



Emulsions

BY

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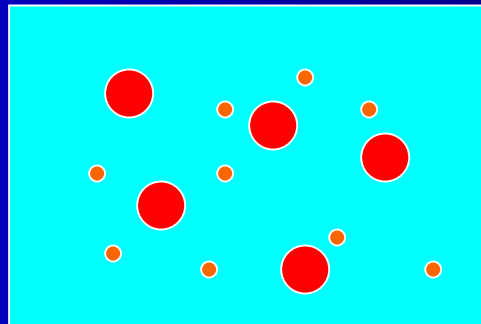
Dept. of Pharmaceutical
Technology (2106)

Scope

- Definition
- Composition
- Type of emulsions
- Determination
- Test
- Selection of ingredients
- Emulsion consistency
- Emulsion theory
- Emulsifying agent
- Preparation
- HLB system
- Stability

Emulsions

heterogenous systems of one liquid dispersed throughout another in the form of droplets usually exceeding 0.1 micrometre in diameter



Compositions

Internal/Discontinuous/Dispersed phase

External/Continuous phase

Emulsifying agent

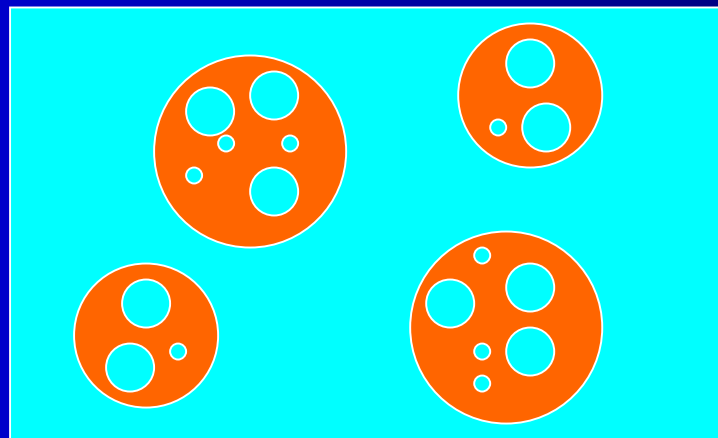
Forms

Liquids

Semisolids

Emulsion Types

1. oil-in-water (o/w)
2. water-in-oil (w/o)
3. water-in-oil-in-water (w/o/w)
4. oil-in-water-in-oil (o/w/o)



Determination of Emulsion Types

- By phase ratio between oil and water phase
- By order of addition
slowly add oil into water → o/w
- By type of emulsifier
phase that the emulsifier is soluble will most probably be continuous phase

Tests for Identification of Emulsion Types

- Dilution test:
emulsion can be diluted only with external phase
- Dye test:
- CoCl_2 /filter paper test:
filter paper impregnated with CoCl_2 and dried (blue) changes to pink when o/w emulsion is added
- Fluorescence:
oils fluoresce under UV light
- Conductivity: for ionic o/w emulsions
o/w emulsions conduct electric current

Choice of Emulsion Types

- Fats or oils for oral administration:
 - o/w is formed to mask unpleasant taste
- For i.v. administration:
 - o/w
 - w/o
- For external application:
 - o/w
 - for water soluble drugs
 - easily wash from skin
 - non greasy texture

- w/o

occlusive effect → influence the
absorption of drugs

cleansing skin

moisturizing creams (designed to
prevent moisture loss from skin)

Choice of Oil Phase

- The type of oil affect on:
 - viscosity
 - spread
 - film forming
 - the transport of drug into skin
- i.e. liquid paraffin (hard, soft and light liquid paraffin), silicone, beeswax, fatty alcohol and so on

Emulsion Consistency

Texture or feel of a product
- viscosity

Rheological properties of emulsion can be controlled by:

1. Volume concentration of dispersed phase:

if increase \longrightarrow viscosity of
product increase

if above about 60% \longrightarrow phase
inversion

2. Particle size of disperse phase:

decrease size → increase viscosity

small globule → increase flocculation →

polydispersed system → lower viscosity

3. Viscosity of continuous phase

4. Nature and concentration of emulsifying system

Purpose of Emulsions

Oral formulation

1. Enhancing bioavailability
2. Giving controlled rate of drug release
3. Affording protection to oxidation or hydrolysis

