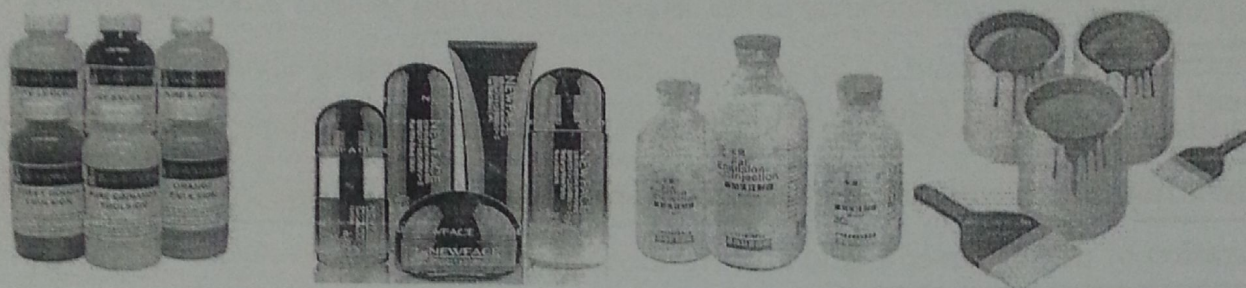


Pharmaceutical Technology II

EMULSION



An emulsion is a heterogeneous system of two immiscible liquids, usually water & oil, one of which is finely subdivided and uniformly distributed as droplets through the other. The dispersed liquid or the (internal phase) consists of globules of diameter usually exceeding $0.1\mu\text{m}$ which are distributed within the external or (continuous phase).

Generally, this system (oil & water) is unstable thermodynamically because the droplets are coalescence or united together to form two separated layers of water & oil. So when they will separate, they will be thermodynamically stable but pharmaceutically the dispersion is unstable; therefore, a third phase or component is necessary which is called the emulsifying agent to maintain the integrity of the product (the miscibility of the two liquids).

In conclusion, emulsion consists of 3 components aqueous phase, oil phase & emulsifying agent.

The aqueous phase may contain water soluble drugs, preservatives, coloring & flavoring agents. Usually it is desirable to use distilled or deionized water because calcium & magnesium ions that are found in hard water can have an influence on the stability of some emulsions.

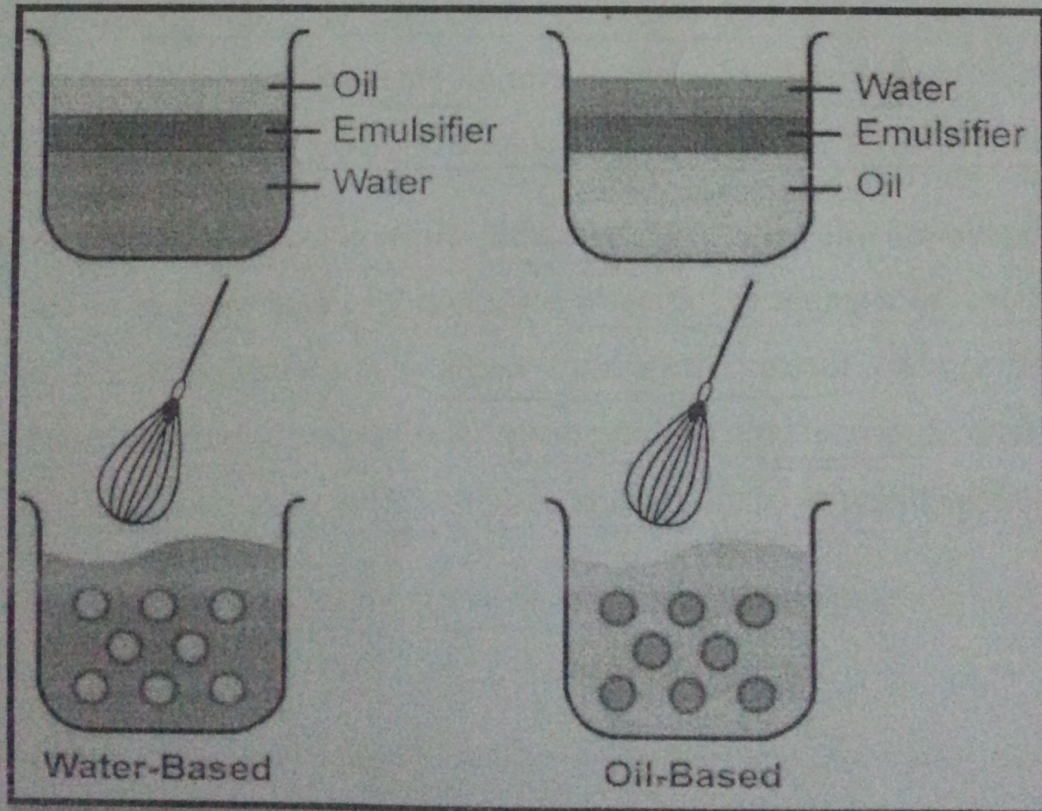
The oil phase frequently consists of fixed oil or volatile oil & some drugs that exist as oil such as oil soluble vitamins (e.g. vit. A & vit.D). Furthermore, antioxidants sometimes added to oil phase to prevent autoxidation of the oil & rancidity and/or destruction of any vitamin present. Flavoring agent & preservative that are oil-soluble can be added to oil phase, but they should exist in enough concentrations to protect both aqueous & oil phase.

