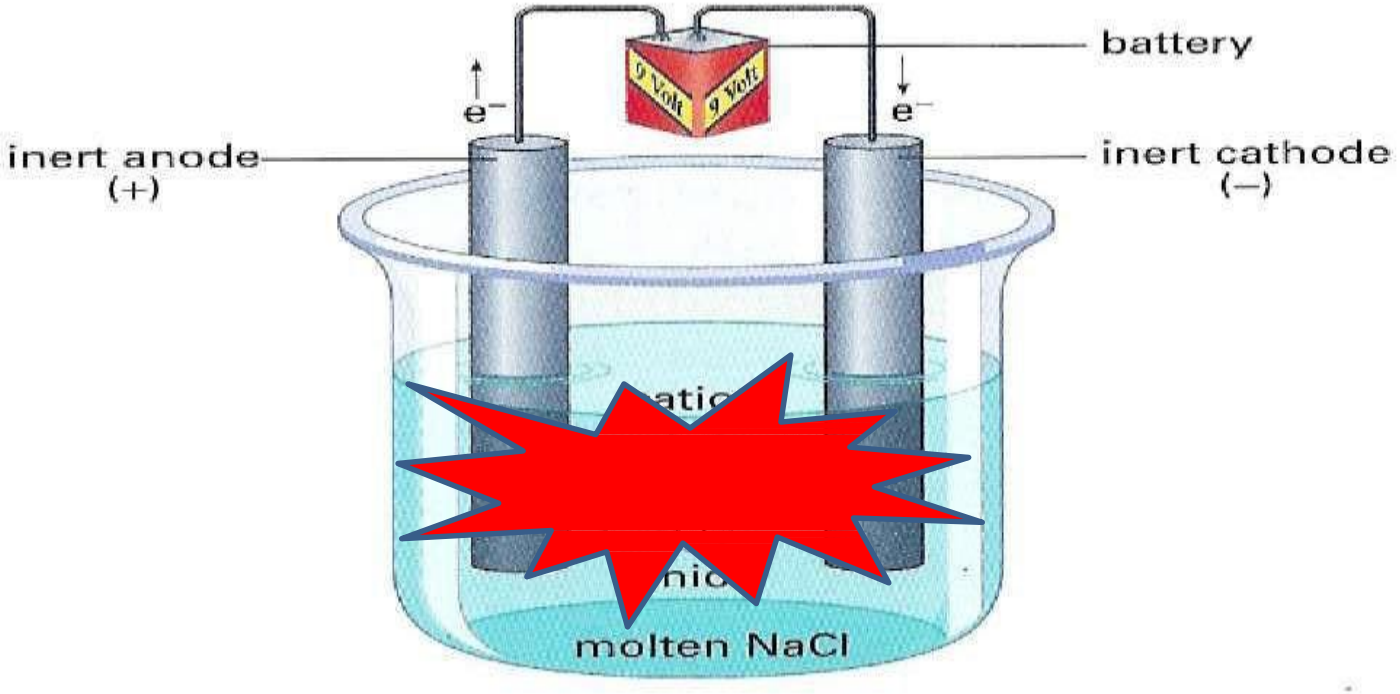
1.Removal of flocculating agent/ electrolyte.

2.Addition of deflocculating agent/ surfactant.

C) Electric arc method:

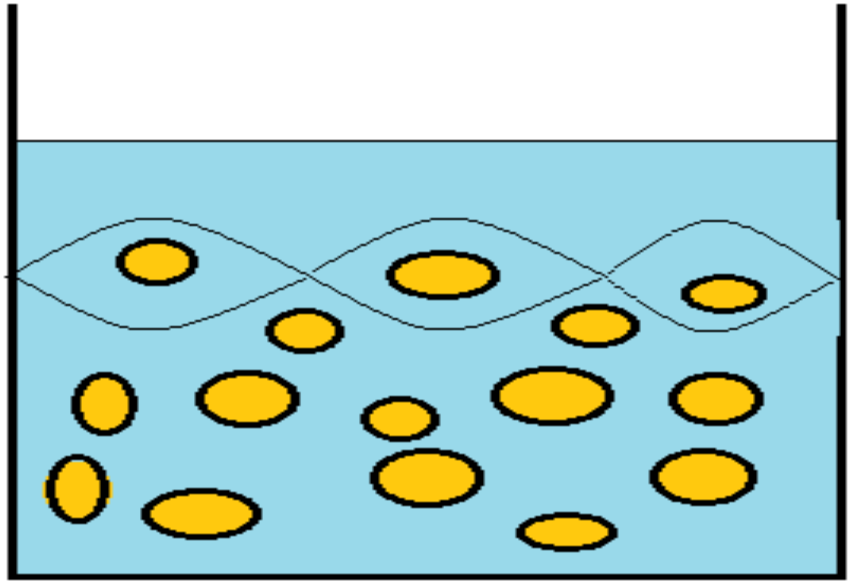
Method suitable for metals- silver, gold.

2 Metal electrodes + cold water ⇨ electric arc formed ⇨ high heat ⇨ metal vapourises ⇩ condense ⇦ colloidal particles + KoH ⇦ Stabilize Dispersion



d) Ultrasonic treatment:

Dispersion medium + Ultrasonic waves ⇒ Cavities & Compressions ⇒ Collapse with force ⇓ Coarse particles breaks ⇐ Colloidal partice + Surfactant ⇐ stabilize dispersion



2. Condensation method (size increasing)

Particles of sub colloidal range aggregate/condense to colloidal range.

Principle:

In supersaturated solution, solute precipitates/ crystallizes in

2 steps- a. nucleation,

b. growth of nuclei

Nuclei is cluster./ group of ions/ molecules.

A stable nuclei attract ions/molecules on surface, size grows

to colloidal range.

a) <u>Addition of non-solvent:</u>

Sulfur soluble in alcohol (solvent),
insoluble in water (non-solvent)

Concentrated + excess ➔ sulfur ➔ size grows ➔ colloidal solution of water precipitates range. sulfur in alcohol

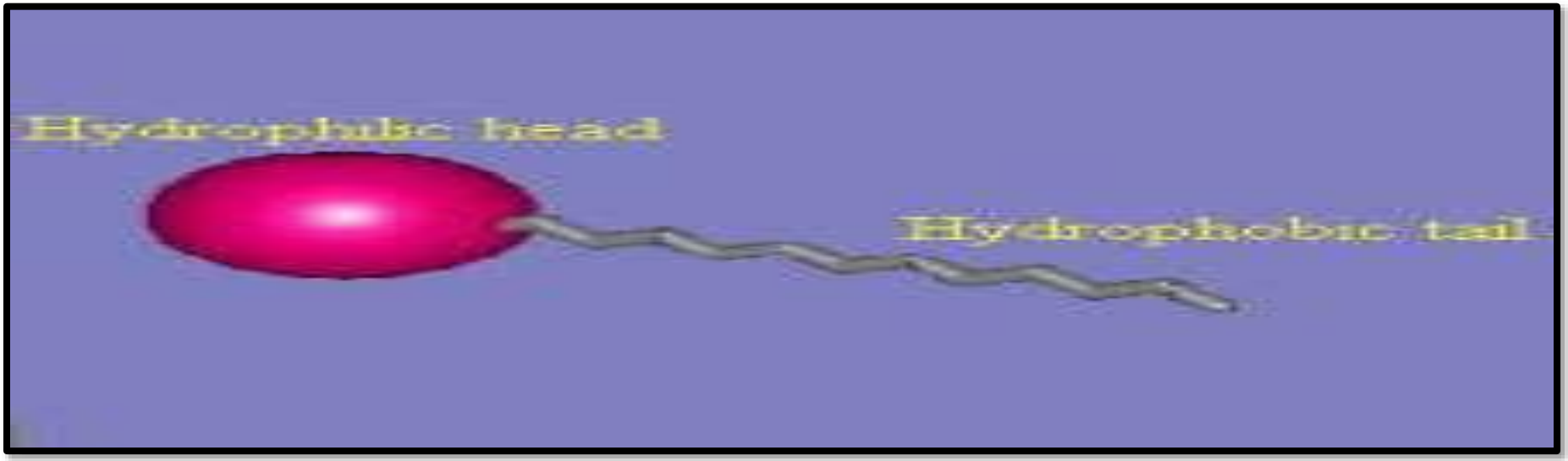
b) <u>Chemical methods:</u>

Chemical reactions of inorganic substances in lyophobic sols form colloids.

1. Gold, silver, platinum-reduction
2. Sulfur-oxidation
3. Ferric oxide-hydrolysis
4. Arsenic oxide-double decomposition.

II) Association colloids/ Amphiphiles:

Amphiphiles are molecules/ions having affinity for both polar and non-polar solvents.



