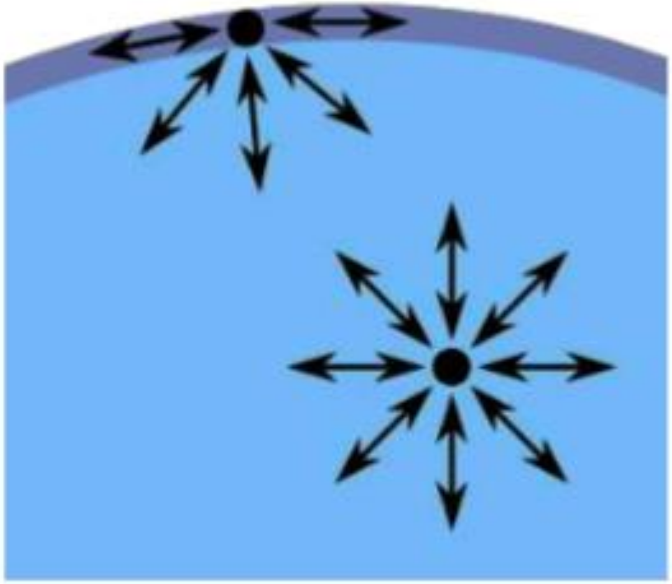
Surfactants

Surfactants – Surface Active Agents

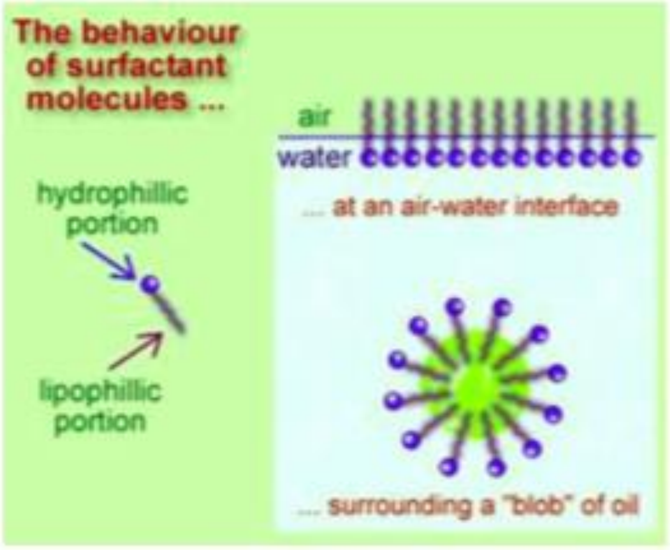
Definition

➢Surface tension:

The molecules at the surface do not have other molecules on all sides of them and therefore are pulled inwards. This creates some internal pressure and forces liquid surfaces to contract to the minimal area.



➢Surfactants: are substances that absorb to surfaces or interfaces, causing a marked decrease in the surface tension.



Surfactants

Their importance in pharmaceutical technology

promotion of wetting, dissolution and dispersion

promotion of absorption,
(increase the bioavailability)

development of new drug carriers

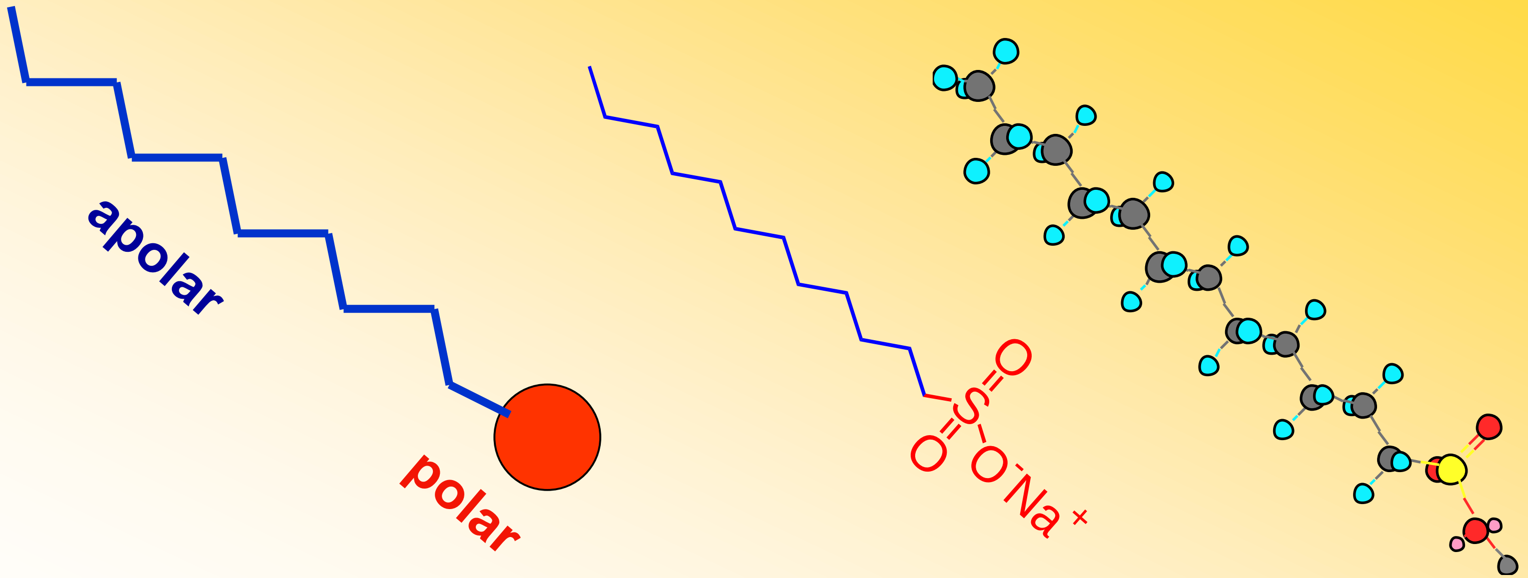
Surfactants

New Drug Delivery Systems

	Emulsions	Microemulsions	Vesicles
Disperse systems	simple or complex		micelles liposomes niosomes
Application	Controlled drug delivery systems elimination of incompatibility	nutrition	Controlled drug delivery systems targetted drug intake

