PV® BOOKS

THEORY CUM PRACTICAL

A Text Book of

PHYSICAL PHARMACEUTICS-II

Strictly As Per Syllabus Prescribed for B. Pharmacy, Semester-IV by Pharmacy Council of India, New Delhi

DR. SHALINI SHARMA
RAVIKIRAN MAHESHRAO SURYAWANSHI
DR. JAGDEEP SINGH DUA

Pee Vee (Regd.)

CONTENTS
(THEORY)
UNIT-I

UNIT-II

UNIT-III

UNIT-I

1 COLLOIDAL DISPERSIONS

Colloidal dispersions: Classification of dispersed systems & their general characteristics, size & shapes of colloidal particles, classification of colloids & comparative account of their general properties. Optical, kinetic & electrical properties. Effect of electrolytes, coacervation, peptization & protective action.

SELECTED DEFINITIONS

Colloidal dispersion: It is a heterogeneous system consist of dispersed phase and dispersion medium in which the particle size of dispersed phase ranges from 1nm to 1μm.

Molecular dispersions: It is the dispersion in which the size of particle is less than 1 nm.

Colloidal dispersions: These are the dispersion in which the size of particle is from 1 nm to 0.5 μm.

Coarse dispersions: These are the dispersion in which the size of particle is greater than 0.5 μm.

Lyophilic colloid : If the dispersed phase interact to a great extent with the dispersion medium, then colloid is called a lyophilic colloid.

Lyophobic colloids: If the dispersed phase has little or no affinity to interact with dispersion medium, then colloid is called a lyophobic colloid.

Peptization: It is the process in which aggregates are break into colloidal size particle in the presence of peptizing agent.

Critical Micelle Concentration(CMC): The concentration at which micelles begins to form.

Tyndall Effect: When a beam of light is pass through a colloidal solution, the path of light gets illuminated. This phenomenon is known as Tyndall Effect.

Brownian movement: The continuous collisions between the colloidal particles and molecules of dispersion medium produce zigzag movement of colloidal particles which is known as Brownian movement.

Electrophoresis: The movement of colloidal particles through a liquid under the influence of electric field.

Donnan effect: It describe the behaviour of charged particle near semi permeable membrane that sometime fails to distribute equally across the two side of membrane. This is due to the presence of different charged substance which are unable to pass through membrane and therefore they create uneven electrical charge.

Sedimentation potential: It is the potential difference develop when particles settle under the influence of gravity. It is reverse of electrophoresis.

Dispersion medium	Type of colloidal dispersion	Example
Liquid	Foam	Soap, beer, lemonade
Solid	Solid Foam	Pumice stone
Gas	Liquid Aerosol	Fog, dust
Liquid	Emulsion	Milk, rubber
Solid	Gel	Butter, Cheese
Gas	Solid Aerosol	Dust
Liquid	Sol	Paste, ink
Solid	Solid sol	Pearls, gem stones

1.2 SIZE & SHAPES OF COLLOIDAL PARTICLES

1.2.1 PARTICLE SIZE

The colour of colloidal dispersions is affected by the size of the particles present. If the particles in a red gold sol are large in size, the dispersion occurs on a blue colour. While Antimony and arsenic trisulfides change from red to yellow as the particle size is decreased.

Based on the size of the dispersed phase, three types of dispersed systems are generally considered:

(a) Molecular dispersions: The size of particle in case of molecular dispersion is less than 1 nm. They are invisible in electron microscope. They can pass through ultrafilter and semipermeable membrane. They undergo rapid diffusion. Examples: Oxygen molecules, ordinary ions, glucose

(b) Colloidal dispersions: The size of particle in case of colloidal dispersion is from 1 nm to 0.5 μm. They are detected by ultramicroscope. They can pass through filter paper but do not pass semipermeable membrane. They diffuse very slowly. Example: Colloidal silver sols, natural and synthetic polymers, cheese, butter, jelly, paint, milk, shaving cream, etc.

(c) Coarse dispersions: The size of particle is greater than 0.5 μm. They are visible under microscope. They do not pass through normal filter paper. They do not dialyze through semipermeable membrane. They do not diffuse. Example: Grains of sand, most pharmaceutical emulsions and suspensions, red blood cells.

1.2.2 PARTICLE SHAPE

The shape of colloidal particles is also important. On extending the particle, the specific surface also get increased and therefore there will be greater opportunity for attractive forces to establish between the particles of the dispersed phase and the dispersion medium. Other properties such as flow, sedimentation, and osmotic pressure are also affected by changing in the shape of colloidal particles. Particle shape is also related to pharmacological action.

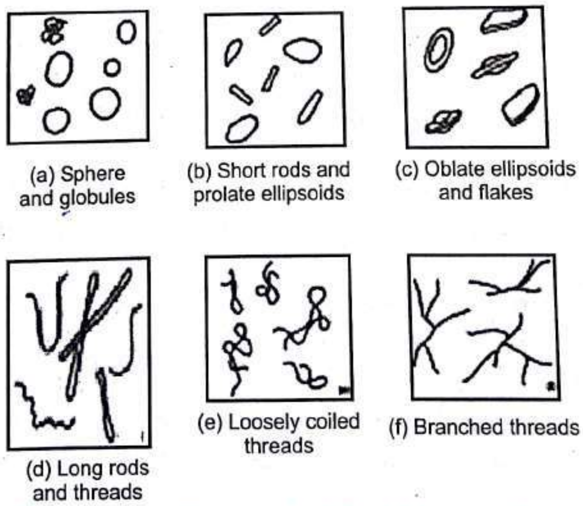


Figure 1.1: Shape of colloidal particle

Other characteristics of dispersed phase include Surface area and Surface charges. The large surface area of colloidal particles act as catalyst and it also increase the solubility of drug particles. The charge on colloidal particles provide information regarding the stability of colloids.

1.3 CLASSIFICATION OF COLLOIDS

Depending on the nature of the interaction between the dispersion medium and the dispersed phase, colloids can be classified into lyophilic, lyophobic and association.

1.3.1 LYOPHILLIC COLLOIDS

The term lyophillic consist of lyo and philic. Lyo means **'liquid'** and philic means **'loving'**. If the dispersed phase interact to a great extent with the dispersion medium, then colloid is called a lyophillic colloid. If dispersion medium is water then they are called hydrophillic colloids and if dispersion medium is non aqueous organic solvents then they are called lipophillic colloids. Lyophillic colloids are thermodynamically stable and therefore they are difficult to coagulate. They can be readily reconstituted by simply mixing. They are also called intrinsic colloid. Examples : starch, rubber, protein

1.3.2 LYOPHOBIC COLLOIDS

The term lyophobic consist of lyo and phobic. Lyo means **'liquid'** and phobic means **'hating'**. Hence, they are liquid-hating. If the dispersed phase has little or no affinity to interact with dispersion medium, then colloid is called a lyophobic colloid. They are thermodynamically unstable. They require stabilizing agents for their preservation. They are also known as **extrinsic colloids.** Examples are sols of metals like silver and gold, sols of metallic hydroxides, etc. They are difficult to prepare as they require some special methods. They are prepared by dispersion method and condensation methods.

(a) **Dispersion methods:** In this method coarse particles are reduced in size. Dispersion can be achieved

(1) By the use of high-intensity ultrasonic generators with frequencies in excess of 20,000 cycles per second.

(2) 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 vapor, which condenses to form colloidal particles.

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

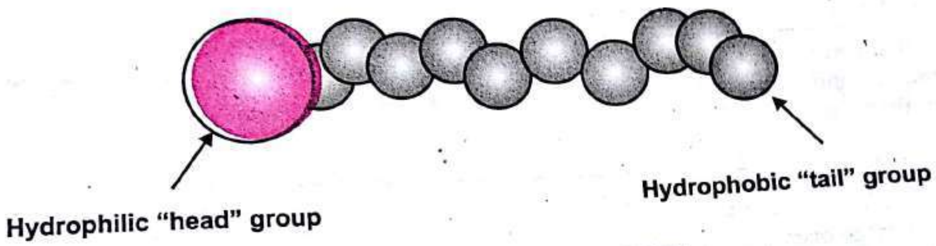
(4) Colloid mills is also used in which the material is sheared between two rapidly rotating plates set close together.