Amphiphiles + water

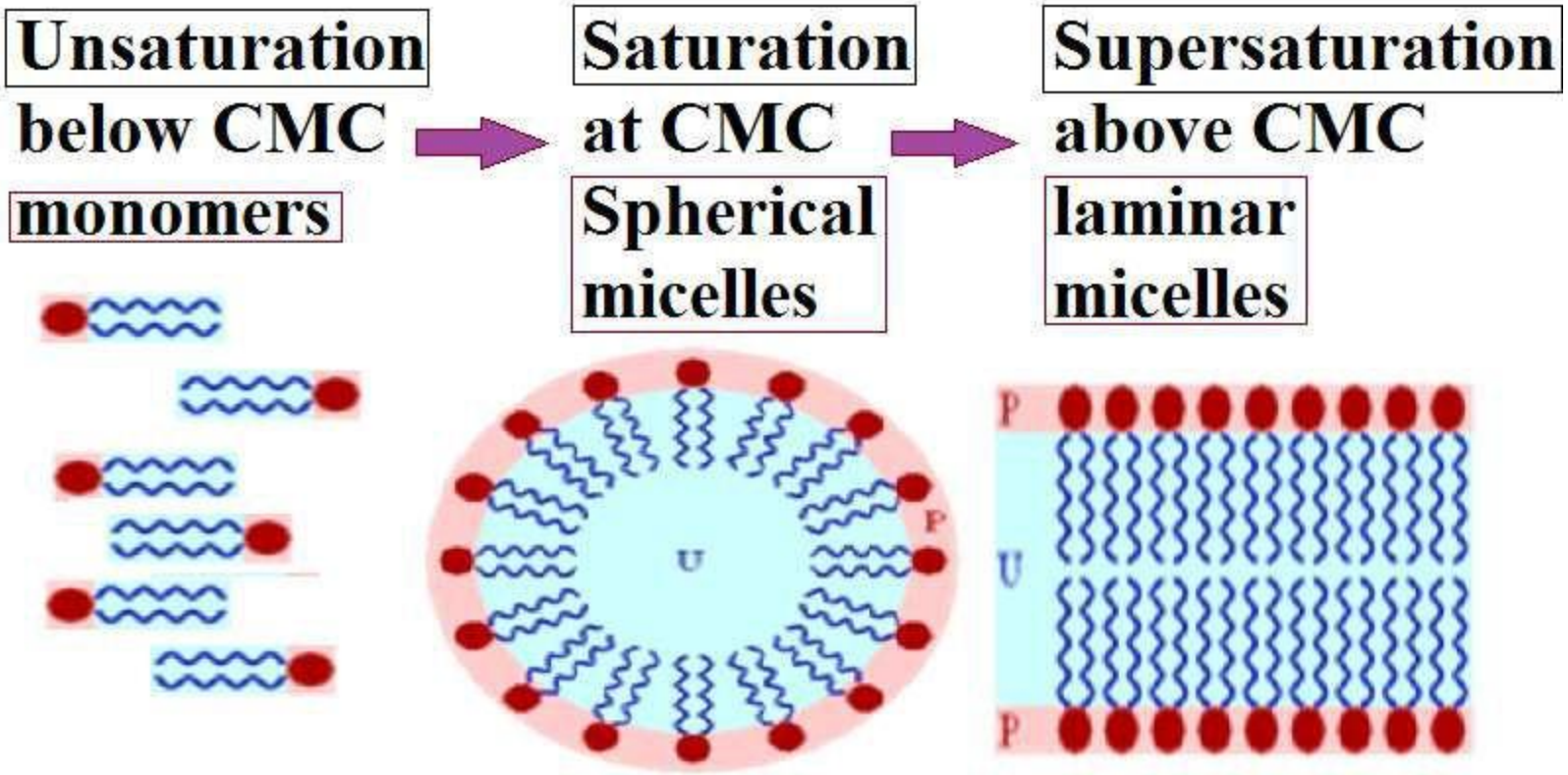
In low conc.➔ momomers of sub-colloidal size

In CMC conc.➔ MICELLES of colloidal size (50 A^0)

CMC (Critical Micellar Concentration):

It is defined as a concentration range of surfactants at which micelles start forming. CMC is concentration range.

Mechanism:



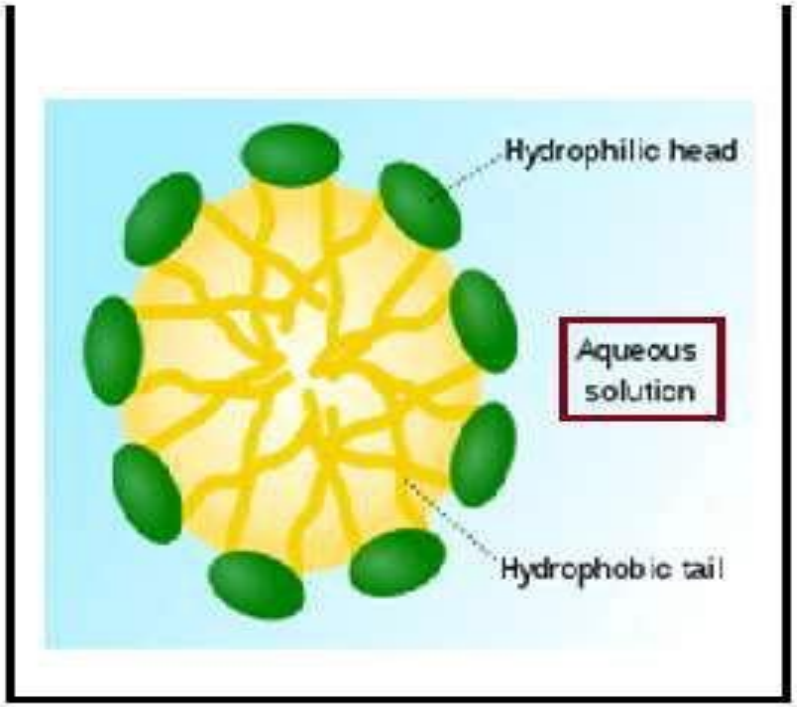
SLS has CMC range of 1-2% W/W

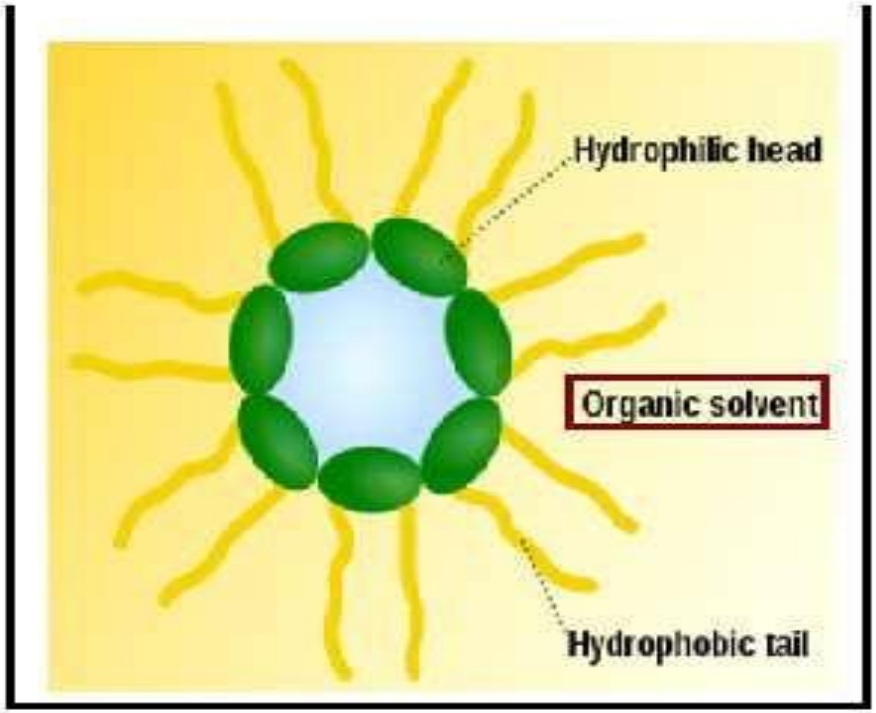
Krafft point (Kt):

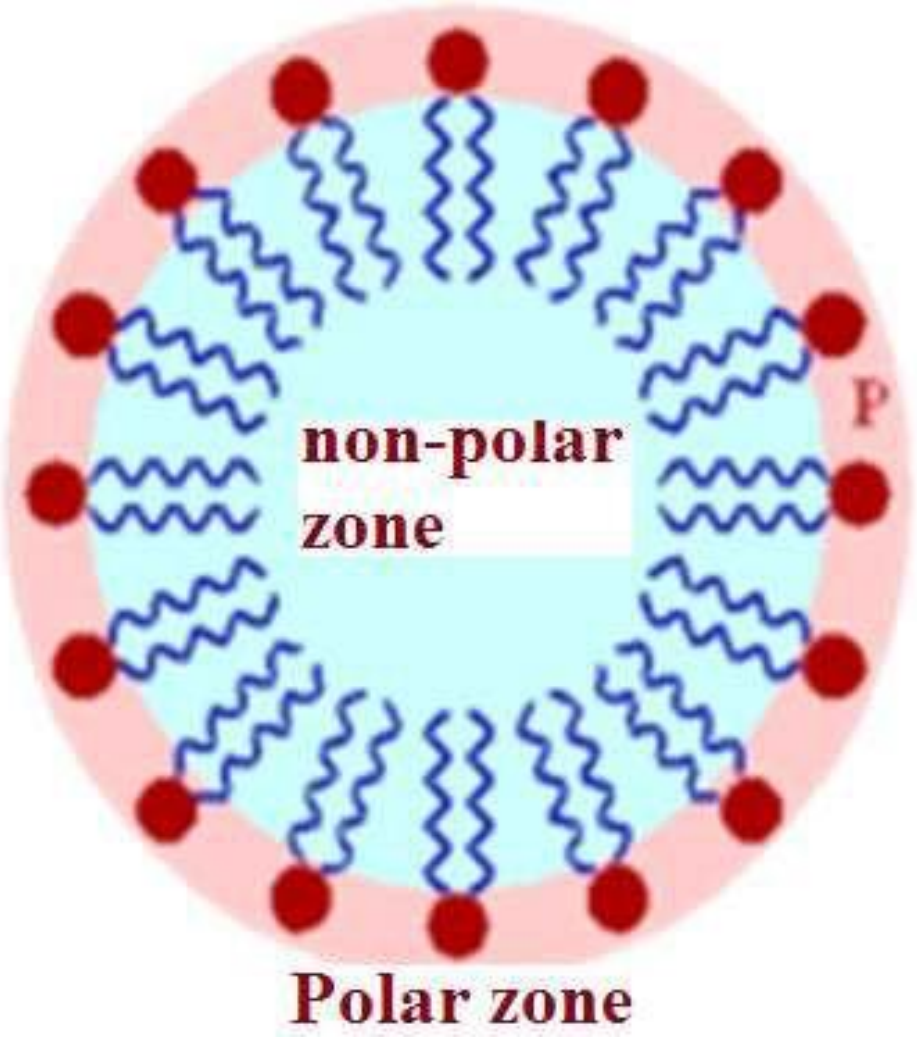
This is defined as the temperature at which solubility of surfactant is equal to the CMC.