Surfactants

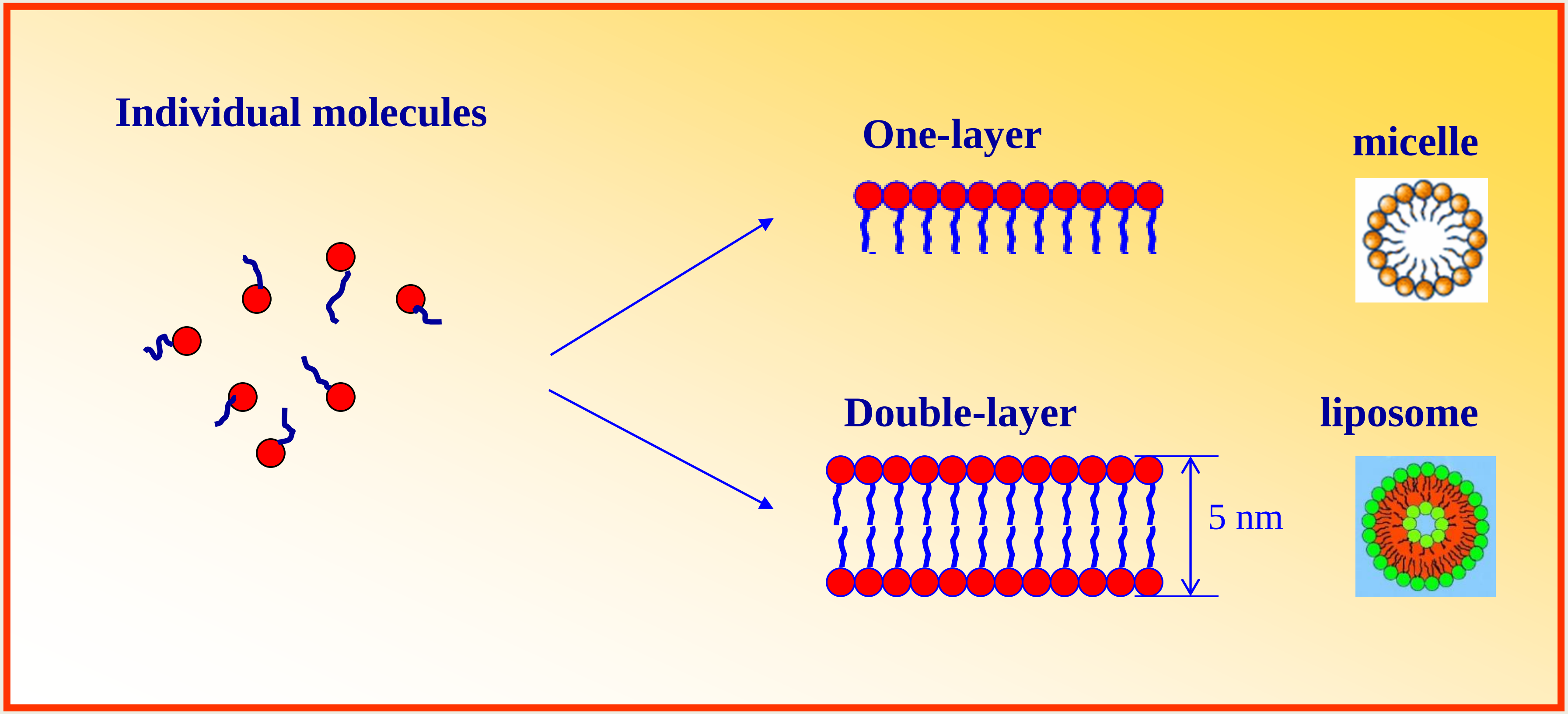
Molecular structures of emulgents



Sodium-dodecil-sulphate

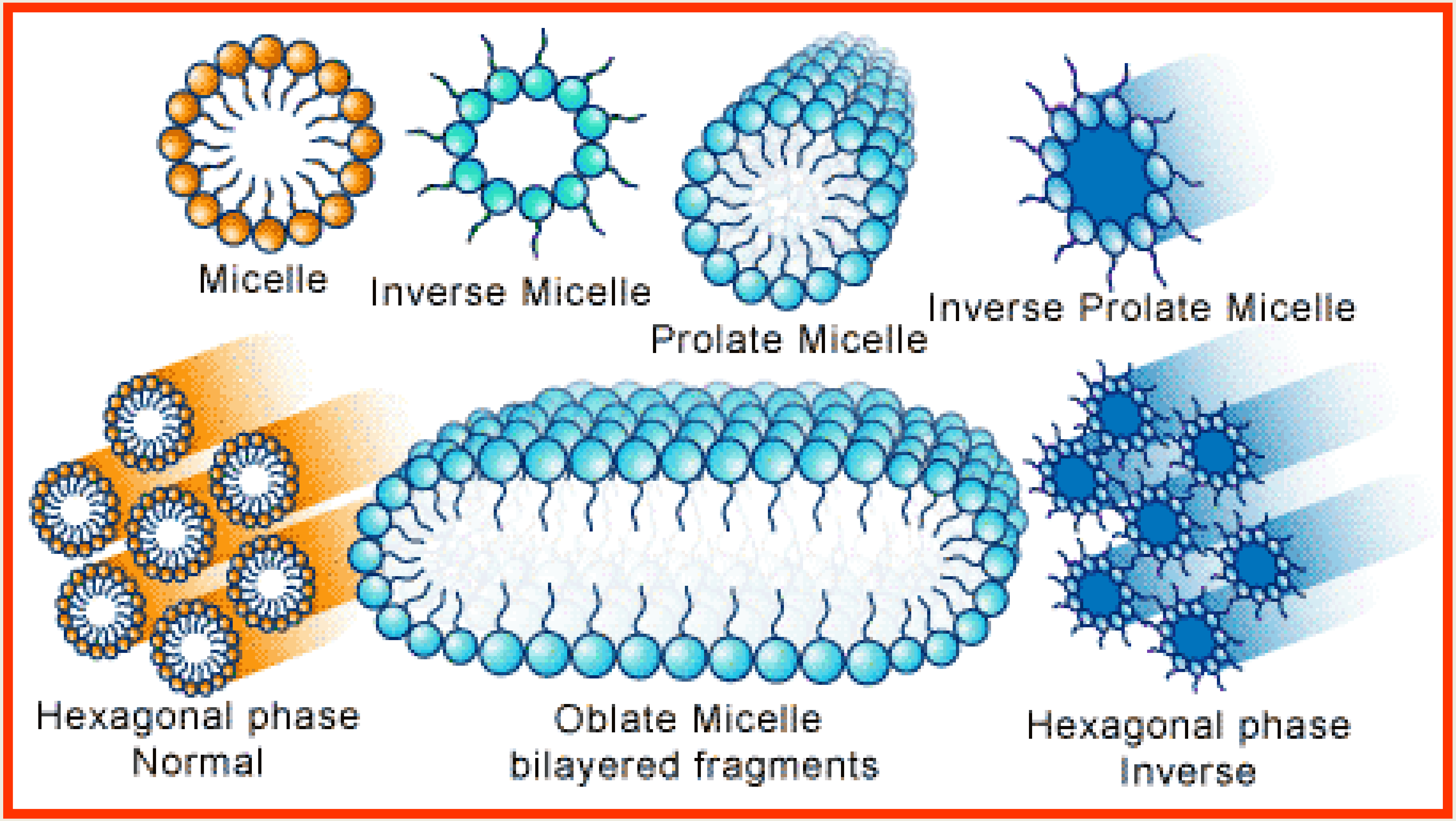
Surfactants

Spheric structures of surfactants



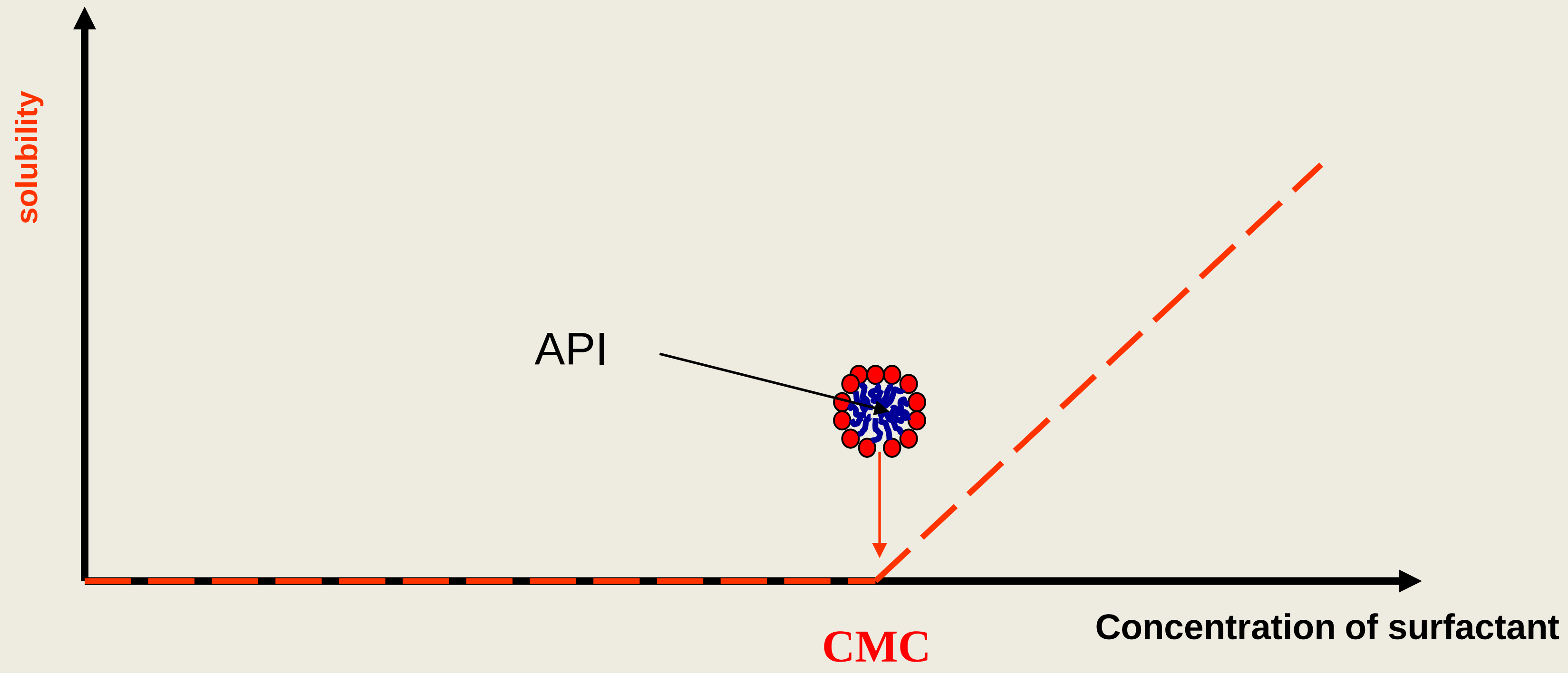
Surfactants

Structures, what can be formed by surfactants



Surfactants

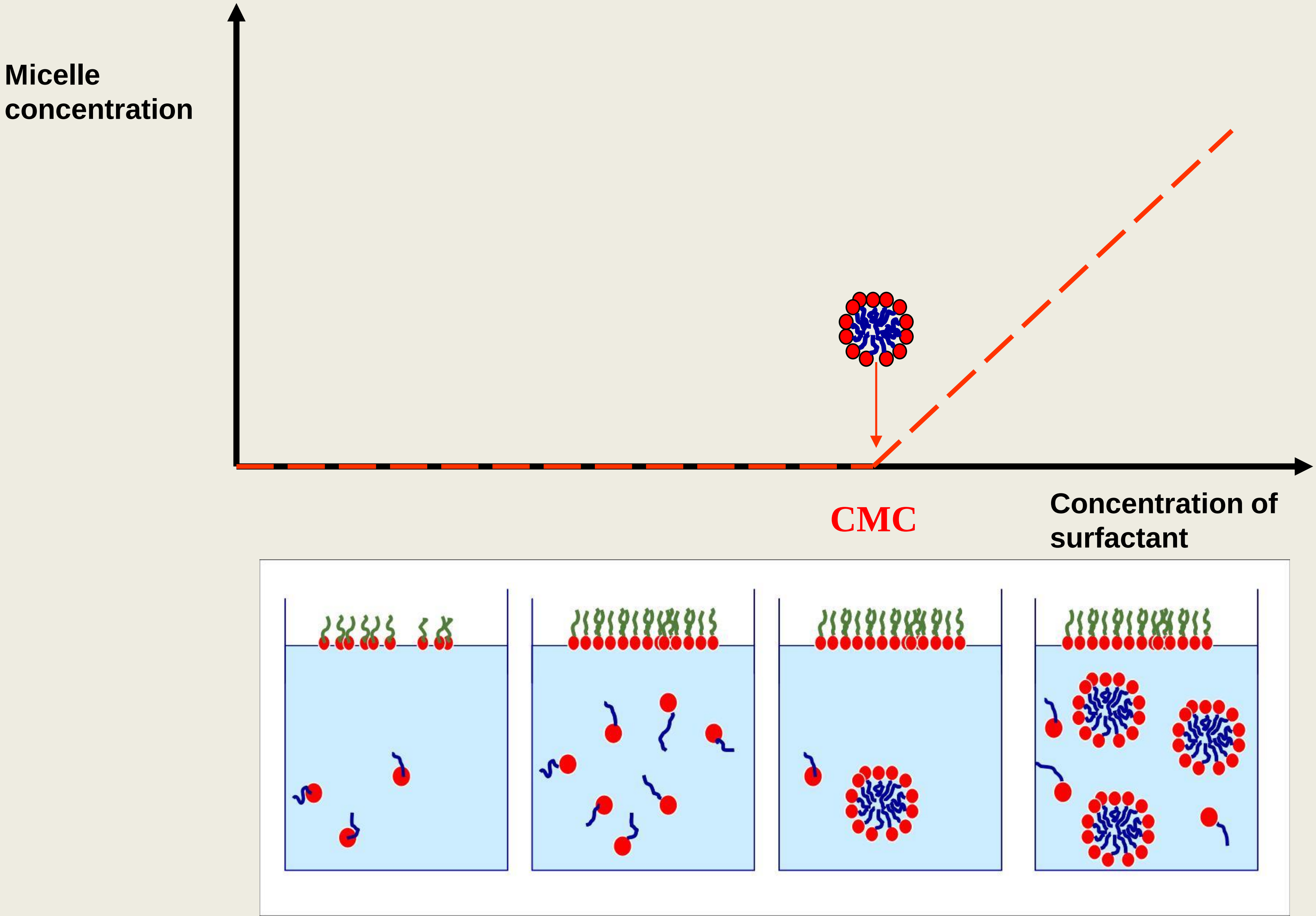
solubilization



The solubility (and so the bioavailability) of poorly soluble APIs can be increased by the application of the proper amount of surfactant to form micelles.
(Those systems, where the diameter of the micelles is not more than the size of the molecules from what are built up the micelles, are called solubilizated solution.)

