

# Introduction

## Definition:

An emulsion is a mixture of two or more liquids that are normally immiscible, one of which is dispersed as finite globules in the other.

- The particle size of the globules range from 0.25 to 25  $\mu$ m.
- The dispersed liquid is known as the internal or discontinuous phase, whereas the dispersion medium is known as External or continuous phase.
- These are thermodynamically unstable systems, hence a suitable emulsifying agent is used to stabilize it.

# Classification

Based on the nature of dispersed phase, emulsions are classified as,

- 1. Oil-in-water (o/w)
- 2. Water-in-oil (w/o)



1. <u>Oil-in-water type-</u> Here the dispersed phase is oil & the continuous phase is water.

2. <u>Water-in-oil type</u>- Here the dispersed phase is water and the continuous phase is oil.



#### Based on globule size, emulsions are classified as,

1. <u>Microemulsions</u>: These contain globules of the size about 0.01micrometer. Droplets of such dimension cannot refract light & are invisible to naked eye. Therefore, micro-emulsions are transparent systems. They show enhanced bioavailability of drug, which are poorly soluble in water.

Ex: Etoposide & Methotrexate

2. <u>Fine Emulsions</u>: Normally these have a milky appearance & the globule size ranges from 0.25 to 25micro meter

#### C. Special type- Multiple Emulsions:

These are 'emulsion-within-emulsion' and designated as w/o/w or o/w/o. Ex: w/o/w emulsion is prepared by incorporating the emulsion w/o in an aqueous phase.

The drug that is incorporated in the innermost phase must cross two phase boundaries before getting absorbed.

These have been proposed in oral sustained release or intramuscular therapy.



- A number of tests have been proposed to determine the type of emulsion.
  - They are:
    - 1. Dilution Test
    - 2. Conductivity Test
    - 3. Dye Solubility Test
    - 4. Cobalt Chloride Test
    - 5. Fluorescence Test
    - 6. Creaming Test
- The identity of emulsion should be confirmed by at least two test procedures.



## 1. Dilution test:

- The type of emulsion is determined by diluting an emulsion with oil or water.
- An o/w emulsion can be easily diluted with an aqueous solvent (e.g. milk, water) whereas a w/o emulsion can be diluted with an oily liquid.
- Addition of the wrong liquid will cause cracking of the emulsion. 2. Conductivity Test:
- The principle is that an emulsion with an water continuous phase will transmit an electrical current whereas one with an oily continuous phase will not.
- This can be conformed by the deflection of indicator in voltmeter.
- This may give false results with non-ionic o/w emulsions.

## 3. Dye solubility Test:

- The principle is that the dye can be dispersed uniformly throughout the phase in which it is more soluble.
- Water soluble dyes e.g. amaranth, methylene blue are readily tint water phase of o/w emulsion.
- Oil soluble dyes e.g. Sudan III, scarlet red color the oil phase of w/o type emulsion.
- Normally the dye powder is dusted on the emulsion for better results.
- It is better to sprinkle water- and oil-soluble dyes on two samples of the same emulsion.
- 4. Cobalt Chloride Test:
- If a filter paper soaked in a cobalt chloride solution and allowed to dry turns from blue to pink on exposure to an emulsion, it indicates that the emulsion is of the o/w type.
- This may not work if emulsion is unstable or breaks in the presence of electrolytes.

## **5. Fluorescence Test:**

- If a drop of an emulsion is exposed to UV radiation and observed under a microscope a w/o emulsion should show continuous fluorescence while an o/w type would show only spotty fluorescence.
- This is because many oils have the property to exhibit fluorescence on exposure to UV light.

## 6. Creaming Test:

- Direction of creaming precisely identifies the emulsion type if the densities of aqueous and oil phase are known.
- w/o emulsions normally cream downward as oil is less denser than water.
- o/w emulsions normally cream upwards.



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# **Pharmaceutical Applications**

- Mask the unpleasant taste: Orally unpleasant taste drugs can be incorporated in the dispersed phase to mask the taste .e.g. laxatives, phenolphthalein, vitamin A
- Improved bioavailability: Absorption of drugs has been found to be faster & better when formulated as emulsions .e.g. griseofulvin, insulin, heparin
- 3. Both the type of emulsions are used to prepare pharmaceutical preparations for external use & cosmetic preparations such as creams and lotions.
  - Sustained release medication: Water soluble antigenic materials are dispersed in mineral oil and are given as intramuscular injections. These preparations act as depots in the muscle and release antigen from the oil slowly, over a long period.
    - Multiple emulsions (emulsion-in-emulsion) are also suggested to provide sustained release of drugs.