Surfactant Applications:

1. Prevent hydrolytic/ oxidative decomposition.
2. Improving solubility of poorly soluble drugs by **micellar solublization.**







Non-ionic surfactant TWEEN-80

1.Benzene, toulene- **non polar** –dissolve in core/ center near tails.

2.Phenol, salicylic acid- **semi polar -** benzene ring dissolve in center, hydrocarbon chain dissolve near heads.

3.P-hydroxy benzoic acid – **polar -** dissolves near heads

Formulation factors:

1.Type of surfactant:

a. non-ionic➔ internal & external use.

b. ionic ➔only external use. Internal use-toxicity.

2.Concentration of surfactant:

a. Low conc. ➔ micelles not formed, drug precipitates.

b. at CMC conc. ➔ Micelles formed, improve solubility, absorption etc.,

c. High conc. ➔ drug tightly binded by laminar micelles, reduced absorption, action.

Surfactant high conc. cause toxicity.

PURIFICATION OF COLLOIDAL DISPERSION:

1. Dialysis
2. Electrodialysis
3. Ultrafiltration

a) Colloidal dispersions + electrolytes → Stable colloids

b) Stable colloids have **dispersed particles, electrolytes, dispersion medium.**

c) Purification is separation of dispersed particles only.

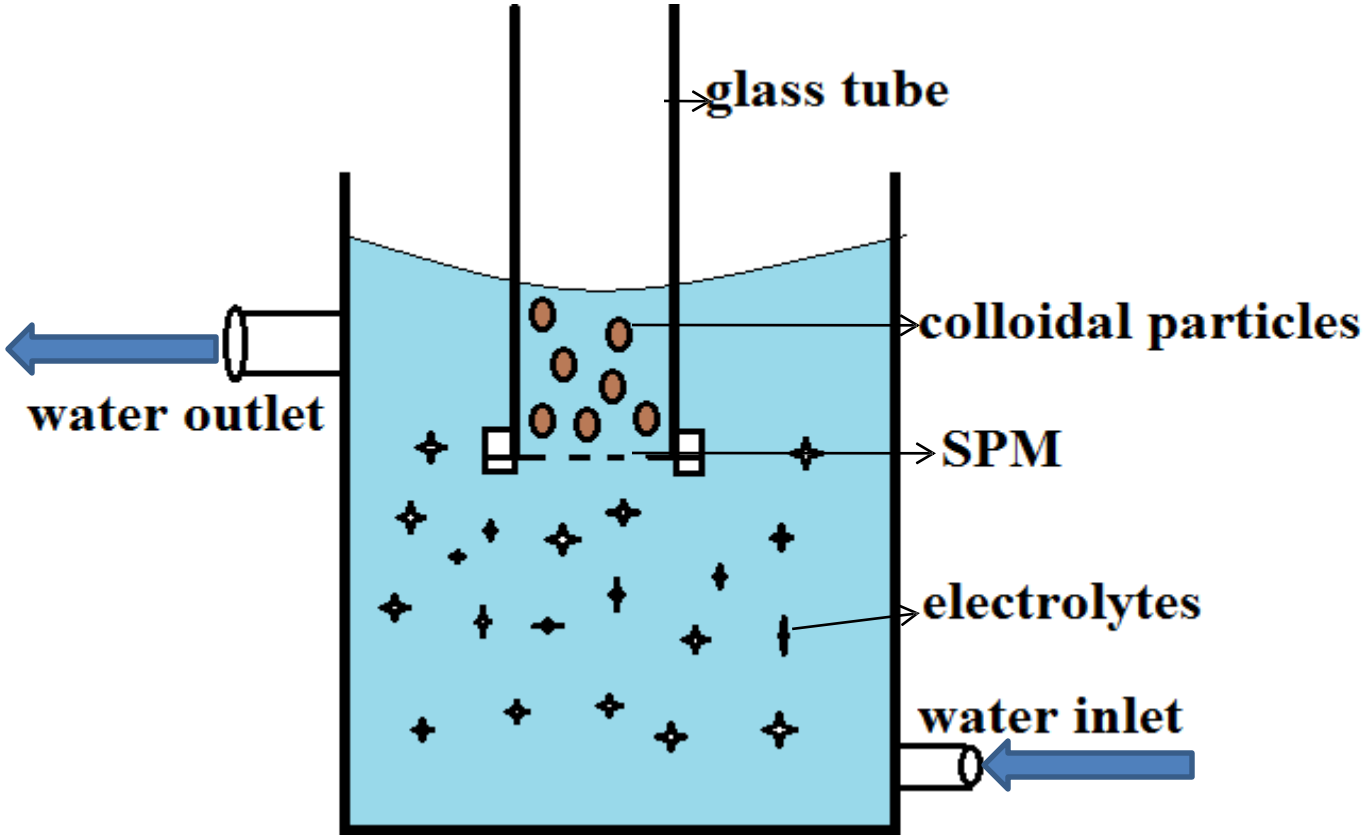
1.Dialysis:

Semi permeable membrane has fine pore.

Ions/small molecules – pass

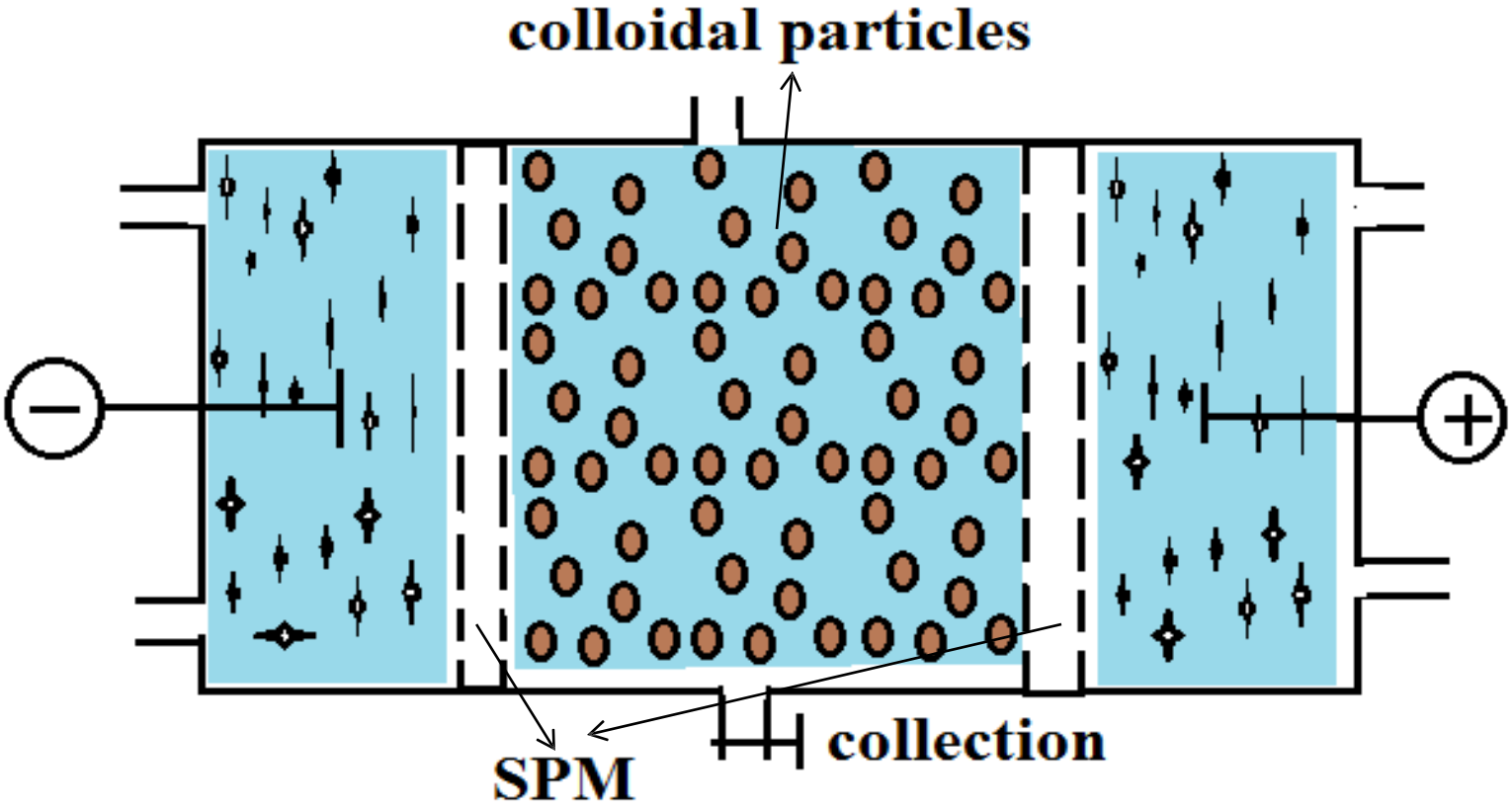
Colloidal particles (large)- retained.