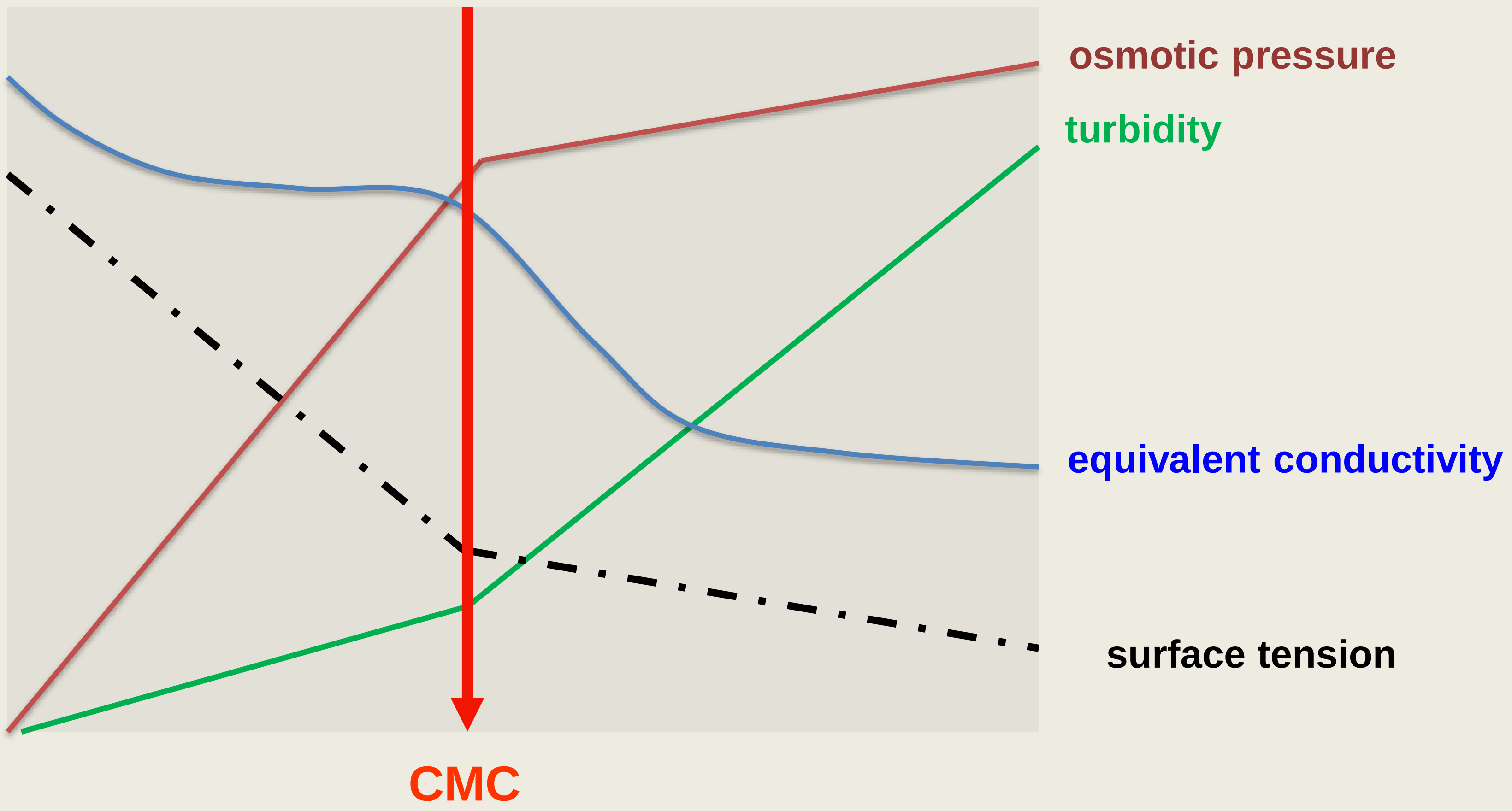
Surfactants

Critical micelle concentration



Surfactants

Determination od critical micelle concentration



Surfactants' classification

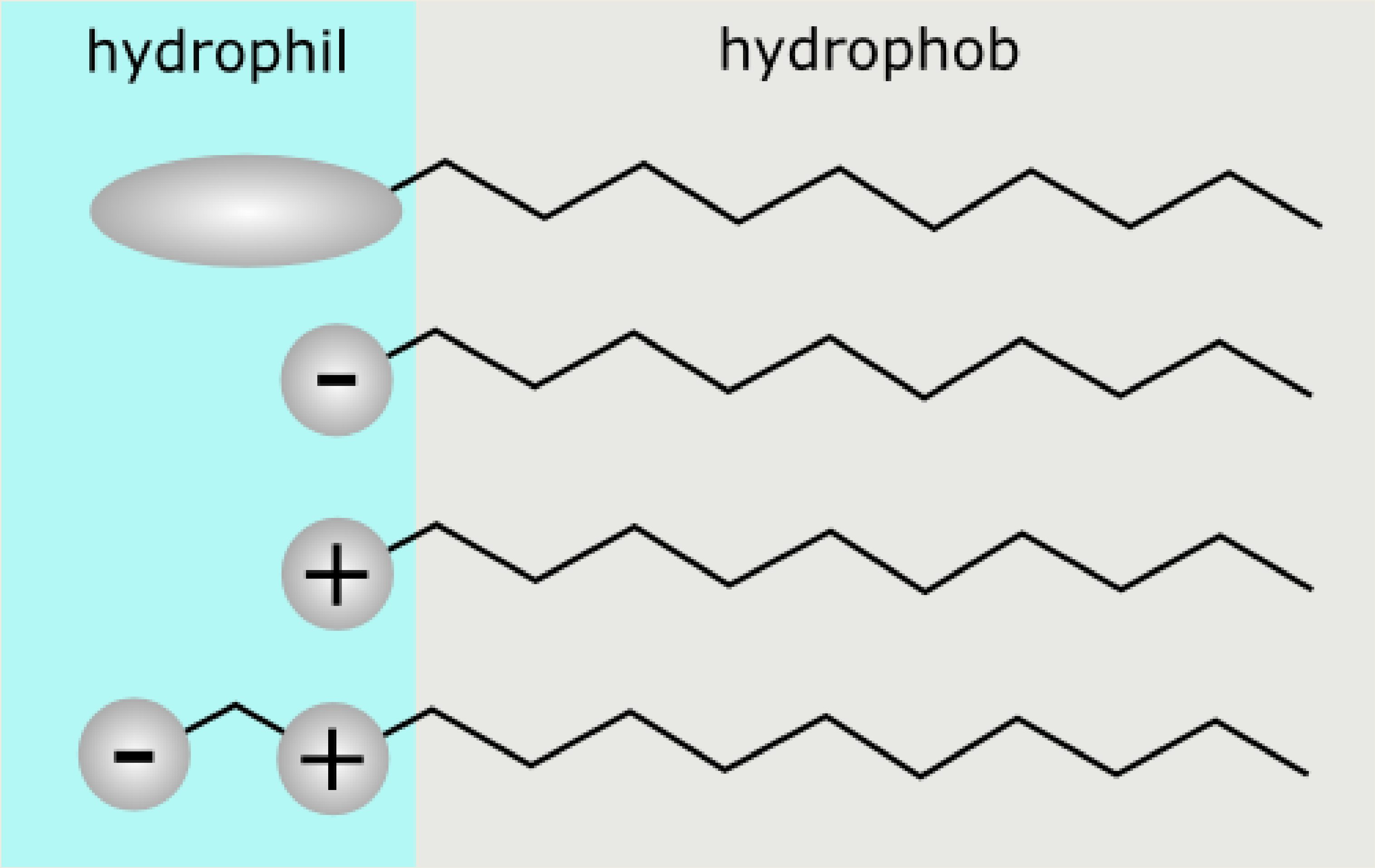
according to their origin

- natural
- synthetic

according to their structure

- non-ionic
- ionic
    - cationoc
    - anionic
    - amphoteric

Surfactants' classification according to the structure



Surfactants

Surfactants with natural origin

Vegetable origin, carbohydrate polymer derivatives:

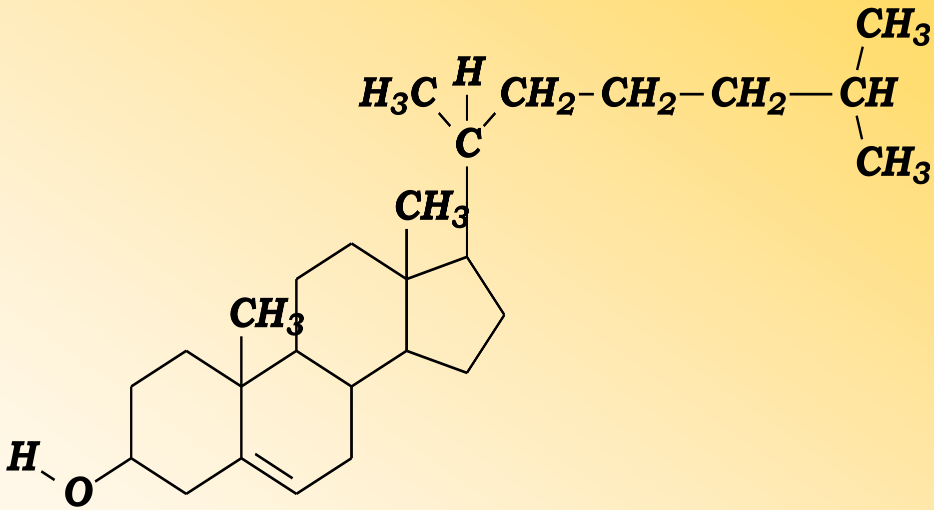
Acacia, tragacantha, agar-agar, pectin

proteins:

