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Research Paper

A Review on Basics of Pharmaceutical Emulsion.

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Abstract :-
The pharmaceutical term "emulsion"is most time used to indicate preparations prepared for internal use.this pharmaceutical dosage form is thermodynamically unstable and must be stabilized by the addition of emulsifying agent.(The immiscible liquids made miscible with the help of emulsifying agent).Emulsified system range from lotions having comparatively low viscosity to creams which are more viscous.There are two basic types of emulsions, i.e, oil in water (O/W) and water in oil (W/O). In addition to these two types, a relatively complex emulsion,called multiple emulsions can be formulated. Emulsion are generally have certain advantages over the dosage forms as well as the drug solubilized may be more bioavailable gastrointestinal problems as well as first pass metabolic effect are also avoided.

Keywords :- *Emulsion, Emulsifying agent, Stability of emulsion.*

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I. INTRODUCTION :-

An emulsion is a two phase system consists two completely immiscible liquid one of which is dispersed as fine globules into others.Emulsion is biphasic system prepared by combining two immiscible liquid.

- **DISPERSED PHASE**: - It is also known as **dispersed phase/internal phase**. The phase which is dispersed into dispersion medium is known as dispersed phase.
- **DISPERSIONMEDIUM**: - It is also known as **continuous phase/external phase** in which the dispersion medium is dispersed is known as dispersion medium.

EMULSION:- It is thermodynamically unstable system which can be stabilized by the presence of an emulsifying agent (emulsifier).Emulsifying agent is an intermediate or interphase between two dispersion phase or dispersion medium system. In Pharmaceutical practical the emulsion is used for liquid preparation for oral use. Emulsion is also used for external use is referred to lotion or liniments. The particle size of globules is ranging from 0.1 to 100 micrometer. System of at least two immiscible phases are called dispersion. A disperse system is made of a dispersed phase in a continuous flow.

There are three major types of dispersions based on the physics of dispersed phase, namely the following: foam of a gas in a liquid mixture; suspensions of a solid in a liquid blend; as well as emulsion of a liquid in a liquid system. [1] Emulsion is a mixture of two immiscible liquids, which generally forms during various chemical processes/equipment such as water flooding of heavy oil reservoirs, water treatment membranes, and packed bed separators. [2] For instance, emulsions can be categorized as water-in-oil emulsion (with water droplets as a dispersed phase in the flow of oil as the continuous phase), oil-in-water emulsions (with oil droplets in the flow of water), and more complex configurations of emulsions such as water-in-oil-in-water, Oil-in-water-in-oil emulsions.[3] Crude oil is blend of hydrocarbons with different sizes that can have various applications in the chemical and energy industries. The type and composition of crude oils (as vital factors) play important roles in the development of emulsions. Water-in crude oil emulsions are stable in the dispersions of water droplets in a continuous flow of oil, stabilized by heavy particles/components (naturally occurring emulsifiers) present in the oil. Emulsion formation is a recurring issue that is undesirable in the oil industry as it might cause flow blockage, inefficient separation, operational problems, corrosion, and consequently, adding high costs to the transportation, processing, and separation units.[4] For instance, the dispersed water droplets occupy a considerable volume of the processing facilities and pipelines, VOLUME 97, JANUARY 2019 Leading to appreciable variations in the normal operating conditions and an increase in operational expenses. Furthermore, the physical properties of oil are significantly altered owing to the presence of emulsions.[5]

