Interfacial Phenomena

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Chapter objectives

At the conclusion of this chapter student should be able to:

1. Differentiate among different types of interfaces and describe relevant examples in the pharmaceutical sciences.
2. Understand the terms surface tension and interfacial tension and their application in pharmaceutical sciences.
3. Appreciate the different methods of surface and interface tension measurements and calculations.
4. Define surface free energy.
5. Understand the mechanisms of adsorption on liquid and solid interfaces.
6. Classify surface-active agents and appreciate their applications in pharmacy.

Surface and Interfacial Tensions

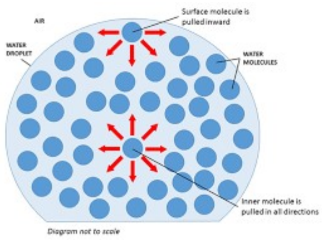
- Interface is the boundary between two phases.
- Surface is a term used to describe either a gas-solid or a gas-liquid interface.
- Interfacial phase is a term used to describe molecules forming the interface between two phases which have different properties from molecules in the bulk of each phase.

Surface and Interfacial Tensions

Phase	Interfacial Tension	Types & Examples of Interface
Gas - gas	-	**No interface possible**
Gas - liquid	**yLV**	**Liquid surface, body of water exposed to atmosphere**
Gas - solid	**ySV**	**Solid surface, table top**
Liquid - liquid	**yLL**	**Liquid-liquid interface, emulsion**
Liquid - solid	**yLS**	**Liquid-solid interface, suspension**
Solid - solid	**ySS**	**Solid-solid interface, powder particles in contact.**

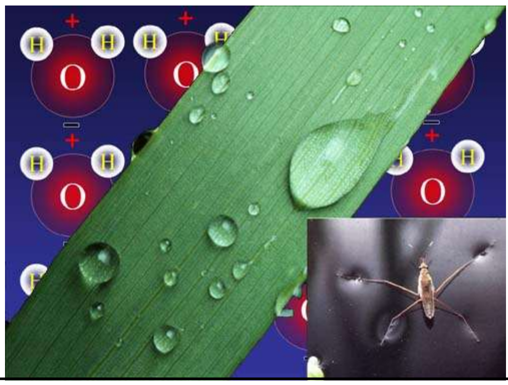
Surface and Interfacial Tensions

- Molecules in the bulk liquid are surrounded in all directions by other molecules for which they have an equal attraction (only cohesive forces).
- Molecules at the surface can only develop cohesive forces with other molecules that are below and adjacent to them; and can develop adhesive forces with molecules of the other phase.
- This imbalance in the molecular attraction will lead to an inward force toward the bulk that pulls the molecules of the interface together and contracts the surface, resulting in a ***surface tension*.**



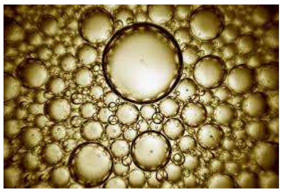
Surface and Interfacial Tensions

- Surface tension is the work per unit area (force per unit length) that must be applied parallel to the surface to counterbalance the net inward pull. It has the units of dynes/cm or N/m.
- The term ***surface tension*** is reserved for the tensions:
  - Liquid-vapor = γLV (written simply as γL).
  - Solid-vapor = γSV (written simply as γS).



Surface and Interfacial Tensions

- Interfacial tension is the work per unit area (force per unit length) existing at the interface between two immiscible liquid phases (units are dynes/cm or N/m).
- The term ***interfacial tension*** is used for the force between:
  - Two liquids = γLL
  - Two solids = γSS
  - Liquid-solid = γLS



Surface and Interfacial Tensions

- Interfacial tensions are normally weaker than surface tensions because the adhesive forces between two liquid phases forming an interface are greater than that between liquid and gas phases.

Substance	Surface tension (at 20 °C) (mN m^{-1})	Interfacial tension (at 20 °C) against water (mN m^{-1})
Water	72	-
Glycerol	63	-
Oleic acid	33	16
n-Octanol	27	8.5

Surface and Interfacial Tensions

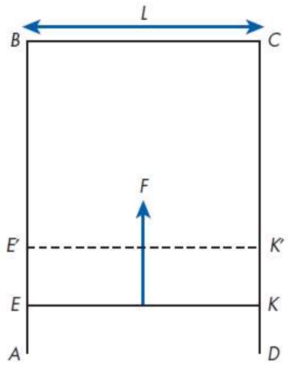
TABLE 3.1 Surface Tension of Water at Various Temperatures

Temperature (°C)	Surface Tension (dynes/cm)
0	76.5
20	72.8
30	71.2
75	63.5
100	58.0

Surface tension

- It is possible to illustrate surface tension by using a wire frame ABCD.
- The ABCD part of the frame is rigid, and only the EK part can slide along the frame sides AB and DC.
- If a soap solution is placed on the frame, it will create a thin film, and then the film will try to shrink itself, forcing the movable part of the frame (EK) to move closer to the BC side.
- The new position of the movable part will be E′K′.
- The force *F* required to move the EK part is proportional to the surface tension *g* times 2 (since the film has two surfaces) times the length *L* of the EK bar:

$$F = g \times 2 \times L$$



Surface free energy

- The surface layer of a liquid possesses additional energy as compared to the bulk liquid.
- If the surface of the liquid increases (e.g. when water is broken into a fine spray), the energy of the liquid also increases.
- Because this energy is proportional to the size of the free surface, it is called a ***surface free energy:***

$$W = \gamma \Delta A$$

W:surface free energy (ergs)

γ: surface tension (dynes/cm)

ΔA: increase in area (cm^2).

- Therefore, surface tension can also be defined as the surface free energy per unit area of liquid surface.

