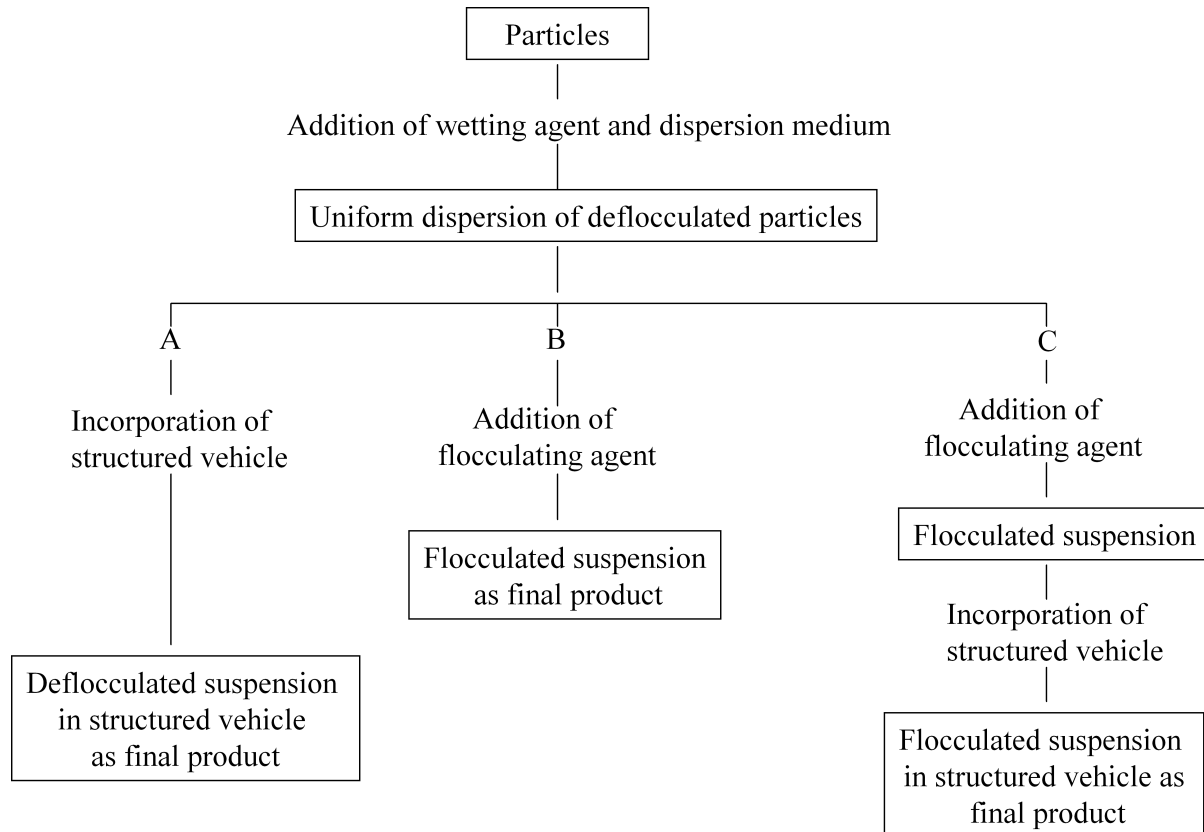


Important question

Q1-Explain the formulation of suspension.

A1- **Method of preparation**

The preparation of suspension includes three methods: (1) use of controlled flocculation and (2) use of structured vehicle (3)- combination of both of the two pervious methods. The following is the general guidelines to suspension formulation:



**A-Structured vehicle**

- Structured vehicles called also thickening or suspending agents. They are aqueous solutions of natural and synthetic gums. These are used to increase the viscosity of the suspension.
- Methyl cellulose, carboxymethyl cellulose, sodium carboxymethyl cellulose, acacia, gelatin and tragacanth are the most commonly used structured vehicle in the pharmaceutical suspensions. These are non-toxic, pharmacologically inert, and compatible with a wide range of active and inactive ingredients.

- These structured vehicles entrapped the particle and reduces the sedimentation of particles. Although, these structured vehicles reduces the sedimentation of particles, not necessarily completely eliminate the particle settling. Thus, the use of deflocculated particles in a structure vehicle may form solid hard cake upon long storage.
- The risk of caking may be eliminated by forming flocculated particles in a structured vehicle.
- Note that too high viscosity isn't desirable and it causes difficulty in pouring and administration. Also, it may affect drug absorption since they adsorb on the surface of particle and suppress the dissolution rate.
- Structured vehicles are pseudoplastic or plastic in their rheological behaviors
- In the following table is summary of suspending agents

**Q2-Evaluation of suspension and sedimentation parameter.**

A2- Suspensions are evaluated by determining their physical stability. Two useful parameters for the evaluation of suspensions are sedimentation volume and degree of flocculation. The determination of sedimentation volume provides a qualitative means of evaluation. A quantitative knowledge is obtained by determining the degree of flocculation.

- 1. Sedimentation volume: (F)**, sedimentation volume of a suspension is expressed by the ratio of the equilibrium volume of the sediment,  $V_u$ , to the total volume,  $V_o$  of the suspension.

$$F = V_u/V_o$$

The value of F normally lies between 0 to 1 for any pharmaceutical suspension. The value of F provides a qualitative knowledge about the physical stability of the suspension.

F= 1	No sedimentation, no clear supernatant
F =0.5	50% of the total volume is occupied by sediment
F > 1	Sediment volume is greater than the original volume due to formation of floccules which are fluffy and loose

- 2. Degree of flocculation: (β)**, degree of flocculation is the ratio of the sedimentation volume of the flocculated suspension, F, to the sedimentation volume of the deflocculated suspension,  $F_{\infty}$

$$\beta = F / F_{\infty}$$

$(V_u/V_o)$  flocculated

$$\beta = \frac{\text{-----}}{\text{-----}}$$

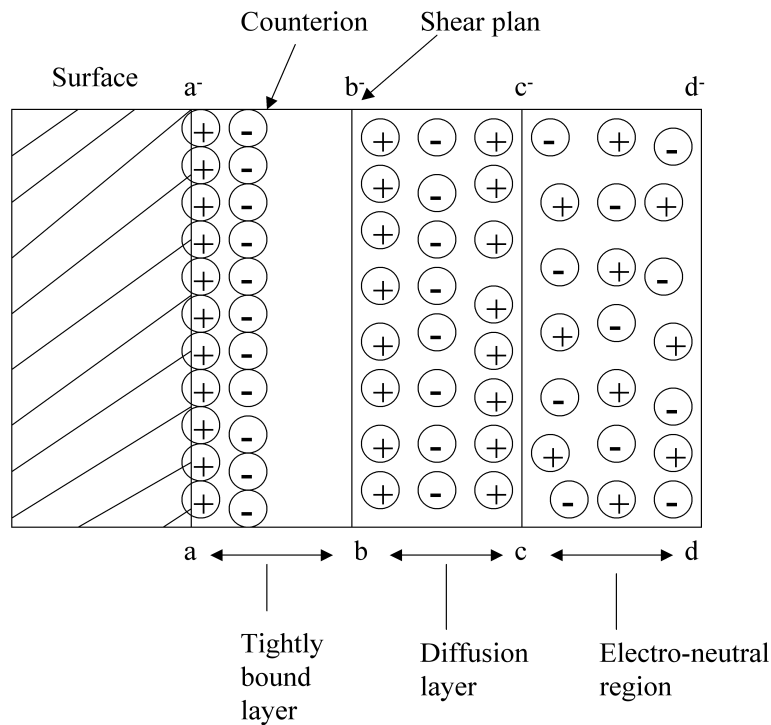
$(V_u/V_o)$  deflocculated

When the total volume of both the flocculated and the deflocculated suspensions are same; the degree of flocculation,  $\beta = (V_u)_{\text{floc}} / (V_u)_{\text{defloc}}$ . The minimum value of  $\beta$  is 1; this is the case when the sedimentation volume of the flocculated suspension is equal to the sedimentation volume of deflocculated suspension.  $\beta$  is more fundamental parameter than  $F$  since it relates the volume of flocculated sediment to that in a deflocculated system

