



## Lecture 4

# Interfacial Phenomena

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## Overview

### Liquid interfaces

- Surface tension
- Interfacial tension
- Surface free energy
- Measurement of tensions
- Spreading coefficient

### Surface active agents

- Classification
- Reduction of surface tension
- Micellisation
- Adsorption
- HLB system
- Wetting

# Learning Objectives

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 and spreading coefficient.
5. Understand the mechanisms of adsorption on liquid and solid interfaces.
6. Classify surface-active agents and appreciate their applications in pharmacy.
7. Differentiate between different types of monolayers and recognize basic methods for their characterization.



## Liquid interfaces

Surface tension

Interfacial tension

Surface free energy

Measurement of tensions

Spreading coefficient

# Liquid Interfaces

*Interface* is the boundary between two phases.

*Surface* is a term used to describe either a gas-solid or a gas-liquid interface.

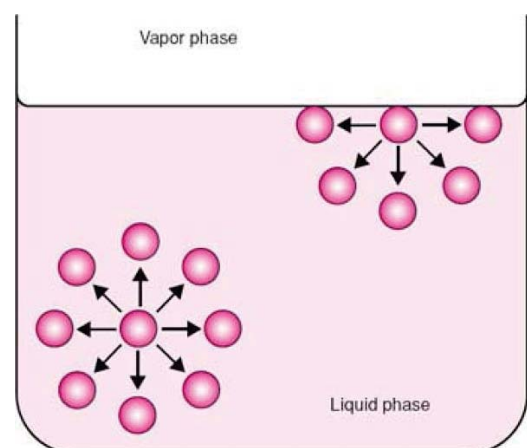
*Interfacial phase* is a term used to describe molecules forming the interface between two phases which have different properties from molecules in the bulk of each phase.



## Surface Tension

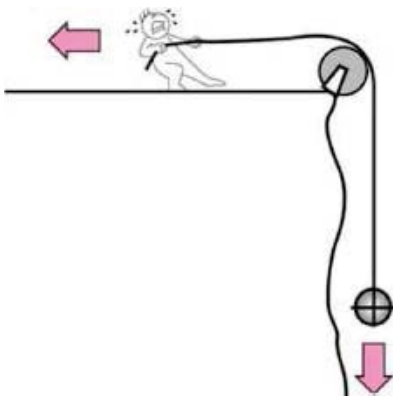
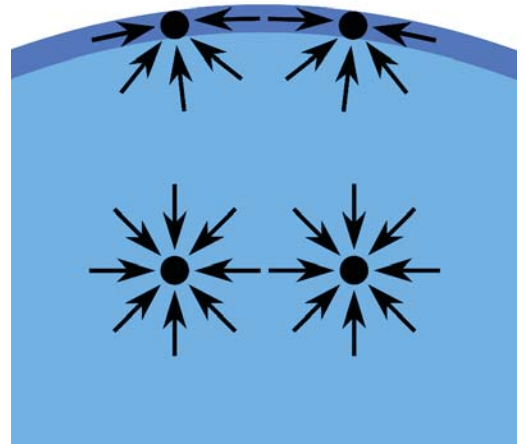
Molecules in the bulk liquid are surrounded in all directions by other molecules for which they have an equal attraction (only cohesive forces).

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.



# Surface Tension

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 tension* is the 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.



## Interfacial Tension

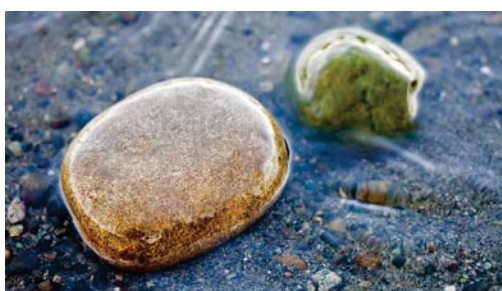
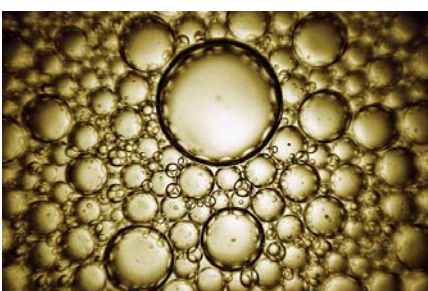
*Interfacial tension* is the force per unit length existing at the interface between two immiscible phases (units are dynes/cm or N/m).

