

Pharmaceutics I

صيدلانيات 1

Unit 7

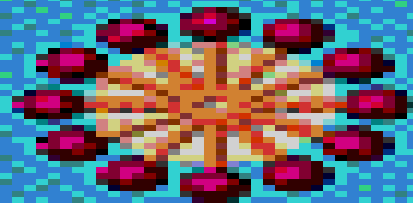
EMULSIONS

- 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.
- Most emulsions will have droplets with diameters of 0.1-100 μm and are inherently unstable systems;
- the dispersed phase is the internal phase,
- the dispersion medium is the external or continuous phase.

Type of emulsion

O/W type

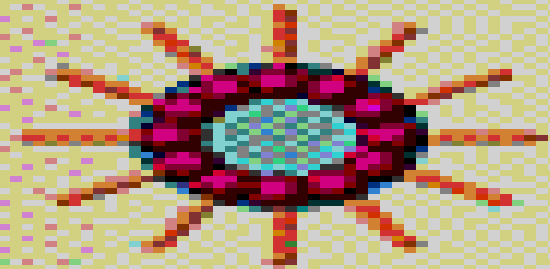
Water



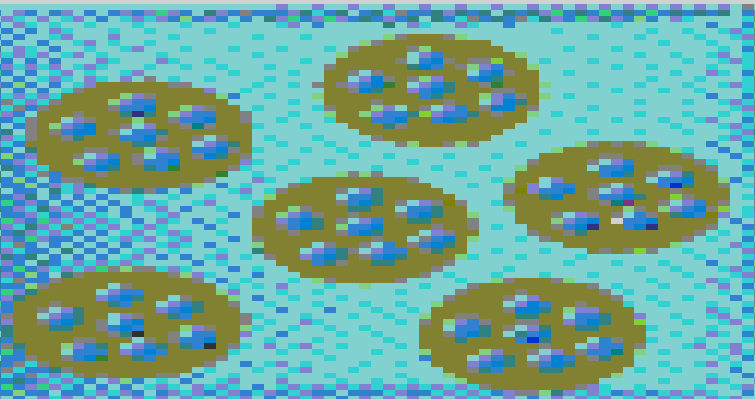
Oil in Water

W/O type

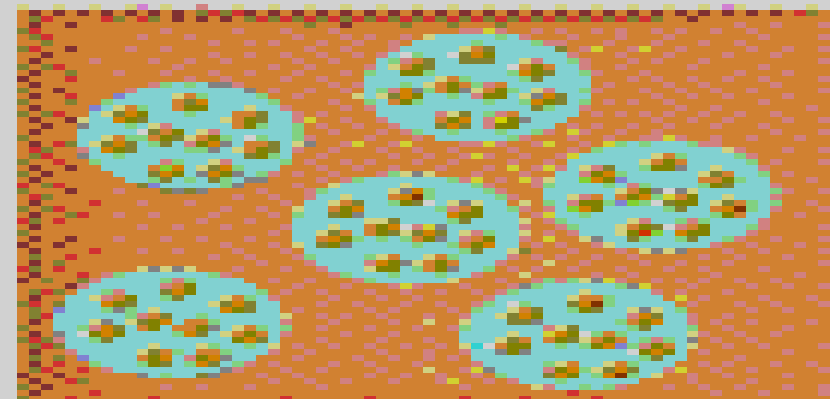
Oil



Water in Oil



W/O/W type



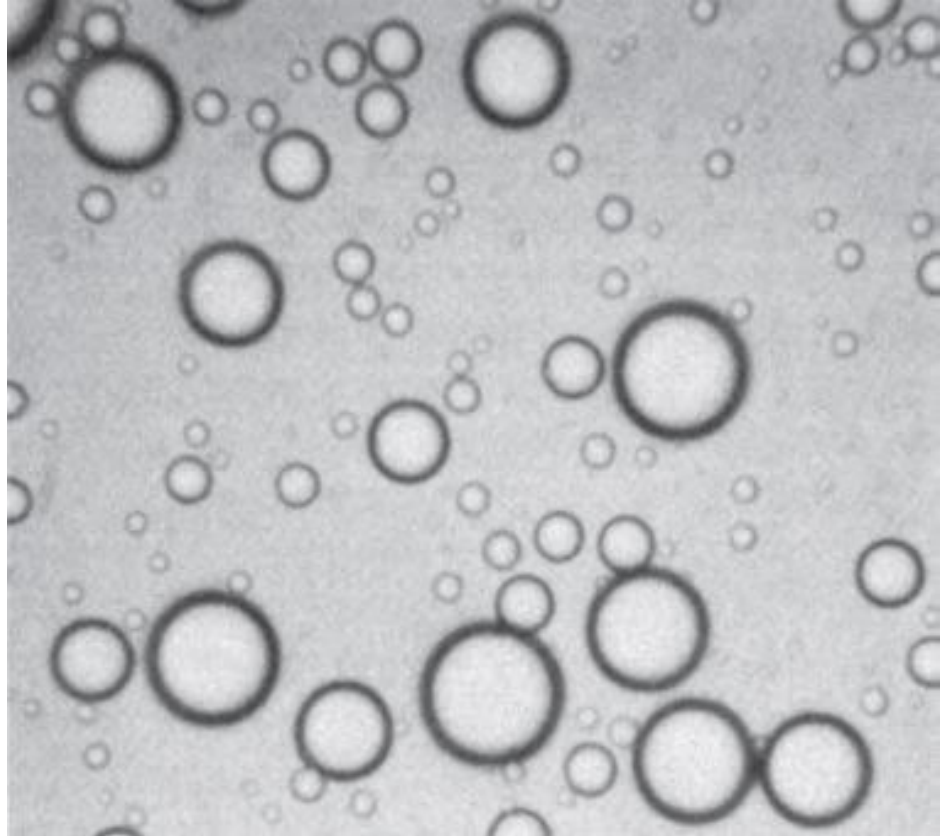
O/W/O type

Types of emulsions

- Emulsions with an oleaginous internal phase and an aqueous external phase are *oil-in-water* (o/w) emulsions.
- emulsions having an aqueous internal phase and an oleaginous external phase are termed *water-in-oil* (w/o) emulsions.
- More complicated emulsion systems may exist: for example, an oil droplet enclosing a water droplet may be suspended in water to form a water-in-oil-in water emulsion (w/o/w).
- Such systems or their o/w/o counterparts are termed *multiple emulsions and are of interest as delayed-action drug delivery systems.*

Example:

- **Mineral oil in water emulsion.**
- **The largest oil globule measures approximately 0.04 mm.**



Micro emulsions

- Unlike the coarse emulsions, microemulsions are homogeneous, transparent systems that are thermodynamically stable.
- they form spontaneously when the components are mixed in the appropriate ratios.
- They can be dispersions of oil in water or water in oil, but the droplet size is very much smaller (5-140 nm) than in coarse emulsions.
- Advantages over coarse emulsions: transparency stability.
- But they require much larger amounts of surfactant for their formulation,

Microemulsions

Microemulsions are for

- Oral
- Topical
- Parenteral administration.



