# Emulsions

غير ممتزجين

- 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.

- At least 2 phases:
  - ✓ Disperse or internal phase
  - ✓ Continuous or external phase.

هو السائل الموجود على شكل قطرات صغيره

هو الوسط الذي تنتشر داخله هذه القطرات

* عندما نقول إن سائلاً مبعثر داخل سائل اخر فهذا يعني ان احد الطورين لا يذوب في الاخر لكن نستطيع تشتيته على شكل قطرات صغيره بمساعده وسائل معينه

Lec عبارة عن ٨٠٪ حفظ و ٢٠٪ وهم

# Emulsions

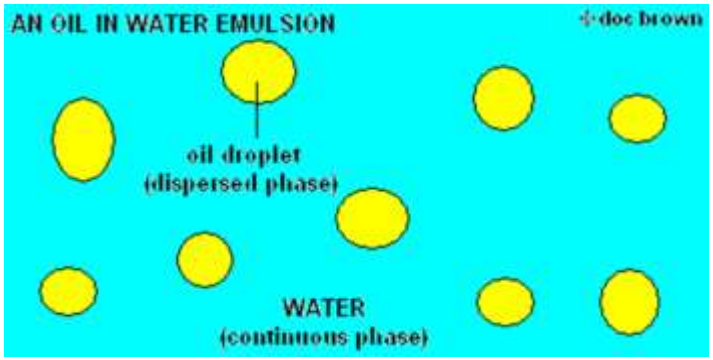
# Emulsion types

oil water

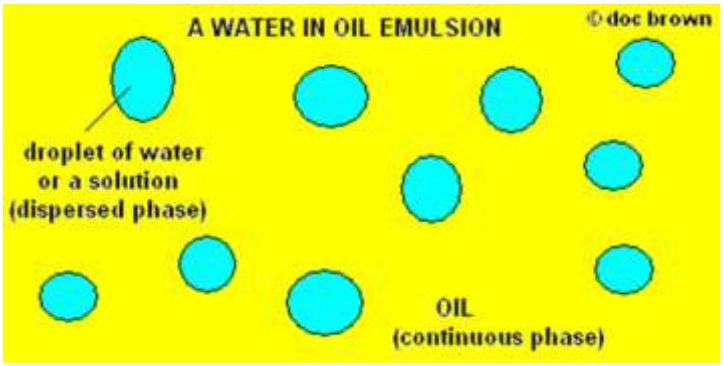
- **O/W emulsions.** oil in water ⇒ oil = internal Phase & water = external Phase
- **W/O emulsions.** water in oil ⇒ water = internal Phase & oil = external Phase
- **Multiple emulsions (e.g. W/O/W emulsions for delayed action drug delivery).**

* هذا يعني انه ماء داخل زيت ، ثم هذا النظام كله مبعثر داخل ماء ، و يستخدم غالبًا في توصيل الدواء متأخر أو مضبوط

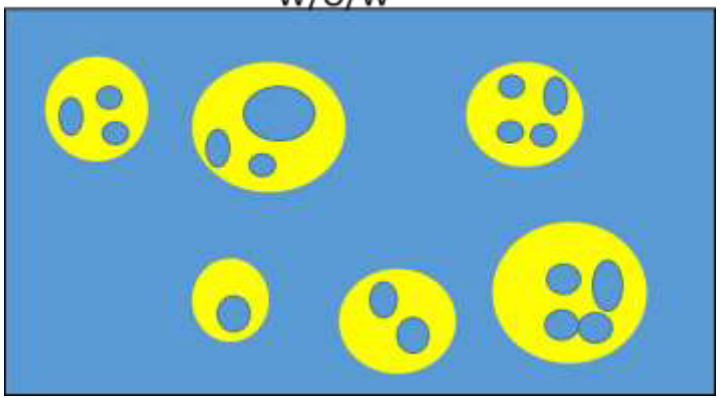
o/w emulsion



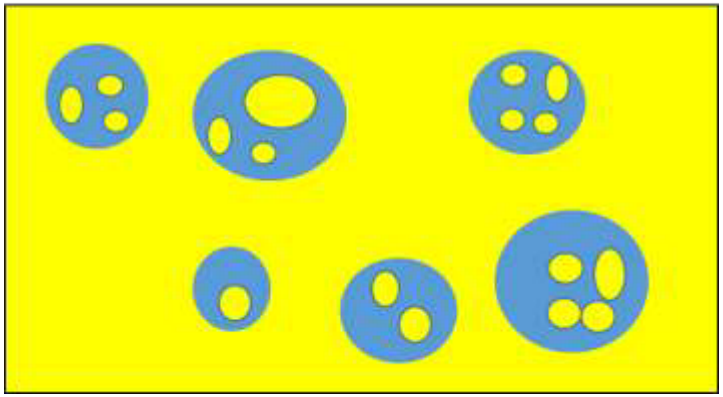

w/o emulsion




W/O/W



O/W/O



تحديد نوع ال emulsion

# 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.

* لماذا يمتزج فقط مع continuous phase ؟ لانه هو الوسط المسيطر على سلوك ال emulsion

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

قياس التوصيل الكهربائي

* طور خارجي (ماء) ← يوصل كهرباء * طور خارجي (زيت) ← لا يوصل كهرباء أو توصيل ضعيف

- **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.