The term **interfacial tension** is used for the force between:

Two liquids =  $\gamma_{LL}$

Two solids =  $\gamma_{SS}$

Liquid-solid =  $\gamma_{LS}$



# Interfacial Tension

The term **surface tension** is reserved for the tensions:

Liquid-vapor =  $\gamma_{LV}$  (written simply as  $\gamma_L$ ).

Solid-vapor =  $\gamma_{SV}$  (written simply as  $\gamma_S$ ).

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



## 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)

$\gamma$ : surface tension (dynes/cm)

$\Delta A$ : increase in area (cm<sup>2</sup>).

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



# Surface Free Energy

Each molecule of the liquid has a tendency to move inside the liquid from the surface; therefore, when the surface is increased, the liquid takes the form with minimal surface and as a result, minimal surface energy:

**Sphere!**



## 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:

$$\gamma = \frac{1}{2} r h \rho g$$

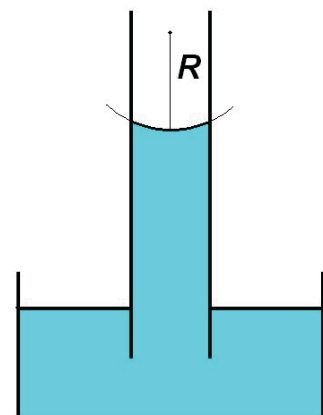
$\gamma$ : surface tension

$r$ : radius of capillary

$h$ : height

$\rho$ : density of the liquid

$g$ : acceleration of gravity



This method cannot be used to obtain interfacial tensions.





