

Emulsions

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Credit: Shorooq Abukhamees, PhD



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Emulsions

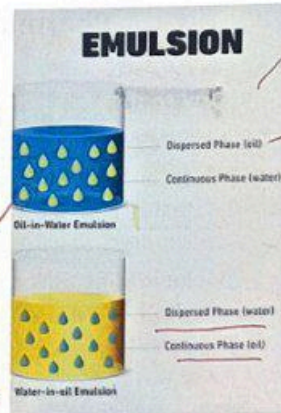
• يكون من 2 مادتين ساطين
يس معش ذ المبات بعض زي
صلا زيت بالمحيطات يوبوا و اساطين
و يشكلوا layer

• An emulsion consists of two immiscible liquids, one of which is uniformly dispersed throughout the other as fine droplets normally of diameter 0.1-100 μm .

• له اذ خضيبه كثير
رجسته بعين بصير عذري
ح نيلت من ااماده لقليلة
بلماده المسمرة و يتكون صخره
صيرك انا صيخت Emulsion

- At least 2 phases:
- ✓ Disperse or internal phase
- ✓ Continuous or external phase
- ✓ Emulsions can be transparent or translucent for emulsion composed of droplets approximately < 200 nm to milky white and opaque for emulsion containing larger droplets

• له اول ما سركه من 200 nm
شور بصير و تبلش قطرات
الماده لقليله تتجمع و تكون ملي
طبقتين ترجع زي قبل ما خضيبه



oil in water
يعني زيت جوا الماء
Dispersed phase
و الوسط الخارجى الكبير هو ماء
Continuous phase
فهنا زيت على ماء
Water in oil
يعني ماء جوا الزيت
Dispersed phase
و الوسط الخارجى الكبير هو زيت
Continuous phase
فهنا ماء على زيت



يكتلمه انه كيفي حجم الجزيئات اذ بال emulsion
ممكن يغير من لونه و شكله

transparent or translucent - most (يكون اقل من 200 nm)

• اما اذا كانت حجم ال drop اكبر من 200 يكون
لون ايضا او خيلسي و يكون معتم

milky to & white
translucent or transparent

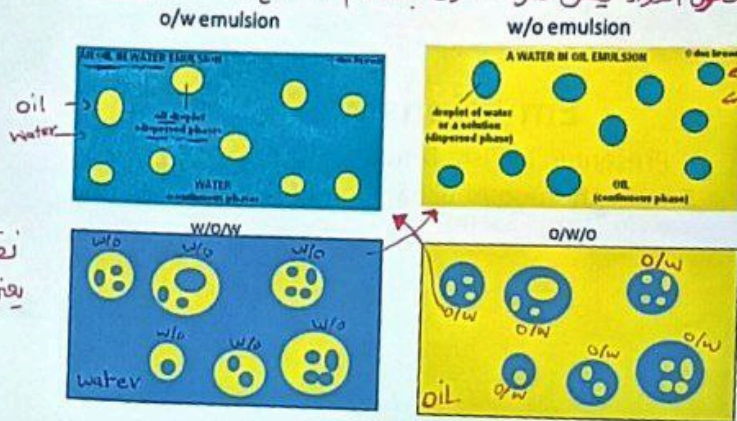
كلما زادت Size of droplets
صا عندي ال emulsion اقل
شفافية اية ايه
بصير opaque

Emulsion types

dispersed phase
continuous phase

in → O/W emulsions.
W/O emulsions.

Multiple emulsions (e.g. W/O/W emulsions for delayed action drug delivery).



نوع O/W/O
مادة موزونة مثل tablet
بمقدار (الوقت) بدهم وقت ليطول
في الجسم يتفاعل مع أكبر واحد
في صورة O/W/W emulsion
Water بعد ذلك مع O/W
الغرض

w/o/w
نقسمها لجزئين (w/o)/w
(water in oil)
بدائرة ككلمة
in water

في هون سلايد لذكورة حزين موجود عند
ذكورة اسراء رشفه ؟ يعني يخرج للسلايد
لقدام



Pharmaceutical application of emulsions

Why emulsions?

عن طريق الفم
① Oral route:

بش ساه افضل لطريقه ال oral
لتحسين الطعم وتسهيل
البلع للدوية اي ما يتوجب الا
oil phase
بزيد امتصاصه / ادوا عبر
intestinal walls
والادوية اللادوية الى قنون في زيت
والادوية الي يتحرك في الماء
مع بعض بنفس التراكيب

- Oral administration of oils or oil-soluble drugs (o/w emulsions).
To enhance palatability of oils when given orally by disguising both taste and oiliness (Taste, odor and oiliness typical of oils are suppressed when administered in the internal phase of an emulsion).
- Increasing absorption of oils and oil-soluble drugs through intestinal walls. An example is griseofulvin suspended in oil in an oil-in-water emulsion.
- Formulation of oil- and water-soluble drugs together.

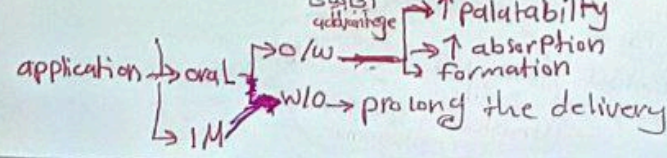
يعني انا جعلت الطعم ما يحسن انه فيزيت بالادوا وانه طعم الزيت مش زكي
ناجسوه بطريقه (o/w)
بغير زي ال aqueous
ال intestinal stomachs
بتمص ال aqueous media
فيكون صعبا اقله الدوا لي يتوجب
بال O/W فيقله (o/w)

Note: Medicinal oils for the local effect of constipation and oral food supplements oil such as fish liver oil + oral delivery of drugs and vitamins of low aqueous solubility small droplets >> large surface area available for contact at the absorption site

w/o emulsions can be used to prolong the delivery of water soluble antigens as The vaccine must first diffuse from the aqueous droplets through the oily external phase before it reaches the tissue.

زيت ما اخذنا بالبيوكيم انه
في ادوية Soluble lipid
هاتنوع ال ال جالز يماثل
Vitamin KEDA

يعني ال w/o يستخدمه عشاق الادوا لطلع ابدا
لانه تبيتيه يتغير الامعاء و تقريبا شوي شوي وتطلع antigens
يعني هي ما يكون فيها حساب مفادة يتطلعها شوي والجسم يتصد ال ال ليه في تستخدم
بال vaccine يكون تأثيره اطول لسنين



Pharmaceutical application of emulsions

Why emulsions?