### Q3- Note on electro kinetic properties

#### A3- Electrokinetic Properties

- Dispersed solid particles in a suspension may have charge in relation to their surrounding vehicle. These solid particles may become charged through one of two situations.
  1. Selective adsorption of a particular ionic species present in the vehicle. This may be due to the addition of some ionic species in a polar solvent. Consider a solid particle in contact with an electrolyte solution. The particle may become positively or negatively charged by selective adsorption of either cations or anions from the solution.
  2. Ionization of functional group of the particle. In this situation, the total charge is a function of the pH of the surrounding vehicle.



- In the above figure, the particle is positively charged and the anions present in the surrounding vehicle are attracted to the positively charged particle by electric forces that also serve to repel the approach of any cations. The ions that gave the particle its charge, cations in this example, are called potential-determining ions. Immediately adjacent to the surface of the particle is a layer of tightly bound solvent molecules, together with some ions oppositely charged to the potential-determining ions, anions in this example. These ions, oppositely charged to the potential-determining ions, are called counterions or gegenions. These two layers of ions at the interface constitute a double layer of electric charge. The intensity of the electric force decreases with distance from the surface of the particle. Thus, the distribution of ions is uniform at this region and a zone of electroneutrality is achieved.

#### **-Nernst and zeta potential-**

- The difference in electric potential between the actual surface of the particle and the electroneutral region is referred to as Nernst potential. Thus, Nernst potential is controlled by the electrical potential at the surface of the particle due to the potential determining ions. Nernst potential has little effect in the formulation of stable suspension.
- The potential difference between the ions in the tightly bound layer and the electroneutral region, referred to as zeta potential (see the figure), has significant effect in the formulation of stable suspension. Zeta potential governs the degree of repulsion between

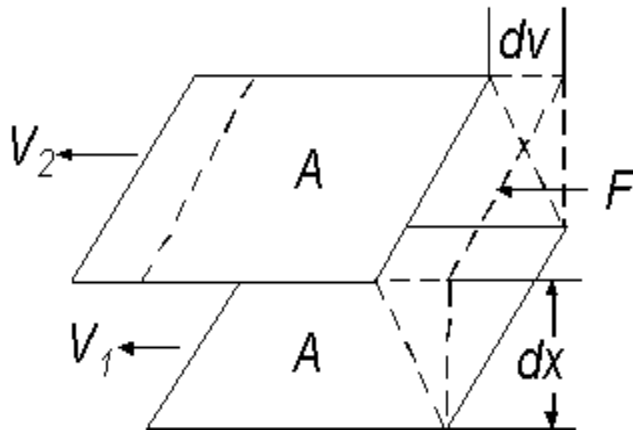
adjacent, similar charged, solid dispersed particles.

If the zeta potential is reduced below a critical value, the force of attraction between particles succeed the force of repulsion, and the particles come together. This phenomenon is referred to as flocculation and the loosely

#### Q4 Define Newtonian and non Newtonian flow with rheogram

##### Viscosity

Viscosity is the measure of the internal friction of a fluid. This friction becomes apparent when a layer of fluid is made to move in relation to another layer. The greater the friction, the greater the amount of force required to cause this movement, which is called *shear*. Shearing occurs whenever the fluid is physically moved or distributed, as in pouring, spreading, spraying, mixing, etc. Highly viscous fluids, therefore, require more force to move than less viscous materials.



Isaac Newton defined viscosity by considering the model represented in the figure above. Two parallel planes of fluid of equal area  $A$  are separated by a distance  $dx$  and are moving in the same direction at different velocities  $V_1$  and  $V_2$ . Newton assumed that the force required to maintain this difference in speed was proportional to the difference in speed through the liquid, or the velocity gradient. To express this, Newton wrote:

where  $h$  is a constant for a given material and is called its viscosity.

The velocity gradient,  $dv/dx$ , is a measure of the change in speed at which the intermediate layers move with respect to each other. It describes the shearing the liquid experiences and is thus called *shear rate*. This will be symbolized as  $S$  in subsequent discussions. Its unit of measure is called the *reciprocal second* ( $\text{sec}^{-1}$ ).

The term  $F/A$  indicates the force per unit area required to produce the shearing action. It is referred to as *shear stress* and will be symbolized by  $F'$ . Its unit of measurement is *dynes per square centimeter* ( $\text{dynes/cm}^2$ ).

Using these simplified terms, viscosity may be defined mathematically by this formula:

$$\eta = \text{Viscosity} = \frac{F'}{S} = \frac{\text{shear stress}}{\text{shear rate}}$$

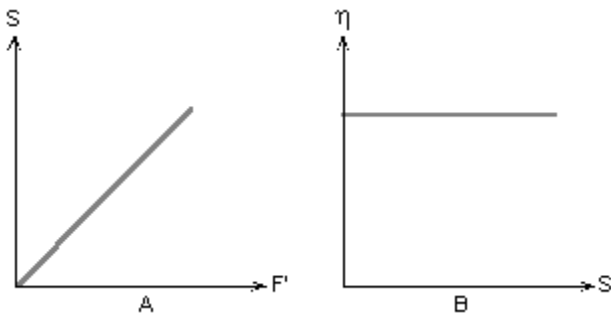
The fundamental unit of viscosity measurement is the *poise*. A material requiring a shear stress of one dyne per square centimeter to produce a shear rate of one reciprocal second has a viscosity of one poise, or 100 centipoise. You will encounter viscosity measurements expressed in *Pascal-seconds* (Pa·s) or *milli-Pascal-seconds* (mPa·s); these are units of the International System and are sometimes used in preference to the Metric designations. One Pascal-second is equal to ten poise; one milli-Pascal-second is equal to one centipoise.

Newton assumed that all materials have, at a given temperature, a viscosity that is independent of the shear rate. In other words, twice the force would move the fluid twice as fast.

As we shall see, Newton was only partly right.

### Newtonian Fluids

This type of flow behavior Newton assumed for all fluids is called, not surprisingly, *Newtonian*. It is, however, only one of several types of flow behavior you may encounter. A Newtonian fluid is represented graphically in the figure below. Graph A shows that the relationship between shear stress (F') and shear rate (S) is a straight line. Graph B shows that the fluid's viscosity remains constant as the shear rate is varied. Typical Newtonian fluids include water and thin motor oils.



What this means in practice is that at a given temperature the viscosity of a Newtonian fluid will remain constant regardless of which Viscometer model, spindle or speed you use to measure it. Brookfield Viscosity Standards are Newtonian within the range of shear rates

generated by Brookfield equipment; that's why they are usable with all our Viscometer models. Newtonians are obviously the easiest fluids to measure - just grab your Viscometer and go to it. They are not, unfortunately, as common as that much more complex group of fluids, the non-Newtonians, which will be discussed in the next section.

