California Northstate University College of Pharmacy

To Advance the Art and Science of Pharmacy

Emulsions:

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DISPERSION

- A liquid preparation containing undissolved or immiscible drug distributed throughout a vehicle.
- The substance distributed is termed dispersed phase.
- The vehicle is termed dispersing phase or dispersion medium.
- All this make a dispersed or disperse system (Dispersion)

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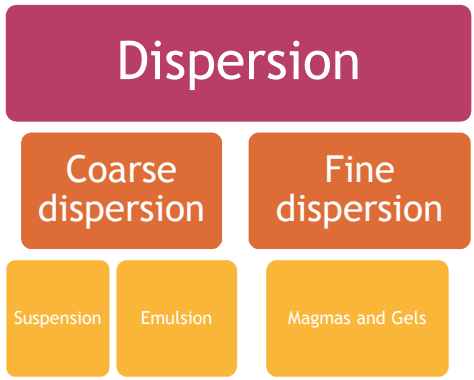

Based on the particle size of the dispersed phase.

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WHAT IS AN EMULSION?

- Any two liquids that are immiscible may form an emulsion.

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EMULSIONS

- Purpose:
  - Increased drug stability.
  - Increased drug solubility.
  - Prolonged drug action (bioavailability).
  - Improved taste.
  - Improved appearance.

PHASES OF EMULSION

- One phase is aqueous(w).
- 2nd phase is oily(o).
- Dispersed phase: _____ phase or discontinuous phase.
- Dispersion medium: external phase or _____ phase.
- if water is internal phase the emulsion is __.
- If water is _____ phase the emulsion o/w.

EMULSIFYING AGENT

- Prevents phase separation thus stabilizing the emulsion by lowering the interfacial tension. They are either:
- Natural emulsifying agent:
  - Acacia
  - Tragacanth
  - Agar
  - Pectin
  - Gelatin
  - Methyl cellulose
  - Carboxymethyl cellulose
- Synthetic emulsifying agent: are anionic, cationic or nonionic named surfactants.
- The type of emulsion is determined by HLB ___ ___ ___

HOW STABLE IS AN EMULSION?

- What do we add to ensure that the Pharmaceutical emulsion is sufficiently stable?
- Emulsifying Agent

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ANOTHER EXAMPLE OF AN EMULSION

- I consist of fatty globules that are surrounded by a layer of casein and suspended in water.
- Who am I?

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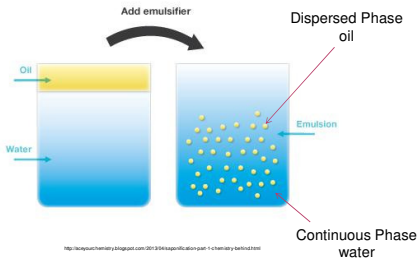
EMULSION



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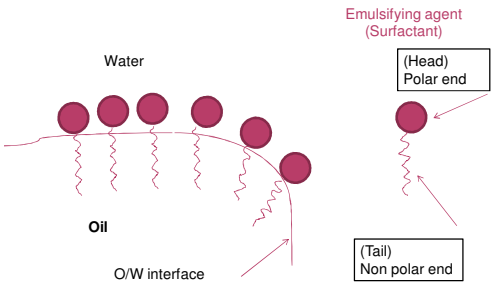
EMULSIFYING AGENT MECHANISM



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MEDICINAL EMUSLIONS

- Medicinal Emulsion intended for oral administration are usually stabilized Oil in water dispersion o/w.
- Castor oil Emulsion: used as laxative

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EMULSIFICATION? HOW

1. Surface Tension reduction:

- Emulsifying agent(surfactant or wetting agents) are used to reduce interfacial tension of two immiscible liquids thus reducing the repellent forces between liquids.

2. Oriented Wedge Theory:

Monolayers of emulsifying agent are curved around the droplet of the internal phase.

Emulsifying agent that are greatly hydrophilic promote an oil-in-water emulsion.

Emulsifying agents that are greatly hydrophobic promote a water-in-oil emulsion.

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3. Plastic Film Theory

- The emulsifying agent is placed at the interface between the oil and water.
- Surrounding the droplets of the internal phase as a thin layer of film adsorbed on the surface of the drops.
- The film prevents the contact and coalescing of the dispersed phase.

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EMULSIFYING AGENT

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EMULSIFYING AGENT

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HLB Value	Surfactant Application
0-3	Antifoaming agents
4-6	W/O emulsifying agent
7-9	Wetting agent
8-18	O/W emulsifying agent
13-15	Detergents
10-18	Solubilizing agent

Ref: Comprehensive pharmacy review 7th edition p.51

SURFACTANTS

- Anionic: sodium lauryl sulfates and soaps
- Cationic: benzalkonium chloride used as ____?___ __?____ effect
- Non ionic:
  - Sorbitan esters: Spans are hydrophobic form w/o emulsions. Have low HLB value (1-9)
  - Polysorbates: Tweens are hydrophilic form o/w emulsions. Have high HLB value (11-20)

EMULSION STABILIZED BY SYNTHETIC EMULSIFYING AGENT

- Oil miscible phase and water miscible phase are both heated to 70-80°C
- Then combined with stirring until emulsion cools.
- Note: heat labile ingredients are to be added in the final emulsion after it has cooled to 40°C.

