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RESEARCH ARTICLE

Current Compensations in Emulsion Type Pharmaceutical Formulation: An Overview

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ABSTRACT

In modern years, the quantity of medicine and drug treatments has larger extremely which are moderately often more strong. Pharmacy research reveals exclusive data which is growing day by day. Emulsion are important dosage formulation they are continuously used from ancient time. In this overview we discuss the development of emulsion technology also focused on properties of emulsion & formulation methods by different equipment used for this consideration. With different identification tests. Multiple emulsion, Microemulsion, Non-aqueous emulsion, Liposome emulsion, Emulsion polymerization, Nanoemulsion are new trends in emulsion technology.

Keywords: Microemulsion, multiple emulsion, multiple emulsions, nanoemulsion oil/water, oil-in-water-in-oil emulsions, water/oil, water-in-oil-in-water

INTRODUCTION

They are oral and semisolid preparations in which medicaments are dissolved in liquid. Emulsions are defined as thermodynamically unstable heterogeneous biphasic system in which one phase is dispersed other liquid phase. In emulsion, both phases are liquid and those agents which are used to prepare emulsion are known as emulsifying agents such as acacia. The range of the molecules of emulsion is 0.1–100 µm. Milk is the ideal and natural emulsion.

This biphasic system consisting immiscible liquids, where one phase is dispersed as fine droplets in other liquid phase which is alleviated by the presence of an emulsifying agent. The phase that is present as fine droplet is called the disperse phase/internal phase, and the phase in which the droplets are suspended is known as the continuous phase/external phase.

The diameters of the droplets constituting the dispersed phase usually range from approximately 10 nm to 100 µm, i.e. the droplets may exceed the usual size limits for colloidal particles.[1]

The majority of emulsions have droplets with diameters of 0.1–100 µm. An emulsion is stable if it shows properties such as uniform dispersion of fine and monosized droplets of the internal phase, which should not aggregate, and if they do, must not combine to form large droplet. The internal droplets should not cream up or down, and if they do, the cream layer should be redispersible.[1]

THE STABLE EMULSION HAVE THE FOLLOWING PROPERTIES[2]

1. They must not containing phase inversion.
2. They must not degraded by microbes on storage.
3. It must be stable at various temperature (50°C, 400°C, and 500°C).
4. It should not form any layer to the surface of cream.
5. They should not be rancid or degraded by oxidation as oil and phase.

If there is any deviation from this ideal behavior, emulsions are considered as instable.

TYPES OF EMULSION[2,3]

1. Oil/water (o/w)
   - Dispersed phase - oil
   - Continuous phase - water.
2. Water/oil (w/o)
   - Dispersed phase - water

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- Continuous phase - oil.

3. Multiple emulsion
   a. Water-in-oil-in-water (w/o/w)
   b. Oil-in-water-in-oil (o/w/o).
4. Miscellaneous

They have commonly in the range of 0.25–25 µm.

Oil in water

An emulsion is termed an o/w emulsion if the dispersed phase is an organic material and the continuous phase is water or an aqueous solution and is termed w/o if the dispersed phase is water or an aqueous solution and the continuous phase is an organic liquid (an "oil") [Figure 1].

When the oil phase is dispersed as globules throughout an aqueous continuous phase, the system is referred to an o/w emulsion. It is formed if the aqueous phase constitutes more than 45% of total weight and if a hydrophilic emulsifier is used.

For example: Sodium laureth sulfate, sodium oleate, and glyceryl monostearate.

Water in oil

A w/o emulsion is sometimes called an inverse emulsion. The term "inverse emulsion" is misleading, suggesting incorrectly that the emulsion has properties that are the opposite of those of an emulsion. Its use is, therefore, not recommended.[1]

If an aqueous phase is dispersed as globules and the oil phase serves as the continuous phase, the emulsion is termed as w/o emulsion.

For example: Spans, cholesterol, and wool fats [Figure 1].

Multiple emulsion

These emulsions recognized as emulsions of emulsions, liquid membrane system, or double emulsions. They are also novel carriers having both o/w and w/o emulsions found in the one system [Table 1]. The inner dispersed droplets in multiple emulsions are separated from the outer liquid phase by a layer of another phase.[4] This is mainly stabilized by lipophilic and hydrophilic surfactants, respectively.

a. w/o/w emulsion system
   In this system, an organic phase separates internal and external aqueous phases. In further words, it is a system in which oil droplets may be surrounded by an aqueous phase, which in turn encloses one or some water droplets.
b. o/w/o emulsion system
   In this system, an aqueous phase separates internal and external oil phase. In further words, it is a system in which water droplets may be surrounded in oil phase, which in true encloses one or additional oil droplets [Figure 2].