### Non-Newtonian Fluids

A non-Newtonian fluid is broadly defined as one for which the relationship F'/S is not a constant. In other words, when the shear rate is varied, the shear stress doesn't vary in the same proportion (or even necessarily in the same direction). The viscosity of such fluids will therefore change as the shear rate is varied. Thus, the experimental parameters of Viscometer model, spindle and speed all have an effect on the measured viscosity of a non-Newtonian fluid. This measured viscosity is called the *apparent viscosity* of the fluid and is accurate only when explicit

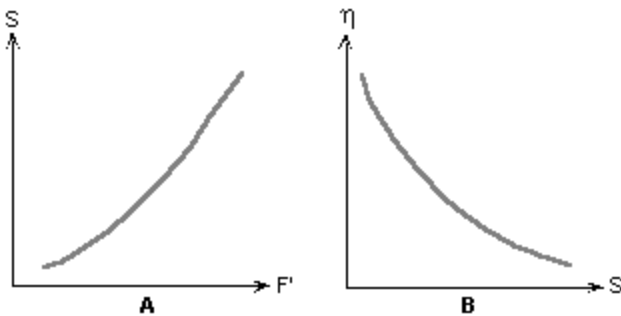
different shapes and sizes. As they pass by each other, as happens during flow, their size, shape, and cohesiveness will determine how much force is required to move them. At each specific rate of experimental parameters are furnished and adhered to.

Non-Newtonian flow can be envisioned by thinking of any fluid as a mixture of molecules with of shear, the alignment may be different and more or less force may be required to maintain motion.

There are several types non-Newtonian flow behavior, characterized by the way a fluid's viscosity changes in response to variations in shear rate. The most common types of non-Newtonian fluids you may encounter include:

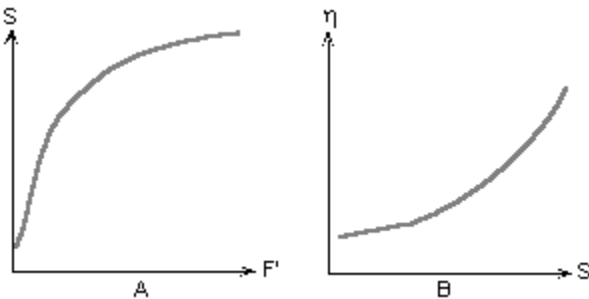
#### Pseudoplastic

This type of fluid will display a decreasing viscosity with an increasing shear rate, as shown in the figure below. Probably the most common of the non-Newtonian fluids, pseudo-plastics include paints, emulsions, and dispersions of many types. This type of flow behavior is sometimes called *shear-thinning*.



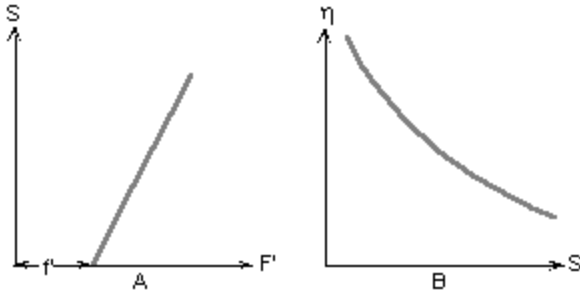
#### Dilatant

Increasing viscosity with an increase in shear rate characterizes the dilatant fluid; see the figure below. Although rarer than pseudoplasticity, dilatancy is frequently observed in fluids containing high levels of deflocculated solids, such as clay slurries, candy compounds, corn starch in water, and sand/water mixtures. Dilatancy is also referred to as *shear-thickening* flow behavior.



#### Plastic

This type of fluid will behave as a solid under static conditions. A certain amount of force must be applied to the fluid before any flow is induced; this force is called the *yield value*. Tomato catsup is a good example of this type fluid; its yield value will often make it refuse to pour from the bottle until the bottle is shaken or struck, allowing the catsup to gush freely. Once the yield value is exceeded and flow begins, plastic fluids may display Newtonian, pseudoplastic, or dilatant flow characteristics. See the figure below.



So far we have only discussed the effect of shear rate on non-Newtonian fluids. What happens when the element of time is considered? This question leads us to the examination of two more types of non-Newtonian flow: *thixotropic* and *rheopectic*.

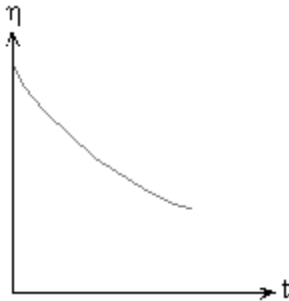
### Q5 Define Thixotrophy

#### Thixotropy and Rheopexy

Some fluids will display a change in viscosity with time under conditions of constant shear rate. There are two categories to consider:

##### Thixotropy

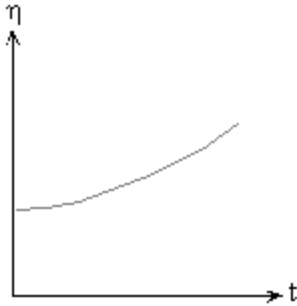
As shown in the figure below, a thixotropic fluid undergoes a decrease in viscosity with time, while it is subjected to constant shearing.



##### Rheopexy

This is essentially the opposite of thixotropic behavior, in that the fluid's viscosity increases with time as it is sheared at a constant rate. See the figure below.

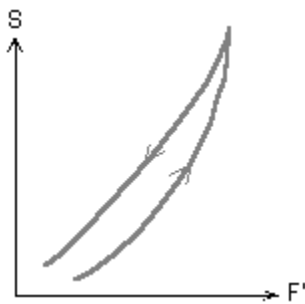




Both thixotropy and rheopexy may occur in combination with any of the previously discussed flow behaviors, or only at certain shear rates. The time element is extremely variable; under conditions of constant shear, some fluids will reach their final viscosity value in a few seconds, while others may take up to several days.

Rheoplectic fluids are rarely encountered. Thixotropy, however, is frequently observed in materials such as greases, heavy printing inks, and paints.

When subjected to varying rates of shear, a thixotropic fluid will react as illustrated in the figure below. A plot of shear stress versus shear rate was made as the shear rate was increased to a certain value, then immediately decreased to the starting point. Note that the *up* and *down* curves do not coincide. This *hysteresis loop* is caused by the decrease in the fluid's viscosity with increasing time of shearing. Such effects may or may not be reversible; some thixotropic fluids, if allowed to stand undisturbed for a while, will regain their initial viscosity, while others never will.

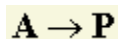


The rheological behavior of a fluid can, of course, have a profound effect on viscosity measurement technique. Later we will discuss some of these effects and ways of dealing with them

**Q6 Derive the first order reaction**

**A6 First Order Reaction**

For a general unimolecular reaction



where **A** is a reactant and **P** is a product, the reaction rate expression for a first order reaction is

$$r = -\frac{d[\mathbf{A}]}{dt} = k[\mathbf{A}] \quad (1)$$

**This means that the reaction rate is proportional to the concentration of a single reactant raised to the first power.**

Separation of the variables in equation (1)

$$\frac{d[\mathbf{A}]}{[\mathbf{A}]} = -k dt \quad (2)$$

and integration of equation (2)

$$\int_{[\mathbf{A}]_0}^{[\mathbf{A}]} \frac{d[\mathbf{A}]}{[\mathbf{A}]} = -k \int_{t_0}^t dt \quad (3)$$

yields

$$\ln[\mathbf{A}] = -kt + C \quad (4)$$

The constant of integration **C** can be evaluated by using boundary conditions. When  $t = 0$ ,  $[\mathbf{A}] = [\mathbf{A}]_0$ .  $[\mathbf{A}]_0$  is the initial concentration of **A**.