- Solution inside membrane – dialysate
- Solution outside membrane – diffusate



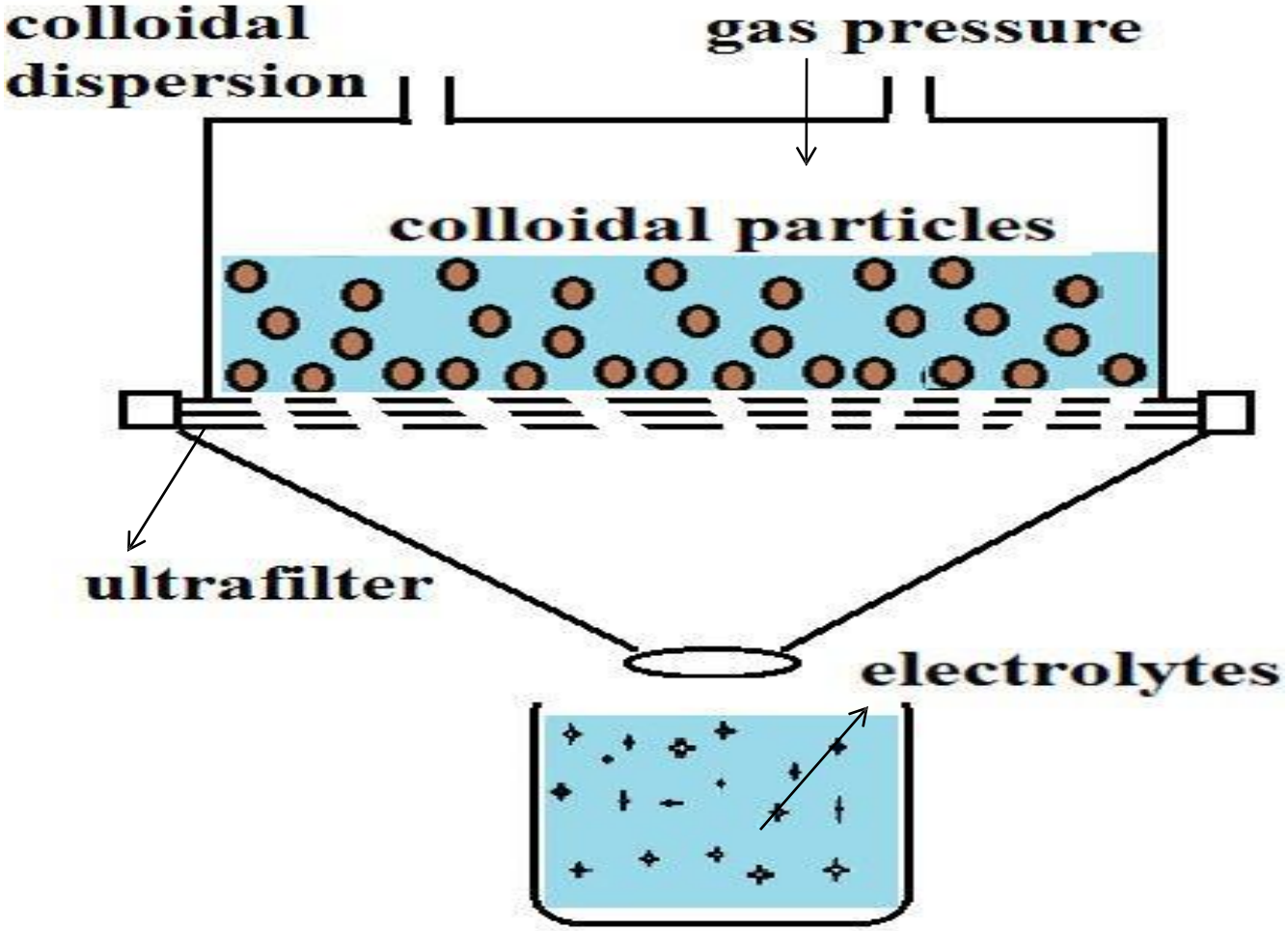
2. Electrodialysis:

- This is similar to diffusion but enhanced by applying potential difference.
- Non-ionic impurities can not be separated.



3. Ultrafiltration:

- Ordinary filter paper has large pore size – not useful
- Ordinary filter paper impregnated with **collodion** has small pores – separate colloid particles.



Pharmaceutical applications of purification:

1.Membrane filters &artificial membranes are used as models to explain principle of diffusion of drug through natural membranes.

2.Drug-protein binding effects can be studied.

3.Principle in haemodialysis technique.

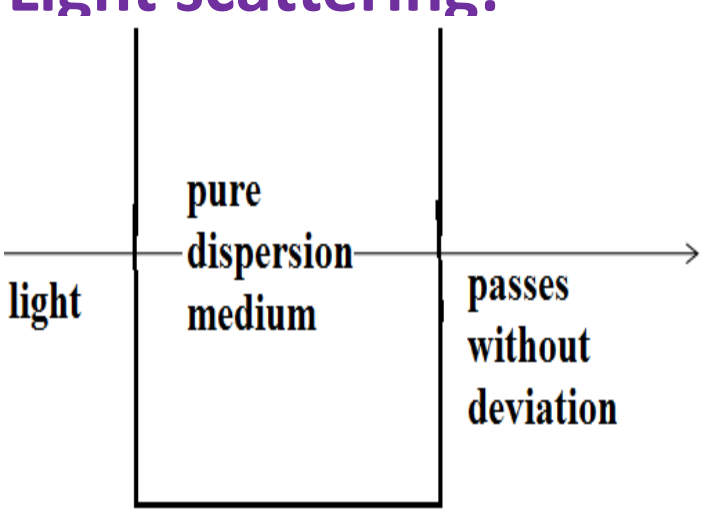
PROPERTIES OF COLLOIDS:

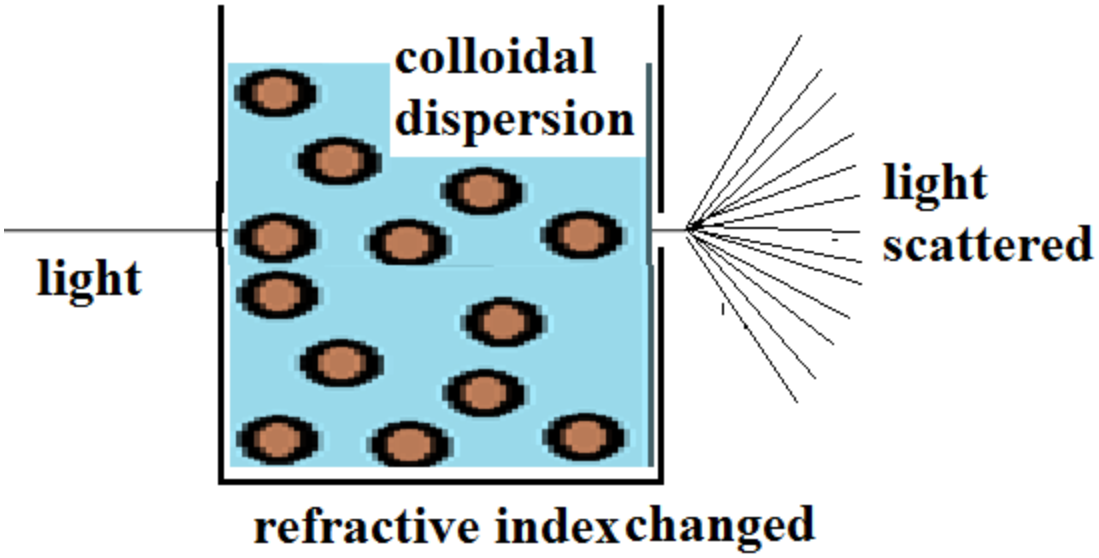
1. Optical properties
2. Kinetic properties
3. Electrical properties

1. Optical properties:

Useful to measure size, shape, structure & molecular weight of colloids. Includes light scattering & turbidity.

