Emulsion Overview

What is an emulsion?
- An emulsion is a mixture of two immiscible (unblendable) substances.
- One substance (the dispersed phase) is dispersed in the other (the continuous phase).

Example: Oil in water emulsion (O/W)
- Oil: Dispersed phase (discontinuous, inner, internal phase)
- Water: Continuous phase (outer, external phase)

Emulsion Overview

Some common type two-phase systems

<table>
<thead>
<tr>
<th>Continuous phase</th>
<th>Disperse phase</th>
<th>System</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gas</td>
<td>Solid</td>
<td>Smoke</td>
</tr>
<tr>
<td>Liquid</td>
<td>Gas</td>
<td>Foam</td>
</tr>
<tr>
<td>Liquid</td>
<td>Solid</td>
<td>Dispersion</td>
</tr>
<tr>
<td>Liquid</td>
<td>Liquid</td>
<td>Emulsion</td>
</tr>
<tr>
<td>Solid</td>
<td>Gas</td>
<td>Foam</td>
</tr>
</tbody>
</table>

Emulsification
- Emulsification is the process by which emulsions are prepared
- Emulsions are thermodynamically unstable systems because the contact between oil and water molecules is unfavorable, and so they will always breakdown over time.
Emulsion Overview

Emulsification

- The preparation of emulsions that are kinetically stable over a time period that is of practical use to the cosmetic industry requires the incorporation of substances known as stabilizers.
- Stabilizers can be classified according to their mode of operation as either:
  - Emulsifiers
  - Texture modifiers

Emulsifiers

- An emulsifier is a surface-active substance that, when present at low concentration in a system, has the properties of:
  - adsorbing on to the surfaces of interfaces of the system
  - altering to a marked degree the surface or interfacial free energies of the surfaces (or interfaces).
- Examples: phospholipids, small molecule surfactants and solid particles.

Texture modifiers

- A texture modifier is a substance that either increases the viscosity of the continuous phase (thickening agent) or forms a gel network within the continuous phase (gelling agent).
- The texture modifiers help slowing down the movement of droplets due to gravity or Brownian motion.

- Most of the texture modifiers form hydrated lyophilic colloids (called hydrocolloids) that form multimolecular layers around emulsion droplets.

Texture modifiers may be classified as:

- Vegetable derivatives, e.g., acacia, tragacanth, agar, pectin, carrageenan, lecithin.
- Animal derivatives, e.g., gelatin, lanolin, cholesterol
- Semi-synthetic agents, e.g., methylcellulose, carboxymethylcellulose
- Synthetic agents, e.g., Carbopols®
Surface-Active Agents

- Interface - a boundary between any two immiscible phases.
- Surface - an interface where one phase is a gas, usually an air.
- Interfacial free energy - the minimum amount of work required to create the interface.
- The interfacial free energy per unit area - what we measure when we determine the interfacial tension between two phases → surface (interfacial) tension.

Emulsification by Surface-Active Agents

- Surface (interfacial) tension is the minimum amount of work required to create unit area of the interface or to expand it by unit area.
- Surface (interfacial) tension is also a measure of the difference in nature of the two phases meeting at the interface (or surface).
- The greater the dissimilarity in their nature, the greater the surface (or interfacial) tension between them.

- Surface tension of liquid - a measure of the interfacial free energy per unit area of the boundary between the liquid and the air above it.
- When we expand an interface, therefore, the minimum work ($W_{min}$) required to create the additional amount of that interface is the product of the interfacial tension ($\gamma$) and the increase in area of the interface ($\Delta A$):

$$W_{min} = \gamma \times \Delta A$$

- A surface-active agent is, therefore, a substance that at low concentration adsorbs at some or all of the interface in the system and significantly changes the amount of work required to expand these interfaces.
- To reduce the interfacial tension & thereby promote droplet formation (the free energy increase of forming new surface is directly proportional to the interfacial tension)
- To stabilize emulsion droplets from flocculation & coalescence
Emulsification by Surface-Active Agents

General Structural features and Behavior of Surface Active Agents: Amphipathic structure

- A lyophobic group: very little attraction to the solvent
- A lyophillic group: strong attraction to the solvent.

