

MUNI
PHARM

Interfacial Phenomena I

Physical chemistry

Basic concepts

Phase – a homogeneous part of a heterogeneous system separated from other phases by the phase interface (the system's properties are step-changed to the phase interface).

The properties of the phase interface are influenced by the properties of the two interconnecting phases.

Phase interfaces are divided according to the state of the matter of the phases in contact:

- **interface liquid/gas (l/g)**
 - **interface liquid /liquid (l/l)**
 - **interface solid/gas (s/g)**
 - **interface solid /liquid (s/l)**
 - **interface solid /solid (s/s)**
- } **mobile interfaces**

Phase interfaces liquid/gas and solid/gas are known as **surfaces**.

Phase interface from a molecular perspective

The **phase interface size determines the effect of the phase interface on the system properties** (i.e. ratio of the number of molecules at the interface to the number of molecules in the bulk phase).

Large specific surface are common in:

- Heterogeneous colloidal dispersion systems (particle size 1 nm - 1 μm)
- Microporous solid substances

Interface phenomena:

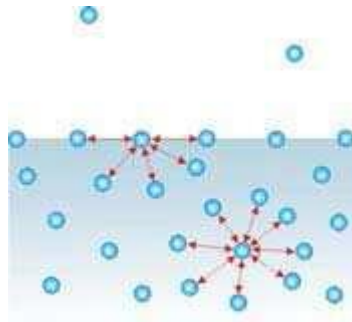
- Surface tension
- Spreading and wetting (capillary phenomena)
- The stability of dispersion systems
- Adsorption
- Micelles and cell membrane formation

These phenomena are influenced by forces that originate in **interatomic or intermolecular interactions.**

Phase interface gas-liquid

Interactions between molecules different from interactions in the phases take place on the phase interfaces – difference most obvious in the case of pure interface liquid / vapor – **surface tension**

$$\sigma = F / \ell \quad [\text{N.m}^{-1}]$$



Surface tension is the force acting in the plane of the liquid surface. It causes the liquid to try to reduce its surface area – **spherical shape** (droplet formation).

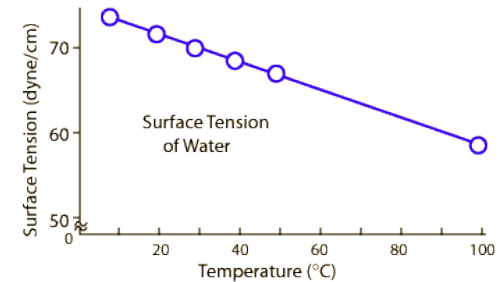
When the surface of the fluid increases, some molecules have to get from the inside to the surface – work needs to be done, so called **surface energy**.

$$\gamma = dW / dS \quad [\text{J.m}^{-2} = \text{N.m.m}^{-2} = \text{N.m}^{-1}]$$

Phase interface gas-liquid

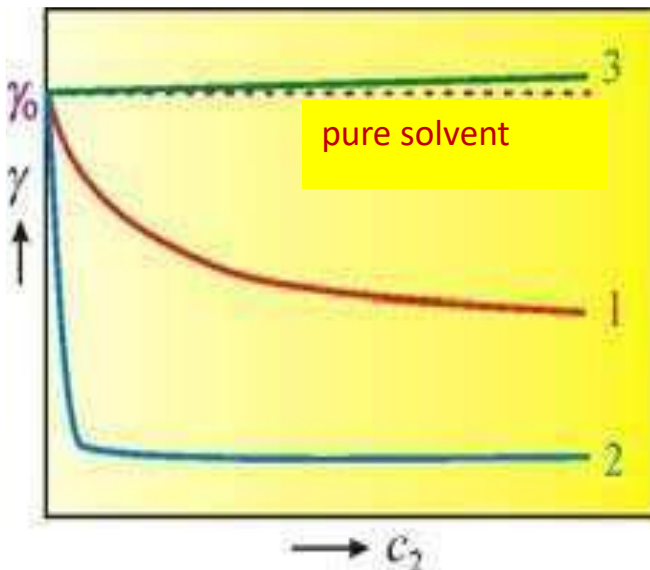
The surface tension depends on the **temperature**:

- with increasing temperature the surface tension always decreases.



The surface tension of solutions:

- varies with concentration and type of added compounds



1 – simple organic compounds

2 – surfactants

3 – inorganic electrolytes (increase surface tension)

dash line - no effect on surface tension (e.g. sugar solutions in water)

Phase interface gas-liquid

Practical consequences of surface tension

Surface tension is responsible for the formation of droplets. The **droplet size** depends on the size of surface tension and hence on the liquid used.

