National University

Technology of Solid Dosage Forms &Disperse Systems

Pharmaceutical Emulsions and Creams

General description

- Emulsions and creams are disperse systems in which an insoluble liquid phase is dispersed within a second liquid phase.
- Creams are emulsions that offer greater consistency (viscosity) and are applied topically.

- Emulsions and creams are either oil in water (o/w) in which oil is the disperse phase and water the external phase, or water in oil (w/o), in which water is the disperse phase and oil is the external phase.

- There are further more structurally complex types, termed multiple emulsions. These are termed water in oil in water (w/o/w) and oil in water in oil (o/w/o) emulsions.

- However, the pharmaceutical uses of these are extremely limited due to their possible reversion to the parent primary emulsion.

- The major use of emulsions is as cream formulations (for external application); however, they may also be administered intravenously,rectally or orally.

Advantages

- 1. Used to deliver drugs that exhibit a low aqueous solubility.
- 2. Used to mask the taste of therapeutic agents, by dissolving the drug in the internal phase of an o/w emulsion.

- 3.Commonly used to administer oils that have a therapeutic effect.
- 4.If the therapeutic agent is irritant when applied topically, the irritancy may be reduced by formulation of the drug within the internal phase of an o/w emulsion.

- 5. Could be employed to administer drugs to patients who have difficulty swallowing solid-dosage forms.
- 6. Emulsions are employed for total parenteral nutrition(TPN).

Disadvantages

- 1. They are thermodynamically unstable and so must be formulated to stabilise the emulsion from separation of the two phases.
- 2. Difficult to manufacture.

Theories of emulsification

- The system attempts to lose this excess free surface energy to its surrounding by coalescence of the droplets. Addition of emulsifier which concentrates at an interface, thereby altering the surface free energy.

Go and read further for:

- The role of surface-active agents.
- The role of hydrophilic polymers.
- The role of adsorbed particles.

In emulsion stability.

Determination of emulsion type

- When oil, water and the specified emulsifying agents are mixed together, the resultant emulsion type is defined by the stability of the droplet phase; the phase of lower stability (i.e. the greater rate of coalescence) coalesces to form the external phase.

Factors that determine Emulsion Type prduced

(1) phase volume of the internal phase.

(2) the chemical properties of the film

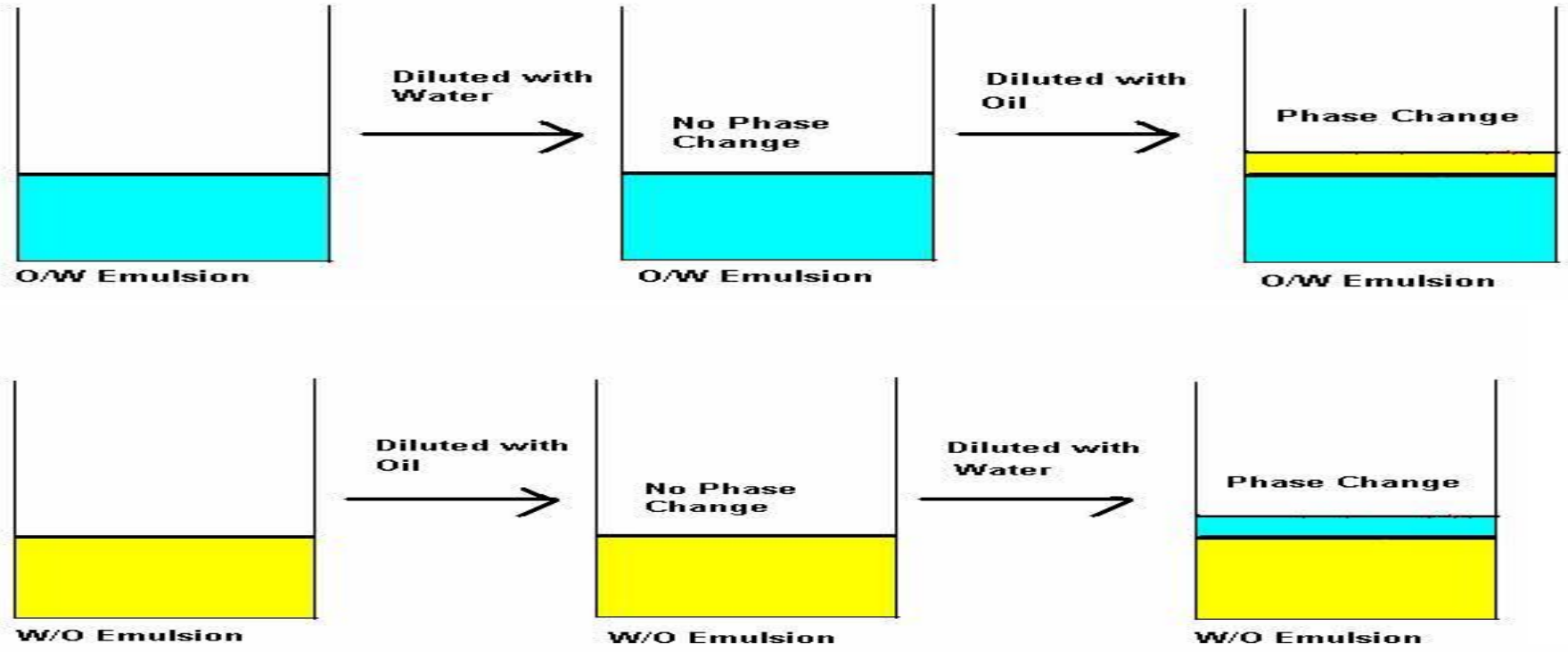
surrounding the internal phase.