* صبغه زيتيه :-

o/w ← اللون ح يظهر في قطرات الزيت ، الخلفيه (ماء) عديمه اللون

w/o ← اللون ح يظهر في الخلفيه لان الزيت طور خارجي .

# Pharmaceutical application of emulsions

## Why emulsions?

* الزيوت غالبًا طعمها ٤- طعم مزعج في رائحه غير جيده في ملمس دهني
لكن عندما تكون الزيوت داخل internal Phase ، تقل هذه الصفات ويصبح تناولها سهل .

### Oral route:

- 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.

* emulsions يسمح بوضع مكونات مختلفه الذوبان في نفس المستحضر

### IM route:

- 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.

depot therapy ٥- ان الدواء لا يتحرر دفعه واحده ، بل تدريجيًا

# Pharmaceutical application of emulsions

## Why emulsions?

**IV route:**

- 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.

**Topical applications** (both o/w and w/o emulsions) ⟹

**Rectal route**

* حسب الهدف المطلوب :-
- سهولة الغسل
- التر طيب
- الملمس ( زيتي أو مائي )
- الحماية

# Formulation of emulsions

## Stability problems

مشاكل الثبات

1. Sedimentation and creaming.

نزول القطرات الى الاسفل — صعود القطرات الى الاعلى

2. Coalescence or cracking.

اندماج القطرات مع بعض — انفصال الطورين

3. Phase inversion.

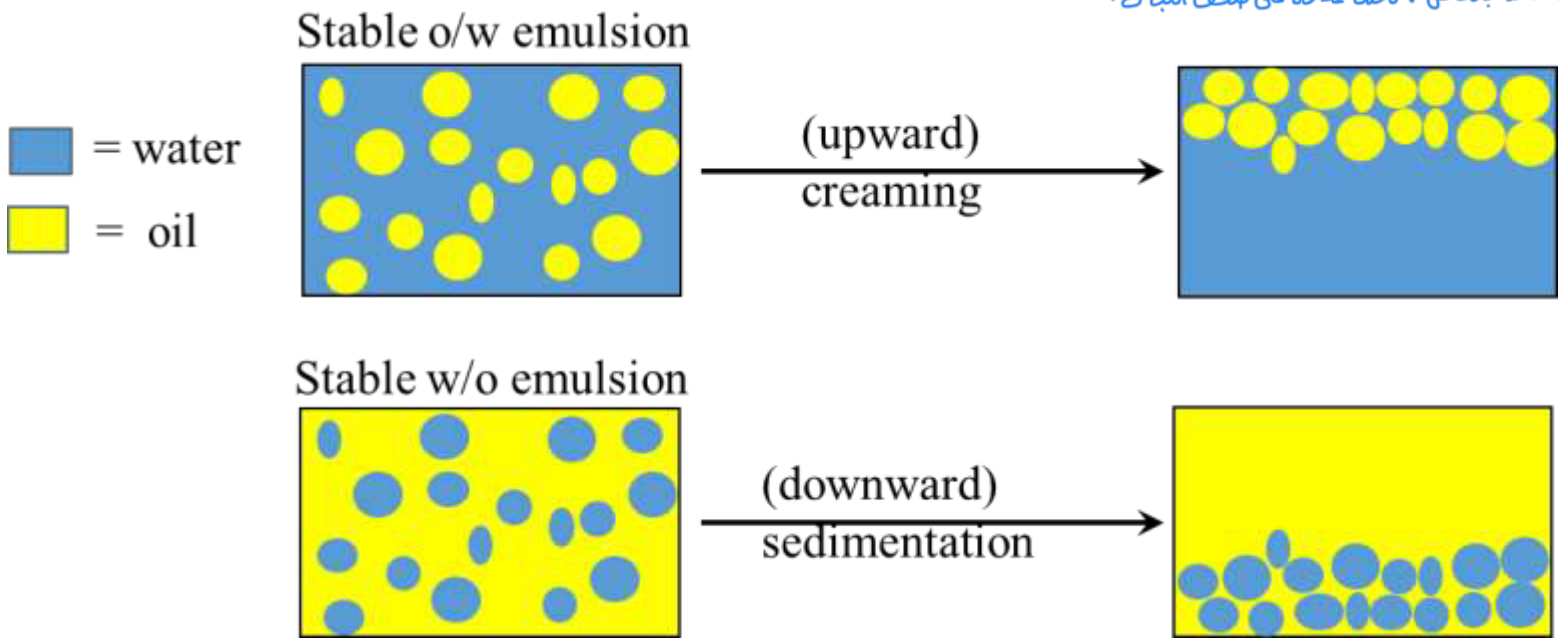
انقلاب نوع emulsion من o/w إلى w/o أو العكس

# Stability of emulsions

## Creaming and sedimentation:

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

* ولا حظ ؛ هذا التحرك لا يعني دائما ان emulsion قد فسد بالكامل ، لكنه علامه على ضعف الثبات .



# Stability of emulsions

## Creaming and sedimentation:

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

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

* سرعه القطرات تتأثر بـ :-
- حجم القطرات
- فرق الكثافه بين الطورين
- لزوجه الطور الخارجي
- الجاذبيه

- 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 ŋ, and where g is the acceleration due to gravity.