(5) **Peptization:** It is the process in which aggregates are break into colloidal size particle in the presence of peptizing agent. Peptizing agent may be liquid, electrolytes and non electrolytes.

(b) **Condensation Method:**This method involve high degree of initial supersaturation and then the formation and growth of nuclei. Supersaturation can be achieved by change in solvent or reduction in temperature. Other condensation methods depend on a chemical reaction, such as reduction, oxidation, hydrolysis, and double decomposition.

1.3.3 ASSOCIATION COLLOIDS

They are also considered as Amphiphillic colloids. At low concentrations, the amphiphiles exist separately. As the concentration is increased, aggregation occurs over a narrow concentration range. These aggregates are called micelles.



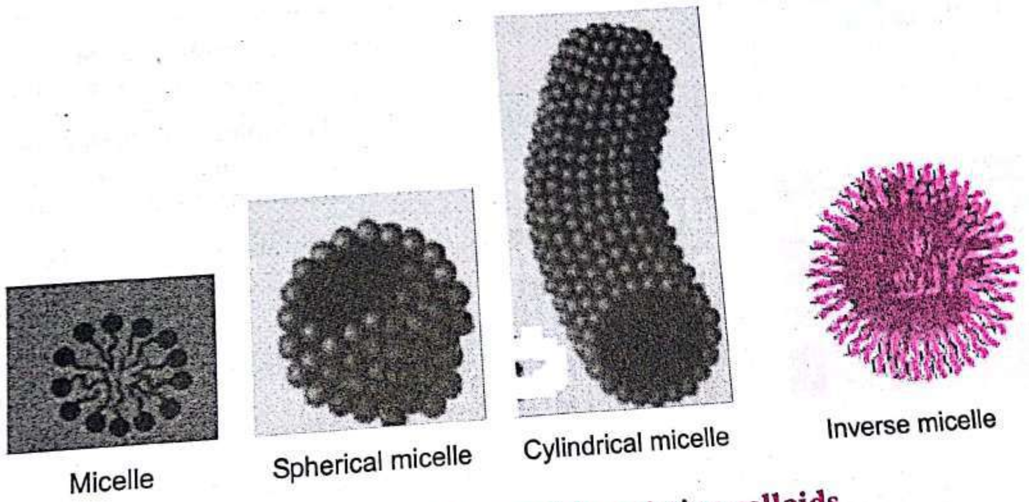


Figure 1.2: Shape of Association colloids

The concentration at which micelles begins to form is called the critical micelle concentration(CMC). Below the CMC, surface active agents undergo adsorption at the air–water interface. With increasing the concentration of surfactants, molecules get accumulated at the interface . At one point where both the interface and the bulk phase become saturated with monomers. This is the CMC. Beyond CMC, on adding more surfactant micelles formation take place in the bulk phase, and therefore the free energy of the system is reduced.

Table 1.2 General properties of different types of colloids

Lyophillic colloids	Lyophobic colloids	Association Colloids
They are liquid loving colloids	They are liquid hating colloids	These are aggregates of surface active agents.
Their sols are **easy** to prepare and can be prepared directly by mixing colloid with liquid.	Special methods are employed to prepare lyophobic sols	They form readily when concentration is equal to CMC.
Lyophilic sols are stable in presence of electrolytes at low concentration but get precipitate at high concentration	Lyophobic sols are unstable in presence of electrolytes at low concentration but stable at high concentration	CMC get decreased in presence of electrolytes
The lyophilic colloids are highly viscous in nature and have higher viscosity than that of the medium.	The Lyophobic colloids have almost same viscosity as that of medium	Not greatly increase in viscosity
Reversible	Irreversible	Reversible
Dispersed phase is large organic molecules of colloidal size	Dispersed phase is inorganic molecules	Dispersed phase is micelles of organic molecules or ions but size below colloidal range
They are solvated	They are little solvated	Hydrophilic or lipophillic side of molecule is solvated depending on the medium.
They are less charged	They are highly charged	They are charged micelles.

1.4 PROPERTIES OF COLLOIDS

1.4.1 OPTICAL PROPERTIES

a. **Tyndall effect:** Tyndall, in 1869, observed that when a beam of light is pass through a colloidal solution, the path of light gets illuminated. This phenomenon is known as Tyndall Effect. The light is scattered due to presence of particles in colloidal solution. The intensity of the scattered light is related to the difference between the refractive indices of the dispersed phase and the dispersion medium.

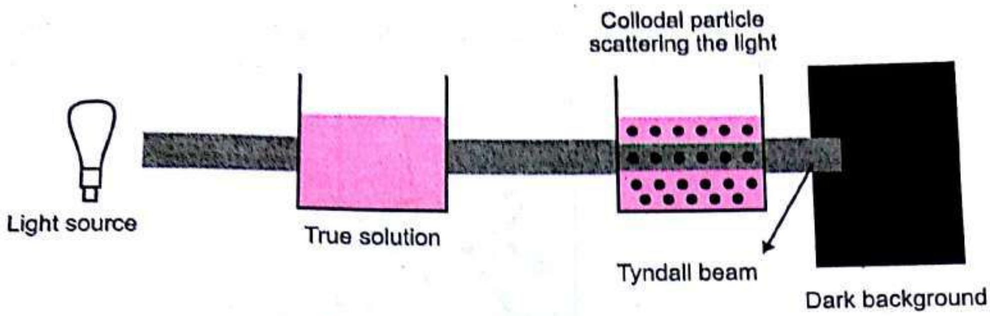


Figure1.3: Faraday Tyndall effect

b. **Electron Microscope:** The electron microscope is useful to yield actual particles pictures. They are used to observe the size, shape, and structure of colloidal particles. The main feature of electron microscope is its high resolving power.

c. **Ultramicroscope:** When an intense light beam is passed through the sol against a dark background at right angles to the plane of observation. The particles will appear as the bright spots which can be observed and counted.

d. **Light Scattering:** It is used to get information on the shape and size of particles. Scattering can be described in terms of the turbidity, τ. The turbidity can be calculated from the intensity of the scattered light. It is also used to determine the molecular weight of the colloid by using following equation

$$\frac{Hc}{\tau}=\frac{1}{M}+2Bc \qquad (1.1)$$

where
τ is the turbidity
c is the concentration of solute in g/cm^3 of solution,
M is the molecular weight
B is an interaction constant
H is optical constant for a particular system

A plot of Hc/τ against concentration give a straight line with a slope of 2B. The intercept of which is $1/M$.

1.4.2 KINETIC PROPERTIES

This property related to the motion of particles

a. **Brownian Motion:** There are continuous collisions between the colloidal particles and molecules of dispersion medium which are in constant motion. This produce zigzag movement of colloidal particles which is known as Brownian movement. Due to very small size particles, the motion of the molecules cannot be observed. The addition of the viscosity enhancing agents such as glycerin decreases and finally stops the Brownian movement.