Spreading Coefficient

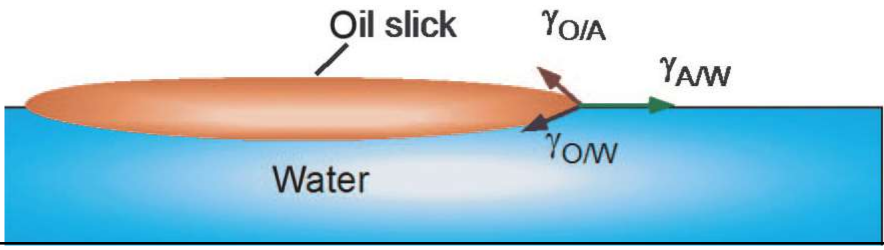
- When a liquid such as oleic acid is placed on the surface of water, it will spread as a film if the force of adhesion between oleic acid and water molecules is greater than the cohesive forces between oleic acid molecules themselves.

$$\textit{Spreading coefficient (S)} = \gamma S - (\gamma L + \gamma LS)$$

- *γS:* surface tension of the sublayer liquid
- *γL:* surface tension of the spreading liquid
- *γ LS:* interfacial tension between the sublayer and the spreading liquid.

Spreading Coefficient

- When $\gamma S > (\gamma L + \gamma LS)$, ($S$ is positive), Spreading occurs.
- When $\gamma S < (\gamma L + \gamma LS)$, ($S$ is negative), the substance forms globules or a floating lens and fails to spread over the surface (e.g. mineral oil on water).



Spreading Coefficient

Example

Spreading Benzene over Water

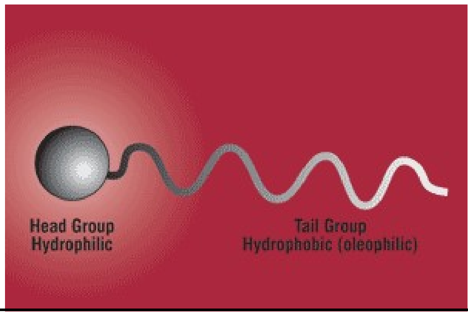
- If the surface tension of water γS is 72.8 dynes/cm at 20°C, the surface tension of benzene, γL, is 28.9 dynes/cm, and the interfacial tension between benzene and water, γLS, is 35.0 dynes/cm, what is the spreading coefficient?

Answer

$$S = 72.8 - (28.9 + 35.0) = 8.9 \text{ dynes/cm}$$

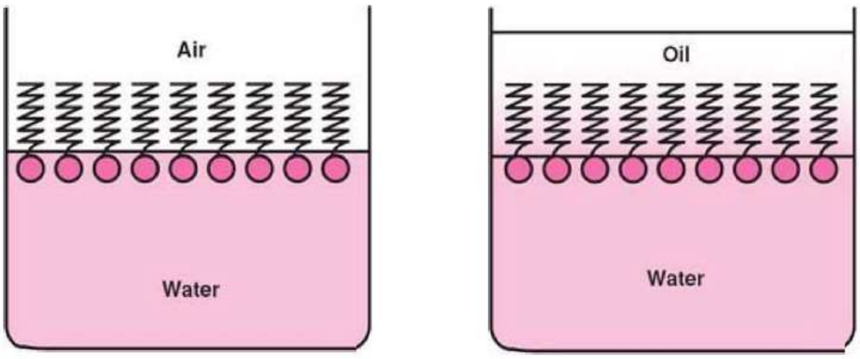
Surface Active Agents (Surfactants)

- Molecules and ions that are adsorbed at interfaces are termed ***surface-active agents*** or ***surfactants.***
- Surfactants have two distinct regions in their chemical structure, one of which is water-liking *(hydrophilic)* and the other of which is lipid-liking *(lipophilic)*. These molecules are referred to as ***amphiphile.***



Surface Active Agents (Surfactants)

- When such molecule is placed in an air-water or oil-water system, the polar groups are oriented toward the water, and the nonpolar groups are oriented toward the air or oil.



Classification of Surfactants

Non-ionic surfactants

- Have low toxicity and high stability and compatibility, e.g.
- Sorbitan esters (spans) and Polysorbates (tweens).

