

EMULSIONS-II

Preparation of Emulsions

- **Preparation Of Emulsions**
- Preparation of emulsions depends on the scale at which it is produced.
- **On small scale** mortar and pestle can be used but its efficiency is limited. To overcome these drawback small electric mixers can be used although care must be exercised to avoid excessive entrapment of air.
- **For large scale** production mechanical stirrers are used
 - to provide controlled agitation and shearing stress
 - to produce stable emulsions.

1- Dry Gum Method

In this method the oil is first triturated with gum with a little amount of water to form the primary emulsion. The trituration is continued till a characteristic 'clicking' sound is heard and a thick white cream is formed. Once the primary emulsion is formed, the remaining quantity of water is slowly added to form the final emulsion.

2- Wet Gum Method

As the name implies, in this method first gum and water are triturated together to form a mucilage. The required quantity of oil is then added gradually in small proportions with thorough trituration to form the primary emulsion.

Once the primary emulsion has been formed remaining quantity of water is added to make the final emulsion.

3- Bottle Method

This method is employed for preparing emulsions containing volatile and other non-viscous oils. Both dry gum and wet gum methods can be employed for the preparation.

As volatile oils have a low viscosity as compared to fixed oils, they require comparatively large quantity of gum for emulsification.

In this method, oil or water is first shaken thoroughly and vigorously with the calculated amount of gum. Once this has emulsified completely, the second liquid (either oil or water) is then added all at once and the bottle is again shaken vigorously to form the primary emulsion. More of water is added in small portions with constant agitation after each addition to produce the final volume.

Preparation of emulsions- large scale

Heat :

Emulsification by vaporization

Emulsification by phase inversion

Low energy emulsification

Several procedures may be applied for emulsion preparation, and these range from simple pipe flow (**low agitation energy L**); static mixers and general stirrers (**low to medium energy, L–M**); high-speed mixers such as the Ultraturrax (**M**); colloid mills and high-pressure homogenizers (**high energy, H**); and ultrasound generators (**M–H**).

Equipments

- Static mixers
- Ultraturrax
- Colloid mills
- High-pressure homogenizers
- Ultrasound generators

high-pressure homogenizers

The emulsion phases are pumped together under high pressure into a small volume or through a small orifice – the interaction chamber – where pressures in the tens of thousands of PSI create very high shear forces.

Droplet size as small as 0.2 μm .

Physical Stability of Emulsions

Emulsions are thermodynamically unstable. The instability problems seen in emulsions during are given below.

- Creaming
- Flocculation
- Coalescence (agglomeration)
- Phase decomposition (Breaking)
- Phase inversion
- Ostwald Ripening (Disproportionation)

A physically stable emulsion should be able to reach its initial state homogeneously with little agitation, with no separation during the shelf life, no dispersed phase, and should be able to flow easily.

a) Creaming and Sedimentation

- This process results from external forces usually gravitational or centrifugal. When such forces exceed the thermal motion of the droplets (Brownian motion), a concentration gradient builds up in the system with the larger droplets moving faster to the top (if their density is lower than that of the medium) or to the bottom (if their density is larger than that of the medium) of the container. In the limiting cases, the droplets may form a close-packed (random or ordered) array at the top or bottom of the system with the remainder of the volume occupied by the continuous liquid phase.

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- The creaming rate is inversely proportional to viscosity.
 - The physical stability of the emulsion can be increased by increasing the viscosity of the external phase.
 - (viscosity enhancing agents such as methyl cellulose, gummi tragacanthae, sodium ainate)
 - Creaming is faster in case of the emulsions with larger droplets compared to smaller ones. So, the diameter of the droplets is the most important factor in determining the rate of creaming.
 - (homogenization)

b) Flocculation:

- Flocculation of the dispersed phase may occur before, during, or after creaming.
- It is defined as the reversible aggregation of inner phase droplets.
- It is affected by surface charge of emulsifying globules.
- In situations where there is no protective mechanical barrier at the interface, for example, if the amount of emulsifier is not sufficient, the emulsion droplets rapidly agglomerate and coagulate.
- During flocculation, the interfacial film and particles maintain their individuality.
- Redispersibility of aggregates depends on the strength of the interaction between the particles.
- This interaction is determined by:
 - the concentration of soluble materials such as electrolytes and ionic emulsifiers.
 - the chemical properties of the emulsifiers,
 - the phase volume ratio,

c) Coalescence:

- Coalescence is the process in which two or more droplets merge together to form a single larger droplet.
- This refers to the process of thinning and disruption of the liquid film between the droplets with the result of fusion of two or more droplets into larger ones.

c) Coalescence:

The limiting case for coalescence is the complete separation of the emulsion into two distinct liquid phases.

The driving force for coalescence is the surface or film fluctuations which results in close approach of the droplets whereby the van der Waals forces is strong thus preventing their separation.

d) Phase separation-Breaking:

- The creaming phase should be considered different from phase separation; because phase separation is non-reversible, but the creaming is a reversible event.
- Cream floks can be redispersed easily by agitation and a homogeneous mixture can be obtained; because the fat globules are still surrounded by a protective film formed by the emulsifier.
- Globules can not be dispersed by mixing when the film surrounding the droplets is broken.
- The phase separation dependents on
 - the droplet size,
 - the viscosity of the dispersion medium and
 - the phase volume ratio.

e) Phase inversion:

Conversion of a W/O type of emulsion to O / W type or otherwise is called phase inversion.

