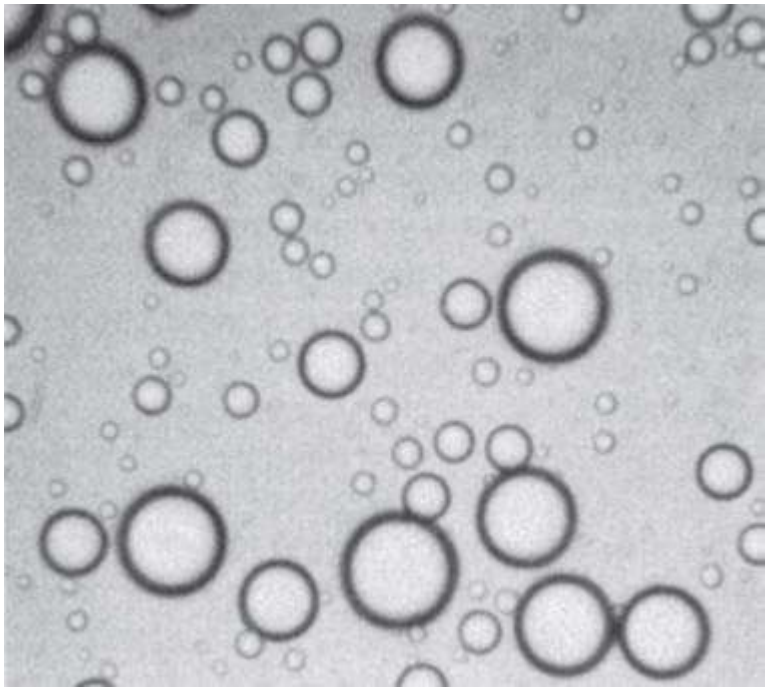
Emulsions

Chapter 13

Introduction

- An emulsion is a dispersion in which the dispersed phase is composed of small globules of a liquid distributed throughout a vehicle in which it is immiscible
- Depending on their constituents, the viscosity of emulsions can vary greatly and pharmaceutical emulsions may be prepared as liquids or semisolids.



Introduction:

- Many pharmaceutical preparations that are actually emulsions are not classified as such because they fit some other pharmaceutical category more appropriately.

- For instance, emulsions include certain lotions, liniments, creams, ointments that are discussed various designations

(مسميات مختلفة)

- Two immiscible components formulated by:

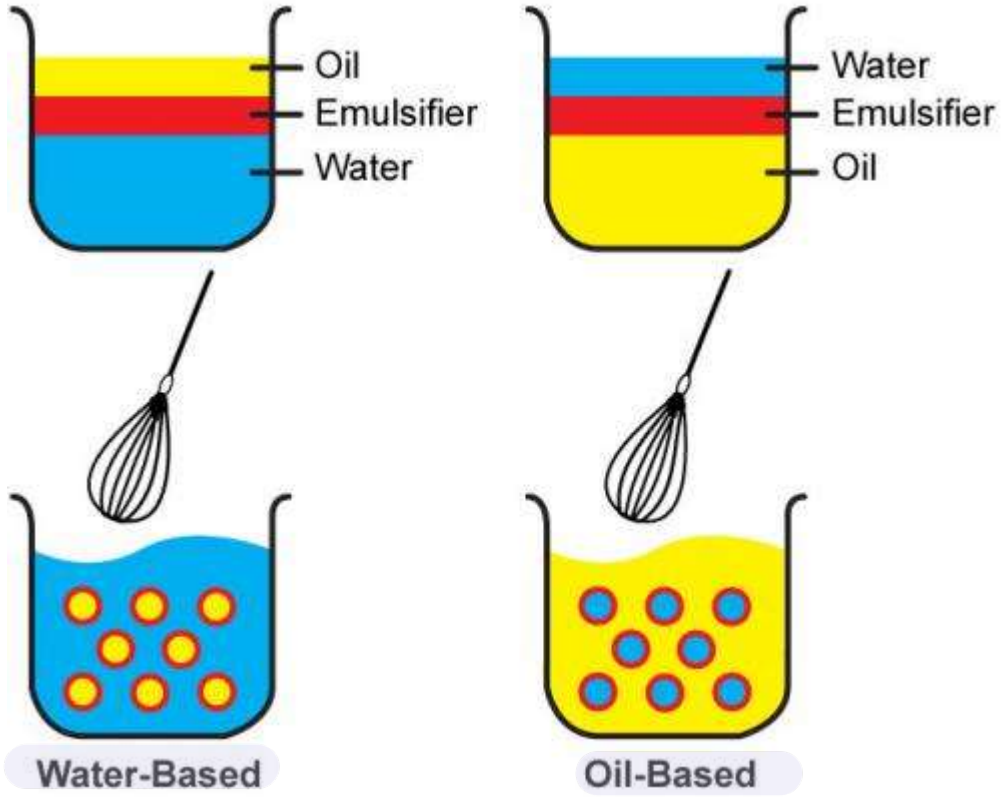
1. Emulsifying agents
2. Energy: to make the three ingredients (water, oil, emulsifying agents) come together and form and emulsion

- The dispersed liquid is the internal or discontinuous phase
- The dispersion medium is the external or continuous phase

Introduction

- Energy can be supplied by:

1. Triturating the ingredients in a mortar with a pestle
2. Heating the ingredients
3. Shaking the ingredients in a bottle
4. Extruding the ingredients through a small orifice (فتحة) of an homogenizer
5. Mechanically blending the ingredients with a high speed mixer or blender


Oil
Emulsifier
Water
Water-Based
Water
Emulsifier
Oil
Oil-Based

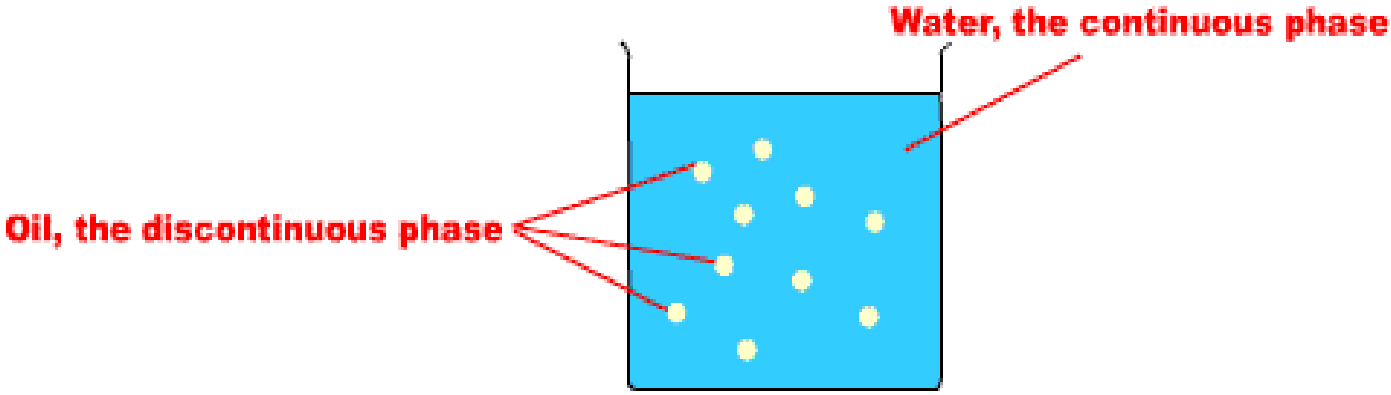


Figure 1a: O/W emulsion

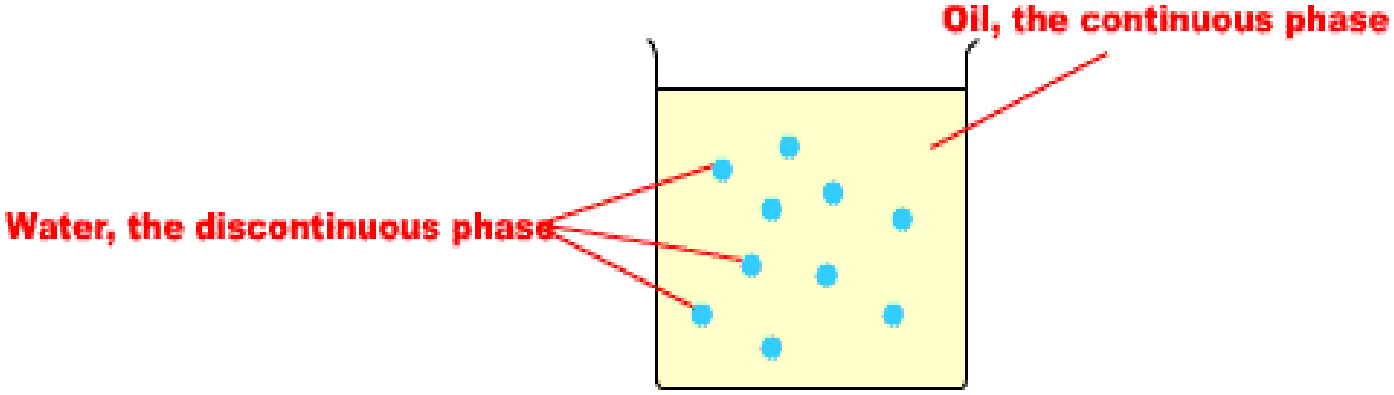


Figure 1b: W/O emulsion

Introduction

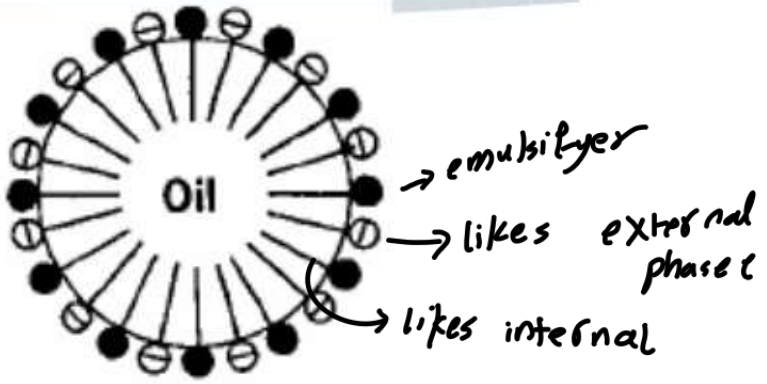
Oil-in-water (o/w) emulsion

- Oils, petrolatum hydrocarbons, or waxes are the dispersed phase
- Aqueous solution is the continuous phase
- Aqueous phase constitutes > 45% of the total weight
- Hydrophilic emulsifier
- Miscible with water
- Water washable قابل للغسل
- Non occlusive مايكون طبقة عازلة
- Non greasy ← ليس دهني

Water-in-oil (w/o) emulsion

- Water or aqueous solutions are the dispersed phase
- Oleaginous solution is the continuous phase
- Aqueous phase constitutes < 45% of the total weight
- Lipophilic emulsifier بحب الزيت
- Not water washable
- Occlusive مثل الفازلين ، عازل
- Greasy دهني

Monomolecular adsorption



Rule of Bancroft: The type of the emulsion is a function of the relative solubility of the surfactant, the phase in which it is more soluble being the continuous phase.

