

1. COLLOIDAL DISPERSIONS

Introduction

Particulate systems or dispersions, generally, are of three types – molecular, colloidal, and coarse dispersions. This classification is based on the size of the dispersed particles in the dispersion medium. Blood is a complex dispersed system in which plasma is the dispersion medium. It is composed of almost all the three types of dispersed phases. Nutrients such as peptides, proteins, and glucose form the molecular dispersion. The serum albumin forms the colloidal dispersion and the blood cells such as red blood cells may be considered to form the coarse dispersion.

Colloidal particles in colloidal solution or dispersion have a large specific surface area contributing for their unique properties to be discussed later in this chapter. To understand the increase in surface area, let us consider a cube of 1 cm edge and a volume of 1 cm³. This cube has a total surface area of 6 cm². If this cube is subdivided into smaller cubes with the edge of 100 μm, the total surface will increase by 600000 cm², though the volume remains the same. Thus, specific surface, which is defined as the surface area per unit weight or unit volume, has increased by 10⁵ times by subdivision of the cube with 6 cm².

A special significance of colloidal dispersions is that most of its properties can be used for the determination of molecular weight of macromolecules such as proteins and polymers and of their homogeneity. For example, insulin is a monodisperse system with a molecular weight of 6000 whereas gelatin is found to be a polydisperse with fractions of molecular weight 10,000 to 100,000 g/mole (or daltons). Many of the colloidal solution of polymers are used as viscosity enhancers or viscosity builders in pharmaceutical preparations.

Colloidal dispersions

Colloidal dispersions or *colloids* consist of two distinct phases - a dispersed phase and a dispersion phase or medium. The dispersed phase is also called as internal or discontinuous phase and the dispersion medium, as external or continuous phase or simply medium.

Colloidal state is due to a state of subdivision of the dispersed phase. Thus, it is the particle size that distinguishes colloidal dispersions from solutions and coarse dispersions. Dispersed phase in the colloidal state may have the dimensions in the range of 0.001 μ to 0.5 μ .

Solids may be dispersed in colloidal state into paste (zinc oxide in zinc oxide paste and starch in petrolatum, tooth paste containing dicalcium phosphate or calcium carbonate with sodium carboxy methylcellulose) or into liquid (bentonite magma) or into gas (smoke, dust etc.). Liquids may also be dispersed into solid (absorption bases), in aqueous medium (Hydrophilic Petrolatum USP) or in liquid (mineral oil emulsion) or in gas (mist, fog etc.) Gases form colloidal dispersion with solids (solid foam) and with liquids (carbonated beverages).

Molecular dispersion, colloidal dispersion and coarse dispersion from one another may be distinguished as follows:

	Molecular/dispersions (true solution)	Colloidal dispersions	Coarse dispersions
Size	0.001 micron	> 0.001 micron to 0.5 micron	> 0.5 micron
Visibility	Invisible even in electron microscope	Detected in an ultramicroscope and visible in an electron microscope	Visible to naked eye and in light microscope
Retention	Pass through ultra-filter and ordinary filter paper	Pass through ordinary filter paper but are retained by dialysis or ultrafiltration membrane	Do not pass even through ordinary filter
Diffusion	Undergo rapid diffusion	Diffuse very slowly	Do not diffuse

Note: 1 micron or micrometer (1 μ) = 10^{-6} meter 10^{-3} mm or 10^{-4} cm

The size of colloidal particles contributes to optical and kinetic properties and the charges present on the particles account for their electrical properties. They usually carry a charge either positive or negative on their surface.

Types of colloids

Colloidal dispersions can be broadly classified into two types - lyophilic and lyophobic. A third type is the association colloid with both the tendencies (i.e., lyophilic and lyophobic). This classification is based on the affinity or interaction between the disperse phase and dispersion medium. (*lyo* means solvent, *philic* means loving, and *phobic* means hating)

1. Lyophilic colloids

When there is considerable interaction (or affinity) between the disperse phase and the dispersion medium, a lyophilic colloid is formed. In this dispersion, the colloidal particles are solvated and they are mostly solids in liquids. Lyophilic colloid may be hydrophilic or lipophilic. If water is the dispersion medium, it is hydrophilic. With lipophilic colloids, non-aqueous vehicle forms the dispersion medium.

Hydrophilic colloids: Hydrophilic colloids may be subdivided as (a) *True solutions*; water-soluble polymers such as acacia and povidone (polyvinyl pyrrolidone) form molecular dispersion in water but the molecules are of colloidal dimensions and hence are classified under colloids. b) *Gelled solutions*: These are solutions of polymers at high concentrations. They are also formed at temperatures at which their solubility in water is low. Solutions of gelatin and starch set to gels on cooling whereas solution of methyl cellulose sets to a gel on heating. If water is the dispersion medium, they are called hydrogels. c) *Particulate dispersions*: They do not form molecular dispersions but they are present as minute particles of colloidal dimensions. Bentonite forms hydrosol with water.

Lipophilic colloids: *Lipophilic colloids* exhibit affinity for oils and hence are called oleophilic. Oils are non-polar and some examples are mineral oil, vegetable oils such as cotton seed oil and essential oils such as lemon oil. Lipophilic colloids may also be true solutions, gelled solutions or particulate dispersions.

Polystyrene and gum-rubber form colloidal solutions with benzene. Aluminium stearate dissolves or disperses in cotton seed oil. Activated charcoal forms particulate dispersion or sol in all oils.

Lyophilic colloidal dispersions are thermodynamically stable. Lyophilic substances form colloidal dispersions spontaneously with the dispersion medium. They are also reversible i.e. they are again formed after the dispersion medium has been removed i.e. the residue obtained after the removal of dispersion medium forms again a colloidal dispersion on adding to the dispersion medium.

2. Lyophobic colloids

Lyophobic means solvent-hating. In lyophobic dispersions, the colloidal particles exhibit little interaction or affinity with the dispersion medium. Hence in lyophobic collidal dispersions, the particles are not solvated.

Lyophobic colloids may be *hydrophobic and lipophobic*. Hydrophobic dispersion have water as dispersion medium and the particles are not hydrated. Hydrophobic colloids may have lipophilic substances as disperse phase in water. For example, Substance like polystyrene (or gum-rubber), steroids, and magnesium stearate form hydrophobic colloidal dispersions with water. Hydrophobic colloids are formed with substances like gold, silver and sulfur in water. Lipophobic dispersions are water-in-oil emulsions.

3. Association colloids

Association colloids result from the formation of 'micelles' (a micelle is formed by a group of surfactant molecules) when a surfactant in sufficient amount is added to the dispersion medium (water). As a surfactant has two distinct portions of opposing affinities (polar and non polar) within its molecule, the molecules tend to associate to form groups called micelles within the medium. The micelles are of colloidal dimensions. Such micelles are formed at and above a concentration called *critical micellar concentration* of the surfactant. Some 50 or more molecules aggregate together to form micelles which are of the order of 50\AA ($0.005\ \mu$) in diameter. They are thermodynamically stable and also reversible.

Various colloids are differentiated as follows:

	Lyophilic colloid	Association colloid	Lyophobic colloid
<i>Disperse phase</i>	Consists of large organic molecules of colloidal dimensions or particulate substances.	Consists of aggregate (micelles) of small organic molecules or ions of sub-colloidal sizes. e.g.: surfactants form associated colloids (micelles) in water.	Consists of inorganic particles (i.e., aggregate of atoms; e.g., gold colloid.)
<i>Solvation</i>	Disperse phase particles are solvated with dispersion medium	Hydrophilic portions of the molecule are solvated i.e., hydrated	No solvation (i.e., little interaction between disperse particles and the dispersion medium)
<i>Spontaneity</i>	Spontaneously formed once the disperse phase comes in contact with dispersion medium. They are thermodynamically stable and are also reversible.	Spontaneously formed at and above the critical micellar concentration (CMC). They are thermodynamically stable and are reversible.	Does not form spontaneously but it needs special methods for the formation. Hence they are thermodynamically unstable and are irreversible.
<i>Viscosity due to disperse phase</i>	Viscosity of the dispersion medium is increased. At sufficiently high concentrations they may become a gel. Viscosity is related to the solvation effects and gel formation and to the shape of the disperse phase molecules.	Viscosity increases as micelles increase in number and become asymmetric.	Viscosity is not increased.
<i>Effect of electrolytes</i>	Dispersions are stable generally in the presence of low concentrations of electrolytes. But at high concentrations, the	Electrolytes reduce CMC and at higher concentrations salting out of the disperse phase occurs.	Sensitive even to low concentrations of electrolytes. This is due to neutralisation of

	disperse phase may be salted out (coagulation)		the charge on the colloidal particles. Lyophilic colloids exert a protective effect on lyophobic colloids.
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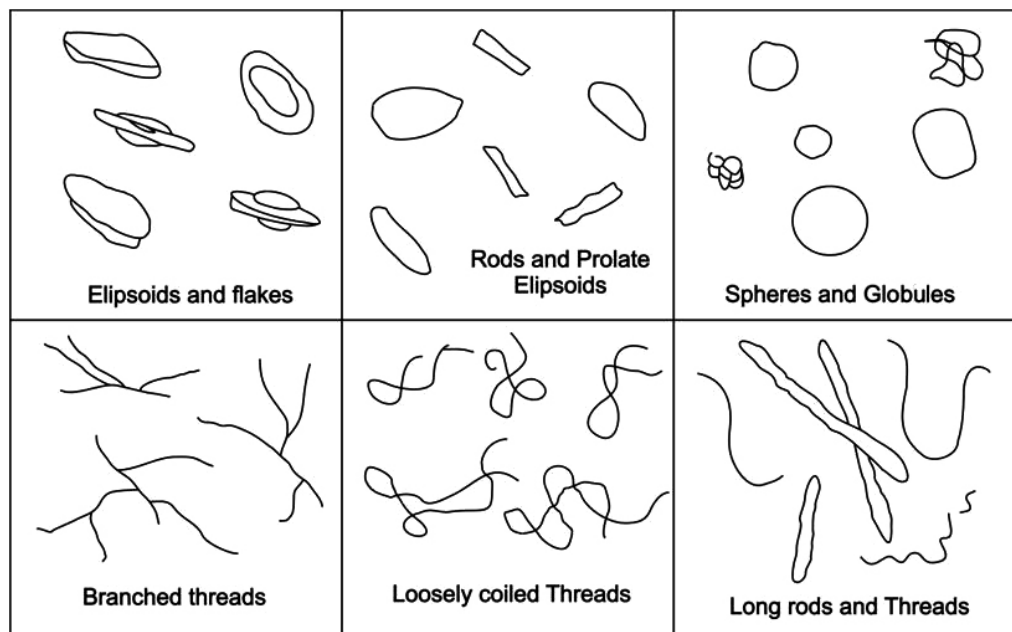


Fig. 1.1. Different shapes of colloidal particles

Properties of Colloids

Properties of colloids may be classified into optical properties, kinetic properties and electric properties.

1. Optical properties

The optical properties may be discussed under Faraday Tyndall effect, electron microscope and light scattering.

(a) The Faraday Tyndall effect

When a narrow strong beam of light is passed through a colloidal dispersion, the path of the light can be observed at right angles under an ultra-microscope. These colloidal particles appear as bright spots against a dark background due to the scattering of light by the colloidal particles on the path of the beam. This optical property is actually due to discrete variations in the refractive index caused by the presence of particles (or by small scale density fluctuations.)

(b) Electron Microscope

The ordinary light microscope cannot reveal the structural details of particles which are separated by smaller distances since the resolving power is about 2000 \AA (0.2μ). The electron microscope has a higher resolving power of about 5 \AA as it employs electron beam with wavelength of about 0.1 \AA . The resolving power is directly related to the wavelength of the radiation. The shorter the wavelength, the more efficient is the resolving power.

The electron microscope is used to get pictures of actual particles. It is used to study the size, shape and structure of colloidal particles.

(c) Light Scattering

The scattering of light and the intensity of the scattered light depend upon the following factors.

1. wavelength of the incident beam
2. intensity of incident beam
3. difference in the refractive index between the particles and the medium
4. volume of the particles as well as the number of particles involved in the scattering of light.

The intensity of light scattered may vary at different angles and can be used to obtain some indication as to the shape of the macromolecules (colloidal particles). It may be used to obtain the molecular weight and the equation giving the relationship is given as

$$\frac{Hc}{\tau} = \frac{1}{M} + 2Bc \quad \dots(1)$$

where τ = turbidity measured at 90° to the incident beam.

c = concentration of the solute in grams/liter

M = molecular weight.

B = interaction constant related to the degree of non-ideality of the solution.

H = a constant for a particular system and is given by the equation

$$H = \frac{32\pi^3 n^2 \left(\frac{dn}{dc}\right)^2}{3\lambda^4 N} \quad \dots(2)$$

where n = refractive index

$\frac{dn}{dc}$ = change in refractive index with concentration

N = Avogadro's number

λ = wavelength

A plot of $\frac{Hc}{\tau}$ versus c yields a straight line at low concentration with a slope of $2B$. The intercept on the $\frac{Hc}{\tau}$ axis will give the value of $1/M$ and hence the molecular weight.

Light scattering, apart from the molecular weight determination is used for the study of proteins, synthetic polymers, association colloids and lyophobic sols. Light scattering may be used to study the pattern of self-association and it showed that bile salts associate to form dimers, trimers and tetramers. Colloids may exhibit color due to the wavelength of the scattered light. For example, a colloidal dispersion of gold chloride is deep red in color and that of silver iodide is yellow.

2. Kinetic properties

Kinetic properties may be classified as follows:

	Thermally induced	Gravitationally induced	Externally induced
(a)	Brownian movement	Sedimentation	Viscosity
(b)	Diffusion		
(c)	Osmosis		

(a) Brownian motion (or movement)

The macromolecules or the colloidal particles are engaged continuously and randomly in motion within the medium. These molecules or particles are buffeted by the molecules of the dispersion medium. This random movement and bombardment with the molecules of the dispersion medium are increased and become erratic and such a movement of colloidal particles (zig-zag movement) within the medium is termed *Brownian motion*. Brownian motion is decreased by an increase in viscosity of the medium and the motion may also be stopped by increasing this viscosity to a certain level.

(b) Diffusion

Diffusion is a process where the solute molecules move from a region of higher concentration to one of lower concentration until the concentration of the system attains equilibrium and it is due to Brownian motion.