② IM route: w/o
 ابرة بالعضل

- ① Slow release
- ② greater antibody response
- ③ longer immunity

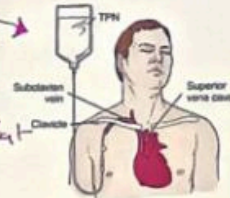
• IM depot therapy: Intramuscular injections of some water-soluble vaccines (w/o emulsions) provide slow release and therefore a greater antibody response and longer-lasting immunity.



A. IV route: o/w
 متعة اقول

• IV (o/w) emulsions for hydrophobic drugs.

• Total parenteral nutrition (TPN) makes use of a sterile oil-in-water emulsion to deliver oily nutrients intravenously to patients, using non-toxic emulsifying agents, such as lecithin.



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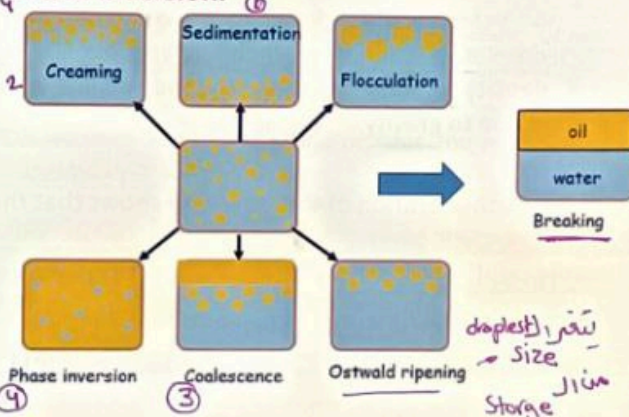
ب. Topical applications (both o/w and w/o emulsions)
 مستخدم لكريكات أكثر شي

C. Rectal route
 حقن شرجية

Formulation of emulsions

Stability problems

- ① Sedimentation and creaming ← لا تسفل / لا تطفو
- ② Coalescence or cracking ← تدخل droplets مع بعض
- ③ Phase inversion ← فصل زيت عن مائي / two layer



④ نبدأ o/w ثم w/o

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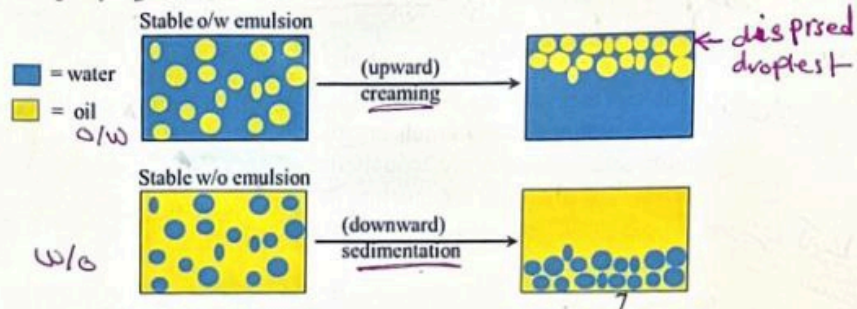
Stability of emulsions

سحب
Sedimentation ↓
↓ down ↓ Set ↓
(w/o)
Creaming ↑ up
(o/w)

Creaming and sedimentation:

- As the dispersed droplets are subjected to gravity force, they tend to move upward (creaming) or downward (sedimentation), but not both.
- Creaming usually happens in o/w emulsions.
- Sedimentation usually happens in w/o emulsion.

In most cases oil is less dense than water, hence generally:
تخفيف أقل مشان هيك بتطخوا للأعلى



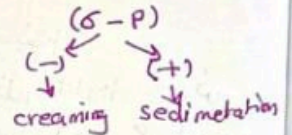
Stability of emulsions

Creaming and sedimentation:

- The rate of sedimentation or creaming is described by Stoke's law.

$$v = \frac{2r^2(\sigma - \rho)g}{9\eta}$$

velocity ← v = $\frac{2r^2(\sigma - \rho)g}{9\eta}$
 ↑ radius of globule, ↑ density of globule, ↑ density media, ↓ gravity, ↓ viscosity



- Where v = velocity of sedimentation or creaming of a dispersed droplet or globule of radius r , and density σ , in a liquid of density ρ , and viscosity η , and where g is the acceleration due to gravity.

كيف تقلل سرعة لرفع

- A theoretical consideration of this equation shows that the rate of creaming will be reduced by:

- ✓ Reduction in the globules size ↓ r
- ✓ A decrease in density difference between the two phases. ↓ (σ - ρ)
- ✓ An increase in the viscosity of the continuous phases ↑ η

$$v = \frac{2r^2(\sigma - \rho)g}{9\eta}$$

Stability of emulsions

Creaming and sedimentation:

The process is **reversible** and **gentle shaking redistributes** the droplets throughout the **continuous phase**.

إذا عملنا shaking تخلط
ال droplet مع المستمر
صاي الغليوة (reversible)

However, **creaming is undesirable** because:

إذا ما اختلطوا يكون
العينة غير مقبولة

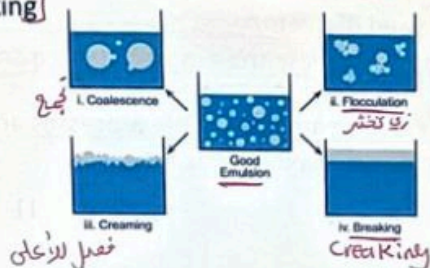
if shaking is not thorough, it is **inelegant** and **inaccurate** dosing is possible

غير دقيقة

غير النقية

احتمال

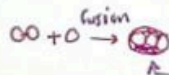
Additionally, **creaming increases the likelihood of coalescence** fusion of globules and therefore **break down** of the emulsion due to **cracking**



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Stability of emulsions

Cracking or coalescence:



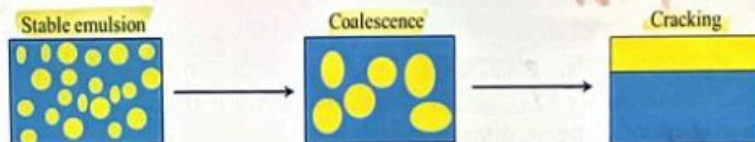
Coalescence is the **fusion** of **two or more droplets** of the disperse phase forming **one droplet**.

