

## **CHAPTERWISE NOTES**

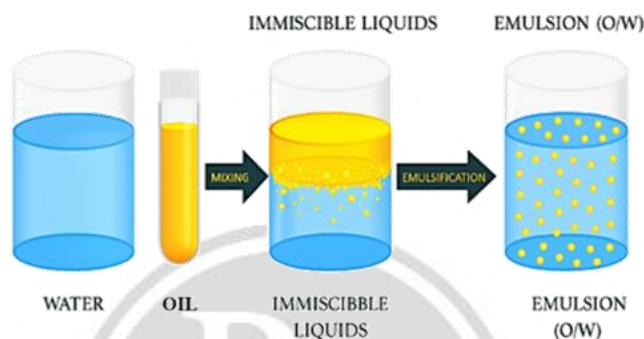
# **Emulsion**

## PHARMACEUTICAL TECHNOLOGY & MODERN PHARMACEUTICS

### Emulsion

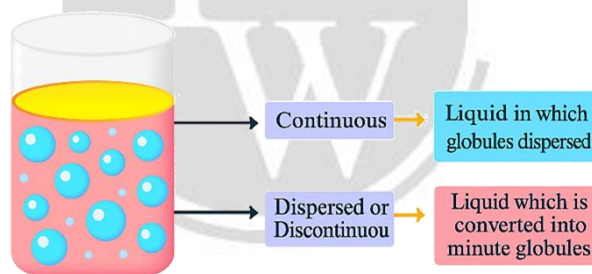
#### ➤ EMULSIONS (LIQUID-LIQUID SYSTEM)

- \* An **emulsion** is a **mixture of two immiscible liquids**, where one is dispersed in the other as tiny droplets.
- \* ⚠ **Thermodynamically unstable** → tends to separate unless stabilized by an **emulsifier**.



#### ➤ Phases of an Emulsion

EMULSION CONSISTS OF TWO PHASES



◆ Phase Type	💧 Description
<b>Disperse Phase</b>	Internal / Discontinuous phase (droplets)
<b>Continuous Phase</b>	External phase (surrounds the droplets)

#### Types of Emulsions

1. **O/W (Oil-in-Water)**
  - Oil droplets in 💧 water
  - Found in: *Lotions, vanishing Creams, Milk*
2. **W/O (Water-in-Oil)**
  - 💧 Water droplets in ● oil
  - Found in: *Butter, Cold Creams*
3. **Multiple Emulsions**
  - O/W/O** → Oil in Water, then in Oil
  - W/O/W** → Water in Oil, then in Water
  - Uses: *Controlled Drug Release, Cosmetics*

### Emulsifiers (Stabilizers)

- Role: ↓ **Surface tension** b/w two immiscible liquids
- Help form & stabilize the emulsion

### Size & Appearance

Type	Droplet Size	Appearance
<b>Emulsion</b>	0.1 – 10 $\mu\text{m}$	White, milky
<b>Microemulsion</b>	10 – 100 nm	Transparent
<b>Micelles</b>	5 – 20 nm	Clear, not true emulsion

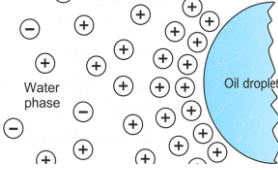
✦ **Note:** *Micelles = lipid-surfactant structures, not droplets.*

◆ **O/W** = Washable, non-greasy, absorbs quickly

◆ **W/O** = Greasy, occlusive, better for dry skin

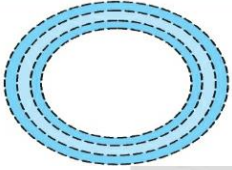
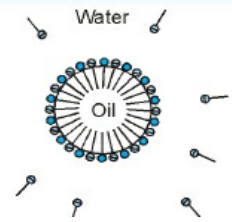
◆ **Microemulsions** = Thermodynamically **stable** but require surfactants

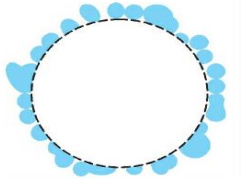
### Theory of Emulsification:

