

SURFACE AND INTERFACIAL PHENOMENA

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Surface and Interfacial Phenomena



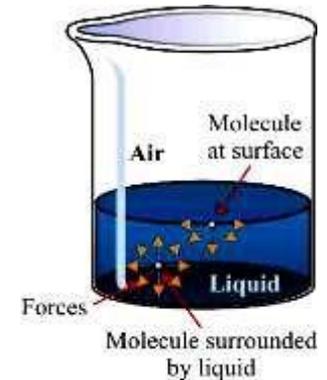
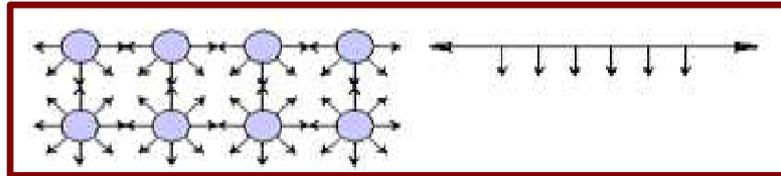
Interface

- ❑ ***Interface*** is the boundary between two or more phases exist together
- ❑ The properties of the molecules forming the interface are different from those in the bulk that these molecules are forming an ***interfacial phase***.
- ❑ Several types of interface can exist depending on whether the two adjacent phases are in solid, liquid or gaseous state.
- ❑ Important of Interfacial phenomena in pharmacy:
 - ❖ Adsorption of drugs onto solid adjuncts in dosage forms
 - ❖ Penetration of molecules through biological membranes
 - ❖ Emulsion formation and stability
 - ❖ The dispersion of insoluble particles in liquid media to form suspensions.

LIQUID INTERFACES

Surface and Interfacial Tensions

- In the liquid state, the cohesive forces between adjacent molecules are well developed.



- ***For the molecules in the bulk of a liquid***

They are surrounded in all directions by other molecules for which they have an equal attraction.

- ***For the molecules at the surface (at the liquid/air interface)***

- Only attractive **cohesive forces** with other liquid molecules which are situated below and adjacent to them.
- They can develop **adhesive forces** of attraction with the molecules of the other phase in the interface
- The net effect is that the molecules at the surface of the liquid experience an inward force towards the bulk of the liquid and pull the molecules and contract the surface with a force F .

 To keep the equilibrium, an equal force must be applied to oppose the inward tension in the surface.

 Thus **SURFACE TENSION** [γ] is the force per unit length that must be applied parallel to the surface so as to counterbalance the net inward pull and has the units of **dyne/cm**

 **INTERFACIAL TENSION** is the force per unit length existing at the interface between two immiscible liquid phases and has the units of **dyne/cm**.

 Invariably, interfacial tensions are less than surface tensions because an adhesive forces, between the two liquid phases forming the interface are greater than when a liquid and a gas phase exist together.

 If two liquids are completely miscible, no interfacial tension exists between them.

 Greater surface tension reflects higher intermolecular force of attraction, thus, increase in hydrogen bonds or molecular weight cause increase in ST

The work W required to create a unit area of surface is known as **SURFACE FREE ENERGY/UNIT AREA** (ergs/cm²)

erg = dyne . cm

Its equivalent to the surface tension γ

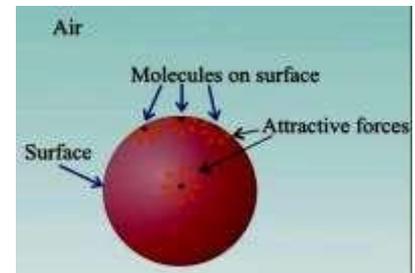
$$W = \gamma \Delta A$$

Thus the greater the area A of interfacial

contact between the phases, the greater the free energy.

For equilibrium, the surface free energy of a system must be at a minimum.

Thus Liquid droplets tend to assume a spherical shape since a sphere has the smallest surface area per unit volume.



Measurement of Surface and Interfacial Tensions

Methods for measuring surface and interfacial tension

- 1 Capillary rise method**
- 2 Ring (Du Nouy) tensiometer**
- 3 Drop weight method (Stalagmometer)**

The choice of the method for measuring surface and interfacial tension depend on:

- **Whether surface or interfacial tension is to be determined.**
- **The accuracy desired**
- **The size of sample.**

Capillary Rise Method

The Principle

❖ When a capillary tube is placed in a liquid, it rises up the tube a certain distance. By measuring this rise, it is possible to determine the surface tension of the liquid. **It is not possible, to obtain interfacial tensions** using the capillary rise method.

❖ **Cohesive force** is the force existing between like molecules in the surface of a liquid

❖ **Adhesive force** is the force existing between unlike molecules, such as that between a liquid and the wall of a glass capillary tube

✓ **When the force of Adhesion is greater than the cohesion, the liquid is said to wet the capillary wall, spreading over it, and rising in the tube.**



➤ If a capillary tube of inside radius = r immersed in a liquid that wets its surface, the liquid continues to rise in the tube due to the surface tension, until the upward movement is just balanced by the downward force of gravity due to the weight of the liquid

➤ The upward component of the force resulting from the surface tension of the liquid at any point on the circumference is given by:

$$a = \gamma \cos \theta$$

Thus the total upward force around the inside circumference of the tube is

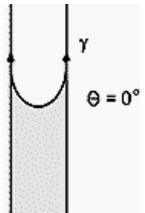
$$a = 2 \pi r \gamma \cos \theta$$

Where

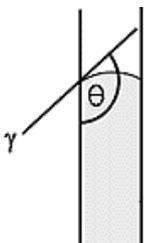
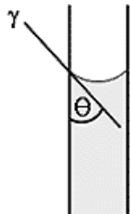
θ = the contact angle between the surface of the liquid and the capillary wall

$2 \pi r$ = the inside circumference of the capillary.

For water the angle θ is insignificant, i.e. the liquid wets the capillary wall so that $\cos \theta = \text{unity}$



Cont. angle water and glass



Cont. angle Mercury and glass

The downward force of gravity

(mass x acceleration) is given by

$$\pi r^2 h (\rho - \rho_0) g + w$$

Where:

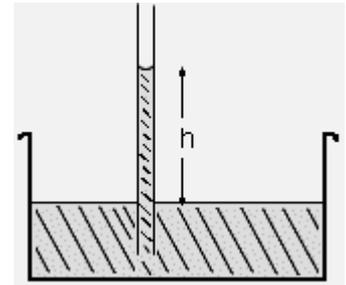
πr^2 = the cross-sectional area

h = the height of the liquid column to the lowest point of the meniscus

$(\rho - \rho_0)$ = the difference in the density of the liquid ρ and its vapor ρ_0

g = the acceleration of gravity

w = the weight of the upper part of the meniscus.



At Maximum height, the opposing forces are in equilibrium

$$2 \pi r \gamma \cos \theta = \pi r^2 h (\rho - \rho_0) g + w$$

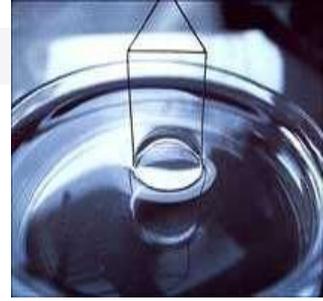
ρ_0 , θ and w can usually be disregarded

Hence the surface tension can be calculated.

$$2 \pi r \gamma = \pi r^2 h \rho g$$

$$\gamma = 1/2 r h \rho g$$

Ring (Du Nouy) Tensiometer



- For measuring surface and interfacial tensions.