Cracking

This ends up to the **separation** of the disperse phase as a separate layer (**phase separation**).



Coalescence is an **irreversible** process and **redispersion cannot be achieved by shaking**.

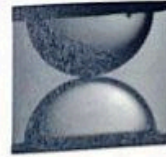


fusion of two or more droplet to form one droplet

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phase separation

Coalescence



- **Coalescence** describes the **irreversible** process in which dispersed phase droplets merge to form a larger droplet.
- The process will continue until **cracking**: in this case, there is **complete separation of oil and water phases**.

Why
ديناميكا حرارية

• Coalescence and cracking occur **because** emulsions are **thermodynamically unstable systems** hence to enhance their **stability**, the dispersed **droplets come closer to each other** and **fuse in an attempt to decrease the exposed surface area**.

عشاقهم ميسر
مستقرين
كيف يتبادل تصابع القلط
انها تدمج الجزيئات
لتعوضها عن مساحة السطح

• Coalescence and cracking are **irreversible processes** and **re-dispersion** cannot be achieved by shaking.

Stability of emulsions

بعضين طرائق عشاق تصنع رصير عندي

creaming ← القلط
cracking ←

How to **enhance stability** (to prevent **creaming and cracking**)?

- **Globule size:** ① **Smaller particles** have **slower** creaming or sedimentation than larger particles (Stoke's law).
- Stable emulsions require a maximal number of **small sized (1-3 μm)** globules and as few as possible larger (**>15 μm**) diameter globules.
- A **homogenizer** will efficiently **reduce droplet size** by **forcing the emulsion through a small aperture** to reduce the size of the globules. ②
- Additionally, **reducing droplet size** may additionally **increase the viscosity** if more than **30% of disperse phase is present**.



جهاز يعمل mixing
بقل حجم ال-globules

اذا اجتمعت لي على
توصير

- ① ↑ viscosity (n)
- ② ↓ droplet (r) size

صاحب اسلاید لکھو

How to enhance stability (to prevent creaming and cracking)?

3) **By keeping the concentration of dispersed phase > 20%.**

Emulsions containing > 20% dispersed phase result in hindrance of movements of the droplets → Therefore there will be reduction in the rate of creaming compared to emulsions where the dispersed phase is < 20%.

4) **Higher percentages of oil phase (o/w).**

Higher amounts of solid fats in the oily phase (i.e. high ratios of solid fat to liquid fats).

نفساً نقطہ ای فوقہ بس حد
o/w

درازا درشتا رمارا الكمانه
disperse > 20
بترید ال
Viscosit
↑ n → ↓ V

Stability of emulsions



How to enhance stability (to prevent creaming and cracking)?

□ **Viscosity of the continuous phase:**

✓ Increasing the viscosity of the continuous phase will reduce the potential for globule creaming and hence coalescence as this reduces the movement of globules.

✓ **How to increase viscosity?**

➢ Viscosity enhancing agents, which increase the viscosity of the continuous phase, may be used in o/w emulsions, e.g. tragacanth, sodium alginate and methylcellulose.

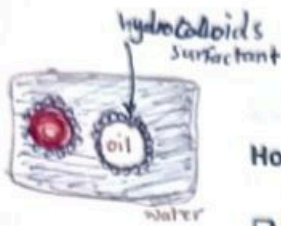
➢ Decreasing the droplet size of the internal phase.

↑ viscosity
↓ rate
↓ movement
↓ creaming & coalescence

بصورت
باعد نفس الكلام

صاحه عشان
و نرها بصر
هو اد
بصيفه عشان ازید ال viscosity





Stability of emulsions

How to enhance stability (to prevent cracking)?

Using emulsifying agents (hydrocolloids, surfactants and other):

- Forming interfacial film mechanical barrier which decreases the potential for coalescence.
- Surfactants may reduce the interfacial tension between the two phases.
- Hydrocolloids enhance the viscosity of the medium.

Note: Care should be taken for any effects that could affect the interfacial film (chemical, physical or biological effects).

anion ← رقيق
 emulsion ← طابا
 cation ← عكسي

↑
 هيكلي لماري تكون
 سبب في نمو الميكروبات

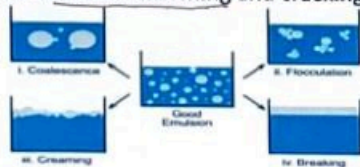
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Stability of emulsions

How to enhance stability (to prevent creaming and cracking)?

Storage temperature:

- Extremes of temperature can lead to an emulsion cracking.
- When water freezes it expands, so undue pressure is exerted on dispersed globules and the emulsifying agent film, which may lead to cracking. probably because the ice formation disrupts the interfacial film around the droplets.
- Conversely, an increased temperature decreases the viscosity of the continuous phase and disrupts the integrity of the interfacial film.
- An increasing number of collisions between droplets will also occur, leading to increased creaming and cracking.



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كيف نعالج
 1. Cracking
 → emulsifying agent
 ① interfacial film mechanical barrier ↓ coalescence
 ② ↓ interfacial tension
 ③ ↑ viscosity

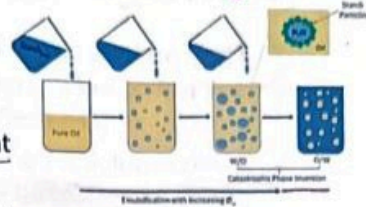
باختصار
 زيادة درجة الحرارة
 أو نقصانها كثيرا
 يسبب
 Cracking & creaming

Starch
 كان ٥/٥٠ ٥/١٠٠
 هذا يقيناً مادة كبرى من ل
Stability of emulsions

إذا قويت أو تجاوزت ١.٧٤
 صير الحالة

Phase inversion

- Emulsion type is determined by:
 - The oil to water ratio (amounts).
 - The solubility of the emulsifying agent



- [Phase inversion] is the process in which an emulsion changes from one type to another, say o/w to w/o.
- The most stable range of disperse phase concentration is 30-60%. If the amount of disperse phase approaches or exceeds a theoretical maximum of 74% of the total volume, then phase inversion may occur.
- Addition of substances which alter the solubility of an emulsifying agent may also cause phase inversion.
- The process is irreversible.

