Pharmaceutics I

Lecture (12)

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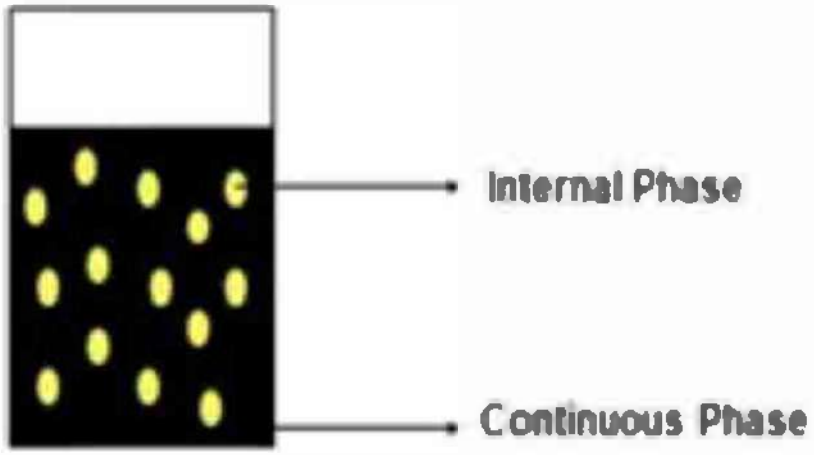
Pharmaceutical Emulsions

Introduction

An emulsion is a thermodynamically unstable two – phase system consisting of at least two immiscible liquid phases, one of which is dispersed uniformly as globules throughout the other liquid phase, and stabilized by the presence of an emulsifying agent.

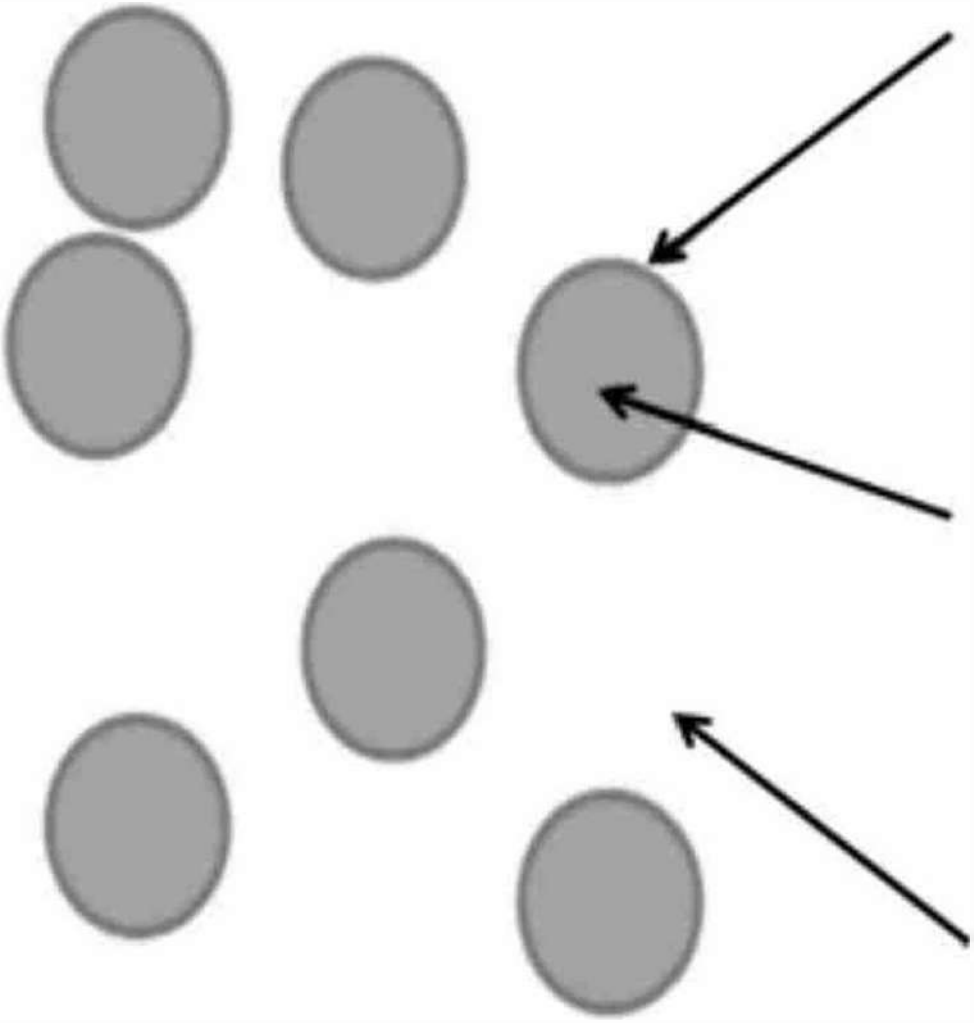
The liquid that is dispersed into small droplets is called the dispersed phase, internal phase or discontinuous phase while, the other liquid is called the dispersion medium, external or continuous phase.



