

EMULSIONS



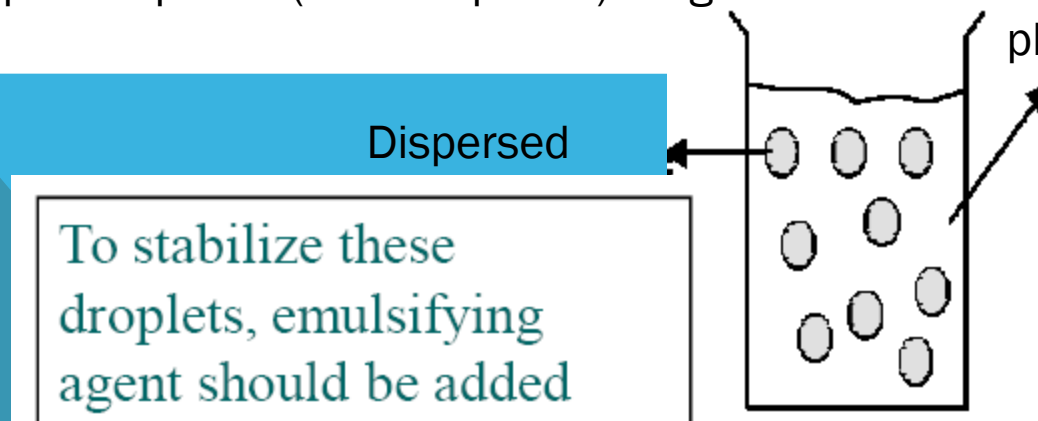
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EMULSIONS:

Definition: It is thermodynamically unstable system consisting of at least two immiscible, one of them is finely subdivided and uniformly distributed as droplets throughout the other.

liquid phases one of which is dispersed as globules (the dispersed phase) in the other liquid phase (the continuous phase) stabilized by presence of emulsifying agent.

Particle diameter of dispersed phase (Internal phase) ranged from 0.1 to 10 μm .



ADVANTAGES OF EMULSIONS

1. Mask the taste of certain medicinal agents.
2. The penetration and spreadability of emulsion constituents is increased when administered in emulsion form.
3. Antiseptics are found to be more efficacious in o/w emulsion.
4. Locally the absorption and penetration of medicaments may be controlled by the proper selection of emulsion type.
5. w/o emulsion has a greater emollient effect when applied externally.
6. o/w emulsions applied to the skin readily washed off from the skin and clothes.

PHARMACEUTICAL APPLICATIONS OF EMULSIONS:

1. They can mask the bitter taste and odor of drugs,
e.g. castor oil, cod-liver oil etc.
2. They can be used to prolong the release of the drug
thereby providing sustained release action.
3. Essential nutrients like carbohydrates, fats and
vitamins can all be emulsified and can be administered
to bed ridden patients as sterile intravenous
emulsions.
4. Emulsions provide protection to drugs which are
susceptible to oxidation or hydrolysis.
5. Intravenous emulsions of contrast media have been
developed to assist in diagnosis.
6. Emulsions are used widely to formulate externally
used products like lotions, creams, liniments etc.

Types Of Emulsions:

- 1- Oil in water emulsions
- 2- Water in oil emulsions
- 3- Multiple emulsions (O/W/O) or (W/O/W) in which small water droplet can be enclosed in a larger oil droplet which itself dispersed in water.
- 4- Microemulsions if the dispersed globules are of colloidal dimensions. It exhibits the properties of hydrophobic colloids.

DIFFERENCE BETWEEN O/W AND W/O EMULSIONS:

(o/w)	(w/o)
Water is the dispersion medium and oil is the dispersed phase	Oil is the dispersion medium and water is the dispersed phase
non greasy and easily removable from the skin	greasy and not water washable
used externally to provide cooling effect e.g. vanishing cream	used externally to prevent evaporation of moisture from the surface of skin e.g. Cold cream
preferred for internal use as bitter taste of oils can be masked.	preferred for external use like creams.