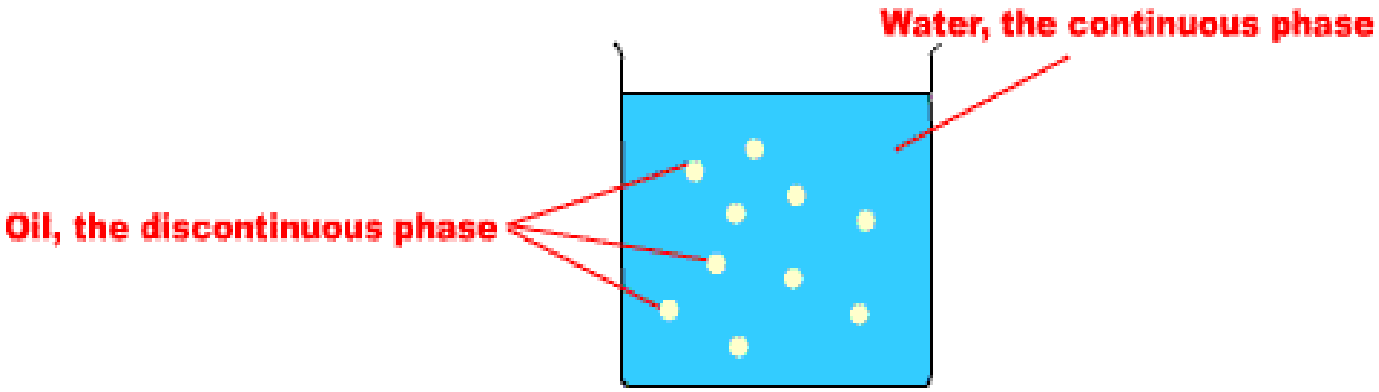


Figure 1a: O/W emulsion

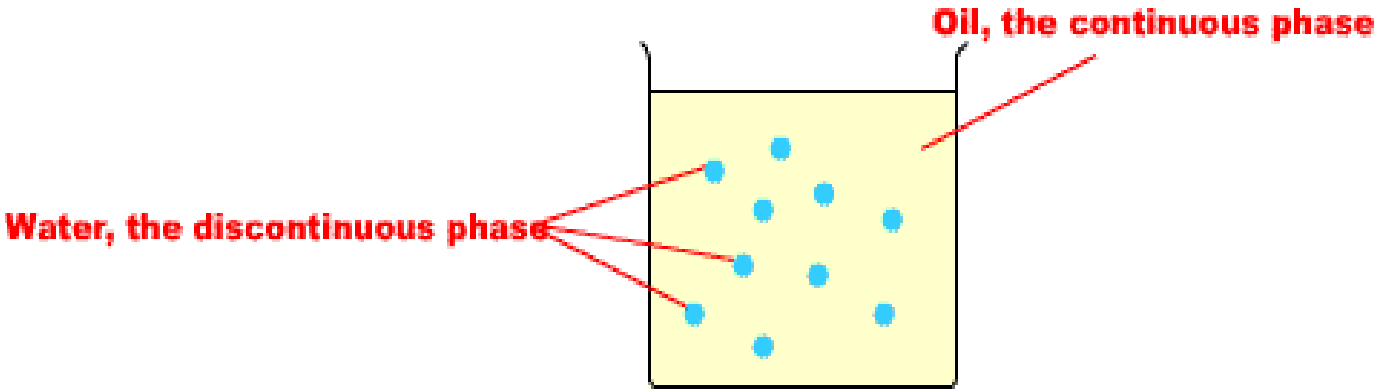


Figure 1b: W/O emulsion

Emulsions

- Orally (o/w) emulsion:
  - Mask the taste of a bitter drug
  - May enhance bioavailability of a drug

لـ(التوافر الحيوي)

كم يحدث امتصاص للدواء من الجسم اذا أخذناه orally

- Topically: Lotions and creams:
  - Creams are thick emulsions
  - Lotions are fluid emulsions (some lotions actually are suspensions rather than emulsions)
- Parenteral nutrition

تغذية بالوريد

parenteral (IV)

oral.

topical

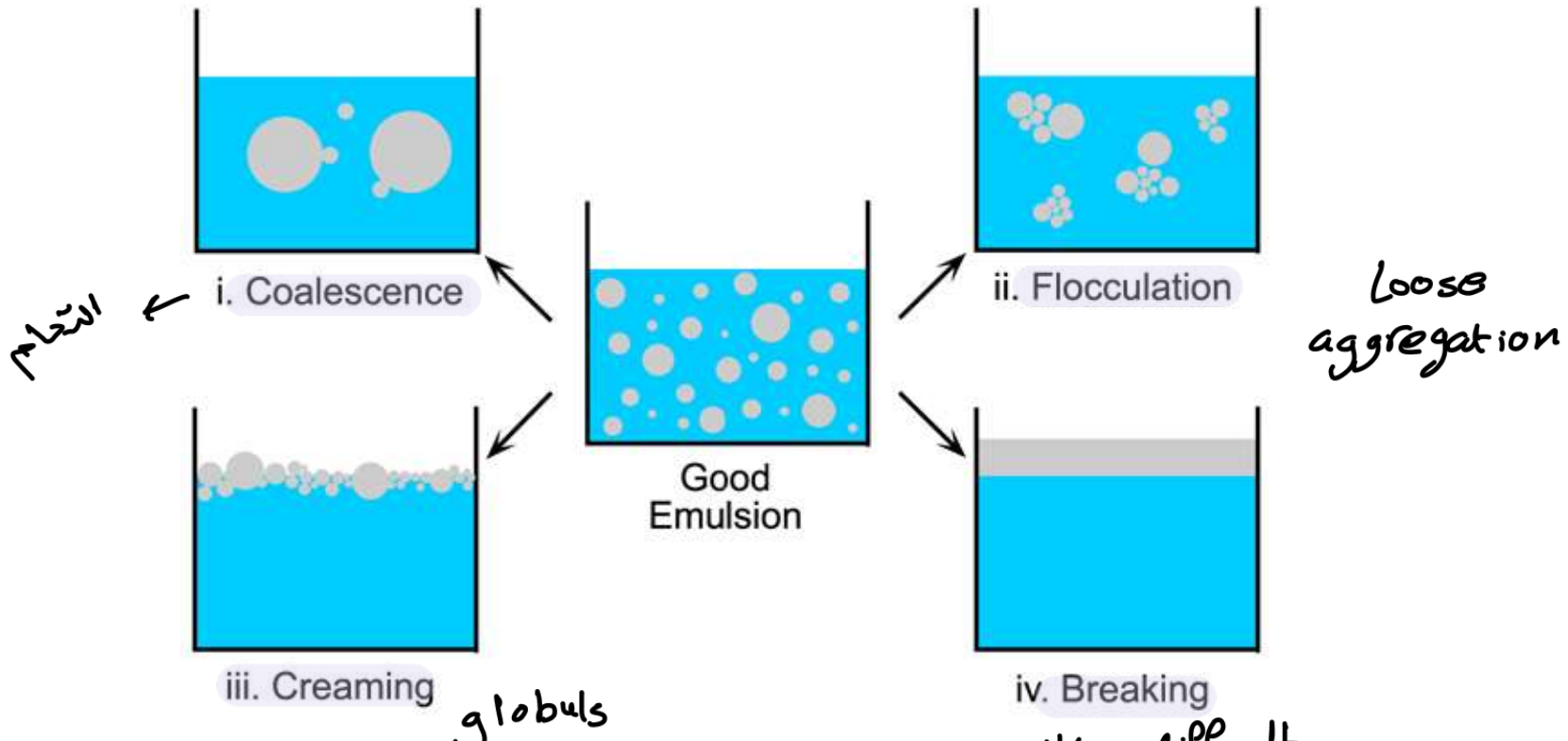
Stability

Three levels of instability:

1. Creaming: occurs when dispersed oil droplets merge and rise to the top of an o/w emulsion or settle to the bottom in w/o emulsions. In both cases, the emulsion can be easily redispersed by shaking.
2. Coalescence: the fusion of the dispersed phase droplets. Viscosity adjustment and using an optimum phase:volume ratio may minimize coalescence
3. Phase inversion: a change from w/o to o/w (or vice versa) may occur. This is considered a type of instability by some.