The principle

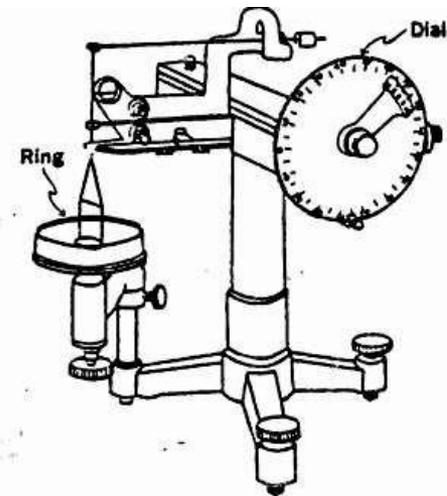
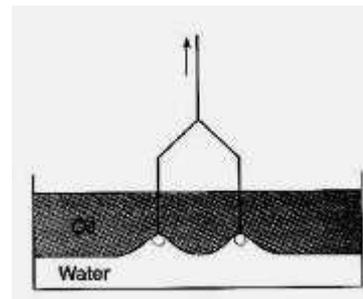
- the principle of the instrument depends on the fact that: the force necessary to detach a platinum-iridium ring immersed at the surface or interface is proportional to the surface or interfacial tension.
- The force of detachment is recorded in dynes on a calibrated dial
- The surface tension is given by:

$$\gamma = F / 2 \pi (R_1 + R_2)$$

Where:

F = the detachment force

R_1 and R_2 = the inner and outer radii of the ring.



Cenco DuNouy tensiometer.

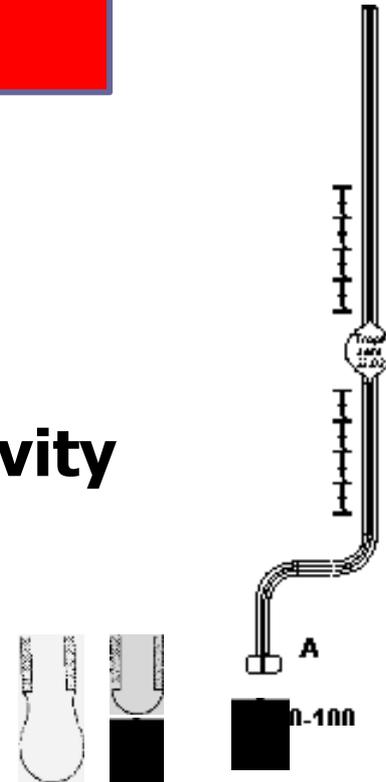
Drop Weight and drop volume method

If the volume or weight of a drop as it is detached from a tip of known radius is determined, **the surface and interfacial tension** can be calculated from

$$\gamma = \frac{\Phi \, m \, g}{2 \pi r} = \frac{\Phi \, V \, \rho \, g}{2 \pi r}$$

Where m = the mass of the drop
 V = the volume of the drop
 ρ = the density of the liquid
 r = the radius of the tip
 g = the acceleration due to gravity
 Φ = a correction factor

- ❑ *The correction factor is required as not all the drop leaves the tip on detachment*
- ❑ *The tip must be wetted by the liquid so as the drop doesn't climb the outside of the tube.*

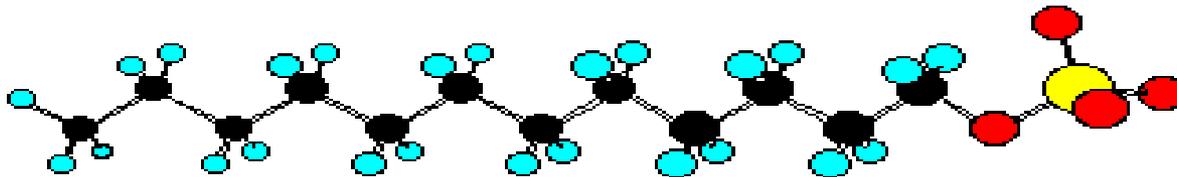
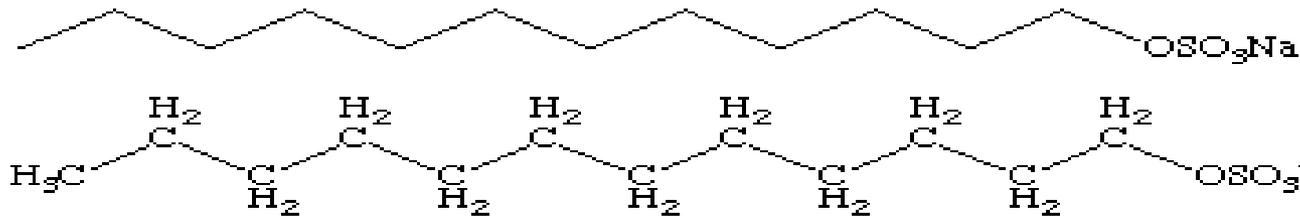


Surface Active Agents

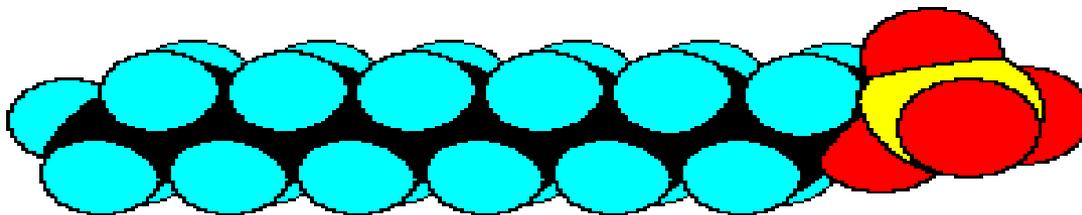
Surface Active Agents

A surfactant molecule is depicted schematically as a cylinder representing the hydrocarbon (**hydrophobic**) portion with a sphere representing the polar (**hydrophilic**) group attached at one end.

The hydrocarbon chains are straight because rotation around carbon-carbon bonds bends, coils and twists them.



Sodium Lauryl Sulfate molecule



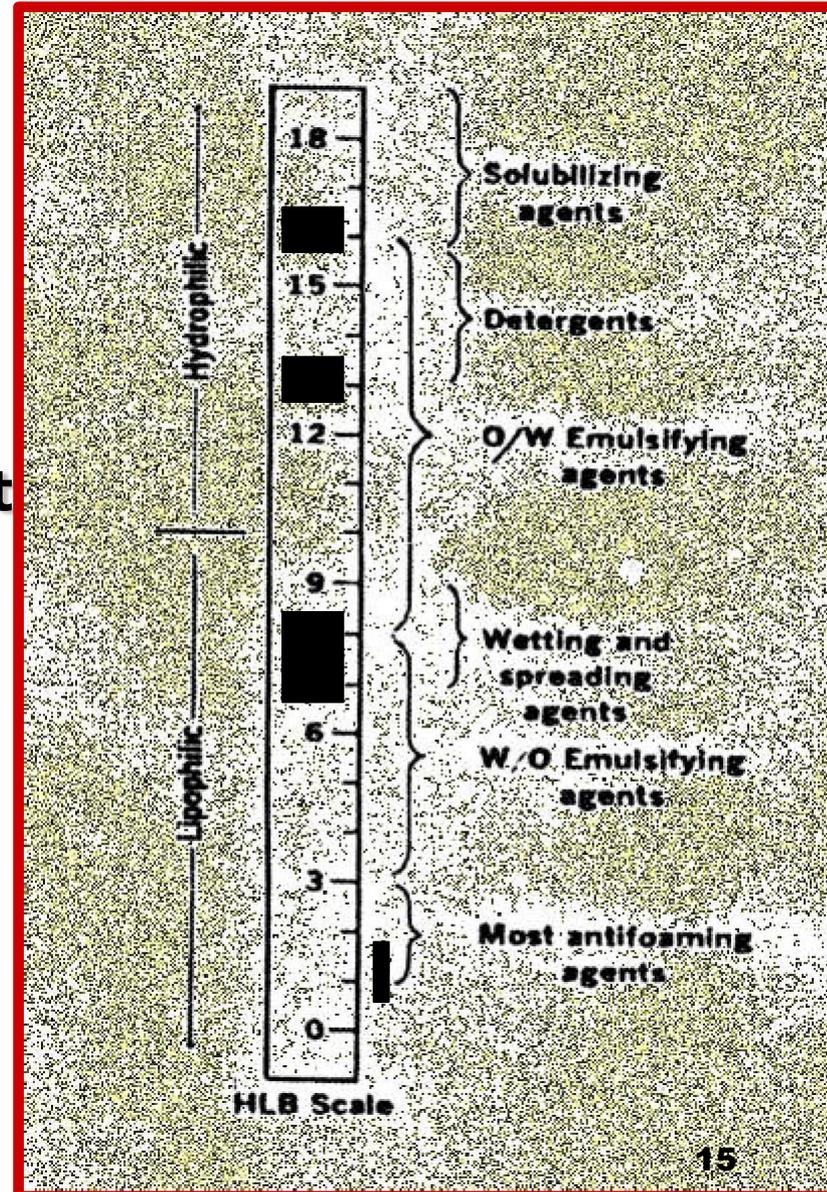
Surface Active Agents

Surface Active Agents

- Molecules and ions that are adsorbed at interfaces are termed **surface active agents, surfactants or amphiphile**
- The molecule or ion has a certain affinity for both polar and nonpolar solvents.
- Depending on the number and nature of the polar and nonpolar groups present, the amphiphile may be **hydrophilic, lipophilic** or be reasonably well-balanced between these two extremes.
- It is the amphiphilic nature of surface active agents which causes them to be adsorbed at interfaces, whether these be liquid/gas or liquid/liquid.