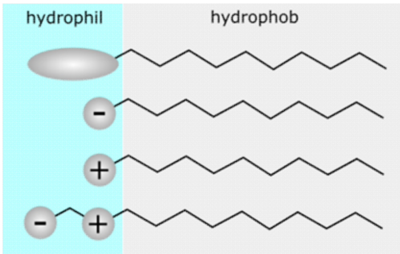
Anionic surfactants

- Have bacteriostatic action
- e.g. Sodium Lauryl Sulphate

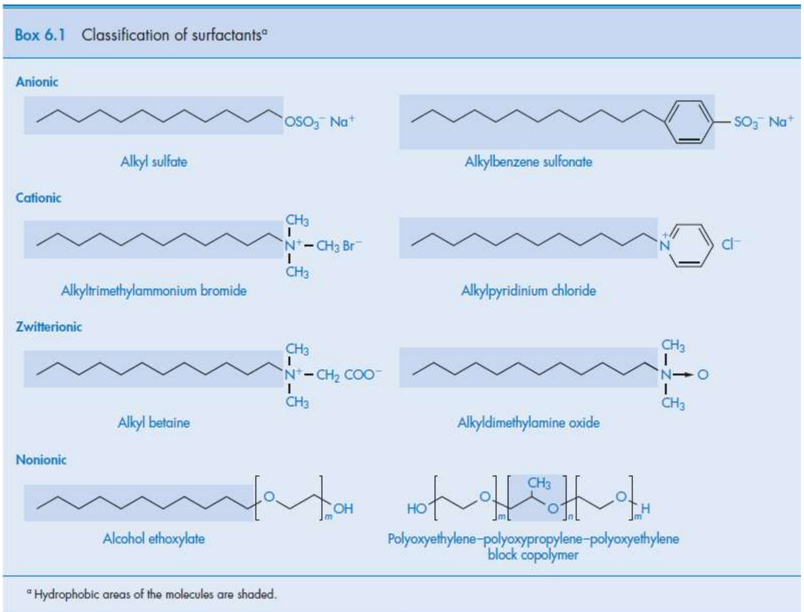
Cationic surfactants

- Have bactericidal activity
- e.g. benzalkonium chloride

Ampholytic Surfactants

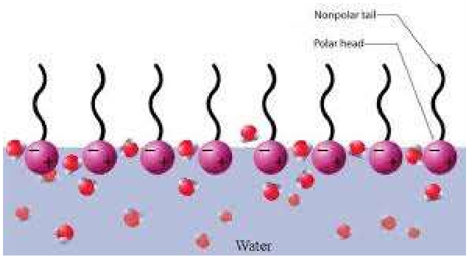


Classification of Surfactants



Reduction of Surface Tension
Principle

- When surfactants are dissolved in water they can reduce surface tension by replacing some of the water molecules in the surface so that the forces of attraction between surfactant and water molecules are less than those between water molecules themselves, hence the contraction force is reduced.



Reduction of Surface Tension
Effect of Structure on Surface Activity

- The surface activity (surface tension reduction) of a particular surfactant depends on the balance between its hydrophilic and hydrophobic properties.
- An increase in the length of the hydrocarbon chain (hydrophobic) of a surfactant increases the surface activity.
- Conversely, an increase in the length of the ethylene oxide chain (hydrophilic) of a non-ionic surfactant results in a decrease of surface activity.

Reduction of Surface Tension

Surface Excess Concentration

- ***Surface excess concentration (Γ)*** is the extra amount per unit area of the solute that is present in the surface
- It represents the difference between the amount per unit area of a solute in the surface of a real system and that of a hypothetical system (without adsorption).
- Surface excess is expressed by the Gibbs equation:

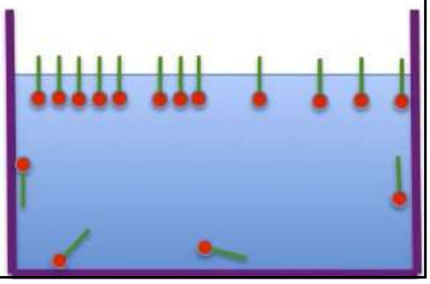
$$\Gamma = \frac{1}{RT} \times \frac{d\gamma}{d\ lnc}$$

Γ = surface excess (g/cm^2)

R = gas constant (8.314 J mol^{-1} K^{-1})

T = absolute temperature (kelvins)

c = concentration (mol m^{-3})



Reduction of Surface Tension

Surface Area

- The ***surface area*** *(A)* is the area occupied by one surfactant molecule at the solution surface.
- It can be calculated from the equation:

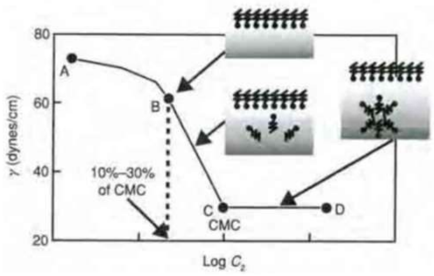
$$A = \frac{1}{N_a \times \Gamma}$$

N_a= Avogadro number (6.023 x 10^{23} molecules mol^{-1})

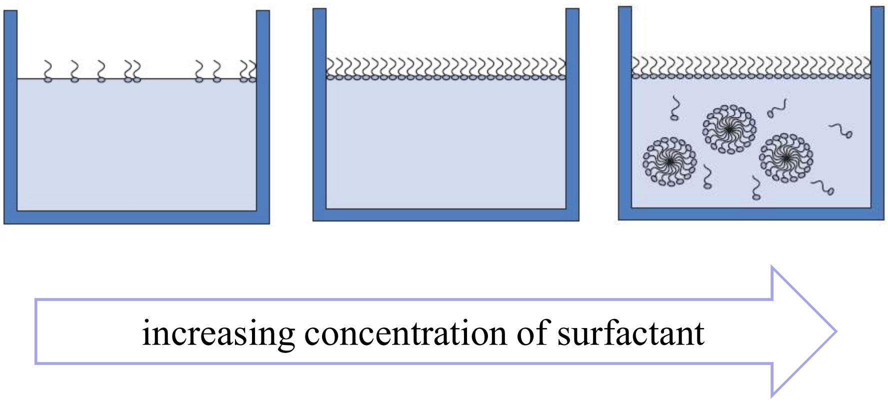
Micellization

- Micelles are formed when the concentration of a surfactant reaches a given concentration called ***critical micelle concentration (CMC)*** in which the surface is saturated with surfactant molecules.

- When the concentration of the surfactant is increased above the CMC, the number of micelles increases but the free surfactant concentration and surface tension stays constant at the CMC value.

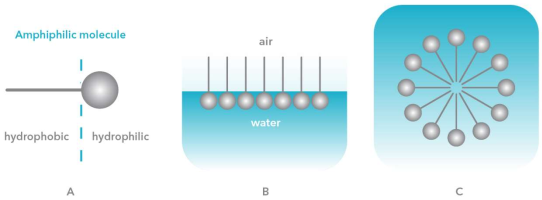


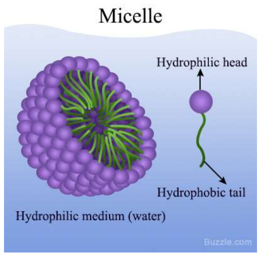
Micellization



Micellization

- Micelles are dynamic structures and are continually formed and broken down in solution (they are not solid spheres).
- The main reason for micelle formation is to obtain a minimum free energy state.
- In a micelle, polar or ionic heads form an outer shell in contact with water, while non polar tails are sequestered in the interior to avoid water.