Light scattering:



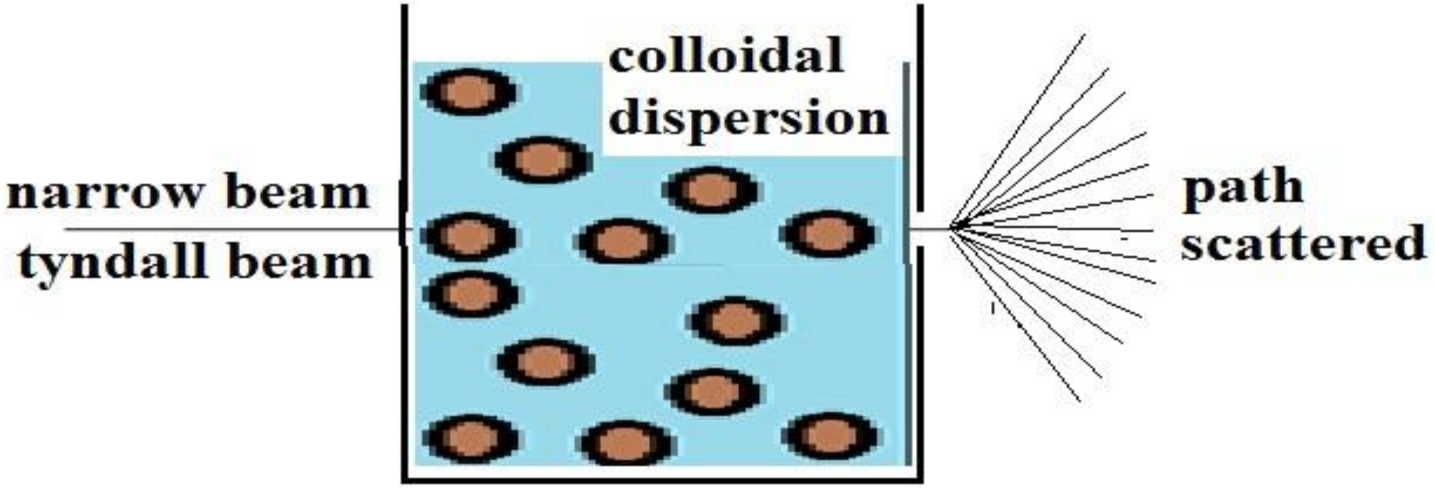


Mechanism:

Light + dispersed particle ➔ polarize atoms/molecules ➔ dipoles ➔ Emmitt light in all directions ➔ **light scattering**

Tyndall effect:

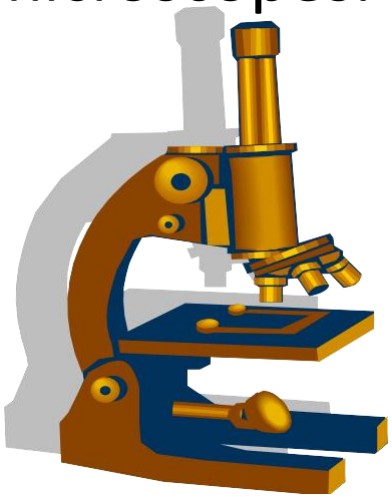
Light scattering is clearly visible in **dark back ground** at **perpendicular angle**.



Light scattering studied in light, ultra, electron microscopes.

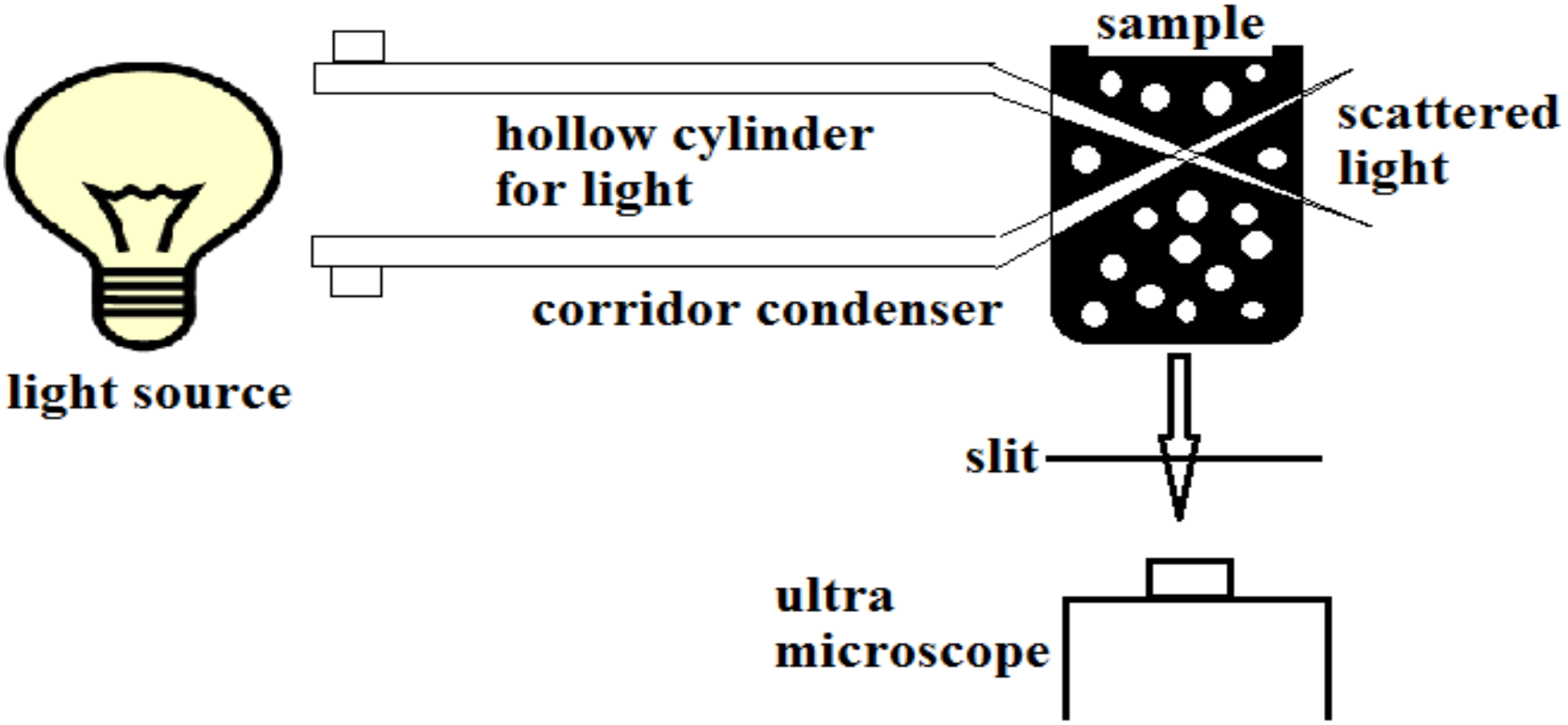
1. Light microscope:

- Source of radiation – visible light
- 2 separate particles are visible if distance between them is 0.2µ.
- Not suitable for colloidal particles.



2. Ultra microscope (dark-field microscope):

- Used to observe tyndall effect,
- Dispersed particles appear as bright spots in dark back ground.
- Used to determine zeta potential.



3. Electron microscope:

- Used to measure particle size, shape, structure .
- Radiation source – high energy electrons ($\lambda = 0.1A^0$)
- As wave length decreases resolution increases.
- Particle photographs can be taken.

Turbidity (τ):

This method is used to estimate **concentration** of dispersed particles and **molecular weight** of solute.

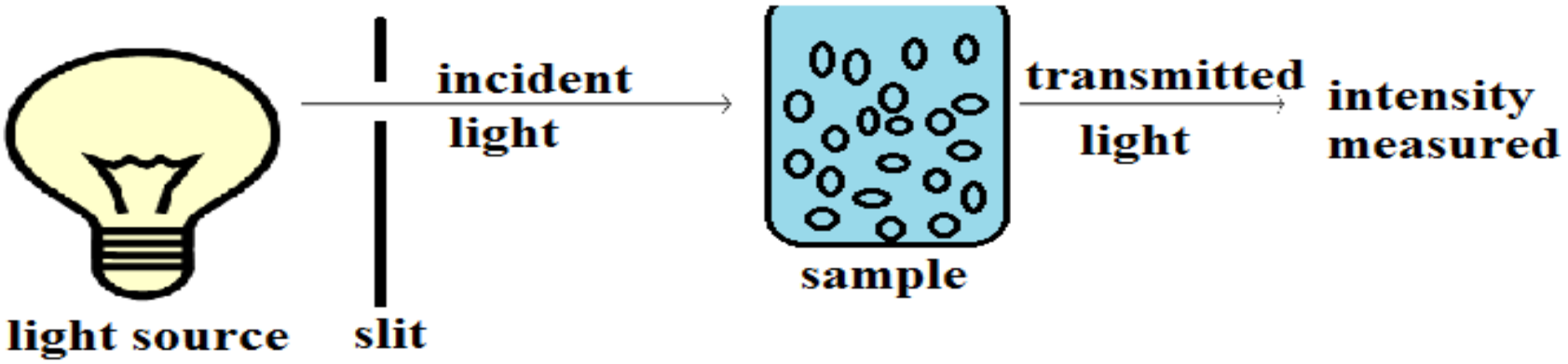
Equipments used

1.Spectrophotometer

2.Nephelometer.

1. Spectrophotometer:

Measures intensity of transmitted light.