Topical formulation

1. Easily applied and can be formulated to eliminate oiliness and staining
2. Carrying water which is an excellent softener to skin

Emulsion Theory

- To explain how emulsifying agents act in promoting emulsification and in maintaining the stability of the resulting emulsion
 - Surface tension theory (important in initial formation)

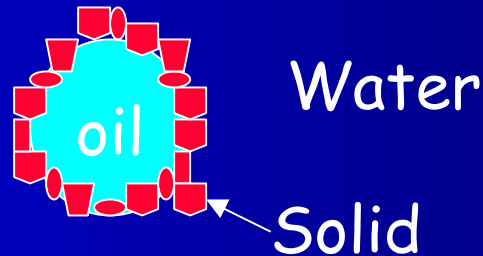
The force causing each liquid to resist breaking up into smaller particles is called **interfacial tension**. Surfactants promote the lowering of this resistance
 - Surface orientation theory

Emulsifying agent having a greater hydrophilic character than hydrophobic character will promote an o/w emulsion

- Plastic or interfacial film theory
emulsifying agent surrounding the droplets of the internal phase as a thin layer of film adsorbed on the surface of the droplets, prevent the contact and coalescing of the internal phase
- Rate of coalescence theory
- Phase volume theory

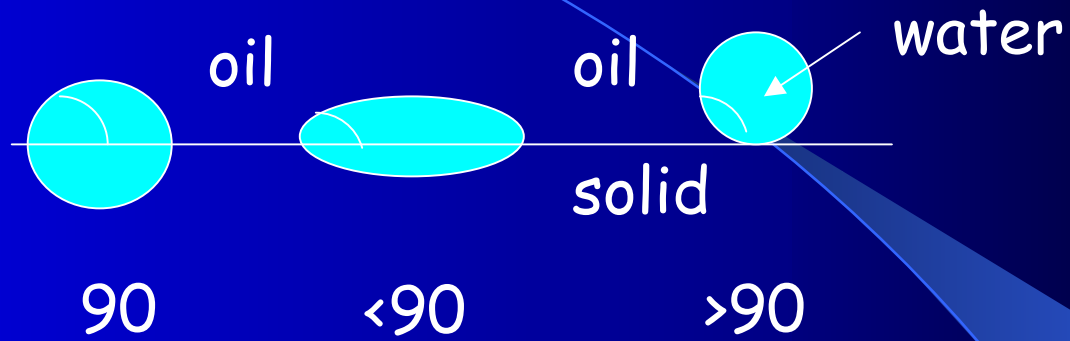
Film

- Monomolecular film
- Multimolecular film
- Solid particle film



$$E = \gamma_{o/w} (1 - \cos \theta)$$

- E = the energy to expel an absorbed particle from the interface into the phase that it is predominant wet
- θ = its contact angle between solid and water phase



interface
most stable

$$\gamma_{s/w} < \gamma_{s/o}$$

o/w

$$\gamma_{s/w} > \gamma_{s/o}$$

w/o

Mechanism

- To form droplets
 - surface free energy or surface tension
 - system at its lowest free energy is thermodynamically stable
 - emulsions are not thermodynamically stable
- To stabilize droplets (by surfactants or polymers)
 - by reducing the interfacial tension
 - by packing of the emulsifier molecules

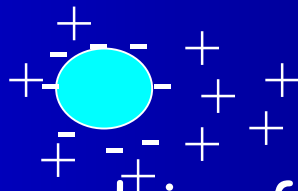
Microemulsions

- The droplet size is below 0.15 micrometer
- Transparent
- Form spontaneously during preparation
- Thermodynamically stable (no change spontaneously, and if forced to change, it will return to the stable state)

Emulsifying agents

- must be present at the interface to prevent coalescence of the internal phase:
 1. To reduce the interfacial tension
 2. To be interfacial barrier (most influence on emulsion stability)
 - increase viscosity of continuous phase
 - energy barrier

the electric double layer



the steric repulsion from absorbed polymer

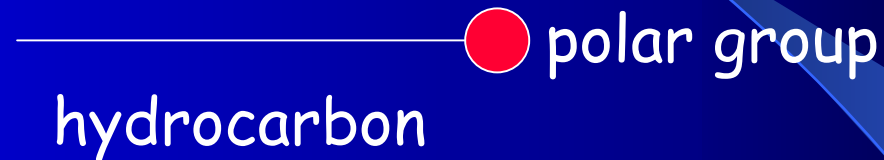


Compositions

- Emulsifying agents, Emulsifiers, Emulgents, Surfactants
 - primary
 - auxiliary
- The other formulation additives
 1. Preservatives: MP:PP 10:1
 2. Antioxidants: BHT, BHA etc.
 3. Humectants: propylene glycol, glycerol, sorbitol