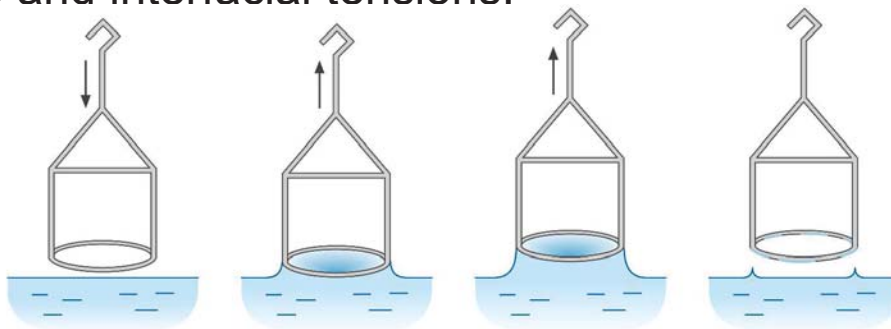
# Measurement of Tensions

## 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.



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13

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# Surface Active Agents

Classification

Reduction of Surface Tension

Micellisation

Adsorption

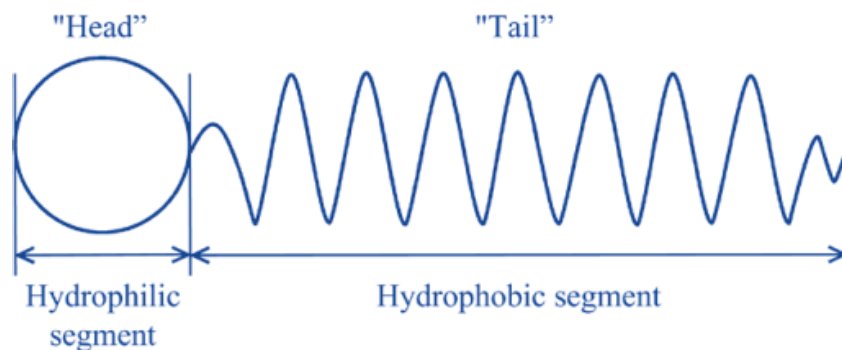
HLB system

Wetting

# Surface Active Agents

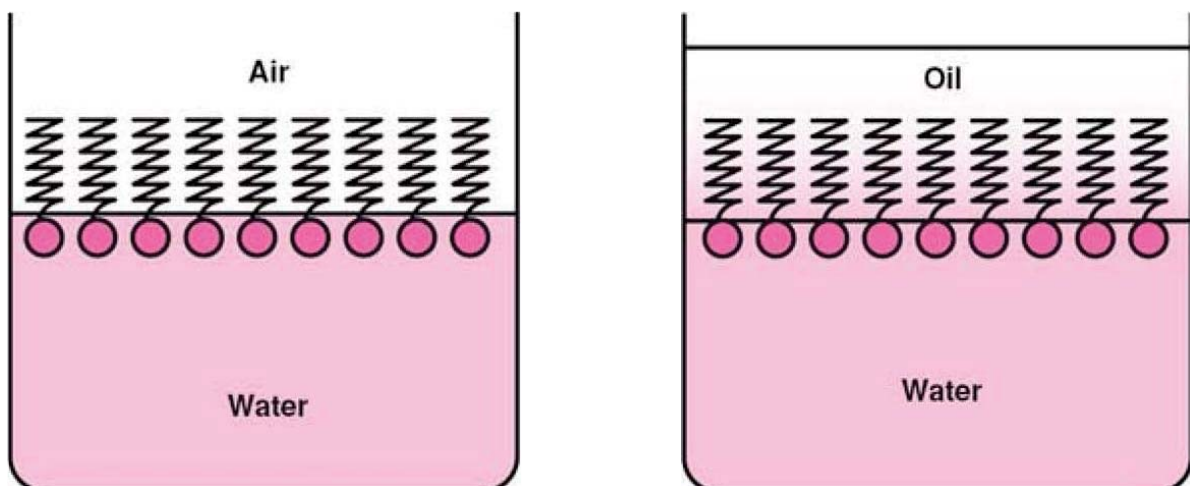
Molecules and ions that are adsorbed at interfaces are termed **surface-active agents** or **surfactants**.

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

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

## Non-ionic surfactants

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

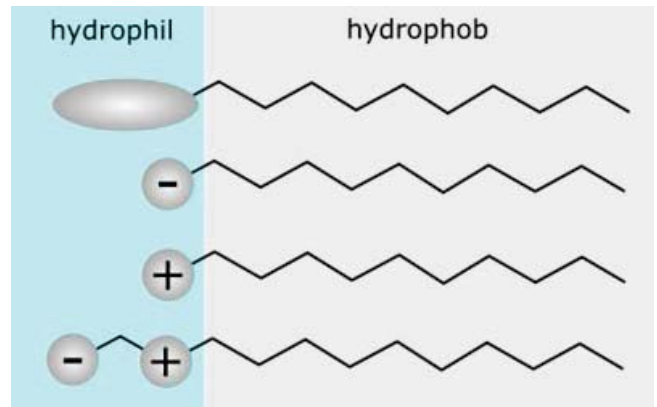
## Anionic surfactants

Have bacteriostatic action  
e.g. Sodium Lauryl Sulphate

## Cationic surfactants

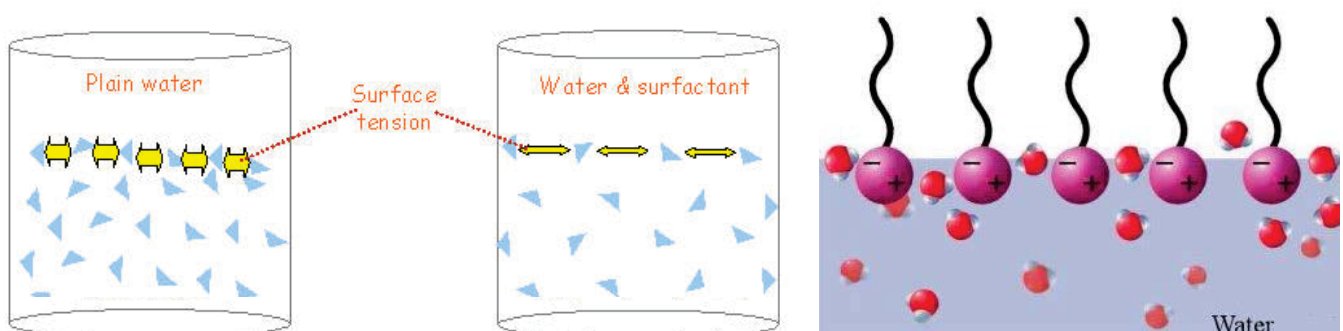
Have bactericidal activity  
e.g. benzalkonium chloride