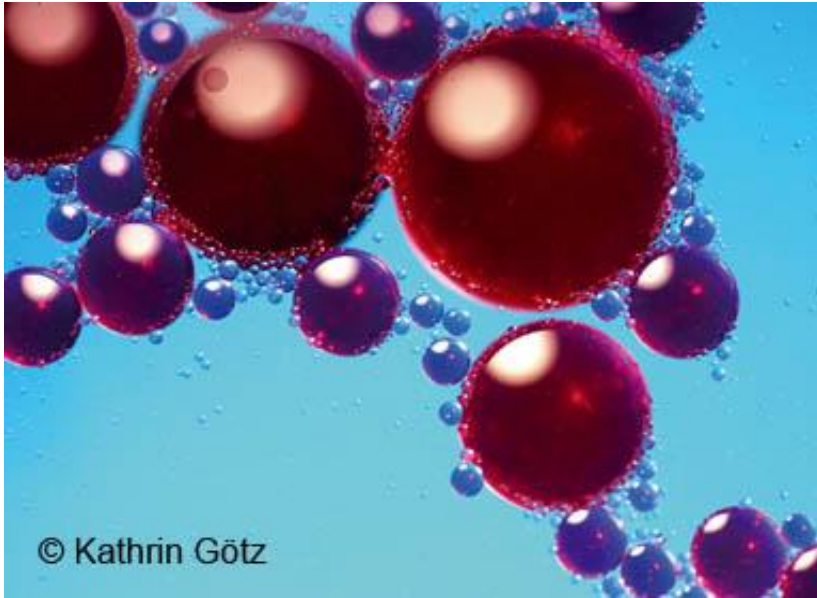
They offer the advantage of:

- spontaneous formation
- transparency stability
- ease of manufacturing and scale-up
- thermodynamic stability
- improved drug solubilization and bioavailability.

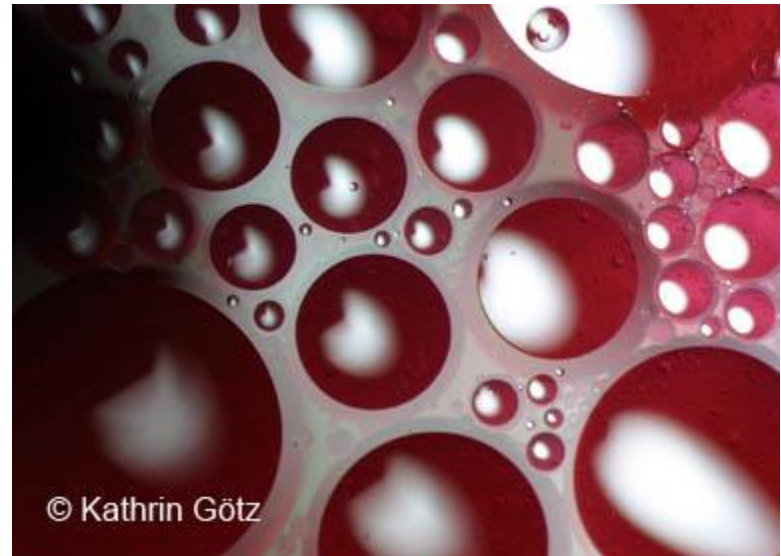
Tests for identification of emulsion type

1. miscibility tests with oil or water: The emulsion will only be miscible with liquids that are miscible with its continuous phase;
2. conductivity measurements: Systems with aqueous continuous phases will readily conduct electricity, whereas systems with oily continuous phases will not;
1. staining tests: Water-soluble and oil-soluble dyes are used, one of which will dissolve in, and colour the continuous phase.

Staining tests

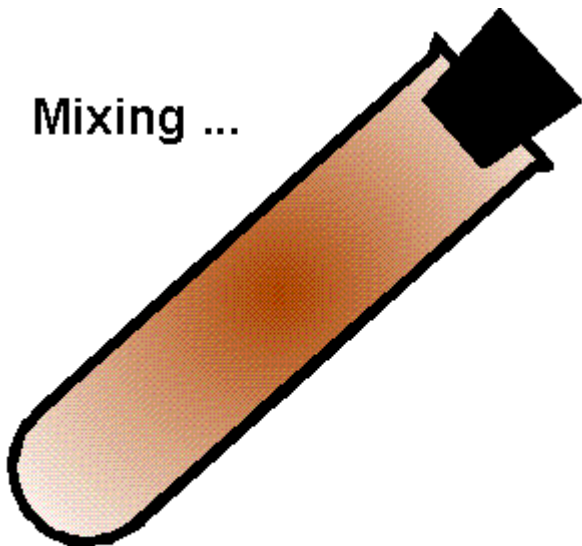


O/W emulsion



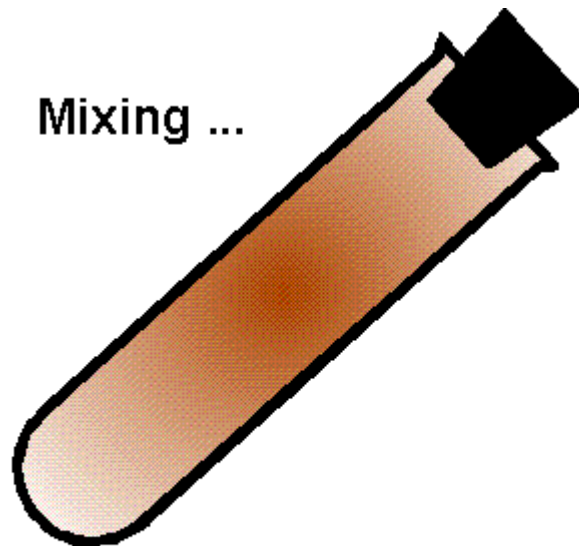
W/O emulsion

Mixing ...



W/O

Mixing ...



O/W

- an o/w emulsion may be diluted or extended with water or an aqueous preparation and a w/o emulsion, with an oleaginous or oil-miscible liquid.
- Generally, to prepare a stable emulsion, a third phase, an *emulsifying agent*, is necessary.
- Depending on their constituents, the viscosity of emulsions can vary greatly and pharmaceutical emulsions may be prepared as liquids or semisolids.

- **liquid emulsions may be employed:**
- **orally,**
- **topically,**
- **or parenterally;**
- **semisolid emulsions, topically.**

PURPOSE OF EMULSIONS AND OF EMULSIFICATION

- Emulsification enables the pharmacist to prepare relatively stable and homogeneous mixtures of two immiscible liquids.
- For orally administered emulsions, the o/w type permits palatable administration of an otherwise distasteful oil by dispersing it in a sweetened, flavored aqueous vehicle.
- The reduced particle size of the oil globules may render the oil more digestible and more readily absorbed,
- render the oil more effective in its task, as for example, the increased efficacy of mineral oil as a cathartic when emulsified.

- **Emulsions to be applied to the skin may be o/w or w/o, depending on such factors as:**
 - 1.the nature of the therapeutic agents,**
 - 2.the desirability for an emollient or tissue-softening effect,**
 - 3.the condition of the skin.**

- **The nature of the therapeutic agents:**
- **Medicinal agents that irritate the skin generally are less irritating in the internal phase of an emulsified topical preparation than in the external phase, from which direct contact with the skin is more prevalent.**
- **Naturally, the miscibility or solubility in oil and in water of a medicinal agent dictates to a great extent the vehicle, and its nature in turn suggests the phase of the emulsion that the resulting solution should become.**

- **The condition of the skin:**
- **On the unbroken skin, 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.**

- The desirability for an emollient or tissue-softening effect:
- A w/o emulsion is also more softening to the skin, because it resists drying and removal by contact with water.
- On the other hand, if it is desirable to have a preparation that is easily removed from the skin with water, an o/w emulsion is preferred.