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

✓ Reduction in the globules size. ⟶ كلما كانت القطرات اصغر ، تحركت ببطء اكبر

✓ A decrease in density difference between the two phases. ⟶ اذا كانت كثافه الطورين متقاربه تقل سرعه الانفصال

✓ An increase in the viscosity of the continuous phase. ⟶ كلما زادت اللزوجه ، صعب على القطرات الحركه

# Stability of emulsions

## Creaming and sedimentation:

* عليه creaming تعتبر reversible ، يمكن إعاده توزيع القطرات بالرج الخفيف .

- The process is **reversible** and gentle shaking redistributes the droplets throughout the continuous phase.
- However, creaming is undesirable because:

➢ It is inelegant and inaccurate dosing is possible if shaking is not thorough.

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

1- شكل غير أنيق : - المستحضر يبدو منفصلا وغير مقبول جميلا نيا

2 - احتمال جرعه غير دقيقه : - اذا لم يرج المستحضر جيداً قبل الاستعمال ، قد يأخذ المريض جرعه أقل أو جرعه أعلى

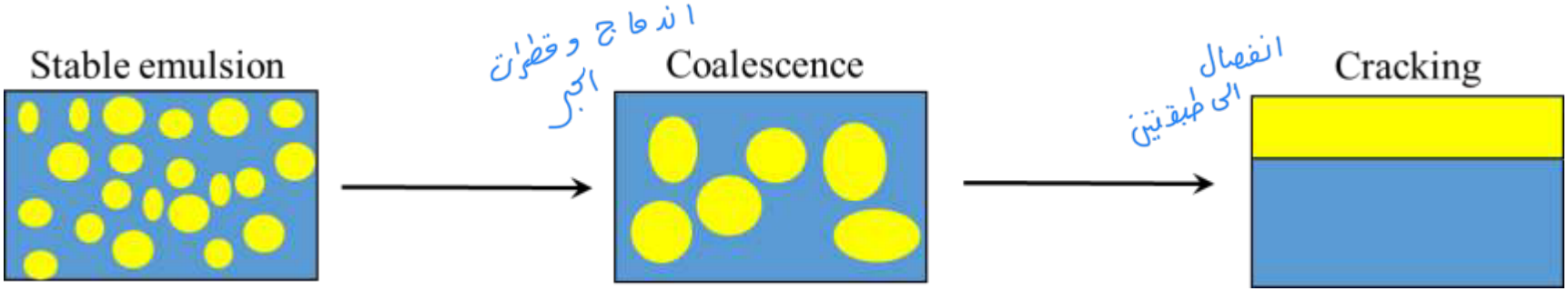
3 - تزيد احتمال Coalescence :- عندما تتجمع القطرات في مكان واحد ، يزداد احتكاكها واحتمال اندماجها ، وهذا قد يسبب cracking

* Creaming ← ليس كارثه بحد ذاته ، لكنه يمهد للكارثه اذا استمر

# Stability of emulsions

## Cracking or coalescence:

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



# Stability of emulsions

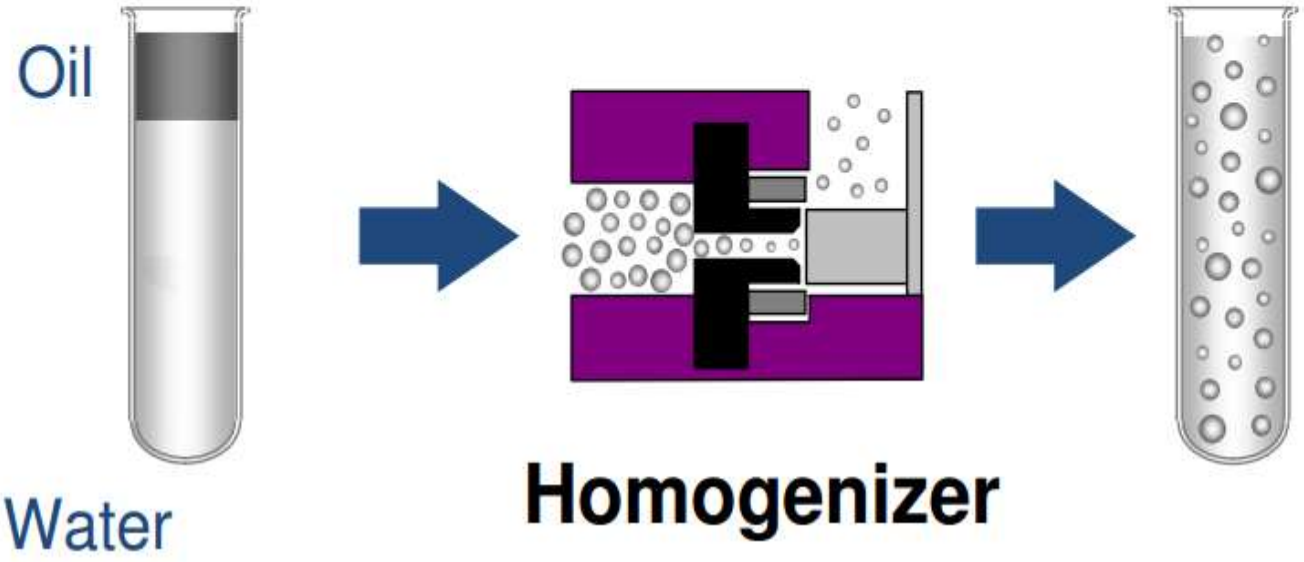
## How to enhance stability (to prevent creaming and cracking)?

- **Globule size:**

- ✓ 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.