## Ampholytic Surfactants



# 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.



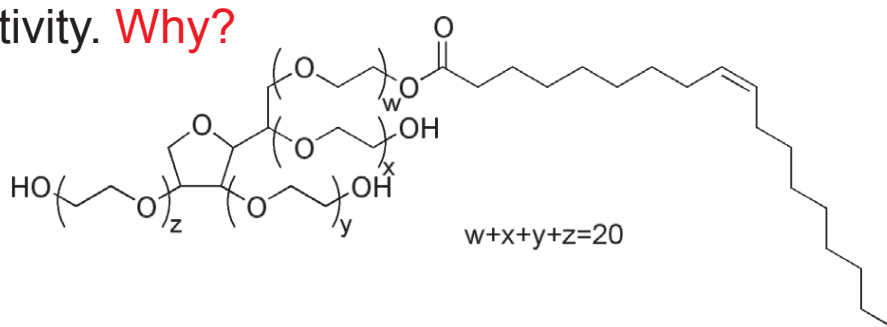
# Reduction of Surface Tension

## 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.

An increase in the length of the ethylene oxide chain (hydrophilic) of a non-ionic surfactant results in a decrease of surface activity. **Why?**



# Reduction of Surface Tension

## Surface Excess Concentration

**Surface excess concentration ( $\Gamma$ )** is the extra amount per unit area of the solute that is present in the surface

It is 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:

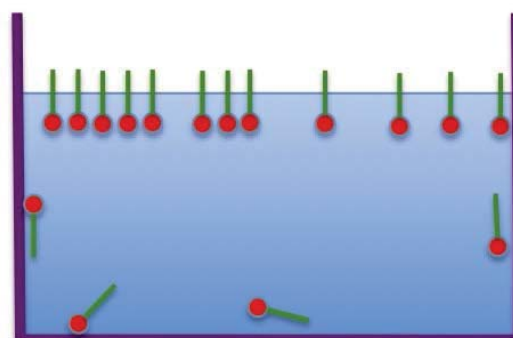
$$\Gamma = \frac{1}{RT} \times \frac{d\gamma}{d \ln c}$$

$\Gamma$  = surface excess (g/cm<sup>2</sup>)

$R$  = gas constant (8.314 J mol<sup>-1</sup> K<sup>-1</sup>)

$T$  = absolute temperature (kelvins)

$c$  = concentration (mol m<sup>-3</sup>)



# Reduction of Surface Tension

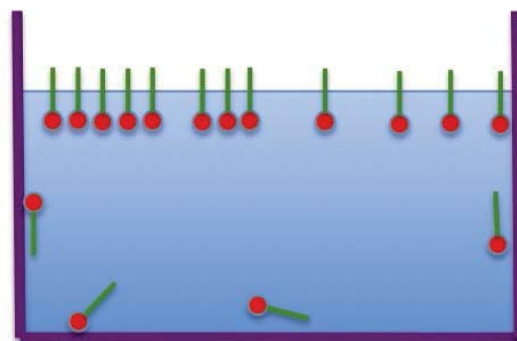
## Surface Area

The **surface area** ( $A$ ) is the area occupied by one surfactant molecule at the solution surface.

It can be calculated from the equation:

$$A = \frac{1}{N_A \Gamma}$$

$N_A$  = Avogadro number ( $6.023 \times 10^{23}$  molecules  $\text{mol}^{-1}$ )

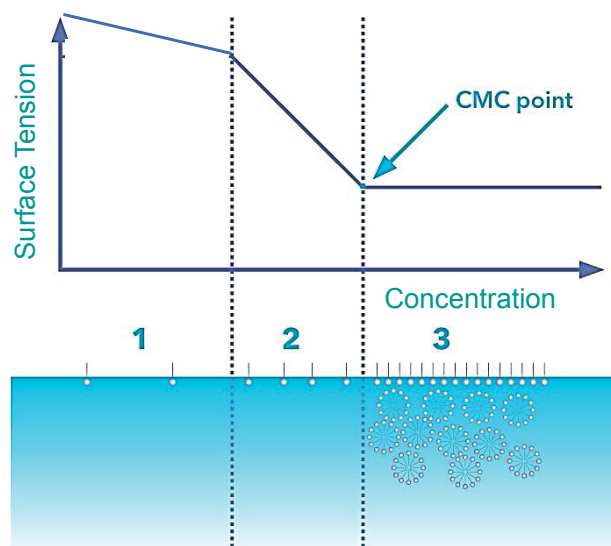


## Micellisation

### Definition

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



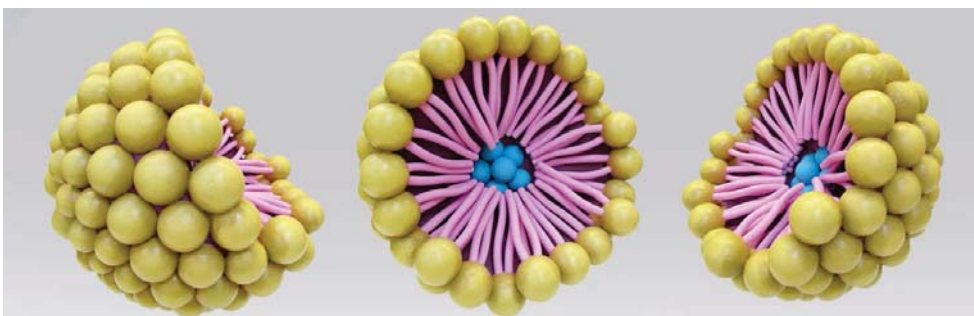
# Micellisation

## Definition

Micelles are dynamic structures and are continually formed and broken down in solution (they are not solid spheres).