[Formulation] of emulsions

[Emulsifying agents (emulsifiers):

- An emulsifying agent is any material that enhances the stability of an emulsion (i.e. Prevention of coalescence and reducing creaming).
- The ideal emulsifying agent is
 - colourless, odourless, tasteless,
 - non-toxic,
 - non-irritant
- able to produce stable emulsions at low concentrations.
- Emulsifying agents are either: types
 - Hydrocolloids.
 - Surface active agents (SAA) (surfactants).
 - Finely divided solids.
 - Auxiliary emulsifiers.

Stable emulsion
 هذه (تدبر) ان اقله

اضافى

← أظفها أروع → ^{skin} **Dermatological emulsions** → ^{lotions} _{creams}

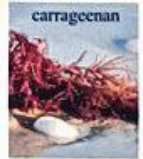
- They are the largest class of emulsions used in pharmacy and range in consistency from fluids lotions and liniments to semisolids (creams). *مستحلبات لوضع على الجلد لتحتوي على الدواء المرصود*
- A w/o emulsion can usually be applied more evenly, because the skin is covered with a thin film of sebum, and this surface is more readily wetted by oil than by water. *بدون استخدام متساوي* → oily secretion *الزهم*
- A w/o emulsion is also more softening to the skin, because it resists drying and removal by contact with water. *تقدم الخافض*
- Dermatological emulsions can facilitate drug permeation into and through the skin by occlusion. *سه تدخل ادوا جوا الجلد*



Emulsifying agents
Hydrocolloids

Natural Polysaccharides:

- The main problem with these agents is their natural variability between batches and microbial contamination. *اختلافات طبيعية*
- These materials should not be used externally as they leave a sticky feel on the skin. *تكون*
- Acacia is the best emulsifying agent for extemporaneously prepared oral emulsions as it forms a thick film at the oil-water interface to act as a barrier to coalescence. It is too sticky for external use. *أساسيا*
- Tragacanth is used to increase the viscosity of an emulsion and prevent creaming. *صمغ*
- Other polysaccharides, such as starch, pectin and carrageenan, are used to stabilize an emulsion. *صمغ*



• مما اذيت على الجلد عشان
تقل ملمس لزوج على skin
صمغ عربي

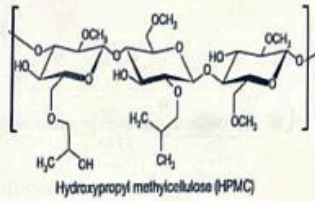
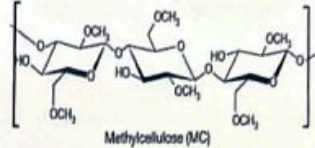
Emulsifying agents Hydrocolloids

Semi-synthetic polysaccharides:

- These are derived from the naturally occurring polysaccharide cellulose and generally form o/w emulsions.

Examples include low-viscosity grades of

- ✓ Methylcellulose (MC)
- ✓ Carboxymethylcellulose (CMC)
- ✓ Hydroxypropylmethylcellulose (HPMC)



Synthetic hydrocolloids:

- ✓ Carbopol
- ✓ Polyvinyl alcohol (PVA)
- ✓ Polyvinyl pyrrolidone (PVP)

بيقرضوا للماء ويصير لهم
Swelling بغير حجمهم
وتزيد الـ Viscosity

قليل استعمالهم orally
يستخدوا للعين أو
الـ Skin

hydrophilic hydrophobic

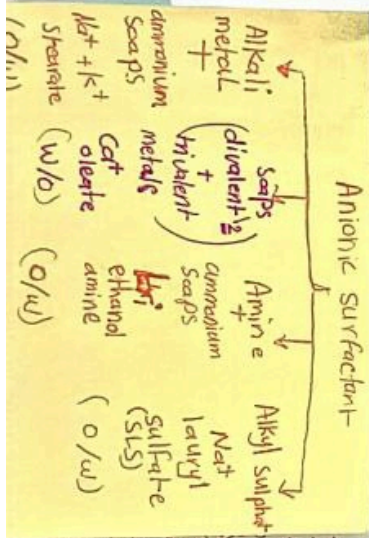
Emulsifying agents Surfactants

Anionic surfactants:

- These are organic salts which, in water, have a surface-active anion.
- Some examples include:
 - ① Alkali metal and ammonium soaps (salts of long chain fatty acids) such as sodium stearate and potassium oleate (o/w).
 - ② Soaps of divalent and trivalent metals such as calcium oleate (w/o).
 - ③ Amine and ammonium soaps such as triethanolamine oleate (o/w).
 - ④ Alkyl sulphates such as sodium lauryl sulphate (SLS) (o/w).

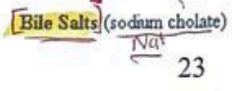
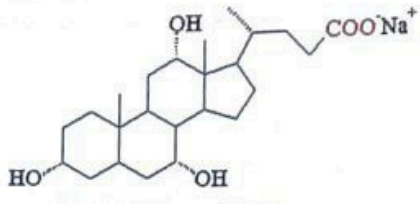
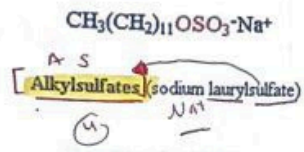
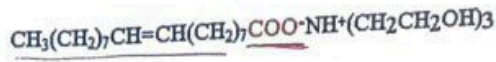
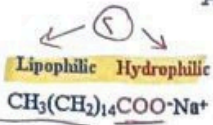
Disadvantages:

- Incompatible with some organic and inorganic cations and with large organic cations such as cetrimide.
- They are irritant internally so widely used in external preparations as o/w emulsifying agents.
- pH sensitivity: They must be in their ionized form to be effective and emulsions made with anionic surfactants are generally stable at more alkaline pH.



لا تقبل حساسون لظروف
استعمال خارج
قد يتم تكون بشكل الباتين
عشان تستغل
ولذلك تكون مع
anionic surfactant

Anionic Surfactants: Soaps



أمين دا ليك استرا صابون
Bile Sats
B S ←
A S ←
Alkyl Sulfates

④ ~~~~~

Emulsifying agents
Surfactants

(+) Cationic surfactants:

- These are usually quaternary ammonium compounds which have a surface-active cation.
- Examples include cetrimide and benzalkonium chloride.
- They are used in the preparation of o/w emulsions for external use and must be in their ionized form to be effective.
- The cationic surfactants also have antimicrobial activity.