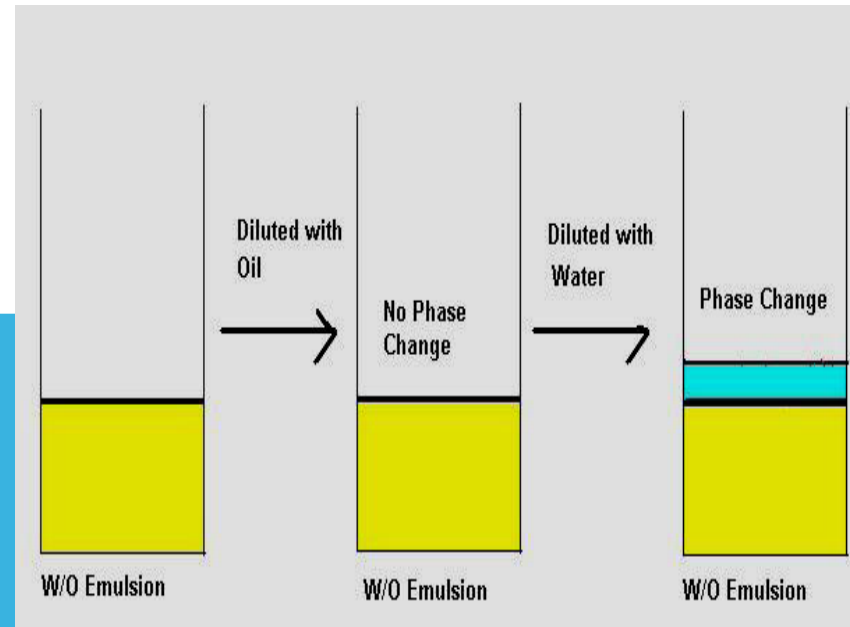
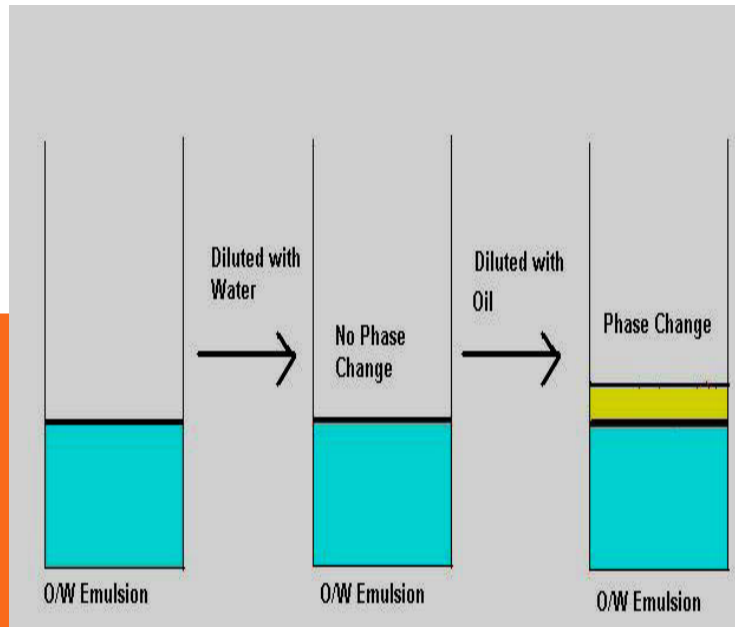
TESTS USED TO IDENTIFY EMULSION TYPE:

1. Phase dilution method

based on the solubility of external phase of emulsion.