Hydrophilic Lipophilic Balance

- A scale showing classification of surfactant function on the basis of HLB values of surfactants.
- The higher the HLB of a surfactant the more hydrophilic it is.
- Example: Spans with low HLB are lipophilic. Tweens with high HLB are hydrophilic.



Hydrophilic Lipophilic Balance

Determination of HLB

- Polyhydric Alcohol Fatty Acid Esters (Ex. Glycerol monostearate)

$$\text{HLB} = 20 \left(1 - \frac{S}{A} \right)$$

S = Saponification number of the ester

A = Acid number of the fatty acid

- Surfactants with no Saponification no (Ex. Bees wax and lanolin)

$$\text{HLB} = \frac{E + P}{5}$$

E = The percent by weight of ethylene oxide

P = The percent by weight of polyhydric alcohol group in the molecules

- Surfactants with hydrophilic portion have only oxyethylene groups

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

When a liquid is placed on the surface of other liquid, it will spread as a film if the adhesion force is greater than the cohesive forces.



As surface or interfacial work is equal to surface tension multiplied by the area increment.

➤ The *work of cohesion*, which is the energy required to separate the molecules of the spreading liquid so as it can flow over the sub-layer=

$$W_c = 2 \gamma_L$$

Where 2 surfaces each with a surface tension = γ_L

➤ The *work of adhesion*, which is the energy required to break the attraction between the unlike molecules=

$$W_a = \gamma_L + \gamma_s - \gamma_{LS}$$

Where: γ_L =the surface tension of the spreading liquid

γ_s =the surface tension of the sublayer liquid

γ_{LS} =the interfacial tension between the two liquids.

➤ Spreading occurs if the work of adhesion is greater than the work of cohesion, i.e. $W_a > W_c$ or $W_a - W_c > 0$

Spreading Coefficient is The difference between the work of adhesion and the work of cohesion

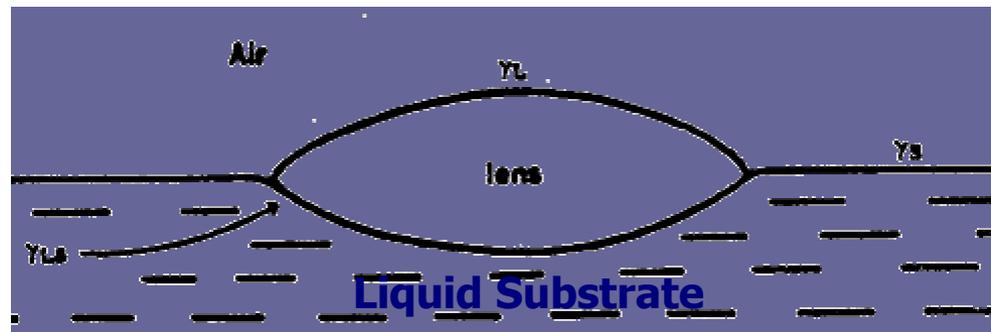
$$S = W_a - W_c = (\gamma_L + \gamma_S - \gamma_{LS}) - 2\gamma_L$$

$$S = \gamma_S - \gamma_L - \gamma_{LS}$$

$$S = \gamma_S - (\gamma_L + \gamma_{LS})$$

Spreading occurs (S is positive) when the surface tension of the sub-layer liquid is greater than the sum of the surface tension of the spreading liquid and the interfacial tension between the sub-layer and the spreading liquid.

If $(\gamma_L + \gamma_{LS})$ is larger than γ_S , (S is negative) the substance forms globules or a **floating lens** and fails to spread over the surface.



Factor affecting Spreading Coefficient

Molecular Structural:

- The greater the polarity of the molecule → the more positive [S] as ethyl alcohol and propionic acid
- Non polar substances as Liquid petrolatum have negative [S] fail to spread on water
- For organic acids, as Oleic acid, the longer the carbon chain → decrease in polar character → decrease [S]
- Some oils can spread over water because they contain polar groups as COOH and OH

Cohesive forces:

Benzene spreads on water not because it is polar but because the cohesive forces between its molecules are much weaker than the adhesion for water.

Application of Spreading coefficient in pharmacy

- ✓ **The requirement of film coats to be spreaded over the tablet surfaces**
- ✓ **The requirement of lotions with mineral oils to spread on the skin by the addition of surfactants**

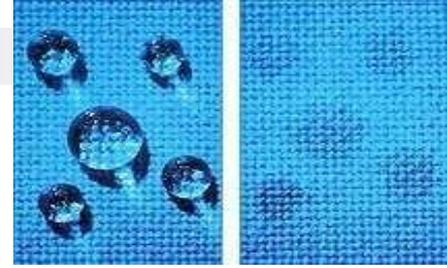
Classification of Surface Active Agents

Functional Classification

According to their pharmaceutical use, surfactants can be divided into the following groups:

- Wetting agents**
- Solubilizing agents**
- Emulsifying agents**
- Dispersing, Suspending and Deflocculating agents**
- Foaming and antifoaming agents**
- Detergents**

Wetting agents



- ❖ **Wetting agent is a surfactant that when dissolved in water, lower the contact angle and aids in displacing the air phase at the surface and replacing it with a liquid phase.**
- ❖ **Solids will not be wetted if their critical surface tension is exceeded than the surface tension of the liquid. Thus water with a value of 72 dynes/cm will not wet polyethylene with a critical surface tension of 31 dynes/cm.**
- ❖ **Based on this concept we should expect a good wetting agent to be one which reduces the surface tension of a liquid to a value below the solid critical surface tension.**

According to the nature of the liquid and the solid, a drop of liquid placed on a solid surface will adhere to it or no. which is the wettability between liquids and solids.

When the forces of adhesion are greater than the forces of cohesion, the liquid tends to wet the surface and vice versa. Place a drop of a liquid on a smooth surface of a solid. According to the wettability, the drop will make a certain angle of contact with the solid.

A contact angle is lower than 90° , the solid is called wettable

A contact angle is wider than 90° , the solid is named non-wettable.

A contact angle equal to zero indicates complete wettability.