PREPARATION OF EMULSIONS

- **Emulsifying Agents**

- The initial step in preparation of an emulsion is selection of the emulsifier.
- To be useful in a pharmaceutical preparation, the emulsifying agent:
 1. must be compatible with the other formulative ingredients and must not interfere with the stability or efficacy of the therapeutic agent.
 2. It should be stable and not deteriorate in the preparation.
 3. The emulsifier should be nontoxic with respect to its intended use and the amount to be consumed by the patient.
 4. Also, it should possess little odor, taste, or color.
 5. It should have the capability to promote emulsification and to maintain the stability of the emulsion for the intended shelf life of the product.

emulsifiers and stabilizers for pharmaceutical systems

1. Carbohydrate materials
2. Protein substances
3. High–molecular-weight alcohols
4. Wetting agents (surface active agents)
5. Finely divided solids

Carbohydrate materials

- such as the naturally occurring agents acacia, tragacanth, agar, chondrus, and pectin.
- These materials form hydrophilic colloids which when added to water and generally produce o/w emulsions.

Protein substances

- such as gelatin, egg yolk, and casein.
- These substances produce o/w emulsions.

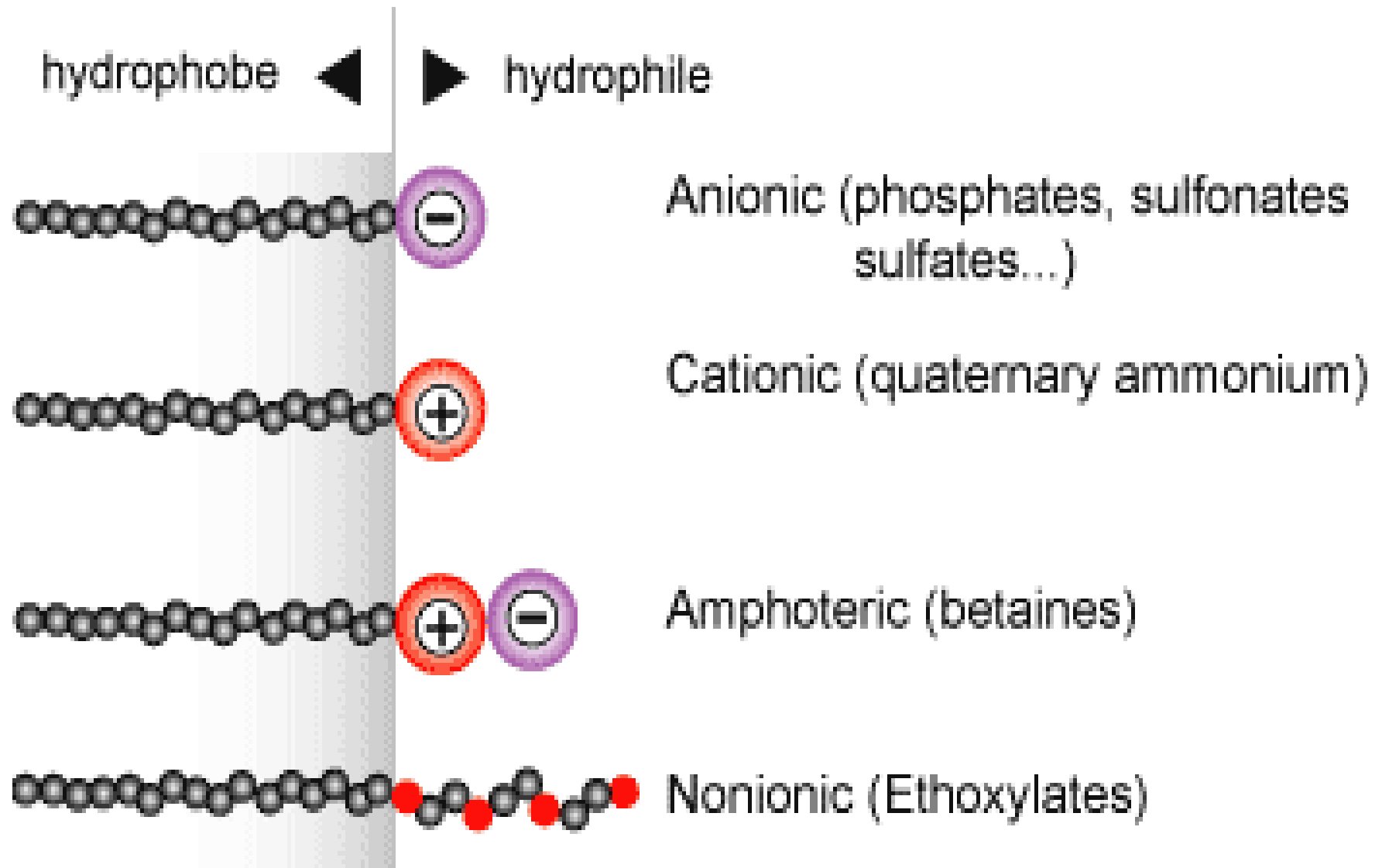
High-molecular-weight alcohols

- such as stearyl alcohol, cetyl alcohol, and glyceryl monostearate.
- These are employed primarily as thickening agents and stabilizers for o/w emulsions of certain lotions and ointments used externally.
- Cholesterol and cholesterol derivatives may also be employed in externally used emulsions to promote w/o emulsions.

Wetting agents (surface active agents)

- may be anionic, cationic, or nonionic.
- These agents contain both hydrophilic and lipophilic groups,
- In anionic agents, the lipophilic portion is negatively charged, but in the cationic agent, it is positively charged.
- Owing to their opposing ionic charges, anionic and cationic agents tend to neutralize each other and are thus considered incompatible.

SYNTHETIC EMULSIFIERS



Emulsifying agents

```
graph TD; A[Emulsifying agents] --> B[Synthetic]; A --> C[Natural]; B --> D[Anionic]; B --> E[Cationic]; B --> F[Nonionic]; D --> G[Alkali soaps]; D --> H[Amine soaps]; D --> I[Sulphated comp.]; F --> J[Glycerol esters]; F --> K[Sorbitan esters]; F --> L[Polysorbates]; F --> M[Higher fatty alcohol];
```

Synthetic

Natural

Anionic

Cationic

Nonionic

Alkali soaps

Amine soaps

Sulphated comp.