- ✓ Additionally, reducing droplet size may additionally increase the viscosity if more than 30% of disperse phase is present.

# Emulsion Processing: Homogenizers



# 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.

* زيادة اللزوجة ← تقلل حركة القطرات ← تقلل Creaming ← تقلل coalescence

### ✓ 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.

# 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.

* interfacial film ← يتشكل حول القطرات ، فيعمل كحاجز ميكانيكي يمنع اندماجها

تزيد لزوجة الوسط

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

* اي عامل (كيميائي ، فيزيائي ، حيوي) يمكن ان يؤذي interfacial film ، بالتالي يضعف الثبات

# Stability of emulsions

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

### ❑ *Storage temperature*:

* درجات حراره قصوى تودي ← cracking

- 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.

* تجمد الماء ← يتمدد و يضغط على ← القطرات ← الغشاء المستحلب ← وهذا يودي الى كسر المستحلب ( emulsions )

- Conversely, an increased temperature decreases the viscosity of the continuous phase and disrupts the integrity of the interfacial film. An increasing number of collisions (تصادمات) between droplets will also occur, leading to increased creaming and cracking.

* التخزين الخاطئ يفسد المستحلب حتى لو كانت تركيبته ممتازة
emulsion

# Stability of emulsions

**Phase inversion** →

تحول نوع emulsion من
o/w → w/o
w/o → o/w

- 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.

* تركيز disperse phase يكون الحبيبات ثباتا عندما يكون بين 30-60% ولكن اذا اقترب او تجاوز 74% فسوف يحدث inversion
- 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 and able to produce stable emulsions at low concentrations.
- **Emulsifying agents are either:**

* الانواع الرئيسيه من ٤

✓ Hydrocolloids.

✓ Surface active agents (SAA) (surfactants).

✓ Finely divided solids.

✓ Auxiliary emulsifiers.

# Emulsifying agents

## Hydrocolloids

* مشاكل المواد الطبيعية :-
1- تختلف من دفعة لأخرى
2- معرضة للتلوث الميكروبي
3- تعطي ملمسًا لزجا على الجلد

### Natural Polysaccharides:

- The main problem with these agents is their natural variability between batches and microbial contamination.
- These materials should not be used externally as they leave a sticky feel on the skin.
- *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.

لزج جدًا

- Tragacanth is used to increase the viscosity of an emulsion and prevent creaming.
- Other polysaccharides, such as starch, pectin and carrageenan, are used to stabilize an emulsion.

# 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)

* هذه المواد غالبًا التي تباتًا وتجانسًا من المواد الطبيعيه ، وتي فع اللزوجه وتساعده emulsions .

### Synthetic hydrocolloids:

✓ Carbopol

✓ Polyvinyl alcohol (PVA).

✓ Polyvinyl pyrolidone (PVP)

# Emulsifying agents

## Surfactants

مواد تعطي في الماء ايونًا سالبًا فعالًا
( الايون الفعال سالبا )

1

### Anionic surfactants:

- These are organic salts which, in water, have a surface-active anion.
- Some examples include:

✓ Alkali metal and ammonium soaps (salts of long chain fatty acids) such as sodium stearate and potassium oleate (o/w).

✓ Soaps of divalent and trivalent metals such as calcium oleate (w/o).

✓ Amine and ammonium soaps such as triethanolamine oleate (o/w).

✓ Alkyl sulphates such as sodium lauryl sulphate (SLS) (o/w).

* كلها تعطي emulsions o/w او w/o يعطي calcium oleate

### 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. ← مهيجه داخليًا
- 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.

* ثباتها يكون افضل في الوسط القلوي

* كل surfactant يمتلك :-
- رأساً محباً للماء
- ذيلاً محباً للزيت
وهذا ما يجعله يتموضع عند سطح الفصل بين الزيت والماء

# Anionic Surfactants: Soaps

**Lipophilic** **Hydrophilic**

$CH_3(CH_2)_{14}COO^-Na^+$

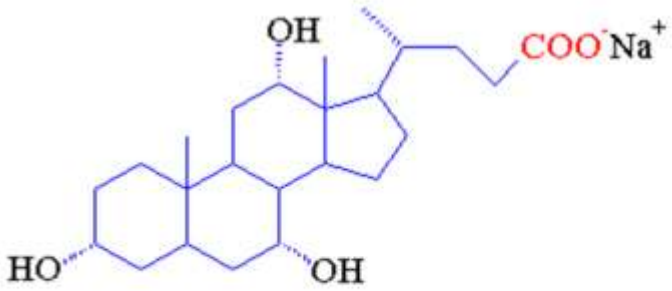
**Alkali Soaps** (sodium palmitate)

$CH_3(CH_2)_7CH{=}CH(CH_2)_7COO^-NH^+(CH_2CH_2OH)_3$

**Amine Soaps** (triethanolamine oleate)

$CH_3(CH_2)_{11}OSO_3^-Na^+$

**Alkylsulfates** (sodium laurylsulfate)




**Bile Salts** (sodium cholate)

# Emulsifying agents

## Surfactants

مواد يكون فيها الأيون الفعال سطحيًا موجبًا.

2 **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 (bactericidal) activity.