Emulsions are a part of a more general class of two – phase systems of matter called colloids. Although the terms colloid and emulsion are sometimes used interchangeably, emulsion tends to imply that both the dispersed and the continuous phase are liquid.

Emulsions are kinetically unstable systems because the globules of the dispersed liquid tend to recombine to form large globules (coalescence) until all of the dispersed globules have coalesced. An emulsifying agent is usually added to the system to prevent the coalescence of the globules and maintain the integrity of the individual globules of the dispersed phase.

Fluid emulsions can also suffer from creaming; the migration of one of the substances to the top of the emulsion.



Emulsion Composition

The interfacial layer (emulsifying agent) is essential to stabilize the emulsions.

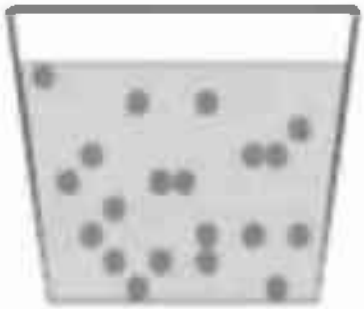
Oily phase (dispersed phase) has limited effects on the properties of the emulsion.

Aqueous phase (continuous medium). Aqueous chemical reactions affect the interface and hence the emulsion stability.

A

A. Two immiscible liquids, not emulsified.

B

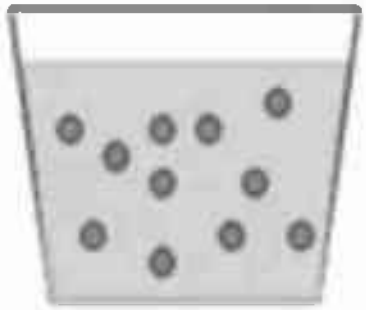


B. An emulsion of Phase B dispersed in Phase A.

C

C. The unstable emulsion progressively separates.

D



D. The surfactant positions itself on the interfaces between Phase A and Phase B, stabilizing the emulsion.

Over time, emulsions tend to revert to the stable state of oil separated from water. Surface active substances (surfactants) can increase the kinetic stability of emulsions greatly so that, once formed, the emulsion does not change significantly over years of storage.

Emulsions are thermodynamically unstable systems and thus do not form spontaneously. Energy input through shaking, stirring, homogenizers, or spray processes are needed to form an emulsion.

Emulsions tend to have a cloudy appearance, because of many phase interfaces (the boundary between the phases is called the interface) which scatter light that passes through the emulsion.

Types of Emulsions

Pharmaceutical emulsions can be classified based on the dispersed phase into:

Oil – in – water (o/w): oil droplets dispersed in water. Oil is the dispersed phase and an aqueous solution is the continuous phase.