Factors Affecting Micellization

Structure of the hydrophobic group

- Increase in length of the hydrocarbon chain results in a decrease in CMC and an increase in micellar size.
- The decrease in CMC for compounds with identical polar head groups is expressed by the linear equation:

$$\log [CMC] = A - Bm$$

where m is the number of carbon atoms in the chain and A and B are constants for a homologous series.

Factors Affecting Micellization

Nature of the hydrophilic group

- Non-ionic surfactants generally have very much lower CMC values and higher aggregation numbers than their ionic counterparts with similar hydrocarbon chains.
- An aggregation number is a description of the number of molecules present in a micelle once the critical micelle concentration (CMC) has been reached.
- An increase in the ethylene oxide chain length of a non-ionic surfactant makes the molecule more hydrophilic and the CMC increases.

Factors Affecting Micellization

Nature of the hydrophilic group

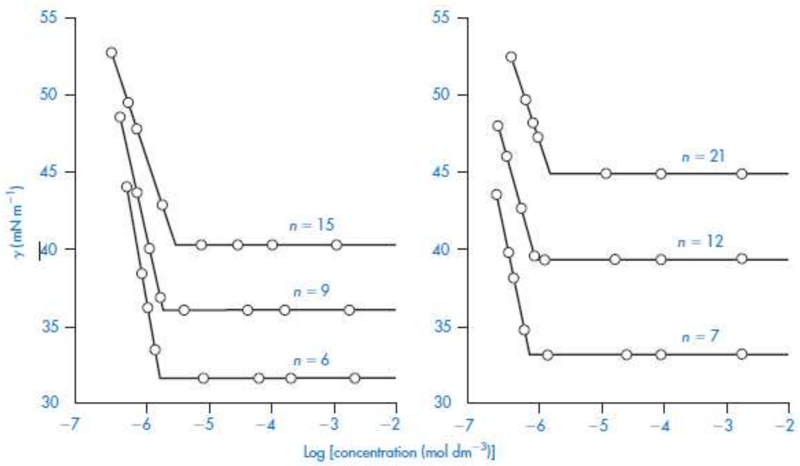


Figure 6.4 Surface tension versus log concentration plots for nonionic surfactants with the general formula $CH_3(CH_2)_{15}(OCH_2CH_2)_nOH$ for a series of ethylene oxide chain lengths, *n*.
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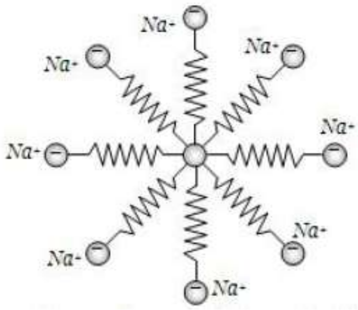
Factors Affecting Micellization

Addition of electrolytes

- Electrolyte addition to solutions of ionic surfactants decreases the CMC and increases the micellar size.
- This is because the electrolyte reduces the forces of repulsion between the charged head groups at the micelle surface, allowing the micelle to grow.



Factors Affecting Micellization

Type of counterion

- Micellar size increases for a cationic surfactant as the counterion is changed according to the series $Cl^- < Br^- < I^-$, and for a particular anionic surfactant according to $Na^+ < K^+ < Cs^+$.
- Ionic surfactants with organic counterions (e.g. maleates) have lower CMCs and higher aggregation numbers than those with inorganic counterions.

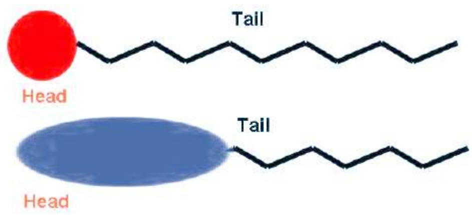
Factors Affecting Micellization

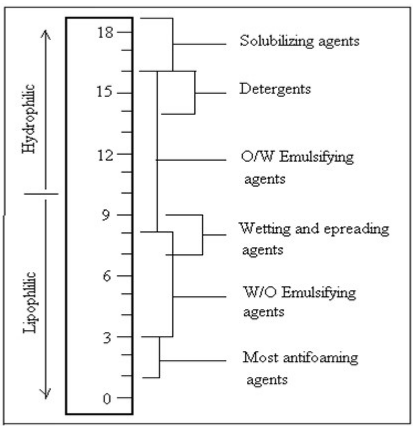
Temperature

- For non-ionic surfactants, Increasing temperature increases micellar size and decrease CMC.
- The effect of temperature stops at a characteristic temperature called the *cloud point* where the solution becomes turbid due to the separation of the solution into two phases.
- This behavior is characteristic of non-ionic surfactants containing polyoxyethylene chains, which exhibit reverse solubility versus temperature behavior in water.
- Temperature has a comparatively small effect on the micellar properties of ionic surfactants.

HLB system

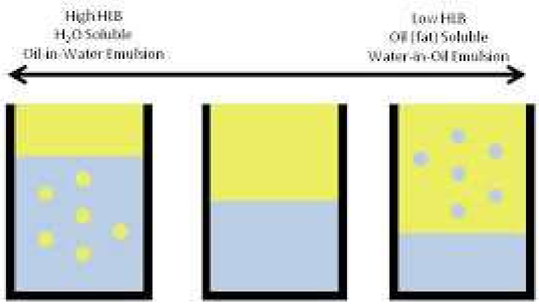
- The ***hydrophile-lipophile balance (HLB)*** system is an arbitrary scale for expressing the hydrophilic and lipophilic characteristics of an emulsifying agent.