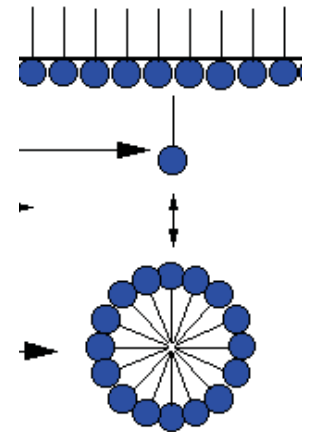
The main reason for micelle formation is to obtain a minimum free energy state.

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.



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25



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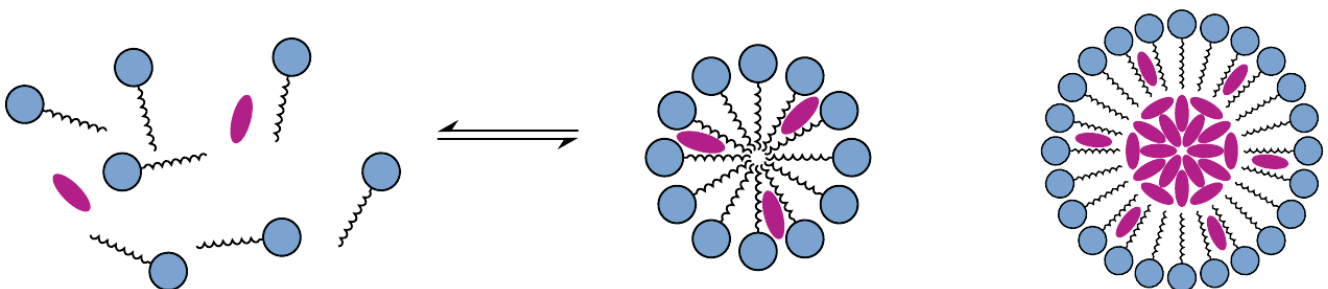
# Micellisation

## 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.



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# Micellisation

## Factors Affecting Micellisation

### *Structure of the surfactant*

Increase in length of the hydrocarbon chain results in a decrease in CMC and an increase in micellar size.

An increase in the ethylene oxide chain length of a non-ionic surfactant makes the molecule more hydrophilic and the CMC increases.

### *Type of counterion*

Micellar size increases for a cationic surfactant as the counterion is changed according to the series  $\text{Cl}^- < \text{Br}^- < \text{I}^-$ , and for a particular anionic surfactant according to  $\text{Na}^+ < \text{K}^+ < \text{Cs}^+$ .



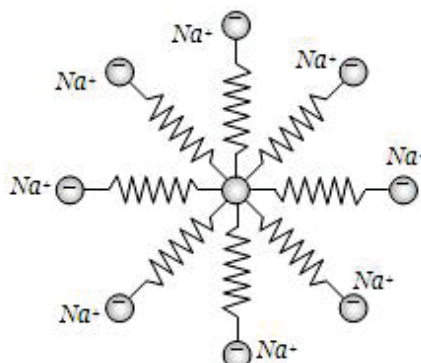
# Micellisation

## Factors Affecting Micellisation

### *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.



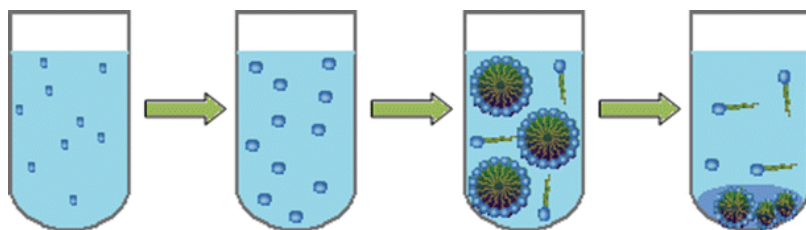
# Micellisation

## Factors Affecting Micellisation

### *Effect of 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 become turbid due to the separation of the solution into two phases.