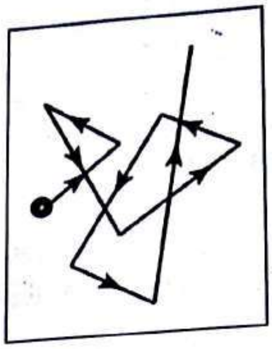


Figure1.4: Brownian movement of Colloidal Particles

b. **Diffusion:** The particle diffuse from a region of higher concentration to lower concentration until the concentration of the system is uniform throughout. According to Fick's first law, the amount, dq, of substance diffusing in time, dt, across a plane of area, S, is directly proportional to the change of concentration, dc, with distance travelled, dx. It is expressed as

$$dq = -DS\frac{dc}{dx}dt \tag{1.2}$$

Where

D is the diffusion coefficient

The measured diffusion coefficient is used to determine the molecular weight of spherical molecules, by use of the following equation

$$D = \frac{RT}{6\pi\eta N}\sqrt[3]{\frac{4\pi N}{3Mv^2}} \tag{1.3}$$

Where

M is molecular weight

v' is the partial specific volume

R is molar gas constant

N is Avogadro number

r is radius of spherical particle

T is absolute temperature

η is viscosity

c. **Osmotic pressure:** The osmotic pressure, π, of a dilute colloidal solution is described by the van't Hoff equation

$$\pi = \frac{C_g}{M} RT \qquad (1.4)$$

Where

c_g is the grams of solute per liter of solution
M is the molecular weight
T is absolute temperature
R is molar gas constant

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

d. **Sedimentation:** The rate of sedimentation is given by Stokes's law:

$$v = \frac{2r^2(\rho - \rho_0)g}{9\eta_0} \qquad (1.5)$$

Where

g is the acceleration due to gravity
v is velocity
ρ is density of spherical particle
ρ_0 is density of medium
η_0 is viscosity

When the particles settle on the basis of their molecular weight, the following equation is used to determine molecular weight (M)

$$M = \frac{RT_s}{D(1 - \bar{v}\rho_0)} \qquad (1.6)$$

Where

T_s is absolute temperature
R is molar gas constant
D is diffusion coefficient
ρ_0 is density of medium
v' is the partial specific volume

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

$$\eta = \eta_0(1 + 2.5\phi) \qquad (1.7)$$

Where

η_0 is the viscosity of the dispersion medium
η is the viscosity of the dispersion when the volume fraction of colloidal particles present is φ.

According to the Mark–Houwink equation, intrinsic viscosity $[\eta]$ is used to calculate the molecular weights of polymers.

$$[\eta] = KM^a \quad (1.8)$$

Where

K and a are constants characteristic of the particular polymer–solvent system.

SOLVED PROBLEM

Exercise 1.1

Calculate molecular weight of cellulose acetate fraction when the value of constant K = 5 x 10^{-5} and a = 1.29 at 25⁰C. The intrinsic viscosity was found to be 1.20

Solution

$[\eta] = KM^a$

$\log [\eta] = \log K + a \times \log M$

$\log (1.20) = \log (5 \times 10^{-5}) + 1.29 \log M$

or $\log M = \log (1.20) - \log (5 \times 10^{-5}) / 1.29$

$\log M = 0.079 + 4.301 / 1.29$

$\log M = 3.395$

$M = \text{Antilog}(3.395) = 2483.133$

Answer- 2483.133

1.4.3 ELECTRICAL PROPERTIES

The properties of colloids is to carry charges on the surface of a particle either by ionisation or by adsorption.

a. Electrophoresis

The movement of colloidal particles through a liquid under the influence of electric field is called Electrophoresis. On applying electric field across the colloidal solution, the colloidal particles migrate to oppositely charged electrode. This phenomenon is known as electrophoresis.

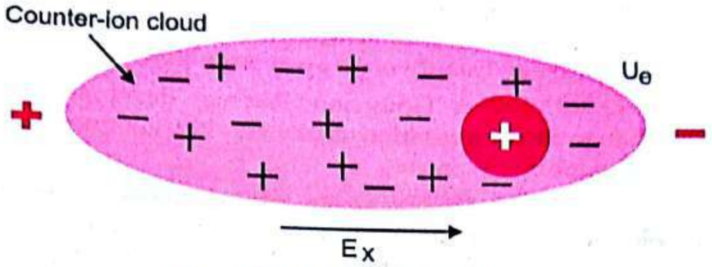


Figure1.5: Electrophoresis

The rate of migration of particle is observed by means of an 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

$$\zeta = \frac{v}{E} \times \frac{4\pi\eta}{\varepsilon} \times (9 \times 10^4) \quad (1.9)$$

Where

ζ is zeta potential

v is the velocity of migration in an electrophoresis tube of a definite length in cm,

η is the viscosity of the medium,

ε is the dielectric constant of the medium,

E is the potential gradient, , in volts/cm.

The term v/E in the equation is known as the mobility.

b. Electric Double Layer:

In this theory, at the first layer charge is imparted to the particles by situating ions which are adsorbed preferentially at immovable points and the second layer consists of diffused mobile ions. The charge present on both the layers are equal. This two-layer arrangement develop **zeta or Electrokinetic potential**.

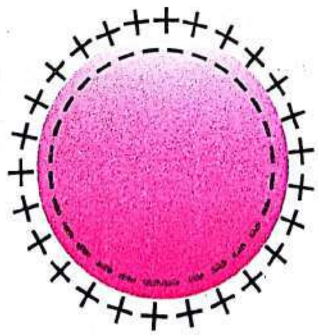


Figure1.6: Electric double layer

There are several theories to describe it

Helmholtz Double Layer theory: The theory states that the surface charge is neutralized by opposite sign counterions placed at distance of (d) away from the surface.

Gouy-Chapman Double Layer Theory: Gouy and Chapman developed *diffuse double layer*. According to this the change in concentration of the counter ions near a charged surface follows the Boltzman distribution

Stern Modification of the Diffuse double Layer: Stern, therefore, modified the Gouy-Chapman diffuse double layer. His theory states that ions do have finite size, so cannot approach the surface closer than a few nm. Stern also supposed that it is possible that some of the ions are specifically adsorbed by the layer which is called Stern Layer.

c. **Donnan Membrane effect:** It describe the behaviour of charged particle near semi permeable membrane that sometime fails to distribute equally across the two side of membrane. This is due to the presence of different charged substance which are unable to pass through membrane and therefore they create uneven electrical charge. This is known as Donnan effect.

For example: Suppose on one side of a semipermeable membrane, sodium chloride is placed in solution and on the 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 the membrane are considered to be equal.

Outside (o)	Inside (i)
	R^-
Na^+	Na^+
Cl^-	Cl^-

As the principle of escaping tendencies states that The concentration in dilute solutions of sodium chloride must be the same on both sides of the membrane. So

$$[Na^+]_0[Cl^-]_0 = [Na^+]_i[Cl^-]_i \qquad (1.10)$$

In case of electroneutrality, on the outside

$$[Na^+]_0 = [Cl^-]_0 \qquad (1.11)$$

And on the inside

$$[Na^+]_i = [R^-]_i + [Cl^-]_i \qquad (1.12)$$

On substituting eq 1.11 and 1.12 in eq 1.10, we get

$$\frac{[Cl^-]_0}{[Cl^-]_i} = \sqrt{1 + \frac{[R^-]_i}{[Cl^-]_i}} \qquad (1.13)$$

The equation gives the ratio of concentrations of the diffusible anion outside and inside the membrane at equilibrium.

Higuchi modified the Donnan membrane equilibrium, equation. He included polyelectrolyte sodium carboxymethylcellulose for enhancing the absorption of drugs such as sodium salicylate and potassium benzylpenicillin.

If [Cl^-] in above equation (eq 1.13) is replaced by the concentration of the diffusible drug, anion [D^-] at equilibrium, and [R^-] is used to represent the concentration of sodium carboxymethylcellulose at equilibrium. Then equation will be

$$\frac{[D^-]_o}{[D^-]_i} = \sqrt{1+\frac{[R^-]_i}{[D^-]_i}} \qquad (1.14)$$

The addition of an anionic polyelectrolyte to a diffusible drug anion should enhance the diffusion of the drug out of the chamber.

SOLVED PROBLEM

Exercise 1.2

As per Donnan Membrane effect, Calculate the ratio of salicylate on the two sides of the membrane at equilibrium, if the equilibrium concentration of carboxyethylcellulose is 2.1 × 10^{-2} g equivalent/liter and the equilibrium concentration of Magnesium salicylate is 7.0 × 10^{-3} g equivalent/liter.

Solution

$$\frac{[D^-]_o}{[D^-]_i} = \sqrt{1+\frac{[R^-]_i}{[D^-]_i}}$$

$$\frac{[D^-]_o}{[D^-]_i} = \sqrt{1+\frac{21\times10^{-3}}{7\times10^{-3}}}$$

Answer- 2

d. **Others:** Electroosmosis is other method for getting the zeta potential by mesuring the rate of flow of liquid through the plug under standard conditions. *Sedimentation potential* is the potential difference develop when particles settle under the influence of gravity. It is reverse of electrophoresis. The *streaming potential* is potential occurs due to forcing a liquid to flow through a plug or bed of particles.