HLB system

- Agents with HLB value of 1-8 are lipophilic and suitable for preparation of w/o emulsion, and those with HLB value of 8-18 are hydrophilic and good for o/w emulsion.
- The oil phase of an o/w emulsion requires a specific HLB, called the ***required hydrophile-lipophile balance*** **(RHLB).**



HLB system

Calculation

- **Example: Calculation of HLB Value for Oil-in-Water Emulsions**

Ingredient	Amount	**RHLB (O/W)**
Beeswax	15 g	9
Lanolin	10 g	12
Paraffin wax	20 g	10
Cetyl alcohol	5 g	15
Emulsifier	2 g	
Preservative	0.2 g	
Color	As required	
Water, purified	q.s. 100 g	

HLB system

Calculation

- **Example: Calculation of HLB Value for Oil-in-Water Emulsions**

One first calculates the overall RHLB of the emulsion by multiplying the RHI.B of each oil-like component (items 1-4) by the weight fraction that each oil-like component contributes to the oil phase. The total weight of the oil phase is 50 g. Therefore,

Beeswax	**15/50 x 9**	**= 2.70**
Lanolin	**10/50 x 12**	**= 2.40**
Paraffin	**20/50 x 10**	**= 4.00**
Cetyl alcohol	**5/50 x 15**	**= 1.50**
Total RHLB for the emulsion		**= 10.60**

HLB system

Calculation

- **Example: Calculation of HLB Value for Oil-in-Water Emulsions**
- Next, a blend of two emulsifying agents was chosen, one with an HLB above the RHLB of the emulsion (Tween 80, HLB = 15) and the other with an HLB below the RHLB (Span 80, HLB = 4.3)
- Calculate the percentages of the emulsifiers using the formula:

$$\%\,\boldsymbol{Surfactant\ with\ HLB_{high}} = \frac{\boldsymbol{RHLB - HLB_{low}}}{\boldsymbol{HLB_{high} - HLB_{low}}}$$

$$\%\,\boldsymbol{Tween} = \frac{10.6 - 4.3}{15 - 4.3} = 0.59$$

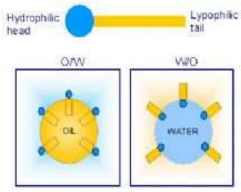
- Therefore, 2 g x 0.59 = 1.18 g of Tween 80 and the remainder, 0.82 g, must be supplied by Span 80

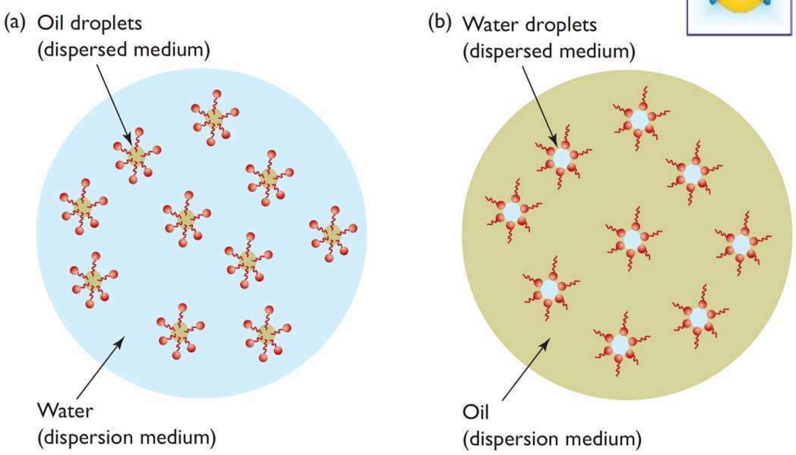
Applications of surface active agents

- Emulsifying agents
- Detergents
- Wetting agents
- Solubilizing agents
- Antibacterial
- Absorption enhancers