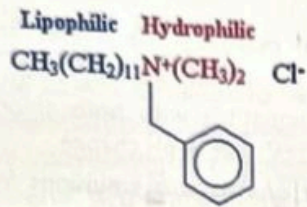
Disadvantages:

1. They are sensitive to anionic surfactants and drugs.
2. Emulsions formed by a cationic surfactant are generally stable at acidic pH.
3. They are more toxic than other surfactants.

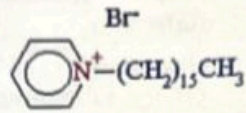
← استعراضهم قليل

cationic ammonium surface-active cationic	external acidic pH	toxic sensitive to anionic surfactant
anionic organic salt surface-active anion	external alkaline pH	nontoxic sensitive to cation surfactant long in organic organic
		o/w emul Soaps lecithin Cat oleate

Cationic Surfactants: Inverted Soaps



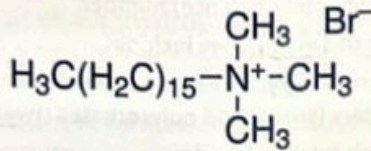
Quaternary Ammonium Salts
 (lauryldimethylbenzylammonium chloride)



Pyridinium Salts
 (Cetylpyridinium bromide)

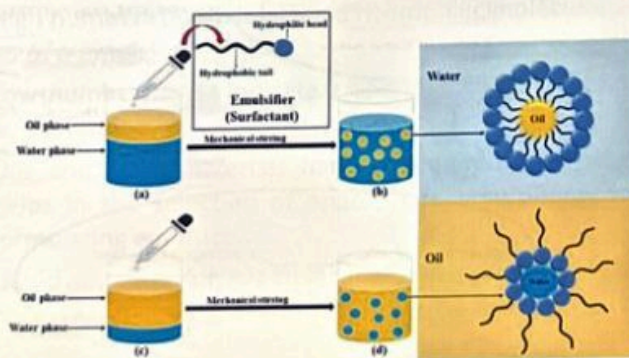
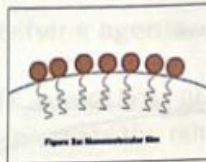
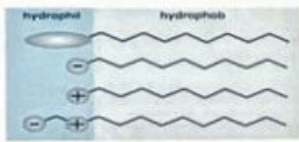
Pyridinium

4 Ammonium Salt

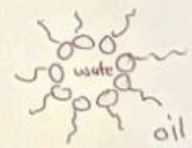


Cetrimide (cetyltrimethylammonium bromide)
 o/w emulsifier, but also preservative

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لأنه الـ oil و hydrophilic
 ← hydrophilic
 ← hydrophobic



26

Emulsifying agents Surfactants



[Non-ionic surfactants]

- They are synthetic materials and make up the largest group of surfactants.
- The non-ionic surfactants are compatible with both anionic and cationic substances and are highly resistant to pH change.
- They are used to produce either [o/w or w/o] emulsions for both external and internal use.
- The type of emulsion formed depends on the balance between hydrophilic and lipophilic groups which is given by the HLB (hydrophilic-lipophilic balance) number.
- Examples of the main types include:
 - A. (Esters) such as glycol esters, glycerol esters, macrogol esters, sorbitan esters (spans) and polysorbates (tweens).
 - B. (Amides) such as alkanolamides.
 - C. (Ethers) such as macrogol ethers and poloxamers.

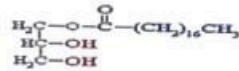
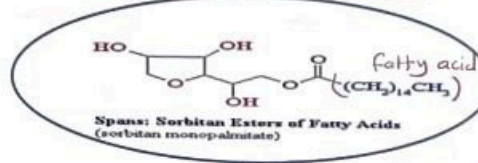
27

Nonionic Surfactants

من الحفظ

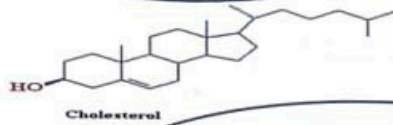
Lipophilic Hydrophilic
 $\text{CH}_3(\text{CH}_2)_n\text{OH}$

Fatty Alcohols
($n=11$, lauryl, $n=15$, cetyl, $n=17$, stearyl alcohol)

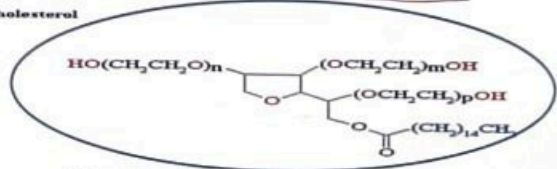


Partial Fatty Acid Esters of Multivalent Alcohols
(glycerol monooleate)

$\text{HO}(\text{CH}_2\text{CH}_2\text{O})_n-(\text{CH}_2)_{11}\text{CH}_3$
Brij: Polyethyleneglycol (PEG) Ether
(PEG-200 lauryl ether, Brij 30)



$\text{HO}(\text{CH}_2\text{CH}_2\text{O})_n-\text{C}(=\text{O})-(\text{CH}_2)_{16}\text{CH}_3$
Cremophor: Polyethyleneglycol (PEG) Fatty Acid Ester
(PEG-400 stearate)



Polysorbates, Tweens: PEG-Sorbitan Fatty Acids Esters
(PEG-200-sorbitan monooleate, Polysorbate 60)

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o/w or w/o depend → length { hydrocarbon (hydrophobic) Chain, polyoxyethylene (hydrophilic) Chain } → depend Fatty acid Chain

صه عند دكتور عربيا

o/w or w/o emulsifiers depending on the length of the hydrocarbon chain (hydrophobic) and the length of polyoxyethylene chain (hydrophilic)

Spans: w/o emulsifiers, the hydrophilic/hydrophobic balance depends on the length of the fatty acid chain.