1.5 STABILITY OF COLLOIDS

Stability of colloid prevent them for aggregation. There are two mechanisms for colloid stabilization one is Steric stabilization (in which each particle is surrounded with solvent sheath to prevent adherence due to Brownian movement) and other is electrostatic stabilization (in which particle are provided with electric charges)

1.5.1 EFFECT OF ELECTROLYTES

Effect of electrolytes 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 four scientist: Derjaguin, Landau, Verway, Overbeek).

According to this theory, distance between two colloidal particle 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 particle will form aggregate.

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

Lets explain this theory with the help of diagram of potential energy vs interparticle distance.

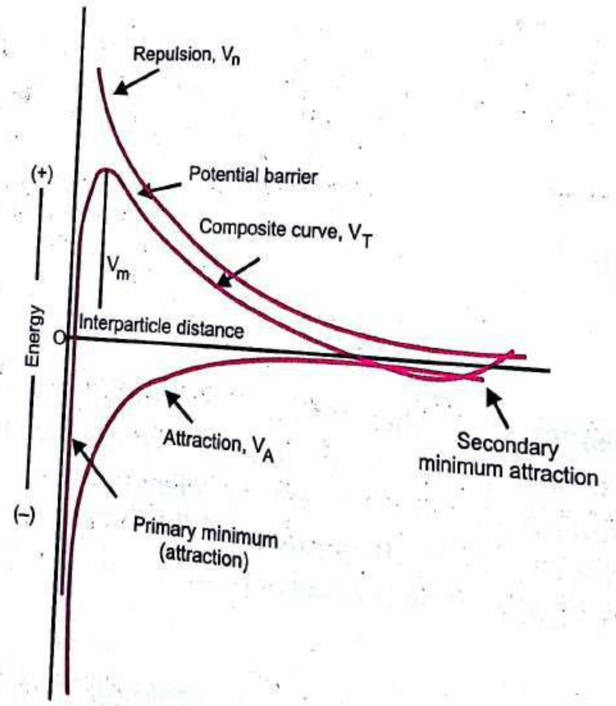


Figure1.7: potential energy vs interparticle distance

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

Lets consider the effect of electrolyte. In the absence or removal of electrolytes, the interparticle repulsion decreased to such extent that coagulation occurs. The particle deposit at the bottom as hard cake. This behaviour is correspond to primary minimum in DLVO theory.

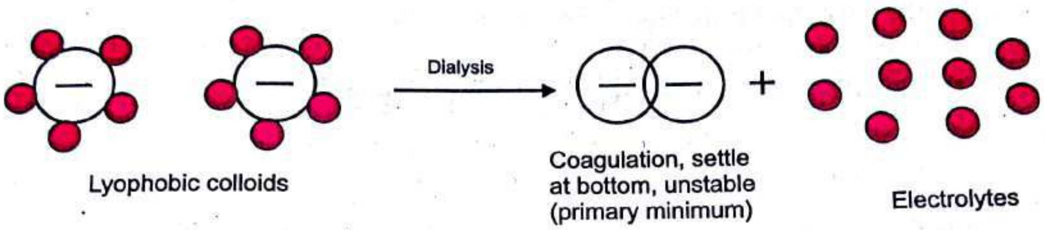


Figure 1.8: In absence of electrolytes

(2) **Secondary minimum:** When distance between the particles are large. Particles experience attractive force and aggregates are formed. This is secondary minimum.

Lets consider the effect of electrolyte. On addition of excess of electrolytes, the floccule formation occur. This behaviour is correspond to secondary minimum in DLVO theory.

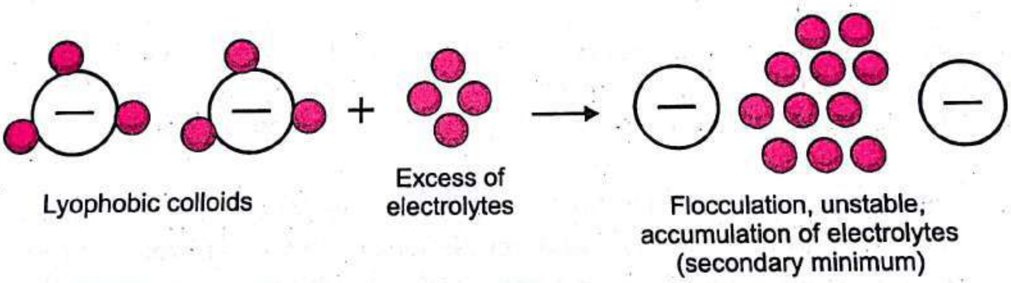


Figure 1.9: On addition of excess of electrolytes

(3) The accumulation of opposite charged ions to lyophobic 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."

Effect of electrolyte on Lyophillic colloid

Lyophobic colloids are thermodynamically stable. But particles undergo aggregation, coagulation or precipitation. This is due to following reason

1. 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.
2. The addition of non solvent such as alcohol to hydrophilic colloids cause dehydration of particles. When small amount of electrolytes are added it cause flocculation

The coagulation power in lyophillic colloid is given by Hoffmeister series. The precipitating power is depend on the hydration of the ion and hence to its capacity to detach water molecules from the colloidal particles. Several anions of the Hofmeister series in decreasing order of precipitating power are:

citrate>tartrate>sulphate>acetate>chloride>nitrate>bromide>iodide.

1.5.2 COACERVATION

When two opposite 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.

1.5.3 PEPTIZATION

It is the process in which aggregates are break into colloidal size particle in the presence of peptizing agent. Peptizing agent may be liquid, electrolytes and non electrolytes. It is responsible for the formation of stable dispersion of colloidal particles in dispersion medium.

On addition of electrolyte to a freshly precipitated substance, the particles adsorb one particular type of ions of the electrolyte and get dispersed due to electrostatic repulsi... produce colloidal size particles. A few exampl...

phenomenon is called protection. The colloids that are used to stabilize other colloids is called protective colloid.

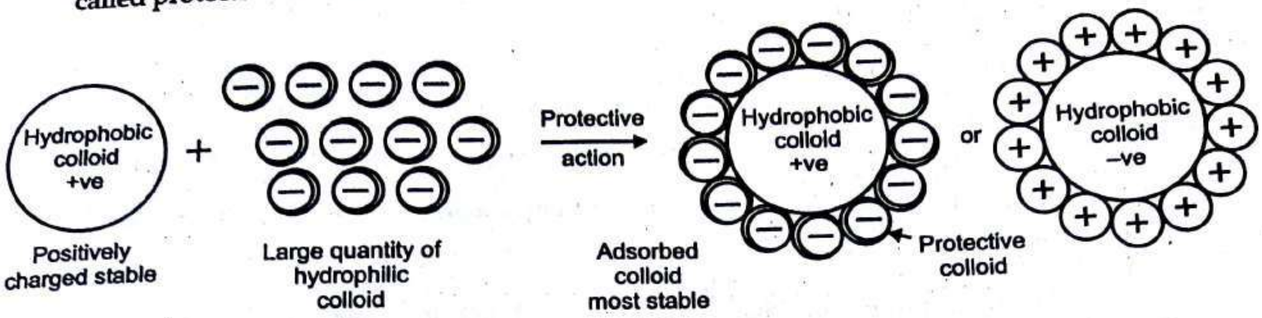


Figure 1.10: protective colloid

The protective ability of colloids is measured as **Gold number**. Gold number is defined as number of milligram of protective colloid required in 10 ml of red gold sol to prevent the change in color from red to violet on addition of 1ml of 10% solution of sodium chloride. If the gold number is less then the protective action will be more.

Table 1.3 Gold number of few protective colloids are

Protective colloids	Gold number
Albumin	0.1
Acacia	0.1-0.2
Tragacanth	2
Gelatin	0.005-0.01

UNIT-II

2 RHEOLOGY

Rheology: Newtonian systems, law of flow, kinematic viscosity, effect of temperature, non-Newtonian systems, pseudoplastic, dilatants, plastic, thixotropy, thixotropy in formulation, determination of viscosity, capillary, falling Sphere, rotational viscometers

SELECTED DEFINITIONS

Rheology: It is the science of the flow of a material.