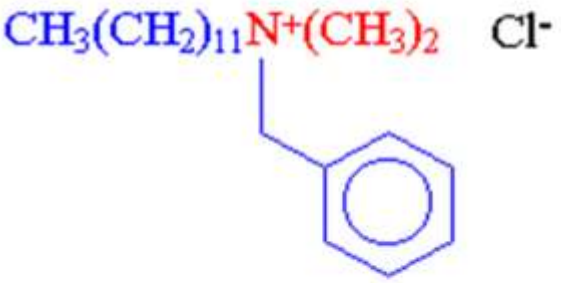
**Disadvantages:**

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

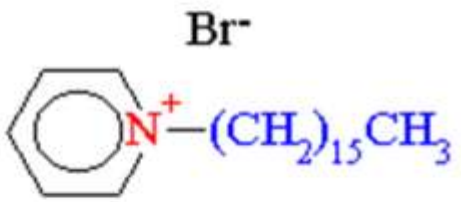
- It must be in the ionized form to work.

# Cationic Surfactants: Inverted Soaps

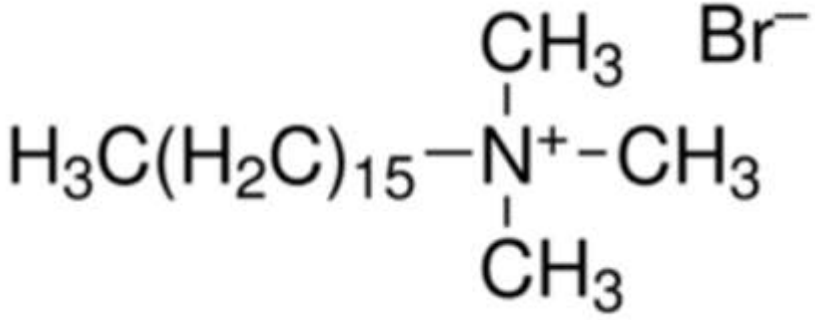
Lipophilic Hydrophilic




**Quaternary Ammonium Salts**
(lauryldimethylbenzylammonium chloride)

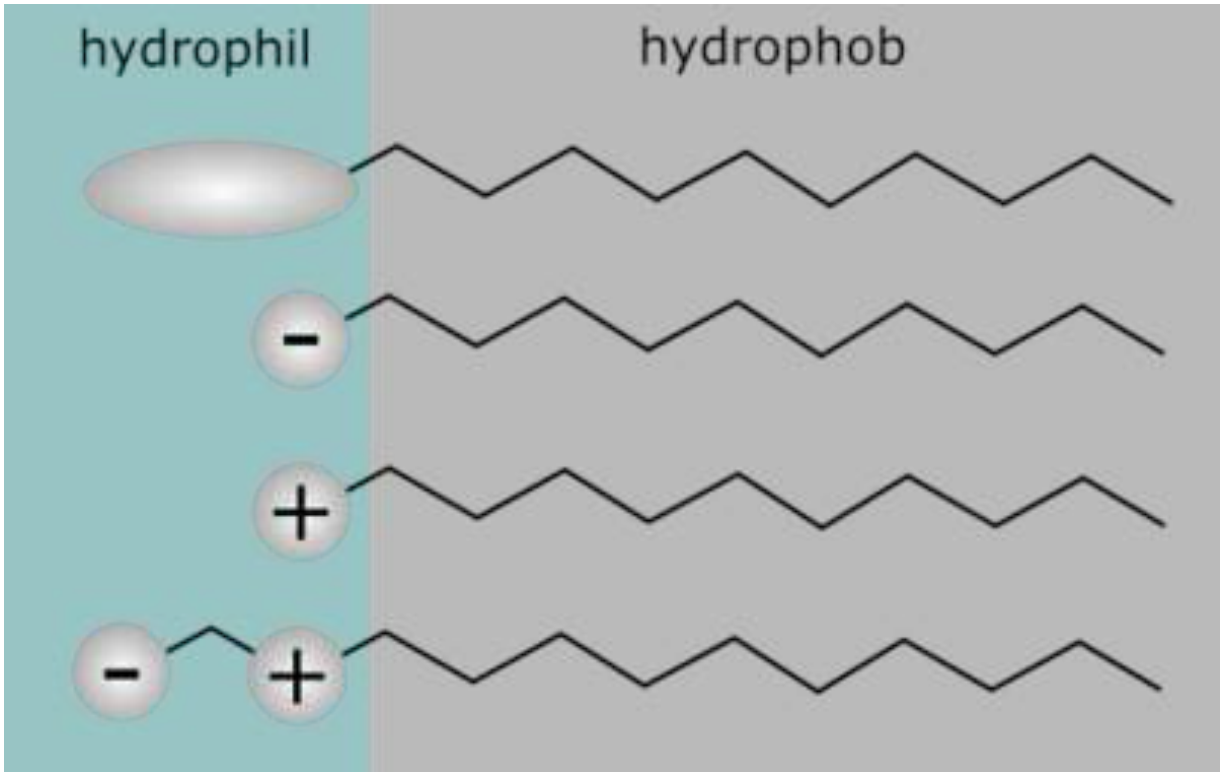



**Pyridinium Salts**
(Cetylpyridinium bromide)




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

يعمل ك


hydrophil
hydrophob
-
+
-
+

# Emulsifying agents
## Surfactants

* ميزاتها :-
1- متوافقه مع المواد الانيونيه والكاتيونيه
2- مقاومه لتغيرات الـ PH
3- يمكن استخدامها داخليا وخارجيا
4- يمكن ان تكون w/o و o/w

3

### 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:

✓ Esters: such as glycol esters, glycerol esters, macrogol esters, sorbitan esters (spans) and polysorbates (tweens).

