

## **EMULSIONS**

An emulsion is a dispersion in which the dispersed phase is composed of small droplets of a liquid distributed throughout a vehicle in which it is immiscible (Fig.1).

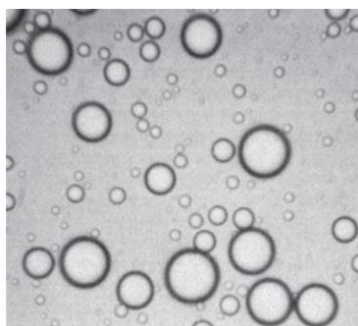


FIGURE 1: Oil in water emulsion.

In emulsion terminology, the dispersed phase is the internal phase, and the dispersion medium is the external or continuous phase. Emulsions with an oleaginous internal phase and an aqueous external phase are oil-in-water (o/w) emulsions. Conversely, emulsions having an aqueous internal phase and an oleaginous external phase are termed water-in-oil (w/o) emulsions. Because the external phase of an emulsion is continuous, an o/w emulsion may be diluted with water and a w/o emulsion with an oleaginous liquid.

If the dispersed droplets are of colloidal dimensions (1 nm to 1  $\mu$ m diameter) the preparation is called a microemulsion and the product is transparent or translucent.

The viscosity of emulsions can vary greatly and they may be prepared as liquids or semisolids. Liquid emulsions may be employed orally, topically, or parenterally while semisolid emulsions employed topically. Many employed preparations that are actually emulsions are not classified as emulsions because they fit some other pharmaceutical category more appropriately. For instance, emulsions include certain lotions, creams and ointments but they are not commonly called emulsions.

## **Advantages**

1. They can mask the bitter taste and odor of drugs, thereby making them more palatable. 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 IV emulsions.
4. Emulsions provide protection to drugs which are susceptible to oxidation or hydrolysis.
5. Emulsions are used widely to formulate externally used products like lotions, creams, etc.
6. The reduced particle size of the oil droplets make them more readily absorbed.

## **Disadvantages**

1. In practice, very few poorly soluble compounds can be successfully delivered as emulsions because of low oil solubility. It is mainly limited to oily materials that are miscible with oils.
2. Re-crystallization and globule size growth of the emulsion can be difficult to identify, particularly in low dose formulations. High opacity of the milk-like liquid prevents the visual check.

## **Identification of emulsion type**

Several simple methods are available for distinguishing between o/w and w/o emulsions. The most common of these involve:

1. Miscibility with oil or water. The emulsion will only be miscible with liquids that are miscible with its continuous phase.
2. Conductivity measurements. Systems with aqueous continuous phases will readily conduct electricity, whereas systems with oily continuous phases will not.
3. Staining test. Water-soluble and oil-soluble dyes are used, one of which will dissolve and stain the continuous phase.

## **FORMULATION OF EMULSIONS**

The smaller the globules of the disperse phase, the slower will be the rate of creaming in an emulsion. The size of these globules can also affect the viscosity of the product, i.e, the smaller the globules, the higher viscosity.

In many cases simple blending of the oil and water phases with a suitable emulgent system may be sufficient to produce satisfactory emulsions. Homogenizers (such as the Silverson mixer-homogenizer) can also be used to reduce globule size still further. The initial blending may be accomplished on a small scale by the use of a pestle and mortar or by using a mixer fitted with an impeller type of agitator, the size and type of which will depend primarily on the volume and viscosity of the product.

Colloid mills are also suitable for the preparation of emulsions. The extensive shearing of the product they produce emulsions of very small globule size.

Because of the very wide range of emulsifying agents available, considerable experience is required to choose the best emulsifying system for a particular product. The final choice will depend on the properties and use of the final product and the other materials required to be present.

Fat or oil drugs for oral administration are formulated as o/w emulsions. In this form, the presence of a flavor in the aqueous phase will mask any unpleasant taste.

Emulsions for intravenous administration must also be of the o/w type, although intramuscular injections can also be formulated as w/o products if a water-soluble drug is required for depot therapy (S.R).

Emulsions are most widely used for external application. Semisolid emulsions are termed creams and more fluid-containing preparations are called either lotions or liniments (liniments are intended for skin massage). Both o/w and w/o types are available.

In most cases, the oil phase of an emulsion is the active agent, and therefore its concentration in the product is predetermined. Castor oil and cod liver oil are examples of medicaments which are formulated as emulsions for oral administration.

A high viscosity is necessary in order to maintain a physically stable emulsion. It is important, however, that these products should be shaken and poured easily from the container. On the other hand, the main disadvantage with low-viscosity emulsions is their tendency to cream easily.

### **The HLB balance**

The inclusion of an emulsifying agent(s) is necessary for the emulsification process during manufacture, and also to ensure emulsion stability during the shelf-life of the product.

A useful method has been suggested for calculating the quantities of these emulsifying agents necessary to produce physically stable emulsion. This is called the hydrophile-lipophile balance (HLB) method.