Temperature has a comparatively small effect on the micellar properties of ionic surfactants.

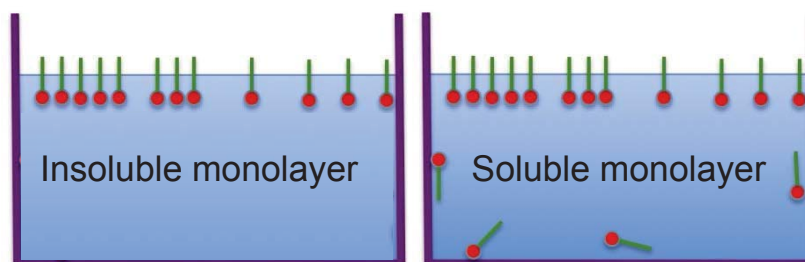


# Micellisation

## Insoluble Monolayers

Insoluble amphiphilic compounds (e.g. surfactants with very long hydrocarbon chains) can also form films on water surfaces when they are dissolved in a volatile solvent and carefully injected onto the surface.

They differ from soluble amphiphilic compounds in that all the molecules injected on to the surface stay at the surface, and do not continually move back and forward between the surface and the bulk of the solution in equilibrium.





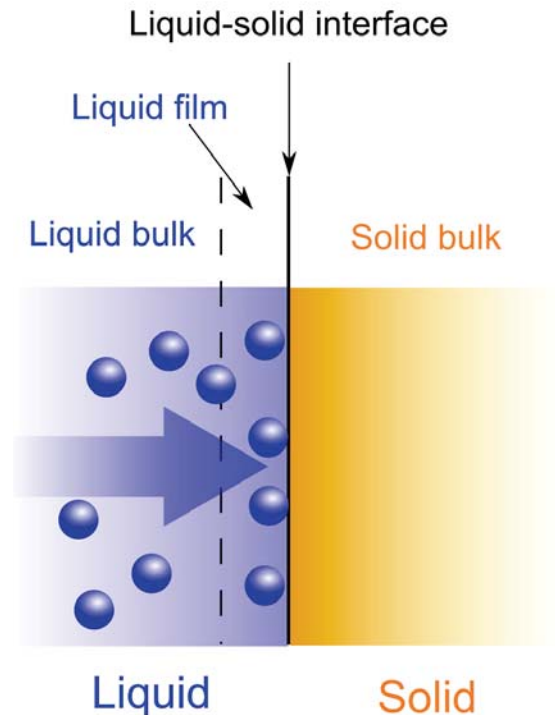
# Adsorption

## Types of Adsorption

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

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.



# Adsorption

## Langmuir Equation

Adsorption may be analysed using the Langmuir equation:

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

$x$  = amount of solute adsorbed.

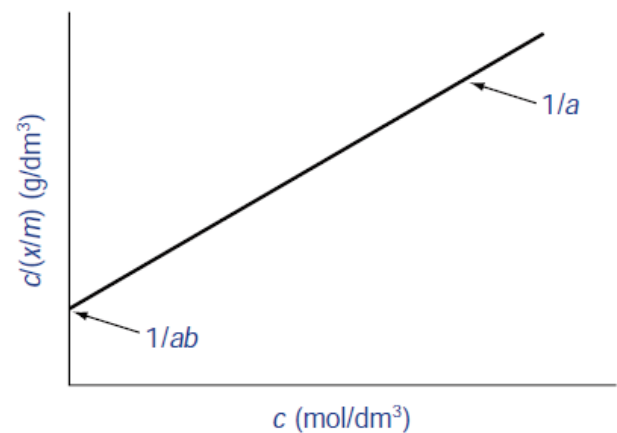
$m$  = weight of adsorbent.

$c$  = 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 ( $1/a$ ) by plotting  $c/(x/m)$  against  $c$



# Adsorption

## Factors Affecting Adsorption at S-L Interface

### *Solubility of the adsorbate*

The extent of adsorption of a solute is inversely proportional to its solubility in the solvent from which adsorption occurs.

### *pH*

For simple molecules adsorption increases as the ionization of the drug is suppressed, reaching a maximum when the drug is completely unionized.



# Adsorption

## Factors Affecting Adsorption at S-L Interface

### *Nature of the adsorbent*

The extent of adsorption is proportional to the surface area of the adsorbent. Thus, the more finely divided or the more porous the solid, the greater its adsorption capacity.