Diffusion is given by Fick's law

$$dq = -DS \frac{dc}{dx} . dt \quad \dots (3)$$

D = diffusion coefficient and is defined as the amount of material diffusing (dq) per unit time across unit area 'S' when concentration gradient $\frac{dc}{dx}$ is unity. Diffusion coefficient is a measure of mobility of the dissolved molecules of colloidal dispersion in a liquid medium.

It is possible to compute the molecular weight of approximately spherical particles from the diffusion coefficient by substituting the data obtained from diffusion experiments. The expression to calculate the molecular weight is given as

$$D = \frac{RT}{6\pi r \eta N} \sqrt[3]{\frac{4\pi N}{3M\bar{v}}} \quad \dots(4)$$

Where M = molecular weight

\bar{v} = partial specific volume (volume in cm³ of 1 g of solute)

η = viscosity of the solvent

R = molar gas constant

T = absolute temperature

r = radius of spherical particle

N = Avogadro's number

Using this method, the molecular weight of egg albumin and haemoglobin have been obtained.

(c) Osmotic pressure

Using osmotic pressure, it is possible to estimate the molecular weight of colloid (colloidal particles) and this is based on Vant Hoff's equation (The osmotic pressure of colloidal solutions is usually very small).

$$\pi = cRT \quad \dots (5)$$

Replacing the c (concentration) with $\frac{c_g}{M}$ the equation is

$$\pi = \frac{c_g}{M} \cdot RT \quad \dots (6)$$

where c_g = gram of solute per liter of solution

M = molecular weight

This equation is valid for very dilute solutions in which the interaction between the solute and the solvent molecules is little and the particles are spherical.

When the solute molecules become solvated (i.e. because of interaction between solute and solvent molecules) there is deviation and the plot of $\frac{\pi}{c_g}$ versus c_g will not be linear and it is necessary to extrapolate the curve to infinite dilution to obtain $\frac{RT}{M}$. The equation is then written as given below when there is interaction between the solvent and the solute molecules.

$$\frac{\pi}{c_g} = \frac{1}{M}RT + Bc_g \quad \dots (7)$$

where B = a constant and is the slope for any particular system and it gives the degree of interaction between the solvent and the solute molecules.

Using this method, the molecular weight of polymers has been obtained.

(d) Sedimentation

Brownian motion keeps the dissolved molecules of colloidal dimensions (macromolecules) or colloidal particles in continuous random motion. Hence it offsets sedimentation due to gravity. Therefore, stronger force must be employed to bring about sedimentation of colloidal particles. Even the usual laboratory centrifuges cannot cause sedimentation. This can be undertaken by the use of *ultracentrifuge*. This produces sedimentation at a reasonable rate.

In this method, the colloidal dispersion is placed in a glass cell in the ultracentrifuge rotor and arranged in such a way that light passing through the cell may be photographed. The centrifuge is rotated at 50,000 rev/min and higher. The rate of sedimentation is derived from the change in the light absorption or a change in refractive index during centrifugation. The change in refractive index is translated into peaks on a photographic plate. The peaks obtained are termed as *Schlieren patterns* and the peak gives the position of boundary at each time. The boundary (x) refers to the boundary between the solvent and the high molecular weight component (dispersed in the medium) in the centrifuge cell. The boundary and hence the sedimentation is located by a change in refractive index.

Svedberg sedimentation coefficient as it is called is given by

$$S = \frac{\ln\left(\frac{x_2}{x_1}\right)}{\omega^2(t_2 - t_1)} \quad \dots (8)$$

where x_1 and x_2 are measured on the *Schlieren photographs* obtained at times t_1 and t_2 . ω is equal to 2π times the speed of the rotor in revolutions per second.

The molecular weight of a polymer is obtained by using the expression.

$$M = \frac{RTS}{D(1 - \bar{v}\rho_0)} \quad \dots (9)$$

where R = gas constant

T = absolute temperature

\bar{v} = partial specific volume of the polymer

ρ_0 = density of the solvent

S = *Svedberg sedimentation coefficient* determined at 20°C

D = diffusion coefficient obtained by calculation from diffusion data collected at 20°C

With ultracentrifugation (sedimentation rate method) it is possible not only to determine the molecular weight but also to determine the relative homogeneity of a polymer with respect to molecular weight. If a sample consists of a component of definite molecular weight, the *Schlieren pattern* yields a single sharp peak at any moment during the run. If several peaks appear on the *Schlieren pattern*, it indicates components with different molecular weights. Thus, insulin is found to be a monodisperse (homogeneous) system with a molecular weight of about 6000 and gelatin, a polydisperse system with fractions of molecular weight from 10,000 to 1,00,000.

(e) Viscosity

Viscosity studies provide not only the molecular weight of polymers but also information regarding the shape of the particles in a colloidal dispersion.

Einstein equation provides a quantitative expression for the flow of disperse systems consisting of spherical particles.

$$\eta = \eta_0 (1 + 2.5 \varphi) \quad \dots (10)$$

where η = viscosity of the dispersion

η_0 = viscosity of the dispersion medium

φ = volume fraction of the disperse phase (It is the volume of disperse phase divided by the total volume of the system)

The following viscosity coefficients as applied to colloidal dispersions may be defined with respect to Einstein equation.

Relative viscosity η_{rel} is defined as:

$$\eta_{rel} = \frac{\eta}{\eta_0} = 1 + 2.5 \phi \quad \dots (11)$$

Specific viscosity (viscosity ratio increment) may be defined as the relative increase in viscosity produced by the presence of dispersed phase.

$$\eta_{sp} = \frac{\eta - \eta_0}{\eta_0} = \frac{\eta}{\eta_0} - 1 \quad \dots (12)$$

hence $\eta_{sp} = 2.5 \phi$

In addition, since the volume fraction is directly related to the concentration of the disperse phase, the above equation may be given in the form.

$$\eta_{sp} = Kc \quad \dots (13)$$

where $K = \text{constant}$

$c = \text{concentration (weight of disperse phase in } 100 \text{ cm}^3 \text{ of total dispersion)}$

The above equation applies to dilute systems only. The equation is usually written as a power series for more concentrated dispersions.

$$\eta_{sp} = \alpha c + \beta c^2 + \dots$$

Reduced viscosity is obtained by dividing the above equation through 'c' and the ratio of specific viscosity to concentration is

$$\frac{\eta_{sp}}{c} = \alpha + \beta c + \dots \quad \dots (14)$$

Intrinsic viscosity $[\eta]$ is the intercept on 'y' axis obtained by extrapolating the line obtained by plotting $\frac{\eta_{sp}}{c}$ versus 'c' to definite dilution. (Fig. 1.2)

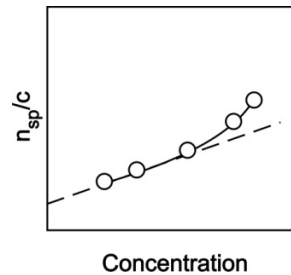


Fig. 1.2

The intrinsic viscosity is used to calculate the approximate molecular weight of a polymer and the equation relating this $[\eta]$ is given

$$[\eta] = KM^a \quad \dots (15)$$

Where, K and a are constant for a given polymer solvent system and are obtained from other experiments at fixed temperatures. M = molecular weight

This method is used to determine the average molecular weights of starch, dextran and gelatin preparations which are used as plasma extenders. The determination of intrinsic viscosity is used as a test in the BP (British Pharmacopoeia) for the standardization of Dextran injection, a plasma substitute.

The shape of the colloidal particles (disperse phase) influences the viscosity of the dispersion medium. Spherical colloidal particles produce dispersions of relatively low viscosity whereas linear colloidal particles produce dispersions of relatively high viscosity. Viscosity increase is due to solvation effect. When the degree of solvation is more, the dispersion becomes more viscous. Thus, if a linear colloid is placed in a solvent for which it has a low affinity, the linear particles tend to assume a spherical shape and as a result, the viscosity falls. Therefore, the viscosity studies provide a means of detecting changes in the shape of flexible colloidal particles and macromolecules.

3. Electric properties of colloids

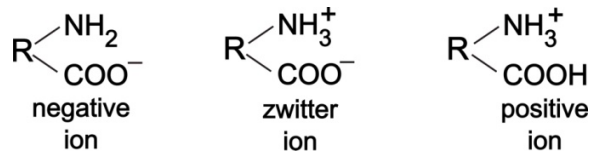
The colloidal particles are either negatively charged or positively charged. The particles are negatively charged in kaolin, sulfur, and arsenious sulfide colloidal dispersion while in ferric hydroxide and other metal hydroxide colloidal dispersions, the particles are positively charged. In

some other colloidal dispersion such as proteins, the charge of the particles may be positive, negative or neutral depending upon the pH of the medium.

The particles in a colloidal dispersion acquire charges from several sources mainly by ionization or by adsorption

Ionization: A fatty acid soap (sodium stearate), which forms micelles of colloidal size in aqueous solution, ionizes to Na^+ and $\text{C}_{17}\text{H}_{35}\text{COO}^-$ so that the micelle particle carries a negative charge.

Proteins contain both basic and acidic groups in the molecule ($\text{NH}_2 - \text{R} - \text{COOH}$). In alkaline solution, the acidic group - COOH ionizes to $-\text{COO}^-$ carrying a negative charge. In acid solution the basic group $-\text{NH}_2$ ionizes to $-\text{NH}_3^+$ so that the particle now carries a positive charge. At an intermediate pH known as iso-electric point, the protein molecule exists as zwitter ion when the net charge is zero provided no other ions are adsorbed. It can be depicted as



(A protein is least soluble at its isoelectric point and can be readily precipitated.)

Adsorption: A non-ionizing colloidal particle may preferentially adsorb ions and thus the particle may acquire a positive or negative charge depending upon which ion (that is anion (-) or cation (+)) is adsorbed. Adsorption of ions, through which particles acquire electric charges usually occur in hydrophobic colloids.

(a) Electric double layer (refer under suspensions also)

The presence of electric charges on the dispersed particles influences the distribution of positive and negative ions in the vicinity of the solution that surround each particle. (Fig. 1.3) Thermal motion also has some influence over the distribution of charges. The resultant effect is that each particle is surrounded by an electric double layer.

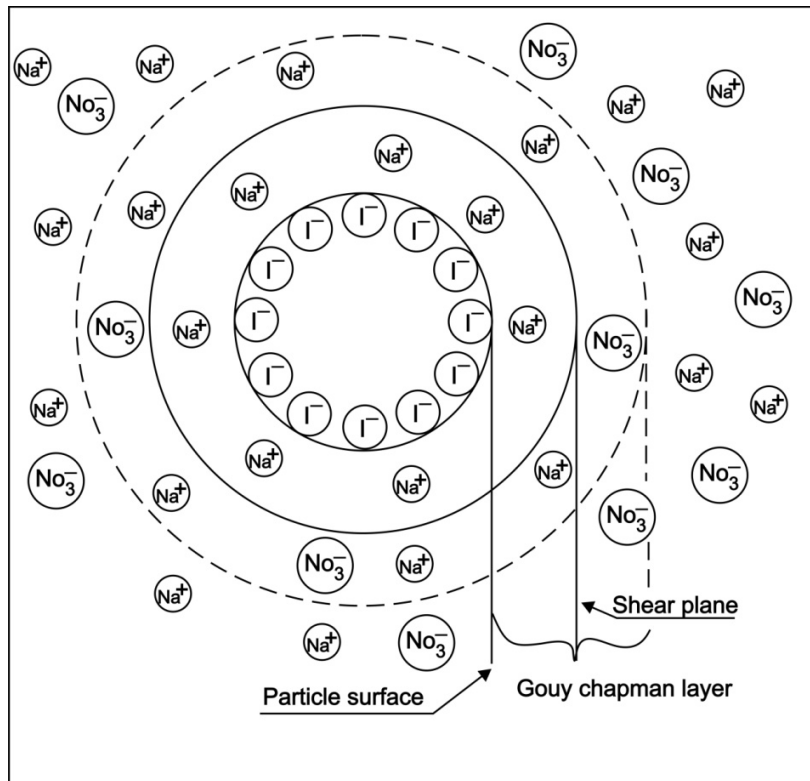
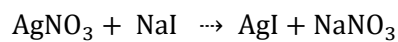


Fig. 1.3

Consider the colloidal dispersion of silver iodide prepared by chemical reaction.



The colloidal dispersion in water as such will contain Ag^+ , I^- , Na^+ , NO_3^- and traces of H^+ and OH^- ions.

If the reaction is conducted with an excess of sodium iodide, the surface layer of silver iodide contains more I^- ions than Ag^+ ions and the aqueous solution contains relatively high concentration of Na^+ and NO_3^- ions, a lower concentration of I^- and traces of H^+ , OH^- and Ag^+ ions.

As the silver iodide particles contain more of I^- ions on their surface, each of the silver iodide particles is negatively charged and it attracts positive ions from the solution and repels negative ions. As a result, the aqueous solution in the vicinity of the surface (of the AgI particle)

contains a much higher concentration of Na^+ ions (called *counter ions or gegenions*) and much lower concentration of NO_3^- ions than in the bulk of the solution. The counter ions Na^+ are pulled closer to its surface and these counter ions tend to stick to the surface as closely as possible as the hydration sphere (the solvated layer on the particle) permits. At the same time, thermal motion (of water molecules) tends to disperse the Na^+ ions throughout the solution. As a consequence, the layer of counter ions surrounding the particle is spread out and however the Na^+ concentration is highest in the immediate vicinity of the negative surface forming a compact layer called Stern layer. The concentration of Na^+ ions decreases with distance from the surface throughout diffuse layer called *Gouy-Chapman* layer. Thus, the negatively charged surface layer is surrounded by a cloud of Na^+ ions (counter ions) required for electro-neutrality. The combination of the two layers of oppositely charged ions constitutes an electric double layer. The thickness of the double layers usually ranges from 10 to 100 Å (0.001 to 0.1 μ)

The presence of electrical double layer around each particle in a colloidal dispersion gives rise to electrokinetic effects. They are electrophoresis, electro-osmosis, sedimentation potential, and streaming potential.

(b) Electrophoresis

When an electric field is applied to a colloidal dispersion, the particles carrying the charge (+ or -) move towards the electrode of opposite charge. When the particles move, the counter ions within the hydration shell (i.e., solvation layer) are dragged along with (the surface of the hydration shell is the plane of shear) and the counter-ions in the free or mobile solvent (i.e. medium) move towards the other electrode. This phenomenon is termed *electrophoresis*.