Turbidity-light intensity relationship

I0 = intensity of incident light

I = intensity of transmitted light

L = length of sample (1 cm)

τ = turbidity

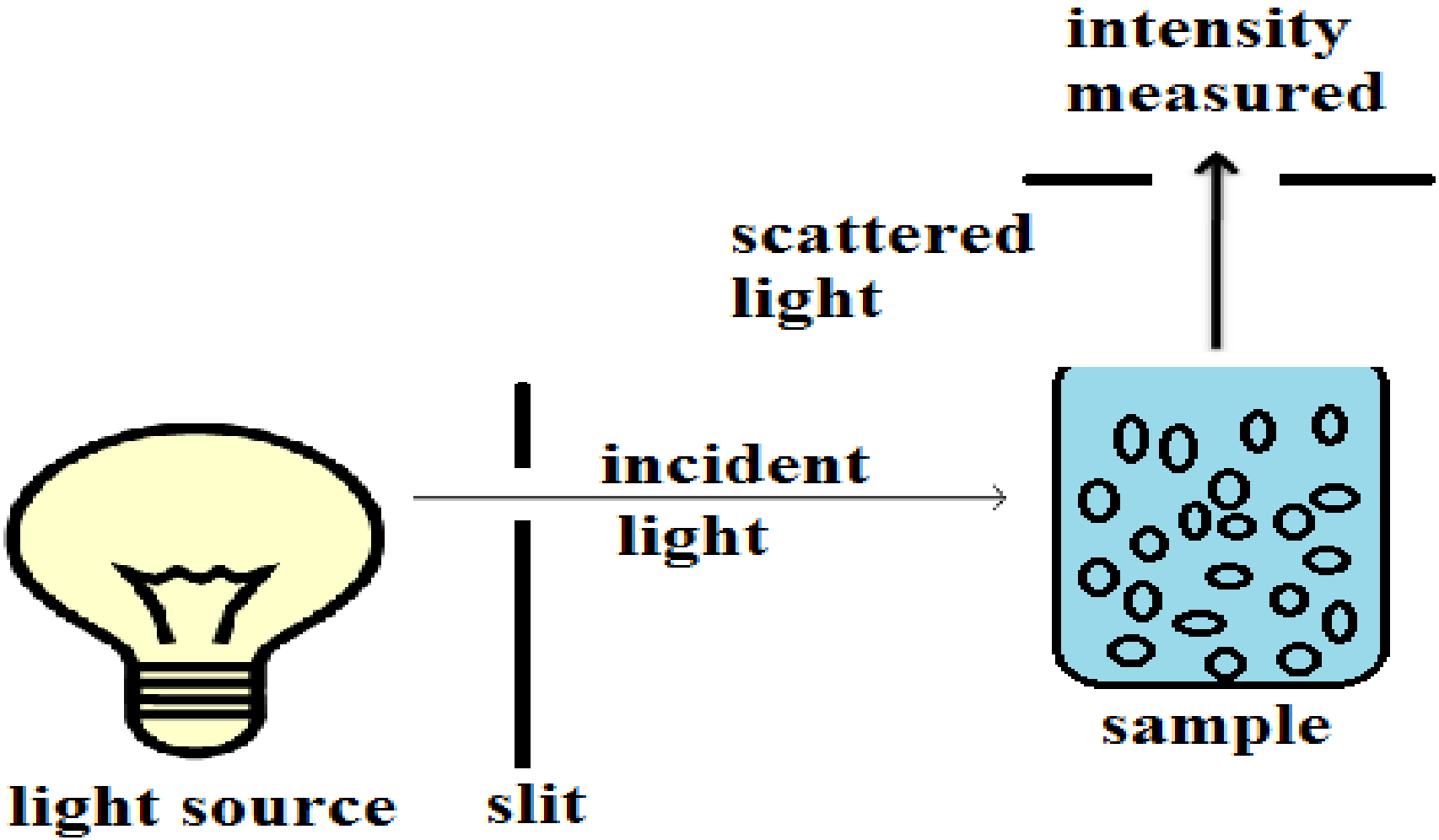
$$I/Io = e^{-\tau L}$$

lyophobic colloids ==> high turbidity ===> high scattering, low transmitance.

lyophilic colloids ==> low turbidity ===> low scattering, high transmitance.

2. Nephelometer:

- Scattered light intensity is measured at 90^0.
- Applicable to lyophilic colloids.



Light scattering – turbidity:

Used to study proteins, polymers, association colloids, lyophilic sols.

Used to measure molecular weight of polymers.

Principle:

Light source > dimensions of → turbidity is measured for
Wavelength particles scattered light.

spherical micelles + light ==> light scattered in all directions

laminar micelles + light ==> adjust in direction of light

$$\tau = 16\pi R_{90}/3$$

$$R_{90} = Ir^2/Io$$

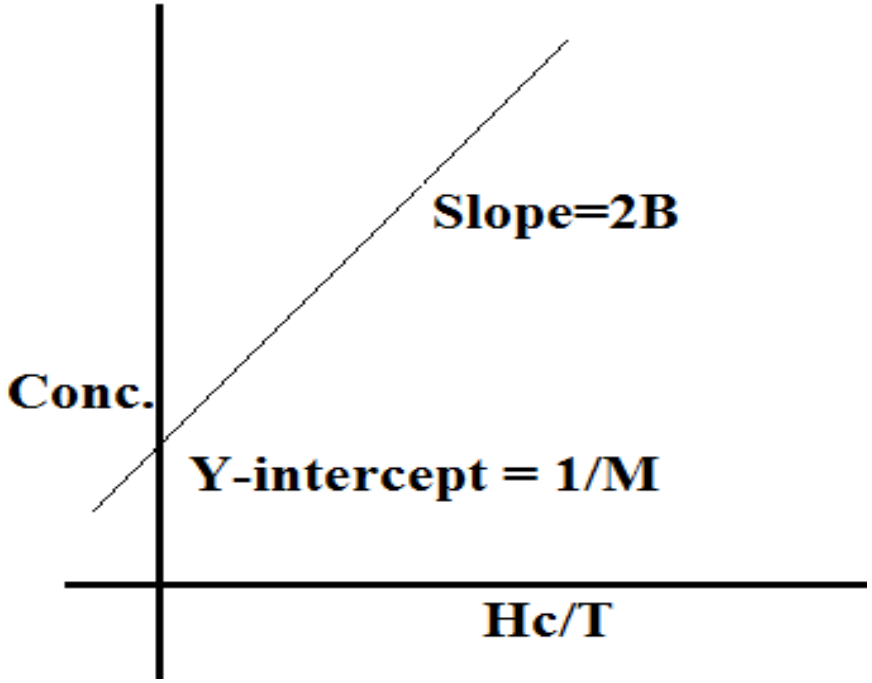
I0 = intensity of incident light I = intensity of scattered light R_{90} = Rayleigh ratio

τ = turbidity

r = distance between scattered particle and point of observation.

Molecular weight – turbidity relation: Graph:

$$\frac{Hc}{\tau} = \frac{1}{M} + 2Bc$$



C = concentration of solute (g/cm^3)

M = average molecular weight of colloid

B = interaction constant of solvent-solute system

H = optical constant depending on refractive index (changes with concentration & wavelength of light used)

2. Kinetic properties:

- Used to detect stability of system, molecular weight of particles, transport kinetics.
- Includes Brownian motion, diffusion, sedimentation, viscosity, colligative properties.

Brownian motion:

- ✓Robert brown theory states colloidal particles (5µm) continuous random motion b/o thermal energy.
- ✓In motion they collide with walls, other particles and change their direction, velocity. (light microscope)
- ✓Particles move against gravitational force.
- ✓Brownian motion stops with increase in size & viscosity.

Diffusion :

Colloidal particles of small size pass through the porous plug b/o brownian motion.

Ficks Ist law: states that particles diffuse spontaneously from a region of high concentration to region of low concentration until diffusion equilibrium is attained.

Application: molecular weight determination.

$$D = \frac{RT}{6\pi\eta_0 N}\sqrt[3]{\frac{4\pi N}{3MV}}$$

D – diffusion experiment

η_0 – capillry viscometer

V – density determination

D = diffusion coefficient of polymer

R = ideal gas constant

T = absolute temperature.

η_0 = viscosity of dispersion medium N= avagardos number

M = molecular weight of polymer

V = partial specific volume of particles.

In **Diffusion experiment** quantity of drug diffused is

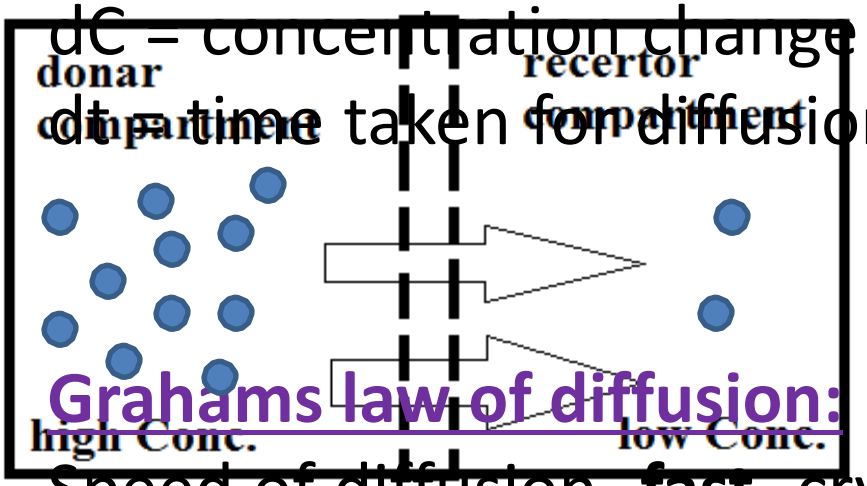
$$\frac{Dq}{dt} = -DS\frac{dc}{dx}$$

Dq = quantity of drug diffused D = diffusion coefficient

S = plane area

dC = concentration change dx = distance travelled

dt = time taken for diffusion.



Grahams law of diffusion:

Speed of diffusion- **fast**- crystalloids (salt, acid, base)

Speed of diffusion- **slow** – colloidal substances (gelatin, albumin)- glue.

Sedimentation:

- This is influenced by gravitational force, applicable for particle size > 0.5 µm.
- Stokes law equation – velocity of sedimentation.
- Colloidal particles have brownian motion → No sedimentation
- Forced sedimentation – ultra centrifuge.

Applications:

1. Molecular weight estimation
2. Study micellar properties of drug.

Colligative properties:

Only **osmotic pressure** is suitable for measurement of molecular weight of dispersed particles.

Viscocity (η):

Affected by many parameters

1.Shape of particle – Spherical (↓ η), Liner shape (↑ η)

2.Affinity of particle to medium - Lyophobic (Liner shape - ↑η)

3.Types of colloid dispersions - dispersion medium of Lyophilic (↑η), Lyophobic (↓ η).