Applications of surface active agents

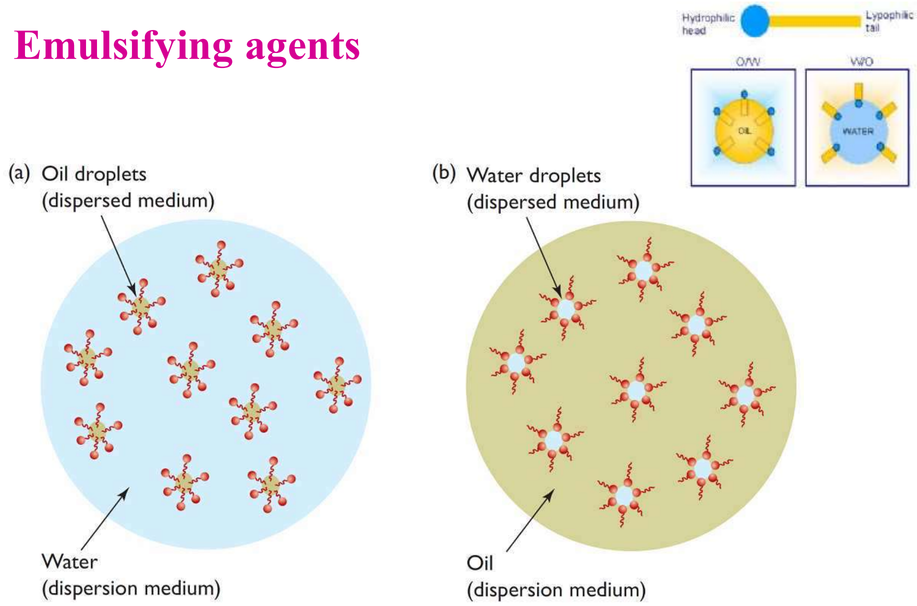
Emulsifying agents





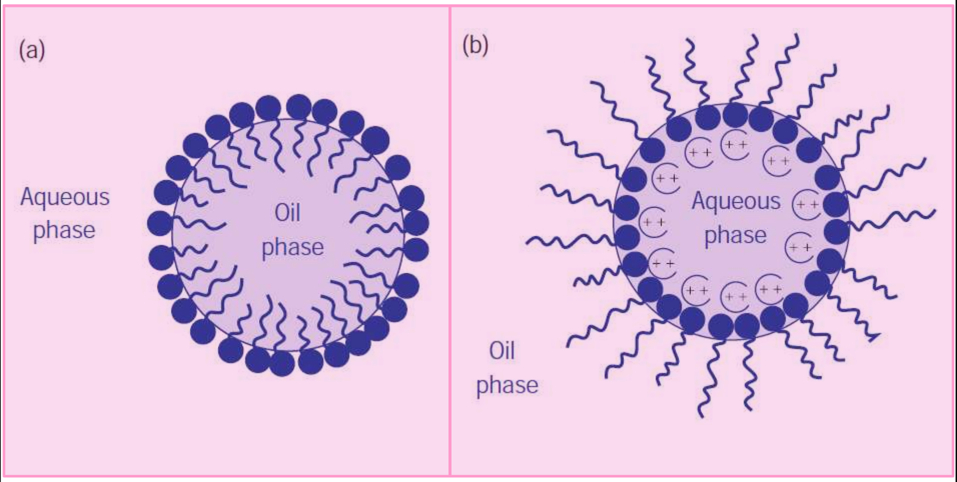
Applications of surface active agents

Emulsifying agents



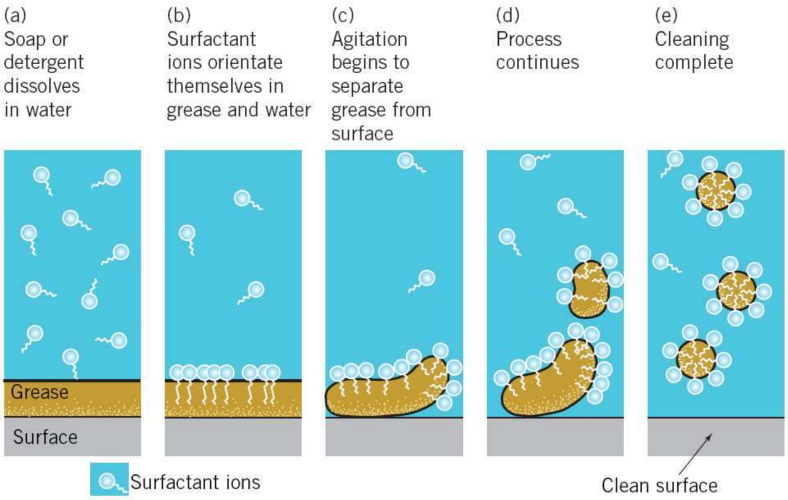
Applications of surface active agents

Emulsifying agents



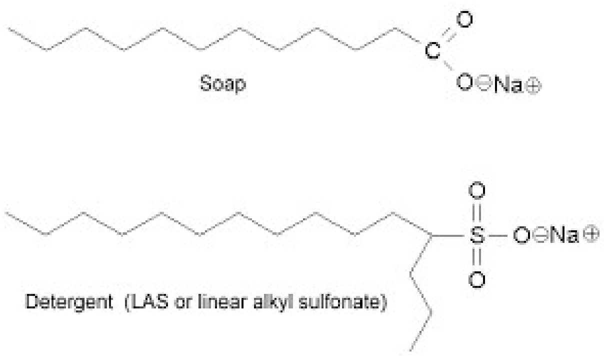
Applications of surface active agents

Detergents



Applications of surface active agents

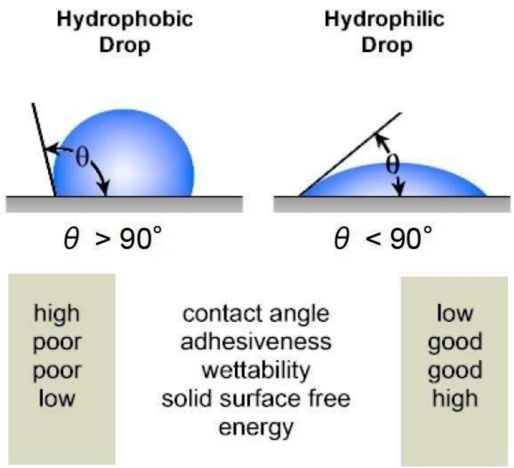
Detergents



Applications of surface active agents

Wetting agents

- A wetting agent is a surfactant that lowers the contact angle by displacing an air phase at the surface, and replacing it with a liquid phase.
- The contact angle is the angle between a liquid droplet and the surface over which it spreads.



Applications of surface active agents

Wetting agents

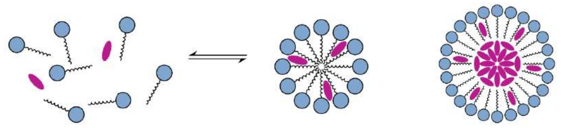
Application of wetting to pharmacy and medicine include:

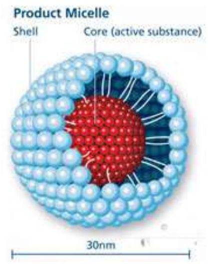
- The displacement of air from the surface of pharmaceutical powders in order to disperse them in liquid vehicles.
- To aid in spreading of medicinal lotions and sprays on surface of skin and mucous membranes.