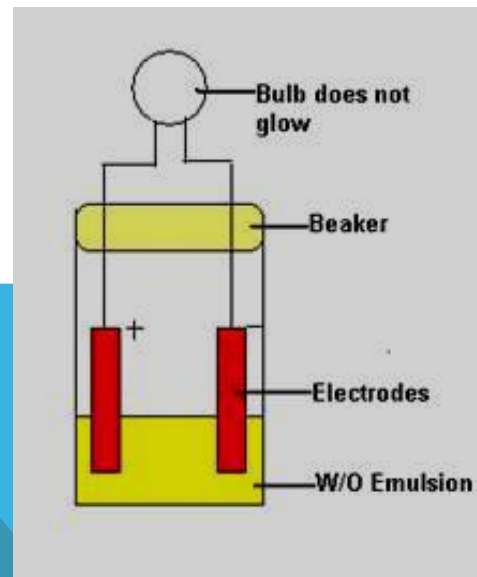
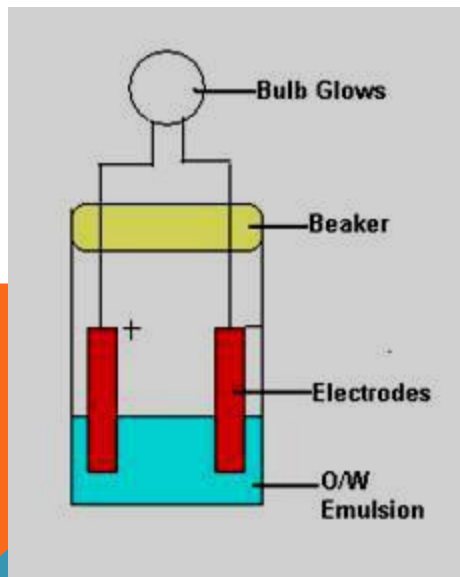
- o/w emulsion can be diluted with water.

w/o emulsion can be diluted with oil.



2. Conductivity Test:

water is good conductor of electricity whereas oil is non-conductor. Therefore, continuous phase of water runs electricity more than continuous phase of oil.

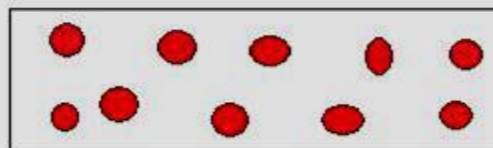


3. Dye-Solubility Test:

when an emulsion is mixed with a water soluble dye such as amaranth (red) or brilliant blue and observed under the microscope. if the continuous phase appears red, then it means that the emulsion is o/w type as water is the external phase if the scattered globules appear red and continuous phase colorless, then it is w/o type. An example of oil soluble dye is red sudan III.



O/W Emulsion



W/O Emulsion

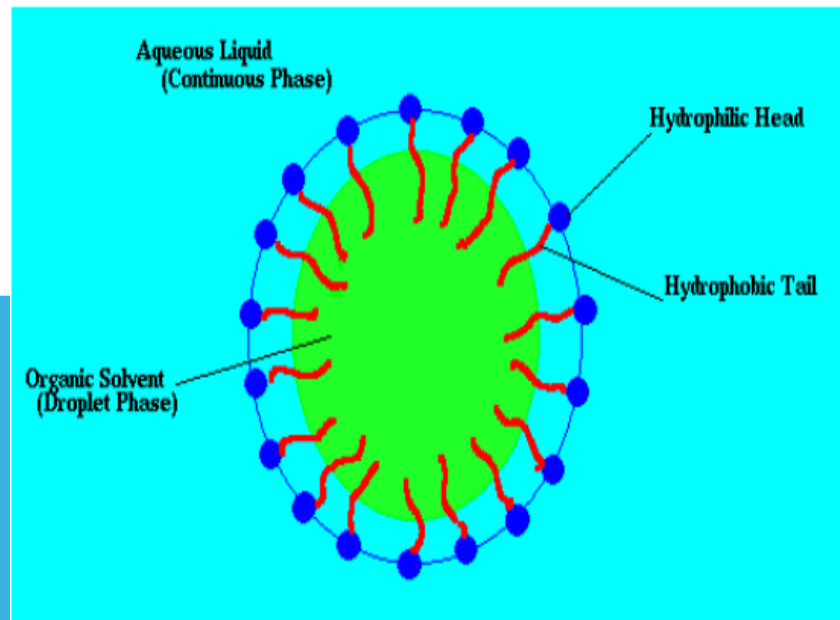
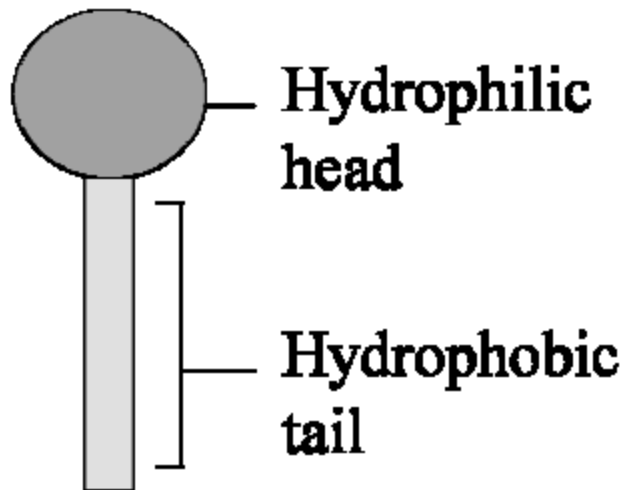
4. Fluorescence test: oils give fluorescence under UV light, while water doesn't. Therefore, O/W emulsion shows spotty pattern while W/O emulsion fluoresces.