Newtonian fluid: The fluid which obeys Newton's law of viscosity are called Newtonian fluid.

Non- Newtonian fluid: Those liquid which do not obey Newton's law of viscosity is termed as Non- Newtonian fluid.

Rate of shear: It is defined as change in velocity between two planes of liquid which is separated by distance.

Shear stress: It is the ratio of shear force to cross sectional area required to bring the flow.

Viscosity or dynamic viscosity: It is defined as resistance provided to a layer of liquid when it moves over another layer of liquid.

Kinematic viscosity: It is defined as the ratio of dynamic viscosity to the density of the fluid.

Plastic viscosity: It is defined as the shearing force greater than yield value is required to induce rate of shear.

Thixotropy: It is defined as isothermal and comparatively slow recovery of a system whose consistency is lost through apart shearing.

Rheopexy: It is a phenomenon in which gel formation takes place more readily when gently shaken or on regular movement.

2.1 INTRODUCTION

Rheology is a Greek word Rheo means 'to flow' and logos mean 'science'. Rheology is the science of the flow of a material. It applies to liquids, solids and semi solids. It also applies to the substance which have complex micro structures such as suspension, muds, sludges etc. The term rheology was invented by Bingham and Crawford. The term also describe deformation of solids.

Rheologic properties of a pharmaceutical system influence the selection of processing equipment during the manufacturing of dosage form and also handling of drugs at the time of administration. The factors such mixing and flow of materials, their packaging into containers, and their removal prior to use influence rheological properties.

The Flow behaviour of liquids have great importance in pharmacy. The classification of material according to types of flow and deformation is divided into two categories: Newtonian and non-Newtonian systems. The fluid which obeys Newton's law of viscosity is termed as **Newtonian fluid** and those liquid which do not obey Newton's law of viscosity is termed as **Non- Newtonian fluid.**

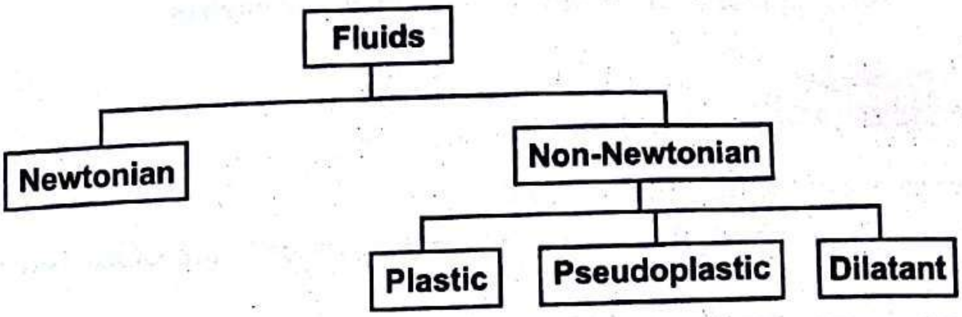


Figure 2.1: Classification of fluid

2.2 NEWTONIAN FLUID

2.2.1 NEWTON'S LAW OF VISCOSITY

This law states that "The shear stress in flowing fluid is directly proportional to the rate of shear."

Mathematically

$$\tau \propto dv/dr \quad (2.1)$$

or

$$\tau = \eta . dv/dr \quad (2.2)$$

Where

η is constant, which is coefficient of viscosity or viscosity or dynamic viscosity

τ is shear stress

dv/dr is rate of shear.

Rate of shear is defined as change in velocity (dv) between two planes of liquid which is separated by distance (dr).

Shear stress (τ) is the ratio of shear force to cross sectional area (F'/A) required to bring the flow.

Viscosity or dynamic viscosity (η) is defined as resistance provided to a layer of liquid when it moves over another layer of liquid.

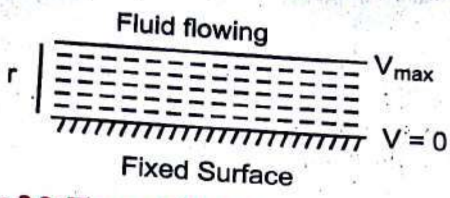


Figure 2.2: Flow of fluid through fixed surface

Suppose we have fixed surface over which the fluid is flowing. The distance between two layer is denoted by r. The layer of liquid which is in contact with fixed surface, they have zero velocity. As we move away from fixed surface the velocity of fluid goes on increasing.

$$\tau = \eta . dv/dr \tag{2.3}$$

or

$$\eta = \frac{\tau}{dv/dr} \tag{2.4}$$

The unit of viscosity is Newton sec m^{-2} or poise.

1 poise = 1/10 Newton sec m^{-2}

The term poise is given on name of French physician Jean Louis Marie Poiseuille. The cgs unit of viscosity is dyne-second per square centimetre (dyne sec cm^{-2}).

SOLVED PROBLEM

Exercise 2.1 How to determine the rate of shear and shearing stress of the oil having viscosity 1×10^{-2} poise. The oil is rubbing with velocity of 20 cm/s and thickness of film is 0.01 cm?

Solution

Rate of shear = dv/ dr = 20/ 0.01 = 2000 s^{-1}

As we know

$$\eta = \frac{\tau}{dv/dr}$$

So τ = (1×10^{-2}) (2000)

Or τ = 20 dyne cm^{-2}

Answer = 20 dyne cm^{-2}

A fluid, whose viscosity does not change with the rate of deformation or shear stain, is called Newtonian fluid. The plot of Newtonian liquid is a straight line. The slope of which is known as fluidity which is equal to reciprocal of viscosity

$\varphi = 1/\eta$

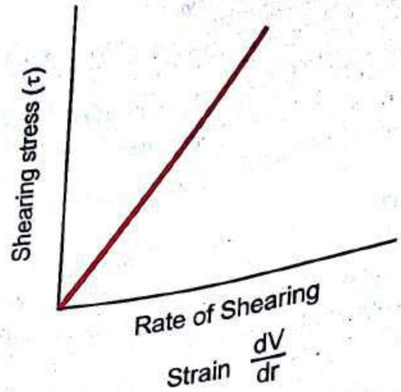


Figure 2.3: Rheogram for Newtonian liquid

2.2.2 KINEMATIC VISCOSITY

It is defined as the ratio of dynamic viscosity (η) to the density (p) of the fluid. (2.6)

Kinematic viscosity = η / p

The SI unit of kinematic viscosity is m^2/s and CGS unit is stokes or centistokes.

SOLVED PROBLEM

Exercise 2.2. Determine kinematic viscosity of liquid having viscosity of that liquid at 25^0 c is found to be 0.55 cp and density is 0.83 g/cm³

Solution;

Kinematic viscosity = η / p

Kinematic viscosity = 0.55/ 0.83 = 0.662 centistokes

Answer = 0.662 centistokes

2.2.3 EFFECT OF TEMPERATURE ON VISCOSITY

The effect of temperature on the viscosity (η) of a liquid is expressed by Arrhenius equation of chemical kinetics:

$$\eta = Ae^{Ea/RT} \quad (2.7)$$

where

A is a constant depending on the molecular weight and molar volume of the liquid and *Ea* is an "activation energy" required to initiate flow between molecules.

T is temperature

2.3 NON NEWTONIAN FLUID

A fluid in which shear stress is not proportional to shear strain. These fluids does not follow Newton's law of viscosity. Non Newtonian fluid follow three type of behaviour such as plastic flow, pseudoplastic flow and dilatants flow.

2.3.1 PLASTIC FLOW

The material which follows plastic flow are called Bingham bodies. Flocculated system are example of plastic flow. On applying shear stress initially floccules will not break and they will move away from each other. When shear stress will be more than yield value, then particle will break and act as individual particle. These particle will follow Newtonian flow. The amount of shear stress are required to break the floccules is called yield value (f).