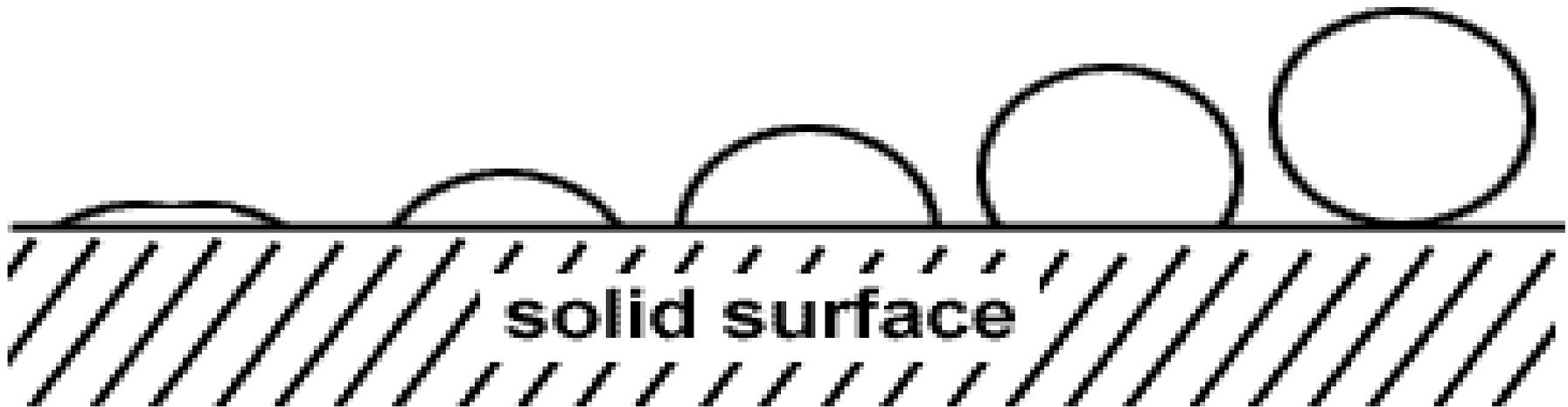


The contact angle of a liquid with a solid is used as wettability index. For $\alpha < 90^\circ$ the liquid wet the wall (eg: water on glass), for $\alpha > 90^\circ$ the liquid does not wet the wall (eg: mercury on glass). If $\alpha = 0^\circ$ the liquid perfectly wet the wall.

**complete
wetting**

incomplete wetting

**no
wetting**



$$\Theta = 0^\circ$$

$$\Theta < 90^\circ$$

$$\Theta = 90^\circ$$

$$\Theta > 90^\circ$$

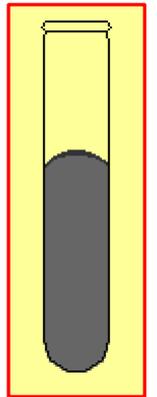
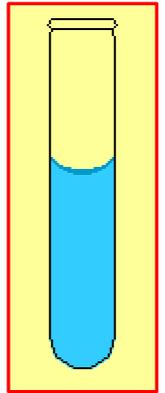
$$\Theta = 180^\circ$$

$$\gamma_s - \gamma_{sL} > 0$$

$$\gamma_s - \gamma_{sL} \approx 0$$

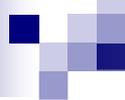
$$\gamma_s - \gamma_{sL} < 0$$

- ❖ **The surface of liquid water (meniscus) has a concave shape because water wets the surface and creeps up the side**
- ❖ **The surface of Mercury has a convex shape it does not wet glass because the cohesive forces within the drops are stronger than the adhesive forces between the drops and glass.**



Micellar Solubilization

- **Surfactant molecules accumulate in the interfaces between water and water insoluble compound. Their hydrocarbon chains penetrate the outermost layer of insoluble compound which combine with the waterinsoluble molecules. Micelles form around the molecules of the waterinsoluble compound inside the micelles' cores and bring them into solution in an aqueous medium. This phenomenon is called micellar solubilization.**
- **The inverted micelles formed by oilsoluble surfactant which dissolves in a hydrocarbon solvent can solubilize water-soluble compound which is located in the center of the micelle, out of contact with the solvent.**



● Micelles of nonionic surfactants consist of an outer shell containing their polyethylene glycol moieties mixed with water and an inner core formed by their hydrocarbon moieties. Some compounds like phenols and benzoic acid form complexes with polyethylene glycols by hydrogen bonding and/or are more soluble in liquids of intermediate polarity like ethanol or ethyl ether than in liquids of low polarity like aliphatic hydrocarbons. These compounds locate in the aqueous polyethylene glycol outer shell of nonionic micelles on solubilization.

Drugs which are soluble in oils and lipids can be solubilized by micellar solubilization.

● As Micellar solubilization depends on the existence of micelles; it does not take place below the CMC. So dissolution begins at the CMC. Above the CMC, the amount solubilized is directly proportional to the surfactant concentration because all surfactant added to the solution in excess of the CMC exists in micellar form, and as the number of micelles increases the extent of solubilization increases .

● Compounds that are extensively solubilized increase the size of micelles in two ways:

- The micelles swell because their core volume is augmented by the volume of the solubilize.
- The number of surfactant molecules per micelle increases.
- The number of surfactant molecules per micelle increases.

Foaming and Anti Foaming agents

❖ ***Foams are dispersion of a gas in a liquid (liquid foams as that formed by soaps and detergents) or in a solid (solid foams as sponges).***



❖ **Foaming agents**

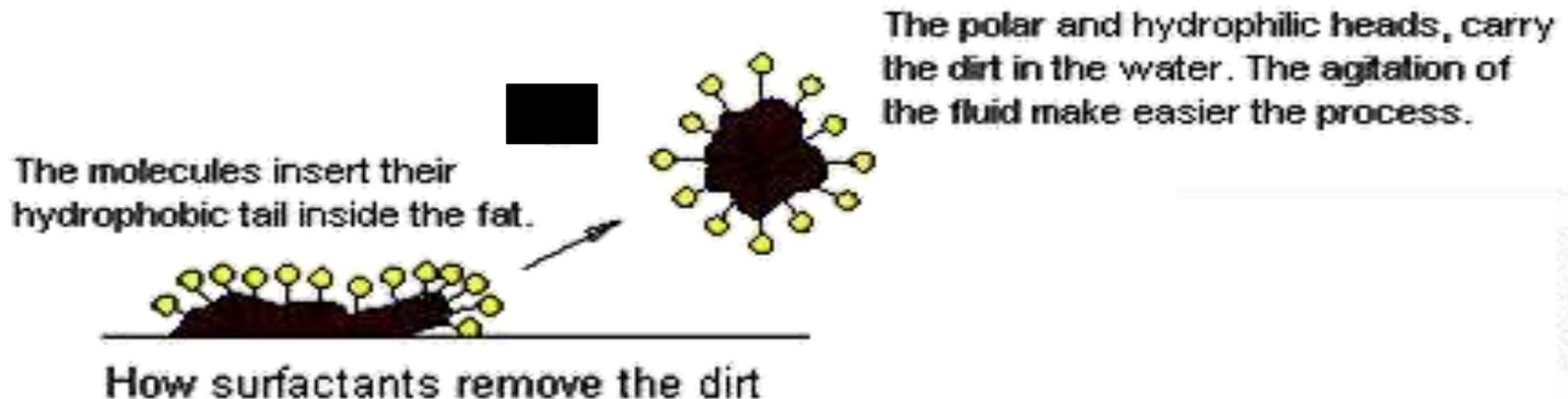
Many Surfactants solutions promote the formation of foams and stabilize them, in pharmacy they are useful in toothpastes compositions.

❖ **Anti Foaming agents**

They break foams and reduce frothing that may cause problems as in foaming of solubilized liquid preparations. in pharmacy they are useful in aerobic fermentations, steam boilers.

Detergents

- Detergents are surfactants used for removal of dirt.
- Detergency involves:
 - Initial wetting of the dirt and the surface to be cleaned.
 - Deflocculation and suspension, emulsification or solubilisation of the dirt particles
 - Finally washing away the dirt.



Structural Classification

- **A single surfactant molecule contains one or more hydrophobic portions and one or more hydrophilic groups.**
- **According to the presence of ions in the surfactant molecule they may be classified into:**
 - ☐ **Ionic surfactants**
 - **Anionic surfactants: the surface active part is anion (negative ion) e.g. soaps, sodium lauryl sulfate**
 - **Cationic surfactants: the surface active part is cation (positive ion) e.g. quaternary ammonium salts**
 - **Ampholytic surfactants: contain both positive and negative ions e.g. dodecyl-B-alanine.**

Ionic surfactants

Anionic surfactants

- ➔ They are the metal salts of long chain fatty acids as lauric acid.
- ➔ *Sodium dodecyl sulfate or Sodium Lauryl Sulfate* is used in toothpaste and ointments
- ➔ *Triethanolamine dodecyl sulfate* is used in shampoos and other cosmetic preparations.
- ➔ *Sodium dodecyl benzene sulfonate* is a detergent and has germicidal properties.
- ➔ *Sodium dialkylsulfosuccinates* are good wetting agents.