Types of instability

by shaking we could get again as emulsion

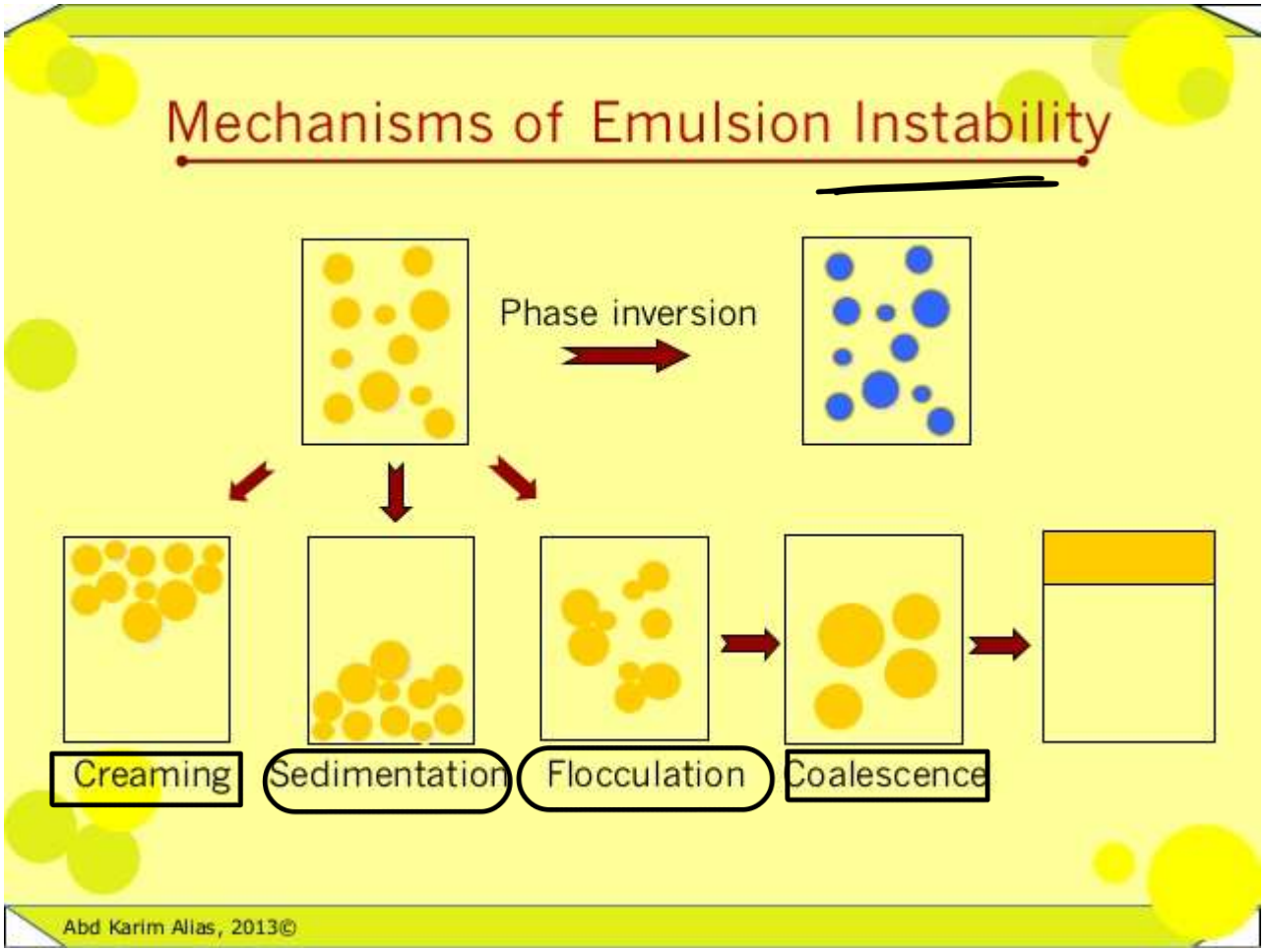


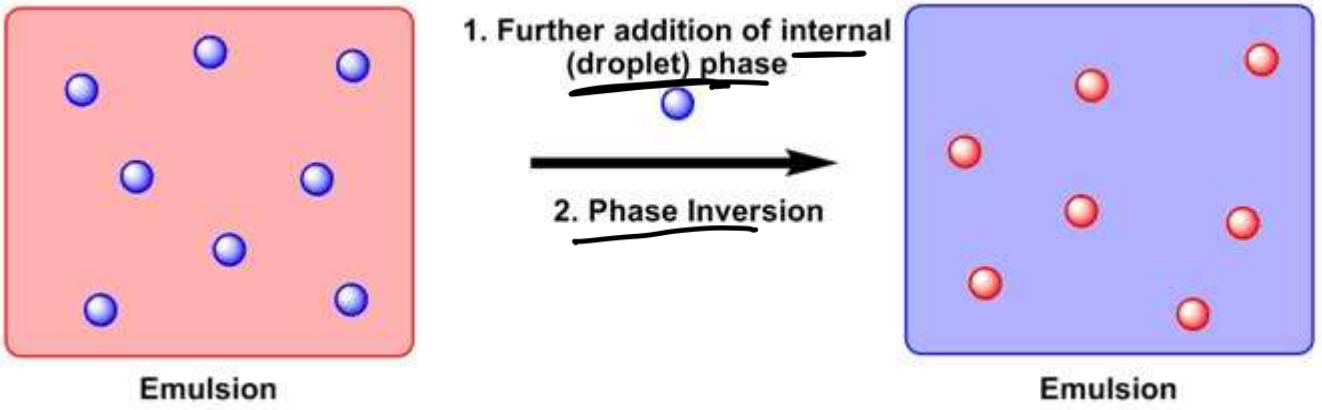
التجلم

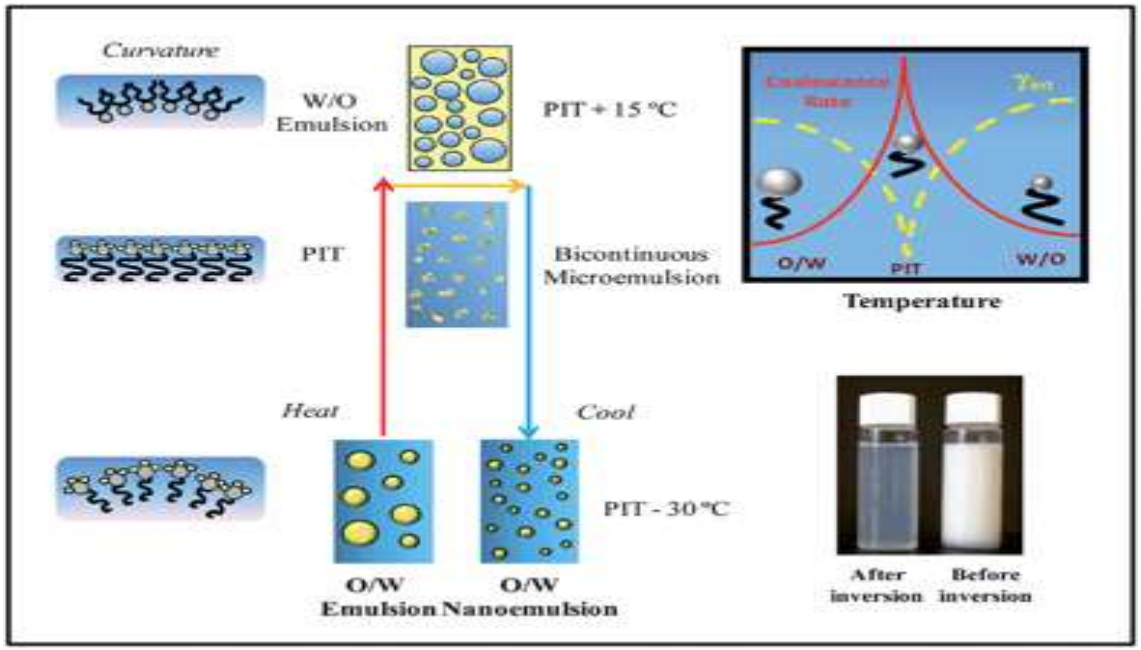
Loose aggregation

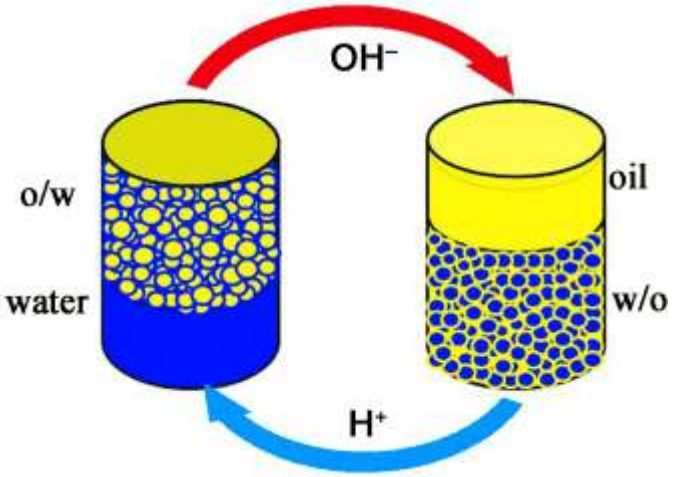
globuls

it's diffcult to reverse it.


Mechanisms of Emulsion Instability
Phase inversion
Creaming
Sedimentation
Flocculation
Coalescence
Abd Karim Alias, 2013©


1. Further addition of internal (droplet) phase
2. Phase Inversion
Emulsion
Emulsion


Curvature
W/O Emulsion
PIT + 15 °C
PIT
Bicontinuous Microemulsion
Heat
Cool
PIT - 30 °C
O/W Emulsion
O/W Nanoemulsion
O/W
PIT
W/O
Temperature
After inversion
Before inversion


OH⁻
o/w
water
oil
w/o
H⁺

Increasing the stability of an emulsion:

1. Use the optimum phase:volume ratio (i.e. the ratio of the internal volume to the total volume of the product) $V_{internal} : V_{tot}$
2. Reduce the globule size of the internal phase
3. Increase the viscosity of the external aqueous phase
4. Adjust the densities of both the internal phase and the external phase so the densities are the same

Emulsifying agent:

- Emulsions are formed by adding an emulsifier or emulsifying agents
- Emulsifying agents are adsorbed onto the oil:water interface:
  - provide a protective barrier around the dispersed droplets
  - reduce the **interfacial tension** of the system
  - Some agents also impart a charge on the droplet surface thereby decrease the physical contact between droplets
- General characteristics: chemically stable in the system, chemically nonreactive with other emulsion components, nontoxic , nonirritating and reasonably odorless.