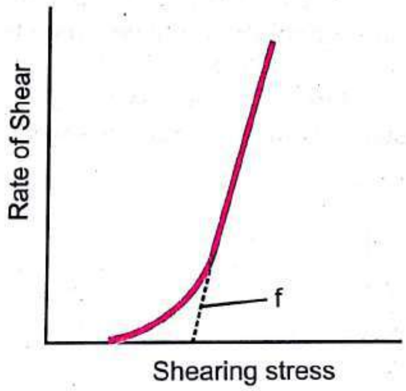


Figure 2.4: Rheogram for plastic material

The rheogram for plastic material shows that the curve does not pass through origin but it intersect the shearing stress axis at a particular point which is yield value. The slope of which is called mobility and reciprocal of mobility is called plastic viscosity (U). Plastic viscosity is defined as the shearing force greater than yield value is required to induce rate of shear.

$$U = (F-f)/G \quad (2.8)$$

Where

f is yield value (dyne cm^{-2})

F is shearing stress

G is rate of shear

Exercise 2.3. Calculate plastic viscosity of a material, whose yield value was found to be 5000 dyne cm^{-2}. If rate of shear was 125 sec^{-1}, when shearing stress above the yield value was 6500dynes/cm^2

$U = (F - f) / G$

$F = 6500 dynes/cm^2$

$f = 5000 \; dyne \; cm^{-2}$

$G = 125 \; sec^{-1}$

So $U = 6500 - 5000 / 125 = 12.0$ poise

Answer = 12.0 poise

2.3.2 PSEUDOPLASTIC FLOW

Pseudoplastic material does not exhibit yield value. Polymer (such as HPMC, CMC) in water is the example of pseudoplastic flow. When polymers are placed between layers of water. Due to hydration, the polymer molecules will swell. These swollen molecules will produce resistance to the flow of water and the solution will become viscous. Now, by applying shear stress, these polymer molecules will dehydrate and these molecules will align themselves in the direction of flow. Thus the material become less viscous as shear rate is increased. The viscosity does not remain constant at different rate of shear. Hence these systems are also known **as shear thinning system.**

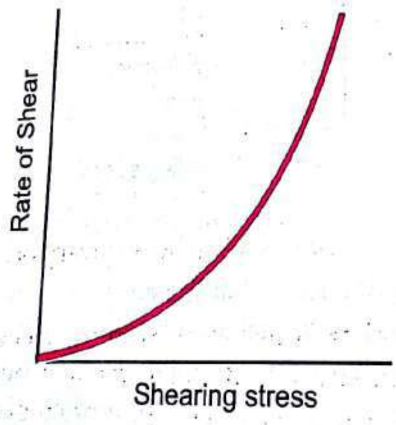


Figure 2.5: Rheogram for pseudoplastic flow

The rheogram for pseudoplastic flow shows that the curve starts from origin but it is non linear. The shear stress F does not increase linearly with shear rate G.

The equation which is used to describe pseudoplastic flow is expressed as

$$F^N = \eta' G \tag{2.9}$$

The exponent N indicates non Newtonian behaviour.

If value of N is one then system follows Newtons law of flow.

If N is greater than one, then it is pseudoplastic material.
If N is less than one, then it is dilatants material
On applying log, the equation can be written as

$$\log G = N \log F - \log \eta' \tag{2.10}$$

This is an equation for straight line.

2.3.3 DILATANT FLOW

Dilatant flow is exhibited by suspension containing more than 50% deflocculated particles. For example corn starch in water. When corn starch molecule is added into water. The quantity of corn starch is more than volume of water. On applying shear stress suddenly, the particles bunch up together and large voids also developed there. Since the amount of vehicle is constant. With further increase in shear rate the particles shows increase resistant to flow and the material become more viscous and attain solid paste like consistency. Therefore it is called **shear thickening system.**

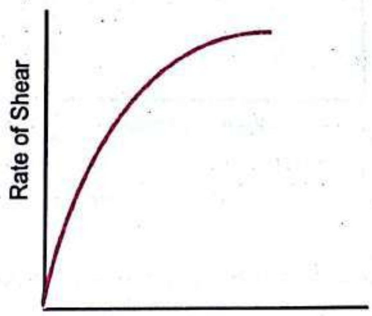


Figure 2.6: Rheogram for dilatants material

2.4 THIXOTROPY

It is defined as isothermal and comparatively slow recovery of a system whose consistency is lost through shearing.

Example of pseudoplastic system showing thixotropy include HPMC (hydroxyl propyl methyl cellulose) in water. Initially HPMC form random network of hydrated elongated particle i.e Gel and viscosity get increased. On application of shearing stress these particles align themselves parallel to the direction of flow and interparticle attractions are broken. Then gel get converted into sol and viscosity get decreases. On removal of shearing forces, again gel network is reformed and viscosity also increases, not immediately but after some time lag.

GEL (V↑) $\xrightarrow{\text{On application of shear stress}}$ SOL (V↓) $\xrightarrow{\text{On removal of shear stress}}$ GEL (V↑)

The rheogram shows that a hysteresis loop is obtained. On applying shearing stress an up-curve is obtained while on removal of shear stress a down-curve is obtained. But these curves are not super-imposable. The viscosities of down-curve are lower than tht up-curve.

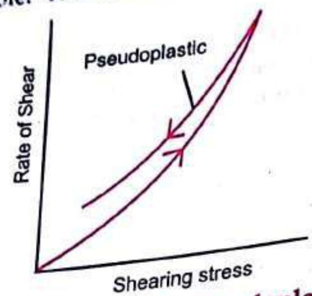


Figure 2.7: Thixotropy in pseudoplastic system

2.4.1 NEGATIVE THIXOTROPY

Negative Thixotropy is a phenomenon in which there is increase in viscosity on down curve. Example of negative thixotropy include suspension containing less number of floccules while more number of deflocculated particles. On application of shear stress number of flocculated particles increase and as a result viscosity also increases. The viscosity obtained on down –curve is greater than that of up-curve.

The rheogram of negative thixotropy shows that the down-curve appears above the up-curve. The graph also shift toward right indicating that system is gaining viscosity. But it is up to a limit. Beyond the limit, if the shear stress increases, there will be no increase in viscosity.

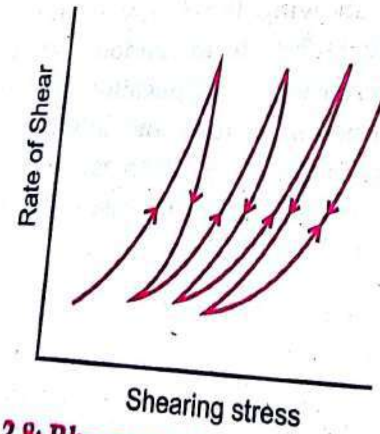


Figure 2.8: Rheogram for negative thixotropy

2.4.2 RHEOPEXY

Rheopexy is a phenomenon in which gel formation takes place more readily when gently shaken or on regular movement. This is because on gentle movement mild turbulence occur which helps in the dispersion of particles to obtain random orientation and therefore network is re-established.

2.4.3 BULGES AND SPURS:

The example of bulges include aqueous bentonite magma(10-15% by wt) At rest crystalline plate are irregularly arranged while On applying shear crystalline plate are arranged to form "house Of cards structure".

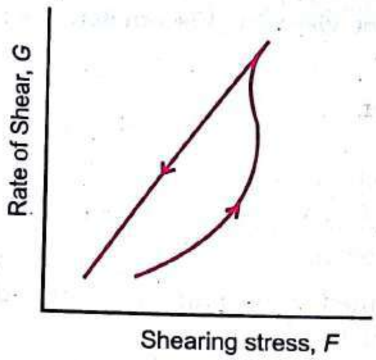


Figure 2.9: Rheogram of a thixotropic material showing a bulge

The spur value represents a sharp point of Structural break down at a low shear rate in the up-curve Example is procaine penicillin gel in Intra muscular injection

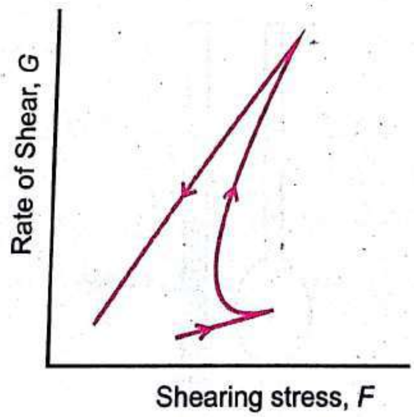


Figure 2.10: Rheogram of a thixotropic material showing a spur value

2.4.4 THIXOTROPY IN FORMULATIONS

Thixotropy is an important property in liquid pharmaceutical systems. Greater the thixotropy, the lower the rate of settling. A well formulated thixotropic suspension will not

easily settle in the container and it will become fluid by shaking and ease to dispense. It also maintain particle in suspended state. A similar behaviour is desirable with emulsions, lotions, creams, ointments, and parenteral suspensions to be used for intramuscular depot therapy.