Cationic surfactants

- ➔ **These are chiefly quaternary ammonium compounds.**
- ➔ **They have bacteriostatic activity probably because they combine with the carboxyl groups in the cell walls and of microorganisms by cation exchange, causing lysis.**
- ➔ **Among the most popular antiseptics in this category are benzalkonium chloride, cetylpyridinium chloride and cetyltrimethylammonium bromide,**

Ampholytic Surfactants

- ➔ **These are the least common, e.g. dodecyl- β -alanine**

Non-ionic surfactants

- ➔ **Widely used in pharmaceutical formulations e.g. Tweens, Spans, Brij and Myrj.**
- ➔ **They are polyethylene oxide products.**
- ➔ **Surfactants based on sorbitan are of pharmaceutical importance.**
- ➔ **Esterification of the primary hydroxyl group with lauric, palmitic, stearic or oleic acid forms sorbitan monolaurate, monopalmitate, monostearate or monooleate**
These are water-insoluble surfactants called Span 20, 40, 60 or 80, respectively.
- ➔ **Addition of about 20 ethylene oxide molecules produces the water-soluble surfactants called polysorbate or Tween 20, 40, 60 or 80.**

Oriented Adsorption of surfactant at Interfaces

As a Surface active substance contains a hydrophilic and a hydrophobic portions, it is adsorbed as a monolayer at the interfaces.

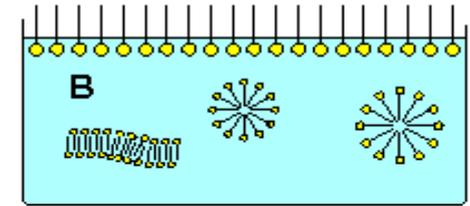
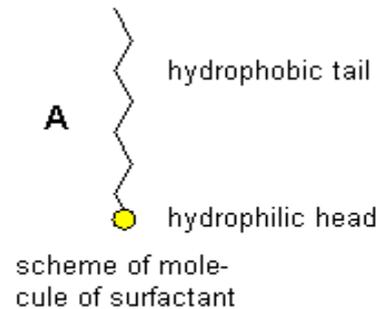
At water-air interface

Surfaceactive molecules will be adsorbed at water-air interfaces and oriented so

that the hydrocarbon chains of are pushed out of the water and rest on the surface, while the polar groups are inside the water. Perhaps the polar groups pull the hydrocarbon chains partly into the water.

At oil-water interface

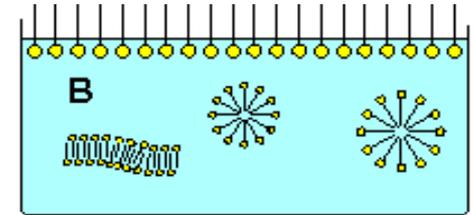
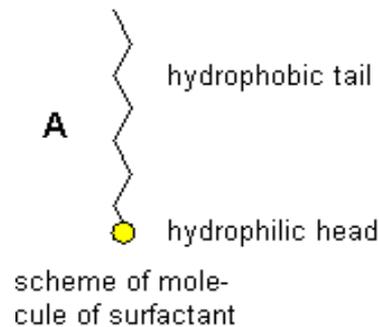
Surfaceactive molecules will be oriented so that the hydrophobic portion is inside the oil phase and the hydrophilic portion inside the water phase.



Surfactants arrange themselves on the water surface like a monolayer of molecules, and inside it as micelles and membranes tied by their hydrophobic tail. As the cohesion of these molecules is inferior to that of the molecules of water, the surface tension of water is lowered.

At low surfactant concentrations:

The hydrocarbon chains of surfactant molecules adsorbed in the interface lie nearly flat on the water surface.



Surfactants arrange themselves on the water surface like a monolayer of molecules, and inside it as micelles and membranes tied by their hydrophobic tail. As the cohesion of these molecules is inferior to that of the molecules of water, the surface tension of water is lowered.

At higher concentrations:

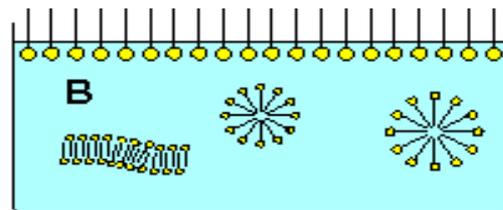
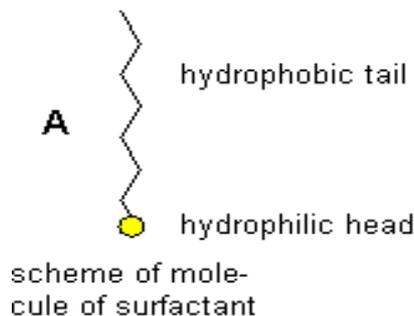
They stand upright because this permits more surfactant molecules to pack into the interfacial monolayer.

As the number of surfactant molecules adsorbed at the water-air interface increased, they tend to cover the water with a layer of hydrocarbon chains. Thus, the water-air interface is gradually transformed into a non polar-air interface. This results in a decrease in the surface tension of water.

Micelle Formation

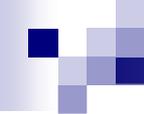
When the surfactant molecules adsorbed as a monolayer in the water-air interface have become so closely packed that additional molecules cannot be accommodated with ease, the polar groups pull the hydrocarbon chains partly into the water. At certain concentration the interface and the bulk phase become saturated with monomers. Excess surfactants add will begin to agglomerate in the bulk of the solution forming aggregates called **Micelles**, and the free energy of the system is reduced

The lowest concentration at which micelles first appear is called the critical concentration for micelle formation [**CMC**]



Surfactants arrange themselves on the water surface like a monolayer of molecules, and inside it as micelles and membranes tied by their hydrophobic tail. As the cohesion of these molecules is inferior to that of the molecules of water, the surface tension of water is lowered.