Each surfactant has an HLB number representing the relative proportions of the lipophilic and hydrophilic parts of the molecule. High numbers (e.g., 20, 30, 33, etc.) indicate a surfactant exhibiting mainly hydrophilic or polar properties, whereas low numbers represent lipophilic or non-polar characteristics.

### **The phase inversion temperature**

An o/w emulsion stabilized by non-ionic emulgents will invert to form a w/o product *on heating*. This is because, as the temperature increases, the HLB value of a non-ionic surfactant will decrease as it becomes more hydrophobic. At a temperature at which the emulgent has equal hydrophilic and hydrophobic tendencies the emulsion will invert. This temperature is called the phase inversion temperature. The stability of an emulsion is related to the phase inversion temperature of its emulsifying agent.

## **CLASSIFICATION OF EMULSIFYING AGENTS**

There are different classes of emulsifying agents (also called emulsifiers or emulgents) but one factor common to all of them, which is their ability to form an adsorbed film around the dispersed droplets between the two phases. The emulsifying agents can be classified as shown below.

### **I. Synthetic emulgents**

**1. Anionic surfactants:** in aqueous solutions, these compounds dissociate to form negatively charged anions that are responsible for their emulsifying ability. They are widely used because of their cheapness, but because of their toxicity are only used for externally applied preparations. Example is sodium stearate.

**2. Cationic surfactants:** these materials dissociate to form positively charged cations in water that provide the emulsifying properties. The most important group of cationic emulgents consists of the quaternary ammonium compounds. Like many anionic emulgents, if used on their own they will produce only poor emulsions, but if used with non-ionic emulgents (auxiliary) they will form stable preparations. Example is Tween.

**3. Amphoteric surfactants:** this type possesses both positively and negatively charged groups, depending on the pH of the system. They are cationic at low pH and anionic at high pH. They are not widely used as emulsifying agents. Example is lecithin.

### **II. Natural emulgents**

Naturally occurring materials often suffer from two main disadvantages: they show batch-to-batch variation in composition and hence in emulsifying properties, and are susceptible to bacterial growth. For these reasons they are not widely used in manufactured products requiring a long shelf-life, but rather for extemporaneously prepared emulsions designed for use within a few days of manufacture. Example is acacia.

### **III. Semisynthetic emulgents**

In order to reduce the problems associated with natural emulgents, semisynthetic derivatives are available. Several grades of methylcellulose and carmellose sodium are available. Methylcellulose, for example, is used to stabilize Liquid Paraffin Oral Emulsion.

#### **Other formulation additives**

In addition to the emulgents, other additives such as buffers, preservatives, thickening agents, flavors, colors and sweeteners are also used.

### **PHYSICAL STABILITY PROBLEMS**

A stable emulsion is one in which the dispersed globules retain their initial character and remain uniformly distributed throughout the continuous phase. Below are some cases of physical instability.

#### **Creaming**

It is the separation of an emulsion into two regions, one of which is richer in the disperse phase than the other. A simple example is the creaming of milk, when fat globules slowly rise to the top of the product. This is not a serious instability problem as a uniform emulsion can be reformed simply by shaking the product (reversible case). It is, however, undesirable because of the increased likelihood of coalescence of the droplets, owing to their close proximity to each other. A creamed emulsion is also inelegant and, if the emulsion is not shaken adequately, there is a risk of the patient obtaining an incorrect dosage.

According to Stokes' law, to slow the rate of creaming the following methods can be used:

1. Production of an emulsion of small droplet size.
2. Increase in the viscosity of the continuous phase.
3. Control of disperse phase concentration: It is not easy to stabilize an emulsion containing less than 25% disperse phase, as creaming will readily occur. A higher

disperse phase concentration would result in a hindrance of movement of the droplets and hence in a reduction in rate of creaming.

Although it is theoretically possible to include as much as 75% of an internal phase, it is found (practically) that at about 60% concentration phase inversion occurs.

Finally, it must be realized that some of the factors above are interrelated. For example, homogenization of the emulsion would decrease globule size and, by thus increasing their number and increasing the viscosity of the product.

### **Flocculation**

Flocculation involves the aggregation of the dispersed globules into loose clusters within the emulsion. The individual droplets retain their identities but each cluster behaves physically as a single unit. This would increase the rate of creaming. As flocculation must precede coalescence, any factor preventing or retarding flocculation would therefore maintain the stability of the emulsion.

### **Coalescence**

The coalescence (breaking) of oil globules in an o/w emulsion is resisted by the presence of a mechanically strong adsorbed layer of emulsifier around each globule. Coalescence results in separation of the two phases and emulsion failure (irreversible case).

Coalescence is usually attributed to the failure of the emulsifying agent in doing its job. It is necessary therefore, to ensure that any emulgent system used is not only physically but also chemically compatible with the active agent and with the other emulsion ingredients. Ionic emulsifying agents, for example, are usually incompatible with materials of opposite charge. Anionic and cationic emulgents are thus mutually incompatible.