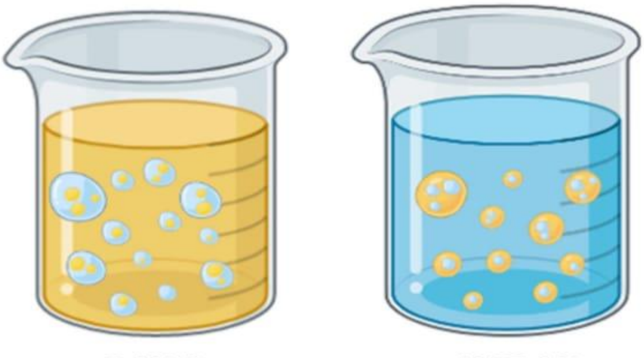
TYPES OF EMULSION:-

1) **Primary emulsion** containing one internal phase, for example

a) Water in oil emulsion (w/o):-

b) Oil in water emulsion (o/w):-

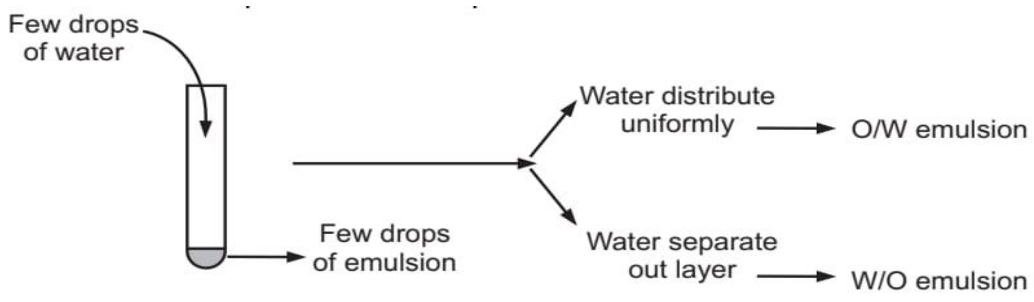
2) **Secondary emulsion** also known as multiple emulsion contain two internal phases for instances, multiple emulsions are water-in-oil-in-water (w\o\w) or oil-in-water-in-oil (o\w\o).



It can be used to delay released or to increase the stability of the active compound.

Identification Tests for Emulsion:-

1) Dilution test :-

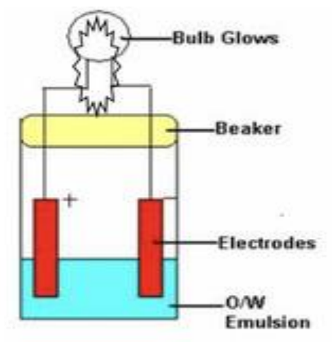


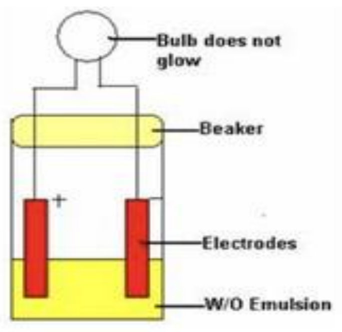
The addition of water to w/o emulsion and oil to o/w emulsion leads to cracking of emulsion and also leads to separation of the phases and dilution of emulsion.

2) Conductivity test :-

Water is a good conductor of electricity where as oil is an non conductor of electricity the conductivity test can be performed by dipping a pair of electrodes connected to a low voltage bulb which glows on passing the electric current through the emulsion o/w type due to presence of water in continuous phase but in case of w/o type the bulb doesn't glow because the oil is present in the continuous phase

i.e- o/w = current flow
w/o = current do not flow

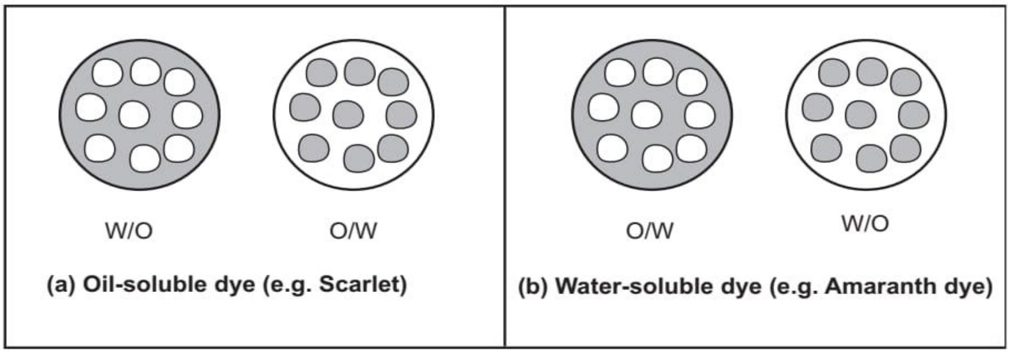




Conductivity test diagram

3) Dye test :-

The water soluble dye will dissolve in aqueous phase (water) where as oil-soluble dye will dissolve in the oily phase (oil) for e.g. amaranth solution used for o/w emulsion, scarlet/sedan used for w/o emulsion.