Surface-active agent dissolves in water solvent, the lyophobic (hydrophobic) group distorts the structure of water (by breaking hydrogen bonds between the water molecules and by structuring the water in the vicinity of the hydrophobic group), resulting in, some of the surface-active agents are expelled to the interfaces of the system, with their hydrophobic group oriented so as to minimize contact with water molecules.

The surface of the water molecule become covered with a single layer of the surface-active agent molecules with their hydrophobic groups oriented predominantly to the air.

Air is nonpolar in nature, same as hydrophobic group-decrease in the dissimilarity of the two phases contacting each other at the surface resulting in a decrease in surface tension of the water.

Critical Micelle Concentration
Emulsification by Surface-Active Agents

• Surfactants as Emulsifying Agents
• Regardless of their classification, all emulsifying agents must be:
  - Chemically stable in the system,
  - Inert and chemically non-reactive with other emulsion components,
  - Nontoxic and nonirritant
  - Reasonably odorless and not cost prohibitive

Emulsification by Surface-Active Agents

Criteria for Surfactant Selection
• Hydrophilic surfactant ➞ O/W emulsion
• Lipophilic surfactant ➞ W/O emulsion
• Compatibility
• Give stable emulsion at low concentration
• Use combination of surfactant

Emulsification by Surface-Active Agents

General Structural features and Behavior of Surface Active Agents: Amphipathic structure
• In a highly polar solvent such as water:
  - Lyophobic (hydrophobic) group may be hydrocarbon, fluorocarbon, siloxane chain.
  - Lyophilic (hydrophilic) group may be ionic or highly polar groups.

Emulsification by Surface-Active Agents

• An emulsifier is a type of surfactant typically used to keep emulsion (mixtures of immiscible fluids) well dispersed.
• Surfactants typically have a hydrophobic (water-hating) and a hydrophilic (water-liking) end.

Emulsification by Surface-Active Agents

• Surfactants are classified as

<table>
<thead>
<tr>
<th>Class</th>
<th>Example</th>
<th>Charge</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anionic</td>
<td>Soap: RCOONa⁺ (e.g., Sodium stearate)</td>
<td>Negative</td>
</tr>
<tr>
<td></td>
<td>Alkylbenzene sulfonate: RC₆H₄SO₃Na⁻</td>
<td>Negative</td>
</tr>
<tr>
<td>Cationic</td>
<td>Salt of a long-chain amine: RNH₃⁺</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td>Quaternary ammonium chloride: RN(CH₃)₃Cl⁻</td>
<td>Positive</td>
</tr>
<tr>
<td>Nonionic</td>
<td>Monoglyceride of long-chain fatty acid: RCOOCH₂CHOHCH₂OH</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Polyoxyethylenated alkylphenol: RC₆H₄(OC₂H₄)xOH</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Polyoxyethylenated alcohol: R(OC₂H₄)xOH</td>
<td>None</td>
</tr>
<tr>
<td>Amphiphatic</td>
<td>Long-chain amino acid: RNH₂CH₃COO⁻</td>
<td>Variable</td>
</tr>
<tr>
<td></td>
<td>Sulfobetaine : RN⁺(CH₃)₂CH₂CH₂SO₃⁻</td>
<td>Variable</td>
</tr>
</tbody>
</table>
**Hydrophilic-Lipophilic Balance (HLB)**

- All surfactants have a water-loving part and an oil-loving part.
- Ratio of water-loving part and oil-loving part → balance
- \( HLB = \text{Hydrophilic-Lipophilic Balance} \)
- The hydrophilicity and lipophilicity are different among emulsifiers, and the balance between the two is called HLB value.
- The value ranges from 0 to 20.
- Low HLB ⇒ soluble/dispersed in oil
- High HLB ⇒ soluble/dispersed in \( \text{H}_2\text{O} \)