Fact of Emulsifying Agents

- Structure



- Reside at interface
- When the concentration is increased in excess of *CMC* (the critical micellization concentration), micelles is formed

Properties

1. Compatible with the other ingredients
2. Not interfere with the stability or efficacy of the therapeutic agent
3. Stable and not deteriorate in the preparation
4. Nontoxic
5. Little odor, taste or color
6. Promote emulsification and to maintain the stability

Emulsifier Classification

According to ionic composed of an organic lipophilic group (surface active portion)

- Synthetic and semisynthetic surfactants
 - Anionic
 - Cationic
 - Nonionic
 - Amphoteric
- Naturally occurring materials and their derivatives

Anionic Surfactants

- Soaps

Fatty acid + Base \longrightarrow Soaps

- o/w emulsions

- in acidic condition \longrightarrow precipitated FFA

- external use

- combination of soap (TEA stearate) with an oil-soluble auxiliary emulsifier (cetyl alcohol) \longrightarrow o/w mixed emulsifier

- incompatible with polyvalent cations

Anionic Surfactants (cont.)

- Soap of di/trivalent metal
 - Cal oleate → w/o emulsions
- Amine soaps: $N(\text{CH}_2\text{CH}_2\text{OH})_3$
 - neutral pH
 - incompatible with acids and high concentration of electrolytes
- Sulfated and sulfonated compound:
 - SLS
 - stable over high pH range
 - o/w emulsions

- Sulfated and sulfonated compound (cont.)

- SLS

- fairly resistant to divalent metal ions
 - used in combination with a nonionic oil-soluble emulsifying agent or fatty alcohol to produce a good emulsions

- sodium dioctylsulfosuccinate
 - used as wetting agent

Cationic surfactants

- Quaternary ammonium compounds:
Cetyl trimethylammonium bromide
(Cetrimide) $\text{CH}_3(\text{CH}_2)_{15}\text{N}^+(\text{CH}_3)_3\text{Br}^-$
- Used with nonionic, oil-soluble auxiliary emulsifiers
- Toxicity and irritancy
- Incompatible with anionic surfactants, polyvalent anions and unstable at high pH

Nonionic surfactants

- Low toxicity and irritancy → oral, parenteral
- High degree of compatibility
- Less sensitive to change pH or to addition of electrolytes
- Most of them are based on:
 1. Hydrophobic part: FA or alcohol (C_{12-18})
 2. Hydrophilic part: alcohol (-OH) and/or ethylene oxide (-OCH₂CH₂)

Nonionic surfactants (cont.)

- Glycol and glycerol esters
 - Glyceryl monostearate (a polyhydric alcohol FA ester):
 - strongly hydrophobic material
 - produce w/o emulsions
 - Self-emulsifying glycerol monostearate soap + glyceryl monooleate
 - diethylene glycol monostearate
 - propylene glycol monooleate

Nonionic surfactants (cont.)

- Sorbitan esters
 - the esterification of 1 or more of the hydroxyl groups of sorbitan with either lauric, oleic, palmitic or stearic acid
 - tend to form w/o
 - used with polysorbates to produce o/w or w/o

Nonionic surfactants (cont.)

- Polysorbates (Tween)
 - polyethylene glycol derivatives of the sorbitan ester
 - variation in water solubility based on:
 - type of FA
 - the number of oxyethylene gr. in the polyethylene glycol chains
 - compatible with most anionic, cationic and nonionic materials

- Polysorbates (cont.)
 - provide neutral pH and stable to the effects of heat, pH change and high conc. of electrolytes
 - low toxicity
 - unpleasant taste
 - form complex with preservatives

- Fatty alcohol polyglycol ethers
 - condensation products of polyethylene glycol and fatty alcohols: polyethylene glycol monocetyl ether (Cetomacrogol 1000)
 - high water solubility
 - stable over a wide pH range
 - salted out by high conc. of electrolytes
 - o/w emulsions (should used with oil-soluble auxiliary emulsifier: Cetostearyl alcohol)