4) Fluorescent test :-

Oil has an capability to absorb the UV light and gives fluorescence while water does not gives the fluorescence. Hence, o/w emulsion shows spotty pattern while w/o emulsion fluorescence.

5) Cobalt chloride test :-

Cobalt chloride is water soluble substance. Small amount of cobalt chloride is add in unknown emulsion when the cobalt chloride is dissolve in the emulsion is o/w type because water is continuous.

Methods of preparation :-

1. Dry Gum Method :-
2. Wet Gum Method :-
3. Bottle Method :-

DRY GUM METHOD:

- Measure requires quantity oil.
- Calculated quantity of gum acacia add with rapid triturate.
- Add required quantity of water with rapid triturate until clicking sound occurs.
- Now the product becomes white or nearly white.
- Now the product called primary emulsion.
- Add more water to make required quantity.

WET GUM METHOD:-

- Calculate the quantity of oil, water, gum.
- Gum acacia + water form mucilage.
- Add require quantity of oil in small portion with rapid trituration.
- Product becomes white and nearly white.
- Primary emulsion.
- Add more water in small portion with uniform trituration to produce final volume.
- Stir thoroughly as to form a uniform emulsion.

BOTTLE METHOD:-

- It is only for volatile and non viscous oil.
- Measure quantity of oil and transfer into flask.
- Add gum acacia.
- Now shake the flask until the gum and oil mix properly.
- Add water.
- Shake the mix vigorously to form a primary emulsion.
- Add more water to make up the volume of emulsion.

FORMULATION OF EMULSION

1. Emulsifying agent
2. Preservatives
3. Antioxidants
4. Flavoring agent

EMULSIFYING AGENT: There are larger number of emulsifying agent no single agent have all properties required so two or more emulsifying agent used to make stable emulsion.

IDEAL PROPERTIES OF EMULSIFYING AGENT

1. It should be capable of reducing interfacial tension it should be compatible with other ingredients.
2. It should be non toxic.
3. It should be chemically stable.
4. It should be capable to reduce required consistency.

EMULSIFYING AGENTS:-

1. Natural

- Vegetable source: Agar, Gum acacia, Pectin, Starch, Irishmoss.
- Animal Source: Wolf fat, Egg yolk, Gelatin.

2. Semi synthetic Polysaccharides

- Methyl Cellulose
- Sodium Carboxyl

3. Synthetic

- Anionic

- Cationic
- Non Anionic

4. **Inorganic**

Milk Of Magnesia

- Magnesium oxide
- Magnesium Trisilicate
- Magnesium Bentonite

5. **Organic**

- Alcohol
- Carbo Waxes
- Cholestrol
- Lecithins

ANTIOXIDANT:

During storage fats ands and emulsifying agents undergo oxidative by atmospheric oxygen so to prevent this anti oxidants are used. E.g. tocopherol, Gallic acid, propyl gallate and ascorbic acid.

Flavoring agents:

These are selected by trial and error method.

E.g. vanillin used for- liquid paraffin emulsion.

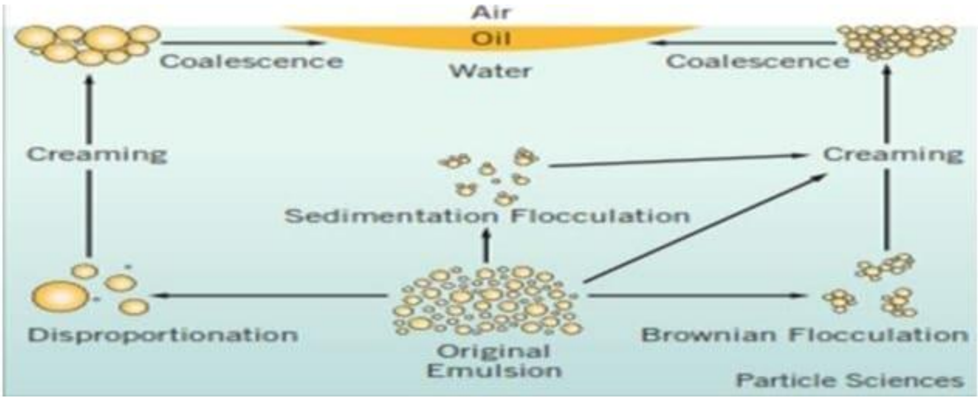
Preservative:

EXAMPLES benzoicacid,methyl and propylparaben, chloroform[0.25%], chloroaerosol [0.1%].

Stability of Emulsion

The process by which an emulsion completely breaks is generally considered and to be governs by four different droplets loss mechanism.

- Brownian flocculation
- Creaming
- Sedimentation flocculation
- Disproportion



Creaming

It is derived from its name the most commonly known example of a de-emulsification process. The separation of milk into it's the cream and skim milk components creaming is not an actual breaking but a separation of the emulsion within the two emulsions one of which the cream is richer in the disperse phase than the other. Creaming is the principle process by which disperse phase separation from an emulsion and its typically the precursor to coalescence.

The creaming rate can be estimated from the stokes equation.

$$\frac{v = 2r^2(p - p_0)g}{9n}$$

Where**,**

v = Creaming rate,

r = Droplet radius

p = Density of droplet

p_0 = Density of the dispersion medium

n = Viscosity of the dispersion medium

g = Local acceleration due to gravity.

Flocculation:-

The aggregation of droplets to give 3d cluster coalescence occurring importantly all droplets maintain their own integrity and remain as totally separated entities it results when there is a weak net attractive between droplets and arises through various mechanism.

Flocculation may be subdivided into two general categories that resulting from sedimentation aggregation as well as from Brownian motion aggregation of the droplets.

Disproportion:-

The pressure of disperse material is greater for little droplets than bigger droplets as per the Laplace equation. It is depend on diffusion of disperse phase molecule from smaller to larger droplets through the continued phase.

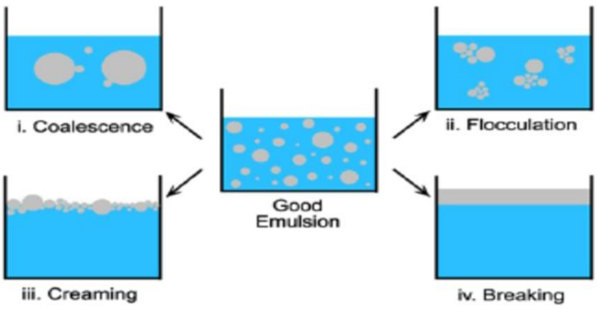
Coalescence :-

In this process emulsifier film around the globules is destroyed to some extent.

A few globule tend to fuse with each other and form bigger globules.

Breaking :-

Completely separation of phases irreversible process. It may be brought about by the addition of an electrolyte by changing the phase volume ratio or by temperature changes by changing chemical nature of emulsifiers.



THEORIES OF EMULSIFICATION:-

Theories of emulsification explain the action of emulsifying agents in stabilizing emulsion. It is the surface or more accurately the interface between the two immiscible liquids that plays the foremost role. Emulsifying agents affect the interface in such a way to obtain stable emulsions (John, 1976). There are many theories proposed to explain the action of emulsifying agents in the stabilizing emulsions. Among these theories, some may be applied. Specific emulsifying agents under certain condition like pH of the system and proportion of the two phases. The most well-known theories include surface tension theory, the oriented wedge theory and the interfacial film theory (Paul,2005).

Surface tension theory

Molecule in a liquid are attracted equally on all sides by the surrounding molecule, however, at the surface, there is inward attraction of molecules due to the imbalance attractive forces. Due to this attraction, a stress or tension is produced called as surface tension (John, 1976). When two immiscible liquids come in contact, the force causing each liquid to resist breakage is known as interfacial tension. In according to surface tension theory of emulsification, the emulsifying agents cause to a reduction in the interfacial tension of the two immiscible liquids, reducing the repellent force between the liquids and withdrawing the attraction of liquids for their own molecule. In this way, the surfactants convert large globules into small ones and avoid small globules from coalescing into large ones (Paul, 2005).