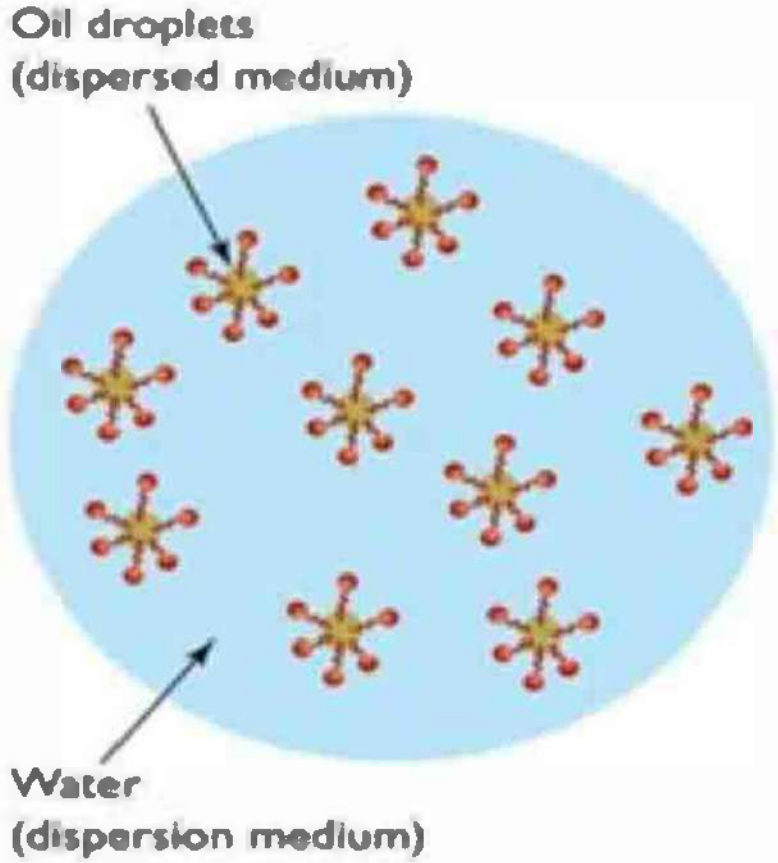
Water – in – oil (w/o): water droplets dispersed in oil. Water or an aqueous solution is the dispersed phase and oil or oleaginous material is the continuous phase.

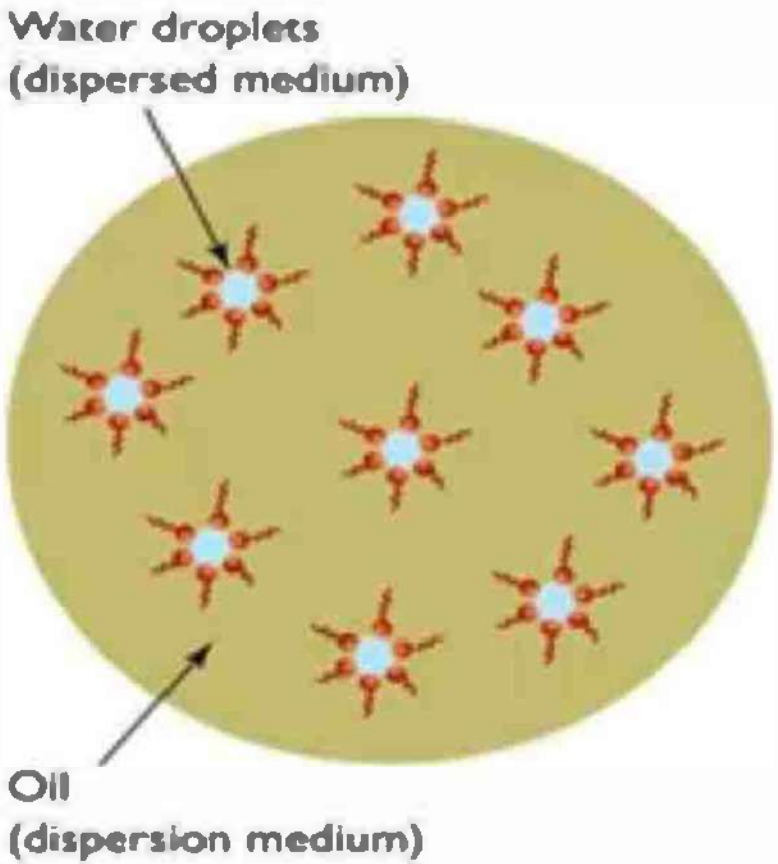
Oil – in – water – in – oil (o/w/o): oil in an aqueous emulsion is dispersed in oil as a multiple emulsion.