Electrophoretic mobility may be observed using electrophoresis cell. The cell is fitted with two electrodes. After taking a colloidal dispersion in the cell, an electric potential is applied across the electrodes. Under the influence of electric field, the colloidal particles move towards the oppositely charged electrode. The velocity of the particles can be measured by timing their movement. This maybe undertaken by observing through an ultramicroscope (and hence called micro-electrophoresis) which is fitted along with.

The rate of movement of individual colloidal particles is a function of charges on the particle and is directly related to the *zeta potential*. The equation relating zeta potential to the mobility of ion is

$$\zeta = \frac{v}{E} \cdot \frac{4\pi\eta}{\epsilon} \times (9 \times 10^4) \quad \dots (16)$$

where ζ = zeta potential in volts

v = velocity of movement of colloidal particles in cm/sec. in an electrophoresis cell
of definite length in cm.

η = viscosity of the medium in poises

ϵ = dielectric constant of the medium

E = externally applied potential gradient in volts/cm.

$\frac{v}{E}$ = mobility

(9×10^4) converts electrostatic units into volts.

When the dispersion medium is water and all the measurements are carried out at 20°C, the equation reduces to approximately

$$\zeta = 150 \frac{v}{E} \quad \dots (17)$$

The electrophoretic mobility of colloidal particles can be obtained from the rate of movement of the boundary of a sol using a simple 'U' tube apparatus. This method is called *moving boundary electrophoresis* and is used when the particles cannot be observed individually with an ultramicroscope. In moving boundary electrophoresis, a sharp boundary is formed between the sol and the pure dispersion medium and its movement in an electric field is observed visually if the disperse phase is colored. If the disperse phase is colorless, the boundary is observed by a change in refractive index along the column using special optical equipment (*Schlieren method*).

This method permits the identification of different colloidal components in a mixture, to study the electrophoretic mobility of the components in the mixture (e.g. proteins) and to estimate the relative amounts present.

(c) Electro-Osmosis

If the charged colloidal particles are rendered immobile, the counter-ions in the free water (dispersion medium) move towards the electrode of opposite charge dragging the water along with. This flow of liquid medium under the influence of electric field is called electro-osmosis and is considered to be opposite in principle to that of electrophoresis. The pressure produced by the process of electro-osmosis is called *electro-osmotic pressure*.

The atmosphere of counter-ions around the particles (apart from the counterions present within the hydration shell of the charged colloidal particles) confers a charge on the dispersion medium. This causes the liquid medium to move towards the opposite electrode under the influence of electric field. This phenomenon can be observed if the tube containing the colloidal dispersion is plugged in the middle with a porous material and across which a potential is applied. This method (electro-osmosis) also provides for obtaining zeta potential.

(d) Streaming potential

It is the converse of electro-osmosis. In this a potential difference is created, if the liquid is forced to flow past a plug or bed of charged particles by applying hydrostatic pressure. The potential difference is created because of the displacement of counterions in the free water. This method too can be used to determine the zeta potential.

(e) Sedimentation potential

This is the reverse of electrophoresis. When the colloidal particles are caused to undergo sedimentation, a potential difference is created.

(f) Donnan Membrane Effect

The presence of charged macromolecules (colloid) on one side of a semipermeable membrane (impermeable to macromolecules) will affect the diffusion of small ions (may be drug ions) through the semipermeable membrane. This effect is due to the electrical gradient across the

membrane and as a consequence, the charged drug ions of the same charge as that of macromolecules are driven to the opposite side of the membrane altering the concentration of the drug ions. This is termed *Donnan membrane equilibrium* or simply *Donnan effect* and may be demonstrated as follows.

Suppose a colloidal solution, the colloidal particles of which carrying negative charges together with its counterions say R^-Na^+ contained in a semipermeable membrane sac is placed in a solution of a drug (such as sodium salicylate) which has ionized into positive and negative ions say Na^+ and D^- . Considering the volumes of solutions on the two sides of the membrane (i.e. inside and outside) are equal, the system at equilibrium is represented as follows

Outside	Inside
(o)	(i)
Na^+	R^- $\left[\begin{matrix} Na^+ \\ D^- \end{matrix} \right]$ Permeable ions
D^-	Na^+ R^- - Non-Permeable ion D^-

In accordance with the principle of escaping tendencies, the concentration of the drug (Na^+D^-) must balance on both sides of the membrane. i.e.

$$[Na^+]_o [D^-]_o = [Na^+]_i [D^-]_i \quad \dots (18)$$

where subscripts o and i indicate outside and inside respectively.

Applying electroneutrality on both sides, the concentration of positively charged ions must balance the concentration of negatively charged ions

i.e., outside: $[Na^+]_o = [D^-]_o$

and inside: $[Na^+]_i = [R^-]_i + [D^-]_i$

Substituting these in the equation (18) we obtain

$$[D^-]_o [D^-]_o = ([R^-]_i + [D^-]_i) [D^-]_i$$

$$\begin{aligned}
[D^-]_o^2 &= [R^-]_i [D^-]_i + [D^-]_i [D^-]_i \\
[D^-]_o^2 &= [D^-]_i^2 + [R^-]_i [D^-]_i \\
&= [D^-]_i^2 \left(1 + \frac{[R^-]_i}{[D^-]_i}\right) \\
\frac{[D^-]_o^2}{[D^-]_i^2} &= 1 + \frac{[R^-]_i}{[D^-]_i} \quad \dots (19) \\
\text{or} \quad \frac{[D^-]_o}{[D^-]_i} &= \sqrt{1 + \frac{[R^-]_i}{[D^-]_i}}
\end{aligned}$$

From the above equation which represents the ratio of concentrations of diffusible drug anion outside and inside the membrane at equilibrium, it may be understood that a charged polyelectrolyte (i.e., macromolecules of colloidal dimensions) inside a semipermeable membrane sac would affect the equilibrium concentration ratio of a diffusible anion. That is it tends to drive the ion (drug ion) of like charge on its side to the opposite side through the semipermeable membrane. It is simple mathematics that when $\frac{[R^-]_i}{[D^-]_i}$ is equal to 15, the ratio of $\frac{[D^-]_o}{[D^-]_i}$ is equal to 4 and when $\frac{[R^-]_i}{[D^-]_i}$ is equal to 120, the ratio $\frac{[D^-]_o}{[D^-]_i}$ will be equal to 11. Thus, the addition of an anionic polyelectrolyte such as sodium carboxy methyl cellulose to a diffusible drug anion such as potassium benzyl penicillin and sodium salicylate enhances the diffusion of drug and thereby increases the absorption. The presence of charged electrolyte not only influences the distribution of drug ion according to *Donnan equilibrium* but will bring about an increase in the rate of transfer of the drug across the membrane.

It was also found that ion exchange resins, sulfate and phosphate ions which do not diffuse through intestinal wall, will drive anionic drug from the intestinal tract into the blood stream.

[Note: Charges on the membrane also influence the permeability of anions and cations. For example, a collodion membrane which possesses fixed anions and mobile cations will be selectively permeable to cations and the anions being repelled by negatively charged membrane.]

Conversely, a membrane with fixed cations and mobile anions will be selectively permeable to anions]

Preparation of Colloids

1. Lyophilic colloids

Owing to the affinity of lyophilic colloids for the dispersion medium, these colloidal sols are formed with relative ease. As there is considerable interaction between the disperse phase and the liquid dispersion medium, (i.e., there is extensive solvation) lyophilic dispersions are formed spontaneously when the material is placed in contact with the liquid. They are thermodynamically stable and reversible.

Acacia and povidone will readily disperse if added to water forming a colloidal solution. Gelatin and starch form colloidal sols spontaneously (especially in hot water) with water.

2. Lyophobic colloids

Most of the lyophobic dispersions are hydrophobic dispersions. They include aqueous dispersions of insoluble organic and inorganic compounds which have a low degree of hydration (i.e., less interaction).

Because, hydrophobic dispersions are intrinsically unstable and there is little interaction between the disperse phase and the dispersion medium (water), preparation of hydrophobic colloids needs special methods. They can be prepared by *dispersion or condensation*. Dispersion methods involve breaking up of disperse phase to small particles of colloidal dimensions through milling and grinding (particle size reduction or comminution) or peptization. Condensation methods involve the aggregation of small molecules or ions to produce particles of colloidal dimensions.

Comminution

Comminution can be carried out by two methods

(a) Dispersion methods: Colloid mills, ball mills and micronizers can be used to reduce the size of particles to colloidal range. In a colloid mill, the coarse material is sheared in a narrow gap between a static cone and a rapidly rotating cone to colloidal sizes.

In electrical dispersion method (*Bredig's arc method*) the dispersions of metals are prepared by producing an electric arc by keeping close together two electrodes made of the metal immersed in water containing traces of KOH as stabilizer in a container cooled by ice externally. The intense heat vaporizes some of the metal and the vapor condenses into colloidal particles in water. Eg. silver, gold, platinum hydrosols.

Colloidal dispersions of many materials such as sulfur and graphite can be obtained by means of ultrasonic waves. Emulsification by ultrasound waves is the method of choice for the preparation of soyabean oil emulsion in water for intravenous injection.

(b) Peptization is a process of dispersion of a precipitated material (flocculated or aggregated) into smaller aggregates of colloidal dimension.

It can be effected by the addition of deflocculating or peptizing agents. Peptizing agents may be surfactants, water soluble polymers, or ions which are adsorbed at the particle surface and they do not allow aggregation and keep the particles in the colloidal dimensions. Peptization occurs in the presence of an electrolyte carrying the same ion or charge as that of the precipitated particles. It is usually undertaken with freshly precipitated particles. For example, when a small volume of very dilute solution of hydrochloric acid is added to a fresh precipitate of silver chloride, it leads to the formation of colloidal solution of silver chloride.

Peptization can also be brought about by the removal of flocculating agents (electrolytes) and their removal results in the disintegration of floccules into small particles of colloidal dimensions. Even washing the gelatinous precipitate of aluminium hydroxide with water bring about peptization. Ferric hydroxide yields a sol when ferric chloride (Fe^{3+} being common ion) is added to it.

Condensation methods

A change in solvent may bring about the formation of colloidal particles by condensation. If an alcoholic solution of resin is poured slowly into water, a colloidal dispersion of resin in water is obtained. In the same manner, when an alcoholic solution of sulfur is mixed with water a bluish white colloidal dispersion of sulphur is produced. This is usually undertaken in the presence of a stabilizing agent to prevent precipitation.

Colloidal dispersion may be obtained by chemical reaction also. Colloidal sulphur may be obtained by bubbling hydrogen sulfide gas into an aqueous Sulphur dioxide solution



Colloidal dispersions of aluminium hydroxide may be prepared by hydrolyzing aluminium chloride



By double decomposition of sodium chloride with silver nitrate, a colloidal dispersion of silver chloride may be obtained.



A colloidal dispersion of ice in ether or chloroform can be obtained by freezing saturated solution of organic solvent in water.

Purification of colloidal dispersion

Most of the hydrosols contain low molecular weight water soluble impurities. Presence of electrolytes as impurities in hydrophobic dispersion has to be avoided as it may coagulate such dispersions. These dissolved impurities are removed by dialysis, electro dialysis and ultrafiltration. However, traces of electrolytes are needed to stabilize the colloidal system.

(a) Dialysis

It is a process based on unequal rates of passage of solutes and solvent through microsporus membrane.

Dialysis can be simply carried out by placing the colloidal sol in a *cellophane sac* and immersing this sac into a large vessel of water. Low molecular weight solute molecules diffuse out into water while the colloidal particles remain inside the sac entrapped. Dialysis rate may be increased by increasing the area through which diffusion occurs, by stirring, and by maintaining a high concentration gradient across the membrane. To maintain a high concentration gradient, the water is replaced continuously or changed repeatedly. Diffusion is continued until the colloidal sol is substantially free from the low molecular weight solute molecules.

Ordinary dialysis is relatively slow and if electrolytes of low molecular weight are the impurities to be removed, the process of dialysis can be speeded up by applying an electric potential. This technique is called electro-dialysis.

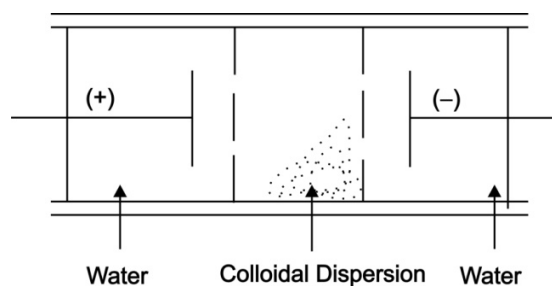


Fig. 1.4 Electro-dialysis cell

An electro-dialysis cell consists of three compartments two outer and one center compartment. (Fig. 1.4) The center compartment is separated from the two other compartments on either side by two dialysis membranes supported by screens. The two outer compartments contain water and also the electrodes and the center compartment the colloidal sol. When an electric potential is applied, the anions move from the sol into the anode compartment while the cations move from the sol into the cathode compartment. The colloidal particles in the center compartment move towards one of the membranes according to the charge they carry. Non electrolyte solute molecules (impurities) diffuse into both the outer compartments. As the density increases due to the accumulation of colloidal particles, they settle to the bottom of the center compartment as shown in Fig.1.4. The supernatant liquid can be changed by decantation and thus the purified colloidal sol is prepared by electro-dialysis and decantation. This process is called *electro-decantation*.

(b) Ultrafiltration

Keeping the colloidal sol in a compartment that is closed by a dialysis membrane of pore size 0.003μ and applying pressure, the liquid and the low molecular weight solute molecules are forced through the membrane. The colloidal particles are retained within the compartment. This separation process is called *ultrafiltration*. Ultrafiltration differs from dialysis only in that the passage of the small molecules of low molecular weight through the membrane is enhanced by

applying usually high positive pressures. As the process uses high pressure, the membrane is usually supported by a fine wire screen.

In order to avoid the increase in the concentration of colloidal particles and to remove the dissolved impurities completely, the water is replaced continuously or repeatedly by equal amounts of de-ionized water. To maintain uniform concentration throughout the colloidal sol, the sol is stirred.