- Fatty acid polyglycol esters
 - stearate esters or polyoxyl stearates
 - i.e. polyoxyethylene 40 stearate (40 = the no. of oxyethylene units)
 - water-soluble
 - used with stearyl alcohol to give o/w
- Poloxalkols
 - polyoxyethylene/polyoxypropylene copolymers
 - used for i.v. fat emulsions

- Higher fatty alcohol
 - saturated aliphatic monohydric alcohols: hexadecyl (cetyl), octadecyl (stearyl)
 - used as auxiliary emulsifiers according to their ability to increase viscosity
 - i.e.

cetostearyl alcohol + SLS/ → o/w
Cetrimide/
Cetomacrogol 1000

Amphoteric surfactants

- charge depending on the pH of the system
 - low pH → cationic
 - high pH → anionic
- i.e. lecithin: used to stabilize i.v. fat emulsion

Naturally Occurring Materials and Their Derivatives

Disadvantage

- batch to batch variation
 - susceptible to bacterial and mold growth
 - susceptible to alcohol, electrolytes
-
- Polysaccharides
 - i.e. acacia, tragacanth, sodium alginate
 - anionic
 - stabilize o/w (internal)
 - forming a strong multimolecular film
 - (hydrophilic barrier) round oil globule

- Semisynthetic polysaccharides
 - to reduce batch to batch variation
 - as o/w emulsifiers or stabilizer
 - i.e. MC (nonionic), CMC (anionic)
- Sterol-containing substance
 - Beeswax: beeswax-borax
 - Wool fat (anhydrous lanolin)
 - fatty alcohol with FA esters of cholesterol and other sterols
 - form w/o
 - emollient property
 - water absorbing property
 - odor: require antioxidant

- Sterol-containing substance (cont.)
 - polyoxyethylene lanolin derivatives
 - water soluble
 - o/w emulsifier
 - emollient property
 - wool alcohol
 - cholesterol together with other alcohols
 - w/o emulsifier
 - no strong odor (but still require antioxidant)
 - Protein substances
 - i.e. gelatin, egg yolk and casein
 - o/w emulsifier
 - gelatin; provide emulsion that is too fluid

Finely Divided Solids

- i.e. bentonite, aluminium magnesium silicate, colloidal silicon dioxide
 - forming a coherent film which physical prevents coalescence of the dispersed globules
 - if the particles are:
 - preferentially wetted by the aqueous phase → o/w emulsion
 - preferentially wetted by the oil phase → w/o emulsion

Preparation

- Method depending on:
 - the nature of emulsion components
 - the equipment available
 - porcelain mortar and pestle
 - bottle
 - homogenizer/ hand homogenizer
 - colloid mill

Continental or dry gum method

- 4:2:1 oil:water:gum → primary emulsion
- Emulsifier is triturated with the oil in perfectly dry porcelain mortar
 - ↓
 - 2 parts of water are added at once
 - ↓
 - triturate immediately, rapidly and continuously (until get a cracking sound)
 - ↓
 - aqueous solution is added (alcohol the last, if any)

bland oil should be added if oil is less than 20%

Prepare 50 ml (4:2:1)

Rx	Calciferol solution	0.15 ml
	Glycerin	0.30 ml
	Water to	5.00 ml

Rx	Calciferol solution	1.5 ml
	Arachis oil	8.5 ml
	Water	5.0 ml
	<u>Acacia powder</u>	<u>2.5 ml</u>

primary emulsion

English or Wet Gum Method

triturate gum with twice its weight
of water in a mortar



oil is added slowly in portions



the mixture is triturated



after adding all of the oil, thoroughly
mixed for several minute

Caution: the mixture become too thick (ropy)
during the process, additional water may
be blended

Bottle or Forbes Bottle Method

- Extemporaneous preparation for volatile oils or oil with low viscosity

gum + 2 parts of oil (dry bottle)



shake



water (volume equal to oil)
is added in portions



shake

Beaker Method

Oil phase: heated about 5-10 degree above the highest melting point of ingredient (water bath)

Water phase: heated to the same temperature of oil phase (water bath)

Add: internal phase into external phase, mix, constant agitation being provided throughout the time of addition

Caution: - not to heat the phase above 85 degree
- rate of cooling determining the final texture and consistency