Emulsifying agent classification:

1. Chemical structure:

- Synthetic
- Natural
- Finely dispersed solids (بشکل جید)
- Auxiliary agents

2. Mechanism of action:

- Surface active agents (adsorb at the oil/water interface forming a monomolecular layer)
- Hydrophilic colloids (form multimolecular layers at the interface)
- Finely divided solid particles (adsorb at the interface and form a layer of particles around the droplets

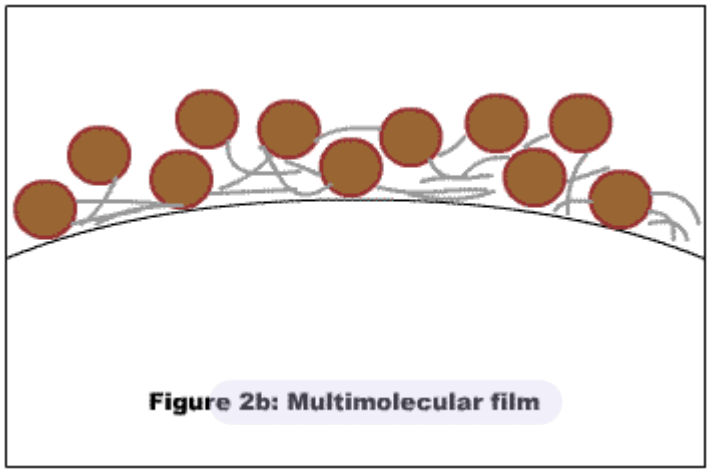


Figure 2b: Multimolecular film

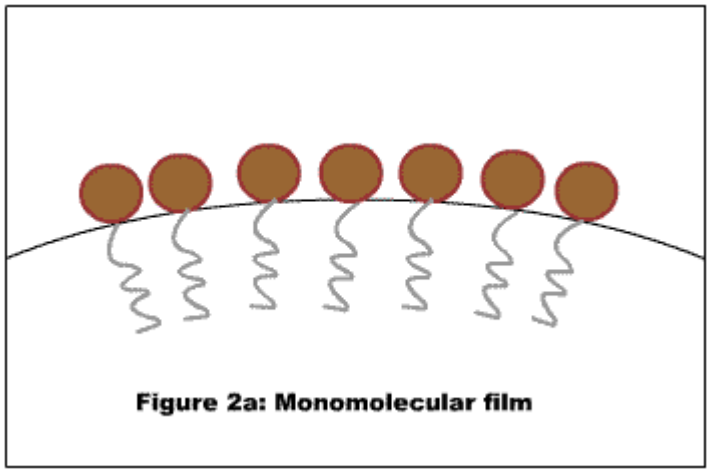


Figure 2a: Monomolecular film

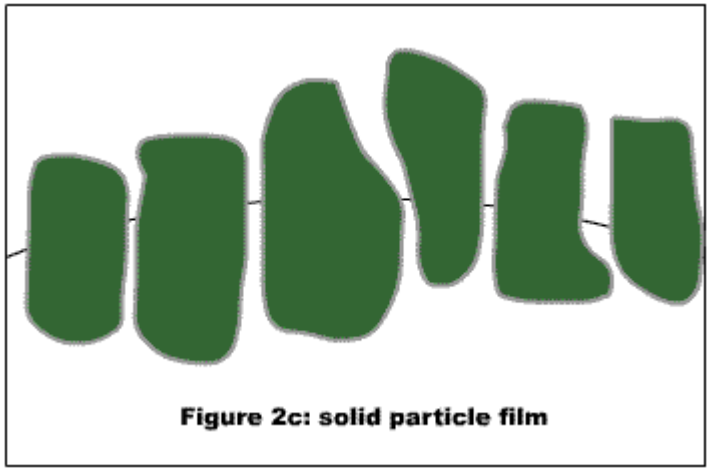


Figure 2c: solid particle film

بقلل التاتر بين الزيت والماء ويتكون o/w او w/o

Synthetic emulsifying agents

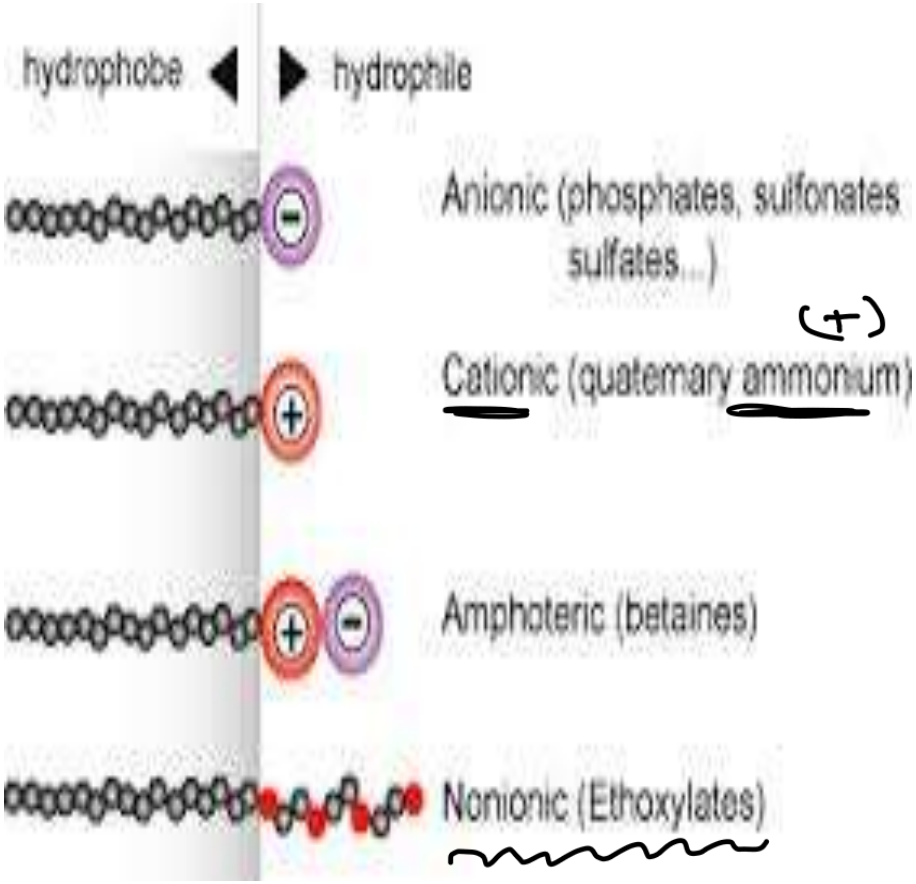
- Have both a hydrophilic part (e.g. carboxyl, hydroxyl, amino groups) and a lipophilic part (e.g. alkyl chain)
- Classified based on the properties of the hydrophilic part as:

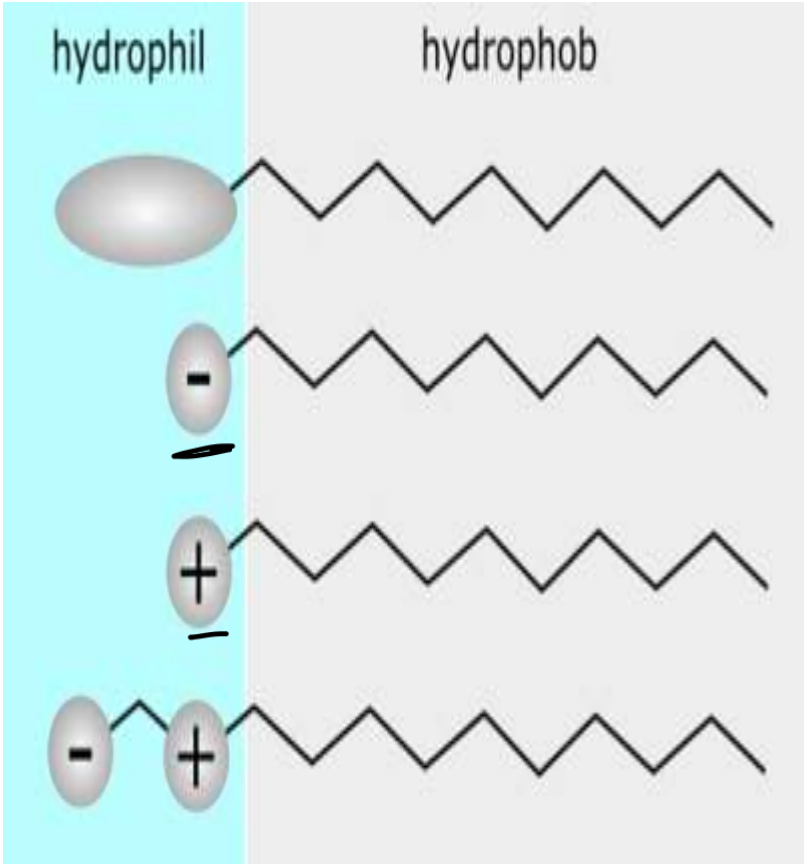
- Anionic (−)
- Cationic (+)
- Nonionic
- Amphoteric (+ و −)

Synthetic emulsifying agents

- When the liquid is in contact with a second liquid in which it is insoluble and immiscible, the force causing each liquid to resist breaking up into smaller particles is called **interfacial tension**
- Substances that reduce this resistance encourage a liquid to break up into smaller drops or particles.
- These tension-lowering substances are *surface active (surfactant)*

(surfactant)

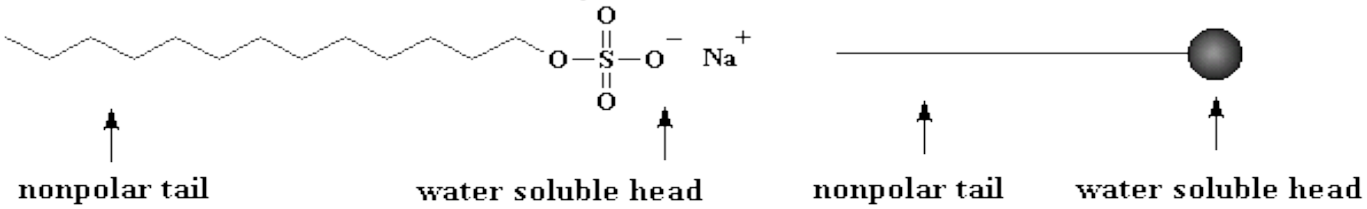

hydrophobe
hydrophile
Anionic (phosphates, sulfonates sulfates...)
Cationic (quatemary ammonium)
Amphoteric (betaines)
Nonionic (Ethoxylates)


hydrophil
hydrophob

Synthetic emulsifying agents: Anionic Surfactants

- Contain, carboxylate, sulfate, and sulfonate groups
- Are soaps and detergents
- Carboxylate surfactants have the tendency to undergo hydrolysis and decompose
- The long alkyl sulfates typically are used as surfactants of which sodium lauryl sulfate is the best known
- Anionic surfactants require a pH greater than 8
- Are used in topical o/w emulsion

hydrophilic surfactant

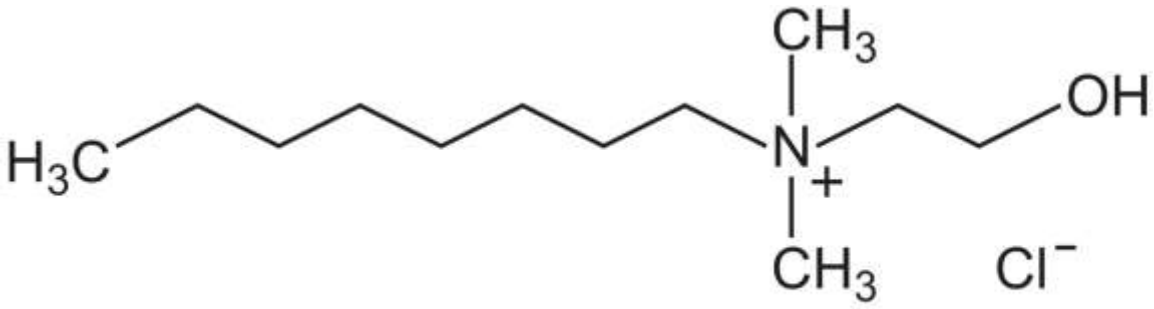


Sodium Lauryl Sulfate

Lazy chemist's representation of Sodium Lauryl Sulfate

Synthetic emulsifying agents: Cationic surfactants

- Are used as bactericidal agents ← قدرة قتل البكتيريا
- Long chain amino and quaternary ammonium salts
- Are used in topical o/w emulsions
- Cationic agents (quarternary ammonium salts) are incompatible with organic anions and are infrequently used as emulsifiers
- cationic surfactants are effective over pH range of 3 to 7