Glycerol esters

Sorbitan esters

Polysorbates

Higher fatty alcohol

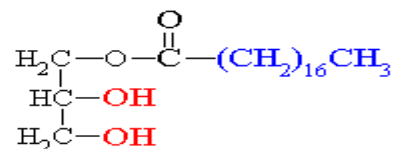
- Nonionic emulsifiers show no inclination to ionize.
- Depending on their individual nature, certain of the members of these groups form o/w emulsions and others, w/o emulsions.
- **Anionic emulsifiers** include various monovalent, polyvalent, and organic soaps, such as triethanolamine oleate, and sulfonates, such as sodium lauryl sulfate.
- Benzalkonium chloride, known primarily for its bactericidal properties, may be employed as a **cationic emulsifier**.
- Agents of the nonionic type include the sorbitan esters (Spans) and their polyoxyethylene derivatives (Tweens)

Nonionic Surfactants

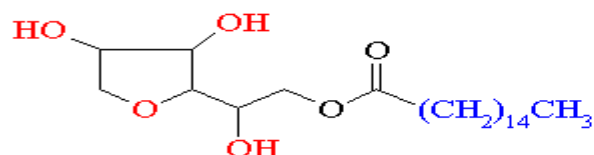
Lipophilic **Hydrophilic**
 $\text{CH}_3(\text{CH}_2)_n\text{OH}$

Fatty Alcohols

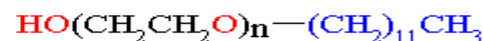
(n=11, lauryl; n=15, cetyl; n=17, stearyl alcohol)



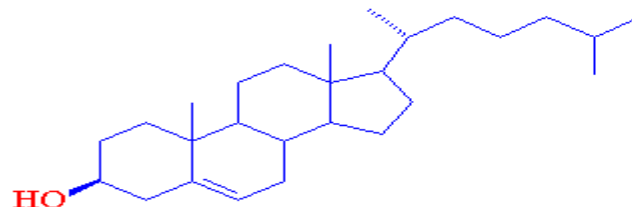
Partial Fatty Acid Esters of Multivalent Alcohols
 (glycerol monostearate)



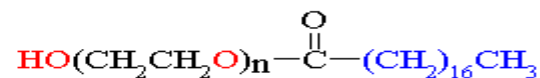
Spans: Sorbitan Esters of Fatty Acids
 (sorbitan monopalmitate)



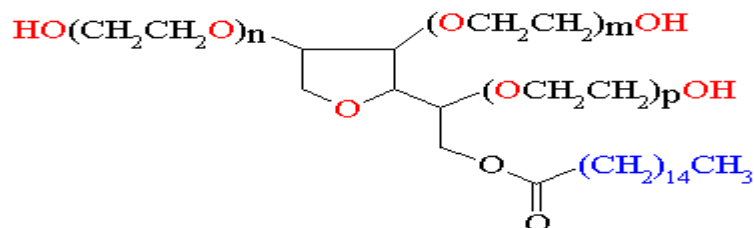
Brij: Polyethyleneglycol (PEG) Ether
 (PEG-200 lauryl ether, Brij 30)



Cholesterol



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



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

Sorbitan esters of fatty acids (Spans)

❖ **Sorbitan is esterified with lauric, palmitic, stearic or oleic fatty acid**

❖ **Variations in the type of fatty acid produce different Spans:**

***Span 20* with lauric acid (sorbitan monolaurate)**

***Span 40* with Palmitic acid (sorbitan monopalmitate)**

***Span 60* with stearic acid (sorbitan monostearate)**

***Span 80* with oleic acid (sorbitan monooleate)**

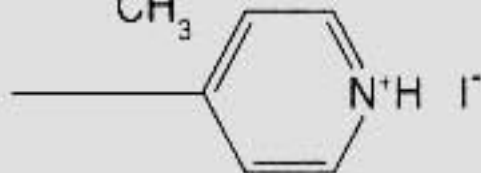
❖ **Form stable w/o emulsions**

Polysorbates (Tweens)

- **Polyethylene glycol derivatives of the sorbitan esters (Polyoxyethylene sorbitan ester of fatty acids).**
- **Variations in the type of fatty acid produce different tweens chain with different oil and water solubility, (Tween 20, 40, 60 and 80).**
- **Polysorbates are generally used in conjunction with the corresponding sorbitan esters to form a complex condensed film at the oil/water interface to produce either o/w or w/o emulsions.**
- **Advantages of tweens:**
 - **Compatible with other types of surfactants**
 - **Stable to heat, pH change and electrolytes**
 - **Low toxicity, for oral and parenteral preparations**
- **Disadvantages:**
 - **Unpleasant taste**
 - **Inactivate some preservatives as parabens by complexation**

- **Nonionic surfactants are effective over pH range of 3 to 10;**
- **cationic surfactants are effective over pH range of 3 to 7;**
- **anionic surfactants require a pH greater than 8**

Table 6.3 Classification of surface-active agents

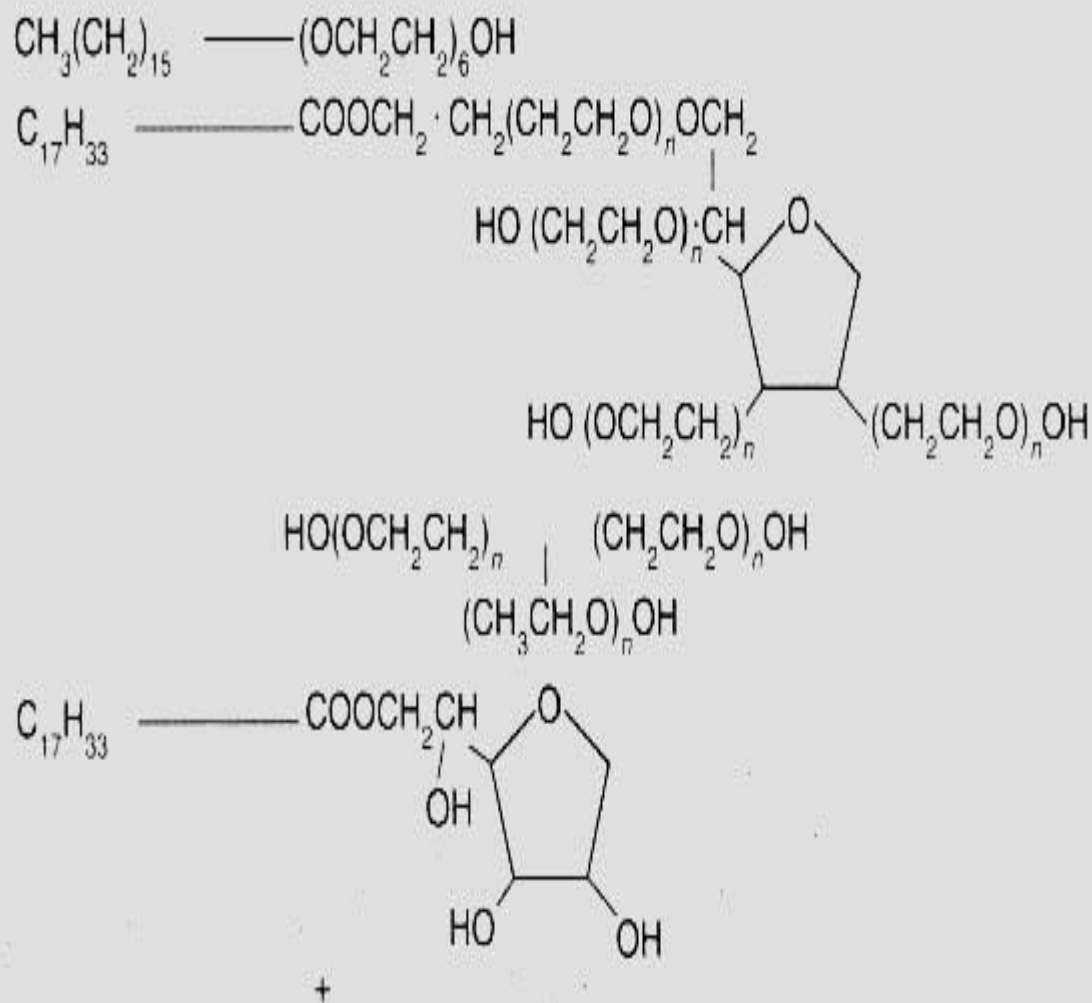
	Hydrophobic	Hydrophilic
<i>Anionic</i>		
Sodium dodecanoate	$\text{CH}_3(\text{CH}_2)_{10}$	$\text{—COO}^-\text{Na}^+$
Sodium dodecyl (lauryl) sulphate	$\text{CH}_3(\text{CH}_2)_{11}$	$\text{—OSO}_3^-\text{Na}^+$
Sodium dioctyl sulphosuccinate	$\text{CH}_3(\text{CH}_2)_7$	$\text{OOC.CHSO}_3^-\text{Na}^+$ $\quad \quad \quad $ $\text{CH}_3(\text{CH}_2)_7\text{.OOC.CH}_2$
<i>Cationic</i>		
Hexadecyl trimethyl ammonium bromide (Cetrimide)	$\text{CH}_3(\text{CH}_2)_{15}$	$\text{—N}^+(\text{CH}_3)_3\text{Br}^-$ $\quad \quad \quad $ CH_3
Dodecyl pyridinium iodide	$\text{CH}_3(\text{CH}_2)_{11}$	
<i>Non-ionic</i>		