- <u>Nutritional supplement</u>: Fats are dissolved in the oil phase & water soluble nutrients are incorporated in the aqueous phase.
- 6. <u>Diagnostic purposes</u>: Radio-opaque emulsions are used as diagnostic materials in X-ray examination.
- 7. <u>Topical use</u>: Concentrated emulsions are used in topical delivery as semisolid vehicles. e.g. cold cream, vanishing cream, benzyl benzoate etc.

#### Disadvantages:

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- Have short shelf life. They are unstable & the insoluble phase separates slowly.
- Appropriate care should be taken in handling and storage as these are packed in glass or plastic containers.
- Thermodynamic instability indicates that the preparation of emulsion is difficult whereas the separation into two liquid phase is spontaneous process.





# **Emulsifying Agents**

- Emulsifying agents act by reducing the interfacial tension between the two phases and forming a stable interfacial film between the two.
- The stability of the prepared emulsion is primarily determined by the strength and nature of the interfacial film formed.
- Examples: Spans, Tweens, Acacia, Gelatin, Soap

#### Ideal Characteristics:

- The agent should be,
- 1. Stable
- 2. Inert
- 3. Free from toxic and irritant properties
- 4. Odourless, colourless, tasteless
- 5. Should produce stable emulsions of desired type at a very low concentrations
- <u>Bancroft's rule</u> describes the relationship between the nature of emulsifying agent and type of emulsion formed.

4	EMULSIFYING AGENTS				
NAT	URAL	SEMI-SYNTHETIC POLYSACCHARIDES	SYNTHETIC		ALCOHOLS
VEGETAI SOURC # Gum a # Tragac # Agar # Pectin # Starch # Irish m	ILE ANIMA E SOURC acia # Wool anth # Egg y # Gelat	AL CE fat # Methyl cellulose yolk # Sodium carboxy tin methyl cellulose	# Anionic # # Cationic # # Non-ionic # #	Milk of magnesia Magnesium oxide Magnesium trisilicate Magnesium alu- minium silicate Bentonite	# Carbowaxe # Cholesterol: # Lecithins

# Formulation

#### Selection of oil phase:-

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Variety of substances have been used for oil phase.

Examples: i) Fixed oils: Corn oil, Soyabean oil, Peanut oil, Sunflower oil

- ii) Aliphatic hydrocarbons: Liquid paraffin, Turpentine oil
- iii) Bees wax, Spermaceti
- iv) Glycerides (Long and medium chain)

b) Selection of Antioxidant: Antioxidants are used to prevent oxidation.
Examples: Ascorbic acid- 0.1 to 1%
Propyl galate (gallic acid)
Tocopherol- 0.5%
Thiourea- 0.005%

#### c) Preservatives:-

Used to hinder the growth of micro-organisms.

Examples: Derivatives of parahydroxy benzoate e.g. Methyl paraben(0.5-1%), Propyl paraben 4° ammonium compounds e.g. Benzal konium chloride, Benzathonium chloride, Cetrimide

#### d) Flavoring Agents:-

Used to mask the unpleasant fragrance.

Examples: Cinnamon syrup, Orange syrup, Cherry syrup, Raspberry syrup etc.

#### e) Selection of emulsifying Agents:-

These are selected depending on the type of emulsion required & on the intended use (internal or external).

i)For internal use, non-ionic and water-soluble emulsifying agents are choosen. E.g. Tweens (Polyoxy ethylene derivatives of sorbitans)

ii)For external use, both ionic and non-ionic emulsifying agents are employed.

e.g. Anionic- sod. Lauryl sulphate

Cationic- 4° ammonium compounds, cetrimide

iii) The use of emulsifying agents from natural origin e.g. Gum tragacanth, pectin, starch etc. should be avoided, because they support the microbial growth.

iv) Inorganic substances such as,

Milk of magnesia(10-20%), Magnesium oxide(5-10%), Magnesium aluminum silicate(1%) are used to prepare coarse o/w type emulsion.

Bentonite (5%) is used to prepare both o/w & w/o type emulsion.