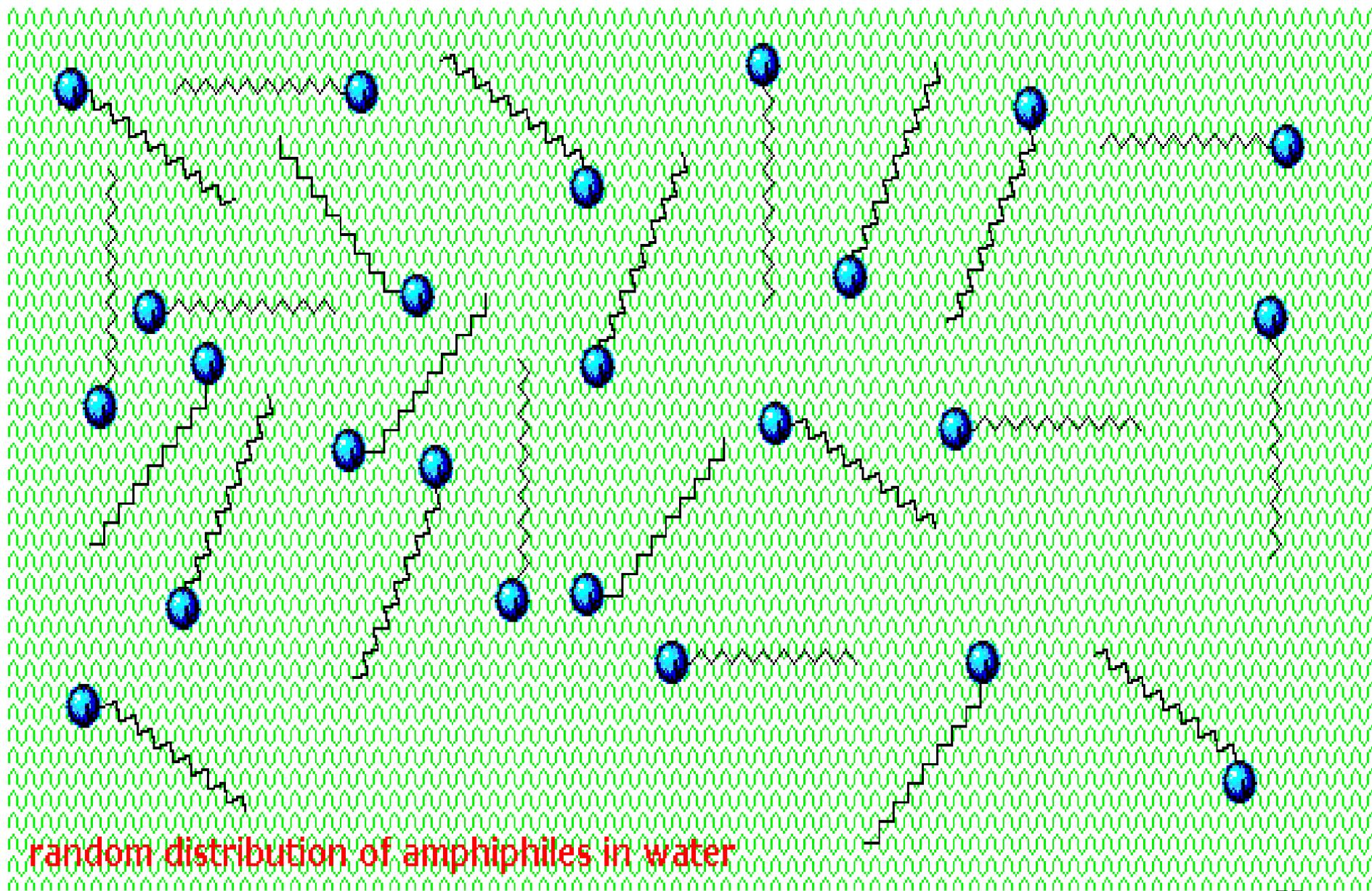


At a given concentration, temperature, and salt content, all micelles of a given surfactant usually contain the same number of molecules, i.e. they are usually monodisperse. For different surfactants in dilute aqueous solutions, this number ranges approximately from 25 to 100 molecules.

The diameters of micelles are approximately between 30 and 80 Å. Because of their ability to form aggregates of colloidal size, surfactants are also called association colloids.

Micelles are not permanent aggregates. They form and disperse continually.

Please wait



random distribution of amphiphiles in water

Surfactant shapes in colloidal solution

- a-** Cone-shaped surfactant resulting in **b-**normal micelles
- c-** Champagne cork shaped surfactant resulting in **d-**reverse micelles with control of their size by the water content
- e-** Interconnected cylinders .
- f-** Planar lamellar phase .
- g-** Onion-like lamellar phase.

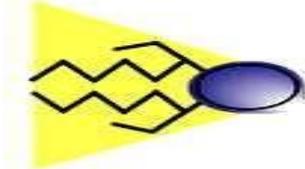
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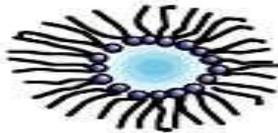
b



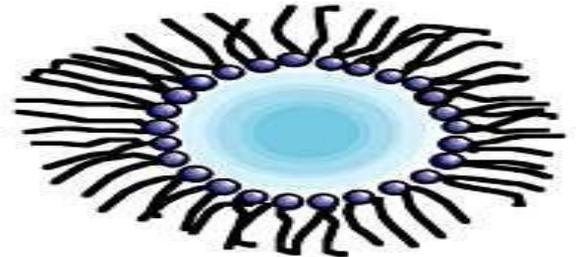
c



d



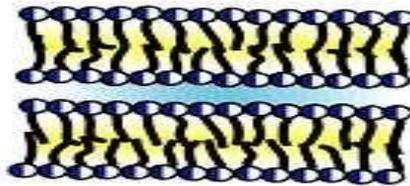
Water →



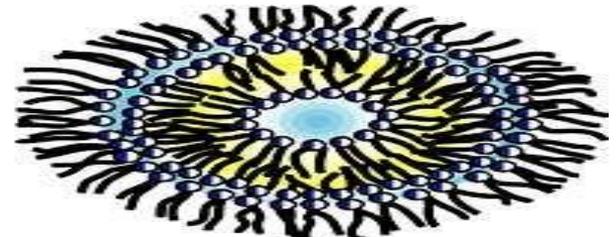
e



f



g



➤ **Normal spherical micelles**

In dilute aqueous solutions micelles are approximately spherical. The polar groups of the surfactants are in the periphery and the hydrocarbon chains are oriented toward the center, forming the core of the micelles

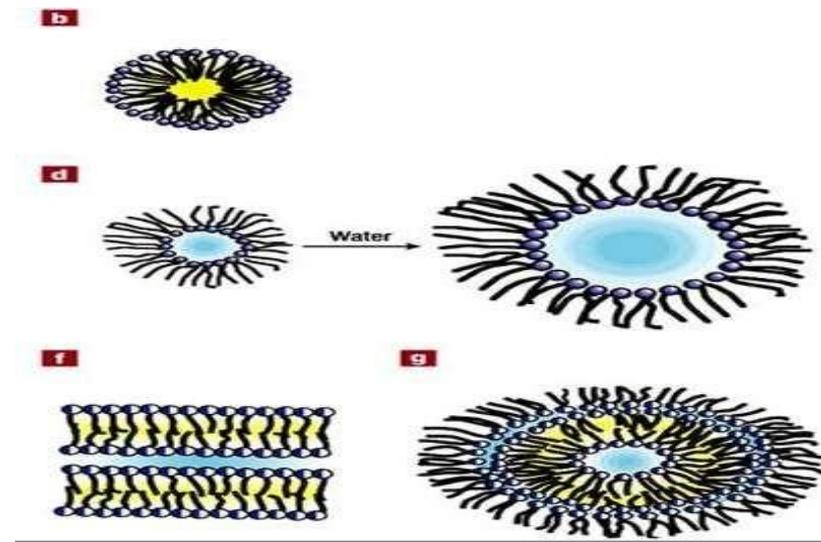


➤ **Inverted spherical micelles**

In solvents of low polarity or oils micelles are inverted. The polar groups face inward to form the core of the micelle while the hydrocarbon chains are oriented outward

➤ **Cylindrical and lamellar micelles**

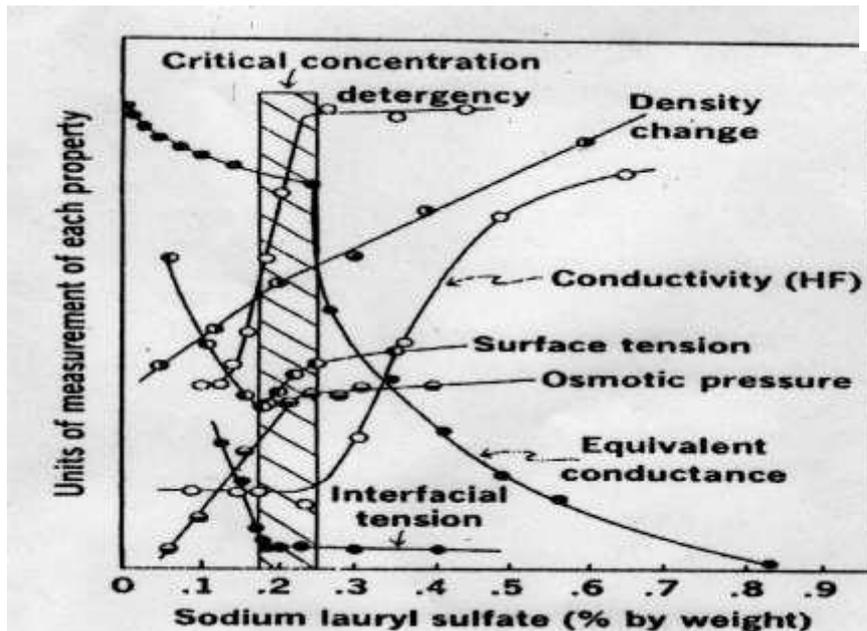
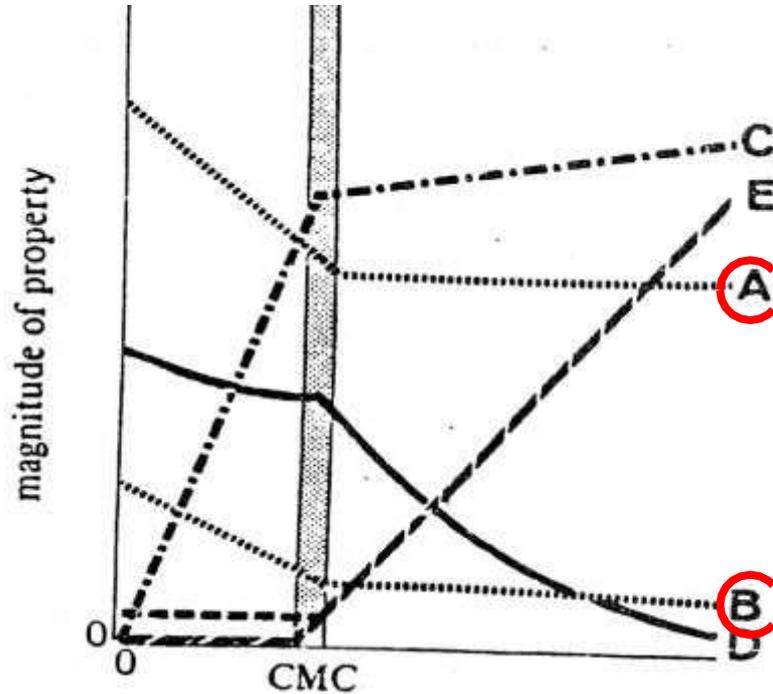
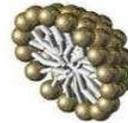
In more concentrated solutions of surfactants, micelles change from spherical either to cylindrical or lamellar phase.