Another example is concentrated parenteral suspensions containing from 40% to 70% w/v of procaine penicillin G in water. It also have a high inherent thixotropy. When the suspension is pass through the hypodermic needle. Consistency is maintained. This helps to formation of a depot of drug at the site of intramuscular injection where drug was slowly removed and made available to the body.

2.5 DETERMINATION OF VISCOSITY

Viscometers are used to determine viscosity. Viscometers are classified as

1. Capillary viscometer
2. Falling Sphere viscometer
3. Rotational viscometers

2.5.1 CAPILLARY VISCOMETER

Example of different capillary viscometers are

a. Ostwald viscometer (named after Wilhelm Ostwald, 1853-1932, one of the major founder of physical chemistry).

b. Ubbelohde viscometer (named after Leo Ubbelohde, 1877-1964, another notable German Chemist)

2.5.2 OSTWALD VISCOMETER:

This is used to determine both kinematic and dynamic viscosities.

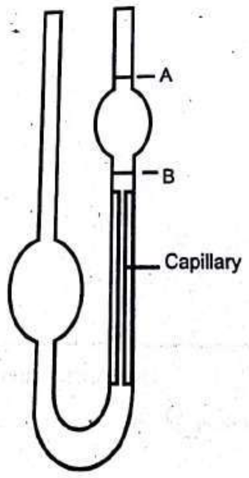


Figure 2.11: Ostwald viscometer

Method:

Ostwald viscometer is fixed to a stand in vertical position. Fluid (under test) is sucked through bulb upto the level above the upper mark A. Then fluid is allowed to flow down until it reaches to mark A. Now start the stop clock. When fluid reaches the mark B, stop the clock. The time required for the fluid to flow from one mark to another is measured. The time of flow of liquid under test is compared with time required for a liquid of known viscosity (water).

Derivation

Suppose η_1 and η_2 are the viscosities of the unknown and the standard liquids, respectively, $p_1$and p_2 are the respective densities of the liquids, and t_1 and t_2 are the respective flow times in seconds, the absolute viscosity of the unknown liquid, η_1, is determined by substituting the experimental values in the equation

$$\frac{\eta_1}{\eta_2} = \frac{p_1 t_1}{p_2 t_2} \tag{2.11}$$

The ratio of η_1/η_2 is called relative viscosity of liquid under test.

The liquid flowing through a capillary tube is based on *Poiseuille's law*

$$\eta = \frac{\pi r^4 t \, \Delta P}{8 l v} \tag{2.12}$$

where

r is the radius of the inside of the capillary,

t is the time of flow,

ΔP is the pressure head in dyne/cm^2 under which the liquid flows,

l is the length of the capillary, and

V is the volume of liquid flowing.

The radius, length, and volume of a given capillary viscometer are invariants. So above equation can then be written as

$$\eta = K.\, t.\, \Delta P \tag{2.13}$$

where

K is constant

The pressure head ΔP depends on density the ρ of the liquid being measured, the acceleration of gravity (constant value), and the difference in heights of liquid levels in the two arms of the viscometer. Suppose the levels in the capillary are kept constant for all liquids. So the viscosities of the unknown and the standard liquids can be written as

$$\eta_1 = K' t_1 \rho_1 \tag{2.14}$$

$$\eta_2 = K' t_2 \rho_2 \tag{2.15}$$

Divide both equations, we get

$$\frac{\eta_1}{\eta_2} = \frac{p_1 t_1}{p_2 t_2} \tag{2.16}$$

2.5.3 UBBELOHDE VISCOMETER

It is also called **suspended-level** viscometer. It is used for higher viscosity cellulosic polymer solutions.

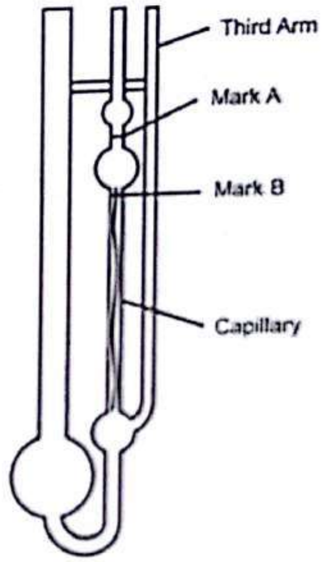


Figure 2.12: Ubbelohde viscometer

This consists of a reservoir on one side and a measuring bulb with capillary on the other. A liquid is introduced into the reservoir and then sucked through the capillary and the measuring bulb. The liquid is allowed to travel through the measuring bulb and the time required for the liquid to cross two calibrated marks is a measure of the viscosity. The Ubbelohde device has a third arm extending from the end of the capillary and opening to the atmosphere. In this way, the pressure head depends only on a fixed height and no longer on the total volume of liquid.

Exercise 2.4

At 20^{0}C the time required for flow of water and organic liquid through Ostwald viscometer is 45 sec and 18 sec respectively. Suppose density of water and liquid are 0.9982 and 1.17 g/ml respectively. The viscosity of water at 20^{0}C is 1.002 centipoise. Calculate viscosity of organic liquid at 20^{0}C

Solution

$$\frac{\eta_1}{\eta_2} = \frac{p_1 t_1}{p_2 t_2}$$

viscosity of water (η_1) = 1.002 centipoise
viscosity of organic liquid (η_2) = ?
density of water (p_1)= 0.9982 g/ml
density of organic liquid (p_2) = 1.17 g/ml
time required for flow of water (t_1)= 45 sec
time required for flow of organic liquid (t_2)= 18 sec

$$\eta_2 = \frac{1.002 \times 1.17 \times 18}{0.9982 \times 45}$$

η_2 = 0.469 centipoise
Answer = 0.469 centipoise

2.5.4 FALLING SPHERE VISCOMETER

It is called as Hoeppler falling sphere viscometer. This viscometer is based on the principle of Stokes' Law.

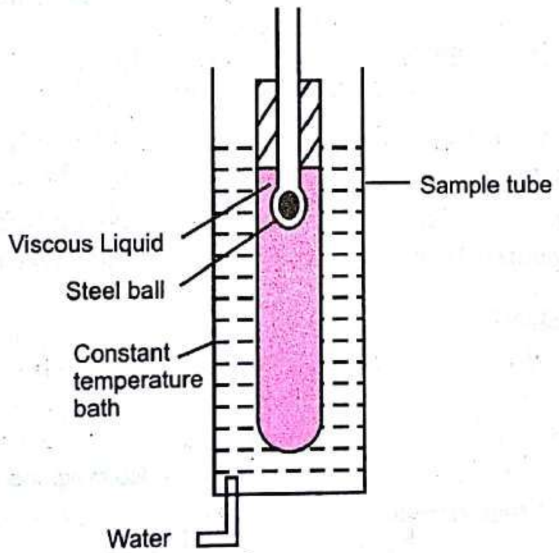


Figure 2.13: Hoeppler falling sphere viscometer

Method:

This type of viscometer consists of a cylindrical glass tube filled by the liquid under investigation. The tube is enclosed by constant temperature jacket in which water is circulated around the tube. A glass or steel ball is allowed to fall down. The falling time is recorded. The viscosity of a Newtonian liquid is then calculated from

$$\eta = t\,(S_b - S_f)\,B \qquad (2.17)$$

where

t is the time interval in seconds for the ball to fall between the two points

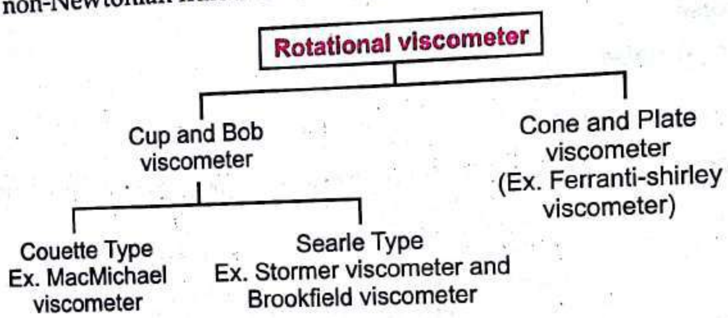
S_b and S_f are the specific gravities of the ball and fluid, respectively, at the temperature being used.