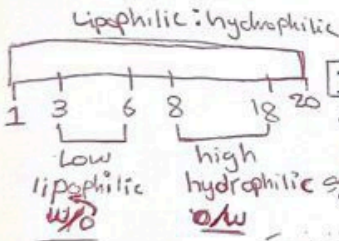
Tweens: o/w or w/o emulsifiers depending on the length of the hydrocarbon chain (hydrophobic) and the length of polyoxyethylene chain (hydrophilic)



Note: solubility characteristics of many non-ionic emulsifying agent change with a rise in temperature;

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Emulsifying agents



The HLB (Hydrophilic lipophilic balance system):

- An HLB number (1-20) represents the relative proportions of the lipophilic and hydrophilic parts of the molecule.
- High numbers (8-18) indicate a hydrophilic molecule, and produce an o/w emulsion.
- Low numbers (3-6) indicate a lipophilic molecule and produce a w/o emulsion.
- Oils and waxy materials have a 'required HLB number' which helps in the selection of appropriate emulsifying agents when formulating emulsions.
- Liquid paraffin, for example, has a required HLB value of 4 to obtain a w/o emulsion and 12 for an o/w emulsion.

4 w/o 12 o/w → Liquid paraffin

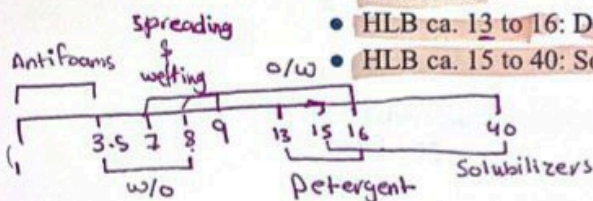
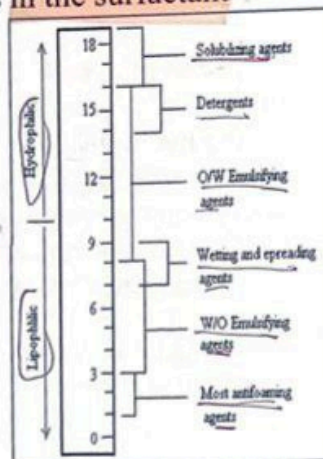
water oil

30

HLB and Use of Surfactants

Amphiphilic surfactants are characterized by the hydrophilic-lipophilic balance (HLB): a relative ratio of polar and non-polar groups in the surfactant

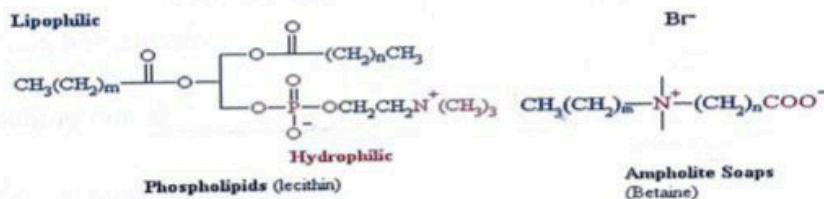
- HLB ca. 3.5 to 8: Water-in-Oil Emulsifiers
- HLB ca. 1 to 3.5: Antifoams
- HLB ca. 7 to 9: Wetting and spreading agents
- HLB ca. 8 to 16: Oil-in-Water Emulsifiers
- HLB ca. 13 to 16: Detergents
- HLB ca. 15 to 40: Solubilizers



Amphoteric (Zwitterionic) Surfactants

Amphoteric Surfactants

ال structure مش حفظ



Proteins (gelatin, casein)

هي مواد تستخدم في تكوين المستحلب تستنت الجزيئات المعلقة في الماء

عوامل الاستحلاب (التي هي) مواد النجول أو عوامل الاستحلاب
 (Finely divided solids)

- Finely divided solids can be adsorbed at the oil-water interface to form a coherent film that prevents coalescence of the dispersed globules.
- Additionally, most of them swell in the dispersing medium resulting in an enhanced viscosity.
- If the particles are preferentially wetted by oil, a w/o emulsion is formed.
- Conversely, if the particles are preferentially wetted by water, an o/w emulsion is formed.
- They form emulsions with good stability which are less prone to microbial contamination than those formed with other naturally derived agents.
- **Examples:**
 - ✓ Natural clays as bentonite and aluminium magnesium silicate.
 - ✓ Synthetic materials as colloidal silicon dioxide (Aerosil®).
 - ✓ Colloidal aluminium and magnesium hydroxides are used for internal preparations.

الطين الطبيعي

Mg+

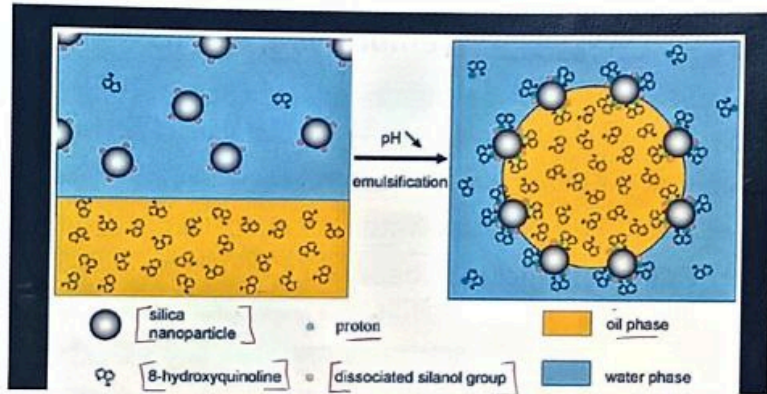


Figure 2c: solid particle film



Choosing an emulsifying agent

emulsifying agent, كيف يتجانس عامل, كيفية اختيار عامل, كيفية اختيار عامل, كيفية اختيار عامل

• The **active ingredients** and the intended use of the product will determine the choice of emulsifying agent.

active ingredient

taste should be

pleasant

• Natural **polysaccharides** (acacia) and **non-ionic emulsifying agents** are useful for **internal emulsions (oral)**.

• The **taste** should be **bland** and **palatable**, again suggesting the natural polysaccharides. E.g. Polysorbates have a **disagreeable taste**, therefore flavouring ingredients are necessary.

هناك جبهة شو معناها

عاطف

• **Soap emulsions** irritate the gastrointestinal tract and have a **laxative effect**.

• A wider range of emulsifying agents can be used **externally**, although the polysaccharides are normally considered **too sticky**.

• Only certain **non-ionic emulsifying agents** are suitable for **parenteral use** including **lecithin, polysorbate 80, methylcellulose, gelatin and serum albumin**.