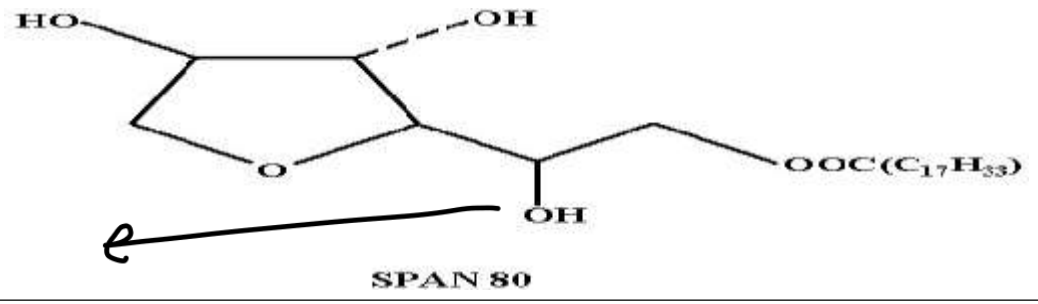
an alkyl quaternary system

Synthetic emulsifying agents: Nonionic surfactants

- Most frequently used of all the surfactants
- Have a neutral pH and resist the addition of acids and electrolytes
- Nonionic surfactants are effective over pH range of 3 to 10;
- They are superior in compatibility, stability, and lack of toxicity
- Divided into:

1. Those that are more hydrophobic
2. Those that are more hydrophilic

في الحالتين بنقدر نستخدمهم



SPAN 80

Natural Emulsifying Agents:

- are natural products derived from plant or animal tissue.
- Most of them form hydrated lyophilic colloids (called **hydrocolloids**) that form multimolecular layers around emulsion droplets.
- Lyophilic: (of a colloid) readily dispersed by a solvent and not easily precipitated.
- Hydrocolloid type emulsifiers have little or no effect on interfacial tension
- They exert a protective colloid effect, reducing the potential for coalescence, by:

- providing a protective sheath around the droplets
- imparting a charge to the dispersed droplets (so that they repel each other)
- swelling to increase the viscosity of the system (so that droplets are less likely to merge)

Natural Emulsifying Agents:

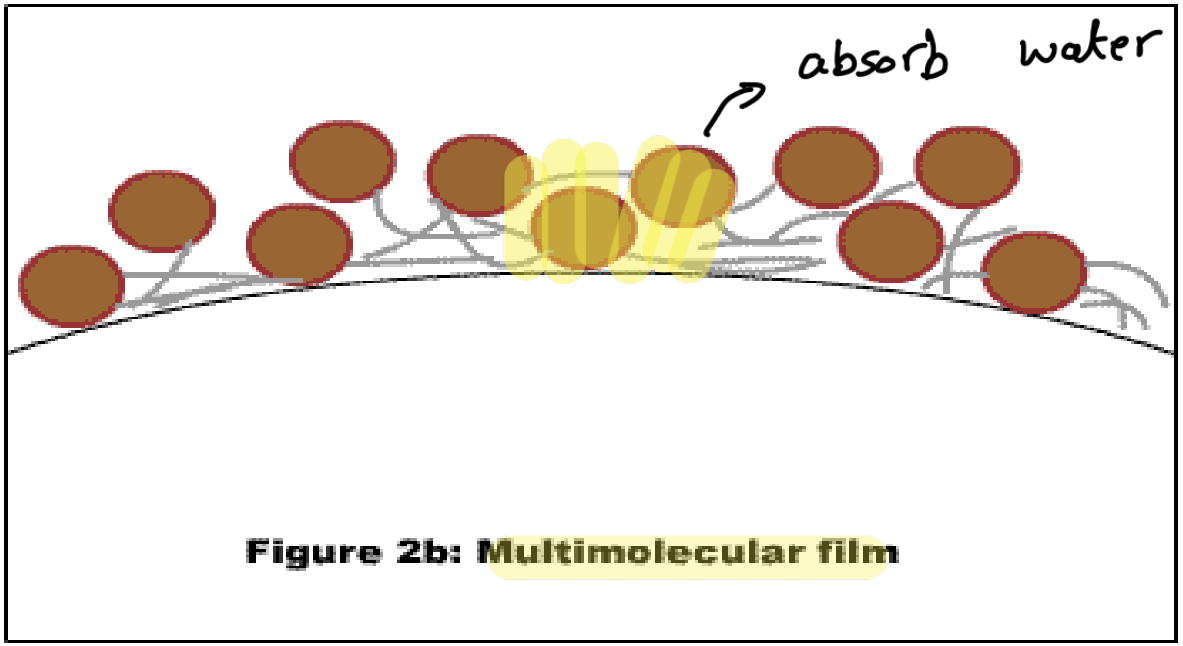


Figure 2b: Multimolecular film

Natural Emulsifying Agents:

Hydrocolloid emulsifiers may be classified as:

1. Vegetable derivatives, e.g., acacia, tragacanth, agar, pectin, carrageenan
2. Animal derivatives, e.g., gelatin, lanolin, cholesterol, lecithin
3. Semi-synthetic agents, e.g., methylcellulose, carboxymethylcellulose
4. Synthetic agents, e.g., Carbopols®

Natural Emulsifying Agents: Vegetable hydrocolloids

- have the advantages of being inexpensive, easy to handle, and nontoxic.
- Their disadvantages are that they require relatively large quantities to be effective as emulsifiers, and they are subject to microbial growth and thus their formulations require a preservative.
- Vegetable derivatives are generally limited to use as o/w emulsifiers.
- Form multimolecular film around the droplets

Natural Emulsifying Agents:

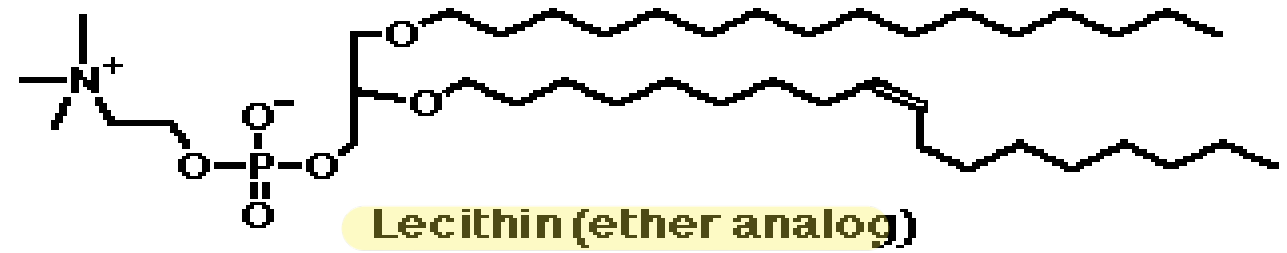
Animal derivatives

- Lecithin and cholesterol form a monomolecular layer around the emulsion droplet instead of the typically multimolecular layers.
- Cholesterol is a major constituent of wool alcohols and it gives lanolin the capacity to absorb water and form a w/o emulsion.
- Lecithin (a phospholipid derived from egg yolk) produces o/w emulsions because of its strong hydrophilic character.
- Animal derivatives are more likely to cause allergic reactions and are subject to microbial growth and rancidity.
- Their advantage is in their ability to support formation of w/o emulsions.

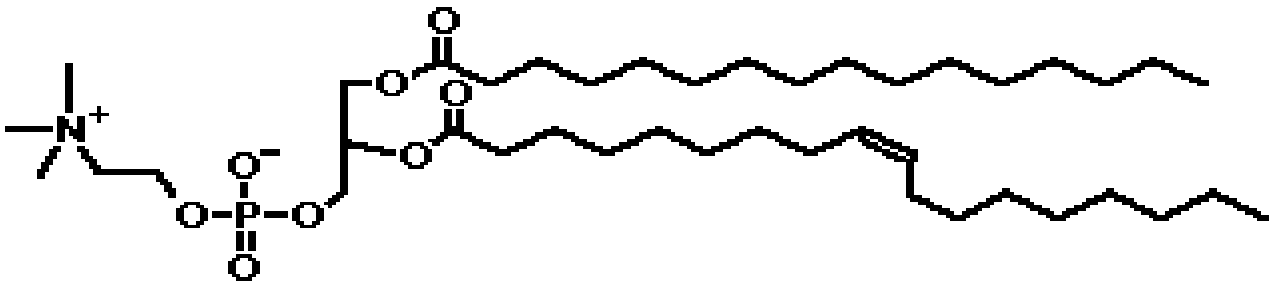
Natural Emulsifying Agents: Animal derivatives

- **Wool alcohols** are the principle component of **lanolin**
- **Lanolin** is a natural product obtained from the fleece of sheep.
- Sebum is extracted from the **wool**, cleaned and refined to produce anhydrous **lanolin**.