Substituting the values above into equation (4) one obtains:

$$\ln[\mathbf{A}]_0 = -k(0) + C \quad (5)$$

Therefore the constant of integration is

$$C = \ln[\mathbf{A}]_0 \quad (6)$$

Substituting equation (6) into equation (5) leads to the integrated rate law:

$$\ln \frac{[\mathbf{A}]}{[\mathbf{A}]_0} = -kt \quad (7)$$

**Plotting  $\ln [A]$  or  $\ln [A] / [A]_0$  against time creates a straight line with slope  $-k$ .  
The plot should be linear up to a conversion of about 90 %.**

Equation (7) can also be written as:

$$[A] = [A]_0 \cdot e^{-kt} \quad (8)$$

This means that the concentration of **A** decreases exponentially as a function of time.

The rate constant **k** can also be determined from the half-life  $t_{1/2}$ . Half-life is the time it takes for the concentration to fall from  $[A]_0$  to  $[A]_0/2 \implies [A] = 1/2 [A]_0$ .

Equation (7) is rewritten as:

$$k \cdot t_{1/2} = \ln \frac{[A]_0}{[A]_0/2} \implies k = \frac{\ln 2}{t_{1/2}} \quad (9)$$

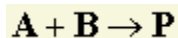
Thus, half-life of a first order reaction is independent of the initial concentration of the reactant.

**Q7 Derive the second order reaction**

## A7 **Second Order Reaction**

**The rate of a second order reaction is proportional to either the concentration of a reactant squared, or the product of concentrations of two reactants.**

For the general case of a reaction between **A** and **B**, such that



the rate of reaction will be given by

$$r = \frac{d[A]}{dt} = -k \cdot [A][B] \quad (1)$$

**1. Initial concentrations of the two reactants are equal:**

Equation (1) can be written as:

$$-\frac{d[A]}{dt} = k \cdot [A]^2 \quad (2)$$

Separating the variables and integrating

$$\int_{[A]_0}^{[A]} \frac{d[A]}{[A]^2} = -k \int_{t_0}^t dt \quad (3)$$

gives

$$\frac{1}{[A]} = kt + C \quad (4)$$

Provided that  $[A] = [A]_0$  at  $t = 0$ , the constant of integration  $C$  becomes equal to  $1/[A]_0$ .

Thus the second order integrated rate equation is

$$\frac{1}{[A]} - \frac{1}{[A]_0} = kt \quad (5)$$

**A plot of  $1/[A]$  vs  $t$  produces a straight line with slope  $k$  and intercept  $1/[A]_0$ . The plot should be linear up to a conversion of about 50 %.**

## 2. Starting concentrations of the two reactants are different:

If  $[A]_0$  and  $[B]_0$  are different the variable  $x$  is used.

Noting that  $d[A] = -dx$ , the general rate equation (1) can be expressed by

$$\frac{dx}{([A]_0 - x)([B]_0 - x)} = kdt \quad (6)$$

$[A]_0 - x = [A]$ ,  $[B]_0 - x = [B]$  and  $x$  is the decrease in the concentration of  $A$  and  $B$  respectively.

In order to integrate the left-hand side of equation (6), it is necessary to perform a partial fraction expansion. The fraction on the left hand-side of equation below is splitted into a sum of simple fractions on the right hand-side.

$$\frac{1}{([\mathbf{A}]_0 - \mathbf{x})([\mathbf{B}]_0 - \mathbf{x})} = \frac{\mathbf{c}'}{([\mathbf{A}]_0 - \mathbf{x})} + \frac{\mathbf{c}''}{([\mathbf{B}]_0 - \mathbf{x})} \quad (7)$$

$\mathbf{c}'$  and  $\mathbf{c}''$  are two constants. Putting them back over a common denominator

$$= \frac{\mathbf{c}'([\mathbf{B}]_0 - \mathbf{x}) + \mathbf{c}''([\mathbf{A}]_0 - \mathbf{x})}{([\mathbf{A}]_0 - \mathbf{x})([\mathbf{B}]_0 - \mathbf{x})} \quad (8)$$

leads to

$$1 = (\mathbf{c}'[\mathbf{B}]_0 + \mathbf{c}''[\mathbf{A}]_0) - (\mathbf{c}' + \mathbf{c}'')\mathbf{x} \quad (9)$$

Provided that  $-\mathbf{x}(\mathbf{c}' + \mathbf{c}'') = 0$

$$1 = (\mathbf{c}'[\mathbf{B}]_0 + \mathbf{c}''[\mathbf{A}]_0) \quad \text{and} \quad \mathbf{c}' = -\mathbf{c}'' \quad (10)$$

The equations above allow to determine the factors  $\mathbf{c}'$  and  $\mathbf{c}''$ :

$$-\mathbf{c}''([\mathbf{B}]_0 - [\mathbf{A}]_0) = 1 \quad (11)$$

$$\mathbf{c}' = -\frac{1}{[\mathbf{A}]_0 - [\mathbf{B}]_0} \quad \text{and} \quad \mathbf{c}'' = \frac{1}{[\mathbf{A}]_0 - [\mathbf{B}]_0} \quad (12)$$

Using  $\mathbf{c}'$ ,  $\mathbf{c}''$  notation equation (6) becomes the form

$$\frac{\mathbf{c}' d\mathbf{x}}{([\mathbf{A}]_0 - \mathbf{x})} + \frac{\mathbf{c}'' d\mathbf{x}}{([\mathbf{B}]_0 - \mathbf{x})} = \mathbf{k} d\mathbf{t} \quad (13)$$

whose integration

$$\frac{1}{[\mathbf{A}]_0 - [\mathbf{B}]_0} \int \left[ \frac{1}{[\mathbf{B}]_0 - \mathbf{x}} - \frac{1}{[\mathbf{A}]_0 - \mathbf{x}} \right] d\mathbf{x} = \mathbf{k} \int d\mathbf{t} \quad (14)$$

results in

$$\frac{1}{[A]_0 - [B]_0} \ln \frac{[A]_0 - x}{[B]_0 - x} = kt + C \quad (15)$$

where  $C$  is the constant of integration.

Using the condition that  $x = 0$ , when  $t = 0$ , the value of  $C$  can be found:

$$C = \frac{1}{[A]_0 - [B]_0} \ln \frac{[A]_0}{[B]_0} \quad (16)$$

and equation (15) becomes

$$\ln \frac{[A]_0 - x}{[B]_0 - x} = kt ([A]_0 - [B]_0) + \ln \frac{[A]_0}{[B]_0} \quad (17)$$

**If  $[A]_0 > [B]_0$ , then a plot of**

$$\ln \frac{[A]_0 - x}{[B]_0 - x} \quad (18)$$

**against  $t$  will have a positive slope, equal  $([A]_0 - [B]_0) \cdot k$ .**

Because equivalent amounts of **A** and **B** are reacting,  $[A]$  can be expressed in terms of  $[B]$ :

If the experimental method yields reactant concentrations rather than  $x$ , the equivalent form of equation (17) is

$$\ln \frac{[A]}{[B]} = kt ([A]_0 - [B]_0) + \ln \frac{[A]_0}{[B]_0} \quad (19)$$

The rate constant can be determined using equation (20), provided that the initial concentration of **A** is twice the initial concentration of **B** (see [Kinetic equations - Reaction Second Order - Download PDF file](#)):

$$\ln \left[ \frac{1}{2} \left( \frac{x_0}{x} + 1 \right) \right] = x_0 \cdot kt \quad (20)$$

where  $x_0 = [B]_0$  and  $x = [B]$ .