Water – in – oil – in – water (w/o/w): water in oil emulsion is dispersed in water as a multiple emulsion.

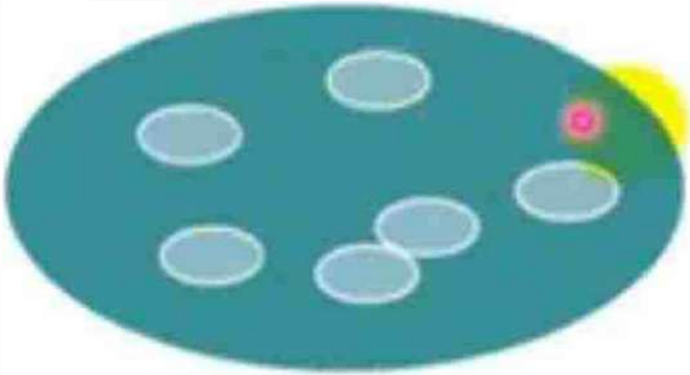
Oil – in – water (o/w) emulsions are used for oral and intravenous administration.

Water – in – oil (w/o) emulsions are used as intramuscular injections for a depot effect (extended – release or long – acting effect).

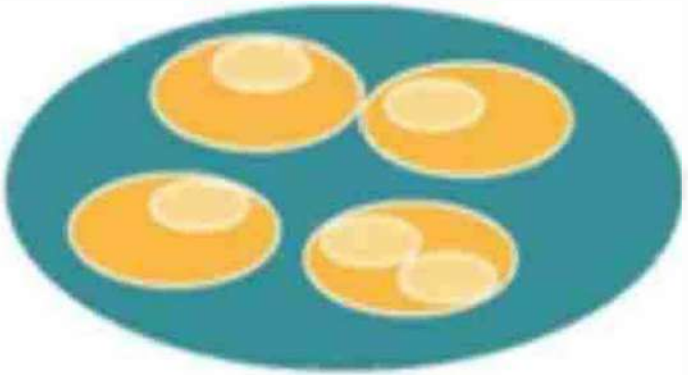




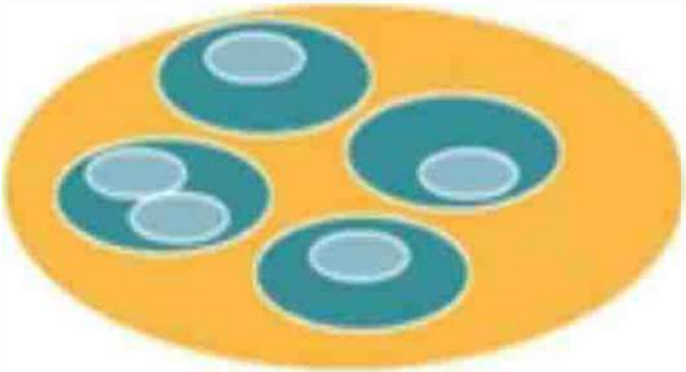
Single Phase System



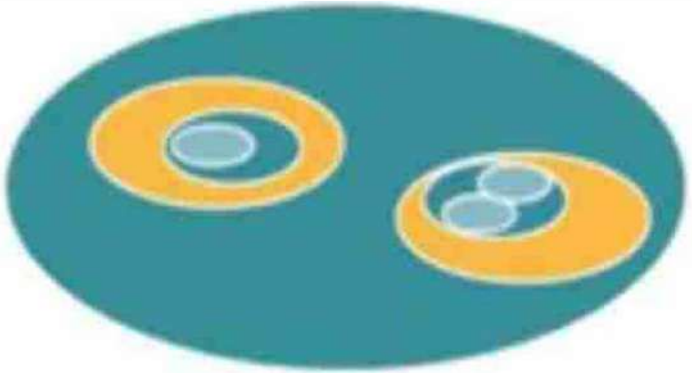
Oil in Water Emulsion



Water in Oil Emulsion



Water in Oil in Water Triple Emulsion



Water

Water Soluble Drug

Oil

Oil Soluble Drug

Pharmaceutical emulsions can also be divided according to droplet size into microemulsions, nanoemulsions and macroemulsions.