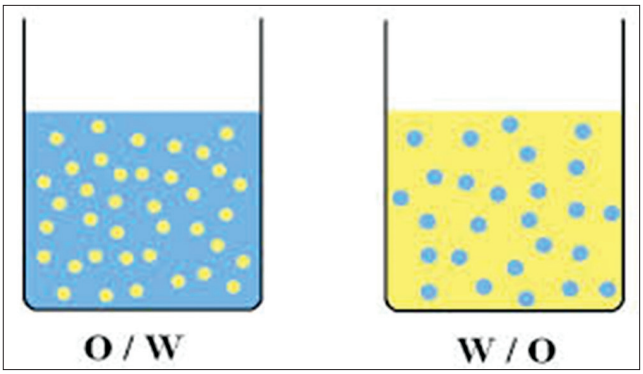

Figure 1: Oil/water and water/oil type emulsion

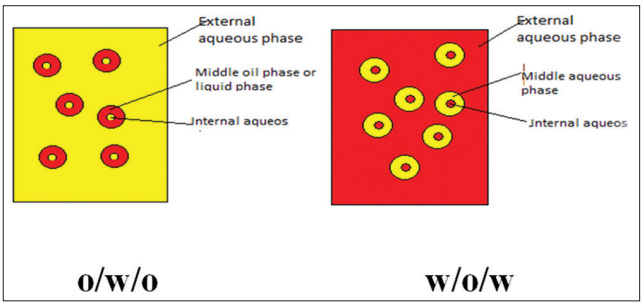

Figure 2: Oil-in-water-in-oil and water-in-oil-in-water type of emulsion

Table 1: Types of emulsion on the basis of size

Emulsion	Globule size range
Coarse emulsion	25.0 µm
Fine emulsion	5.0 µm
Microemulsion of micellar emulsion	10–75 µm

Types of emulsion on the basis of size

Miscellaneous

This type of emulsion is commonly in the range of 0.25–25 µm.

Emulsion is prepared for[2]

1. Enhance the stability of those drugs which are unstable in aqueous solution.

Table 2: Comparison of different emulsion[5]

Criteria	Microemulsion	Multiple emulsion	Non-aqueous emulsion	Liposome emulsion	Emulsion polymerization	Nanoemulsion
Type	Both o/w or w/o	w/o/w or o/w/o	o/o type	o/w or w/o	o/w or w/o	o/w or w/o
Particle size	0.01–10 µm	0.1–100 µm	0.1–100 µm	0.1–100 µm	0.1–100 µm	10–200 nm
Surfactant	All	Lipophilic and non ionic	Oil soluble	HLB 4–7	Mostly w/o	All
Composition	Oil + water + surfactant + cosurfactant	Oil + water + surfactant	Oil + surfactant	Oil + water + Lipophilic material + surfactant	Oil + water + surfactant + polymer material	Oil + water + surfactant
Phase	Single phase	Triple phase	Single phase	Double phase	Double phase	Single phase
Purpose	Rapid action	Prolonged action and taste masking	Reservoir	Drug targeting	Manufacture of polymer	Rapid action
Marketed example	Sandimmune neoral novartis	Sorbitan monooleate, sorbitan trioleate	Silicone (dimethicone, cyclopentasiloxane)	Lubrizol liposome emulsion	TufCOR™	Indomethacine, indobene gel

o/w: Oil/water, w/o/w: Water-in-oil-in-water, o/w/o: Oil-in-water-in-oil

2. It improves the appearance of material which is usually intended for topical application.
3. It improves the taste of medicinal agents.
4. It improves penetration.
5. It enhances the rate of absorption.
6. They have prolonged drug action.
7. It improves the solubility.

Tests for identification of emulsion[6] [Table 2]

- Dilution test: Emulsion can be diluted only with external phase
- Dye test: Water or oil-soluble dyes
- $CoCl_2$/filter paper test: Filter paper impregnated with $CoCl_2$ and dried (blue) changes to pink when o/w emulsion is added
- Fluorescence: Some oils fluoresce under UV light.
    1. Wet gum method
    2. Dry gum method
    3. Bottle method
    4. Soap method.

The preparation of emulsion is carried out using thickening agents (emulsifying agent), antimicrobial agents (alcohols, aldehydes, formaldehyde, and phenol), antioxidant (ascorbic acid), and organoleptic agent.

Equipments used[2]

1. Kenwood mixer
2. Silversion mixer
3. The Q.P. emulsifiers
4. Colloid mills
5. Standard slurry type dispersed mixer with the vaned rotor
6. Standard paste type dispersed mixer with the clipped rotor
7. Two-stage homogenizer.