5. Wetting filter paper

Ability of oil and water to wet the filter paper. If the liquid spreads rapidly, leaving a small drop at the center, the emulsion is o/w.

EMULSIFYING AGENTS:

Emulsifier or surface active agent (SAA) is molecule which has two parts, one is hydrophilic and the other is hydrophobic. Upon the addition of SAA, it tends to form monolayer film at the oil/water interface.

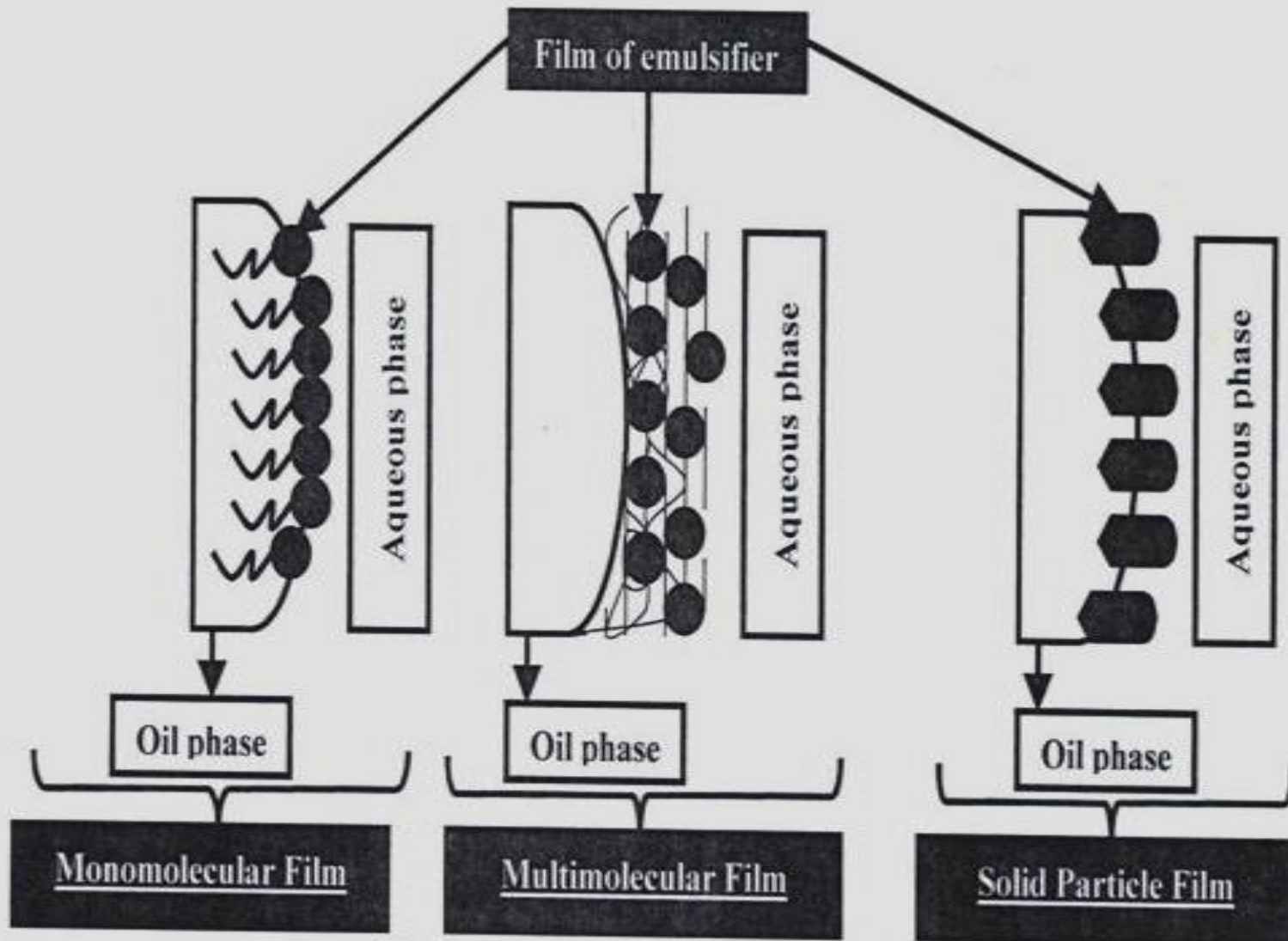


MECHANISM OF ACTION OF EMULSIFYING AGENTS:

When two immiscible liquids are agitated together so that one of the liquids is dispersed as small droplets in the other.

To prevent coalescence between globules, it is necessary to use emulsifying agent.





Diagrammatic Representation of the Films Formed by the Emulsifying Agent at the o/w Interface.

THE PROPERTIES OF IDEAL EMULSIFYING AGENT

1. Non toxic and posses no sensitizing and allergic reactions for emulsion applied to the skin.
2. Ability to form coherent film around the dispersed globules.
3. Reducing the interfacial tension between the dispersed phase and continuous phase.
4. Increasing the viscosity of the external phase, increasing the emulsion stability.
5. Chemically stable
6. Resist decomposition with yeasts, fungi and bacteria.
7. Cheap, disagreeable odor and taste
8. Suitable over wide range of different pairs of liquids.

TYPES OF EMULSIFIERS

True or primary emulsifying agent, which is capable of forming and stabilizing emulsion e.g. acacia, tweens, spans.