The emulsifying agent is the most important component in emulsion formulation in term of achieving stability.

The general mechanism of emulsifying agent is that:

they form a film (thin layer) around the dispersed globules; this film acts to prevent coalescence and separation of the dispersed liquid as a separated phase.

-the system is heterogeneous system before the addition of the emulsifying agent will convert to a homogeneous one after the addition of the emulsifying agent.



Types of Emulsions:

According to the phases, emulsion has two types:

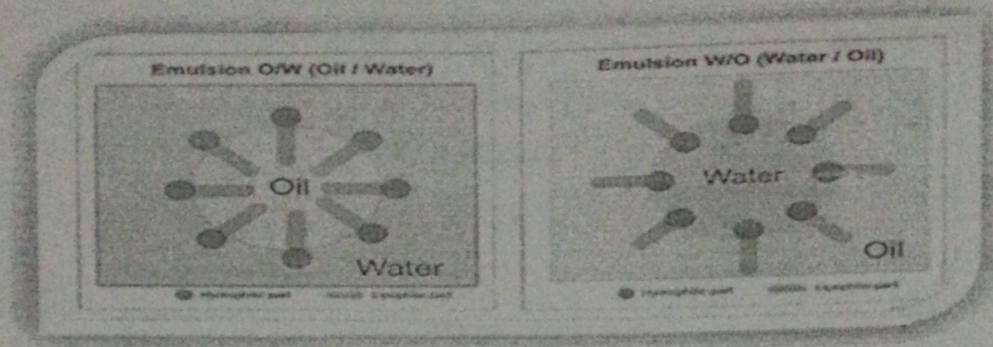
*Oil in Water Emulsion (O/W)

Pharmaceutical emulsions usually consist of mixtures of aqueous phase with various oils and waxes. If the oil droplets are dispersed throughout the aqueous phase, the emulsion is termed oil-in-water (o/w). Fats or oils for oral administration, either as medicaments in their own right, or as vehicles for oil soluble drugs, are always formulated as oil in water (o/w) emulsions. They are non-greasy and are easily removable from the skin surface and they are used externally to provide cooling effect and internally to also mask the bitter taste of oil. Water soluble drugs are more quickly released from o/w emulsion.

*Water in Oil Emulsion (W/O)

A system in which the water is dispersed as globules in the oil continuous phase is termed water-in-oil emulsion (w/o). Water-in-oil emulsions will have an occlusive effect by hydrating the stratum corneum and inhibiting evaporation of eccrine secretions.

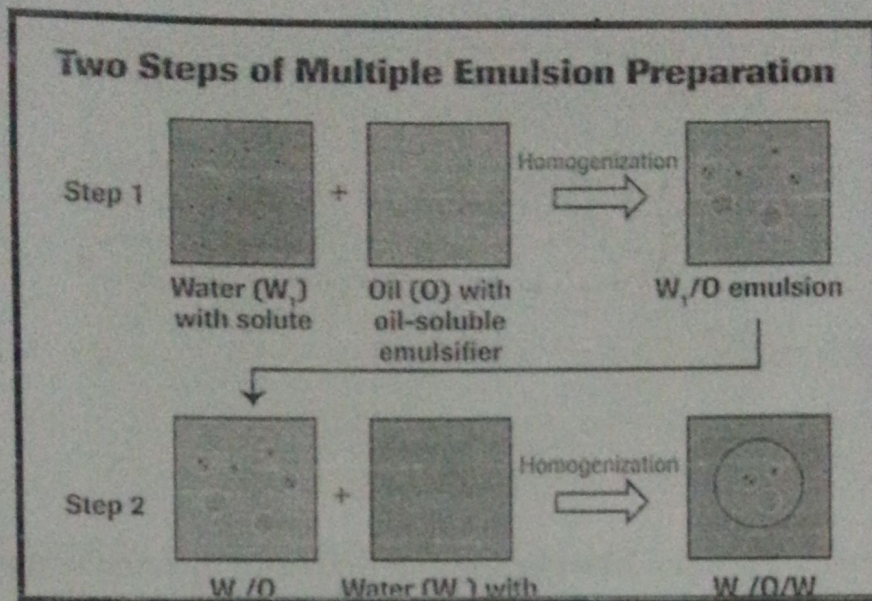
It has an effect on the absorption of drugs from w/o emulsions. W/o emulsion is useful for cleansing the skin of oil soluble dirt, although its greasy texture is not always cosmetically acceptable. They are greasy and not water washable and are used externally to prevent evaporation of the moisture from the surface of skin e.g. cold cream. Oil soluble drugs are more quickly released from w/o emulsion. They are preferred for formulation meant for external use like cream w/o emulsion.