Ultrafiltration has been used to separate and purify colloidal sols. An ultrafilter may be an ordinary filter paper impregnated with collodion (Cellulose tetranitrate dissolved in a mixture of ether and alcohol in the ratio of 3:1) or cellophane (a regenerated cellulose in swollen gel sheet) or cellulose acetate.

Stability of Colloids

The stability of a colloidal dispersion depends on two factors

1. presence of charge (+ or -) on the dispersed colloidal particles
2. Solvent sheath surrounding each dispersed particle

When the colloidal particles collide as a result of *Brownian movement*, the above two factors will prevent mutual adherence. It may be said that the stability of lyophobic colloid is largely due to the electric charges on the surface of the dispersed particles and for lyophilic sols it is the solvent sheath that is significant in stabilizing the system.

In a lyophobic sol as already mentioned, the particles are stabilised by the presence of electric charges on their surfaces. The like charges present on their surfaces prevent the coagulation of the particles. Coagulation is a process where the colloidal particles aggregate together resulting in the precipitation of the dispersed particles and ultimately the colloid dispersion breaks up i.e., becomes unstable. Coagulation (or aggregation of colloidal particles) may be brought about by the addition of electrolytes which reduce the zeta potential (the sign and magnitude of charge on the particle). The coagulating power of electrolytes depends on the valency of the active ion (ion causing coagulation). The higher the valency of the ion, the greater is the precipitating power. This is known as the *Schulze-Hardy* rule.

The stability of lyophobic colloids is described by DLVO theory (*Derjaguin, Landau, Verwey and Overbeek*). The forces operating on colloidal particles in a dispersion are the repulsive and attractive forces. The repulsive forces are due to overlapping of electrical double layer and the attractive forces are due to London type *van der Waals* forces. The potential energy of repulsion (V_r) is shown in Fig. 1.5 and also the potential energy of attraction V_a . V_0 indicates the composite potential energy, (i.e. interaction curve).

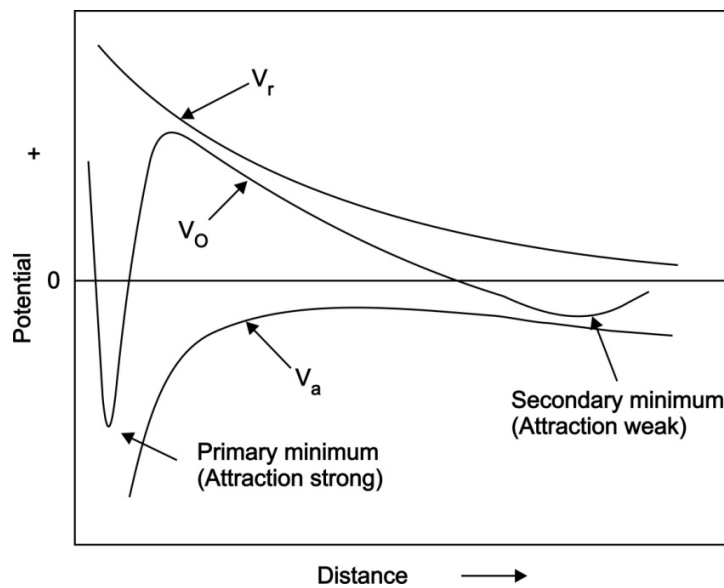


Fig. 1.5

As two particles approach each other in the medium a weak attractive force exists beyond the range of electrical double layer repulsive forces. This attractive region is called the *secondary minimum*. It is responsible for flocculation. This is significant in the controlled flocculation of suspended particles in a coarse dispersion (a suspension). If the thermal energy is equal or greater than the repulsive barrier (V_r) the particles come closer and encounter strong attraction in the *primary minimum* shown in the figure. When the particles get into the primary minimum, they coagulate.

At low electrolyte concentration, the repulsive forces predominate so that the particles experience only a repulsive force upon approach. The particles remain individually and the system is called dispersed or peptized. At a high concentration of electrolyte, the electrical double

layer forces are greatly diminished. As a result, *van der Waals* forces of attraction predominate and the particles encounter net attractive forces ending in coagulation.

Lyophilic and association colloids are thermodynamically stable and they exist in true solution. Hence, they do not coagulate on the addition of moderate amounts of electrolytes. However they coagulate if sufficient amount of electrolyte is added. This is termed 'salting out'. The coagulating power in lyophilic colloids may be given by *Hofmeister or lyotropic series*. Anions of Hofmeister series in decreasing order of precipitating power are citrate, tartrate, sulfate, acetate, chloride, nitrate, bromide and iodide. The precipitating power is due to their ability to dislodge solvent sheath from the colloidal particles.

Even the addition of solvents such as alcohol and acetone which are having greater affinity to water causes coagulation of colloidal particles. Addition of such solvents lowers the dielectric constant of the medium which is unfavorable for the colloidal particles.

Coacervation

When oppositely charged hydrophilic colloids are mixed, the colloidal particles may get separated forming colloid-rich layer. Such a formation of colloid-rich layer is termed as coacervation. The process of formation of coacervates is called coacervation. For example, Gelatin and acacia in water form hydrophilic colloids. Gelatin is (below pH 4.7) is positively charged while acacia is negatively charged. If these two oppositely charged colloidal solutions are mixed at a definite proportion, coacervates are formed. Coacervation may also be brought about by the addition of alcohol, sodium sulfate or starch.

When a polar solvent such as alcohol or acetone is added to a hydrophilic colloid, (i.e., a colloidal dispersion in more polar solvent such as water), it will decrease the solubility of colloidal particle in water. To this if a small amount of an electrolyte is added, it may bring about the coagulation or flocculation of the colloidal particles. It may be regarded that flocculation is a transformation of a sol hydrophilic nature to one of more hydrophobic nature.

This coacervation process forms the basis for microencapsulation of drug products. Thus, sulfamethoxazole drug particles can be encapsulated with gelatin-acacia coacervates. An aqueous mixture of sulfathiazole and povidone also results in coacervation by the addition of resorcinol, a coacervating agent for povidone.

Using microencapsulation process to different thicknesses, sustained release dosage forms, which have wide commercial applications, are manufactured.

Sensitization and Protection

When a small amount of hydrophilic or hydrophobic colloid is added to a hydrophobic colloid of opposite charge, the hydrophobic colloid becomes sensitive.

Sensitization is attributed to a reduction in zeta potential below the critical value (the value below which coagulation occurs). It is also reasoned that it is due to a reduction in the thickness of the ionic layer surrounding the colloidal particles.

However, addition of large amounts of hydrophilic colloid tends to stabilize the system because of adsorption of hydrophilic colloid particles forming a protective cover on the hydrophobic colloid particles. This phenomenon is called *protection*. The hydrophilic sol used for the purpose of protecting the hydrophobic colloid is known as protective colloid. This protective power of hydrophilic colloid may be given in terms of “*gold number*”.

The *gold number* is the weight in milligrams of the protective colloid (on dry basis) needed to prevent a color change from red to violet in 10 ml of gold sol on the addition of 1 ml of 10% solution of sodium chloride. Gold numbers of some protective colloids are given below.

Protective colloid	Gold number (mg)
Gelatine	0.006 - 0.01
Albumin	0.1
Acacia	0.1 - 0.2
Tragacanth	2

2. RHEOLOGY

Introduction

Rheology is the science of flow of materials under stress. Flow property of materials is mainly of two types – Newtonian and non-Newtonian. In the case of Newtonian flow, the viscosity of materials remains the same whatever be the stress applied. The Newtonian systems may be of different viscosities from low viscosity (such as water) to high viscosity (such as honey). The difference in viscosities is due to differences in the resistance offered to the flow by the respective liquid.

The Newtonian systems are again put into different types namely dilatant, plastic, and pseudoplastic systems. Dilatant systems or materials flow immediately once the stress is applied but as the stress is increased, the apparent viscosity of the system increases. At very high stresses the viscosity increases to a greater extent and at high stresses the flow may even stop damaging the stressing system.

The pseudoplastic system also flows immediately once the stress is applied but, in this case, the viscosity decreases on increasing the stress. The plastic system differs from pseudoplastic system by not flowing until a certain minimum stress is not exceeded i.e., the system does not flow at initial mild stresses. The flow occurs only after a minimum stress is exceeded and on further increasing the stress, the viscosity decreases as in the case of pseudoplastic systems. The minimum stress above which the flow starts is termed as yield value. Once the yield value is exceeded, the system starts to flow and on increasing the stress further, there is decrease in viscosity as in the case of pseudoplastic systems. Within the yield value, the plastic system behaves like elastic system. The yield value in plastic systems can be considered as elastic limit. Once this limit is exceeded, the flow starts and on increasing the stress, the viscosity decreases,

Even solids (powders) flow under stress and in this case, there is elastic and plastic flow. Elastic flow refers to the point within which, the solid will regain its original shape on removal of

the stress applied. Once the stress is exceeded greater than the elastic limit, there occurs what is called plastic flow which is irreversible and it ultimately leads to complete deformation. These behaviors assume importance when pharmaceutical powders are subjected to stress to form tablets and the properties of tablets depend on the elastic and plastic deformation.

Rheology

The term rheology was derived from two Greek words namely *rheo* (to flow) and *logos* (science). Rheology is the science that deals with the deformation of matter under the influence of stresses. The stresses may be

- (a) *Tensile stress*: a stress applied perpendicularly to the surface of a body
- (b) *Shearing stress*: a stress applied tangentially to the surface of a body.
- (c) Stress applied at any other angle to the surface of a body can be merely called as *stress*.

The deformation is of two types.

Elastic deformation	Plastic deformation
It is spontaneous and reversible. The work spent for the deformation is recoverable when the body returns to the original position.	It is permanent and irreversible. The work spent for the deformation is dissipated as heat.

The flow properties or viscous behavior of various pharmaceutical products ranging from simple liquids to semisolids such as ointments, gels, creams and pastes are very important for pharmacists in the following areas as detailed below.

1. For fluids

- Mixing of liquids
- Particle size reduction of disperse system with shear.
- Passage through orifices, including pouring, packaging in bottles, and passage through hypodermic needles.

- Fluid transfer, including pumping and flow through pipes
- Physical stability of disperse systems.

2. For semisolids

- Acceptable consistency and smoothness
- Spreading and adherence on to the skin
- Removal from jars or extrusion from tubes
- Capacity of solids to mix with miscible liquids.
- Release of the drug from the base
- Mixing and packing into containers.
- Physical stability and patient acceptability
- Biological availability from skin and gastro-intestinal tract

3. For solids

- Flow of powders from hopper and into die cavities in tableting and flow of powder into capsules during encapsulation.
- Packageability of powdered or granular solids.

4. Processing

- Production capacity of equipment
- Processing efficiency
- Correct choice of production equipment.

Viscosity

Viscosity is qualitatively defined as the resistance of a liquid to flow due to internal friction between different layers of liquid when it flows.

It may be treated mathematically as follows.

When the liquid flows (e.g., liquid passing through a pipe) due to a shearing stress, a plastic deformation occurs. Due to this, there is a change of velocity between different layers of

the liquid. That is, the velocity changes from zero (liquid at the periphery of the pipe) where the distance $x = 0$ from the base to a maximum value u at the topmost layer. (In the case of liquid flowing through a pipe, the velocity will be maximum at the center of the pipe Fig. 2.2).

Let us consider the liquid is made up of infinitely thin parallel layers (laminae) each of area A on a horizontal base as shown in (Fig. 2.1). u

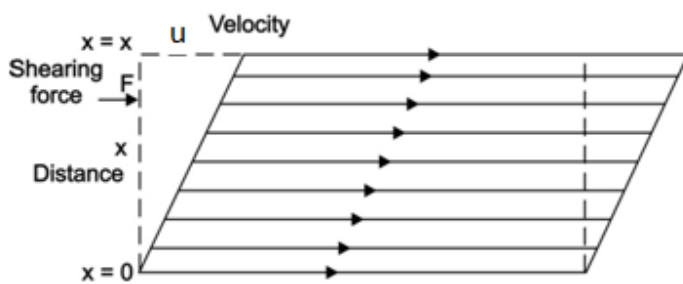


Fig. 2.1

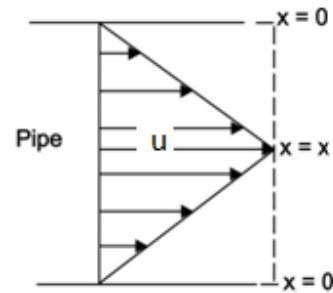


Fig. 2.2

Representation of movement of a liquid in a planar lamina and through a pipe

The infinitesimal difference of velocity du between two layers of liquid separated by an infinitesimal distance dx is the velocity gradient and the change in velocity with distance is the rate of shear and is given by $\frac{du}{dx}$. The force per unit area required to produce a certain rate of shear is called the shearing stress, S , i.e., $S = \frac{F}{A}$.

Shearing stress and shear rate are related by $S \propto \frac{du}{dx}$.

Introducing proportionality constant

$$S = \eta \frac{du}{dx} \quad \dots (1)$$

$$\text{or} \quad \eta = \frac{\text{shearing stress}}{\text{rate of shear}} = \frac{S}{du/dx}$$

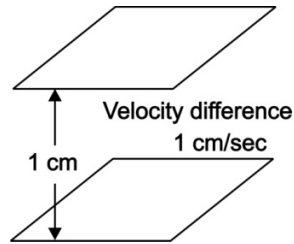


Fig. 2.3

It may also be defined as the force (in dyne/square centimeter) required to maintain a velocity difference of 1cm/sec between two parallel layers of liquid of each one square centimeter separated by a distance of 1 centimeter (Fig. 2.3). If the force required is 1 dyne/square centimeter, the coefficient of viscosity or simply viscosity (η) is said to be one poise (P)

The unit may be obtained by dimensional analysis

$$1 \text{ poise} = 0.1 \text{ Nsm}^{-2}$$

$$\eta = \frac{F}{A} \cdot \frac{dx}{du} = \frac{\text{dyne} \times \text{cm}}{\text{cm}^2 \times \text{cm}/\text{sec}} = \frac{\text{dyne sec}}{\text{cm}^2}$$

(i.e. 0.1. Newton second per square meter)

Newton second is the SI unit for poise.

$$\text{Dyne.sec/cm}^2 \text{ can also be given as g/cm.sec, since, } \frac{\text{dyn.sec}}{\text{cm}^2} = \frac{g \times \frac{\text{cm}}{\text{sec}^2} \times \text{sec}}{\text{cm}^2} = \frac{g}{\text{cm.sec}}$$

Liquids showing high coefficient of viscosity is said to be viscous and the liquid showing less coefficient of viscosity is said to be less viscous or mobile. For mobile liquids, the convenient unit is *centipoise* which is one hundredth of 1 *poise*. The reciprocal of viscosity is called fluidity (ϕ). (The unit is Poise^{-1})

$$\phi = \frac{1}{\eta} \quad \dots (2)$$

Kinematic viscosity

Kinematic viscosity is the absolute viscosity (η) divided by the density of the liquid. The units are *stoke* and *centistoke*.