gelatin, casein, o / w emulsion

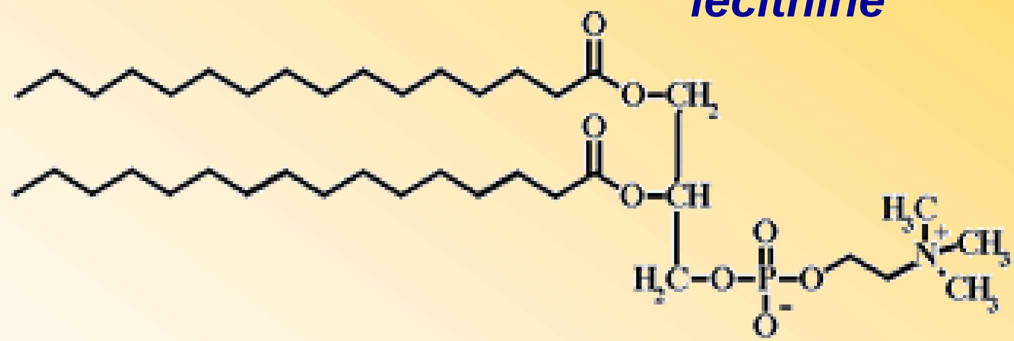
high molecular weight alcohols:

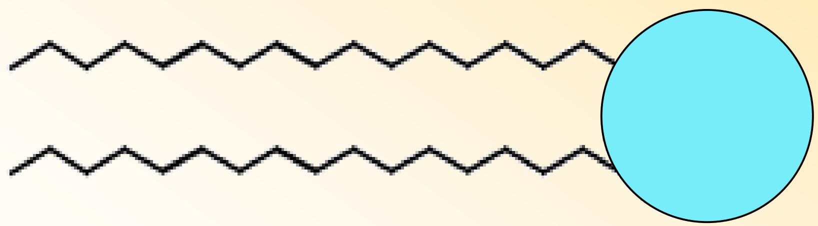
stearyl alcohol, cetyl alcohol, cholesterol



cholesterol

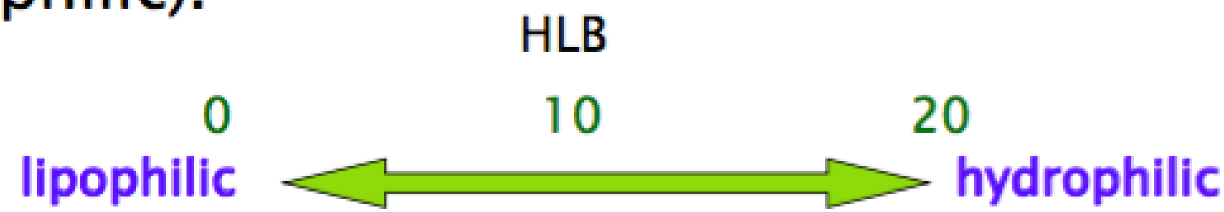
lecithine





Hydrophile-lipophile balance (HLB)

- Hydrophile-lipophile balance：surfactants contain both hydrophilic groups and lipophilic groups with one or the other being more predominant, the hydrophile-lipophile balance (HLB) number is used as a measure of the ratio of these groups. It is a value between 0-40 defining the affinity of a surfactant for water or oil. HLB value of nonionic surfactants ranges from 0-20. HLB numbers >10 have an affinity for water (hydrophilic) and number <10 have an affinity of oil (lipophilic).



Calculation of HLB value by Griffin's method (1949)

$$\mathrm{HLB} = \frac{M_{\mathrm{h}}}{M} \times 20$$

M_h – molecular mass inside the molecule of the hydrophylic part

M – molecular mass of the total molecule

Surfactants

Calculation of HLB

Emulsifier parts

$$HLB = \frac{A * HLB_{\alpha} + (100 - A) * HLB_{\beta}}{100}$$

HLB_{α} , HLB_{β}	**HLB value of emulsifier α** and **emulsifier β**
A	**the ratio of emulsifier α**

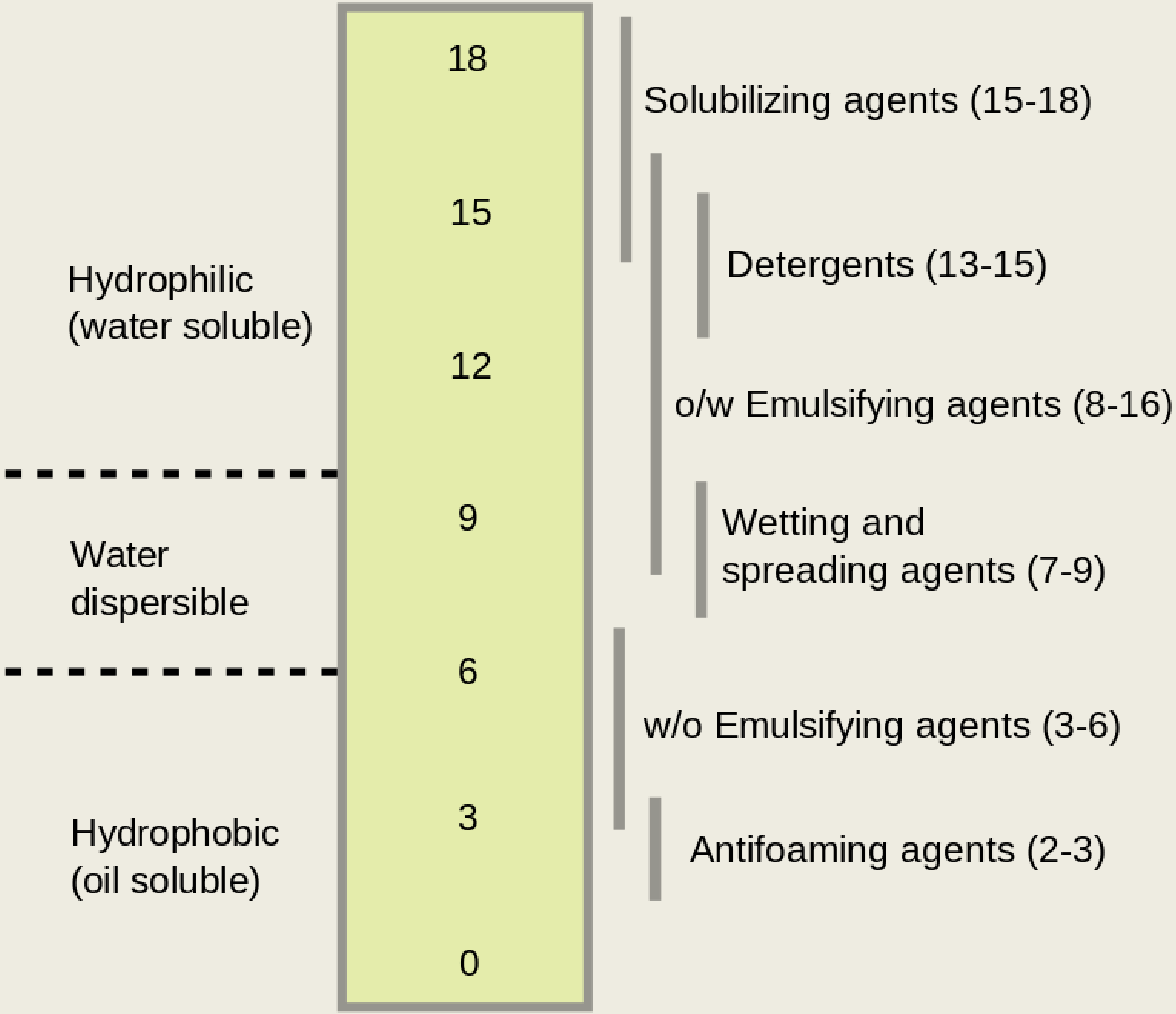
Surfactants

It is an arbitrary scale between 0 and 20 which expresses numerically the size and **strength of the polar portion relative to the non-polar portion of the molecule**.