This phenomenon can be seen during the preparation of the emulsion, during mixing of the two phases, heating and cooling of the emulsion.

Phase inversion is caused by:

- the changes on the phase volume ratio
- the addition of an electrolyte
- changing the pH of the emulsion over time

f) Ostwald Ripening (Disproportionation)

This results from the finite solubility of the liquid phases. Liquids that are referred to as being immiscible often have mutual solubilities that are not negligible. With emulsions, which are usually polydisperse, the smaller droplets will have larger solubility when compared with the larger ones (due to curvature effects). With time, the smaller droplets disappear and their molecules diffuse to the bulk and become deposited on the larger droplets. With time, the droplet size distribution shifts to larger values

Stability tests on Emulsions

It is important to determine the acceptable shelf life in the development of emulsion formulations.

There is no single rapid and sensitive method to measure the instability of the emulsion.

To accelerate the stability program, the emulsions are kept under **stress conditions**.

The forced conditions applied in the evaluation of physical instability are:

- time degeneration (aging) and temperature,
- centrifugation,
- ultracentrifugation
- mixing

Aging and temperature

The shelf life of an emulsion is determined by standing at different temperatures at high temperatures.

In evaluating shelf life, the cycle between two temperatures is important. This cycle should be between 4-45 ° C.

Centrifugation and ultracentrifugation:

- The stability of emulsions can be assessed by creating a certain stress in the emulsions by centrifugation and ultracentrifugation.
- Phase separation by centrifugation is very fast.
- In general, centrifugation is a useful method for predicting the shelf life of the emulsions.

Mixing:

In an emulsion, coalescence does not occur unless there is a collision between the emulsion droplets due to the Brownian movements.

Simple mechanical mixing causing two droplets to collide with each other.

If the emulsions are mixed or shaken too fast emulsions might get disrupted.

Shelf life and Storage

- Should be stored at room temperature and will either be recently or freshly prepared
- Some official preparations will have specific expiry dates.
- Should not be frozen

Containers

- ❑ An amber medicine bottle is used, plain for internal use and ribbed for external use, with an airtight child-resistant closure.
- ❑ Containers with wide mouth are useful for very viscous formulations.

Special labelling and advice for emulsions

- ❑ «shake well before use»
- ❑ «store in cool place» (This is to protect the emulsion against extremes of temperature which will adversely affect its stability)

Composition of Emulsions

- Polar compounds
- Apolar compounds
- Emulsifier
- Stabilizing agents
- Antimicrobial agents
- Antioxydants
- Active Agents

Polar compounds

-Water

- Polyols

- Butylene glycol
- Glycerin
- PEG
- Propylene Glycol

Apolar compounds

- Esters (solid lipids, lanolin, synthetic materials (iso propyl myristate, glyceryl monostearate))
- Ethers
- Fatty acids
- Fatty alcohols
- Hydrocarbons (butane, propane, squalene)
- Others (halo hydrocarbons, vegetable / animal waxes, silicone)

Stabilizing agents

Stabilizing agents increase the emulsion stability by :

- minimizing the phase densities,
- increasing the external phase viscosity
- holding onto the o / w interface.

Stabilizing agents

- Lyophilic colloids (polysaccharides, tragacanth, agar, alginic acid, gelatin, cellulose esters, synthetic-semisynthetic polymers)
- Particulate powder: Bentonite, Mg-Al Silicate, microcrystalline cellulose, oxides and hydroxides
- Gelling agents: amino acids, peptides, proteins, lecithin

Preservatives

It is important to protect emulsions against fungi and yeast.

Due to microbial contamination following properties may change:

- odor
- color
- Viscosity
- Chemical structure of the emulsifiers



Stability problems

Ingredients of emulsions can provide a growth medium for microbes.

Eg:

- Arachis oil supports: *Aspergillus* species
- Liquid paraffin supports: *Penicillium* species

Other contamination sources:

- Natural emulsifying agents: starch and acacia
- Water (if not properly stored)
- Carelessly cleaned equipment
- Poor closures on containers

Preservatives

- Ethanol (20 %)
- Sugar (67 %)
- Polyols (10 %)
- Glycerin (40-50 %)
- Sorbitol



Preservative is not needed

Eg:

- Quaternary ammonium compounds
- benzoic acid
- phenyl mercury nitrate
- parabens

Antioxydants

-In addition to the protection of the active agent, it is also appropriate to add antioxidants to the emulsions for the formulation components such as unsaturated lipids.

- Besides the addition of antioxidants, the use of tightly closed and opaque containers is also important in terms of preventing system from oxidation.

-They should be preferentially soluble in the oily phase

Antioxidants

1) True antioxidants:

Inhibits oxidation by reacting with free radicals and blocking the chain reaction

Eg: Tocopherols, alkyl gallates, butylated hydroxyanisole (BHA), butylated toluene (BHT), nordihydroguaiaretic acid (NDGA)

2) Reducing agents:

They react with reducing agents.

Ascorbic acid, Na and K salts of sulfurous acid

3) Antioxidant synergists:

citric acid, tartaric acid, lecithin, EDTA

Colours and Flavourings

Color is rarely needed in an emulsion, as most have an elegant White colour and thick texture

Oral emulsions usually contain some flavouring agent.