**Q8 classify the various types of viscometer**

A8 Capillary viscometer

Falling sphere viscometer

Cup and bob viscometer

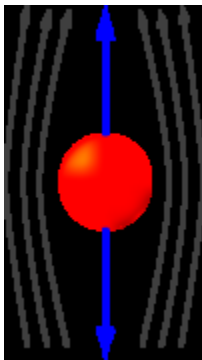
Cone and plate viscometer

v Brookfield viscometer

Ultrasonic Shear Rheometer: -For analyzing protein solution rheology

**Q9 Explain falling sphere viscometer**

A9.vInstron Capillary Rheometer:- Falling sphere viscometers



creeping flow past a sphere

Stokes' law is the basis of the falling sphere viscometer, in which the fluid is stationary in a vertical

glass tube. A sphere of known size and density is allowed to descend through the liquid. If correctly selected, it reaches terminal velocity, which can be measured by the time it takes to pass two marks on the tube. Electronic sensing can be used for opaque fluids. Knowing the terminal velocity, the size and density of the sphere, and the density of the liquid, Stokes' law can be used to calculate the viscosity of the fluid. A series of steel ball bearings of different diameter is normally used in the classic experiment to improve the accuracy of the calculation. The school experiment uses glycerine as the fluid, and the technique is used industrially to check the viscosity of fluids used in processes. It includes many different oils, and polymer liquids such as solutions.

In 1851, George Gabriel Stokes derived an expression for the frictional force (also called drag force) exerted on spherical objects with very small Reynolds numbers (e. g. , very small particles) in a continuous viscous fluid by solving the small fluid-mass limit of the generally unsolvable Navier-Stokes equations:

$$F = 6\pi r\eta v$$

where:

- $F$  is the frictional force,
- $r$  is the radius of the spherical object,
- $\eta$  is the fluid viscosity, and
- $v$  is the particle's velocity.

If the particles are falling in the viscous fluid by their own weight, then a terminal velocity, also known as the settling velocity, is reached when this frictional force combined with the buoyant force exactly balance the gravitational force. The resulting settling velocity (or terminal velocity) is given by:

$$V_s = \frac{2}{9} \frac{r^2 g (\rho_p - \rho_f)}{\mu}$$

where:

- $V_s$  is the particles' settling velocity (m/s) (vertically downwards if  $\rho_p > \rho_f$ , upwards if  $\rho_p <$
- 
- $\rho_f$ ),
- $r$  is the [Stokes radius](#) of the particle (m),
- 
- $g$  is the [gravitational acceleration](#) (m/s<sup>2</sup>),



- 
- $\rho_p$  is the [density](#) of the particles ( $\text{kg/m}^3$ ),
- 
- $\rho_f$  is the [density](#) of the fluid ( $\text{kg/m}^3$ ), and
- 
- $\mu$  is the (dynamic) fluid [viscosity](#) (Pa s).

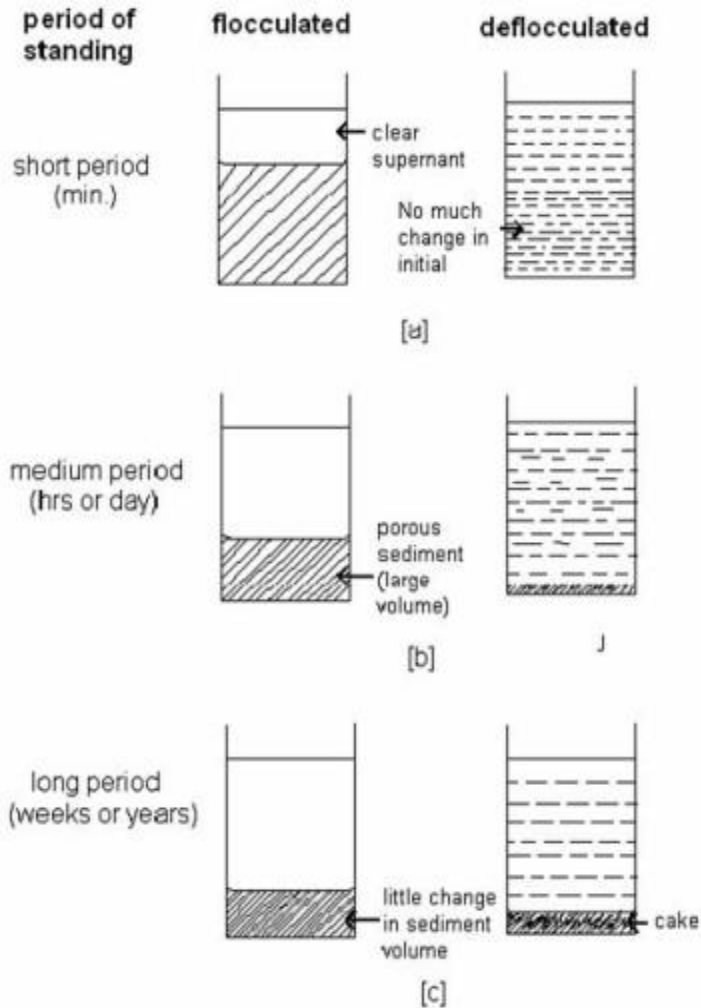
Note that [Stokes flow](#) is assumed, so the [Reynolds number](#) must be small.

## **Q 10 What is the Sedimentation Behaviour Of Flocculated And Deflocculated Suspensions:**

### **A10 Flocculated Suspensions**

In flocculated suspension, formed flocs (loos aggregates) will cause increase in sedimentation rate due to increase in size of sedimenting particles. Hence, flocculated suspensions sediment more rapidly.

Here, the sedimentation depends not only on the size of the flocs but also on the porosity of flocs. In flocculated suspension the loose structure of the rapidly sedimenting flocs tends to preserve in the sediment, which contains an appreciable amount of entrapped liquid. The volume of final sediment is thus relatively large and is easily redispersed by agitation.



**Fig 2.2: Sedimentation behaviour of flocculated and deflocculated suspensions**

### **Deflocculated suspensions**

In deflocculated suspension, individual particles are settling, so rate of sedimentation is slow which prevents entrapping of liquid medium which makes it difficult to re-disperse by agitation. This phenomenon also called 'cracking' or 'claying'. In deflocculated suspension larger particles settle fast and smaller remain in supernatant liquid so supernatant appears cloudy whereby in flocculated suspension, even the smallest particles are involved in flocs, so the supernatant does not appear cloudy.

Electrolytes decrease electrical barrier between the particles and bring them together to form flocules. They reduce zeta potential near to zero value that results in formation of bridge between adjacent particles, which lines them together in a loosely arranged structure.

### **Q11 Write a note on controlled formulation**

A11

Electrolytes act as flocculating agents by reducing the electric barrier between the particles, as evidenced by a decrease in zeta potential and the formation of a bridge between adjacent particles so as to link them together in a loosely arranged structure. If we disperse particles of bismuth subnitrate in water we find that based on electrophoretic mobility potential because of the strong force of repulsion between adjacent particles, the system is peptized or deflocculated. By preparing series of bismuth subnitrate suspensions containing increasing concentration of monobasic potassium phosphate co-relation between apparent zeta potential and sedimentation volume ,caking ,and flocculation can be demonstrated.