# Preparation

The methods commonly used for the preparation of emulsion are,

- 1. Dry gum method
- 2. Wet gum method
- 3. Bottle method
- 4. Other method

#### **Dry Gum Method:**

Measure the required amount of oil in dry measure

Transfer into a dry mortar



Add calculated quantity of gum acacia into it & triturate rapidly to form a uniform mixture

Required amount of water added by continuing the trituration in same direction until clicking sound is produced & the product becomes white or nearly white (This stage is 'Primary Emulsion')

Dilute with excess amount of water or continuous phase to produce required volume





### Wet Gum Method:

Calculate the quantity of oil, water & gum required for preparing the primary solution

Powder the gum acacia in a morter. Add water and triturate it with gum, to form a mucilage

Add the required quantity of oil in small portions with rapid trituration until a clicking sound is produced and the product become white or milky white (Primary Emulsion)

Add more water to produce required volume, strire thoroughly so as to form a uniform emulsion.

Transfer the emulsion to a bottle, cork, label and dispense



Measure the required quantity of oil and transfer it into a large bottle. Add required quantity of powdered gum acacia

Shake the bottle vigorously, until the oil and gum are mixed thoroughly

Add the calculated amount of water all at once

Shake the mixture vigorously to form a primary emulsion

Add more water with constant agitation to produce required volume

#### **Other Methods:**

Various blenders and homogenizers are used for preparing emulsions. Mostly used are, 1. Hand homogenizer

- 2. Silverson mixture homogenizer
- 3. Colloidal mill
- Principle: The large globules in coarse emulsion are broken into smaller globules by passing them under pressure through a narrow orifice.

#### Hand Homogenizer:

- This is hand operated.
- Emulsion is placed in the hopper of the homogeniser.
- The up and down movement of the handle force the emulsion to pass through the fine orifice.
- The oil globules are broken into fine globules of uniform size.

#### Silverson Homogenizer:

- It consists of <u>emulsifier head</u> covered with fine <u>meshed stainless steel sieve</u>.
- The emulsifier head consists of a number of blades which rotate at a very high speed to produce a powerful shearing action.
- The blades are rotated by using an electric motor fitted at the top.

## Working:

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- The emulsifier head is placed in a vessel containing immiscible liquids, in such a way that it should be dipped into it.
- 2. When the motor is started, the liquid is sucked through the holes & oil is reduced into fine globules due to rotation of blades.
- 3. So a fine emulsion is produced which is then expelled out.



# **Stability of Emulsions**

- An emulsion is said to be stable if it remains as such after its preparation i.e. the dispersed globules are uniformly distributed through out the dispersion medium during its storage.
- The following changes usually occur during the storage of an emulsion.
- Flocculation
- 2. Creaming
- 3. Coalescence
- 4. Cracking
- 5. Phase Inversion
- 6. Ostwald Ripening
- **1.Flocculation:** Here the neighboring globules come closer to each other and form colonies in the external phase.
- The extend of flocculation of globules depends on,
- a) Globule size distribution
- b) Charge on the globule surface
- c) Viscosity of the external medium

Flocs slowly move upward or downward leading to creaming.

**Creaming**: It is the concentration of globules at the top or bottom of the emulsion. The floccules either move upward or downward leading to creaming.

It is a reversible process.

Creaming is of two types, 1. upward creaming & 2. downward creaming

Upward creaming is due to the less denser internal phase. Normally observed in o/w type emulsion.

<u>Downward creaming</u> is also possible if the internal phase is heavier. Due to gravitational pull, the globules settle down. Observed in case of w/o emulsion.

Creaming is influenced by: 1. globule size

2. viscosity of dispersion system



 $v = 2r^2 (d_1 - d_2)g/9^{ij}$ 

V = rate of creaming r = radius of globules d1 = density of dispersed phase

d2 = density of continuous phase

g = gravitational constant

 $\mathfrak{n}$  = viscosity of dispersion medium

emulsion.

**<u>4. Cracking</u>**: This is indicated by complete separation of oil and aqueous phases. It is an irreversible process.

Here the protective sheath around the globules is completely destroyed.

The rate of cracking depends on,

Radius of globules

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- Difference in density of dispersed phase & dispersion medium
- III. Viscosity of the dispersion medium
- iv. Storage condition
- v. Freezing should be avoided because it may lead to cracking

**<u>5. Phase Inversion</u>**: It means a change of emulsion type from o/w to w/o or vise versa. It may be due to reasons,

- i. By changing the phase-volume ratio
- ii. By changing the emulsifying agent
- iii. By temperature change

It can be minimised by keeping the concentration of dispersed phase between 30 to 60%

**<u>6.Ostwald Ripening</u>**: This effect is an increase in the average radius of the emulsion droplets with time as the smaller droplets dissolve and redeposit their material onto the larger droplets.

The rate of Ostwald ripening is the rate at which the radius of the emulsions increases with time.



# THANK YOU