(3) viscosity of the internal and external phases.

Tests for identification of emulsion type

- Dilution test (miscibility test)
- Staining test (dye solubility test)
- Conductivity measurement

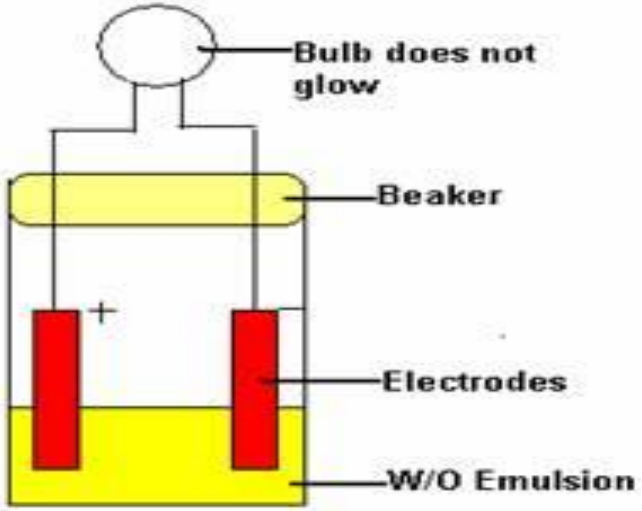
Dilution test (miscibility test)

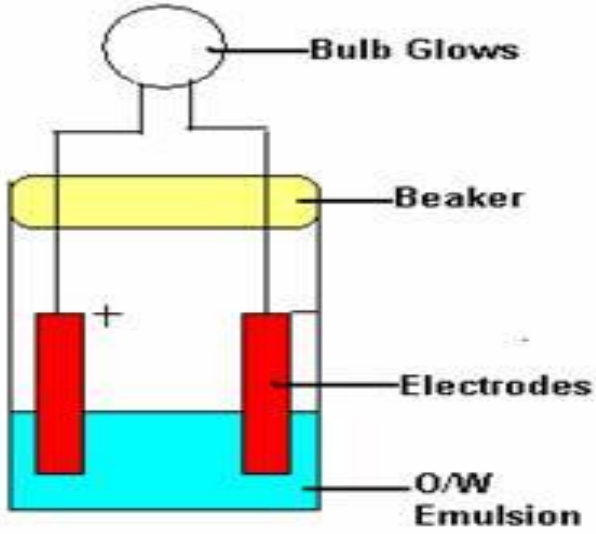


Conductivity Test

- This test is based on the basic principle that water is a good conductor of electricity. Therefore in case of o/w emulsion , this test will be positive as water is the external phase. In this test.