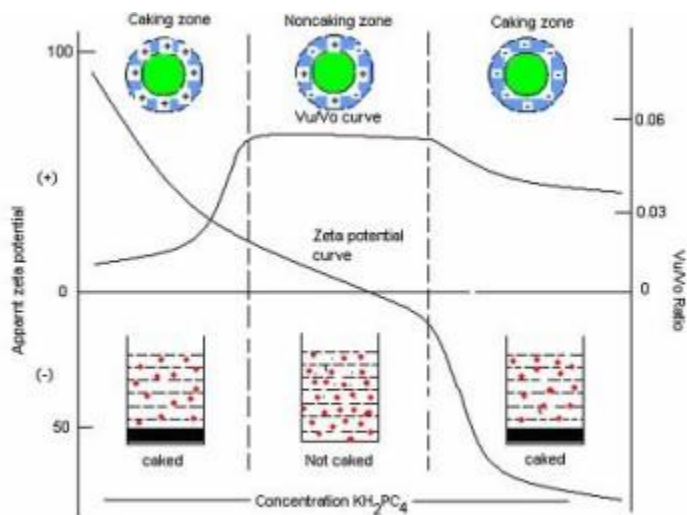


Fig 2.3: Caking diagram, showing the flocculation of a bismuth subnitrate suspension by means of the flocculating agent.

(Reference: From A.Martin and J.Swarbrick, in *sprowls*, American Pharmacy, 6<sup>th</sup> Edition, Lippincott, Philadelphia, 1966,p.205.)

The addition of monobasic potassium phosphate to the suspended bismuth subnitrate particles causes the positive zeta potential to decrease owing to the adsorption of negatively charged phosphate anion. With continued addition of the electrolyte, the zeta potential eventually falls to zero and then increases in negative directions.

Only when zeta potential becomes sufficiently negative to affect potential does the sedimentation volume start to fall. Finally, the absence of caking in the suspensions correlates with the maximum sedimentation volume, which, as stated previously, reflects the amount of flocculation.

### Q12 Explain DLVO Theory

A12

#### DLVO THEORY (GRAPH FROM BOOK)

Half a century ago, Derjaguin and Landau in Russia, and Verwey and Overbeek in Holland, independently and simultaneously proposed a theory to interpret the known

phenomena related to the stability of lyophilic colloids, i.e., systems with small dispersed fragment with no affinity for the dispersing continuous phase. In their honor the theory is now recalled as DLVO theory, and its application range has been extended qualitatively to systems containing fragments of matter up to the 10  $\mu\text{m}$  range, that is at least 100 times larger than the bigger colloids.

This theory assumes that when two interfaces are approaching, as it happens in any dispersed system when two fragments of matter get close enough, then the overall force can be calculated as the combination of the attractive Van der Waals forces and the repulsive electrostatic Coulomb forces.

There is no space here to discuss in details the different expressions of these forces (see FIRP Booklet # 614), and it is only necessary to take for granted that these expressions depend upon the approaching interface geometry and the intrinsic nature of the forces, i.e., the Debye length value on the electrostatic repulsion side, and the Hamaker constant as far as the Van der Waals forces are considered.

Fig. 10 indicates the variations of the overall resulting force as a function of the distance between approaching interfaces. At infinity, which may mean only a few microns in many cases, the force is null. At an extremely short distance, i.e., essentially zero, the two interfaces are in contact and the force is always repulsive. Extremely short range repulsion depending on the inverse of the 12th power of the distance have been proposed for this "compressibility" repulsion.

Depending on the case the force balance can be repulsive (fig. 10-a) or attractive (fig. 10-b) at intermediate distance, which can be as short as 100  $\text{\AA}$ . The occurrence of cases (a) or (b) is commanded by the nature of the fragmented material, the solvent, the state of the interface (charge, adsorbed surfactant) etc.

In case (a), the force is always repulsive from long distance down, and there is a maximum repulsive force referred to as barrier  $V_m$  in fig 10-a. If this barrier happens to be superior to the Brownian motion thermal agitation (which is typically 10 kT), then the kinetic energy of the fragments is not large enough to offset the barrier, and the repulsive force will impede the two interfaces to get close enough for the overall force to be attractive. A high barrier is thus associated to a stable dispersed system.

In the case of fig. 10-b, the force is attractive at all distances and the approach proceeds until the curve minimum is reached, where the most stable state is encountered. By the way this also happens in fig. 10-a case, provided that the energy barrier is overcome.

Depending whether this minimum occurs at short or very short distance, a matter of very few  $\text{\AA}$  indeed, the situation is called flocculation, coagulation or aggregation. Often the word flocculation is kept for a "long" distance aggregation is used when the interfaces are actually in contact with an attraction energy similar to the cohesion/adhesion energy. Fig. 11 has been prepared to summarize the role of the repulsion barrier and the potential minimum in the practical cases of low energy minimum, while coagulation. In this case there are two minima separated by a maximum. The farther minimum

is shallow and at some "long" separation distance. When two particles get close, the potential is slightly attractive and the particles become stuck together at the secondary

minimum, which is said to correspond to a flocculation. Since the attractive energy that corresponds to this minimum is weak, a weak energy input such as a hydrodynamic stirring is generally strong enough to separate again the two particles. As a consequence flocculation is essentially a reversible phenomenon.

On the contrary the principal minimum is associated with a short distance and a very strong attractive energy. The associated situation is termed coagulation, and it is essentially irreversible, since the energy input to reverse it is of the same magnitude that the one which was supplied to the system to make it dispersed in the first place.

If the dispersed phase is a fluid, the bubbles or drops generally coalesce as an instant consequence of the coagulation. If the dispersed phase is solid, then the particle size starts growing upon coagulation. In any case coagulation results in an alteration of the dispersed system which is generally viewed as instability. be returned to a stable system with little energy input On the other hand flocculated systems are in some weakly metastability, and canion

## **Q 12 Define HLB scale and how it can be determined**

### **The Hydrophile-Lipophile Balance (HLB Scale)**

1. Surfactant possess both hydrophilic and lipophilic portions, so there must be some scale to measure the balance between these two opposing tendencies.

2. Griffin (1949) developed an arbitrary scale to serve as a measure of hydrophilic-lipophilic balance (HLB) of surface active agents.

3. This HLB scale is numerical scale extending from 1 to 20.

4. The more hydrophilic surfactants have a high HLB number  $> 10$ , while surfactants with an  $HLB < 10$  are considered to be lipophilic.

5. The HLB value helps in the selection of a proper surfactant for a particular application.

6. The HLB of a number of polyhydric alcohols and fatty acid esters such as glyceryl monostearate, can be calculated by using the formula:

$$HLB = 20(1 - S/A)$$

where S is the saponification number of the ester and A is the acid number of the fatty acid.

7. But the saponification number for many substances like bees-wax and wool-fat derivatives cannot be easily estimated.

8. In such cases, the following relation is used,

$$\text{HLB} = (E + P)/5$$

where E is the percent by weight of oxythelene chains and P is the percent by weight of polyhydric alcohol groups in the molecules.

9. obviously, when the molecule consist only of oxyethylene groups, equation becomes

$$\text{HLB} = E/5$$

10. Davies calculated the HLB values for surface active agents by splitting the various surfactant molecules into their component groups, to each of which is assigned a *group number*.