B is a constant for a particular ball.

Applications: This viscometer is more accurate, low time-consuming and a more user-friendly means of measuring viscosity in a laboratory environment.

2.5.5 ROTATIONAL VISCOMETERS

Rotational viscometers can be used for the accurate measurement of viscosity for both Newtonian and non-Newtonian fluids. The instrument is divided into two major categories



In the *Couette* type of viscometer, the cup is rotated. The viscous drag on the bob due to the sample produce torque which is proportional to the viscosity of the sample.

The *Searle* type of viscometer uses a stationary cup and a rotating bob. The torque resulting from the viscous drag is measured by a spring or sensor used to drive the bob.

2.5.6 CUP AND BOB VISCOMETER

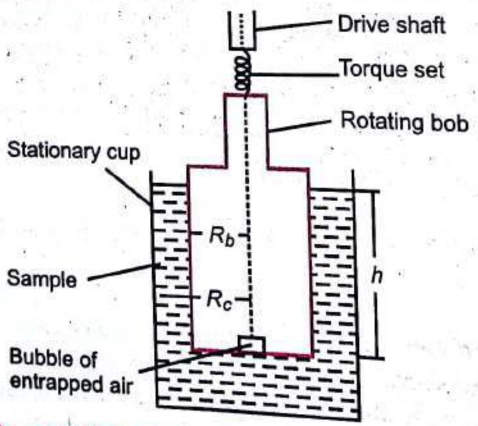


Figure 2.15: Cup and Bob Viscometer

As the name indicates, cup and bob viscometer consist of central cylindrical bob and stationary cup. The sample is sheared in the space between the outer wall of a bob and the inner wall of a cup. A known weight (w) of sample is used. Determine the time taken by bob to rotate for specific number of times and convert it into rpm (revolutions per minute). The rpm (v) value is considered as shear rate while weight (w) as shear stress. By using these values, viscosity of material (η) can be calculated by

$$\eta = K\,(w/v) \qquad (2.18)$$

where K is instrument constant.

2.5.7 CONE AND PLATE VISCOMETER

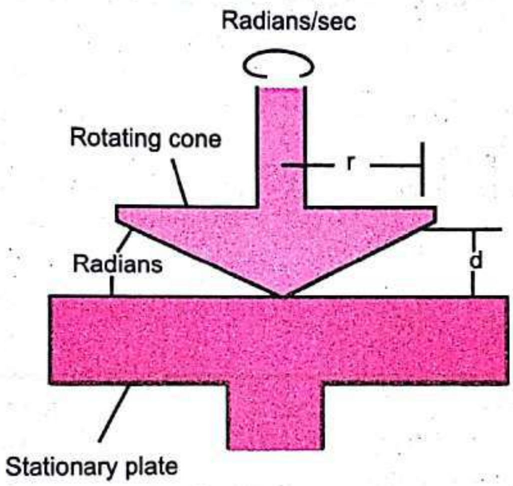


Figure 2.16: Cone and Plate viscometer

It consist of flat stationary plate and a wide angle rotating cone is placed centrally above it. The sample is placed at centre of stationary plate and then it is raised into the position under the cone. As a result the sample is sheared in narrow gap between stationary plate and rotating cone. The rate of shear in rpm is increased or decreased. The torque produced on the cone is measured. The viscosity in case of cone-plate viscometer is measured by

$$\eta = K\,(T/v) \qquad (2.19)$$

where

T is torque reading
V is rpm
K is instrument constant

Plastic viscosity is calculated by

$$U = K\frac{T - T_f}{v} \qquad (2.20)$$

Yield value is calculated by

$$f = K_f \times T_f \tag{2.21}$$

Where

T_f = torque at the shearing stress

K_f = instrumental constant

Exercise 2.5

The following data was collected when an emulsion was analyzed in the cone and plate viscometer.

T = 100 rpm,

T_f = 20 at zero rpm

v (rpm) = 300 rpm

K = 1.226

Calculate plastic viscosity

Solution

$$U = K\frac{T - T_f}{V}$$

U = 1.226 x (100-20/ 300) = 0.327 poise

3 DEFORMATION OF SOLIDS

Deformation of solids: Plastic and elastic deformation, Heckel equation, Stress, Strain, Elastic Modulus

SELECTED DEFINITIONS

Deformation: It is defined as change in the size and shape of an object.

Stress (σ): It is the force per unit area that applies to an object to deform it.

Tensile stress: It is defined as tensile force acting per unit area of the body.

Compressive stress: It is defined as compressive force acting per unit area of the body

Shear stress: It is defined as shear force acting per unit area of the body.

Tensile strain: It is defined as ratio of increase in length to original length of bar

Compressive strain: It is defined as ratio of decrease in length to original length of bar

Elastic Modulus: It is the ratio of stress to strain

Hooke's Law: This law states that ", In an elastic member stress is directly proportional to the strain within elastic limit."

Poisson's ratio: When a material is loaded within elastic limit, the ratio of lateral strain to linear strain remain constant. This phenomenon is called Poisson's ratio.

Elastic deformation: It is the process in which the material return to its original shape when force is removed.

Plastic deformation: It is the process in which the material does not return to its original shape when force is removed

Creep: Progressive, permanent deformation under constant load is called creep.

3.1 INTRODUCTION

Deformation means change in the size and shape of an object. When loads are applied to a body, some deformation will occur resulting to a change in dimension. Lets discuss the **deformation of solids** in terms of the concepts of stress and strain.

3.2 STRESS

Stress (σ) is the force per unit area that applies to an object to deform it. (3.1)

Stress (σ) = Force / Area

Its unit is Nm^{-2} or Pa

3.2.1 TYPE OF STRESS

There are three type of stress

1. Direct stress
2. Indirect stress
3. Combined stress

1. **Direct stress:** These stresses produced under direct loading condition i.e. force will be in line with the axis of member. Based on the type of force acting on the body , it may be tensile or compressive or shear stresses.
   a. **Tensile stress:** It is defined as tensile force acting per unit area of the body. It is that type of force which produce extension or elongate the dimension of the body. These force will be in line with the axis of member. The tensile stress is the ratio of change in length to the original length
   b. **Compressive stress:** It is defined as compressive force acting per unit area of the body. In this the forces applied is opposite to each other. It is that type of force which compress the dimension of the body.
   c. **Shear stress:** It is defined as shear force acting per unit area of the body. When we applied load on the surface of the body. Due to this body develop some resistive force which is parallel to each surface but opposite to direction of force applied.
2. **Indirect stress:** These stress occur due to torque produced in the body.
3. **Combined stress:** These stress are the combination of above two type of stress.

3.3 STRAIN

Strain (ε) is the measure of the amount of deformation. If the bar has original length (L) and when the load is applied on a bar the length of bar will change which is indicated as (ΔL)

Strain (ε) = $\Delta L / L$

It has no unit. (3.2)

3.3.1 TYPE OF STRAIN

1. **Tensile strain:** It is defined as ratio of increase in length to original length of bar
2. **Compressive strain:** It is defined as ratio of decrease in length to original length of bar
3. **Shear strain:** The strain produced by shear force is called shear strain.