*Multiple Emulsions

Multiple emulsions are complex systems. They can be considered as emulsions of emulsions, and have been shown to be secured in cosmetic pharmaceutical and separation sciences. It is a complex type of emulsion system in which many small water droplets can be enclosed within larger oil droplets, which are then dispersed in water; this gives a water-in-oil-in-water (w/o/w) emulsion. The alternative o/w/o emulsion is also possible.

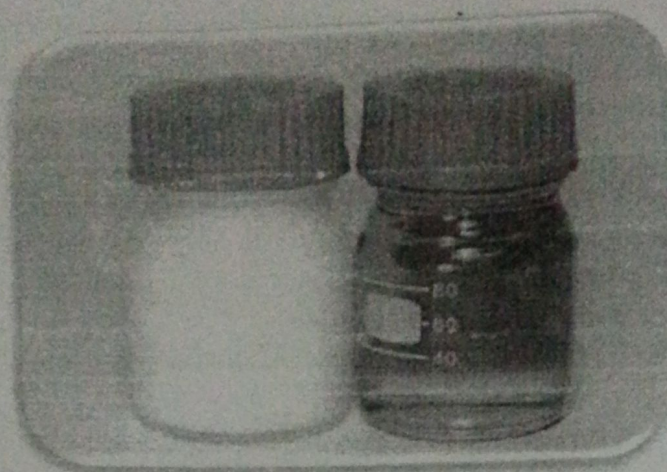
Multiple emulsions have been formulated as cosmetics, such as skin moisturizer. Prolonged release can also be obtained by means of multiple emulsions. These systems have some advantages, such as the protection of the ensnared substances and the possibilities of incorporating several active ingredients in the different compartments. Regardless of their importance, multiple emulsions have limitations because of thermodynamic instability and their complex structure.



*Microemulsions

Unlike the coarse emulsions, microemulsions are homogeneous, transparent systems that are thermodynamically stable (stabilized by interfacial film of surfactant frequently in combination with a co-surfactant with a droplet size usually in the range of 10-100 nm). Moreover, they form spontaneously when the components are mixed in the appropriate ratios. They can be dispersion of oil in water or water in oil, but the droplet size is very much smaller than coarse emulsions.

Although microemulsions have many advantages over coarse emulsions, particularly their transparency & stability, they required much larger amounts of surfactant for their formulation, which restricts the choice of acceptable components.



Difference between Macroemulsion (left) and Microemulsion (right)

Three factors are important in the determining the emulsion's type:

- ① Phase volume ratio: generally the phase which has the lower volume will be the internal phase, but sometimes the internal phase reaches ^{mca} 74% & still consider as internal phase, this occur due to the presence of strong emulsifying agent that coat a large volume of internal phase & disperse it in the internal phase.
- ② Emulsifying agent type: each emulsifying agent preferred one type of emulsion in which it coat the phase that it is insoluble in it & make the phase that it is soluble in it as the external phase. For example acacia, tragacanth & gelatin are water soluble, when used they will give o/w emulsion.
- ③ Order of mixing or Method of preparation: if we add oil gradually to water, then we get o/w emulsion while if we add water gradually drop by drop to oil, so we get w/o emulsion.

Tests for Identifying Emulsion Types

Several tests are used for identifying the emulsion type (w/o or o/w). Although, such tests may be applied rapidly, the results must be interpreted with caution.