11. The summation of the respective group number permits the calculation of the HLB value according to the equation

$$\text{HLB} = \sum (\text{hydrophilic group numbers}) - (\text{lipophilic group numbers}) + 7$$

Solubility in Water HLB Value Description

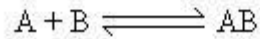
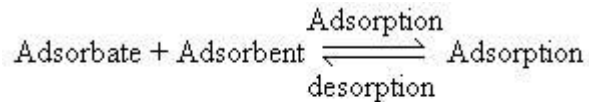
-----  
Insoluble 4 - 5 water in oil  
emulsifier  
Poorly dispersible 6 - 9 wetting agent  
(milky appearance)  
Translucent to 10 - 12 detergent  
clear  
Very soluble 13 - 18 oil in water  
Emulsifier

### is Q13 What is Adsorption Isotherm? Explain various types

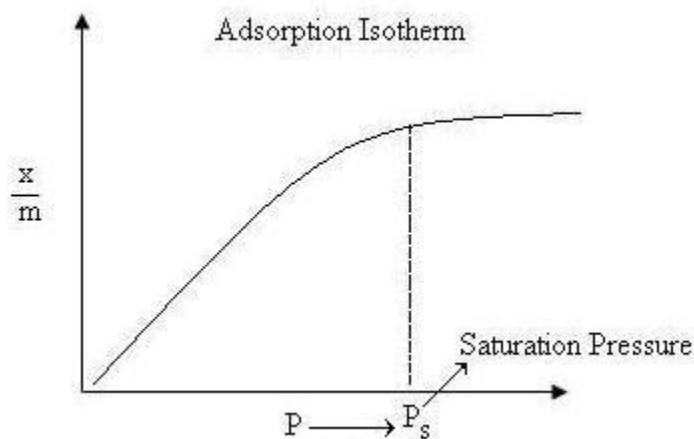
the graph between the amounts of adsorbate (x) adsorbed on the surface of adsorbent (m) and pressure at constant temperature. Different adsorption isotherms have been Freundlich, Langmuir The process of Adsorption is usually studied through graphs know as adsorption isotherm. It and BET theory.

#### Basic Adsorption Isotherm

In the process of adsorption, adsorbate gets adsorbed on adsorbent.



According to Le-Chatelier principle, the direction of equilibrium would shift in that direction where the stress can be relieved. In case of application of excess of pressure to the equilibrium system, the equilibrium will shift in the direction where the number of molecules decreases. Since number of molecules decreases in forward direction, with the increases in pressure, forward direction of equilibrium will be favored.



Basic Adsorption Isotherm

From the graph, we can predict that after saturation pressure  $P_s$ , adsorption does not occur anymore. This can be explained by the fact that there are limited numbers of vacancies on the surface of the adsorbent. At high pressure a stage is reached when all the sites are occupied and further increase in pressure does not cause any difference in adsorption process. At high pressure, Adsorption is independent of pressure.

### Freundlich Adsorption Isotherm

In 1909, Freundlich gave an empirical expression representing the isothermal variation of adsorption of a quantity of gas adsorbed by unit mass of solid adsorbent with pressure. This equation is known as Freundlich Adsorption Isotherm or Freundlich Adsorption equation or simply Freundlich Isotherm.

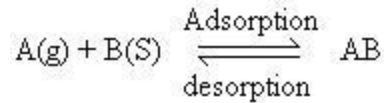


Where  $x$  is the mass of the gas adsorbed on mass  $m$  of the adsorbent at pressure  $p$  and  $k, n$  are constants whose values depend upon adsorbent and gas at particular temperature. Though Freundlich Isotherm correctly established the relationship of adsorption with pressure at lower

values, it failed to predict value of adsorption at higher pressure.

### Langmuir Adsorption Isotherm

In 1916 Langmuir proposed another Adsorption Isotherm known as Langmuir Adsorption isotherm. This isotherm was based on different assumptions one of which is that dynamic equilibrium exists between adsorbed gaseous molecules and the free gaseous molecules.



Where A(g) is unadsorbed gaseous molecule, B(s) is unoccupied metal surface and AB is Adsorbed gaseous molecule.

Based on his theory, he derived Langmuir Equation which depicted a relationship between the number of active sites of the surface undergoing adsorption and pressure.

$$\theta = \frac{KP}{1 + KP}$$

Where  $\theta$  the number of sites of the surface which are covered with gaseous molecule, P represents pressure and K is the equilibrium constant for distribution of adsorbate between the surface and the gas phase .The basic limitation of Langmuir adsorption equation is that it is valid at low pressure only.

At lower pressure, KP is so small, that factor (1+KP) in denominator can almost be ignored. So Langmuir equation reduces to

$$\theta = KP$$

At high pressure KP is so large, that factor (1+KP) in denominator is nearly equal to KP. So Langmuir equation reduces to



### BET adsorption Isotherm

BET Theory put forward by Brunauer, Emmett and Teller explained that multilayer formation is the true picture of physical Adsorption.

One of the basic assumptions of Langmuir Adsorption Isotherm was that adsorption is monolayer in nature. Langmuir adsorption equation is applicable under the conditions of low pressure. Under these conditions, gaseous molecules would possess high thermal energy and high escape velocity. As a result of this less number of gaseous molecules would be available near the surface of adsorbent.



Under the condition of high pressure and low temperature, thermal energy of gaseous molecules decreases and more and more gaseous molecules would be available per unit surface area. Due to this multilayer adsorption would occur. The multilayer formation was explained by BET Theory. The BET equation is given as



The another form of BET equation is high pressure conditions so as to cover the surface with a unilayer of gaseous molecules, Where  $V_{mono}$  be the adsorbed volume of gas at

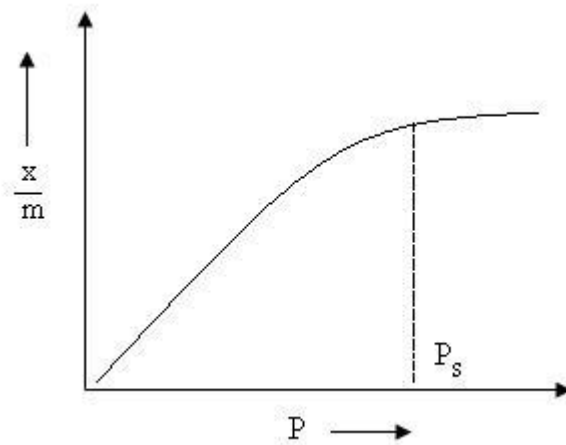


the ratio is designated  $C$ .  $K_1$  is the equilibrium constant when single molecule adsorbed per vacant site and  $K_L$  is the equilibrium constant to the saturated vapor liquid equilibrium.

**Type of Adsorption Isotherm**

Five different types of adsorption isotherm and their characteristics are explained below.

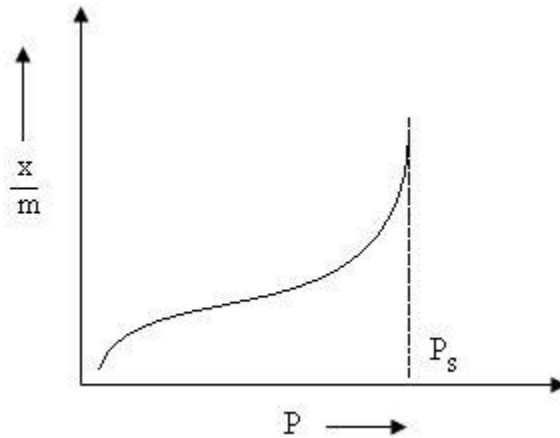
**Type I Adsorption Isotherm**



Type I Adsorption Isotherm

- The above graph depicts Monolayer adsorption.
- This graph can be easily explained using Langmuir Adsorption Isotherm.
- If BET equation, when  $P/P_0 \ll 1$  and  $c \gg 1$ , then it leads to monolayer formation and Type I Adsorption Isotherm is obtained.
- Examples of Type-I adsorption are Adsorption of Nitrogen (N<sub>2</sub>) or Hydrogen (H) on charcoal at temperature near to -1800C.