Viscosity of liquids

Poiseuille was the first scientist who designed an equipment to find out viscosity of liquids. The equipment consists of a tall cylinder attached with a capillary flow tube at its lowest side at right angle to it (Fig. 2.4).

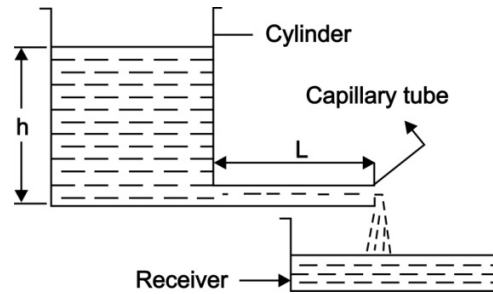


Fig. 2.4

The liquid is filled up to the height ' h ' in the cylinder and a specified volume of liquid is collected into a reservoir through the capillary tube of length l and radius ' r '. Then, the volume of liquid collected is given by

$$V = \frac{\pi p r^4 t}{8 \eta l} \quad \dots (3)$$

where V = volume of liquid collected

p = pressure head due to the liquid and is equal to ' hdg ',

i.e. height \times density \times acceleration due to gravity.

r = radius of the capillary tube.

t = time upto which the liquid was collected.

η = coefficient of viscosity of the liquid.

l = length of the capillary tube.

Rearranging the formula for (η) (viscosity),

$$\eta = \frac{\pi p r^4 t}{8 V l} \quad \dots (4)$$

in which all the parameters are measurable and η can be calculated easily.

Effect of temperature on viscosity

It is fact that as the temperature of a system is increased. viscosity decreases. Approximately for one degree centigrade rise, the viscosity falls by 1 to 10%. It is mathematically given as

$$\eta = Ae^{E_a/RT} \quad \dots (5)$$

Or

$$\ln \eta = \frac{E_a}{RT} + \ln A \quad \dots (6)$$

where A = a constant

R = gas constant

T = thermodynamic temperature

E_a = energy of activation to move one molecule past another

However, there are some exceptions. For example, viscosity of methyl cellulose solution *increases* as the temperature *increases*.

Hence the viscosity is affected by temperature, it is necessary to report the viscosity of a system at a given temperature and in the determination of viscosity of substances, the temperature should be maintained constant throughout the experiment.

Types of Rheological Systems

It is broadly classified into two types

- I. Newtonian systems
- II. Non-Newtonian systems.

1. Newtonian systems

Rheological properties of a system are usually expressed in the form of a graph wherein shearing stress (on the x axis) is plotted against rate of shear (on the y axis) and this is called a *rheogram*.

If a system shows same values of ' η ' (i.e., coefficient of viscosity) at different shearing rates at a given temperature, it is said to be a Newtonian system.

S.No.	Shearing stress	Shear rate	$\eta = \frac{\text{Shearing stress}}{\text{shear rate}}$
1	x_1	y_1	$\frac{x_1}{y_1} = n$
2	x_2	y_2	$\frac{x_2}{y_2} = n$
3	x_3	y_3	$\frac{x_3}{y_3} = n$
.	.	.	.
.	.	.	.
.	.	.	.
n	x_n	y_n	$\frac{x_n}{y_n} = n$

The linear curve passes through the origin indicating that even a mild force can induce a flow. The curve also indicates that the values of η are constant at different shear rates (Fig. 2.5).

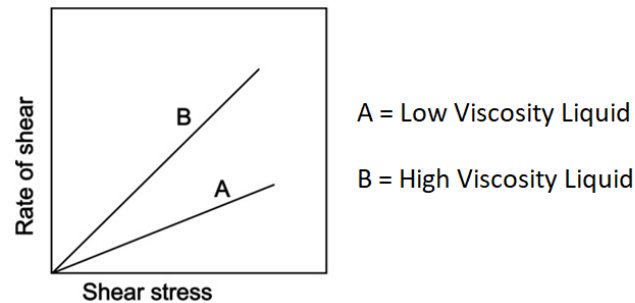


Fig. 2.5 Newtonian flow

Examples of some Newtonian liquids are water, simple organic liquids, solutions containing small solute molecules, dilute suspensions and emulsions.

II. Non-Newtonian systems

A system is said to be non-Newtonian when it shows different η values at different shearing rates at a given temperature. Therefore, the viscosity is often called *apparent* viscosity.

S.No.	Shearing stress	Shear rate	$\eta = \frac{\text{Shearing stress}}{\text{shear rate}}$
1	x_1	y_1	$\frac{x_1}{y_1} = \eta_1$
2	x_2	y_2	$\frac{x_2}{y_2} = \eta_2$
3	x_3	y_3	$\frac{x_3}{y_3} = \eta_3$
.	.	.	.
.	.	.	.
.	.	.	.
n	x_n	y_n	$\frac{x_n}{y_n} = \eta_n$

There are three types of non-Newtonian systems. They are

1. Plastic systems
2. Pseudoplastic systems
3. Dilatant systems

1. Plastic systems

The rheogram of plastic system is shown in (Fig. 2.6).

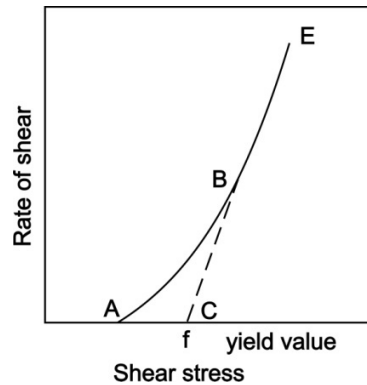


Fig. 2.6 Simple plastic flow

Plastic systems were studied extensively by Bingham and hence, they are called as **Bingham bodies**. In this, the curve is not passing through the origin. It indicates that mild forces cannot induce a flow. The flow is possible only after some shearing stress is exceeded. The

shearing stress at *A* is termed as low or minimum or low 'yield value', which induces a flow. The shear stress at the point *C* is called the *yield value* indicated as "*f*" in the Fig. 2.6. (yield value is an important property of certain pharmaceutical dispersions). At stresses below the yield value '*f*' the substance acts as an elastic material. Then the system is said to behave like a solid for stresses below the yield value. Those substances that exhibit a yield value are, in general, called **Bingham bodies**. It follows that those substances that exhibit no yield value and flows at the smallest shearing stress are termed as fluids. The curve obtained from shear stress *A* to shear stress *C* is not linear (i.e. the curve *AB*). The slope of the curve gradually increases until the point *B* and it indicates a gradual decrease in the viscosity of the system up to the point *B*. Therefore, the system which shows a gradual decrease in viscosity on increasing the shear stress is called '*shear thinning system*'. In this case, the *apparent plastic viscosity* (*U* or η_{pl}) is given by

$$\eta_{pl} \text{ or } U = \frac{S - \text{yield value}}{du/dx} \quad \dots (7)$$

Therefore, the η_{pl} viscosity is the viscosity above yield values.

The curve beyond *B* becomes linear (i.e., from *B* to *E*) and the system behaves just like Newtonian system there afterwards. The slope of the curve is termed as mobility and its reciprocal as plastic viscosity.

Examples of plastic systems are *ointments, pastes and creams and some disperse systems*.

2. Pseudoplastic systems

The rheogram for pseudoplastic system is given in (Fig. 2.7).

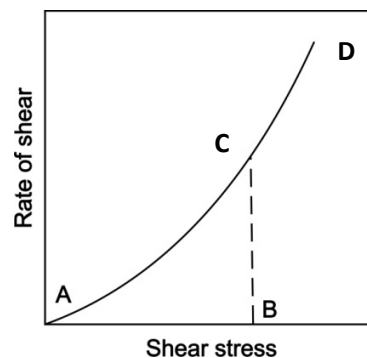


Fig. 2.7

The curve passes through the origin which indicates that mild forces can induce a flow. There is no yield value for this system. The curve obtained from shear stress A to shear stress B is similar to plastic system (i.e., curve AC). Since the system is having both the characters of Newtonian and plastic, it is called pseudoplastic system. This is also a 'shear thinning system'. In this case, the viscosity is given by the empirical power law.

$$\eta = \frac{S^N}{\frac{du}{dx}} \quad \dots (8)$$

where the value of N is greater than 1 (For Newtonian system, the value of N is 1). The values of N varies for different pseudoplastic systems. The greater the value of N the more pseudoplastic is the system. The equation (8) can be rearranged and written in logarithmic form as

$$\log \frac{du}{dx} = N \log S - \log \eta$$

Plotting the log of shearing stress ($\log S$) versus the log of rate of shear, ($\log \frac{du}{dx}$) a straight line is obtained with a slope of N (Fig. 2.8). However, some pseudoplastic suspending agents do not conform to equation (8)

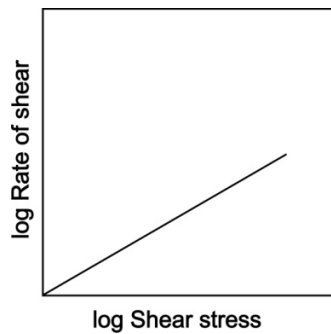


Fig. 2.8 Pseudo-Plastic flow

The curve beyond the point C becomes linear (i.e., from C to D) and the system (Refer Fig 2.7) behaves like Newtonian system there after wards.

To distinguish between plastic and pseudoplastic systems, it is necessary to obtain the flow behavior at low shear rates.

Examples of pseudoplastic system are *liquid dispersions of tragacanth, sodium alginate and sodium carboxymethyl cellulose*.

3. Dilatant systems

Suspensions with high percentage of dispersed solid particles (i.e., with more than 50% of deflocculated solid dispersed phase) exhibit an increase in resistance to flow with increasing rates of shear. They, in fact, increase in volume (with more void space) when sheared and therefore, termed *dilatant*. These Systems show an increase in consistency or viscosity on increasing the shear rate or stress in contrast to 'shear thinning systems' such as pseudoplastic and plastic systems.

The rheogram for dilatant system is given in (Fig. 2.9).

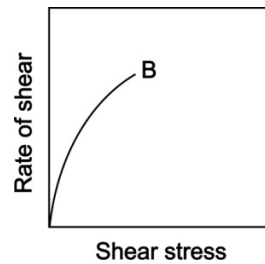


Fig. 2.9

The curve passes through the origin and it indicates that mild forces can induce a flow. The slope of the curve gradually decreases until the point, *B*. In this case, the viscosity of the system gradually increases and hence this system is called '*Shear thickening system*'. When the stress is removed, a dilatant system returns to its original state of fluidity.

The *apparent* viscosity of a dilatant system is given by the empirical power law.

$$\eta = \frac{S^N}{du/dx} \quad \dots (9)$$

where the value of *N* is less than 1.

Both the plastic and pseudoplastic systems show '*shear thinning*' properties and the dilatant systems show '*shear thickening*' properties.

Examples of dilatant system are concentrated deflocculated suspension (about 50% or more) and suspensions of starch in water

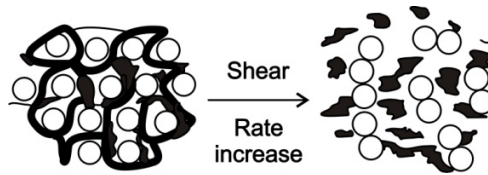
Mechanism of shear thinning

Plastic system is associated with the presence of aggregates or flocculated particles in the dispersion medium. In pseudoplastic system, the macromolecules align with neighboring molecules resulting in entanglement of molecules entrapping the liquid. In both the cases, there is considerable structural build-up increasing the viscosity of the system. Under the influence of shearing stress in both the systems, there is progressive structural breakdown resulting in decrease in viscosity. Greater amount of breakdown occurs at higher shear rates. Consequently, there is gradual decrease in viscosity. Once the structural breakdown is complete with increasing shear rates, the apparent viscosity becomes constant. i.e., the flow becomes Newtonian.

Mechanism of shear thickening

In contrast to shear thinning system, a shear thickening (or dilatant) system exhibits an increase in viscosity with increasing shear stress or shear rate. In dilatant systems, at rest, the particles are closely packed and so a minimum void space is present. The amount of vehicle is just sufficient to fill the minimum void space and the particles can move relative to one another at low rates of shear. At rest the system is reasonably fluid. As the shear rate is increased, the bulk of the system expands, particles become open packed and the void space within the system increases. The vehicle is now insufficient to fill the expanded void space. As one particle moves with respect to another, there is lot of structural build up with increased void spaces with consequent under-lubrication (i.e., insufficient lubrication) by the medium or vehicle and that leads to increased viscosity. Eventually the fluid system becomes a firm paste-like. Hence processing of dilatant systems in a mixer such as colloid mill leads to overloading and damaging the processing equipment especially at high shear rates

The following figure (Fig 2.10) shows dilatant system at rest and at high shear rates.



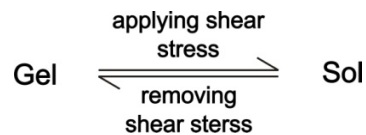
Dilatant system at rest	Dilatant system at high shear rate
Particles closely packed	Particles open packed
Less void space	More void space
Vehicle sufficient to fill the void space	Vehicle not sufficient to fill the void space
Less viscous and pourable	More viscous and non-pourable

Thixotropy

In the case of Newtonian systems, a curve which may be called up-curve is obtained with increase in shear rate. If the rate of shear is reduced after the desired maximum rate has been reached, a down-curve may be obtained. This down-curve and up-curve would be identical and superimposable. Whereas in shear-thinning system (i.e., in non-Newtonian systems), the down-curve can be displaced with respect to the up-curve. This indicates that the material has a different (especially lower) consistency at anyone rate of shear on the down-curve. It may be assumed tacitly that the system adapts itself to changing shear instantaneously. It may also be assumed that the structural build-up may not follow the same route of the structural break-up for its return to its original state i.e., structural build-up will not be the exact inverse copy for the structural break-up) because of changing rate of shear and the time of shear. The plastic and pseudoplastic systems at a given temperature, change their viscosities at varying shearing stresses.