Non-ionic

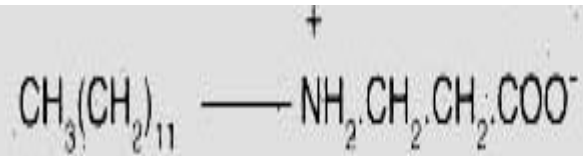
Hexaoxyethylene monohexadecyl ether

Polyoxyethylene sorbitan mono-oleate
(polysorbate 80)

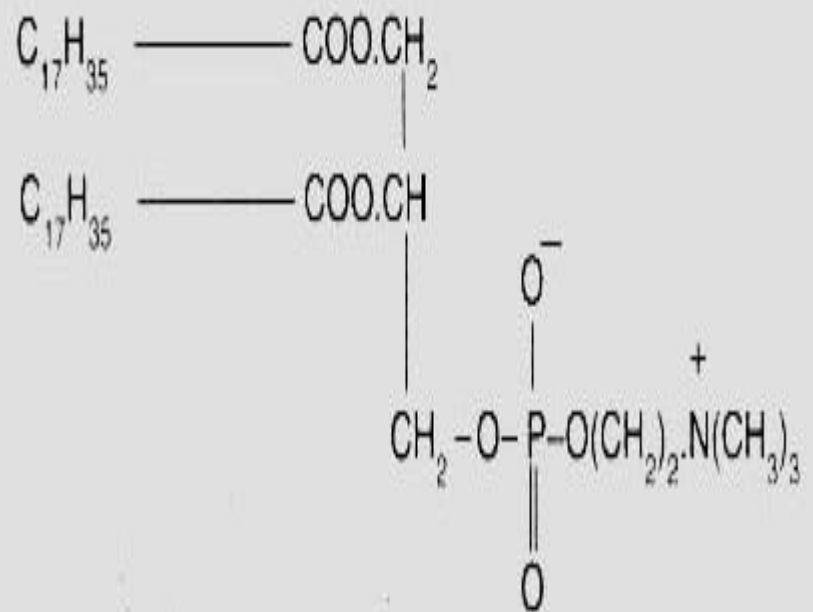
Sorbitan mono-oleate



Ampholytic
N-dodecyl alanine



Lecithin



**TABLE 14.3 ACTIVITY AND HLB VALUE
OF SURFACTANTS**

ACTIVITY	ASSIGNED HLB
Antifoaming	1–3
Emulsifiers (w/o)	3–6
Wetting agents	7–9
Emulsifiers (o/w)	8–18
Solubilizers	15–20
Detergents	13–16

Finely divided solids

- such as colloidal clays, including bentonite,
- Generally, these **form o/w emulsions** when the insoluble material is added to the aqueous phase if there is a greater volume of the aqueous phase than of the oleaginous phase.
- However, if the powdered solid is added to the oil and the oleaginous phase volume predominates, a substance such as bentonite is capable of forming a **w/o emulsion**.

The HLB System And Formulation by the HLB method

The HLB System

- Generally, each emulsifying agent has a hydrophilic portion and a lipophilic portion, with one or the other being more or less predominant.
- emulsifying or surface-active agents may be categorized on the basis of their chemical makeup as to their hydrophil–lipophil balance, or HLB.
- By this method, each agent is assigned an HLB value or number indicating the substance's polarity.
- Although the numbers have been assigned up to about 40, the usual range is between 1 and 20.

- **Materials that are highly polar or hydrophilic have been assigned higher numbers than materials that are less polar and more lipophilic.**
- **Generally, surface active agents having an assigned HLB value of 3 to 6 are greatly lipophilic and produce w/o emulsions,**
- **agents with HLB values of about 8 to 18 produce o/w emulsions.**