Applications of surface active agents

Solubilization

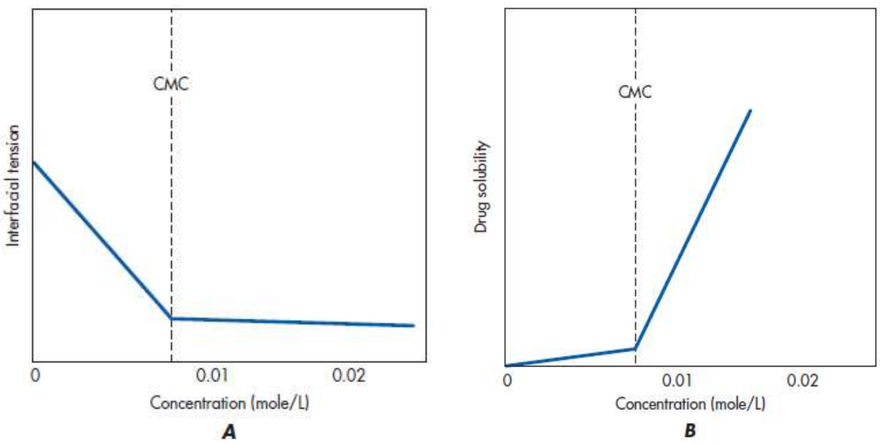
- Solubilization is the process where water-insoluble substances are brought into solution by incorporation into micelle.
- Solubilization does not occur until the micelles are formed (i.e. above CMC)
- The amount of substance solubilized increases as the number of micelles increases.





Applications of surface active agents

Solubilization



A. Changes in the interfacial tension as a function of concentration. ***B.*** Changes in the solubility of a difficult-to-solubilize drug as a function of the concentration of the surface active agent.

Applications of surface active agents

Stability of drugs in solubilized systems

- Solubilization of a drug by incorporation into micelles may affect its stability.
- In a micelle, the drug molecules may be protected from attacking species such as hydronium or hydroxide ions and the stability of the drug may be increased.
- The difference in environment between the micellar and bulk aqueous phases may be such that reaction rates may be radically changed by the transfer of solute to micelles.

Applications of surface active agents

Antibacterial

- Significant antimicrobial effects have been associated with cationic surfactants, in particular the quaternary compounds.
- The action mechanism of quaternary surfactants involves disruption of the cell membrane, protein denaturation, and enzyme inhibition.

Absorption enhancers

Naturally occurring surfactants

Phospholipids

- The phospholipids are widely found in biological membranes and can be used as emulsifiers especially for intravenous fat emulsions, and as a key component of liposomes.

Bile Salts

- Bile salts are carboxylic acids (C22–C28) with a cyclopentenophenanthrene nucleus containing a branched chain of 3–9 carbon atoms ending in a carboxyl group.

Saponins

- Saponins are glycosides found in certain plants which are characterized by their property of producing a frothing aqueous solution.

Measurement of Tensions

Capillary Rise Method

- When a capillary tube is placed in a liquid contained in a beaker, the liquid rises up in the tube to a certain distance.
- By measuring this rise in the capillary, it is possible to determine the surface tension of the liquid using the formula:

$$\gamma = rh\rho g/2$$

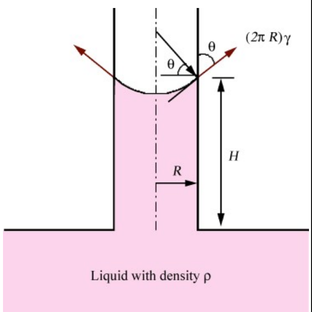
γ: surface tension

r: radius of capillary

h: height

ρ: density of the liquid

g: acceleration due to gravity



- This method cannot be used to obtain interfacial tensions.

Measurement of Tensions

Capillary Rise Method

Example

Calculation of the Surface Tension of Chloroform by the Capillary Rise Method

- A sample of chloroform rose to a height of 3.67 cm at 20°C in a capillary tube having an inside radius of 0.01 cm. What is the surface tension of chloroform at this temperature? The density of chloroform is 1.476 g/cm3.

Answer

$$\gamma = \frac{1}{2} \times 0.01\ cm \times 3.67\ cm \times 1.476 \frac{g}{cm^3} \times 981 \frac{cm}{sec^2}$$

$= 26.6\ g/sec^2$

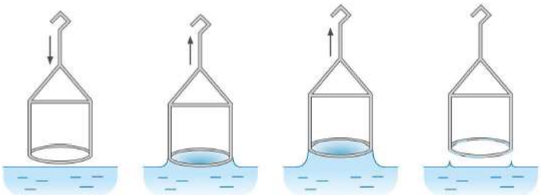
Measurement of Tensions

The DuNoüy Ring Method

- The force necessary to detach a platinum—iridium ring immersed at the surface or interface is proportional to the surface or interfacial tension.
- The surface tension is given by the formula:

$$\gamma = \frac{\text{Dial reading in dynes}}{2 \times \text{Ring circumference}} \times \text{Correction factor}$$

- The **DuNoüy tensiometer** is widely used for measuring surface and interfacial tensions.



Adsorption at the solid–liquid interface

Adsorption is the adhesion of atoms, ions, or molecules from a gas, liquid, or dissolved solid to a surface.

There are two general types of adsorption:

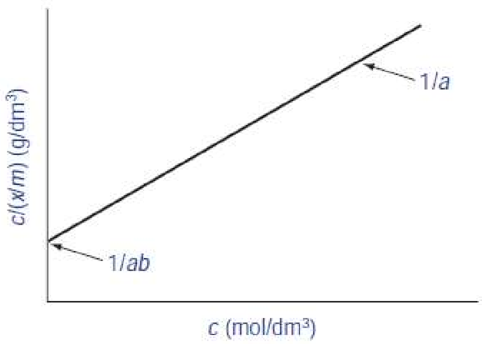
1. Physical adsorption, in which the adsorbate is bound to the surface through the weak van der Waals forces.
2. Chemical adsorption or chemisorption, which involves the stronger valence forces.