METHOD OF PREPARATION OF EMULSION[2,3,8,12]

There are different methods of prepration of emulsion [Table 4].They are also identify By given [Table 3]

(A) Wet gum method

(B) Dry gum method Bottle method

(C) Soap method

Table 3: Types of emulsion

Name of test[6-11]	Apply on	Type of emulsion
1.Dilution test - the emulsion is diluted either with oil or water	Stable and unstable both	w/o and o/w
2.Conductivity test - the basic principle of this test is that water is a good conductor of electricity	Stable and unstable both	w/o and o/w
3.Dye solubility test	Stable and unstable both	w/o and o/w
4.Cobalt chloride test - filter paper soaked in cobalt chloride solution is dipped in to an emulsion and dried	Only stable	o/w
5.Filter paper test	Stable and unstable both	w/o and o/w

w/o: Water/oil, o/w: Oil/water

Table 4: Method of prepration of emulsion

Wet gum method	Dry gum method	Bottle method	Soap method
a.Two parts of water and one parts of acacia both are triturated with a mortar and pestle until the mucilage is obtained b.Oil is to be added drop by drop with continuous trituration by this a cream or primary emulsion is produced **c.**Make up the volume with continuous trituration	a.Oil is mixed with acacia by mortar and pestle until the acacia powder is uniformly distributed b.Purified water is added rapidly with trituration until primary emulsion is obtained c.Add additives and make up the required	a.Oil is mixed with acacia with the bottle uniformly b.Add a measured amount of water and shack until uniform emulsion is produced	a.Oil and aqueous solution which containing a sufficient amount of alkali b.Shaking vigorously to form soap c.This method is suitable for o/w and w/o type of emulsion

w/o: Water/oil, o/w: Oil/water

NEW TRENDS IN EMULSION TECHNOLOGY

Microemulsion

Microemulsions, a moderately recent detection in 1959, have found applications in a wide variety of chemical and industrial processes.[13]

It consists of homogenous and transparent system having low viscosity. This system contains a high percentage of oil, water, and emulsifier mixture.[5,14]

IUPAC defines microemulsion as dispersion made of water, oil, and surfactant(s) that is an isotropic and thermodynamically stable system with dispersed domain diameter varying approximately from 1 to 100 nm, usually 10–50 nm.

Advantages

- It is very easy to prepare.
- It is very good system to raise the rate of absorption.
- It is able to improve the solubility of lipophilic drugs.
- It is thermodynamically more stable system.
- It is the best system to minimize first pass metabolism.

Disadvantages

- Additional use of excess amount of surfactant and cosurfactant in puckers cost.
- Excess concentration of surfactants can lead to mucosal toxicity.

Multiple emulsions

Multiple emulsions are more complex. Their two-phase counterparts from the standpoint of formulation, stability, and drug release.[15]

They are novel carrier system which is complex and polydispersed in nature where both w/o and o/w emulsion exists simultaneously in a single system. Lipophilic and hydrophilic surfactants are used for stabilizing these two emulsions, respectively.

Advantages of multiple emulsions

a. They can mask the bitter taste and odor of drugs, thereby making them more palatable, for example, castor oil, cod liver oil, and chloroquine phosphate.
b. They can be used to prolong the release of

the drug, thereby providing sustained release action.

c. Essential nutrients such as carbohydrates, fats, and vitamins can all be emulsified and can be administered to bedridden patients as sterile intravenous emulsions.
d. Emulsions provide protection to drugs which are susceptible to oxidation or hydrolysis.

LIMITATIONS OF MULTIPLE EMULSIONS

The main problem associated with multiple emulsions is their thermodynamic instability and their complex structure, which has severely limited their usefulness in the many applications of multiple emulsions.

STABILITY OF MULTIPLE EMULSION

- Leakage of the contents from the inner aqueous phase.
- Expulsion of internal droplets in the external phase.
- Constriction or distension of the internal droplets due to osmotic gradient across the oil membrane.
- Flocculation of internal aqueous phase and multiple emulsion droplets.
- Disruption of oil layer on the surface of internal droplets.
- Phase separation.

Nanoemulsion

They are also called miniemulsions. The use of nanotechnology in pharmaceuticals, and medicine has grown over the past few years. They have size 300 nm, so-called nanoemulsions. Nanoemulsions are transparent systems, kinetically stable. They are thermodynamically stable. Nanoemulsions are categorized as multiphase colloidal dispersion.[16]

ADVANTAGES OF NANOEMULSION

- Much higher surface area and free energy than macroemulsions that make them an effective transport system.
- They are not showing problems of inherent creaming, flocculation, coalescence, and sedimentation, which are commonly associated with macroemulsion, which are commonly associated with macroemulsions.
- They are nontoxic and nonirritant.
- They can be taken by enteric route.
- They do not damage healthy human and animal cells.

APPLICATIONS OF NANOEMULSIONS

1. It is used in cosmetics.
2. It is used to deliver either recombinant protein.
3. It is used in antimicrobial.
4. It is used in cell culture technology.
5. It is also used in cancer therapy.
6. Increases the rate of absorption.
7. Helps in solubilizing lipophilic drug.

DISADVANTAGES OF NANOEMULSION-BASED SYSTEMS[11]

1. Use of a large concentration of surfactant and cosurfactants necessary for stabilizing the nanodroplets.
2. Limited solubilizing capacity for high melting substances.
3. The surfactant must be nontoxic for pharmaceutical applications.

CONCLUSION

The role of the pharmacist is continuously increased with the development of technology to achieve the modern technology of emulsion. Their use makes the process fast, easy, smooth, effective, and error free.

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