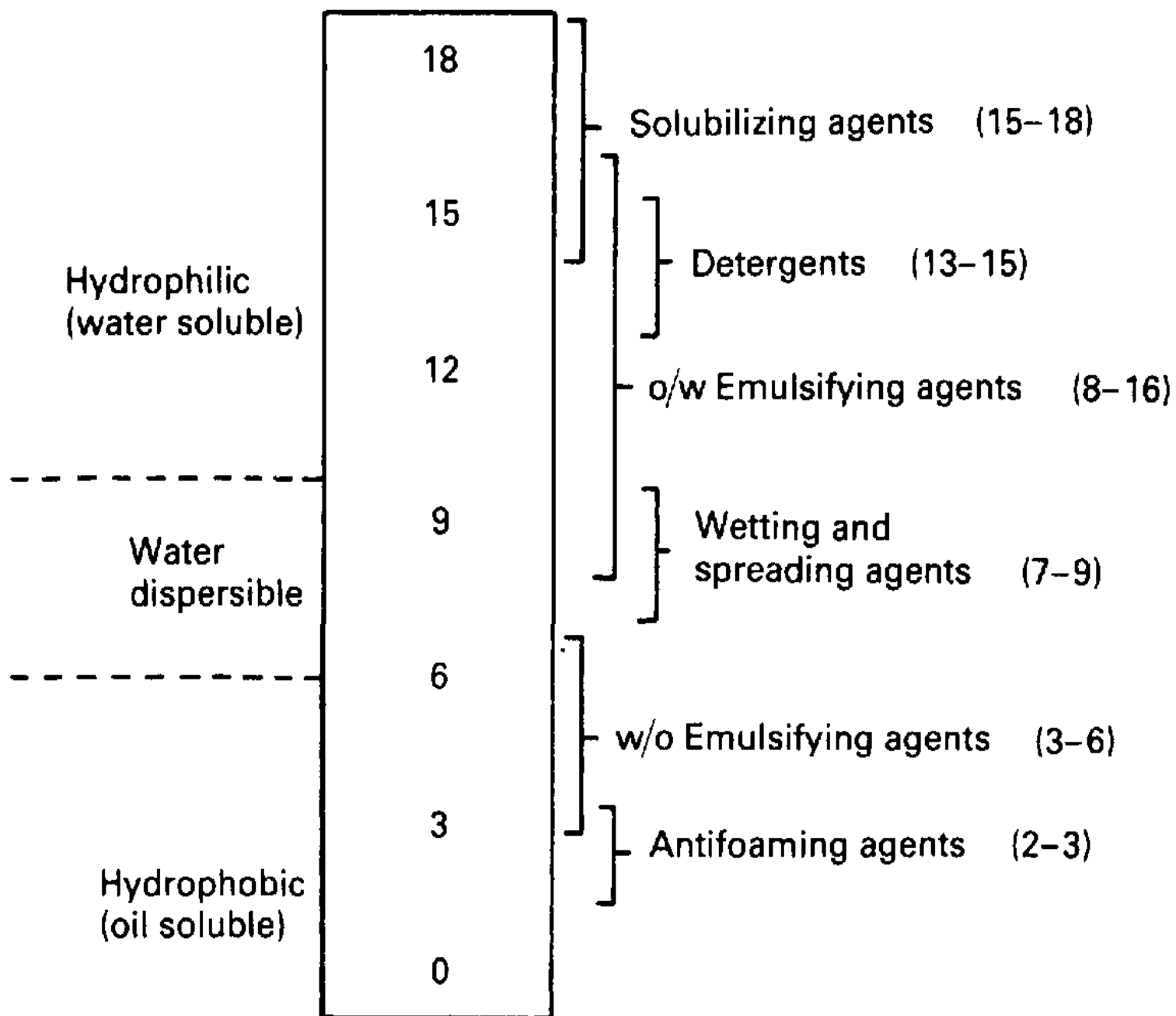


TABLE 14.2 HLB VALUES FOR SELECTED EMULSIFIERS

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 ^a)	9.7
Gelatin	9.8
Triton X-45 ^b	10.4

Methylcellulose	10.5
Polyoxyethylene monostearate (Myrj 45 ^a)	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 ^d	17.0
Sodium oleate	18.0
Potassium oleate	20.0
Sodium lauryl sulfate	40.0

- In the HLB system, in addition to the emulsifying agents, values are assigned to oils and oil like substances.
- One selects emulsifying agents having the same or nearly the same HLB value as the oleaginous phase of the intended emulsion.
- For example, mineral oil has an assigned HLB value of:
- 4 if a w/o emulsion is desired
- 10.5 if an o/w emulsion is to be prepared.

- To prepare a stable emulsion, the emulsifying agent should have an HLB value similar to the one for mineral oil, depending on the type of emulsion desired.
- When needed, two or more emulsifiers may be combined to achieve the proper HLB value.

Formulation by the HLB method

- A useful method has been devised for calculating the relative quantities of these emulgents necessary to produce the most physically stable emulsion for a particular oil/water combination.
- This is called the hydrophile-lipophile balance (HLB) method.
- Although originally applied to non-ionic surfaceactive agents, its use has been extended to ionic emulgents.

- Each surfactant is allocated an HLB number representing the relative proportions of the lipophilic and hydrophilic parts of the molecule.
- Each type of oil used will require an emulgent of a particular HLB number in order to ensure a stable product.
- For an o/w emulsion, for example, the more polar the oil phase the more polar must be the emulgent system.

Table 23.2 HLB values for some pharmaceutical surfactants

Sorbitan trioleate (Span 85)	1.8
Oleic acid	4.3
Sorbitan mono-oleate (Span 80)	4.3
Sorbitan monostearate (Span 60)	4.7
Sorbitan monolaurate (Span 20)	8.6
Polysorbate 60 (polyoxyethylene sorbitan monostearate)	14.9
Polysorbate 80 (polyoxyethylene sorbitan mono-oleate) (Tween 80)	15.0
Polysorbate 20 (polyoxyethylene sorbitan mono-laurate) (Tween 20)	16.7
Potassium oleate	20.0
Sodium dodecyl (lauryl) sulphate	40.0

Table 23.3 Required HLB values for a range of oils and waxes

	For a w/o emulsion	For an o/w emulsion
Beeswax	5	12
Cetyl alcohol	–	15
Liquid paraffin	4	12
Soft paraffin	4	12
Wool fat	8	10

- **Example: o/w emulsion.**

Liquid paraffin	35%
Wool fat	1%
Cetyl alcohol	1%
Emulsifier system	5%
Water	to 100%

- The total percentage of oil phase is 37 and the proportion of each is:
- Liquid paraffin $35/37 \times 100 = 94.6\%$
- Wool fat $1/37 \times 100 = 2.7\%$
- Cetyl alcohol $1/37 \times 100 = 2.7\%$

- this particular formulation requires an emulgent blend of HLB 12.1 in order to produce the most stable emulsion.
- Assuming that a blend of (Span 80) sorbitan mono-oleate (HLB 4.3) and (Tween 80) polyoxyethylene sorbitan mono-oleate (HLB 15) is to be used as the emulsifying system, the proportions of each to be added to the emulsion to provide an HLB of 12.1 are calculated as follows.

- Let A be the percentage concentration of the hydrophilic and B the percentage of the hydrophobic surfactants required to give a blend having an HLB value of x . Then:

$$\% A = \frac{100(x - \text{HLB of } B)}{(\text{HLB of } A - \text{HLB of } B)}$$

$$\% B = 100 - A$$

(Tween80)(HLB 15) (hydrophilic) (A)
(Span 80) (HLB 4.3) (Hydrophobic) (B)

is to be used as the emulsifying system, the proportions of each to be added to the emulsion to provide an HLB of 12.1 are calculated as follows.

- In the example:

$$A = \frac{100(12.1 - 4.3)}{(15 - 4.3)} = 72.9 \%$$

$$B = 100 - 72.9 = 27.1 \%$$

- Because the total percentage of emulgent blend in the formulation is 5, the percentage of each emulsifier will be:

Sorbitan mono-oleate	$5 \times 27.1/100 = 1.36$
Polyoxyethylene sorbitan	
mono-oleate	$5 - 1.36 = 3.64$

Methods of Emulsion Preparation

- Emulsions may be prepared by several methods, depending upon the nature of the components and the equipment.
- On a small scale, as in the laboratory or pharmacy, emulsions may be prepared using porcelain mortar and pestle, a mechanical blender or mixer, such as a Waring blender or a milkshake mixer, a hand homogenizer, a bench-type homogenizer, or sometimes a simple prescription bottle.