4.Molecular weight of polymers – proportional to viscosity.

Einstein equation –calculate viscosity.

$$\eta = \eta_0 (1+2.5\phi)$$

η = viscosity of dispersion medium η_0 = viscosity of dispersed particles ϕ = volume fraction of particles.

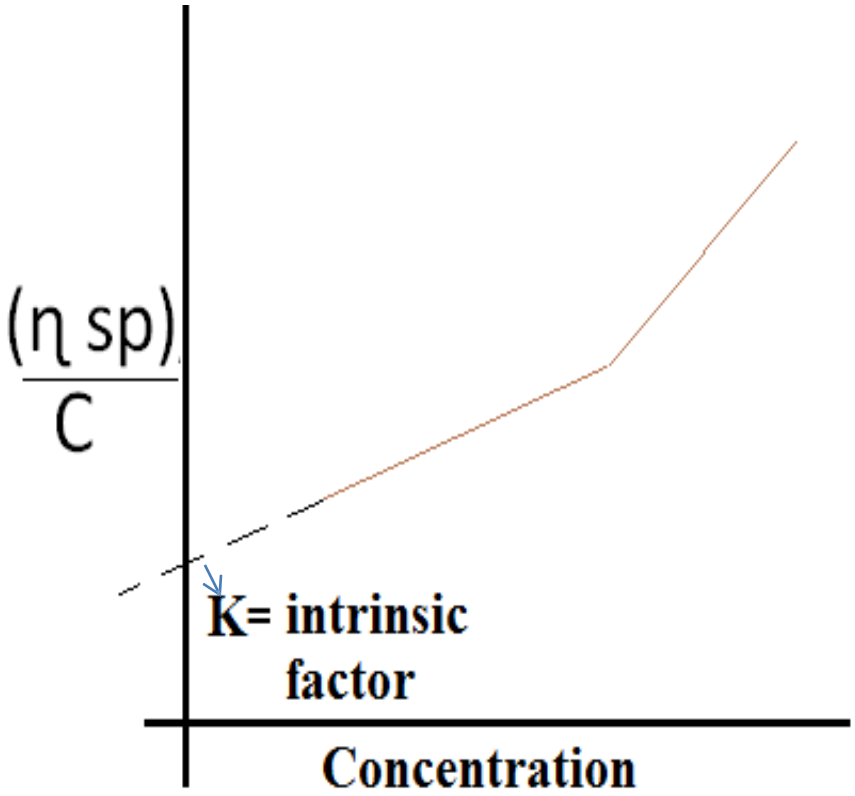
Relative viscosity (η rel) = η/ η0 = 1+2.5ϕ

Specific viscocity (η sp) = η/ η0 -1=

2.5ϕ (η sp) = 2.5ϕ

(η sp)/ϕ = 2.5 (ϕ = concentration of particles)

(η sp)/C = 2.5 = K (K = Intrinsic viscosity factor)



lar weight determination:

Km^a

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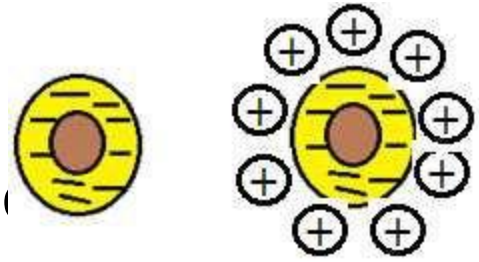
3. Electric properties: Surface charge:



➢Dispersed particles have charge on surfac

➢Dispersed particles added in electrolytic solution forms electrical double layer.

Zeta potential:

✓This is electric potential in the plane of shear of the charged particle.

✓Used in predicting stability of colloidal dispersion

Electrophoresis:

❖Used to determine **sign & magnitude** of zeta potential.

❖This involves movement of charged particles under the influence of an applied potential difference.

Sign:

Particles move towards anode – colloid (-) charged.

Particles move towards cathode – colloid (+) charged

Magnitude:

Rate of migration depends on charge of particle & potential gradient applied.

Ultra microscope measures magnitude, standardized by particles of known potential (RBC of rabbit).

Velocity of particle migration **α** potential gradient applied

V=ζ E

(zeta)ζ= V/E

Velocity also depends on dielectric constant and viscosity.

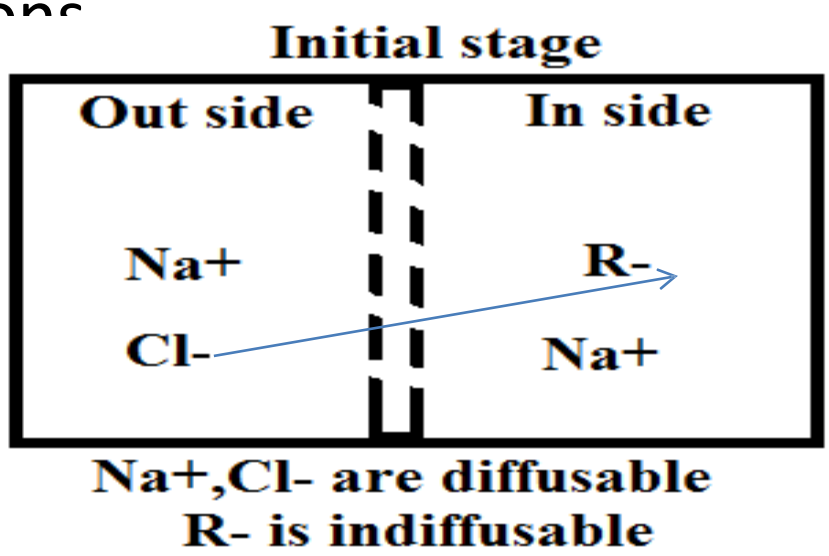
$$\zeta = \frac{V}{E} X \frac{4\pi\eta}{\varepsilon}$$

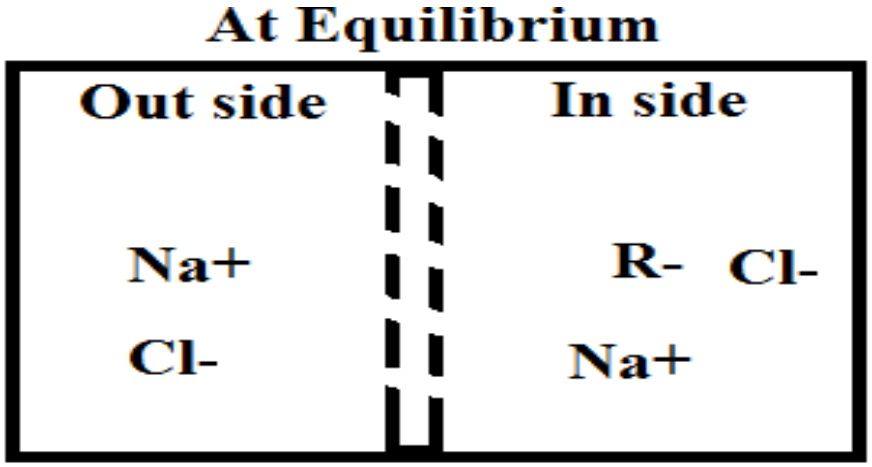
DONNAN- MEMBRANE EQUILIBRIUM:

This principle is used to enhance the absorption of drugs such as sodium salicylate & potassium benzyl penicillin by using **sodium CMC**. ($CMC^- Na^+$)

- Sodium CMC is anionic pro-electrolyte, non diffusable.
- Sodium CMC + anionic drug → drug diffusable, increase absorption of drug.

Other ex:- Ion-exchange resins of sulphate & phosphate ions





At Equilibrium ➔ Charge balance ➔ Electro neutrality

Out side ➔ [Na+]o = [Cl-]o

In side ➔ [Na+]I = [Cl-]I + [R-]I

According to principle of escaping tendency of the electrolytes concentration on both sides of the membrane should be same. (outside = inside)

[Na+]o [Cl-]o = [Na+]I [Cl-]I

Converting to [Cl-] concentrations.

[Cl-]o [Cl-]o = ([Cl-]I + [R-]I) [Cl-]I

$$[Cl-]o^2 = [Cl-]I \left(1 + \frac{[R-]I}{[Cl-]I}\right)$$

$$\frac{[Cl-]o^2}{[Cl-]I^2} = 1 + \frac{[R-]I}{[Cl-]I}$$

[R-] = CMC-

[Cl-] = Drug = [D-]

$$\frac{[Cl-]o}{[Cl-]I} = \sqrt{1 + \frac{[R-]I}{[Cl-]I}}$$

$$\frac{[D-]o}{[D-]I} = \sqrt{1 + \frac{[R-]I}{[D-]I}}$$

Equation helps in selecting appropriate concentration of components.