**Surfactant HLB number and application**

<table>
<thead>
<tr>
<th>HLB range</th>
<th>Main application</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5-3</td>
<td>Anti-foaming agents</td>
</tr>
<tr>
<td>4-6</td>
<td>W/O emulsifiers</td>
</tr>
<tr>
<td>7-9</td>
<td>Wetting agents</td>
</tr>
<tr>
<td>8-18</td>
<td>O/W emulsifiers</td>
</tr>
<tr>
<td>13-15</td>
<td>Detergents</td>
</tr>
<tr>
<td>15-18</td>
<td>Solubilizers</td>
</tr>
</tbody>
</table>

**HLB Calculation: Griffin’s method**

\[ HLB = 20 \times \frac{M_h}{M} \]

- \( M_h \) is the molecular mass of the hydrophilic portion of the molecule.
- \( M \) is the molecular mass of the whole molecule.

**The appearance of the surfactant when added to water is indicative of its likely HLB value.**

<table>
<thead>
<tr>
<th>Appearance in water</th>
<th>HLB Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-dispersed</td>
<td>1-4</td>
</tr>
<tr>
<td>Poorly-dispersed</td>
<td>3-7</td>
</tr>
<tr>
<td>Milky</td>
<td>7-10</td>
</tr>
<tr>
<td>Translucent</td>
<td>10-13</td>
</tr>
<tr>
<td>Clear</td>
<td>13+</td>
</tr>
</tbody>
</table>
Hydrophilic–Lipophilic Balance–HLB

- HLB Calculation: Griffin’s method
- Calculations of Molecular Mass
- Molecular masses of chemical compounds are equal to the sums of the molecular masses of all the atoms in one molecule of that compound.
  - $H_2O = (2 \times \text{atomic mass}) + (1 \times \text{atomic mass})$
  - $CH_2OH = \text{atomic number} \times \text{atomic mass}$
  - $(-CH_2-CH_2-O-) = \text{atomic weight of C, H, O = 12, 1, 16 g/mol, respectively}$

$$H_2O = (2 \times 1) + (1 \times 16) = 18 \text{ g/mol}$$

$$CH_2OH = 1 \times 1 + 2 \times 1 = 3 \text{ g/mol}$$

$$(-CH_2-CH_2-O-) = 2 \times 12 + 4 \times 1 + 3 \times 16 = 88 \text{ g/mol}$$

Hydrophilic–Lipophilic Balance–HLB

- HLB Calculation: Griffin’s method
- Water-wetting and oil-wetting power
- Alkyl chain coupled to polyoxyethylene chain
  $$CH_3(CH_2)_nCH_2(OCH_2CH_2)_mOH$$
  - HLB = % weight content of hydrophilic part of the molecule
  - If $n = 3$, HLB = 7.4
  - If $n = 20$, HLB = 15.6

Hydrophilic–Lipophilic Balance–HLB

- HLB Calculation: Determination of Required HLB
  - Sorbitan monostearate HLB = 4.7 (A) @ 50 %
  - Polyoxyethylene sorbitan monostearate HLB = 14.9 (B) @ 50 %

$$\text{HLB} = xA + (1-x)B$$

- HLB of the mixture of emulsifying agents = ?

Hydrophilic–Lipophilic Balance–HLB

- HLB – pros and cons
  - Positives
    - Excellent starting point
    - Generally produces a fairly good emulsion
  - Negatives
    - Ignores the importance of:
      - Electrical double layer
      - Temperature effects of ethoxylates
      - % of emulsifier to be used
      - Phase volume ratios
      - Component interactions

Type of Emulsion

- Oil-in-Water Emulsion
- Water-in-Oil Emulsion
- Multiple Emulsion

Macroemulsion
Nanoemulsion
Microemulsion
**Type of Emulsion**

- Macroemulsion: particle size > 400 nm (0.4 µm).
- Nanoemulsion (miniemulsion): particle size 100-400 nm.
- Microemulsion: particle size < 100 nm (0.1 µm).
- The appearance of the emulsion is dependent upon the particle size of the discontinuous phase.