Example:

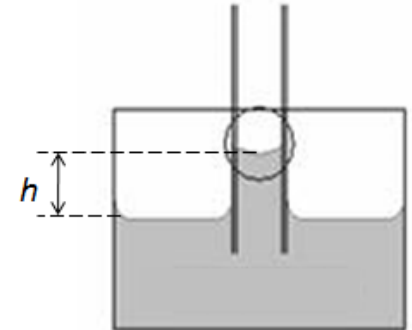
If we have two medicinal products (e.g. solutions) with the same content of active substance and different content of solvent (e.g. ethanol), **we have to dispense a different number of drops to achieve the same dose** of active substance.



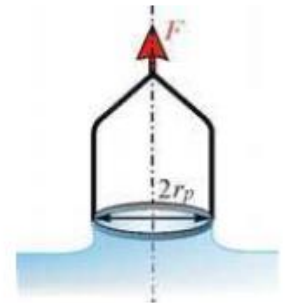
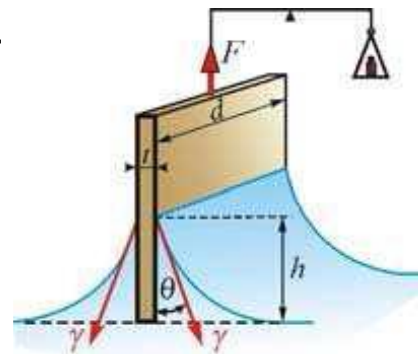
Methods for measuring surface tension

Static methods – monitoring the steady state of equilibrium

- The method of capillary elevation $\frac{\sigma_1}{\sigma_2} = \frac{\rho_1 \times h_1}{\rho_2 \times h_2}$



- Wilhelmy plate method: $F = 2d \sigma$
- Du Noüy Ring method: $F = 4\pi r \sigma$

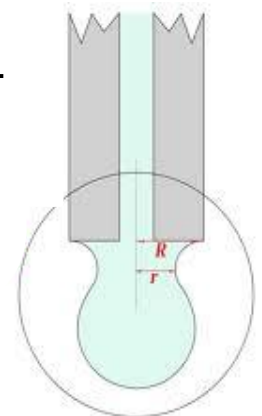


Semi-static methods – achieved equilibrium is unstable

- Method of weighting a drop of liquid (stalagmometry): $mg = 2\pi r \sigma$

$$\frac{m_1}{\sigma_1} = \frac{m_2}{\sigma_2}$$

$$\sigma = \sigma_{H_2O} \times \frac{m}{m_{H_2O}}$$



Heterogeneous dispersion

Classification of heterogeneous systems:

L	L	emulsion
S	L	suspension
G	L	foam
S/L	G	aerosols (dust / fog)
G/L/S	S	solid foam / gel / mixture

The phase interface size determines the total effect on the system properties:

Colloidal dispersion 1-1000 nm

Coarse dispersion $> 1 \mu\text{m}$

Large interface energy = these systems need to be **stabilized**.

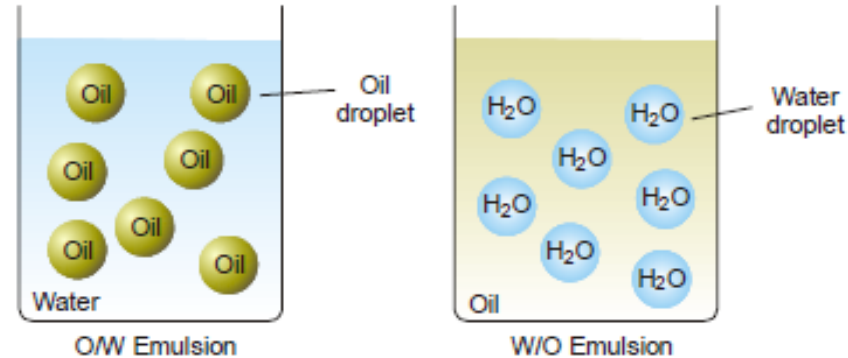
Phase interface liquid-liquid

Emulsions: are formed by dispersion medium and dispersed substance.

The systems of immiscible or limited miscible liquids.