### *Temperature*

Since adsorption is generally an exothermic process, an increase in temperature normally leads to a decrease in the amount adsorbed.



# Adsorption

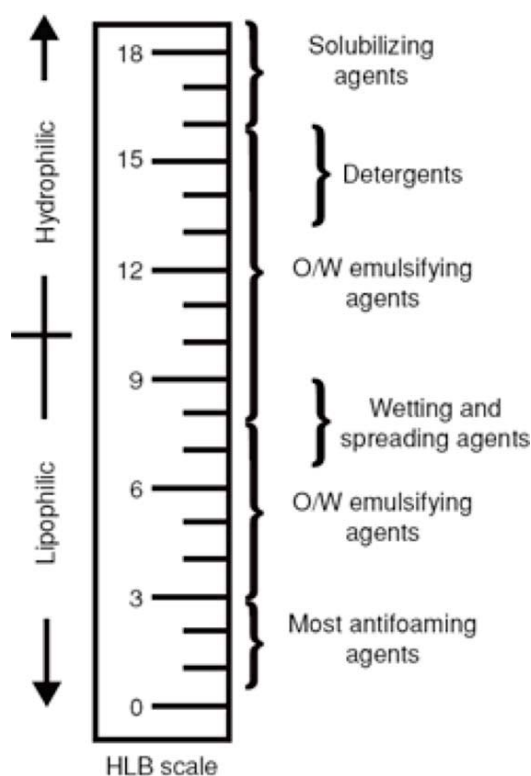
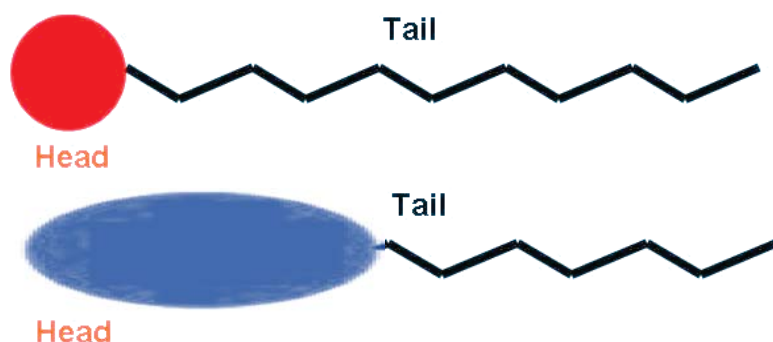
## Pharmaceutical Applications

1. **Adsorption of poisons/toxins:** Activated charcoal are used in adsorbing the toxins and reducing the effects of poisoning by the oral route.
2. **Taste masking:** Drugs such as diazepam may be adsorbed onto solid substrates to minimize taste problems.
3. **Adsorption in drug formulation:**
  1. Suspensions are stabilized by adsorption of surfactants and polymers on the dispersed solid.
  2. Adsorption of surfactants onto poorly soluble solids increase their dissolution rate by increased wetting.
4. **Separation:** HPLC and TLC techniques rely on the principle of adsorption.



## HLB System Definition

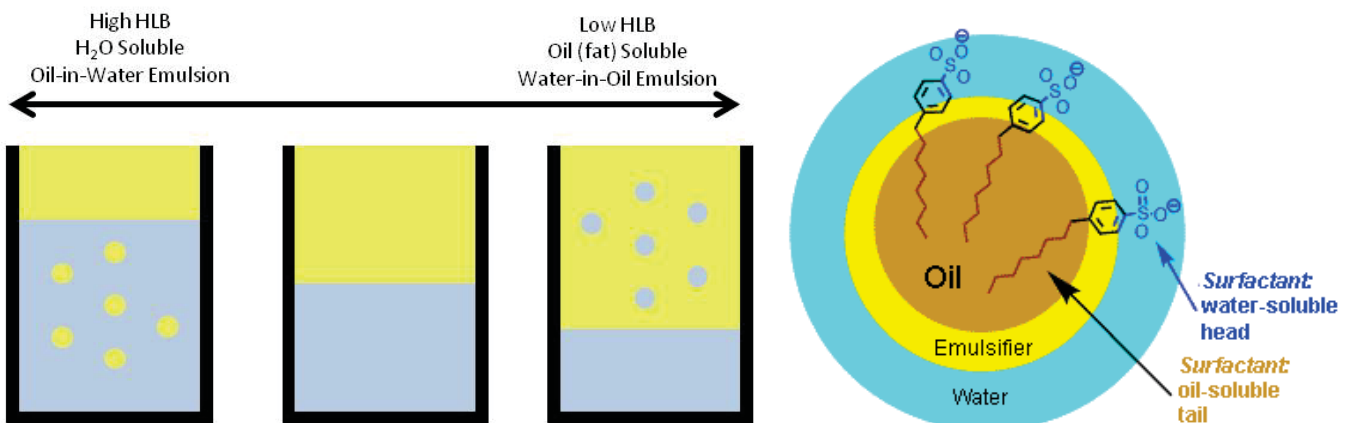
The **hydrophile-lipophile balance (HLB)** system is an arbitrary scale for expressing the hydrophilic and lipophilic characteristics of an emulsifying agent.