<table>
<thead>
<tr>
<th>Particle size (nm)</th>
<th>Size</th>
<th>Appearance</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 400</td>
<td>White</td>
<td></td>
</tr>
<tr>
<td>100-400</td>
<td>Blue White</td>
<td>White</td>
</tr>
<tr>
<td>&lt;100</td>
<td>Translucent</td>
<td></td>
</tr>
<tr>
<td>&lt; 50</td>
<td>Transparent</td>
<td></td>
</tr>
</tbody>
</table>

**Macroemulsions**

- Macroemulsions are inherently thermodynamically unstable systems because the contact between oil and water molecules is unfavorable, and so they will always break down over time.
- They are of two types, based on nature of dispersed phase:
  - Oil-in-Water Emulsion
  - Water-in-Oil Emulsion

**Formation**

- Mechanical energy (e.g. homogenization, stirring)-One of the two immiscible liquids is broken up into particles that are dispersed in the second liquid.
- Particle size > 400 nm-white opaque milky/cream.
- HLB value of emulsifiers used.
- The quantity of emulsifier used - the higher the level of the emulsifier, the smaller the dispersed phase (valid only for suitable HLB emulsifier used).
**Macroemulsions**

**Formation**
- Order of mixing: the phase of the emulsion which is added to the other, often forms the dispersed phase.
- For example: adding Oil into Water \(\rightarrow\) O/W emulsion is likely to be formed.

**Phase Inversion Temperature: PIT**
- As the temperature increases, the water solubility of ethoxylated nonionic emulsifiers becomes poorer (the HLB decreases).
- There is a temperature (PIT) at which the hydrophilic and lipophilic characteristics of the emulsifier are equal (relative to the required HLB of the oil phase).
- At this temperature the emulsion will exhibit a phase inversion.
- The PIT should be at least 20°C higher than the storage temperature.

**Microemulsions**

**Microemulsions are transparent dispersions containing two immiscible liquids with particles of 10–100 nm (0.01–0.1 µm) diameter that are generally obtained upon mixing the ingredients gently.**

**Phase: O/W or W/O.**

**Large amounts of two immiscible liquids (e.g., water and oil) can be brought into a single phase (macroscopically homogeneous but microscopically heterogeneous) by addition of an appropriate surfactant or a surfactant mixture.**

**Technical differentiation between emulsions & microemulsion systems**

<table>
<thead>
<tr>
<th>Macroemulsion</th>
<th>Microemulsion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thermodynamically unstable</td>
<td>Thermodynamically stable</td>
</tr>
<tr>
<td>Direct oil/water contact at the interface</td>
<td>No direct oil/water contact at the interface</td>
</tr>
<tr>
<td>Multiple phase only</td>
<td>May be single or multiple phase</td>
</tr>
<tr>
<td>Cloudy colloidal systems</td>
<td>Optically transparent (Isotropic)</td>
</tr>
</tbody>
</table>

**Microemulsion**

- The essential distinction between macroemulsion and microemulsion is their particle size and stability.
- The macroemulsion is 'kinetically stable'.
- The microemulsion is 'thermodynamically stable'.
- The stability of the microemulsion can be influenced by addition of salt, other additives, temperature or pressure.
Microemulsion

- Microemulsions can be prepared by controlled addition of lower alkanols (butanol, pentanol and hexanol) to milky emulsions to produce transparent solutions comprising dispersions of either water-in-oil (w/o) or oil-in-water (o/w) in nanometer or colloidal dispersions.
- Microemulsion formulation will result in a faster uptake into the skin.

The emulsifying agent is generally 15-30%.
- Cost and safety
- Appropriate selection of ingredients (i.e. surfactants, cosurfactants, oils) are key factors in the formulation of microemulsions.

Nanoemulsions

- Nanoemulsions or miniemulsions or finely dispersed emulsions or ultrafine emulsions.
- The preparation of nanoemulsions requires high-pressure homogenization.
- They are blue white semiopaque emulsion of 100 nm-400 nm drop size.
- The emulsifying agent is generally 1-3% of the oil phase.