Stabilizers or auxiliary agents which although not forming acceptable emulsions when used alone, assist the primary emulsifier in stabilizing the product e.g. tragacanth, agar, stearyl alcohol. They assist the stability by increasing the viscosity of the continuous phase, reducing the tendency of the dispersed phase to coalesce and separate into distinct phase.

Natural

Synthetic

Finely divided solids



Natural emulsifier

form monomolecular and multimolecular film

Advantages: Non toxic and relatively inexpensive

1. Acacia is the best known true emulsifying agent of the natural gum class, acacia emulsions are stable over a pH range of 2-11.

Disadvantages:

- It is incompatible with phenols, tannic acid, heavy metals, sodium borate and high concentration of alcohol.
- Many of phenolic compounds and certain vitamins are readily oxidized by the enzymes found in acacia unless the enzymes are previously destroyed by heat.
- Preparation containing acacia are not resistant to attack by microorganisms and require preservative (0.2% benzoic acid).

NATURAL EMULSIFIERS

2. Tragacanth

- Used in making o/w emulsions, its quantity is one tenth as much as required for acacia. It forms dense emulsions.
- Thus tragacanth contributes to the stability of the emulsion because it imparts high viscosity.
- It is usually used as a thickening agent with acacia to prevent the creaming that occurs when acacia is used alone.