1- Dilution test/miscibility test

Miscibility test involves the addition of continuous phase, e.g. in case of o/w emulsion; the emulsion remains stable upon the addition of water but will become unstable upon the addition of oil and the oil will separate. Vice versa is the case with w/o emulsion.

2- Staining test/dye-solubility test

In this test, a small amount of water soluble dye, such as methylene blue is added to the emulsion, now if water is the continuous phase (o/w emulsion); dye will dissolve uniformly throughout the system. If oil is the continuous phase (w/o emulsion), dye will remain as cluster on the surface of the system.

3- Electrical conductivity test

Water is a good conductor of electricity; hence, an emulsion with water continuous phase will readily conduct electricity while that with oil continuous phase will not.

Purpose of Emulsions and of Emulsification

Pharmaceutically, the process of emulsification enables the pharmacist to prepare relatively stable & homogeneous mixtures of two immiscible liquids. It permits the administration of a liquid drug in the form of minute globules rather than in bulk. The main advantage of such systems is that they increase the solubility and bioavailability of therapeutic drugs as well as the ability to favor the topical transport of hydrophilic drugs.

Classification of the emulsion:

Moreover, emulsions can be classified according to their use into:

1- Emulsion for internal use (oral & intravenous).

2- Emulsion for external use.

1- Emulsion For Internal Use

🍏 Oral Emulsion:

Fat and oils for oral administration are formulated as o/w type of emulsions. In this form, they are pleasant to take, and the inclusion of a suitable flavor in the aqueous phase will mask any unpleasant taste.

E.g. Castor oil in x-ray scanning, prepared as an oral emulsion to mask its disagreeable taste.

Also, the reduced particle size of the oil globules may render the oil more digestible and more readily absorbed, or if that is not the intent, more effective in its task, as for example the increase efficacy of mineral oil as a cathartic when it is in the emulsified form. Normally when fats & oils are ingested, they are emulsified in the duodenum by the bile salts; therefore, in emulsion the fat drug is already emulsified and doesn't need to be emulsified by the body's bile salt resulting in increasing the absorption of fats through the intestinal wall.

🍏 Emulsion for I.V. use:

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

It is prepared for purpose of administration of food (oily food) and medicinal oils like vitamin A, vitamin K and some sex hormones. As well as, this emulsion type could be used for diagnostic test like those of liver function.

Generally i.v. route is risky because the dosage form goes directly to the circulation, so any mistake will be dangerous even air bubble, so caution should be undertaken in the preparation of emulsion for i.v. injection with respect to sterility, globules size uniformity & the choice of the

emulsifying agent since there are some emulsifying agent can be toxic with other may cause allergy & hemolysis.

2- Emulsion For External Use

Emulsions are most widely used for external application. Semisolid emulsions are termed creams and more fluid preparations are called either lotions or, if intended for massage into the skin, liniments. Emulsions to be applied externally to the skin may be prepared as o/w or w/o emulsions, depending on some factors such as the nature of the therapeutic agents to be incorporated into the emulsions, the desirability for an emollient or tissue softening effect of the preparation and the condition of the skin surface.

Properties of emulsion for external use are:

1. It should have a proper consistency.
2. It should be spreads well over an affected area and should not run off.
3. It should be washed easily.
4. It should not stain the cloth.

Medicinal agents that are irritating to the skin generally are less irritating if present in the internal phase of an emulsified topical preparation than in the external phase from which direct contact with the skin is more prevalent. The solubility in oil and in water of a medicinal agent to be used in emulsified preparation would dictate to a great extent the vehicle in which it must be present and its nature would in turn suggest the phase of the emulsion that the resulting solution should be come.

On the unbroken skin, a w/o emulsion can usually be applied more evenly because the skin is covered with a thin film of sebum and this surface is more readily wetted by oil than by water. A w/o emulsion is also more softening to the skin, because it resists drying out and is resistant to removal by contact with water.

O/W emulsion is used for the topical application of water-soluble drugs, mainly for local effect. They do not have the greasy texture associated with oily bases and are therefore pleasant to use and easily washed from skin surfaces.

As mentioned earlier, w/o emulsions will have an occlusive effect hydration of the upper layers of the stratum corneum and the inhibition of evaporation of eccrine secretions. This type of emulsion is useful for cleansing the skin of oil-soluble dirt, although its creasy texture is not always acceptable. O/W emulsions are less efficient as cleansers but are usually more acceptable to the consumer, particularly for use on the hands.

Similarly, moisturizing creams, designed to prevent moisture loss from the skin and thus inhibit drying of the stratum corneum, are more efficient if formulated as w/o emulsions, which produce a coherent, water-repellent film.