Natural Emulsifying Agents: Animal derivatives



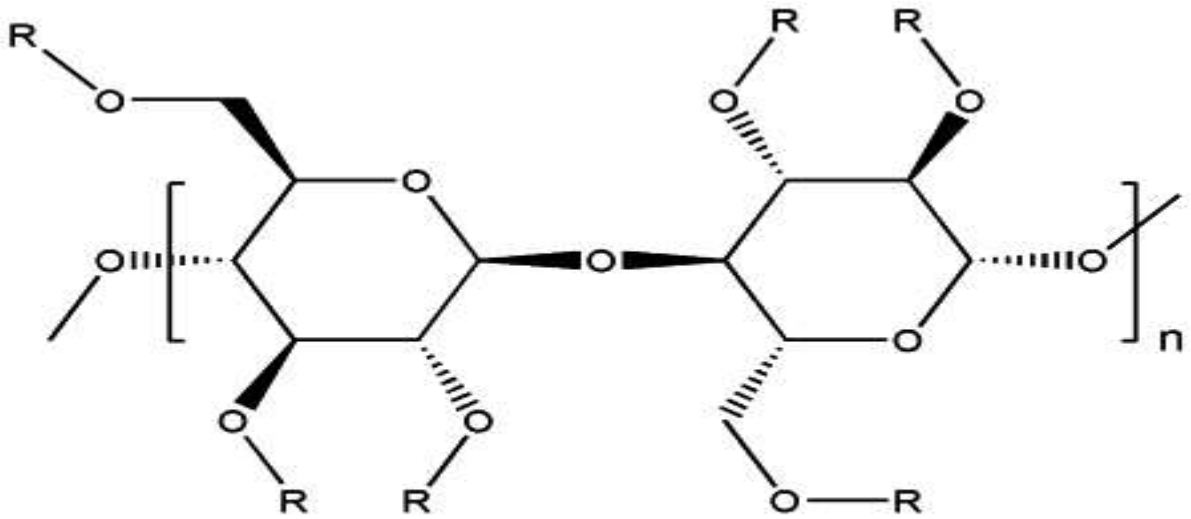
Lecithin (ether analog)



Phosphatidylcholine (lecithin)

Natural Emulsifying Agents: Semi-synthetic agents

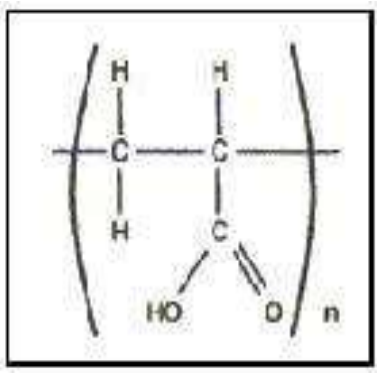
- Semi-synthetic agents are stronger emulsifiers
- are nontoxic,
- and are less subject to microbial growth



Cellulose: R = H
Methyl cellulose: R = CH_3 (40-90%) or H

Natural Emulsifying Agents: Synthetic hydrocolloids

- Are the strongest emulsifiers,
- are nontoxic,
- and do not support microbial growth.
- However, their cost may be prohibitive. ← تكلفة باهظة
- These synthetic agents are generally limited to use as o/w emulsifiers.



General structure of carbopol polymer

Finely divided or dispersed solid particle emulsifiers:

- These agents form a particulate layer around dispersed particles.
- Most will swell in the dispersion medium to increase viscosity and reduce the interaction between dispersed droplets.
- Most commonly they support the formation of o/w emulsions, but some may support w/o emulsions.
- These agents include bentonite, veegum, hectorite, magnesium hydroxide, aluminum hydroxide and magnesium trisilicate.

Auxiliary emulsifying agents

- A variety of fatty acids (e.g., stearic acid), fatty alcohols (e.g., stearyl or cetyl alcohol), and fatty esters (e.g., glyceryl monostearate)
- Serve to stabilize emulsions through their ability to thicken the emulsion.
- Because these agents have only weak emulsifying properties, they are always use in combination with other emulsifiers.

Auxiliary emulsifying agents

Table 22-5. Auxiliary Emulsifying Agents

PRODUCT	SOURCE AND COMPOSITION	PRINCIPAL USE
Cetyl alcohol	Chiefly $C_{16}H_{33}OH$	Lipophilic thickening agent and stabilizer for O/W lotions and ointments
Glyceryl monosterate	$C_{17}H_{35}COOCH_2CHOHCH_2OH$	Lipophilic thickening agent and stabilizer for O/W lotions and ointments
Methylcellulose	Series of methyl ethers of cellulose	Hydrophilic thickening agent and stabilizer for O/W emulsions; weak O/W emulsifier
Sodium carboxymethylcellulose	Sodium salt of the carboxymethyl esters of cellulose	Hydrophilic thickening agent and stabilizer for O/W emulsions
Stearic acid	A mixture of solid acids from fats, chiefly stearic and palmitic	Lipophilic thickening agent and stabilizer for O/W lotions and ointments. Forms a true emulsifier when reacted with an alkali

Semi synthetic

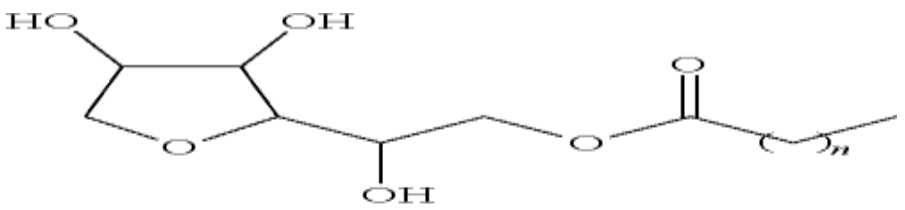
Auxiliary (secondary) emulsifying agents include those compounds that are normally incapable themselves of forming stable emulsion. Their main values lies in their ability to function as thickening agents and thereby help stabilize the emulsion.

The Hydrophile-Lipophile balance (HLB) System

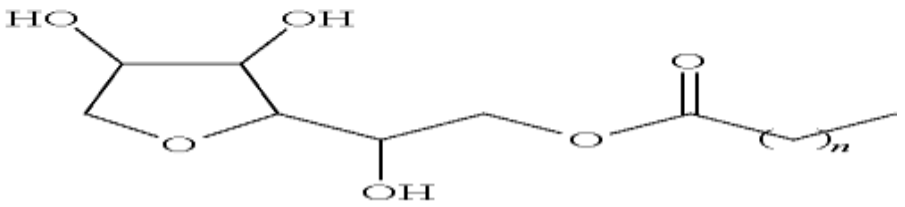
- A system was developed to assist in making systemic decisions about the amounts and types of surfactants needed in stable products.
- The system is called the HLB (hydrophile-lipophile balance) system and has an arbitrary scale of 1 - 20.
- HLB numbers are experimentally determined for the different emulsifiers

The Hydrophile-Lipophile balance (HLB) System

- If an emulsifier has a low HLB number, there is a low number of hydrophilic groups on the molecule and it will have more of a lipophilic character.
- For example, the Spans® (sorbitan esters) generally have low HLB numbers and they are also oil soluble.
- Because of their oil soluble character, Spans® will cause the oil phase to predominate and form an w/o emulsion.



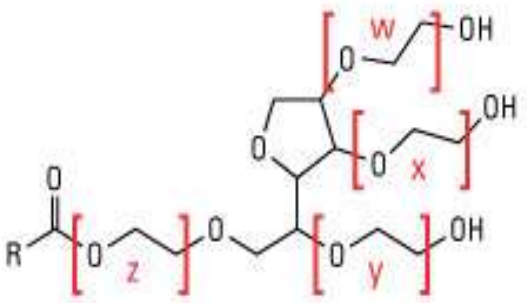
Sorbitan Ester n = 6-12



Sorbitan Laurate (n = 10)

The Hydrophile-Lipophile balance (HLB) System

- The higher HLB number would indicate that the emulsifier has a large number of hydrophilic groups on the molecule and therefore should be more hydrophilic in character.
- The Tweens® (polyoxyethylene derivatives of sorbitan esters) have higher HLB numbers and they are also water soluble.
- Because of their water soluble character, Tweens® will cause the water phase to predominate and form an o/w emulsion.



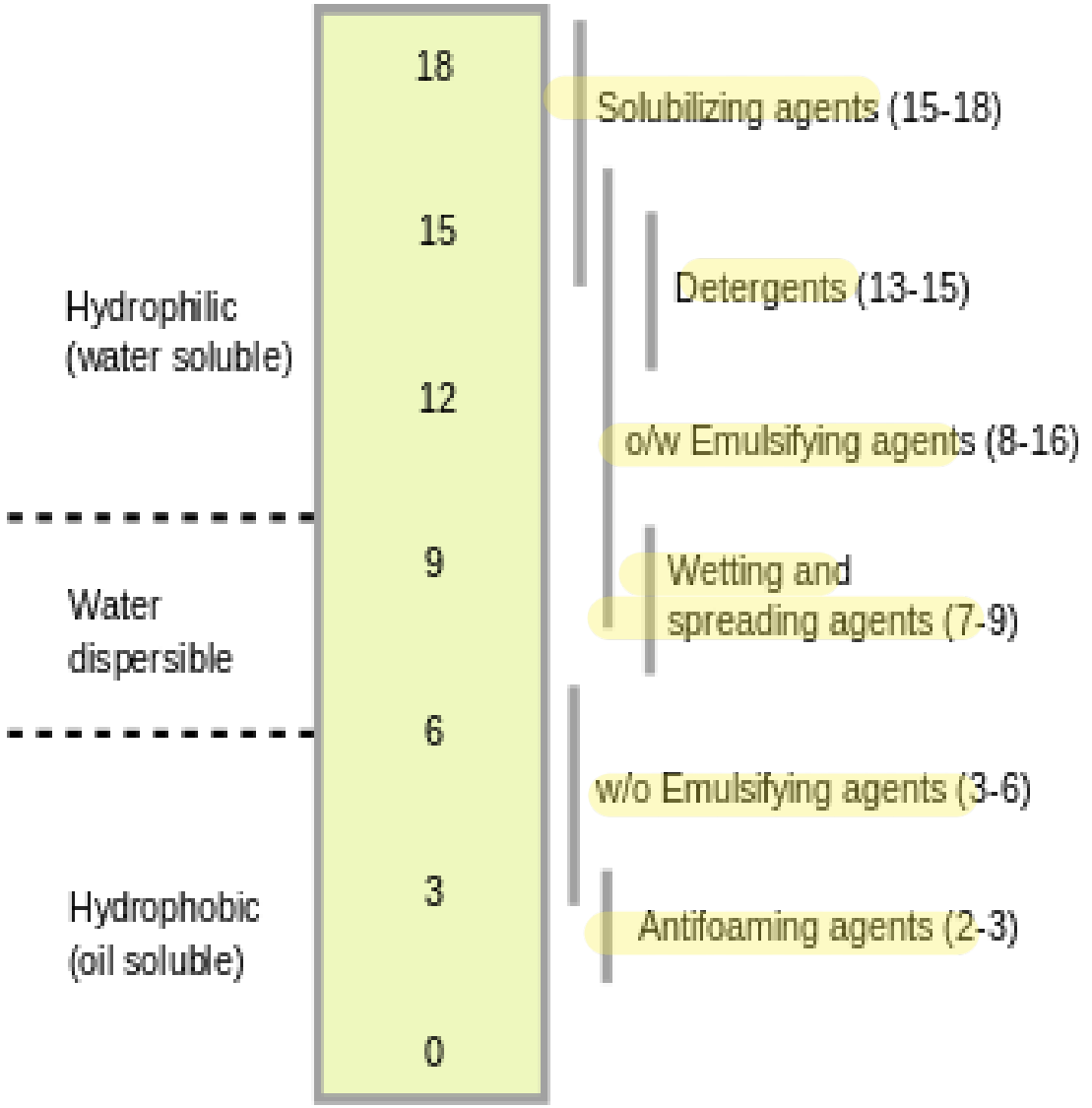
Tween* 20 Detergent

w + x + y + z = 20

R = $CH_2(CH_2)_9CH_3$

MW 1228

- the phase in which the emulsifying agent is more soluble will become the continuous or external phase