By gradually increasing the shearing stress on plastic or pseudoplastic systems, the apparent viscosity gradually decreases as a result of progressive breakdown of structure in the liquid medium at a given temperature. After removing the shearing stress, the viscosity is

regained due to slow rebuilding of structure by Brownian motion but not immediately but after some time lag. Consider the conversion of gel to sol and then sol to gel after removing the stress applied.



The conversion of sol to gel is not instantaneous but requires some time lag indicating its time-dependency.

Plastic and pseudoplastic systems will change their viscosities gradually with respect to time even if a constant shearing stress is applied. They show a lower consistency or viscosity at any one shear rate on the down-curve than it had on the up-curve. It indicates that the build-up of structure does not take place immediately to regain its original consistency when the stress is removed or reduced. This phenomenon, called thixotropy, may now be defined as *a reversible isothermal transition from gel to sol with a comparatively slow recovery from sol to gel on standing or at rest*. In consistent with this definition, thixotropy can be applied only to shear-thinning systems.

A rheogram can be obtained for a shear thinning systems by plotting the rate of shear at various shear stresses. The curve is called 'up curve'. By reducing the shearing stress gradually on the above system, a 'down-curve' is obtained. Both the 'up curve' and 'down curve' are not super-imposable. The down curve is shifted to left side. This means the flow property of the system is not the same before and after the initial determination. Hence the viscosity of the sample depends upon its previous history. Therefore, the viscosities of the 'down curve' are lower than the viscosities of the 'up curve'. As a result, the 'down curve' is shifted to the left side of the 'up curve' in the rheogram (Fig. 2.11).

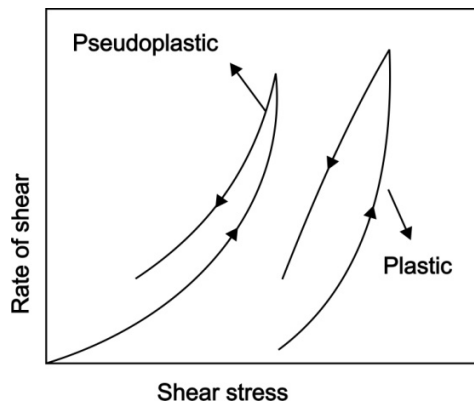


Fig. 2.11 Thixotropy in plastic and pseudoplastic systems

Rheograms obtained with shear-thinning systems are, thus, highly dependent on the rate at which shear is increased or decreased and the length of time the system is subjected to any one rate of shear. Simply saying, it depends on the previous history of the sample taken. The loop between the 'up curve' and the 'down curve' is called 'hysteresis loop'. The area of the loop indicates the extent of structural breakdown.

An example of the system showing thixotropy is bentonite gel. Even the curd obtained from milk can be considered as a thixotropic material.

Bulges and sours

Some dispersions may yield complex hysteresis loop. Though it is not so important, it may need a mention about. For example, a 10 to 15% by weight of aqueous bentonite gel yields a hysteresis loop with a characteristic bulge in the up-curve as shown in the Fig. 2.12. It is assumed to be due to the swelling of bentonite resulting from the crystalline plates of bentonite forming a "house of cards structure"

It is reported that in still more structured system such as procaine penicillin gel, the bulge develops into a spur-like protrusion demonstrating a high yield or spur value as shown in Fig. 2.13. The spur value γ represents a sharp of structural breakdown at low shear stress. It was found gels having definite spur values were very thixotropic, forming intramuscular depots upon injection. Such depots afford prolonged blood levels of the drug.

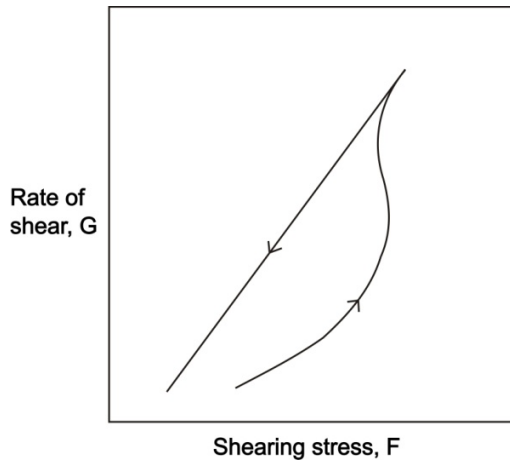


Fig. 2.12 Rheogram of a thixotropic material showing a bulge in the hysteresis loop

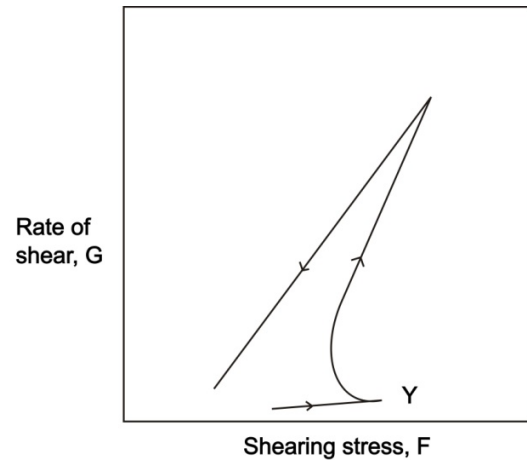


Fig. 2.13 Rheogram of a thixotropic material showing a spur value Y in the hysteresis loop

Negative thixotropy and rheopecy

Certain thixotropic materials show a phenomenon called *negative thixotropy* or *anti-thixotropy*. A thixotropic system such as magnesia magma exhibits an increase rather than a decrease in viscosity on the down curve. The magma which showed normal thixotropy below the shear rates of 30 per second, showed negative thixotropy at shear rates greater than 30 per second. In this the down curve was shifted to right side indicating an increase in viscosity.

The rebuilding of the broken structure after it has been subjected to certain shear rates takes some more time to regain its original consistency. In this case the restoration by Brownian motion is slow if the suspensions or solutions are viscous. However, in such cases gentle agitation or moderate and rhythmic vibration may speed up the rebuilding of the structure. Low shear rates thus hasten the process of regaining the initial high apparent viscosity or the onset of gelation in thixotropic sols. If the sheared dispersion of bentonite in a beaker is subjected to gentle vibration or rotation, the rebuilding of the 'house of cards' is speeded up. This material's recovery of some of its pre-sheared viscosity at a faster rate when it is gently sheared, compared to when it allowed to stand, is called *rheopecy*.

Determination of Flow Properties

For Newtonian systems, the shear rate is directly proportional to the shearing stress and hence it is enough to find a single rate of shear for a shearing stress (i.e., one point determination.) The point obtained for this value in the graph may be extrapolated to the origin i.e., a line passing through the point and origin may be drawn. The line gives a complete rheogram. For non-Newtonian systems, one point determination is useless and hence a multi-point determination should be undertaken. i.e., a number of rates of shear must be obtained at different shearing stresses to obtain a complete rheogram for plastic, pseudoplastic and dilatant systems.

The different instruments used for the determination of flow properties are

1. Ostwalds Viscometer
2. Ubbelohde Suspended Level Viscometer
3. Falling Sphere Viscometer
4. Cup and Bob Viscometer
5. Cone and Plate Viscometer.

Of these five viscometers, the first three viscometers are used for the determination of Newtonian flow and the last two are used for the determination of both Newtonian and non-Newtonian flows.

1. Ostwald's Viscometer

It is also called capillary viscometer. The apparatus (Fig. 2.14) consists of a 'U' tube, the left arm of the tube has a 'bulging' at its lower part and there is a marking 'A' above this bulb. The right arm of the tube also has a 'bulging' at the upper part and just below this bulb is a capillary tube as shown in the figure. There are two markings B and C above and below the bulb of the right arm.

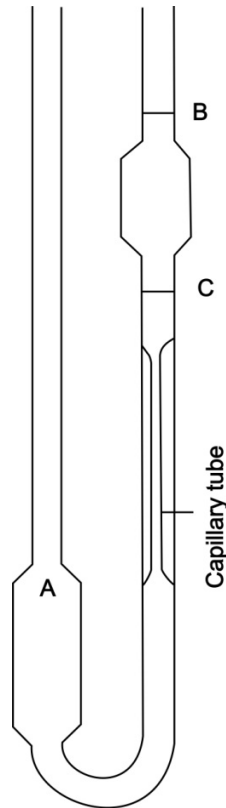


Fig. 2.14 Ostwald's Viscometer

The liquid is poured into the apparatus through the left arm up to the mark *A*. The liquid is then sucked into the right arm slightly above the point *B* and the left arm is closed with the thumb to keep the liquid without dropping down. The apparatus is clamped vertically and the thumb is removed so as to allow the liquid to fall through the capillary under gravity. The time taken for the liquid level to drop down from the point *B* to *C* is noted. The room temperature is also noted. As per Poisuille's equation.

$$\eta = \frac{\pi}{8} \frac{pr^4t}{Vl} = \frac{\pi}{8} \frac{hdgr^4t}{Vl} \quad \dots (10)$$

$$\eta = ctd$$

where *c* is instrument constant

The instrument constant is usually supplied along with the instrument by the manufacturer. By knowing the value of the time t to flow from the mark B to C and the density of the liquid d , the absolute viscosity of the liquid can be found out.

The relative viscosity of the liquid with respect to water can be found out as follows.

The experiment is first undertaken for water as described above with the instrument. After cleaning and drying the instrument, the experiment is carried out with the liquid whose relative viscosity is to be found out.

$$\frac{\eta_l}{\eta_w} = \frac{ct_l d_l}{ct_w d_w} = \frac{t_l d_l}{t_w d_w} \quad \dots (12)$$

The viscosity of water η_w at a given temperature (may be room temperature) is found out. Then t_l , d_l , t_w , and d_w are determined. From these values, the relative viscosity of the liquid with respect to water can be found out. The relative viscosity of the liquid may be converted to absolute viscosity by multiplying the relative viscosity with the absolute viscosity of water. The viscosities of the liquid can be found out at different temperatures by keeping the instrument in a thermostat.

Sometimes the viscosity of the liquid is expressed as *kinematic* viscosity

$$v = \frac{\eta}{\rho} = \frac{\text{absolute viscosity}}{\text{density of the liquid}} \quad \dots (13)$$

Experimental precautions

1. Streamline flow must occur in the capillary
2. Unnecessary long flow time should be avoided.
3. There should not be any air bubble.
4. The instrument should be thoroughly cleaned and dried for each liquid.
5. Adequate temperature control should be ensured.
6. Correction may be made for surface tension which tends to raise or lower the meniscus of the liquid in the tube.

The disadvantage with the Ostwald's viscometer is that for relative viscosity determination, volume of liquid put into the apparatus should be constant so as to get correct reproducible result.

To avoid the above difficulties, Ubbelohde viscometer is used.

2. Ubbelohde viscometer

It is a modified Ostwald's viscometer and in this another vertical tube (third arm) is attached to the bulb below the capillary part of the right arm parallel to 'U' tube as shown in (Fig. 2.15).

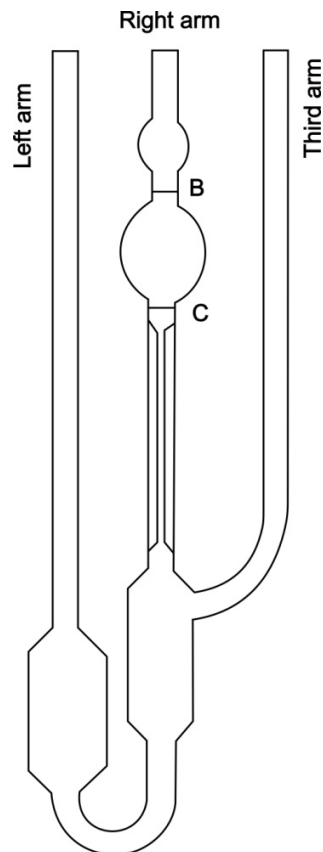


Fig. 2.15 Ubbelohde viscometer

A volume of liquid just sufficient to fill the bulb in the left arm is poured. By closing the left arm and the third arm with the thumbs, the liquid is sucked into the right arm (i.e. central tube) upto a level just above the point *B*. The central arm is now closed with the thumb after removing the thumbs from the other two arms and that keeps the level of the liquid just above the mark *B*. As the liquid below the capillary tube is ventilated down by the third arm, the volume of

liquid in the right arm (central tube) remains constant. The rest of the experiment is similar to as described under Ostwald's viscometer.

3. Falling sphere viscometer (Hoeppler falling ball viscometer)

As per Stoke's law, a body falling through a viscous medium, experiences a resistance or viscous drag that opposes the motion of the body. When the body falls through a liquid under the influence of gravity during which acceleration of the motion occurs at the initial period but when the gravitational force (acceleration) is balanced by the viscous drag, the body falls down at a uniform terminal velocity which can be determined in the falling sphere viscometer.

Viscous drag on the sphere = force responsible for downward motion due to gravity.

$$3\pi \eta du = \frac{\pi}{6} d^3 g (\rho_s - \rho_l) \quad \dots (14)$$

where η = coefficient of viscosity

d = diameter of the sphere

g = acceleration due to gravity

u = terminal velocity

ρ_s = density of the sphere

ρ_l = density of the liquid

Rearranging the above equation

$$\eta = \frac{d^2 g (\rho_s - \rho_l)}{18u} \quad \dots (15)$$

The diameter of the sphere may be obtained by using vernier caliper. ρ_l (density of the liquid) is determined using specific gravity bottle and the terminal velocity (u) by using the falling sphere viscometer and from these values the viscosity of the liquid may be calculated.