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[gelatin و albumin] بستي [lecithin و polysorbate]

only certain non ionic اي للحقن

poly saccharid acacia + non ionic internal oral Soap emulsions external

Auxiliary emulsifying agents

→ **Sterol-containing substances:** w/o

• These agents act as **water-in-oil** emulsifying agents.

• Examples include **beeswax, wool fat** and **wool alcohols**



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- **Antioxidants (Stabilizers)** ← المواد اذنه بتكسر عا نا كسر زيفيا
- Some oils are liable to **degradation** by **oxidation** and therefore **antioxidants** may be added to the formulation.
- They should be **preferentially soluble** in the oily phase.

قابلية للذوبان بشكل تفضيلي



- **Colours and flavourings**
- Colour is rarely needed in an emulsion, as most have an elegant **white** colour and **thick texture** ← حلس
- Emulsions for oral use will **usually** contain some **flavouring agent**. ←

هادي لون بار emulsion
هو مستحلب الحليب شولونه
white + thick texture

بغير طعم

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(المواد الحافظة للميكروبات) Antimicrobial preservatives

تلوث

- **Contamination** may be introduced from a variety of **sources** including: مصادر التلوث
 - a. **Water** if not properly stored.
 - b. **Natural emulsifying agents**, e.g. **starch** and **acacia**
 - c. **Carelessly cleaned equipment**. ← بلا مبالاة
 - d. **Poor closures on containers**. ← اغلاق مسيئة

- **Microbes** produce unpleasant **odours**, **colour changes** and **gases**. (1) (2) (3) ← شوي متقل
- Additionally, they may affect the emulsifying agents, possibly causing the **breakdown** of the emulsion. (4)

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خصائص

Properties of an ideal Antimicrobial preservatives?

1. Should be free from toxic effects, odour, taste (for internal use) and colour.
2. Should be bactericidal rather than bacteriostatic.
3. Have a rapid action and wide antibacterial spectrum over a range of temperatures and pH.
4. Additionally emulsion ingredients should not affect their activity and they should be resistant to attack by microorganisms.

emulsion
بالتفاح
تأثير على

الـ

Partition coefficient (P) = $\frac{X_o}{X_w}$

$$P = \frac{X_{oil}}{X_{water}}$$

$$P = \frac{X_o}{X_w}$$

مما يكون مساويا

$$X_{oil} < X_{water}$$

له مساوات
أكثر يعني

better antimicrobial activity
لأنه في وسط لتمر microbial

- The effect of the partition coefficient is also important:
- A preservative with a low oil/water partition coefficient will have a higher concentration in the aqueous phase and hence better antimicrobial activity.
- A combination of preservatives may give the best preservative cover for an emulsion system.

له لوظائف أكثر من بيطني
preservatives
Best

39

Antimicrobial preservatives

Some preservatives in use are listed below:

1. Benzoic acid: effective at a concentration of 0.1% at a pH below 5.
2. Esters of parahydroxybenzoic acid such as methyl paraben (0.01-0.3%).
3. Chloroform, as chloroform water (0.25% v/v).
4. Chlorocresol (0.05-0.2%).
5. Phenoxyethanol (0.5-1.0%).
6. Benzyl alcohol (0.1-3%).
7. Quaternary ammonium compounds, e.g. cetrimide, which can be used as a primary emulsifying agent but can also be used as a preservative.
8. Organic mercurial compounds such as phenyl mercuric nitrate and acetate (0.001-0.002%).



كأنوع الـ
serfactant

انه تسمى
serfactant

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Emulsions for oral use



- **Acacia gum** is usually used when making extemporaneous **o/w emulsions** for oral use, **unless otherwise specified**.
- If using acacia, a **primary emulsion** should be prepared first.
- This is a **thick stable emulsion** prepared using **optimal proportions** of the ingredients.
- These **vary** with the nature of the oil.

Table 46.1 : Parts of Oil : Water : Gum, for primary emulsion

Type of oil	Example	Quantities for primary emulsion		
		Oil	water	Gum
Fixed	Almond oil	4	2	1
	Arachis oil	4	2	1
	Castor oil	4	2	1
	Cod liver oil	4	2	1
Mineral	Liquid paraffin	3	2	1
Volatile	Turpentine oil	2	2	1
	Cinnamon oil Peppermint oil	2	2	1
Oleo-resin	Male fern extract	1	2	1

صبيحة
معدنية
طبيعية

41

Identification of emulsion type

Miscibility test: An emulsion will only mix with a liquid that is miscible with its continuous phase. Therefore an o/w emulsion is miscible with water, a w/o emulsion with an oil.

miscible
Liquid emulsion
o/w → water
w/o → oil

Conductivity measurement: Systems with an aqueous continuous phase will conduct electricity, whilst systems with an oily continuous phase will not.

use house
o/w → conduct
w/o → not
كهرباء

Dye test: If an oil-soluble dye is used, macroscopically o/w emulsions are paler in colour than w/o emulsions and vice versa. If examined microscopically, an o/w emulsion will appear as coloured globules on a colourless background whilst a w/o emulsion will appear as colourless globules against a coloured background.

o/w paler than w/o
لأن استخراجه
صبغة - oil
أما إذا استخدمت
aqueous-soluble dye
result ↓

الطريقة
باستخدام
المايكروسكوب

Important: Watch videos

يجب تنزيل حبيبات صبغة بنزوبالزيت

42 يجب رفع تكشفي مكان وجود الزيت

إذا كان o/w يجب كل emulsion و oil
وفيها قطرات ماء ربح تروح الصبغة على الزيت

color ← oil →
water → color less

transparent

تلخيص من سلايد اعل ٤٧

Methods

(Continental) Dry method

4:2:1
oil water gum



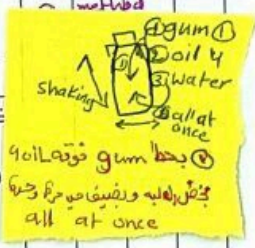
English (wet)

4:2:1
oil water gum



Bottle (Forbes)

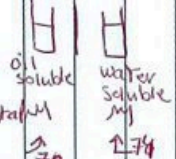
Volatile oils
oleaginous substance
low viscosities



important to minimize initial amount of time

Beater

Synthetic or non-gum or surfactant



Internal or external mixing -> beater / mortar / blender

Auxiliary

blender or homogenizer

stability improved
size

Self emulsifying Soap

2 -> cat 2
soft (olive) oil

cat 2 w/s emulsion (certain vegetable oleic acid lime water) mix lime water

emulsifying agent
cat 2 salt
resistant emulsifying
cat 2
oleate
Calcium Lipo
Calcium Lipo

4 oil و gum و مجرد بعضين بظ powder بدو هاضيف
Water
gum
oil
Slowly
more stable
formed creamy white
cracking
Dry powder = oil + gum

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).