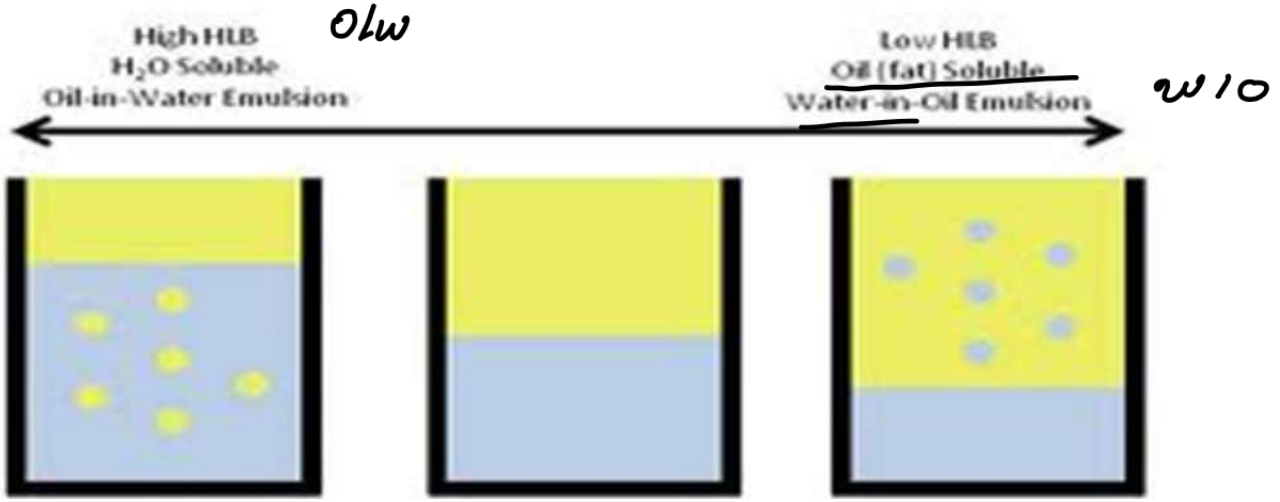
The Hydrophile-Lipophile balance (HLB) System

- Combinations of emulsifiers can produce more stable emulsions than using a single emulsifier with the same HLB number. The HLB value of a combination of emulsifiers can be calculated as follows:

$$HLB = \frac{(Quantity\ of\ surfactant\ 1)(HLB\ surfactant\ 1) + (quantity\ of\ surfactant\ 2)(HLB\ surfactant\ 2)}{quantity\ of\ surfactant\ 1 + quantity\ of\ surfactant\ 2}$$

$$HLB = \frac{(\text{Quantity of surfactant 1})(\text{HLB surfactant 1}) + (\text{quantity of surfactant 2})(\text{HLB surfactant 2})}{\text{quantity of surfactant 1} + \text{quantity of surfactant 2}}$$

HLB value	Surfactant properties
0 – 3	anti-foaming agent
4 – 6	W/O (water in oil) emulsifier
7 – 9	wetting agent
8 – 18	O/W (oil in water) emulsifier
13 – 15	detergents
> 15	solubiliser or hydrotrope



- *Wetting agents are surfactants with HLB values of* ***7 to 9. Wetting agents aid in attaining intimate contact*** between solid particles and liquids.
- *Emulsifying agents are surfactants with HLB values of* ***4 to 6 or 8 to 18. Emulsifying agents reduce interfacial tension*** between oil and water, minimizing surface energy through the formation of globules.
- *Detergents are surfactants with HLB values of* ***13 to 15. Detergents will reduce the surface tension and*** aid in wetting the surface and the dirt. The soil will be emulsifed, and foaming generally occurs → washing away of the dirt.
- *Solubilizing agents have HLB values of* ***15 to 20.***

- *e.g.What is the HLB value of a surfactant system composed of 20 g Span 20 (HLB = 8.6) and 5 g Tween 21 (HLB = 13.3)?*

$$HLB = \frac{(20g)(8.6) + (5\ g)(13.3)}{(20g) + (5\ g)}$$

$= 9.54$

tend to be (o/w)

Commonly Used Emulsifiers And Their HLB Values

TABLE 14.2 HLB VALUES FOR SELECTED EMULSIFIERS

AGENT	HLB
Ethylene glycol distearate	1.5
Sorbitan tristearate (Span 65[a])	2.1
Propylene glycol monostearate	3.4
Triton X-15[b]	3.6
Sorbitan monooleate (Span 80[a])	4.3
Sorbitan monostearate (Span 60[a])	4.7
Diethylene glycol monolaurate	6.1
Sorbitan monopalmitate (Span 40[a])	6.7
Sucrose dioleate	7.1
Acacia	8.0
Amercol L-101[c]	8.0
Polyoxyethylene lauryl ether (Brij 30[d])	9.7
Gelatin	9.8
Triton X-45[b]	10.4
Methylcellulose	10.5
Polyoxyethylene monostearate (Myrj 45[e])	11.1
Triethanolamine oleate	12.0
Tragacanth	13.2
Triton X-100[b]	13.5
Polyoxyethylene sorbitan monostearate (Tween 60[a])	14.9
Polyoxyethylene sorbitan monooleate (Tween 80[a])	15.0
Polyoxyethylene sorbitan monolaurate (Tween 20[a])	16.7
Pluronic F 68[f]	17.0
Sodium oleate	18.0
Potassium oleate	20.0
Sodium lauryl sulfate	40.0

Design an experiment to show the influence of HLB combinations on emulsion formation and stability using Tween® 20 and Span® 85 as surfactants

- Refer to pg 107

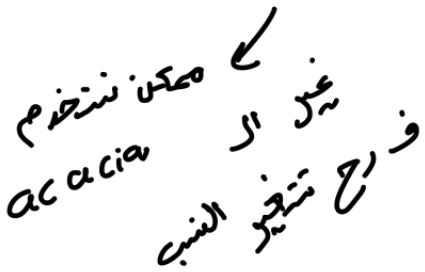
Methods of compounding emulsions: 1. Continental (Dry gum or 4:2:1) Method

- The continental method is used to prepare the initial or primary emulsion from oil, water, and a hydrocolloid or "gum" type emulsifier (usually acacia).
- The primary emulsion, or emulsion nucleus, is formed from 4 parts oil, 2 parts water, and 1 part emulsifier.
- In a mortar, the 1 part gum is levigated with the 4 parts oil until the powder is thoroughly wetted; then the 2 parts water are added all at once, and the mixture is vigorously and continually triturated until the primary emulsion formed is creamy white and produces a "cracking" sound as it is triturated (usually 3-4 minutes).

Methods of compounding emulsions:

2. English (Wet Gum) Method

- In this method the order and techniques of mixing are different.
- The 1 part gum is triturated with 2 parts water to form a mucilage; then the 4 parts oil is added slowly, in portions, while triturating.
- After all the oil is added, the mixture is triturated for several minutes to form the primary emulsion.
- Generally speaking, the English method is more difficult to perform successfully, especially with more viscous oils, but may result in a more stable emulsion.
- The ratio of oil: water: emulsifier depend on oil and emulsifier being used



Methods of compounding emulsions: 3. Bottle (Forbes) Method

- This method may be used to prepare emulsions of volatile oils, or oleaginous substances of very low viscosities. It is not suitable for very viscous oils since they cannot be sufficiently agitated in a bottle.
- This method is a variation of the dry gum method.
- One part powdered acacia (or other gum) is placed in a dry bottle and four parts oil are added. The bottle is capped and thoroughly shaken. To this, the required volume of water is added all at once, and the mixture is shaken thoroughly until the primary emulsion forms.
- It is important to minimize the initial amount of time the gum and oil are mixed. The gum will tend to imbibe the oil, and will become more waterproof.

Methods of compounding emulsions:

4. Beaker Method

- When synthetic or non-gum emulsifiers are used, the previous methods become meaningless.
- The most appropriate method for preparing emulsions from surfactants or other non-gum emulsifiers is to begin by dividing components into water soluble and oil soluble components.
- All oil soluble components are dissolved in the oily phase in one beaker and all water soluble components are dissolved in the water in a separate beaker.
- Both phases (i.e. beakers) are heated to approximately 70°C over a water bath (the aqueous phase should be heated to a few degree higher).
- The internal phase is then added to the external phase with stirring until the product reaches room temperature.
- The mixing of such emulsions can be carried out in a beaker, mortar, or blender.

Methods of compounding emulsions:

5. Auxiliary Methods

- Instead of, or in addition to, any of the preceding methods, the pharmacist can usually prepare an excellent emulsion using an electric mixer or blender.
- An emulsion prepared by other methods can also usually be improved by passing it through a hand homogenizer, which forces the emulsion through a very small orifice, reducing the dispersed droplet size to about 5 microns or less.
- The formulation usually is improved in both stability (because droplet size is reduced) and appearance

Methods of compounding emulsions: In Situ Soap Method

- Self emulsifying emulsions
- The two types of soaps developed by this method are calcium soaps and soft soaps (olive oil soap).
- Calcium soaps are w/o emulsions that contain certain vegetable oils, such as oleic acid, in combination with limewater (synonym: Calcium Hydroxide Solution, USP).
- They are prepared simply by mixing equal volumes of the oil and limewater. The emulsifying agent in this instance is the calcium salt of the free fatty acid formed from the combination of the two entities.
- In the case of olive oil, the free fatty acid is oleic acid and the resultant emulsifying agent is calcium oleate.