The oriented wedge theory of emulsion

According to this theory the oil-like or non-polar ends of the emulsifying agents turn towards the oil as well as the polar ends towards the polar liquid. The oriented wedge theory of emulsions indicates that isthe non-polar end of the emulsifying agent is smaller, the emulsion will be oil-in-water (o/w) as well as if the polar end is smaller, the emulsion will be water-in-oil (w/o) (Harkins and Norvil, 1925).

The interfacial film theory

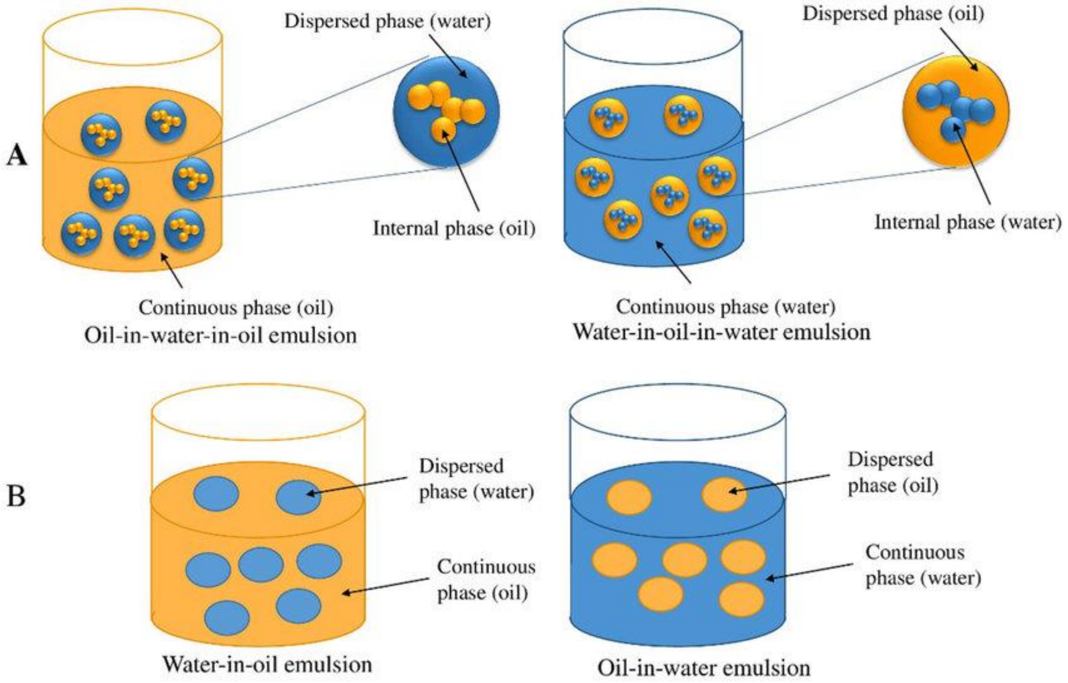
The interfacial film theory suggests that is the emulsifying agents make an interface between the two immiscible phases of the emulsion, surrounding the droplets of the internal phase as a thin film. This film prevents the coalescence of the dispersed phase (Paul, 2005).

Pharmaceutical applications of emulsion :-
1. The Oral, Rectal and Topical administration of oil soluble drugs.
2. Intramuscular injection of water insoluble drug or vaccine to provide slow release.
3. Intravenous emulsion containing fats, carbohydrates and vitamin as a nutrition.
4. Emulsion is used to improve bioavailability. The unpleasant taste and odour can be masked by emulsification.
5. The absorption and penetration of medicament are enhanced by emulsification.

ADVATAGES OF EMULSION
- Unpleasant oil can be administered in pleasant form.
- Unpleasant oil soluble drugs can be administered in pleasant form.
- The aqueous phase is easily flavoured.
- The rate of absorption is increased.
- It is possible to include two incompatible ingredients one in each phase of emulsion.
- Prevent oxidation.