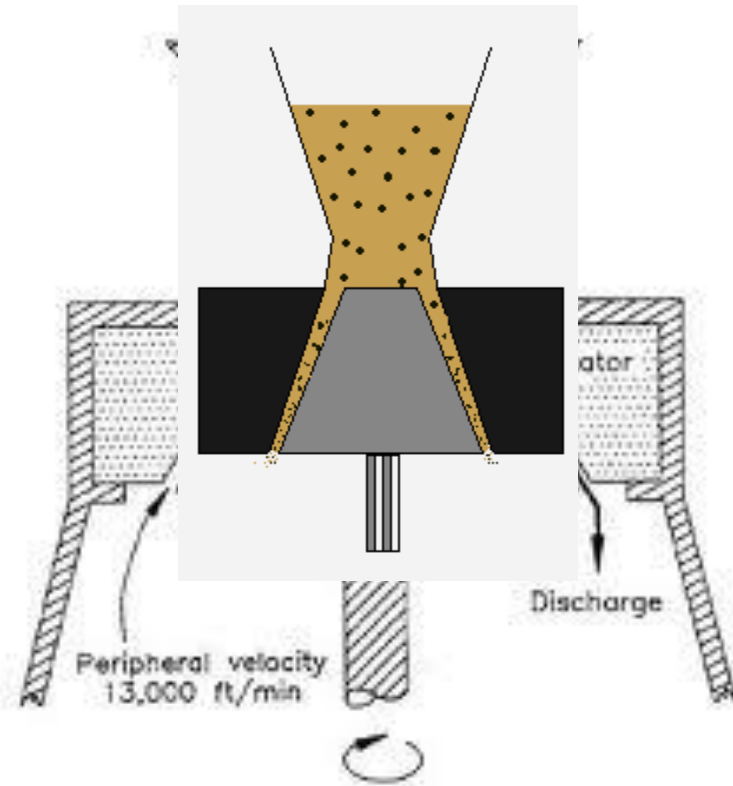
Laboratory preparation of an emulsion using a hand homogenizer.



Homogenizer



- On a large scale, large mixing **tanks** may be used to form the emulsion through the action of a **high-speed impeller**.
- As desired, the product may be rendered finer by passage through a **colloid mill**, in which the particles are sheared between the small gap separating a high-speed rotor and the stator, or by passage through a **large homogenizer**, in which the liquid is forced under great pressure through a small valve opening.



colloid mill

the small-scale extemporaneous preparation of emulsions

- three methods may be used:
 1. the *continental* or *dry gum method*,
 2. the *English* or *wet gum method*,
 3. the *bottle* or *Forbes bottle method*.

The quantities for primary emulsion are as follows:

A. Fixed oil, e.g., almond, castor, arachis and cod liver oil. dry gum method

oil	water	gum
4	2	1

B. Volatile oil, e.g., turpentine, cinnamon and peppermint oil. dry gum method

oil	water	gum
2	2	1

C. Mineral oil (liquid paraffin). wet gum method

oil	water	gum
3	2	1

Continental or Dry Gum Method

- The continental method is also referred to as the 4:2:1 method because for every 4 parts by volume of oil, 2 parts of water and 1 part of gum are added in preparing the initial or *primary emulsion*.
- For instance, if 40 mL of oil is to be emulsified, 20 mL of water and 10 g of gum would be employed in the primary emulsion, with any additional water or other formulation ingredients added afterward.
- In this method, the acacia or other o/w emulsifier is triturated with the oil in a perfectly dry Wedgwood or porcelain mortar until thoroughly mixed.

- A mortar with a rough rather than smooth inner surface must be used to ensure proper grinding action and reduction of the globule size.
- A glass mortar is too smooth to produce the proper reduction of the internal phase.
- After the oil and gum have been mixed, the two parts of water are added all at once, and the mixture is triturated immediately, rapidly, and continuously until the primary emulsion is creamy white and produces a crackling sound to the movement of the pestle.

- **Generally, about 3 minutes of mixing is required to produce a primary emulsion.**
- **Other liquid formulative ingredients that are soluble in or miscible with the external phase may then be mixed into the primary emulsion.**
- **Solid substances such as preservatives, stabilizers, colorants, and any flavoring material are usually dissolved in a suitable volume of water (assuming water is the external phase) and added as a solution to the primary emulsion.**

- Any substances that might interfere with the stability of the emulsion or the emulsifying agent are added as near last as is practical.
- For instance, alcohol has a precipitating action on gums such as acacia, thus no alcohol or solution containing alcohol should be added directly to the primary emulsion, because the total alcoholic concentration of the mixture would be greater at that point than after other diluents were added.

(Fixed Oil)Caster Oil Emulsion

Rx

Ricin Oil *16 ml*

GUM acacia Q.S.

Water 80 ml

Fiat: emuls

Sig. Stat

Uses: Castor oil is administered orally as a purgative.

- When all necessary agents have been added, the emulsion is **transferred to a graduate and made to volume** with water previously swirled about in the mortar to remove the last portion of emulsion.

- Rather than using a mortar and pestle, the pharmacist can generally prepare an excellent emulsion using the dry gum method and an electric mixer or blender.

English or Wet Gum Method

- By this method, the same proportions of oil, water, and gum are used as in the continental or dry gum method, but the order of mixing is different, and the proportion of ingredients may be varied during the preparation of the primary emulsion
- Generally, a mucilage of the gum is prepared by triturating in a mortar granular acacia with twice its weight of water.
- The oil is then added slowly in portions, and the mixture is triturated to emulsify the oil.

- Should the mixture become too thick, additional water may be blended into the mixture before another portion of oil is added.
- After all of the oil has been added, the mixture is thoroughly mixed for several minutes to ensure uniformity.
- Then, as with the continental or dry gum method, the other formulative materials are added, and the emulsion is transferred to a graduate and brought to volume with water.

Bottle or Forbes Bottle Method

- The bottle method is useful for the extemporaneous preparation of emulsions from volatile oils or oleaginous substances of low viscosities.
- Powdered acacia is placed in a dry bottle, two parts of oil are added, and the mixture is thoroughly shaken in the capped container.
- A volume of water approximately equal to that of the oil is then added in portions and the mixture thoroughly shaken after each addition.

- When all of the water has been added, the primary emulsion thus formed may be diluted to the proper volume with water or an aqueous solution of other formulative agents.
- This method is not suited for viscous oils because they cannot be thoroughly agitated in the bottle when mixed with the emulsifying agent.
- When the intended dispersed phase is a mixture of fixed oil and volatile oil, the dry gum method is generally employed.

Auxiliary Methods

- An emulsion prepared by either the wet gum or the dry gum method can generally be increased in quality by passing it through a hand homogenizer.
- In this apparatus, the pumping action of the handle forces the emulsion through a very small orifice that reduces the globules of the internal phase to about 5 μm and sometimes less.