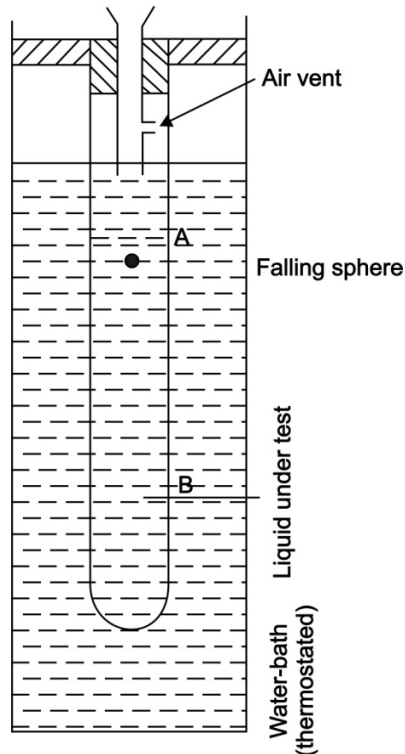


Fig. 2.16 Falling sphere viscometer

The apparatus (Fig. 2.16) consists of a tube having two markings *A* and *B* marked on the outer surface of the tube. The tube is filled with the liquid whose viscosity is to be determined. The tube is clamped vertically inside a constant temperature bath. Sufficient time is allowed to get all the air bubbles removed and the whole set up to attain the equilibrium temperature. A steel sphere (ball) is cleaned and allowed to reach the same temperature as that of the experiment by keeping in a thermostat. There is a guide tube on the fall tube through which the ball is allowed to fall and a hole in the guide tube prevents any airlock. The time t' taken for the sphere to fall from *A* to *B* is noted. The terminal velocity is the ratio of the distance between the two markings *A* and *B* and the time t' . By substituting all the values in the equation, the coefficient of the viscosity of the liquid is calculated.

The equation is given assuming that the sphere is falling through a medium of infinite dimension. But in the experiment the liquid is contained in a cylinder. A correction factor (*F*) is introduced to nullify the effect of wall on the fall of the sphere.

$$F = 1 - \frac{2.104d}{D} + 2.09 \frac{d^3}{D^3} \quad \dots (16)$$

where d = diameter of the sphere

D = diameter of the tube

and the corrected viscosity = $\eta \times F$

The instrument can be used over a range of 0.5 to 200,000 poise. For best results, the ball (density) should be such that it takes not less than 30 seconds to fall from mark A to B .

(Red Wood Viscometer: It consists of a cylinder having an outlet at its bottom with a valve. Two sizes are available called No.1 and No.2. The specifications are detailed in British Pharmacopoeia. The liquid is filled up to the mark made in the cylinder. The valve is fully opened and the time taken for the liquid to drain out fully is reported as Redwood seconds. Thus, it is an empirical instrument.)

4. Rotational viscometer

In rotational viscometers a solid rotating body is immersed or suspended in a liquid/semi solid (whose viscosity is to be measured) and is subjected to a retarding force due to the viscous drag which is proportional to the viscosity of the liquid. The advantages of rotational viscometers are:

- (a) it is possible to vary the shear rate over a wide range of values and
- (b) measurements can be made continuously for extended periods at a given shear rate or shear stress.

Therefore, the rotational viscometer, with accurate temperature control, are useful for measuring the time dependency as well as shear dependency of the viscosities of non-Newtonian systems. The rotational viscometers are

1. Concentric cylinder viscometer (or co-axial cylinder viscometer or cup and bob viscometers)
2. cone and plate viscometers.

Cup and Bob viscometer

The cup and bob viscometer (Fig. 2.17) consists of an outer cylinder *A*, (cup) which acts as a container for the liquid, and can be rotated at different speeds (different shearing stresses). An inner cylinder *B* (bob) is suspended freely by a torsion wire. Rotation of the outer cylinder *A* produces movements within the liquid in the gap separating the two cylinders and as a result the torque (indicating rate of shear) produced is transmitted to the inner cylinder *B*. This torque (*T*) is measured in terms of angular deflection θ of a pointer which moves on a scale.

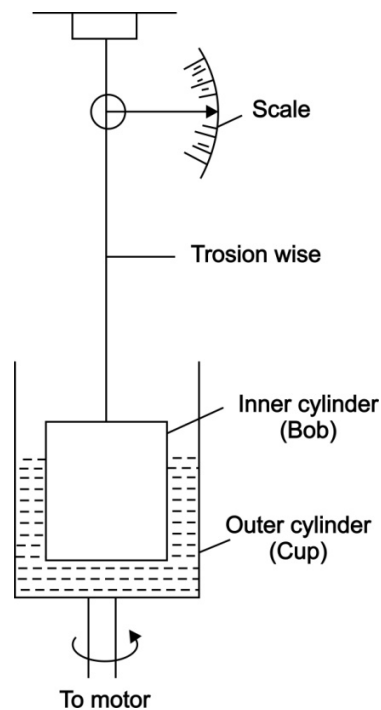


Fig. 2.17 Concentric cylinder viscometer (Cottrell type)

If a steady laminar flow occurs within the liquid, the viscosity is calculated as follows:

$$\eta = \frac{T_o \left(\frac{1}{r_1^2} - \frac{1}{r_2^2} \right)}{4\pi h \omega} \quad \dots (17)$$

Where, T_o = torque in dynes cm.

r_1 and r_2 = radii of the inner and outer cylinders

h = height of the inner cylinder surrounded by the liquid.

ω = angular velocity of the outer cylinder

There are two types of viscometers

- (a) *Couette type viscometer*: The cup is revolved. The viscous drag on the bob produced by the liquid results in a torque which is proportional to viscosity e.g: *Mac Machael viscometer*.
- (b) *Searle type viscometer*: It involves the principle of rotating the bob instead of the cup. e.g.: ***Stromer viscometer*** (Fig.2.18). For systems of viscosity more than 20 centipoise, it may be used. In this the cup is placed in a thermostat (constant temperature bath) on a stand and the bob is suspended into it. Both the cup and bob are allowed to reach the equilibrium temperature. The bob can be rotated by placing weight on a hanger through a winding pool which is attached to a hanger through a pulley. The number of revolutions of the bob can be counted with the help of a revolution counter. The data are converted to rpm. The weight is increased and the whole procedure is similar to the above.

The rpm value can be converted to actual shear rates. The weight added can be transposed into the units of shear stress, dynes/cm²

Formula for shear rate = $k_g \cdot n$ where n is adjustable speed i.e. rpm and k_g = shear rate factor

Formula for shear stress = $K_F \cdot S$. Where, S is dial reading and K_F , shear stress factor.

A rheogram can be obtained by plotting rpm versus the weight added. Making use of appropriate constants, rpm values are converted to actual shear rates (sec⁻¹) and the weights added into the units of shear (dynes cm⁻²) In this case, the viscosity is calculated as follows

$$\eta = K_v \frac{w}{v} \quad \dots (18)$$

where w = weight in grams

v = rpm generated due to w

K_v = instrument constant which can be determined by analysing an oil of known viscosity using the instrument.

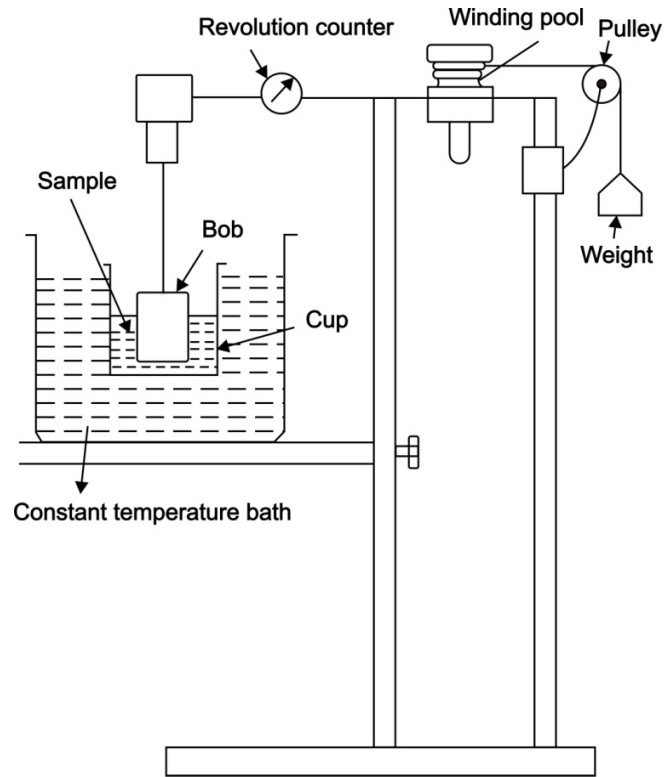


Fig. 2.18 Strome Viscometer (Searle type)

The plastic viscosity may be calculated using the formula, when Strome viscometer is used.

$$U = K_v \frac{W - W_f}{V} \quad \dots (19)$$

where W_f yield value intercept in grams.

The yield value of a Bingham body (f) (plastic system) is given by the expression.

$$f = K_f \times W_f \quad \dots (20)$$

Where

$$K_f = K_v \times \frac{2\pi}{60} \times \frac{1}{2.303 \log \left(\frac{R_2}{R_1} \right)} \quad \dots (21)$$

where R_2 = radius of the cup

R_1 = radius of the bob

Disadvantages of cup and bob viscometer

1. If the gap between the cup and bob is larger, there will be no uniform rate of shear.
2. Frictional heating may develop at higher rates of shear and hence a constant temperature bath is used to offset the temperature effect on viscosity of the liquid.
3. Filling and cleaning are often difficult.
4. The instrument requires more sample.
5. *Plug flow development:* In the cup and bob viscometer there is a variable shear stress within the sample across the gap between the cup and bob. This variation is mainly dependent upon the gap. In Searle type viscometer, the bob is rotated and the cup is stationary. For the bob to be rotated, the shearing stress should necessarily be higher than the yield value. It may happen so, for a certain shearing stress of the bob, (though it is sufficiently high to exceed the yield value) the shearing stress developed at the inner surface of the cup may be less than the yield value. In such a situation, the material at the inner surface of the cup remains as a solid plug without any flow. This phenomenon is plug flow. Chances of plug flow can be minimized by reducing the gap between the cup and bob. For that a bob as large as possible may be used. Laminar flow (rather than plug flow) of the system can be expected only when the shear stress at the wall of the cup exceeds the yield value).

Plug flow may be important when pastes and concentrated suspensions flow out of the container through an orifice. For example, in the case of tooth paste obtained from its container, the paste experiences a higher shear stress when pressed at the circumference of the tube aperture. As a result, the consistency drops at the points of stress and this facilitates extrusion of the paste in the core as a plug. However, this phenomenon is not desirable in obtaining rheograms of plastic systems with cup and bob viscometer.

Cone and plate viscometer

In cone and plate viscometer, all the disadvantages mentioned under cup and bob viscometer are overcome.

The cone and plate viscometer (Fig. 2.19) essentially consists of a smooth plate and a cone. During operation, the sample is placed at the center of the plate, which is then slowly raised

so that the tip of the cone comes in contact with the sample. At this position, the cone to plate angle is ordinarily less than 1° . The sample is sheared in the narrow gap between the plate and the cone when the plate is driven by a variable speed motor. The torque transmitted through the sample to the cone is measured. The viscosity is given by

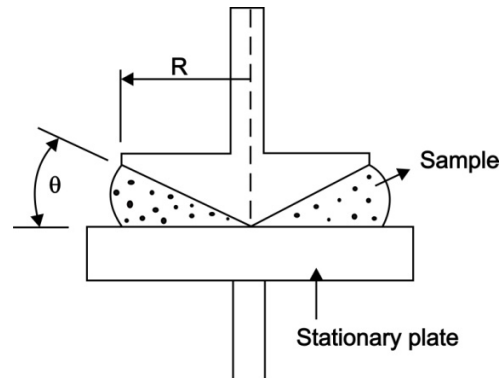


Fig. 2.19 Cone and plate viscometer

$$\eta = \frac{3A/2\pi R^3}{B/Q} \quad \dots (22)$$

where A = torque on the cone

R = radius of the cone

B = radial velocity of the plate

Q = angle between the cone and the plate and is less than $\pi/360$ radians

Advantages:

1. Rate of shear is constant throughout the sample and hence no chance for plug flow.
2. Cleaning is easy and requires less time.
3. Temperature stabilization is also good.
4. It needs very little sample for the study. That is a sample volume of 0.1 to 0.2 ml will do.
5. Rates of shear can be increased or decreased in a predetermined and reproducible manner.
6. This serves as a valuable aid for the determination of hysteresis loop obtained in thixotropic systems and also in determining thixotropic coefficient.

Commercial Viscometers

1. Ferranti - Portable viscometer
2. Brookfield viscometer
3. Ferranti - Shirley cone and plate viscometer
4. Extrusion viscometer

1. Ferranti - Portable viscometer (for bulk liquids)

In this the rotating outer cylinder is inverted and immersed in the liquid. The inner cylinder is attached to a pointer on a scale through a torque spring which is beryllium copper spring. (Fig. 2.20) There is a guard ring shown in Fig. 2.20.

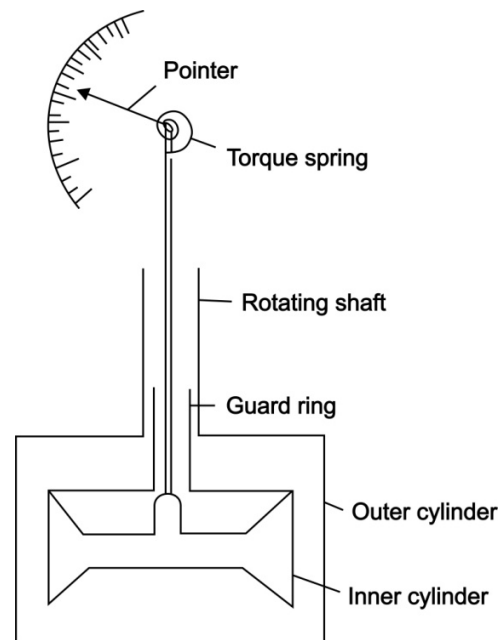


Fig. 2.20 Ferranti portable viscometer

The outer cylinder is driven by a synchronous motor with a three to five speed gear box. The gear box can provide a range of 1 rev/min. up to 300 rev/min. The mean shear rates vary from 930 to 0.15 sec^{-1} . Amount of sample required is usually about 100 ml. For a given rpm (rate of shear) and the angle of deflection (shearing stress), the viscosity may be read directly from the literature table supplied by the manufacturer.

2. Brookfield viscometer

It is used as a comparative instrument (Fig. 2.21) since it does not provide results in terms of absolute shear. A bob is immersed in the sample liquid. The bob carries a rotating spindle which is driven through a calibrated beryllium copper spring which in turn is mounted on a motor shaft. The spindle is also attached to a pointer which gives the displacement of the spindle due to viscous drag of the sample. Since both the pointer and the scale revolve, the readings are complicated. However, it is possible to clamp the pointer. In this viscosity changes cannot be followed while increasing the shearing stress and hence it is used for comparing the apparent viscosities of non-Newtonian systems.