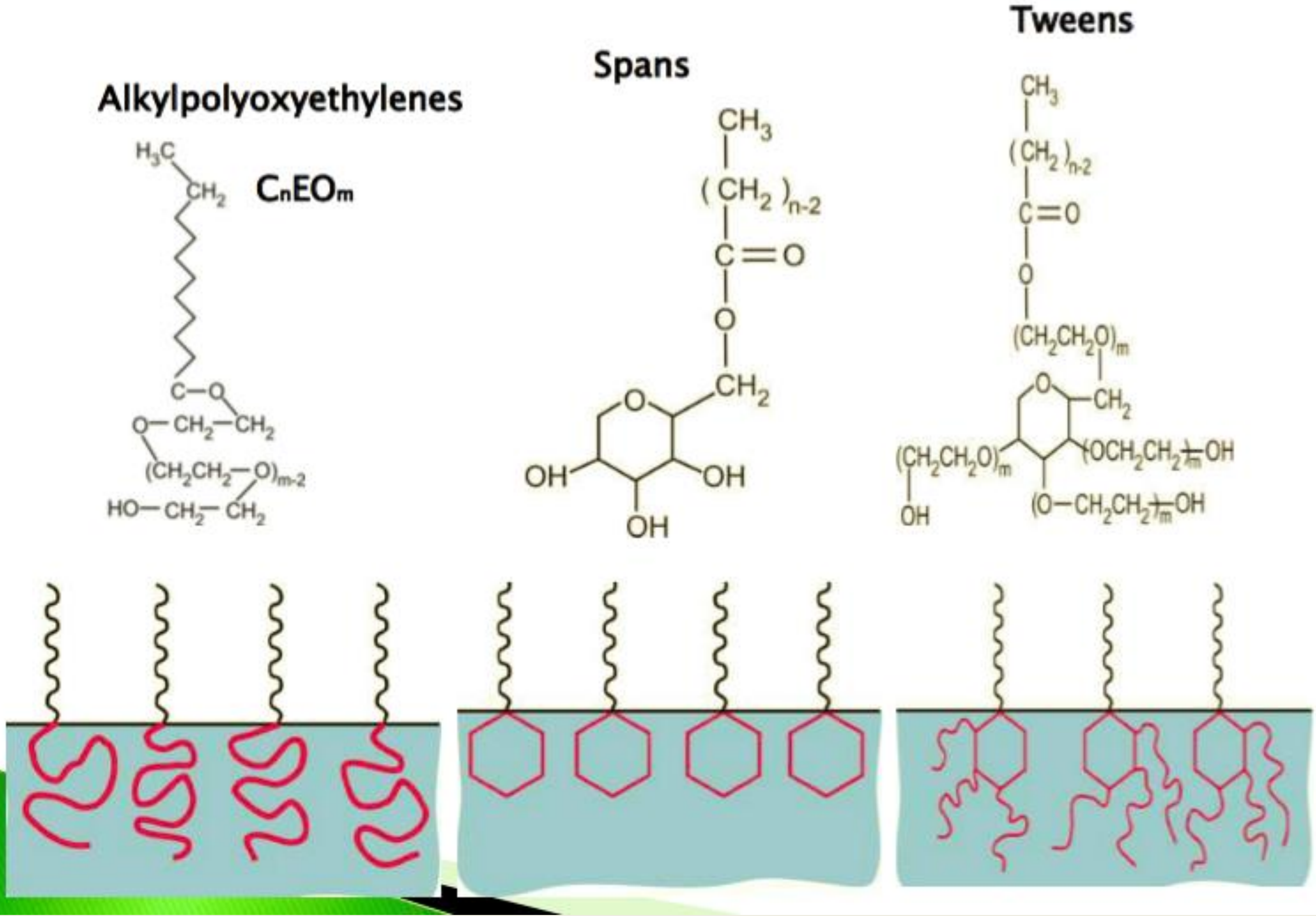
Although originally applied to non-ionic surfactants, its use has now been extended to ionic surfactants (HLB for ionic surfactants are much higher, up to 50, based on the ionization properties.

HLB	application
1-3,5	anti-foaming agents
3,5-8	w/o emulgents
7-9	wetting agents
8-16	o/w emulsifiers
13-16	detergents
15-40	solubilizing agents

Application of surfactants


18
15
12
9
6
3
0
Hydrophilic
(water soluble)
Water
dispersible
Hydrophobic
(oil soluble)
Solubilizing agents (15-18)
Detergents (13-15)
o/w Emulsifying agents (8-16)
Wetting and
spreading agents (7-9)
w/o Emulsifying agents (3-6)
Antifoaming agents (2-3)

1.Nonionic surfactants



Non-ionic surfactants

Brij

Fatty-acid ethers of polyethylenglycols

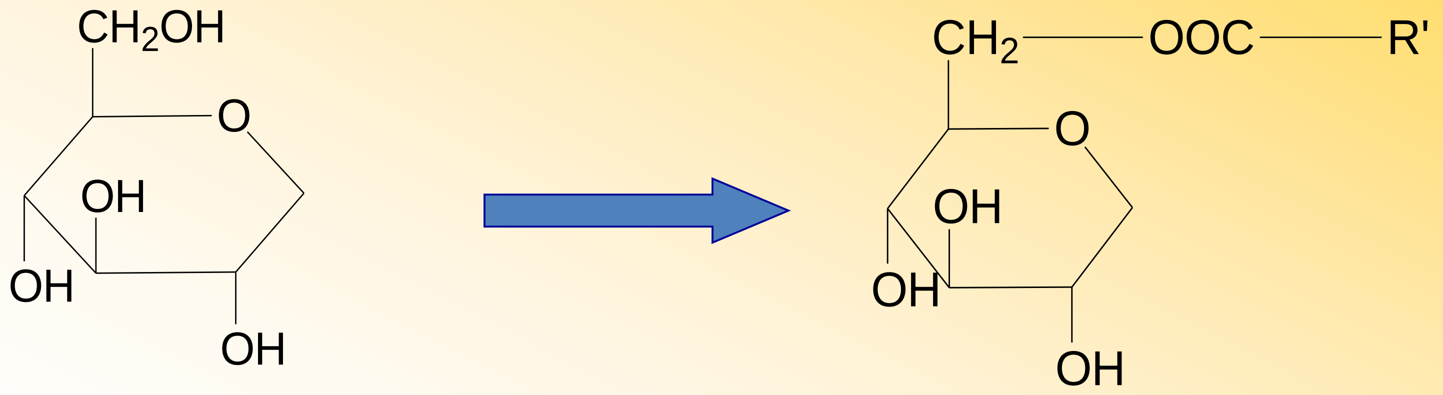
Brij	composition	HLB
30	PEG (4) lauryl ether	9,7
35	PEG (23) lauryl ether	16,9
52	PEG (2)cethyl ether	5,3
58	PEG (20)cethyl ether	15,7
72	PEG (2) stearyl ether	4,9
78	PEG (20)cethyl ether	15,3

Non-ionic surfactants

Span

Fatty acid aesther of sorbitans

The hydrophylcicity of the Spans can be increased by hydrophyl groups (–OH or –CH_2-O-CH_2-O-). (These groups can bound water molecules)



1,5- sorbitan

Non-ionic surfactants

Span	Chemical name	HLB
20	sorbitan monolaurate	8,6
40	sorbitan monopalmitate	6,7
60	sorbitan monostearate	4,7
65	sorbitan tristearate	2,1
80	sorbitan monooleate	4,3
85	sorbitan trioleate	1,8