Changes occurred at the CMC

Properties of surfactant Solutions as functions of concentration:

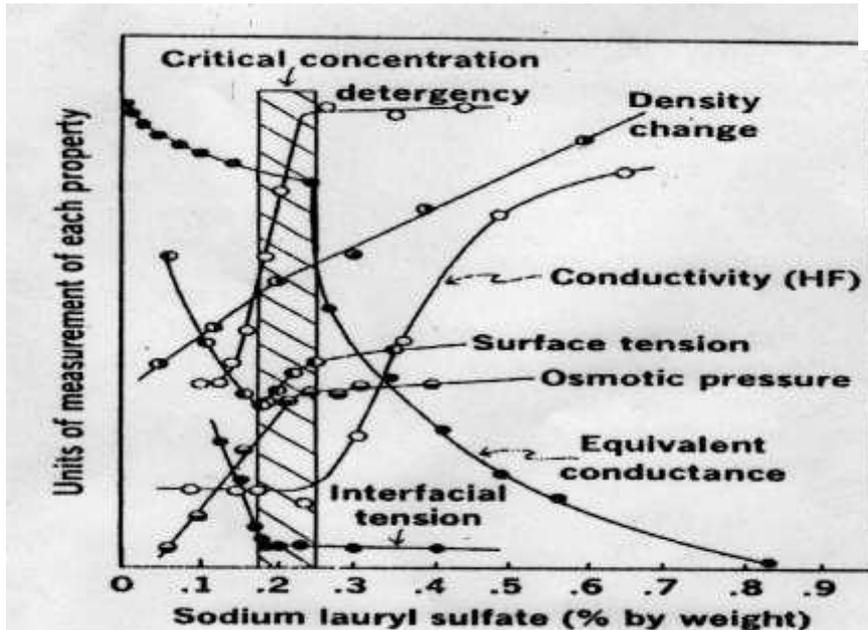
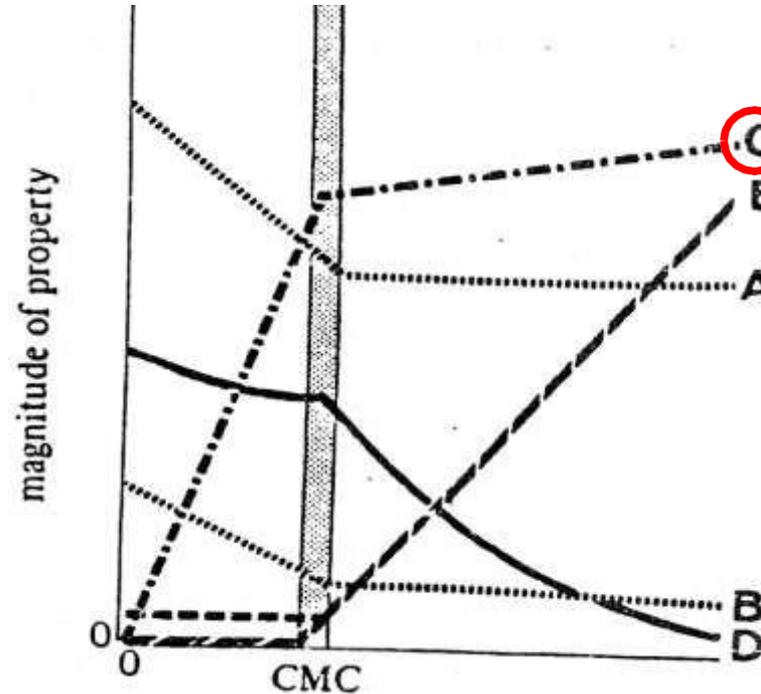
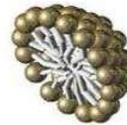
I- A continuous decrease in Surface and interfacial tensions with surfactants concentration until CMC the Surface and interfacial tensions level become constant owing to crowding of surfactant molecules adsorbed at surfaces and interfaces.



A, surface tension
B, interfacial tension
C, osmotic pressure;
D, equivalent conductivity;
E, solubility of compounds with low or zero solubility in water

Changes occurred at the CMC

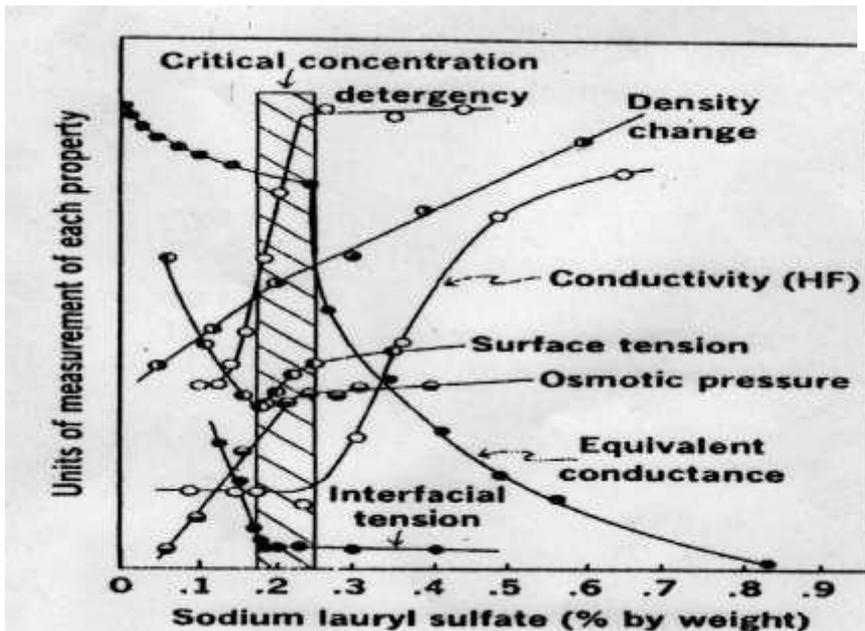
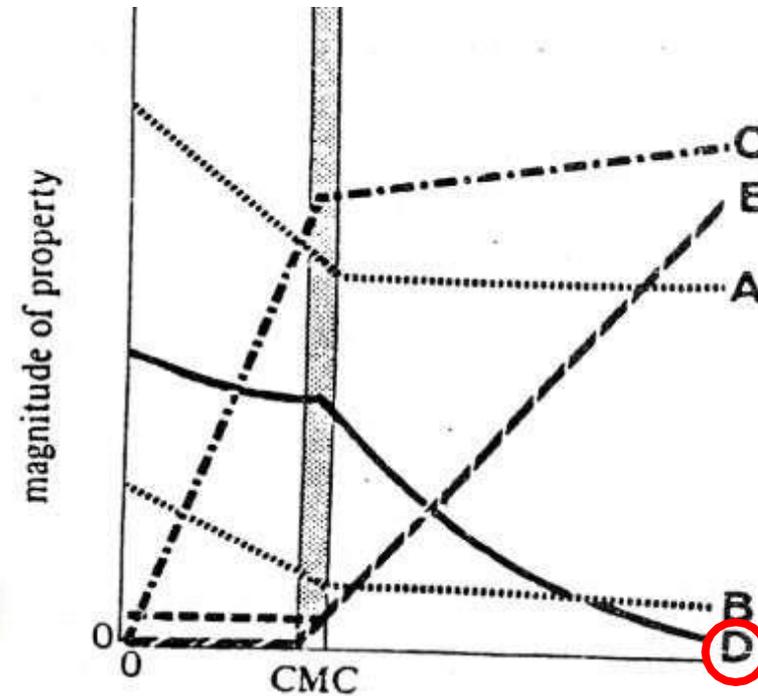
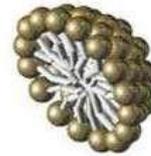
II- The osmotic pressure (and all other colligative properties, lowering of the vapor pressure and of the freezing point), rises much more slowly with increasing surfactant concentration above than it does below the CMC because it depends on the number of dissolved particles.