# HLB System Definition

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)***.



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# HLB System Calculations Example

Calculate the amounts (ml) of each of the emulsifiers (tween 80 and span 80) that are required to prepare the emulsion:

Ingredient	Amount	RHLB (O/W)
1. Beeswax	15 g	9
2. Lanolin	10 g	12
3. Paraffin wax	20 g	10
4. Cetyl alcohol	5 g	15
5. Emulsifiers (Tween 80 + Span 80)	5 ml	
6. Preservative	As required	
7. Color	0.2 g	
8. Water, purified	q.s. 100 ml	

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# HLB System

## Calculations

### Example

First, calculate the overall **RHLB** of the emulsion by multiplying the RHLB of each oil-like component (items 1-4) by their weight fraction from the oil phase. The total weight of the oil phase is 50 g. Therefore:

$$\text{Beeswax } 15/50 \times 9 = 2.70$$

$$\text{Lanolin } 10/50 \times 12 = 2.40$$

$$\text{Paraffin } 20/50 \times 10 = 4.00$$

$$\text{Cetyl alcohol } 5/50 \times 15 = 1.50$$

$$\text{Total RHLB for the emulsion} = 10.60$$



# HLB System

## Calculations

### Example

Next, a blend of two emulsifying agents is 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:

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

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

Therefore,  $5 \text{ ml} \times 0.59 = 2.95 \text{ ml}$  of Tween 80

and the remainder, 2.05 ml, must be supplied by Span 80

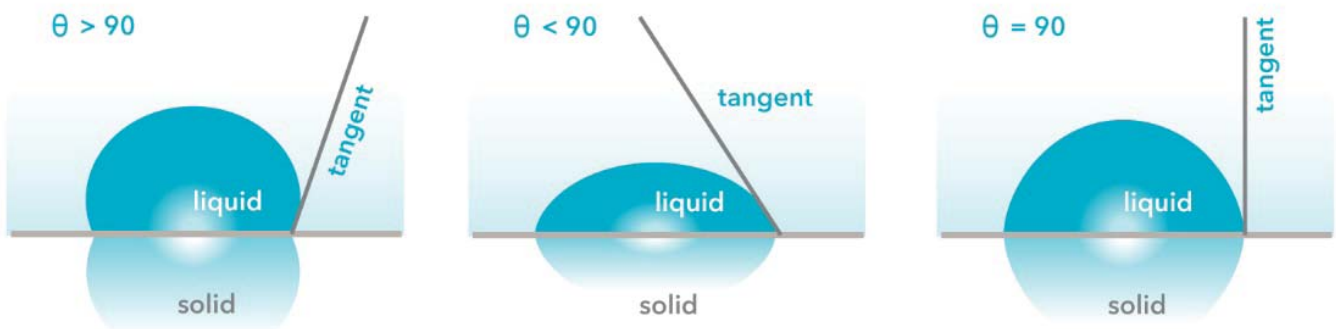


# Wetting

## 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.



# Wetting

## Applications

Application of wetting to pharmacy and medicine include:

1. The displacement of air from the surface of pharmaceutical powders in order to disperse them in liquid vehicles.
2. The displacement of air from the matrix of cotton pads and bandages so that medicinal solutions can be absorbed for application to various body areas.
3. The displacement of air from the surface of the skin and mucous membranes when medicinal lotions and sprays are applied.





# References

1. Attwood, D. & Florence, A. T. 2008. *Physical pharmacy*, London. Chicago, Pharmaceutical Press.
2. Sinko, P. J. M. A. N. 2006. *Martin's physical pharmacy and pharmaceutical sciences: physical chemical and biopharmaceutical principles in the pharmaceutical sciences*, Philadelphia, Lippincott Williams & Wilkins.