Microemulsions: 0.01 – 0.1 μm.

Nanoemulsions: 0.1 – 0.5 μm

Macroemulsions: > 1 μm.

Identification and Determination of Emulsion Type

Miscibility tests (dilution of emulsions): an emulsion will mix with a liquid that is miscible with the continuous phase. Therefore an o/w emulsion is miscible with water and a w/o emulsion is miscible with an oil.

Conductivity measurement: systems with an aqueous continuous phase will conduct electricity, whilst systems with an oily continuous phase will not.

Staining tests: a filter paper soaked in cobalt chloride solution and allowed to dry turns from blue to pink on exposure to stable o/w emulsions.

Dye solubility test: sudan III dye is soluble in oil while, the dye methylene blue is soluble in water.

Advantages of Pharmaceutical Emulsions

Pharmaceutical emulsions may be used to deliver drugs with low – aqueous solubility. For instance, in o/w emulsions, the therapeutic agent is dissolved in the internal oil phase. Following oral administration, the oil droplet containing the drug may be then absorbed using the normal absorption mechanisms of oils. The solubility of many drugs is increased when they are incorporated into emulsions.

Emulsions may be used to mask the unpleasant taste of a therapeutic agent, by dissolving it in the internal phase of an o/w emulsion. The external phase (water) may be then formulated to contain the appropriate sweetening and flavoring agents.

Pharmaceutical emulsions may be used to administer oils having a therapeutic effect. For example, the cathartic effect of liquid paraffin is enhanced following administration to the patient as droplets within an o/w emulsion. Its unpleasant taste or odor can be masked partially or wholly, by emulsification. Furthermore, the taste of the oil can be masked using a sweetening and flavouring agent.

Emulsions are employed for total parenteral nutrition (TPN).

Pharmaceutical emulsions may be employed to deliver drugs to patients who have difficulty to swallow solid dosage forms.

The stability of many drugs which are unstable in aqueous solutions is increased when incorporated into an emulsion.

If the therapeutic agent is irritant when applied topically, irritancy may be reduced by formulating it within the internal phase of an o/w emulsion.

The appearance of oleaginous materials intended for topical applications is usually improved when formulated in an emulsified form.

Prolonged – drug action and increased bioavailability are often obtained when drugs are incorporated into emulsions.

Disadvantages of Pharmaceutical Emulsions

- Pharmaceutical emulsions are thermodynamically and kinetically unstable systems, therefore they must be correctly formulated to avoid the separation of the two phases (emulsion stabilization).
- Pharmaceutical emulsions are sometimes difficult to manufacture.

Pharmaceutical Applications of Emulsions

Oral emulsions: liquid o/w emulsions of water – insoluble liquids such as fat – soluble vitamins are administered orally. The unpleasant taste or odor can be masked by emulsification.

External emulsions: liniments, lotions (liquid) and creams (semi – solid) are topical emulsions for external uses.

Parenteral emulsions: o/w emulsions are used for total parenteral nutrition (TPN) and either o/w or w/o emulsions are used as intramuscular injections. Intramuscular injections of some water – soluble drugs or vaccines are able to provide a slow – release and therefore a greater antibody response and longer – lasting immunity.

- Sterile o/w emulsions are used to deliver oily nutrients and drugs intravenously to patients, using non – toxic emulsifying agents (Tocosol®).

- Emulsions in areosols can be used to produce a foam.

- Rectal administration of oils and oil – soluble drugs, where, the absorption and penetration of medicament is enhanced by emulsification.

O/w emulsions are used instead of w/o emulsions as oral dosage forms because...

The continuous water phase would be more palatable to the mouth and the liquid consistency would be easier to flow through the mouth and down the throat.

By dispersing or milling a foul – tasting drug in the oil phase, the taste buds and smell sense will be unaware of the agent passing by.

In addition, in o/w emulsions, the manufacturer can add sweeteners and flavors to the continuous phase which will be experienced by the taste buds as the medication passes over them.