- The emulsifying agents, mixture of:
  - Ionic surfactant and long-chain alcohol cosurfactant
  - The chain length of cosurfactant is at least 12 carbons
- O/W type
  - Surfactant + cosurfactant + water = micelle
  - Oils added
  - Breakdown of the formed micelle to tiny droplets

Evaluation of Emulsion Type

- Electrical conductivity
  - Electrical conductivity of O/W emulsions is higher than that of W/O emulsions
- Dilution method
  - Evaluated the emulsion type from the dispersion ease at dilution with water
- Dye method
  - Evaluated the emulsion type by dissolving water-soluble and oil-soluble dyes in the emulsion

- Conductivity of o/w and w/o emulsions as a function of volume fraction φ of the discontinuous phase.
Multiple Emulsion

- Water-in-Oil-in-Water type
- Oil-in-Water-in-Oil type

Improving the stability of multiple emulsions is the main issue for the systems.

Preparation of Multiple Emulsions by two-step method

Step 1 Preparation of primary emulsion W/O
- Dropwise addition of the aqueous phase into oil phase, which contains the hydrophobic surfactants
- High shear rate homogenizer may apply to obtain an internal phase size about 1-3 microns.
- Example composition:
  - Brij 92 10%
  - Mineral oil 60%
  - NaCl 0.3%
  - Water to 100%

Step 2 Preparation of W/O/W
- The primary W/O is added dropwise to a water phase, which contains the hydrophilic surfactants.
- Low shear homogenizer must be applied to obtain much larger droplet.
- Example composition:
  - Span 80-Tween 20 5%
  - Primary W/O emulsion 20%
  - Water 75%

Effects of Emulsifiers on W/O/W emulsion
- The optimal HLB value of primary emulsifier is in the range of 3-7.
- The HLB value for secondary emulsifier is 8-16.
- The emulsifier concentration and emulsifier ratio are of great effects on the formation of stable W/O/W emulsion.
- The primary emulsifier can migrate to the external oil phase and it may interact with the secondary emulsifier, therefore, altering the optimal HLB→instability?
Multiple Emulsion

Effects of Emulsifiers on W/O/W emulsion

Example: W/O/W multiple emulsion containing Span 83 and Tween 80

- Span 83 HLB 3.7, the optimum concentration is 20 %
- Tween 80 HLB 15, the optimum concentration is 0.1 %
- High Span 83 concentrations increased the storage modulus $G'$ (solidlike) values and hence enhanced multiple emulsion stability.
- Higher concentration of Tween 80 had a destructive effect on W/O/W emulsion stability.

*J. Jiao, D. J. Burgess, AAPS Pharm. Sci., 5, 1, 2003

Pickering emulsions

- The role of particles in stabilizing emulsions
- The person credited with first investigating particle stabilization in emulsions is Pickering S.U.
- Particles more wetted by water than oil, stabilized O/W emulsions by residing at the interface.
- From this report, the term ‘Pickering emulsions’ has been given to emulsions stabilized by solid particles.

Pickering emulsions

- The role of particles in stabilizing emulsions

- There have been a number of different particle types used as stabilizers in both O/W and W/O emulsions, including silica, metal oxides and sulphates, and clays

- The effectiveness of a specific particle type in stabilizing an emulsion, depends on the emulsion medium, the particle shape and size, particle wettability and inter-particle interactions.

- Unlike surfactants, particles do not affect emulsion stability by significantly reducing the oil–water surface tension.

- For successful stabilization, it is necessary that the particles be approximately orders of size smaller than the droplets, for the particles to be properly located around the droplets.

- The role of particles in stabilizing emulsions

Examples of particulate emulsifiers

<table>
<thead>
<tr>
<th>Compound</th>
<th>Emulsion Type Stabilized</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alumina</td>
<td>W/O</td>
</tr>
<tr>
<td>Bentonite</td>
<td>O/W</td>
</tr>
<tr>
<td>Magnesium Aluminum Silicate</td>
<td>O/W</td>
</tr>
<tr>
<td>Magnesium Oxide</td>
<td>W/O</td>
</tr>
<tr>
<td>Magnesium Triisilicate</td>
<td>W/O</td>
</tr>
<tr>
<td>Titanium Dioxide (coated)</td>
<td>O/W, W/O</td>
</tr>
<tr>
<td>Silica</td>
<td>O/W</td>
</tr>
</tbody>
</table>

References