الطريقة الاقدم
part 4:2:1
من رطوبة
من رطوبة
من رطوبة

Dry powder
gum powder

زيت صلب
الذي يذوب في الماء
مع بعض استنشاق منع

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 trituated 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 trituated 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.

نفس مكونات الطريقة الاقدم

more stable

emulsifier

نفس المكونات التي قبل



Methods of compounding emulsions:

3. Bottle (Forbes) Method بجلا کر آمیختگی بہا المادوں میں اجرائی

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.

لازم ۱۳ دقیقہ موضوع الوقت
 لانہ اذ اجرینا gum + oil
 کثیر وقت (ح) لہووا
 waterproof و مشورہ ریح اقدار اصل الماء علیہ

Methods of compounding emulsions:

4. Beaker Method (مستشرق)

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.

اعلیٰ بیسولہ 70°C (الزیت 70°C) (المادہ بیرونی)

internally / external

عسینا و کلیم مع بیسولہ
 بیسولہ التین
 70°C

Methods of compounding emulsions:

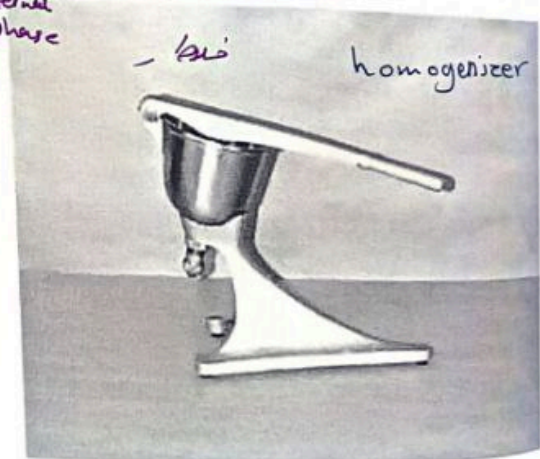
5. Auxiliary Methods

- 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

عنه اذنه الاستقرار
blend



droplets
الاصغر ال
internal
phase



Methods of compounding emulsions:

In Situ Soap Method

لا عمل مكوناته ولا يتم
 تشكيله ^{emulsifier} emulsifying agent

- 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.

مواد زكية مواد قلوية
 ↓
emulsifying agent

Methods of compounding emulsions:

In Situ Soap Method

- A typical example of this emulsion is calamine liniment:
 - Calamine
 - Zinc oxide ZO
 - Olive oil OO
 - Calcium hydroxide solution
 - qs ad 1000.0 mL

حزاد مفارمة

ع تشكيلها emulsifier

لا يكونها المكونات emulsifier
 في
 في حالة In situ soap
 تكونه طاله

من قبل ان يضاف الى الحليب
11.5

Adding ingredients to a primary emulsion:

- ① • Solid substances (active ingredients, preservatives, colors) are dissolved and added as a solution to the primary emulsion
- ② • Volatile ingredients (flavors, odors, or active drugs) should be added once the product has cooled if heat was used
- ③ • Small amounts of oil soluble substances (may be incorporated directly into the primary emulsion)
- ④ • Any substance might reduce the physical stability of the emulsion (i.e. alcohol) should be added to the near end of the process

- ① solid → solution حل
- ② volatile → added once when it has cooled
- ③ Small → incorporated directly
- ④ Any substance → الخطوة التي قبل الاخير
reduce physical

Adding ingredients to a primary emulsion:

- ⑤ • ^{thickening agents} Viscosity enhancers can be added to a primary emulsion to increase stability of the formulation
- ⑥ • The enhancers should be miscible in the external phase of the emulsion
- ⑦ • o/w → hydrocolloids ^{زيتية}
- ⑧ • w/o → viscous oils, fatty alcohols, or fatty acids ^{مائية}

↑ viscosity → ↑ stability → 1° emulsion

Adding ingredients to a primary emulsion:

- When all agents have been incorporated ^{↓ ادخال كل شيء} the emulsion should be transferred ^{↑ نقل} 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

emulsifier →

كمية
تامة لمزيج

(With w/o emulsions:) ^{جافز}

① - Oils and insoluble powders can be incorporated directly into the external phase using a tile and spatula ^{و ليس امزج عليه}

② - 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 ^{جافز}

wetting agent

جافز
او
powder

جافز الجافز
او
او

W/O
Oils & insoluble → external phase

Large → levigating agent
in soluble

Adding ingredients to a commercially prepared emulsion

- With w/o emulsions (cont.):
 - ③ - If an aqueous soluble material ^{مذاب} to be added, ^{بكمية الكفاية} excess emulsifier must be present
 - ④ - For those w/o emulsion that do not have ^{ما في كثير} excess emulsifier, additional emulsifier may have to be added
 - ⑤ - An aqueous solution may be added using a pill tile and spatula, but some may require heat

3 - aqueous soluble → excess emulsifier
 5 - aqueous solution → pill tile & spatula
 4 - w/o → don't have excess

Adding ingredients to a commercially prepared emulsion

- With o/w emulsions:

- ① ^{عند طينة خذ ال} Levigating agents ^{بمادة ناعمة} for aqueous insoluble substances should be water miscible as glycerin, propylene glycol, polyethylene glycol, or alcohol
- ② ^{تفادي} If heat is used to incorporate → work quickly → be careful not to evaporate water from the product → stiff
- ③ ^{wetting agents} In many commercial o/w emulsions, sufficient emulsifying agents is already present in the preparation to accommodate the added oils or powders

Vehicle as external phase Suspension

Flavoring emulsions → in external phase

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

هيك بنكون اخيرا خلصنا 😞
اللهم اني استودعتك ما قرأت وما
حفظت فرده لي عند حاجتي إليه
يارب العالمين 🌻💛



يارب تنجح آيه وتجيب علامة
ترضيتها والكم المثل 💛🌻