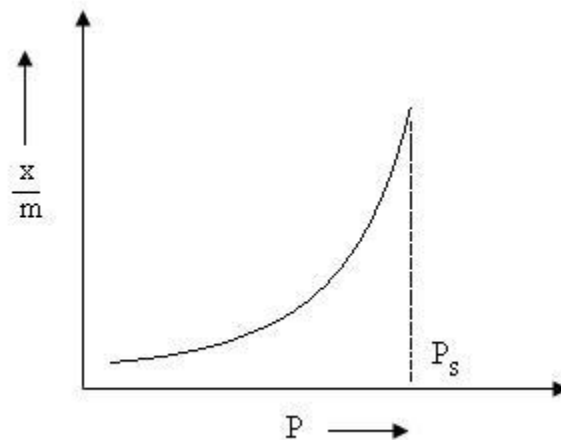
### Type II Adsorption Isotherm



Type II Adsorption Isotherm

- Type II Adsorption Isotherm shows large deviation from Langmuir model of adsorption.
- The intermediate flat region in the isotherm corresponds to monolayer formation.
- In BET equation, value of C has to be very large in comparison to 1.
- [REDACTED]
- Examples of Type-II adsorption are Nitrogen (N<sub>2</sub> (g)) adsorbed at -1950C on Iron (Fe) catalyst and Nitrogen (N<sub>2</sub> (g)) adsorbed at -1950C on silica gel.

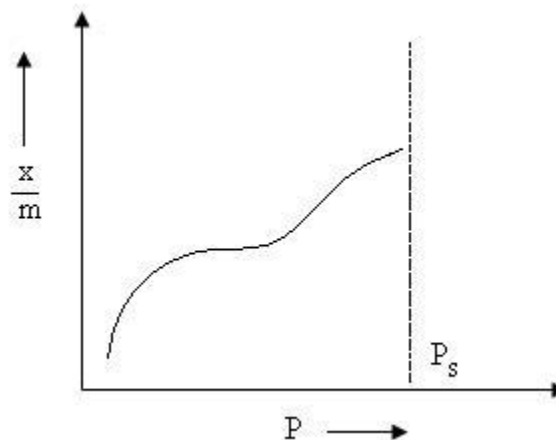
### Type III Adsorption Isotherm



Type III Adsorption Isotherm

- Type III Adsorption Isotherm also shows large deviation from Langmuir model.
- In BET equation value if  $C \lll 1$  Type III Adsorption Isotherm obtained.
- This isotherm explains the formation of multilayer.
- There is no flattish portion in the curve which indicates that monolayer formation is missing.
- Examples of Type III Adsorption Isotherm are Bromine ( $\text{Br}_2$ ) at  $790^\circ\text{C}$  on silica gel or Iodine ( $\text{I}_2$ ) at  $790^\circ\text{C}$  on silica gel.

#### Type IV Adsorption Isotherm



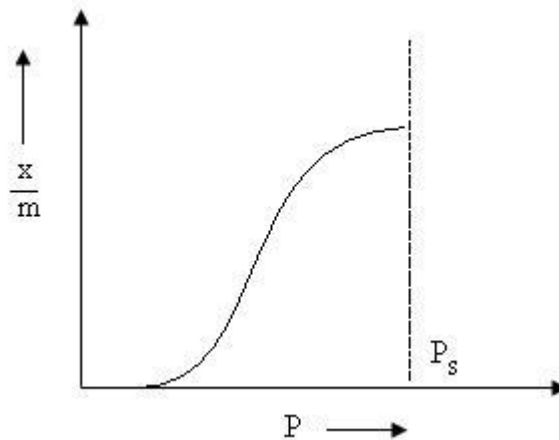
Type IV Adsorption Isotherm

- At lower pressure region of graph is quite similar to Type II. This explains formation of

monolayer followed by multilayer.

- The saturation level reaches at a pressure below the saturation vapor pressure. This can be explained on the basis of a possibility of gases getting condensed in the tiny capillary pores of adsorbent at pressure below the saturation pressure ( $P_s$ ) of the gas.
- Examples of Type IV Adsorption Isotherm are of adsorption of Benzene on Iron Oxide ( $Fe_2O_3$ ) at  $500^\circ C$  and adsorption of Benzene on silica gel at  $500^\circ C$ .

### Type V Adsorption Isotherm



Type V Adsorption Isotherm

- Explanation of Type V graph is similar to Type IV.
- Example of Type V Adsorption Isotherm is adsorption of Water (vapors) at  $1000^\circ C$  on charcoal.
- Type IV and V shows phenomenon of capillary condensation of gas
- 

### Q14 What is Buffers and Buffer Capacity

or **Buffers** are compounds that resist changes in pH upon the addition of limited amounts of acids bases. Buffer systems are usually composed of a weak acid or base and its conjugate salt. The components act in such a way that addition of an acid or base results in the formulation of a salt causing only a small change in pH.

The pH of a buffer system is given by the Henderson-Hasselbach equation:

$$pH = pK_a + \log \frac{[salt]}{[acid]} \text{ (for a weak acid and its salt)}$$

$$pH = pK_w - pK_b + \log \frac{[base]}{[salt]} \quad (\text{for a weak base and its salt})$$

where [salt], [acid] and [base] are the *molar* concentrations of salt, acid and base.

**Buffer capacity** is a measure of the efficiency of a buffer in resisting changes in pH. Conventionally, the buffer capacity ( $\beta$ ) is expressed as the amount of strong acid or base, in gram-equivalents, that must be added to 1 liter of the solution to change its pH by one unit.

Calculate the buffer capacity as:

$$\beta = \frac{\Delta B}{\Delta pH}$$

$\Delta B$  = gram equivalent of strong acid/base to change pH of 1 liter of buffer solution

$\Delta pH$  = the pH change caused by the addition of strong acid/base

In practice, smaller pH changes are measured and the buffer capacity is quantitatively expressed as the ratio of acid or base added to the change in pH produced (e.g., mEq./pH for x volume). The buffer capacity depends essentially on 2 factors:

1. Ratio of the salt to the acid or base. The buffer capacity is optimal when the ratio is 1:1; that is, when  $pH = pK_a$
2. Total buffer concentration. For example, it will take more acid or base to deplete a 0.5 M buffer than a 0.05 M buffer.

The relationship between buffer capacity and buffer concentrations is given by the Van Slyke equation:

$$\beta = 2.3 C \frac{K_a [H_3O^+]}{(K_a + [H_3O^+])^2}$$

where C = the total buffer concentration (i.e. the sum of the molar concentrations of acid and salt).

Just as we must often compromise the optimal pH for a product, so must we compromise on the optimal buffer capacity of our solution. On the one hand, buffer capacity must be large enough to maintain the product pH for a reasonably long shelf-life. Changes in product pH may result from interaction of solution components with one another or with the product package (glass, plastic, rubber closures, etc.). On the other hand, the buffer capacity of ophthalmic and parenteral products must be low enough to allow rapid readjustment of the product to physiologic pH upon administration. The pH, chemical nature, and volume of the solution to be administered must all be considered. Buffer capacities ranging from 0.01 - 0.1 are usually adequate for most pharmaceutical solutions