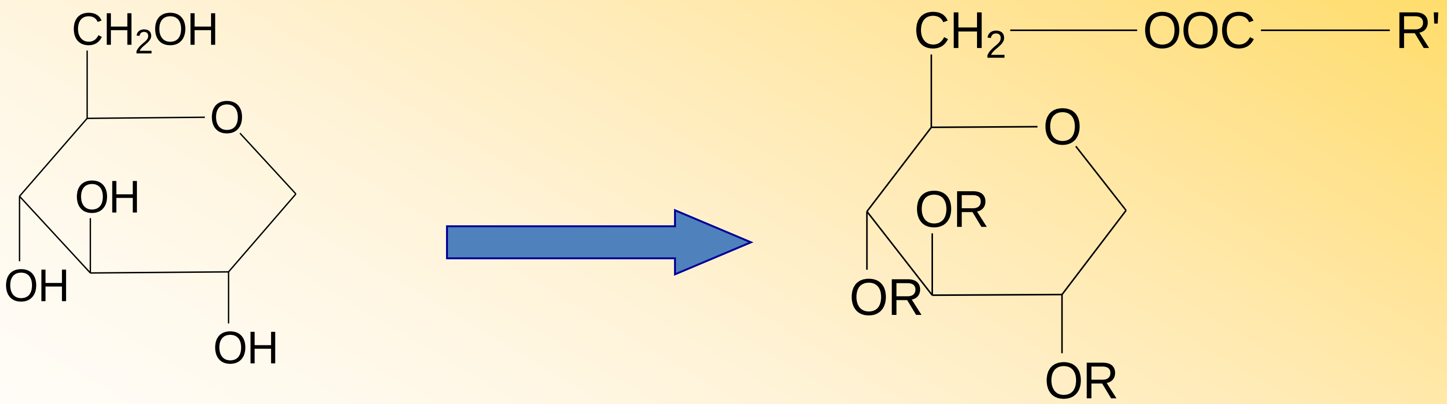
Non-ionic surfactants

Tween

Fatty acid aesthers and polyoxethylen ethers of sorbitan

PEG derivatives of Spans

(the combination of Spans with Tweens can increase the emulsifying effect.



1,5- sorbitan

R=-(CH_2-O-CH_2)-CH_2O

Non-ionic surfactants

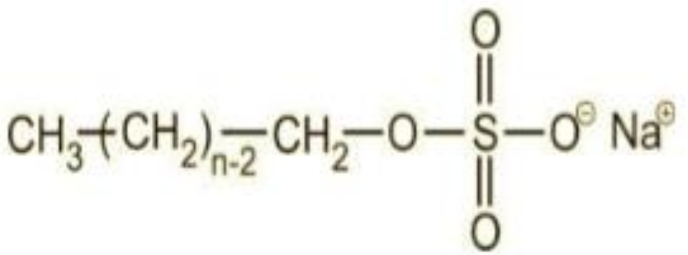
Tween	chemical name	HLB
20	PEG(20) sorbitan monolaurate	**16,7**
40	PEG(20)sorbitan monopalmitate	**15,6**
60	PEG(20)sorbitan monostearate	**14,9**
80	PEG(20)sorbitan monolaurate	**15,0**
85	PEG(20)sorbitan trioleate	**11,0**

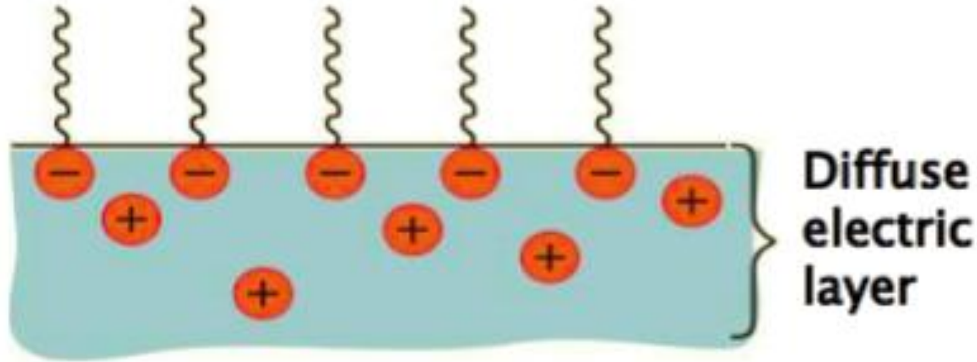
✓Spans are sorbitan fatty acid esters having low HLB values ranging from 1.8 to 8.6.

✓Tweens are polyoxyethylene derivatives of spans. So, they are more hydrophilic having higher HLB values ranging from 9.6 to 16.7.

2.Ionic surfactants

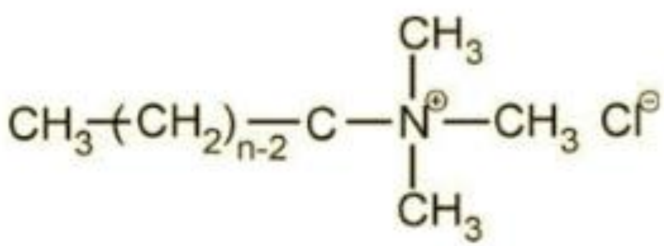
(a) Anionic

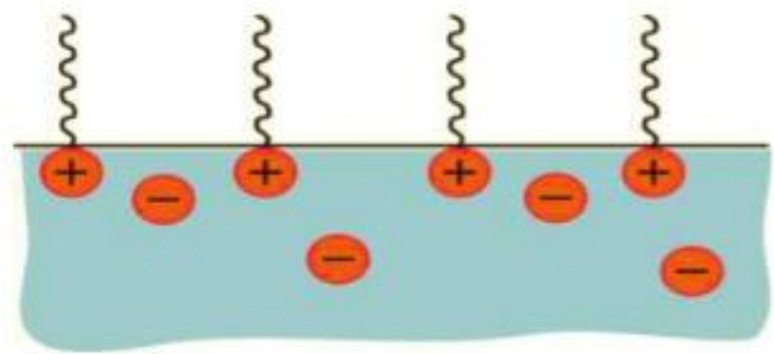




sodium dodecyl sulfate

(b) Cationic





dodecyl trimethyl ammonium chloride

Ionic surfactants

anionic

- alkali metal salts of fatty acids (soaps)

- salts of sulfuric acid esters, sodium-lauryl-sulphate, sulfonates

$$CH_3(CH_2)_{10}CH_2OSO_3Na$$

sodium-lauryl-sulphate

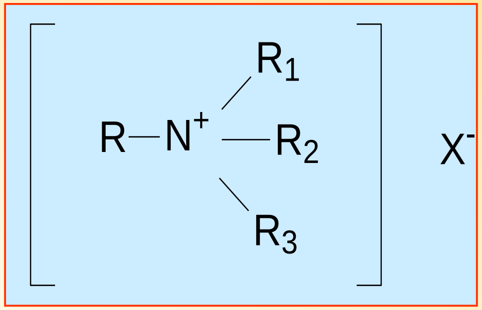
Ionic surfactants

cationic

In these molecules, the Nitrogen or nitrogen containing molecules have a huge importance.

The four hydrogen of the ammonium ion can be substituated by alkil or aril groups (radicals). These structures are called **quaternary ammonium-basis** whom salts are the quaterner ammonium-salts or invert soaps.

Their stucture:



$R_1=R_2=CH_3$

$R_3=CH_3$ or $CH_2C_6H_5$

R= carbon chain (C_{12}-C_{18})

Ionic surfactants

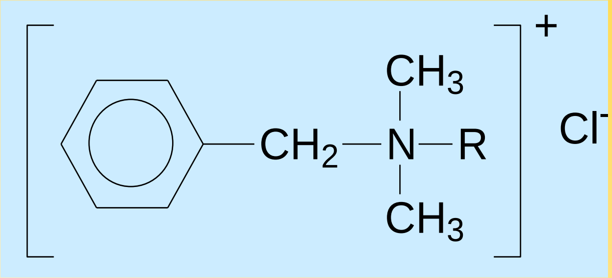
cationic

- *cetavlon: -alkyl trimethyl-ammonium-salts*
- *sapamin: trimetihy-acylamydoalkyl-ammonium -salts*
- *zephirol : -alkyl dimethyl-benzyl-ammonium –salts*
- *sterogenol : the nitrogen is in aromatic ring*
  and to this nitrogen connects a long carbon chain too (Nitrogenol).