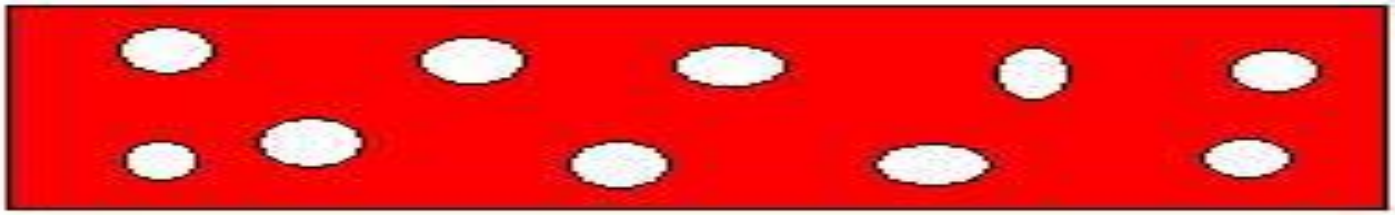
- An assembly consisting of a pair of electrodes connected to a lamp is dipped into an emulsion. If the emulsion is o/w type, the lamp glows.


Bulb does not glow
Beaker
+
Electrodes
W/O Emulsion

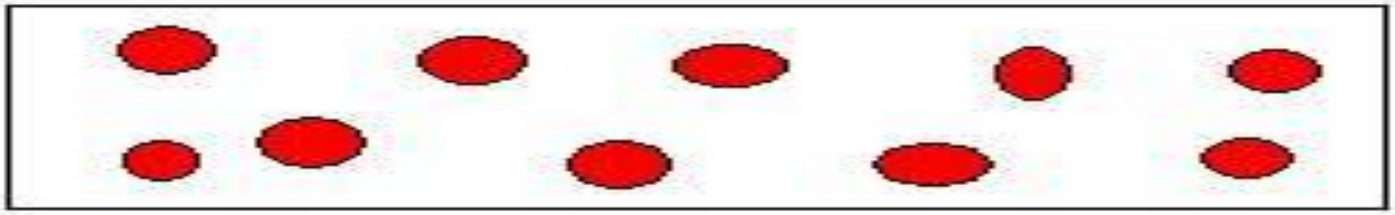

Bulb Glows
Beaker
+
Electrodes
O/W Emulsion

Dye Solubility Test

- In this test, when an emulsion is mixed with a water soluble dye such as amaranth 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 and the dye will dissolve in it to give color but if the scattered globules appear red and continuous phase colorless, then it is w/o type.



O/W Emulsion



W/O Emulsion

- Similarly if an oil soluble dye such as Scarlet red C or Sudan III is added to an emulsion and the continuous phase appears red, then it w/o emulsion.

Emulsifying Agents

- They are the substances added to an emulsion to prevent the coalescence of the globules of the dispersed phase.
- They are also known as emulgents or emulsifiers.
- They act by reducing the interfacial tension between the two phases and forming a stable interfacial film.

- The selection of emulsifying agent plays a very important role in the formulation of a stable emulsion.

Criteria For The Selection of Emulsifying Agents

- It should be able to reduce the interfacial tension between the two immiscible liquids.
- It should be physically and chemically stable , inert and compatible with the other ingredients of the formulation.

- It should be non irritant and non toxic in the conc., used.
- It should be organoleptically inert i.e. should not impart any color , odour or taste to the preparation.

- It should be able to produce and maintain the required viscosity of the preparation.
- It should be able to form a coherent film around the globules of the dispersed phase and should prevent the coalescence of the droplet of the dispersed phase.

- No single emulsifying agent possesses all the properties required for the formulation of a stable emulsion therefore sometimes blends of emulsifying agents have to be taken.

Instabilities In Emulsions

- An emulsion is a thermodynamically unstable preparation so care has to be taken that the chemical as well as the physical stability of the preparation remains intact throughout the shelf life.