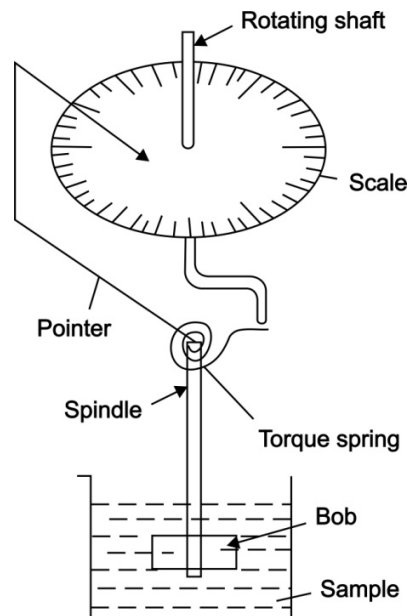


Fig. 2.21 Brookfield Viscometer

3. Ferranti - Shirley cone and plate viscometer

It is very popularly used to study the change of flow properties of a rheological system continuously by varying the shear rates and to study thixotropy.

This viscometer (Fig. 2.22) consists of a stationary flat plate and a rotating cone. The usual plate to cone angle is about 0.3° to 4° so that only small samples (0.1 to 0.2 ml) are required. The plate is maintained at a constant temperature.

The rate of shear for small angles is constant and is given by

$$\frac{A}{B} \quad \dots (23)$$

where $A =$ rotation (rad/sec)

$B =$ cone angle (rad)

The cone is driven by a variable speed motor and the rate of shear is capable of being varied over a wide range from 0 to 18000 sec^{-1} . A torsion spring is interposed between the cone (i.e., the driving shaft of the cone) and the driving shaft in order to measure the shearing stress on a galvanometer connected to a potentiometer circuit.

It is possible to obtain recording of shear rates and shearing stresses simultaneously. This enables to obtain flow curves automatically on an $x - y$ recorder.

A rheological system is taken in between the cone and the plate. The rate of shear is varied continuously and the corresponding shearing stresses are recorded simultaneously on $x - y$ recorder. From the rheograms obtained, one can make out whether the system is Newtonian, plastic, pseudoplastic or dilatant.

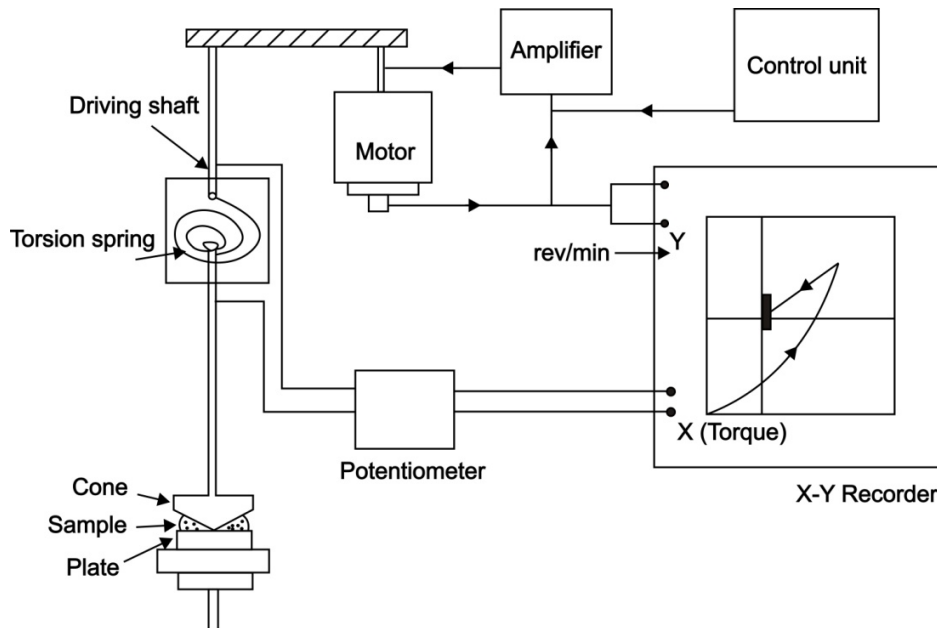


Fig. 2.22 Ferranti-shirely cone and plate viscometer

For thixotropic studies, a sample is placed in between the cone and plate in the instrument. The rate of shear is gradually increased and the corresponding shear stresses are recorded simultaneously on the $x - y$ recorder to get the 'up-curve'. Then the rate of shear is gradually decreased in the sample and the corresponding shearing stresses are recorded simultaneously on the $x - y$ recorder to obtain the 'down curve'. Thus, it is possible to demonstrate the time-dependent effect of stresses on rheological systems as well as how the previous history of the sample alters its physical properties.

4. Extrusion viscometer

It is suitable for butter and semisolid preparations. It consists of a simple cylinder 4 cm long and 1.25 cm in diameter with a circular orifice. Inside the cylinder is a plunger which could be moved at a uniform speed.

A sample of any ointment or paste or cream which has got consumer acceptability is kept in the cylinder. The thrust just required to extrude the material is recorded. Whether the sample of ointment or paste or cream is having the same thrust for the subsequent batches are tested. Any

non-homogeneity due to substandard material, agglomerate of particles or air bubble will be indicated by the fluctuation in the recorded thrust.

Deformation of solids

When a solid body is subjected to opposing forces on its opposite sides, there is a finite change in its geometry or shape depending upon the nature of applied forces or load. The relative amount of deformation produced by such forces is a dimensionless quantity called *strain*. The various types of strains may be tensile strain, compression strain and shear strain. Consider a solid of definite geometry is compressed by forces acting on its opposite sides to cause a reduction in length of ΔH . if the initial length before the application of force is H_0 (Fig. 2.23), the compression strain, Z may be given by the equation

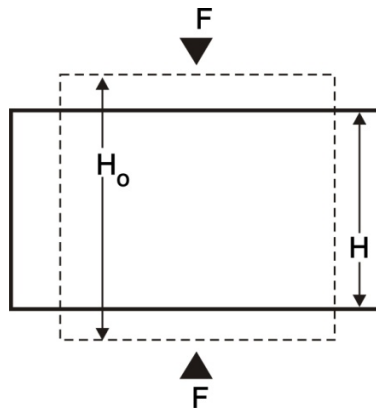


Fig. 2.23

$$Z = \frac{\Delta H}{H_0}$$

The ratio of the force, F required to produce the strain to the area, A over which it acts is called the stress, σ and is given by

$$\sigma = \frac{F}{A}$$

Stress is the force or load applied on solid at a particular area or angle and strain is the effect produced.

Deformation of solids may comprise two components – elastic deformation and plastic deformation.

Elastic deformation

When an external mechanical force is applied to a mass of powder of certain volume contained in a container, the powder particles may repack and this repacking leads to some internal volume reduction. When this repacking resulting in volume reduction becomes more difficult, there may be some type of powder particle deformation on further compression. This powder particle deformation results mainly from the change in intermolecular spacing. This intermolecular spacing is reversible to a large extent on removal of the load. In other words, there is spontaneous reversibility. The solid particles behave like rubber and hence the deformation is said to be elastic. All solids undergo some elastic deformation when subjected to external forces not exceeding the elastic limit. Thus, in the initial stage of stress or applied pressure the deformation of solid material will be elastic. Once the applied load is released or removed, the material will return to its original shape.

Mostly, a solid material, under the initial stages of applied pressure, will be deformed elastically and a change in the shape of the solid material caused by the applied pressure becomes completely reversible and the material will return to its original shape on release of the pressure. The stress-strain relationship for a specimen of solid material is described by **Hooke's law**. For an ideal elastic solid, Hooke's law states that the strain is directly proportional to the applied pressure (or stress) within the elastic limit of the material and can be given by,

$$\sigma = E \cdot \epsilon$$

Where σ = applied pressure or stress

E = Young's modulus of elasticity and it is a measure of the stiffness, hardness, or resistance to elongation.

ϵ = strain

The strain can be given by $\epsilon = \frac{l-l_0}{l_0}$

Where, l_0 = initial length and l = final length. Young's modulus,

The elastic strain results from a change in the intermolecular spacing and for a small deformation. It is reversible. As long as the elastic limit is not exceeded, the material shows elastic deformation. If the elastic limit is exceeded, the deformation of the material becomes irreversible. In pharmaceutical materials such as acetyl salicylic acid and microcrystalline cellulose, elastic deformation assumes the dominant mechanism of compression even within the range of maximum forces normally encountered in practice.

Plastic deformation

In other groups of powdered solids, an elastic limit or yield point is reached and application of load above this limit results in deformation not immediately reversible on removal of applied pressure. In these cases, bulk volume reduction results from plastic deformation and/or viscous flow of the particles. Squeezing of particles into the remaining void space represents the viscous flow of particles. Such a mechanism predominates in materials in which the shear strength (or stress) is less than the breaking strength. When the shear strength is greater the particles may be preferentially fractured or broken. The smaller particles may then fill up any adjacent void or air spaces. Such a fracture is termed brittle fracture. There may also be ductile fracture which is characterized by extensive plastic deformation followed by fracture. All the deformation effects may be accompanied by breaking and formation of new bonds between the particles resulting in consolidation as the new surfaces are pressed together.

Thus, plastic deformation is the permanent change in the shape of the solid material due to applied stress. Plastic deformation depends entirely on crystal defects such as dislocation, grain boundaries and slip planes within the crystals and this in turn is influenced by the rate of crystallization, particle size, the presence of impurities, and the type of crystallization solvent used. The following stress-strain curve (Fig. 2.24) depicts elastic and plastic deformation.

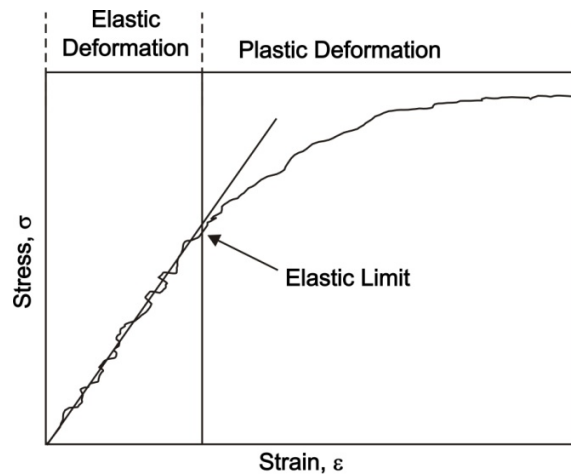


Fig. 2.24 Stress-strain curve showing elastic and plastic deformation regions

Plastic deformation assumes importance because; the plastic deformation permits pharmaceutical excipients and drugs to establish large areas of contact during compaction which assures strong tablets ensuring less friability also.

The student must understand, at this juncture, that when a bed of powder is subjected to compression forces, there is initial repacking followed by elastic and plastic deformation. All these three processes lead to volume reduction resulting in a compact mass of powder or pack, say tablet.

This reduction in volume, which is actually the reduction in void space among powder particles, leads to changes in density of the powder pack. Therefore, in tablet compression, an important concept is relative density. The relative density, D , of a (powder) material is given by

$$D = \rho / \rho_0$$

Where ρ = density of the powder material pack in g/cm^3

ρ_0 = true density (or absolute density) of powder material in g/cm^3

True density can be defined as the density of the powder material in the absence of pores within it. It means the powder pack contains absolutely no void spaces between particles.

In tablet compression, the relative density has a maximum value of 1.0 and this occurs when all the void space is compressed out of the compressed powder and only solid material

(i.e. the tablet) with no pores remains. Attainment of a relative density value of 1.0 is virtually impossible. Usually, relative density values in pharmaceutical tablets may range from 0.4 to 0.95 from loose powder to highly compressed tablets.

Almost all tablets may have some porous structure. The typical density for tablets may vary from 0.7 to 0.95. It means 30% to 10% of tablet volume consists of pores. The relation between relative density and porosity is given by

$$\epsilon = 1 - D$$

Where ϵ = porosity and D = relative density

Heckle equation which relates the applied pressure to porosity, is based on the assumption that void space decrease follows first order process. The Heckel equation is

$$\frac{dD}{dP} = K.(1 - D)$$

Where $\frac{dD}{dP}$ = change in density (hence in porosity) with increase in applied pressure or load

K = slope and is a measure of plasticity. A greater slope indicates greater plasticity of the material.

A = related to the initial repacking when pressure is zero.

Integrating the above equation, we can get

$$\ln \frac{1}{1-D} = K.P + A$$

A Heckel plot can be obtained by plotting $\ln 1/1 - D$ versus P . Such a plot may consist of two regions – an initial non-linear region followed by a linear region. It is to be understood that the Heckel equation does not apply to non-linear portion and it reflects the initial stage of consolidation where significant rearrangement takes place. The terminal portion of the plot is linear which obeys the Heckel equation indicating the deformation properties. The following Heckel plots for three different materials show different terminal slopes indicating different deformation properties.

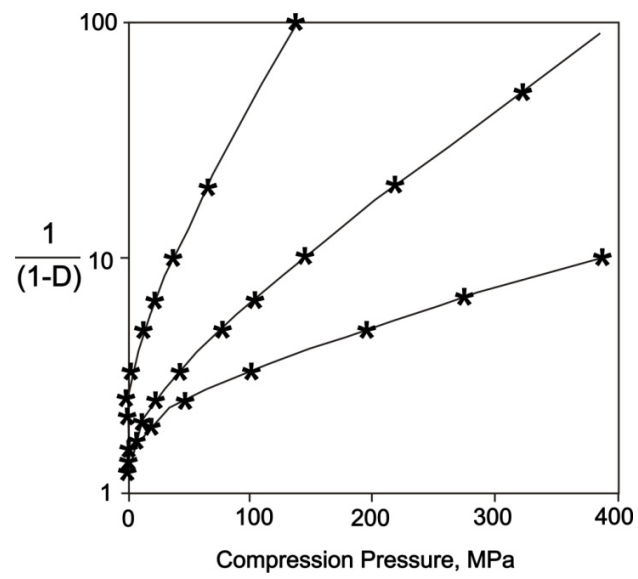


Fig. 2.25 Heckel plot of three pharmaceutical agents