✓ Amides: such as alknolamides.

✓ Ethers: such as macrogol ethers and poloxamers.

* المواد غير الايونيه :-
كثيره الاستخدام
أقل تأثيراً بال PH
يعتمد اختيارها على HLB

اختصار لـ HLB:

Hydrophilic – Lipophilic Balance

يعني:
التوازن بين الجزء المحب للماء والجزء المحب للدهن في المادة المستحلبة.

بمعنى أبسط:
العامل المستحلب فيه جزأين:

- جزء يحب الماء
- جزء يحب الزيت

ورقم HLB يخبرنا:
أي جزء هو الأقوى في هذه المادة؟

———

كيف نفهم الرقم؟

رقم HLB عادة يكون من 1 إلى 20.

إذا كان الرقم منخفض

يعني المادة أكثر محبة للزيت
فتكون أنسب لتكوين:

W/O = Water in Oil

يعني ماء داخل زيت

إذا كان الرقم مرتفع

يعني المادة أكثر محبة للماء
فتكون أنسب لتكوين:

O/W = Oil in Water

يعني زيت داخل ماء

———

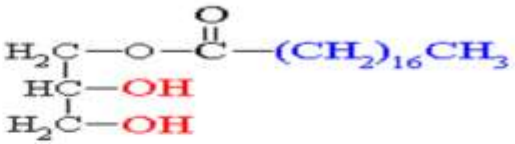
القاعدة الذهبية

# Nonionic Surfactants

Lipophilic Hydrophilic

$CH_3(CH_2)_nOH$

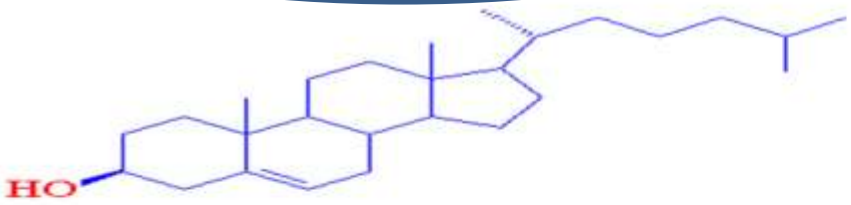
**Fatty Alcohols**
(n=11, lauryl; n=15, cetyl; n=17, stearyl alcohol)



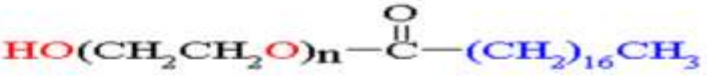
**Partial Fatty Acid Esters of Multivalent Alcohols**
(glycerol monosteatate)

**Spans: Sorbitan Esters of Fatty Acids**
(sorbitan monopalmitate)

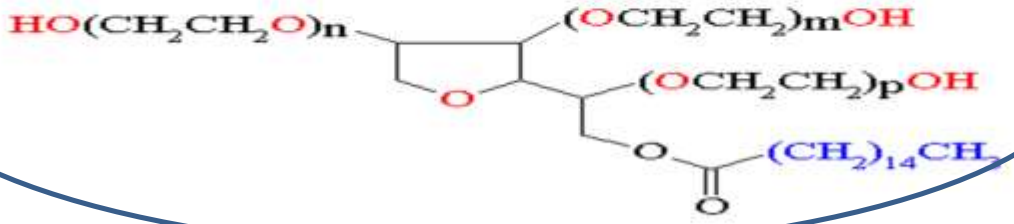
**Brij: Polyethyleneglycol (PEG) Ether**
(PEG-200 lauryl ether, Brij 30)



**Cholesterol**



**Cremophor: Polyethyleneglycol (PEG) Fatty Acid Ester**
(PEG-400 stearate)



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

# 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.

* بعض الزيوت والشموع تحتاج HLB معين حتى يكون emulsions مستقر

- Liquid paraffin, for example, has a required HLB value of 4 to obtain a w/o emulsion and 12 for an o/w emulsion.

* نفس الزيت قد يعطي نوعين مختلفين اذا تغير emulsifying agents

# 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

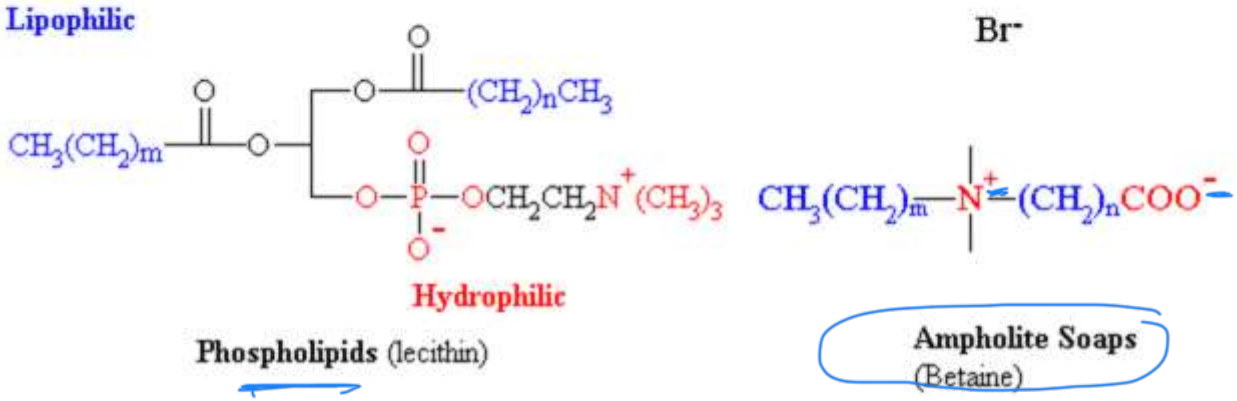
* كلما زادت محبه الماده للماء، زادت قدرتها على :-
• تكوين o/w
• solubilization