There should be

- No appreciable change in the mean particle size or the size distribution of the droplets of the dispersed phase.
- Droplets of the dispersed phase should remain uniformly distributed throughout the system.

Instabilities seen in emulsion can be grouped as:

1.Creaming

- This phenomenon occurs primarily as a result of the density difference between the oil and water phases and involves either the sedimentation or elevation of the droplets of the internal phase, producing a layer of concentrated emulsion either at the top or bottom of the container.

- Patients often believe that an emulsion that shows evidence of creaming has exceeded its shelf-life.

- It is therefore important to understand the physicochemical basis of creaming in emulsions and, in so doing, reduce the rate of or inhibit this phenomenon.

The factors affecting creaming are best described by stoke's law:

$V = 2r^2 (d_1 - d_2) g/9\eta$

- Where V= rate of creaming
- r=radius of globules
- d_1= density of dispersed phase
- d_2= density of dispersion medium
- g= gravitational constant
- η = viscosity of the dispersion medium

So,

- What will you do to decrease Creaming?

2.Cracking

- It refers to the complete coalescence of the internal phase, resulting in the separation of the emulsion into two layers.It occurs due to the destruction of the mono/multilayer film at the interface between the droplet and external phase.

- If an emulsion has cracked it cannot be recovered.

(irreversible instability)

What are the possible reasons of cracking?

This phenomenon may be due to:

1. Incorrect selection of emulsifying agents.
2. Presence of incompatible excipients.
3. Temperature.
4. Microbial spoilage.

3.Flocculation

- Although flocculation may stabilise the formulation, there is also the possibility that the close location of the droplets would enable droplet coalescence to occur if the mechanical properties of the interfacial film are compromised.

4.Phase inversion

- Phase inversion refers to the switching of an o/w emulsion to a w/o emulsion (or vice versa). This is a phenomenon that frequently occurs whenever the critical value of the phase volume ratio has been exceeded.

- In o/w emulsions the frequently phase volume ratio is 74:26 .
- For w/o emulsions this value is 40:60.

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.

The methods commonly used to prepare emulsions can be divided into two categories:

A- Trituration Method

This method consists of dry gum method and wet gum method.

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.

B- 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.

Methods for preparing Emulsions for External use:

- Emulsions meant for external application such as creams, lotions and liniments contain in their formula waxy solids which require melting before mixing.

- Such emulsions may be prepared by melting the oily components separately at 60 0C.

- Similarly in another vessel, the aqueous components are mixed and are warmed gently to 60 C.
- The aqueous phase is then added to the oily phase at the same temperature and stirred until cold.

Proportions of Oil, Water and Gum required for formation of primary emulsion

Type of oil	Oil	Water	Gum
Fixed oil	4	2	1
Mineral oil	3	2	1
Volatile oil	2	2	1

Quality control tests for Emulsions

- 1.Determination of particle size and particle count.
- 2.Determination of viscosity.
- 3.Determination of phase separation.
- 4.Determination of electrophoretic properties.

Stability testing

Stability of emulsions is an important parameter for the formulator.

Stability testing of emulsions involves determining stability at long term storage conditions, accelerated storage conditions, freezing and conditions. Stress conditions are applied in order to speed up the stability testing.

The stress conditions used for speeding up instability of emulsions include:

- Centrifugal force, Agitational force and temperature

- The following physical parameters are evaluated to assess the effect of any of the above stress conditions:

  Phase separation

  Viscosity

  Electrophoretic properties

  Particle size and particle count

Packaging, Labeling and Storage of Emulsions

- Depending on the use, emulsions should be packed in suitable containers. Emulsions meant for oral use are usually packed in well filled bottles having an air tight closure.
- Light sensitive products are packed in amber coloured bottles.

- For viscous emulsions, wide mouth bottles should be used. The label on the emulsion should mention that these products have to be shaken thoroughly before use.
- External use products should clearly mention on their label that they are meant for external use only.

- Emulsions should be stored in a cool place but refrigeration should be avoided as this low temperature can adversely effect the stability of preparation.