Methods of compounding emulsions: In Situ Soap Method

- A typical example of this emulsion is calamine liniment:

- Calamine soothing agent
- Zinc oxide
- Olive oil
- Calcium hydroxide solution
- qs ad 1000.0 mL

Adding ingredients to a primary emulsion:

- Solid substances (active ingredients, preservatives, colors) are dissolved and added as a solution to the primary emulsion
- Volatile ingredients (flavors, odors, or active drugs) should be added once the product has cooled if heat was used
- Small amounts of oil soluble substances may be incorporated directly into the primary emulsion
- Any substance might reduce the physical stability of the emulsion (i.e. alcohol) should be added to the near end of the process

Adding ingredients to a primary emulsion:

- Viscosity enhancers can be added to a primary emulsion to increase stability of the formulation
- The enhancers should be miscible in the external phase of the emulsion
- o/w → hydrocolloids
- w/o → viscous oils, fatty alcohols, or fatty acids

Adding ingredients to a primary emulsion:

- When all agents have been incorporated, the emulsion should be transferred to a calibrated vessel, brought to final volume with water, then homogenized or blended to ensure uniform distribution of ingredients.

Adding ingredients to a commercially prepared emulsion

- With w/o emulsions:

- Oils and insoluble powders can be incorporated directly into the external phase using a tile and spatula
- If a large amount of insoluble powder is being added a levigating agent (i.e. mineral oil) may be necessary that should be miscible with oil phase

Adding ingredients to a commercially prepared emulsion

- With w/o emulsions (cont.):

- If an aqueous soluble material to be added, excess emulsifier must be present
- For those w/o emulsion that do not have excess emulsifier, additional emulsifier may have to be added
- An aqueous solution may be added using a pill tile and spatula, but some may require heat

Adding ingredients to a commercially prepared emulsion

- With o/w emulsions:

- Levigating agents for aqueous insoluble substances should be water miscible as glycerin, propylene glycol, polyethylene glycol, or alcohol
- If heat is used to incorporate → work quickly → be careful not to evaporate water from the product → stiff
- In many commercial o/w emulsions, sufficient emulsifying agents is already present in the preparation to accommodate the added oils or powders

Flavoring emulsions

- Select it based on the external phase
- Flavoring oil can be mixed with emulsifier or with a water miscible solvents as glycerin or ethanol

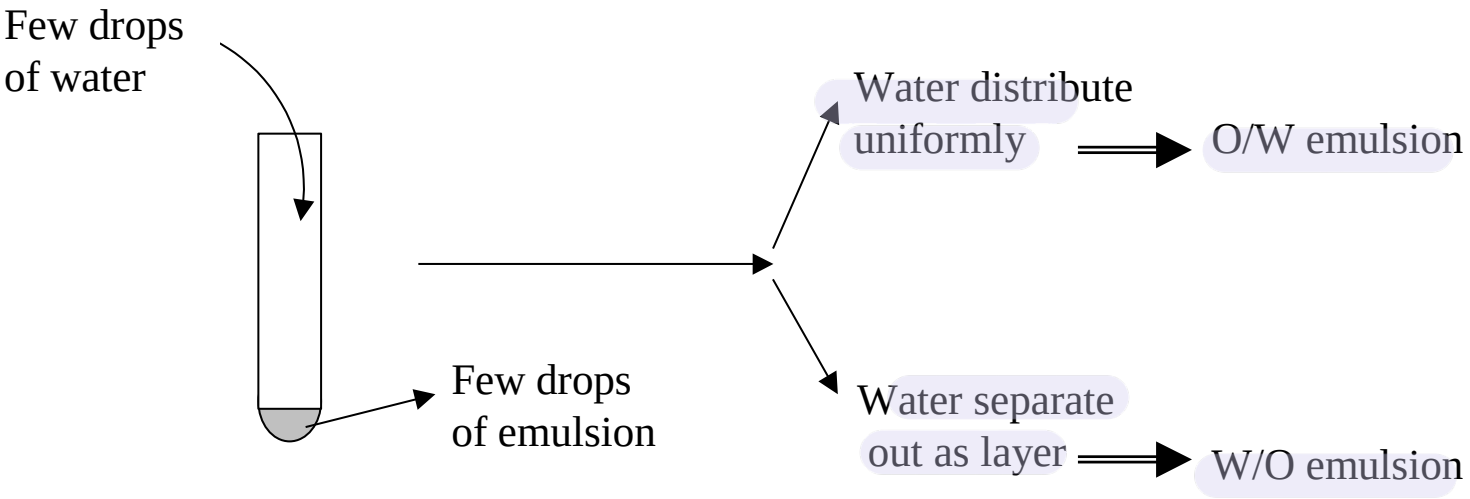
(wetting agent)

Determining type of emulsion: 1. Dilution test

- based on the solubility of external phase:

- o/w emulsion can be diluted with water.

- w/o emulsion can be diluted with oil.



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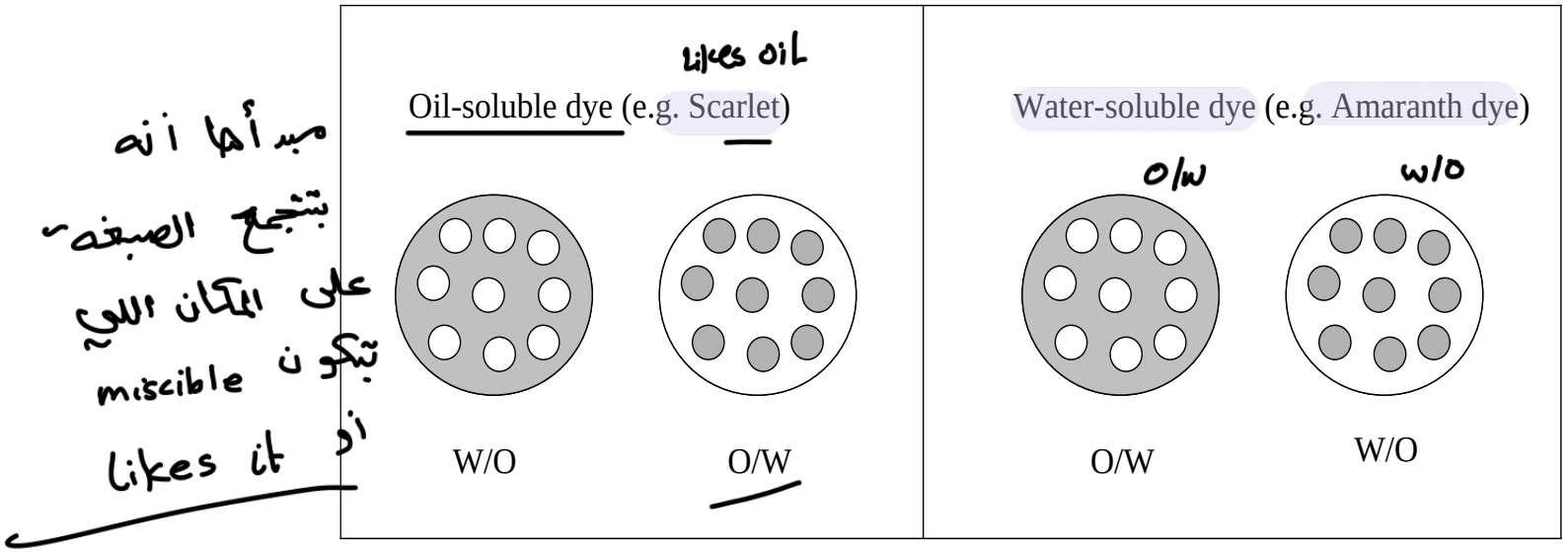
Determining type of emulsion:
2. Dye test:

- Water-soluble dye will dissolve in the aqueous phase.
- Oil-soluble dye will dissolve in the oil phase.



مبدأها انه بتجمع الصبغة على المكان اللي تبكون miscible فيه likes it

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Determining type of emulsion:

3. Drop test:

- Put a drop of the formulation on the surface of water
- If the drop spreads out, the emulsion is an o/w emulsion because the external phase is miscible with water
- If the drop stays as a drop or "balls up", it is a w/o emulsion

Packaging

- Tight containers to avoid loss of water
- Tubes, pumps, squeeze bottles, jars
- If it is liquid:

→enough room for shaking

→Large opening bottle for easy pouring

Observing formulations for evidence of instability:

- Breaking (i.e. separation of an oil phase that is not easily dispersed)
- Crystal growth
- Shrinkage due to water evaporation
- Microbial contamination

Emulsion Contamination

Preservatives

- Aqueous phase support growth of M.O (microorganism)
- Microbes produce changes in emulsion's appearance, cause discoloration and development of gases and odors and change in viscosity
- Microbes may also decompose nonionic and anionic surfactants and other additives as glycerin, gum, and hydrocolloids
- Fungistic and bacteriostatic preservatives (تثبيط (عدم تكاثر البكتيريا) و ليس قتلها)
- Methylparaben, propylparaben, benzoic acid, benzalkonium chloride

Antioxidants

- Rancidification of oils → produce unpleasant odor and taste
- Antioxidants are added to inhibit this process
- Ascorbic acid, Butylated hydroxyanisole, Butylated hydroxytoluene, l-tocopherol

Factors that affect the choice of emulsion type?

- Oil-soluble drug is prepared in o/w emulsion since its solubility and its taste can be masked by adding flavoring agents to the aqueous phase
- For intravenous injection " i.v." o/w emulsion is the only type could be used.
- For intramuscular injection "i.m." both o/w and w/o types of emulsion could be used. Water-soluble drug can be prepared in w/o emulsion to get prolonged action (depot therapy)
- Topical application:

- Semisolid emulsions are called creams and lotions
- Creams are semi-solid or highly viscous liquid emulsions intended for application to the skin
- w/o or o/w

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Microemulsion

- Self reading page 403

Do it by yourself

- **Estimate what type of emulsion will be formed for the following formulation and justify your answer using no more than two lines?**

W/O

Formula	
Mineral oil	150 ml
Anhydrous Lanolin emulsifyer	5 ml
Span 80 W/O emulsifyer	10 ml
Water q.s.	250 ml

بميلوا لحتى يكونوا W/O ب Low HLP

250 − 165 = 85 mL

water phase oil phase

45% > 43% = $\frac{85\ mL}{250\ mL} * 100$

W/O