- A, surface tension*
- B, interfacial tension*
- C, osmotic pressure*
- D, equivalent conductivity*
- E, solubility of compounds with low or zero solubility in water*

Changes occurred at the CMC

III- For ionic surfactants, the equivalent conductivity drops sharply above the CMC.
Only the counterions of non-associated surfactant molecules can carry current.



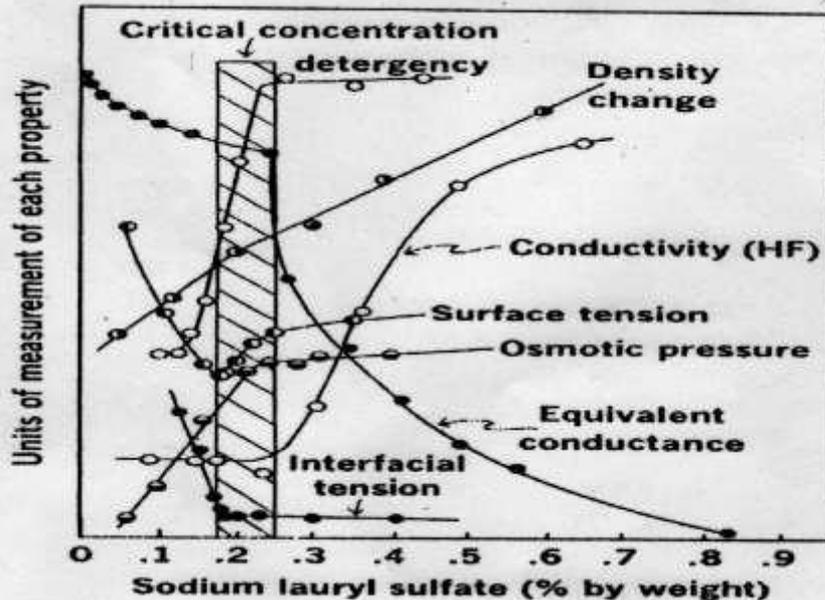
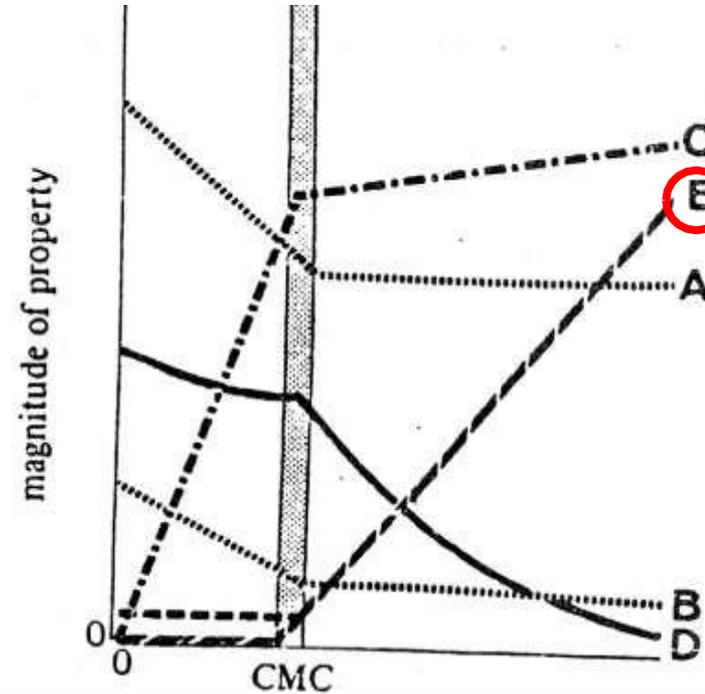
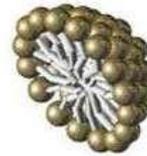
A, surface tension
B, interfacial tension
C, osmotic pressure
D, equivalent conductivity
E, solubility of compounds with low or zero solubility in water

Changes occurred at the CMC

IV-Solubility of many drugs are increased after CMC.

Other solution properties changing at the CMC: intrinsic viscosity and turbidity increase, while diffusion coefficient decreases

All these properties can be used to determine the CMC.



- A, surface tension*
- B, interfacial tension*
- C, osmotic pressure*
- D, equivalent conductivity*
- E, solubility of compounds with low or zero solubility in water*

Factors affecting CMC

For nonionic surfactants

↑ Temperature → ↓ CMC

For ionic surfactants

The CMC are higher for ionic than nonionic surfactants

The charges in the micelle of ionic surfactant are in close, to overcome the resulting repulsion an electric work is required but nonionic surfactants have no electric repulsion to overcome in order to aggregate.

Effect of electrolytes on the CMC of ionic surfactants

The addition of salts to ionic surfactant solutions reduces the electric repulsion between the charged groups and lower CMC values

Effect of Surfactant's structure on CMC

Branched chain systems and double bonds raise CMC

Since the chains must come together inside the micelles

Length of hydrocarbon chain and polarity of Surfactants

Increase in chain length of hydrocarbon facilitate the transfer from aqueous phase to micellar form cause decrease in CMC

Greater interaction with water will retard micelle formation thus ionized surfactants have higher CMC in polar solvents than nonionic Surfactants.

In polar solvents:

↑ Polarity of Surfactant molecules → ↑ CMC

↑ Length of hydrocarbon chain → ↓ CMC

In non-polar solvents:

↑ Polarity of Surfactant molecules → ↓ CMC

↑ Length of hydrocarbon chain → ↑ CMC

Incompatibilities Involving Surfactants

Nonionic surfactants

Nonionic surfactants have few incompatibilities with drugs and are preferred over ionic surfactants. even in formulations for external use, except when the germicidal properties of cationic and anionic surfactants are important.

Nonionic surfactants form weak complexes with some preservatives as phenols, including esters of p-hydroxybenzoic acid (Parabenzes) and with acids like benzoic and salicylic via hydrogen bonds. This reduces the antibacterial activity of these compounds.

Ionic surfactants

Ionic surfactants capable of reacting with compounds possessing ions of the opposite charge. These reactions may bind the surface active ions, sometimes with precipitation. The compounds which react with the surface active ions are also changed, and this may be harmful from the physiological or pharmacological point of view.

- ❖ Incompatibility of surface active quaternary ammonium compounds with bentonite, kaolin, talc, and other solids having cation exchange capacity.**

❖ Anionic surfactants

React with Cationic drugs (alkaloidal salts, local anesthetics, most sympathomimetic, cholinomimetic, adrenergic blocking, skeletal muscle relaxants, antihistamines, many tranquilizing and antidepressant agents) cause precipitation or the drugs lose potency or availability. Drugs with carboxylic, sulfonic or phosphoric acid groups like salicylic and paminobenzoic acids interact with cationic surfactants.

❖ Cationic surfactants

form complex with water soluble polymers containing negatively charged groups, as natural gums (acacia, tragacanth, agar, carrageenin), alginate, sodium carboxy methylcellulose, and Carbopol.