* كلما قلت محبه الماده للماء، اصبحت انسب لـ w/o

# Amphoteric (Zwitterionic) Surfactants

يعني ان المادة قد تحمل شحنة موجبة و شحنة سالبة في نفس الجزيء

## Amphoteric Surfactants




**Phospholipids** (lecithin)

**Ampholite Soaps**
(Betaine)

**Proteins** (gelatin, casein)

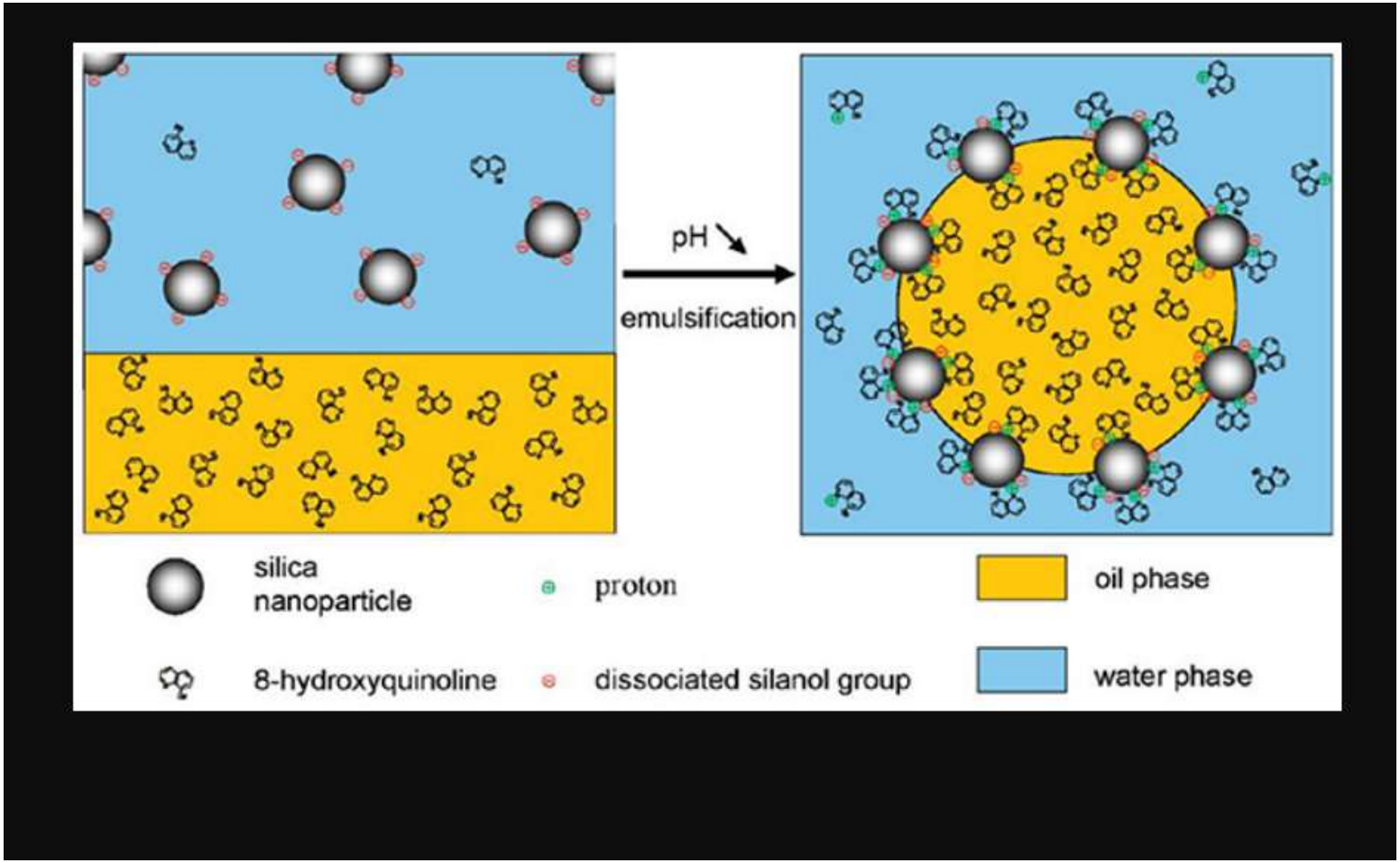
# Finely divided solids

- 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 silicatate.

✓ Synthetic materials as colloidal silicon dioxide (Aerosil®).

✓ Colloidal aluminium and magnesium hydroxides are used for internal preparations.


pH ↘
emulsification
silica nanoparticle
proton
oil phase
8-hydroxyquinoline
dissociated silanol group
water phase

مواد مساعده تدعم الاستحلاب، ليست دائما العامل الرئيسي

# 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

# Choosing an emulsifying agent

- The active ingredients and the intended use of the product will determine the choice of emulsifying agent.
- Natural polysaccharides (acacia) and non-ionic emulsifying agents are useful for internal emulsions.
- The taste should be bland and palatable, again suggesting the natural polysaccharides. Polysorbates have a disagreeable taste, therefore flavouring ingredients are necessary.
- 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.