STABILITY OF EMULSIONS

Stability of Emulsions

Physical

Creaming

Coalescence

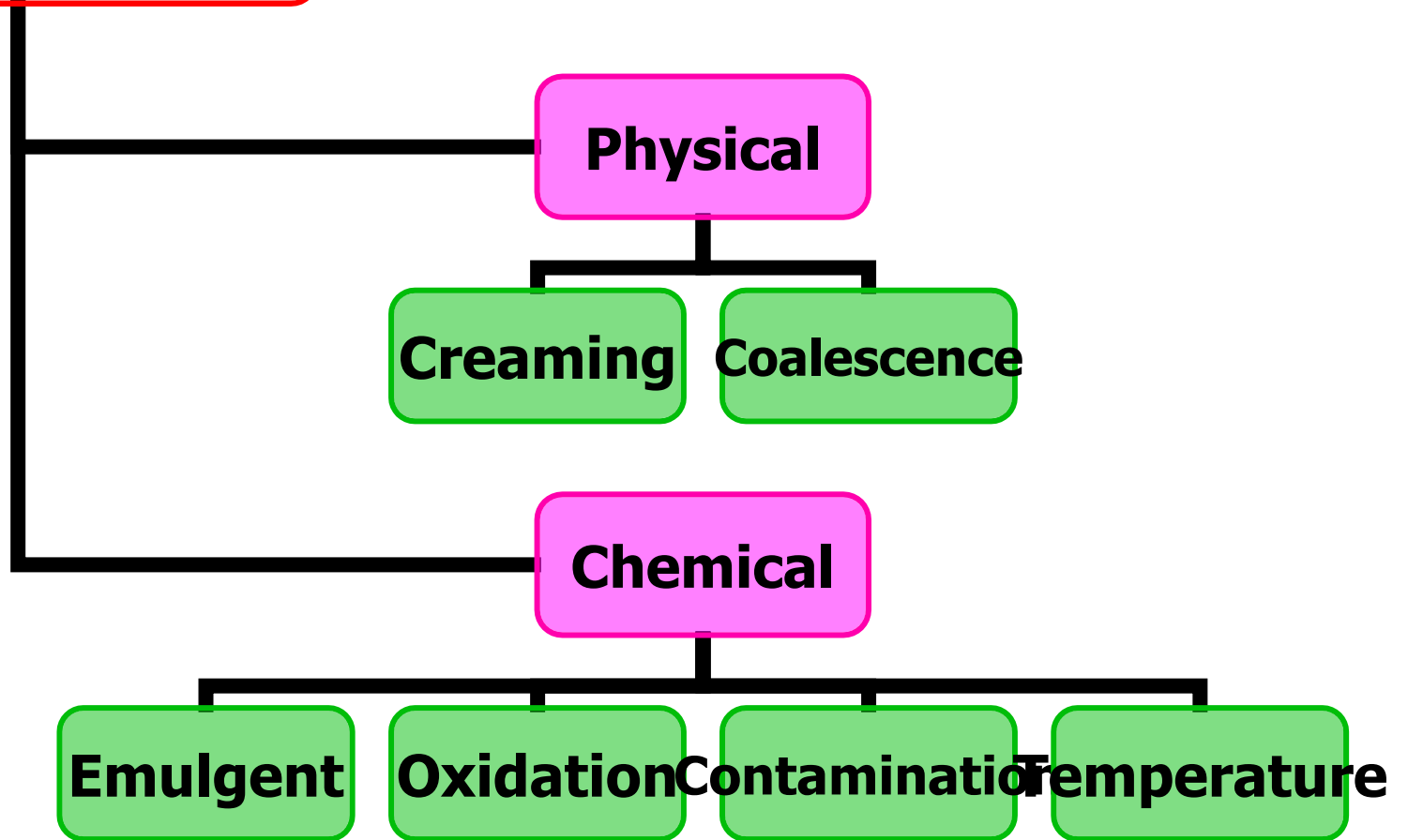
Chemical

Emulgent

Oxidation

Contamination

Temperature



- an emulsion is considered to be physically unstable if
- (a) the internal or dispersed phase upon standing tends to form aggregates of globules,
- (b) large globules or aggregates of globules rise to the top or fall to the bottom of the emulsion to form a concentrated layer of the internal phase
- (c) if all or part of the liquid of the internal phase separates and forms a distinct layer on the top or bottom of the emulsion as a result of the coalescing of the globules of the internal phase.

- **In addition, an emulsion may be adversely affected by microbial contamination and growth and by other chemical and physical alterations.**

Aggregation and Coalescence

- Weak interfaces between droplets break, allowing droplets to merge

– coalescence



- creaming of the emulsion:
- This is the separation of an emulsion into two regions, one of which is richer in the disperse phase than the other.
- provided coalescence is absent, it is a reversible process.
- The term is taken from the dairy industry and is analogous to creaming, or rising to the top of cream in milk that is allowed to stand.

- **The creamed portion of an emulsion may be redistributed rather homogeneously upon shaking, but if the aggregates are difficult to disassemble or if insufficient shaking is employed before each dose, improper dosage of the internal phase substance may result.**
- **Furthermore, a creamed emulsion is not esthetically acceptable to the pharmacist or appealing to the consumer.**
- **More important, it increases the risk that the globules will coalesce.**

- According to Stokes' equation, the rate of separation of the dispersed phase of an emulsion may be related to such factors as the particle size of the dispersed phase, the difference in density between the phases, and the viscosity of the external phase.

$$\frac{dx}{dt} = \frac{d^2(\rho_i - \rho_e)g}{18\eta}$$

- the rate of separation is increased by increased particle size of the internal phase, larger density difference between the two phases, and decreased viscosity of the external phase.

- **Therefore, to increase the stability of an emulsion,**
the globule or particle size should be reduced as fine
as is practically possible, the density difference
between the internal and external phases should be
minimal, and the viscosity of the external phase
should be reasonably high.
- **Thickeners such as tragacanth and microcrystalline**
cellulose are frequently added to emulsions to
increase the viscosity of the external phase.

- Upward creaming takes place in unstable emulsions of the o/w or the w/o type in which the internal phase has a lesser density than the external phase.
- Downward creaming takes place in unstable emulsions in which the opposite is true.

- **Breaking of the emulsion:**
- **More destructive to an emulsion than creaming is coalescence of the globules of the internal phase and separation of that phase into a layer.**
- **Separation of the internal phase from the emulsion is called breaking, and the emulsion is described as being cracked or broken.**
- **This is irreversible, because the protective sheath about the globules of the internal phase no longer exists.**

- Attempts to reestablish the emulsion by agitation of the two separate layers are generally unsuccessful.
- Additional emulsifying agent and reprocessing through appropriate machinery are usually necessary to reproduce an emulsion.

- **Generally, care must be taken to protect emulsions against extremes of cold and heat.**
- **Freezing and thawing coarsen an emulsion and sometimes break it. Excessive heat has the same effect.**
- **Because emulsion products may be transported to and used in locations with climates of extremely high or low temperature, manufacturers must know their emulsions' stability before they may be shipped.**
- **For most emulsions, the industry performs tests at 5°C, 40°C, and 50°C to determine the product's stability.**

- For light-sensitive emulsions, light-resistant containers are used.
- For emulsions susceptible to oxidative decomposition, antioxidants may be included in the formulation and adequate label warning provided to ensure that the container is tightly closed to air after each use.
- Many molds, yeasts, and bacteria can decompose the emulsifying agent, disrupting the system.

- Because fungi (molds and yeasts) are more likely to contaminate emulsions than are bacteria, fungistatic preservatives, commonly combinations of methyl paraben and propyl paraben, are generally included in the aqueous phase of an o/w emulsion.
- Alcohol in the amount of 12% to 15% based on the external phase volume is frequently added to oral o/w emulsions for preservation.