3. Agar, pectin (thickening agent)

4. Methyl cellulose

Is cellulose polymer widely used in the pharmaceutical industry. It is a nonionic emulsifying agent and compatible with other emulsifying agents.

FINELY DIVIDED SOLIDS AS EMULSIFYING AGENTS

as bentonite, magnesium hydroxide and silica gel.

- forming a coherent film which physical prevents coalescence of the dispersed globules.

- if the particles are: preferentially wetted by the aqueous phase o/w emulsion

- If preferentially wetted by the oil phase w/o emulsion



SYNTHETIC EMULSIFYING AGENTS

- form monomolecular film

A- Anionic emulsifying agents

Alkali soap: are salts formed from various fatty acids and alkali metals (soluble soaps)

- e.g. sodium, potassium and ammonium salts of fatty acids (stearic, lauric and oleic acids)

- They are hydrophilic form o/w emulsions

Insoluble soaps e.g. zinc oleate and aluminum stearate for w/o emulsion.

- in acidic condition precipitated Fatty acid decompose the soaps and thus break the emulsion.

- Their unpleasant taste and high alkalinity especially soluble soaps preclude their use for internal administration (for external use)

- incompatible with polyvalent cations (calcium and magnesium)

Sulfated and sulfonated compound

- E.g. Sodium lauryl sulphate
- stable over high pH range
- o/w emulsions

B- Cationic surfactants

- Quaternary ammonium compounds:

E.g. Cetyl trimethylammonium bromide (Cetrimide) and benzalkonium chloride (they have bactericidal properties rather than emulsifiers)