* بعض الزيوت تتأكسد، لذلك نضيف Antioxidants لحماية الزيت الموجود في emulsions

# Antioxidants (Stabilizers)

- 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.

* يجب ان تكون هذه المواد اكثر ذوباناً في الطور الزيتي حتى تعمل في المكان المطلوب

# Antimicrobial preservatives

- Contamination may be introduced from a variety of sources including:

اسباب التلوث

  - ✓ Water, if not properly stored. → ماء لم يخزن جيدًا
  - ✓ Natural emulsifying agents, e.g. starch and acacia → مواد طبيعية
  - ✓ Carelessly cleaned equipment. → اجهزه غير نظيفه
  - ✓ Poor closures on containers. → اغطيه عبوات غير محكمه

- Microbes produce unpleasant odours, colour changes and gases. Additionally, they may affect the emulsifying agents, possibly causing the breakdown of the emulsion.

ماذا تفعل الميكروبات ؟

- روائح كريهه
- تغير في اللون
- انتاج غازات
- قد تخرب العامل المستحلب، فيتدمر المستحلب

# Antimicrobial preservatives

* صفات المادة الحافظة المثالية ، يجب ان تكون:
- غير سامة
- بلا لون
- بلا رائحة
- بلا طعم
- قاتلة للبكتيريا لا مجرد مثبطة
- سريعة الفعل
- واسعة التأثير
- فعالة عبر Rang من الحرارة و pH
- لا تتأثر بمكونات emulsion
- مقاومة لهجوم الميكروبات

Antimicrobial preservatives :

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

Partition coefficient *

اذا كانت المادة الحافظة تميل للطور المائي اكثر ، فتكون فعاليتها المضادة للميكروبات أفضل ، لان الكائنات الدقيقة غالبا تنمو في الطور المائي

لذلك احيانا نستخدم مزيجا من المواد الحافظة للحصول على تغطية أفضل

# 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%).

# Colours and flavourings

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

# Emulsions for oral use

العامل الاكثر استخداماً

- 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 usinSg optimal proportions of the ingredients. These vary with the nature of the oil.

* Primary emulsion = النواه الاساسيه
- يكون سميكاً
- مستقراً
- يحضر بنسب مثاليه ( هذه النسب تختلف حسب نوع الزيت )

# 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

نفس الـ dry
لاكن الترتيب يختلف

- 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

* مقارنه مع الطريقه السابقه ، هذه الطريقه اصعب خصوصاً مع الزيوت عاليه اللزوجه لكنها تعطي emulsion أكثر ثباتاً

# 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.



Dr. Saja Hamed Dr. Tamara Athamneh Dr. Areen Alshweiat

# Methods of compounding emulsions:

## 4. Beaker Method

نستخدم هذا الطريقة عند استخدام

* الطرق السابقة تعتمد اساسا على الصموغ مثل acacia
فإذا كان العامل المستحلب غير صمغي تصبح الطرق السابقة أقل فاعلية

- 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.


Dr.Saja Hamed Dr.Tamara Athamneh Dr.Areen Alshweiat

# 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.

ما معنى In Situ Soap Method؟

يعني تكوين الصابون داخل المستحضر نفسه أثناء التحضير، فيعمل كعامل مستحلب.

هذه تسمى self-emulsifying emulsions

نوعا الصابون المذكوران

* Calcium soaps
* Soft soaps (olive oil soap)

نوع المستحلب المتكوّن

W/O emulsions تعطي غالبًا Calcium soaps

مثال

عند استخدام بعض الزيوت النباتية مثل الزيت المحتوي على oleic acid مع limewater / calcium hydroxide solution،
يتكون:

* calcium oleate

وهذا هو العامل المستحلب الناتج داخل النظام.

الخلاصة

# Methods of compounding emulsions: In Situ Soap Method

- A typical example of this emulsion is calamine liniment:

- Calamine
- 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

* تذوبها اولاً بعد ين تضاف كمحلول لـ Primary emulsion

* يجب ان تضاف بعد ان يبرد المستحضر اذا كان قد استخدم التسخين

# 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

1) التعريف

المستحلب = سائلان غير ممتزجين، أحدهما موزع على شكل قطرات في الآخر.

2) الأنواع

* O/W
* W/O
* Multiple emulsions

3) طرق تمييز النوع

* Miscibility test
* Conductivity
* Dye test

4) التطبيقات

* فموي
* عضلي
* وريدي
* موضعي
* شرجي

5) مشاكل الثبات

* Creaming / sedimentation
* Coalescence / cracking
* Phase inversion

6) تحسين الثبات

* تصغير القطرات
* زيادة اللزوجة
* استعمال emulsifiers
* التخزين المناسب

7) أنواع العوامل المستحلبة

* Hydrocolloids
* Surfactants
* Finely divided solids
* Auxiliary agents

8) HLB

مفتاح مهم جدًا لاختيار الـ surfactant المناسب.

9) المواد الحافظة ومضادات الأكسدة

لمنع التلف الكيميائي والميكروبي.

10) طرق التحضير

* Continental
* English