- A simple experimental method of studying adsorption is to shake a known mass of the adsorbent material with a solution of known concentration at a fixed temperature until no further change in the concentration of the supernatant is observed, that is, until equilibrium conditions have been established.

Adsorption at the solid–liquid interface

- Adsorption may be analyzed using the Langmuir equation:

$$\frac{c}{x/m} = \frac{1}{ab} + \frac{c}{a}$$



x = amount of solute adsorbed.

m = weight of adsorbent.

c = conc. of solution at equilibrium.

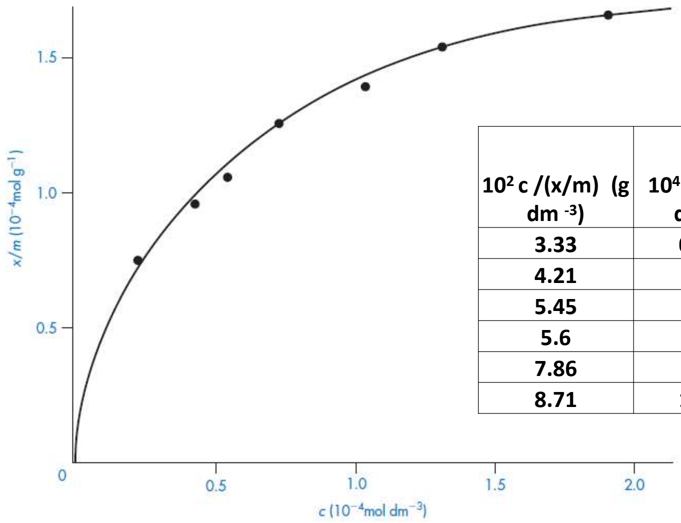
b = constant related to the enthalpy of adsorption

a = constant related to the surface area of the solid

- Values of ***a*** and ***b*** can be determined from the intercept ***(1/ab)*** and slope (1/a) of plots of *c/(x/m)* against *c*

Adsorption at the solid–liquid interface

Example Calculate the Langmuir constants for the adsorption of amitriptyline on carbon black using the following figure and derived data :



10^2 c /(x/m) (g dm $^{-3}$)	10^4 c (mol dm^{-3})	10^3xm (mol g^{-1})
3.33	0.25	0.75
4.21	0.4	0.95
5.45	0.6	1.1
5.6	0.7	1.25
7.86	1.1	1.4
8.71	1.35	1.55

Adsorption at the solid–liquid interface

Answer:

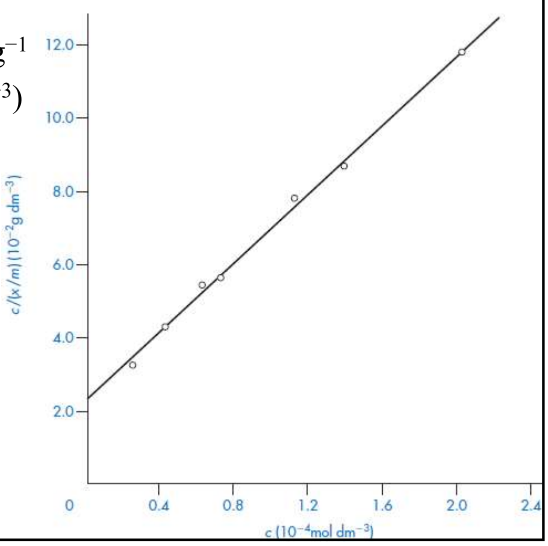
The slope of the plot of c (x/m) against c =4.88×10^{2} g mol^{-1} = 1/a.

Therefore,

a = 1/slope = 2.05×10^{-3} mol g^{-1}

b = 1/($2.35 \times 10^{-2} \times 2.05 \times 10^{-3}$)

= 2.07×10^{4} dm^3 mol^{-1}



Adsorption at the solid–liquid interface

Factors affecting adsorption

- *Solubility of the adsorbate*. In general, the extent of adsorption of a solute is inversely proportional to its solubility in the solvent from which adsorption occurs.
- *pH*. In general, for simple molecules adsorption increases as the ionisation of the drug is suppressed.
- *Nature of the adsorbent*. The extent of adsorption is proportional to the specific surface area.
- *Temperature*. Since adsorption is generally an exothermic process, an increase in temperature normally leads to a decrease in the amount adsorbed.

Adsorption at the solid–liquid interface

Applications

- ***Adsorption of poisons/toxins***.
  - ➢ The 'universal antidote' for use in reducing the effects of poisoning by the oral route is composed of activated charcoal, magnesium oxide and tannic acid.
  - ➢ A more recent use of adsorbents has been in dialysis to reduce toxic concentrations of drugs by passing blood through a haemodialysis membrane over charcoal and other adsorbents.
- ***Taste masking***.
  - ➢ Drugs such as diazepam may be adsorbed onto solid substrates to minimize taste problems, but care should be taken to ensure that desorption does not become a rate-limiting step in the absorption process.

Adsorption at the solid–liquid interface

Applications

- ***Adsorption in drug formulation:***

➢ Suspensions are stabilized by adsorption of surfactants and polymers on the dispersed solid.

➢ Adsorption of surfactants onto poorly soluble solids increase their dissolution rate by increased wetting.

- ***Chromatographic Separation:***

➢ HPLC and TLC techniques rely on the principle of adsorption.