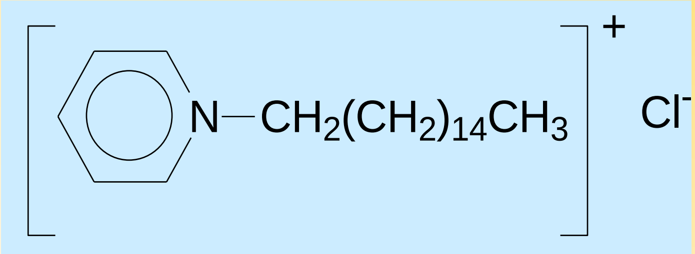
Ionic surfactants

cationic

Benzalkonium chloratum (Zephirol),



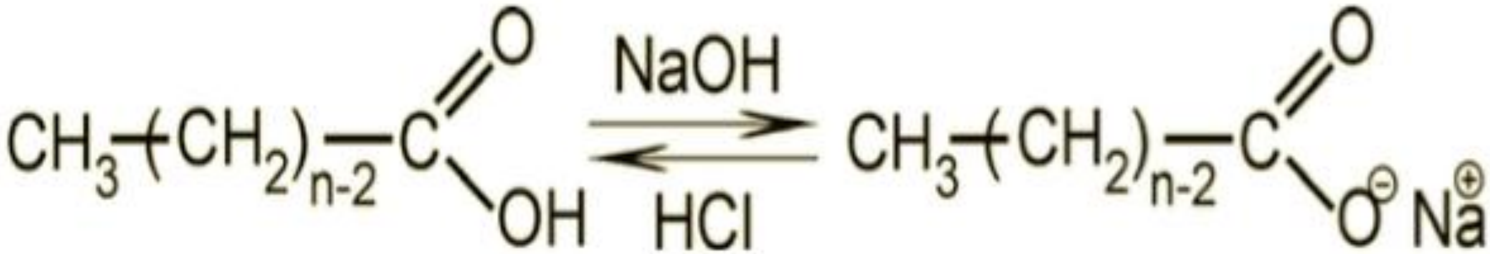
Cetylpyridinium chloratum

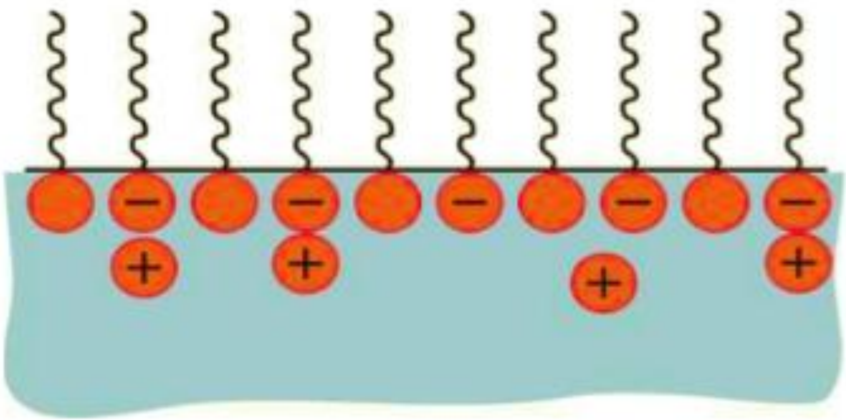


The ionic surfactants can only be applied for external use.

3. Amphoteric surfactants

(a) Natural soaps (alkylcarboxylates), Lipids





Amphoteric surfactants

The amphoteric surfactants may be anionic or cationic according to the pH of the medium.

low pH → cationic

high pH → anionic

Lecithin

stabilizator of the i.v. oil emulsions (for nutrition)
it can build up the walls of the liposomes

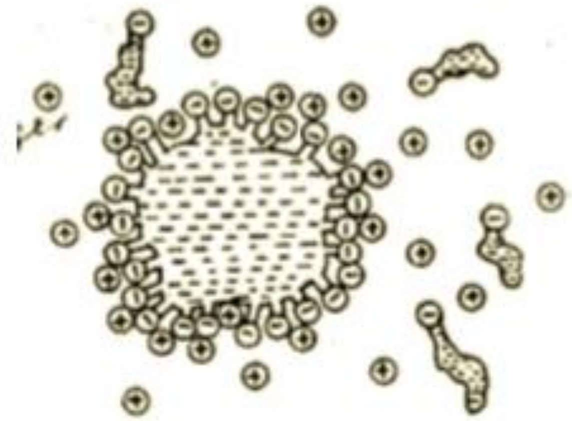
HLB values of ointment's substances

Ointment substance	Type of emulsion	
	o/w	w/o
Cethyl alcohol	15	-
Stearyl alcohol	14	-
Stearic acid	15	-
Lanoline	10	8
Cottonseed Oil	10	5
Beeswax	12	4

Micellar Structure and Shape

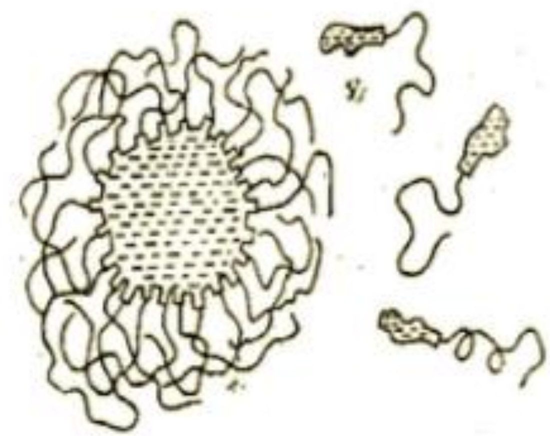
(a) Ionics

- inner core – liquid phase hydrocarbon
- Shell
- diffuse electric double layer



(b) Nonionics

- inner core – liquid phase hydrocarbon
- Shell



Pharmaceutical requirements of a proper surfactant

- promotes and helps to maintain the emulsification
- compatible
- stabile
- non-toxic
- compliant taste, smell and color

Required HLB values

Oil	O/W emulsion	W/O emulsion
Stearic acid	15	6
Cetyl alcohol	15	-------------
Stearyl alcohol	14	-------------
Lanolin, anhydrous	12	8
Mineral oil, light	12	4
Liquid paraffin	10.5	4
Castor oil	14	-------------
Beeswax	9	5
Petrolatum	7-8	4
Wool fat	10	8

Calculation of the required HLB for a mixture of oils, fats or waxes

1. Multiply the required HLB of each ingredient by its fraction from the total oily phase.
2. Add the obtained values to get the total required HLB for the whole oily phase.

Example:

- Liquid paraffin 35%
- Wool fat 1%
- Cetyl alcohol 1%
- Emulsifier system 7%
- Water to 100%

Solution

The total percentage of the oily phase is 37% and the proportion of each is:

Liquid paraffin 35/37 x 100 = 94.6%

Wool fat 1/37 x 100 = 2.7%

Cetyl alcohol 1/37 x 100 = 2.7%

The total required HLB number is obtained as follows:

Liquid paraffin (HLB 10.5) 94.6/100 X 10.5 = 9.93

Wool fat (HLB 10) 2.7/100 x 10 = 0.3

Cetyl alcohol (HLB 15) 2.7/100 X 15 = 0.4

Total required HLB = 10.63

Thank you for your attention!