METHOD OF PREPARATION WITH NATURAL EMULSIFYING AGENT.

Classical acacia stabilized emulsions are prepared by one of the following methods:

1. Dry gum method (Continental) method.
2. Wet gum method (English) method.
3. Bottle method.
4. Nascent soap method.

EMULSION PREPARATION

- The preparation of an emulsion follows two main steps:

1. preparation of a concentrate called the primary emulsion

2. dilution of the concentrate.

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THE PRIMARY EMULSION

	Type of oil		
	Fixed oils Parts/ volume	Mineral oil Parts/volume	Volatile oil Parts/volume
Oil phase	?	3	2
Aqueous phase	2	?	2
Emulsifying agent (gum)	1	1	?

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PRIMARY EMULSION PREPARATION

- Use the ratio of
- oil phase :water phase: emulsifying agent.
- Triturate emulsifying agent with oil in a dry porcelain mortar.
- Why not glass mortar?
- Water is then added all at once, triturated immediately, rapidly and continuously about 3 minutes ⟶ primary emulsion.
- Other ingredient mixed with external phase are then added.

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DRY GUM METHOD (CONTINENTAL) METHOD

- Extemporaneously prepared emulsions for oral administration are usually made by the continental or dry gum method.

1. Mixing the emulsifying gum (usually Acacia) with the oil.
2. The gum and oil then mixed with the aqueous phase to form the primary emulsion.
3. Add remaining water to the primary emulsion.
4. Add colorant, flavoring agent and preservative.

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WET GUM METHOD (ENGLISH) METHOD

- Same proportion of oil,water and gum are used as in the dry gum.
- Order of mixing is different.
- Mucilage of the gum is prepared.
- Oil is added in small proportions and then rapidly mixed to emulsify the oil after each addition.
- Emulsion is made up to volume with remaining water.

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BOTTLE METHOD

- Used for preparation of emulsions from of low viscosity such as _____ oils.
- Ratio of oil to water to gum is _:_:_

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ENHANCING EMULSION STABILITY

- An emulsion stability can be enhanced by passing through _____.
- Emulsion passes through very small holes to reduce the globule size.
- Globules will have uniform in size, thus enhances stability.
- Emulsion is forced through a small aperture.

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STABILITY OF EMULSIONS

- Possibility of break down of emulsions

1. Cracking
2. Creaming
3. Phase inversion.

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CRACKING

- When the disperse phase coalesces (fuse) and forms a separate layer termed coalescence.
- Is it reversible?
- Cracking occurs

1. Oil turns rancid during storage.(due to temp).
2. Incompatible emulsifying agent.
3. Decomposition of the emulsifying agent.

Causing the two phases to separate.

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CREAMING

- When oil separates out, it forms a layer on top of the emulsion, but it usually remains in globules. Product not homogenous.
- Is it reversible?
- Undesirable:

1. As the product appearance is poor.
2. Risk of the patient obtaining an incorrect dose. Why?

- Creaming is reduced if the viscosity of the continuous phase is _____.

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PHASE INVERSION

- When an oil-in-water emulsion changes to a water-in-oil emulsion or vice versa.
- To prepare a stable emulsion a concentration of dispersed phase should be within 30-60% of the total volume. Max is 74%
- If it exceeds this ⟹ at risk of phase inversion.
- Is it reversible upon shaking?

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PACKAGING

- Oral emulsions should always be dispensed in wide mouthed bottles.

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x

HLB CALCULATION:

When using two emulsifying agent

$$\%A = \frac{100 \times (x - HLB_B)}{HLB_A - HLB_B}$$

%A= % of surfactant A needed
%B= % of surfactant B needed
B = 100 – A
Where × is the required HLB_{mix} of the oil mixture.

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HLB

$$HLBmix = \frac{(C_1 \times HLB_1) + (C_2 \times HLB_2) + (C_3 \times HLB_3) \ldots}{C_{Total}}$$

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CALCULATING THE REQUIRED HLB

Rx		HLB
Mineral Oil	30 g	12
Wool fat	1.5g	10
Cetyl Alcohol	1g	15
Emulsifier	5 g	
Water QS AD	90 mL	

If you are using Tween 60 (HLB 14.9) and Span 60 (HLB 4.7), how much of each would you use to fill this Rx?

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Total weight of the oil 30 + 1.5 + 1 = 32.5 g

HLB= the sum HLB requirement of each oil ingredient/ total weight of the oil phase

(30 x 12 / 32.5) + (1.5 x 10/ 32.5) + (1 x 15/ 32.5)=

- 11.07+0.46+ 0.46= 11.99
- HLB $_{mix}$= 11.99

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- If you are using Tween 60 (HLB 14.9) and Span 60 (HLB 4.7), how much of each would you use to fill this Rx?

$$\%A = \frac{100 \times (x - HLB_B)}{HLB_A - HLB_B}$$

X= HLB $_{mix}$
% Tween 60 = %A = [100 X (11.99-4.7)]/ (14.9-4.7)
%A= 100 X (7.29)/10.2
=71.47
B= Span 60= 100-A
B= 100-71.47= 28.53,
A= 71.47% of 5 g= 3.57 g
B= 28.53% of 5g= 1.43 g or B= 5-3.57= 1.43g

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