Types of emulsions: a) **oil in water** (O/W)

b) **water in oil** (W/O)



Applications in pharmacy – creams (O/W, W/O)

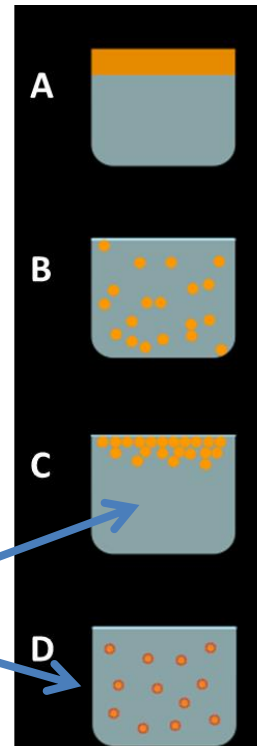
– injections, infusions (O/W)

– ointments (W/O)

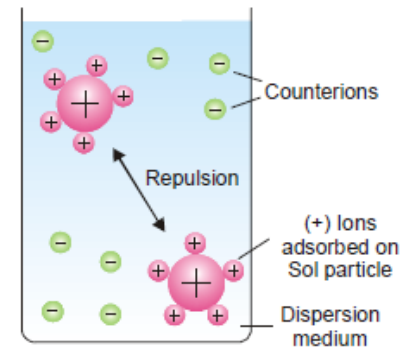
Emulsions may be unstable, their stability must be ensured in an appropriate way.

Coalescence (aggregation of particles or droplets)

Stabilization of the suspension by addition of surfactant (reduction of surface tension)



Phase interface liquid-liquid



Stabilization of emulsions:

1. Electrical double-layer

Repulsive forces between charged droplets prevent coalescence (in diluted emulsions).

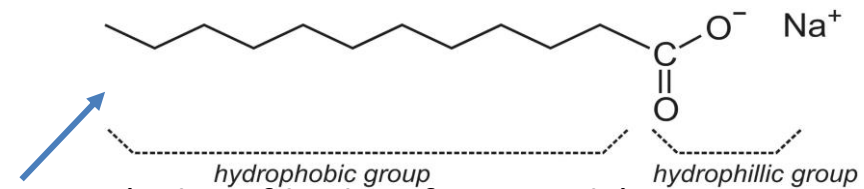
2. Surfactants (emulsifiers)

Types: a) associative (micellar) colloids – soaps (salts of higher fatty acids)

b) macromolecular colloids – hydrophilic (gelatin, dextrans)

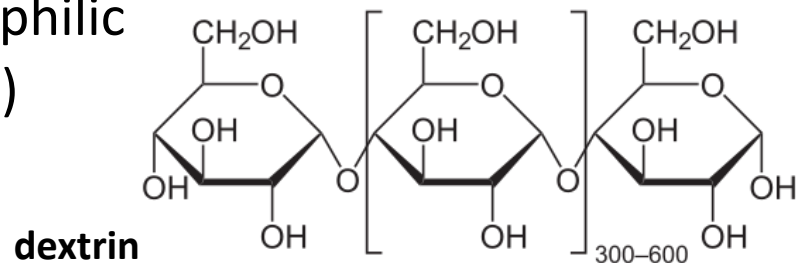
– hydrophobic (rubber, cellulose trinitrate)

c) powders (colloidal SiO_2 , aluminosilicates)



Another division a) ionic surfactants: anionic, cationic, ampholytic

b) non-ionic surfactants: no charge, solubility is due to the presence of hydrophilic groups (eg. $-\text{OH}$, $-\text{NH}_2$)



Phase interface liquid-liquid

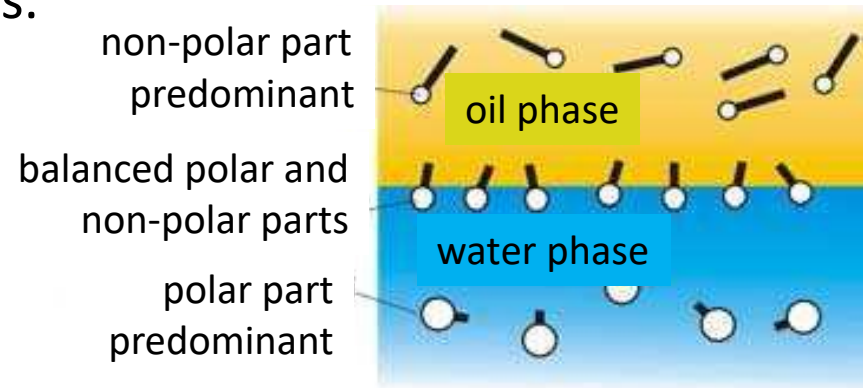
The emulsifying effect

Balanced polar and non-polar part of the molecule (determined by the length of the hydrocarbon chains and by affinity of polar groups to water).

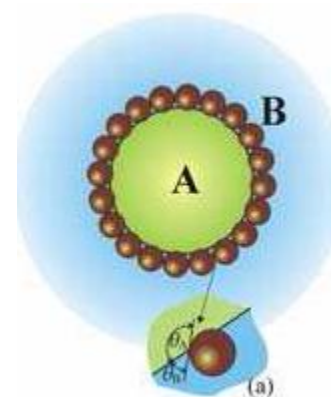
HLB (hydrophilic-lipophilic balance) - characterizes the relationship between hydrophilic and lipophilic parts.