DISAVANTAGES OF EMULSION
- Preparation needs to be shaken well before use.
- A measuring device is needed for administration.
- A degree of technical accuracy is needed to measure a dose.
- Storage condition may affect stability.

Evalution of emulsion :-



Stability testing

Stability testing of emulsion involves determining stability at long term storage condition accelerated storage condition freezing and thawing condition a tress conditions are applied in order to speed up the stability testing.

1. The stress condition used for speeding up instability of emulsion include. Centrifugal force agitation force aging and temperature.
2. Physical parameter are evaluated to assess the effects of any of the above stress condition:

a) Phase separation
b) Viscosity
c) Electrophoretic properties
d) Particle size and particle count

1. Determination of phase separation

This another parameter used for assessing the stability of the formulation

Phase separation may be observed visually or by measuring the volume of the separation phase.

2. Determination of viscosity

This is done to assess the changes that might take place during aging emulsion exhibit in Newtonian type flow characteristics. The viscometers which should be include cone and plate viscometer.

3. Determination of electrophoretic properties

Determination of electrophoretic properties like zeta potential is useful for assessing flocculation since electrical charges on particles influence the rate of flocculation.

4. Determination of particle size and particle count

Determination of changes in the average particle size or the size distribution of droplets is an important parameters used for the evaluation of emulsion it is performed by optical microscopy sedimentation by using Andresen apparatus and coulter counter apparatus.

Types of Surfactant

- **Anionic**
- **Cationic**
- **Non-ionic**
- **Ampholytic**

Sr/No	Surfactant class	Surface charge	Example
01	Anionic (based on sulfate, sulfonoate or carboxylate anions)	The charge is negative	Perfluorooctanoate (PFOA or PFO) Perfluorooctanesulfonate (PFOS) Sodium lauryl ether sulfate (SLES) Alkyl benzene sulfonate Soaps,or fatty acid salts
02	Cationic (based on quaternary ammonium cations)	The charge is positive	Cetyl trimethylammonium bromide(CTAB) Cetylpyridinium chloride (CPC) Polyethoxylated tallow amine (POEA) Benzalkonium choride (BAC) Benzethonium chloride (BZT)
03	Zwitterionic (amphoteric)	Two oppositely charged group	Dodecyl betaine Cocamidopropyl betaine Coco ampho glycinate
04	Non-ionic	No charge groups	Alkyl poly (ethylene oxide) Alkylphenol poly(ethylene oxide) Alkyl polyglucosides,including: octyl glucoside and decyl maltoside Fatty alcohols, including: cetyl alcohol and oleyl alcohol Cocamide MEA Polysorbates, including:Tween 20 and tween 80

Preservative used in emulsion :-

Type	Example	Characteristics
Acid and acid derivatives	Benzoic acid Sorbic acid Propionic acid Dehydoacetic acid	Antifungal
Alcohol	Chlorobutanol Phenoxy-2-ehanol	Eye prep. Synergism
Aldehyde	Formaldehyde Glutaraldehyde	Broad spectrum
Formaldehyde derivatives	Hexamethylenetetramine	Broad spectrum
Phenolic	Phenol cresol chlorothymol P-phenyl phenol P-chlorometaxylenol Methyl-p-hydroxybenzoate Propyl-p-hydroxybenzoate Benzyl-p-hydroxybenzoate Butyl-p-hydroxybenzoate	Broad spectrum
Quaternaries	Chlorohexidine Benzethonium Benzalkonium chloride Cetylpyridium chloride Cetyl methyl ammonium bromide	Broad spectrum
Mercurials	Phenyl mercuric acetate sodium ethyl	Broad spectrum

	mercuric thiosalicylate	

II. Conclusion:

The basics of emulsion are definitely succeeding as well as the proficient development and the production of excellence pharmaceutical emulsions is alsodepends on their basic knowledge of physicochemical properties and stability. This review article provides an overview of emulsion, it's types, tests and important properties of emulsions, with their method of preparation & theories and most suitable emulsifying agents that are of great interest to the researchers as well as pharmaceutical industries.

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