CASE- 1

If [R-]I/[D-]I= 8; then [D-]o /[D-]I = 3 ➔ D out= 3 D in

CASE- 2

If [R-]I/[D-]I= 99; then [D-]o /[D-]I = 10 ➔ D out = 10 D in

(GIT) (Blood)

STABILITY OF COLLOIDS:

Good colloidal dispersions should not change until usage. Colloidal dispersion stable (Brownian motion), unstable (Precipitate)

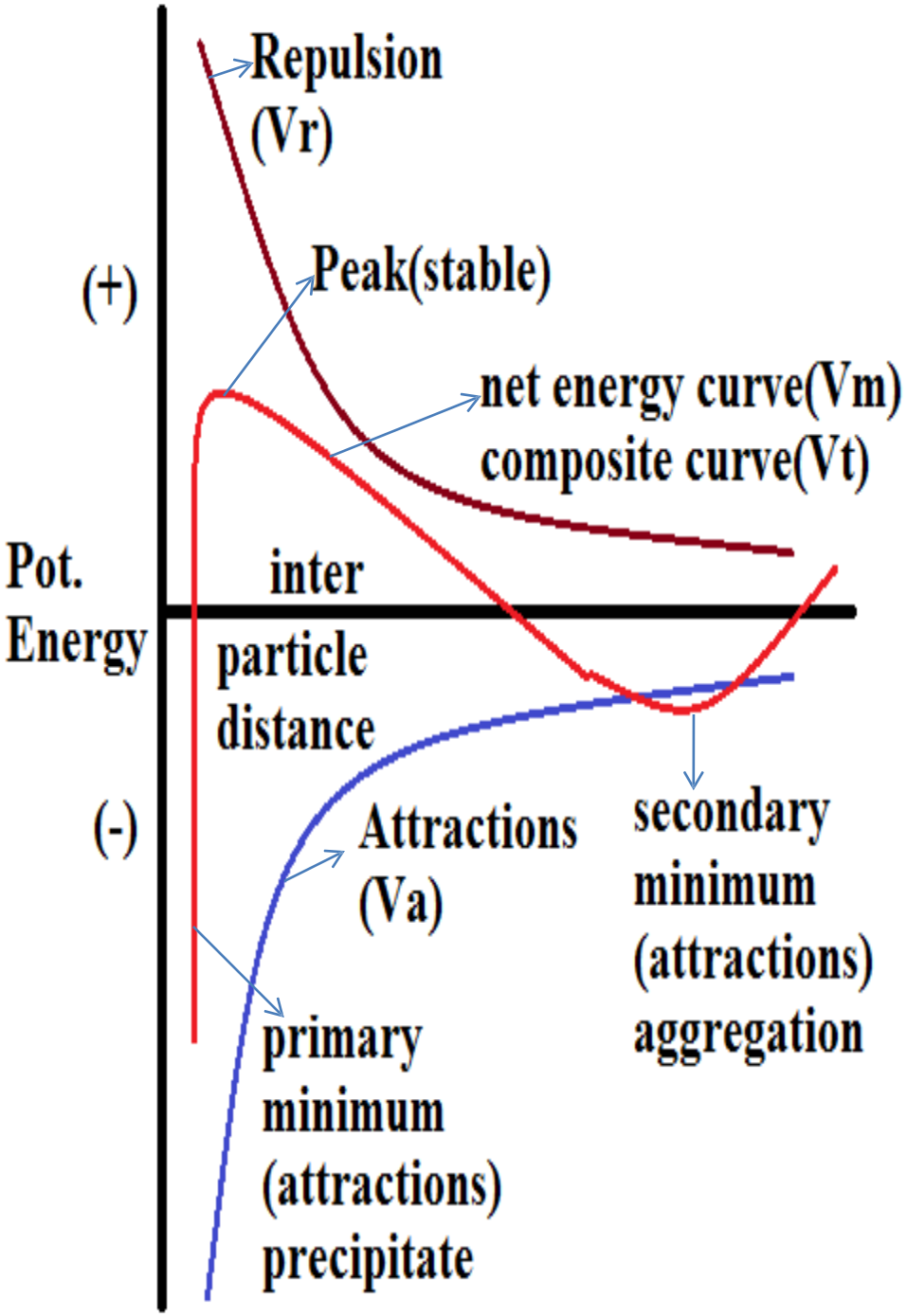
Stability reasons:

1. Lyophilic – solvent sheath on particles.
2. Lyophobic – electric charge on particles.

Lyophobic colloids stability:

DLVO theory- Derjaguin, Landau, Verway & Overbeek

- This theory is based on distance between 2 particles and their interactions
- Colloidal particles exhibit brownian motion causing collisions between particles.
- Amount of electrolytes control stabilization & Precipitation.



Particle interactions:

1.Vanderwaals attraction forces:

Chemical nature, size of particle

Attraction curve (Va)

2.Electrostatic repulsive curve:

Density, surface charge, thickness of EDL.

Repulsion curve (Vr)

Zeta potential stable range 20-50 mv.

3.Net energy interactions:

Algebraic additions of 2 curves (Vt)

Conclusions:

1.Primary minimum:

Particles close ➔ atomic orbital's overlap ➔ Pot. Energy ↑ ➔ Aggregates.

2.Secondary minimum:

Particles separated (1000-2000 A^0) ➔ Attractions ➔

Aggregates.

Used in controlled flocculation.

3.Net energy peak:

At intermediate distance (3-4A^0) ➔ Attractions= Repulsions ➔ Brownian motion ➔ Stable = Zeta potential (50 mv)

Peak height is proportional to Stability.

INSTABILITY OF LYOPHOBIC COLLOIDS:

Breakage of potential energy barrier leads to precipitation/ agglomeration.

Instability Methods:

1.Reducing height of potential ba

2.Increasing the kinetic energy, reduces potential energy

Instability reasons:

1.Removal of electrolyte (1^0 minimum)

2.Addition of electrolyte (2^0 minimum)

3.Addition of electrolytes of opposite charge (2^0 minimum)

1. Removal of electrolyte (1^0 minimum)

Colloids + electrolytes ➔ stable colloidal dispersion

Dialysis = remove Electrolytes ➔ Particles coagulate ➔Settle to bottom.

2.Addition of electrolyte (2^0 minimum)

Stable colloidal dispersion + excess electrolyte ➔ electrolyte Accumulate ➔ instability.

3.Addition of electrolytes of opposite charge (2^0 minimum)

Stable colloidal dispersion + electrolyte opposite charge ➔ attractions between particles ➔ flocculation of particles.

$Al^{+3} > Ba^{+2} > Na^{+}$ $SO_4^{-2} > Cl^{-}$

Schulze-Hardy Rule: Precipitating power of ionic charge

4. Addition of oppositely charged colloid (2^0 minimum)

Bismuth colloids (+) + Tragacanth colloids (-) ➔ Coagulation.

INSTABILITY OF LYOPHILIC COLLOIDS:

Stability – Solvent Sheath

Instability – aggregation/ precip

Instability reasons:

1.Addition of excess electrolyte

2.Addition of oppositely charged colloid

3.Addition of non-solvent.

➢**Addition of excess electrolyte:**

Electrolyte normal Conc➔Zeta potential↓➔No Coagulation Electrolyte high Conc➔ ions + water ➔No solvent for sheath **Hofmeister Rank Order:**

States that the precipitating power of an ion is directly related to ability of that ion to separate water molecule from colloidal particle.

$Mg^{+2} > Ca^{+2} > Na^{+} \quad Cl^{-} > Br^{-} > I^{-}$

- **Addition of oppositely charged colloid**

Gelatin Colloid [+] + Acacia Colloid [-] ➔ Electrostatic attractive forces ➔ Solvent sheath break ➔Particles aggregate.

- **Addition of non-solvent.**

Colloidal Dispersion + Alcohol/Acetone

Water(solvent) + Alcohol/Acetone(non-solvent) ➔ Solution. No water, No solvent Sheath ➔ Unstable colloid.

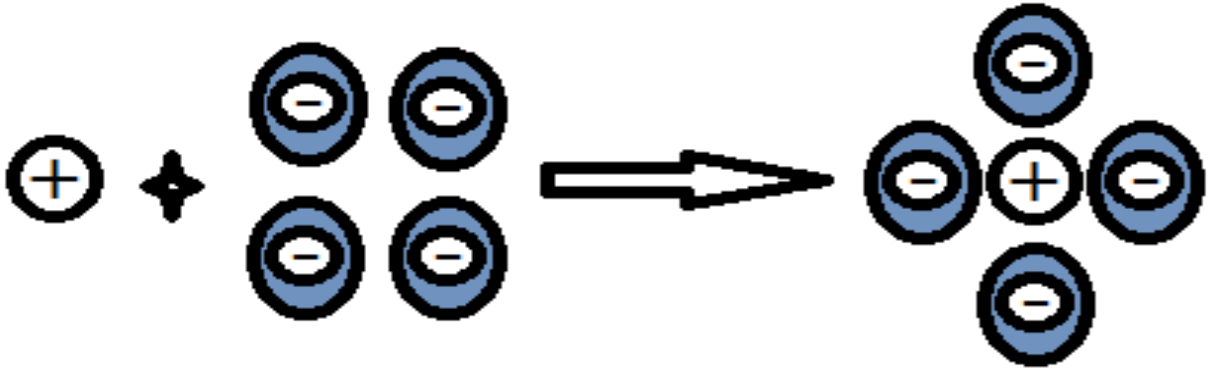
Sensitization & Protective colloidal action:

1.Lyophobic colloid + excess electrolyte ➔ charge neutralize ➔ Precipitation.

2.Lyophobic colloid + Lyophilic colloid (**low Conc**) ➔ **Sensitization** ➔ Add electrolyte ➔Precipitation.

3.Lyophobic colloid + Lyophilic colloid (**High Conc**) ➔ **Protective colloid** ➔ Add electrolyte ➔ ions can not reach particle ➔No Precipitation.

Sensitization



Protective colloid

The colloids that help in stabilizing other colloids are called **Protective colloids.**

This protective colloidal property is measured in **GOLD NUMBER.**

Ex:

1.Colloidal gold (red) + electrolyte → coagulation (violet)

2.Colloidal gold (red) + Gelatin Colloid → Protective Colloid (red)

Thank you…….