Disadvantages: Toxicity and irritancy

Incompatible with anionic surfactants, polyvalent anions
unstable at high pH

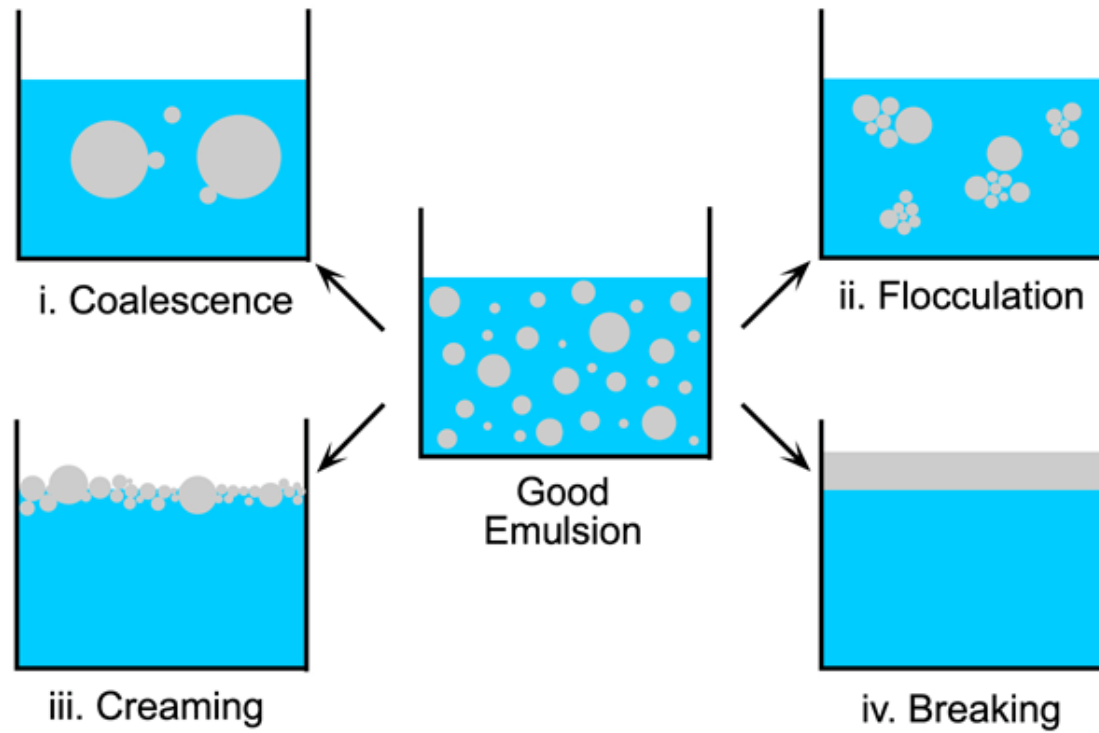
C- Nonionic surfactants

- Low toxicity and irritancy so suitable for oral and Parenteral administration
 - High degree of compatibility
- Less sensitive to change pH or to addition of electrolytes
 - E.g. Tweens (polyethylene fatty acid ester) O/W
 - E.g. Span (sorpitan fatty acid ester) W/O

Hydrophile-Lipophile Balance (HLB):

- HLB: the ratio between the hydrophilic portion of the molecule to the lipophilic portion of the molecule.
- The higher the HLB of an agent the more hydrophilic it is.
 - Spans are lipophilic have low HLB.
 - Tweens are hydrophilic have high HLB.


EMULSION STABILITY



Flocculation and creaming:

- *Flocculation* - *The small spheres of oil join together to form clumps or flocs which rise or settle in the emulsion more rapidly than individual particles.*
- *Creaming* - *it is a concentration of the floccules of the internal phase formed upward or downward layer according to the density of internal phase.*

Factors affect creaming:

- 
- 1- Globule size: increase globule size increase creaming
 - 2- The density of the internal and external phases:
 - 3- Gravity: const, However centrifugation is applied.
 - 4- increase Viscosity decrease creaming

Strategies to reduce creaming:

Principle	Method
<i>Reduce droplet size (r)</i>	Homogenizer
<i>Reduce density difference ($\Delta \rho$)</i>	Add weighting agent are oils that, have a density greater than the density of water
<i>Increase continuous phase viscosity (η)</i>	Add thickening or gelling agent e.g. methylcellulose

Coalescence and Breaking:

- **Coalescence** is the process by which emulsified particles merge with each to form large particles.
- **Breaking** - Due to Coalescence and creaming combined, the oil separates completely from the water so that it floats at the top in a single, continuous layer.



Major differences between creaming and breaking:

Items	Creaming	Breaking
Definition	Formation of upward or downward layer	Separation of emulsion to upward oily layer and downward aq layer
Reverersability	Reversible	irreversible
Agitation	Reconstitute	not reconstituting
Emulsifying film around particles	intact	destroyed
Internal phase globules	Partial or no coalescence	Complete fusion
Effect of phase volume ratio	No or little	in o/w if oil >74%

Phase inversion:

- In phase inversion o/w type emulsion changes into w/o type and vice versa.
- It is a physical instability.
- It may be brought about by:
 - 1- the addition of an electrolyte e.g. addition of CaCl_2 into o/w emulsion formed by sodium stearate can be inverted to w/o.
 - 2- by changing the phase volume ratio
 - 3- by temperature changes.
- Phase inversion can be minimized by:
 - 1- using the proper emulsifying agent in adequate concentration
 - 2- keeping the concentration of dispersed phase between 30 to 60 %
 - 3- storing the emulsion in a cool place.

Cracking

- When an emulsion cracks during preparation, i.e., the primary emulsion does not become white but acquires an oily translucent appearance.
- In such a case, it is impossible to dilute the emulsion nucleus with water and the oil separates out.
- Cracking of emulsion can be due to:
 - 1- addition of an incompatible emulsifying agent
e.g. monovalent soap + divalent soap
e.g. anionic + cationic emulsifying agent
 - 2- chemical or microbial decomposition of emulsifying agent

e.g. alkali soaps decomposed by acids

e.g. monovalent soaps salted out by electrolytes such as NaCl

e.g. nonionic emulsifying agents are incompatible with phenols

e.g. alcohol precipitates gums and gelatin

3- exposure to increased or reduced temperature

4- Addition of common solvent

e.g. addition of a solvent in which the two phases are soluble (alcohol)