↓HLB = **hydrophobic surfactants**,
well stabilized emulsion W / O

↑HLB = **hydrophilic surfactants**,
well stabilized emulsion O / W



Powder emulsifiers - partially wetted by both phases; particle size is important (large particles sediment, small particles leave the interface due to thermal motion).



Phase interface solid-liquid

Suspension

At least two phases, an internal (dispersed) phase is solid; outer dispersed phase is liquid.

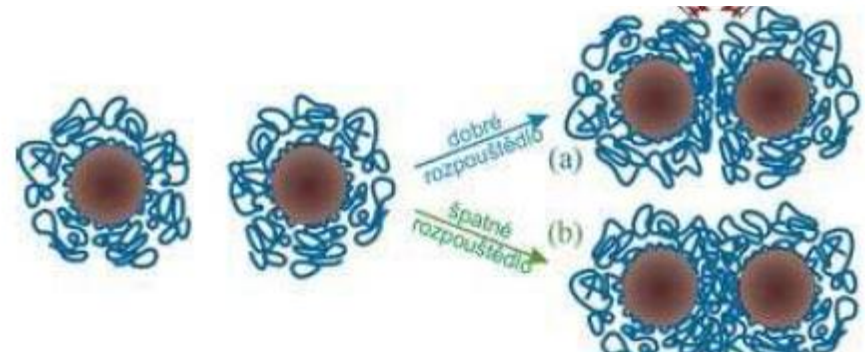
Stabilization of suspension:

1. **Aggregation** (colloidal dispersion 1-1000 nm)

a) **Electrostatic stabilization** – repulsion of particles with the same charge.

b) **Steric stabilization** – addition of a substance which is adsorbed on the particle surface, but also is soluble in the dispersion medium (surfactants, macromolecules).

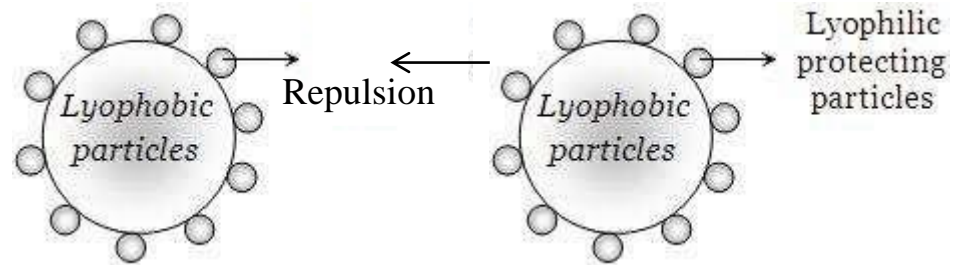
good affinity of the added substance to the solvent - stabilization



bad affinity of the added substance to the solvent - aggregation

Phase interface solid-liquid

c) **Electrosteric stabilization** – addition of **lyophilic colloid** (stable colloid solution) to **lyophobic colloid** (unstable colloid solution), at least one is electrically charged.



d) **Stabilization by solid particles**

2. **Sedimentation** (coarse dispersion > 1 μm)

a) **Sedimentation rate** (Stokes equation):

$$v = \frac{2 r^2 (\rho_1 - \rho_2) g}{9 \eta}$$

r..... radius of particle

ρ_1, ρ_2 ... density of inner and outer phase

η viscosity of outer phase

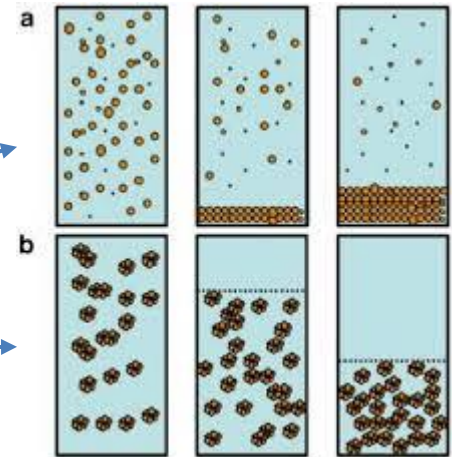
g..... gravitational acceleration



Phase interface solid-liquid-gas

b) **Surface wettability** – influences redispersion of sediment by shaking and aggregate state of suspended drug:

- **non-flocculated** suspension
- **flocculated** suspension
- **flotated** suspension



Suspension	Wettability	Sediment shakeability	Pharmaceutical applicability
non-flocculated	perfect	not easy (caking)	mainly parenteral application
flocculated	good	not problematic	most of the medicinal suspension
flotated	bad	-	no

Influence of wettability

- Addition of a surfactant (steric stabilization).
- Addition of electrolyte increases flocculation of suspensions (suppression of electrostatic stabilization).