Theory	Key Concept	Explanation / Mechanism	Result / Type of Emulsion
<b>Viscosity Theory</b>	Emulsion viscosity affects stability	Viscosity depends on <b>phase-volume ratio</b> and <b>presence of emulgent</b>	Higher viscosity <b>retards coalescence</b> and <b>phase separation</b>
<b>Interfacial Tension Theory</b>	Emulsions are thermodynamically unstable due to <b>interfacial tension</b>	Cohesive forces between oil droplets and adhesive forces between oil and water develop <b>interfacial tension</b> , which <b>promotes coalescence</b>	<b>Surfactants</b> reduce this interfacial tension ↓ ⇒ Easier to break large droplets into smaller ones ⇒ Prevents coalescence ⇒ Stabilizes the emulsion
<b>Adsorption Theory / Electrical Repulsion</b> 	<b>Surfactants</b> stabilize emulsions by forming an <b>electrical double layer</b> around droplets.	<b>Electric repulsion</b> between similarly charged particles prevents coalescence	<b>Stabilizes dispersed phase</b> and prevents merging
<b>Bancroft's Theory</b>	Type of emulsion depends on <b>solubility of surfactant</b>	- Surfactant soluble in <b>water</b> → forms <b>oil-in-water (o/w)</b> emulsion - Surfactant soluble in <b>oil</b> → forms <b>water-in-oil (w/o)</b> emulsion	<b>Determines emulsion type</b> based on solubility behavior

<b>Orientation/Wedge Theory (Hardy-Harkins)</b>	Emulsion type depends on <b>ionic size</b> of metal ions in surfactants	<ul style="list-style-type: none"> <li>- <b>Monovalent ions</b> (<math>\text{Na}^+</math>, <math>\text{K}^+</math>) → favor <b>o/w emulsion</b></li> <li>- <b>Divalent/Trivalent ions</b> (<math>\text{Ca}^{2+}</math>, <math>\text{Mg}^{2+}</math>, <math>\text{Al}^{3+}</math>) → favor <b>w/o emulsion</b></li> <li>- Smaller ionic volume with higher valency → favors w/o</li> </ul>	<b>Predicts emulsion type</b> by metal ion valency & volume
<b>Complex Film Theory (Schulman &amp; Cockbain)</b>	Surfactant forms a <b>rigid interfacial film</b> at high concentration	Densely packed surfactant molecules at the interface create a <b>stable, rigid film</b> , preventing droplet coalescence	<b>Greater interfacial film rigidity = better stability</b>

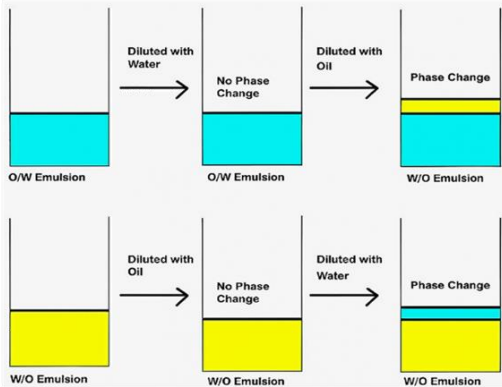
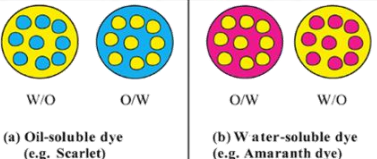
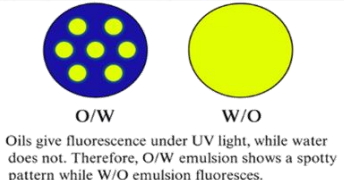
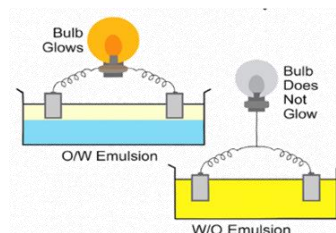
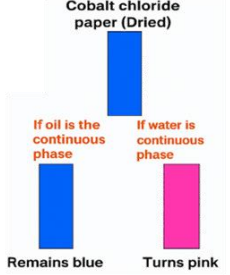
### Types of Emulsifying Agents

Type	Examples	Properties / Mechanism	Additional Examples
<b>Hydrophilic Colloids (Natural/Synthetic Polymers)</b> 	<ul style="list-style-type: none"> <li>- <b>Vegetable:</b> Gum acacia, Tragacanth, Starch</li> <li>- <b>Animal:</b> Gelatin, Wool fat (Lanolin), Egg yolk</li> <li>- <b>Synthetic:</b> Methylcellulose, Hydroxyethyl cellulose</li> </ul>	<ul style="list-style-type: none"> <li>- Do not reduce surface tension</li> <li>- Form rigid, protective films around droplets → prevent coalescence.</li> <li>- Form <b>multimolecular films.</b></li> <li>- Also act as viscosity enhancers</li> </ul>	<ul style="list-style-type: none"> <li>- Sodium alginate</li> <li>- Carbopol</li> <li>- Carboxymethylcellulose (CMC)</li> </ul>
<b>Synthetic Surface Active Agents (Surfactants)</b> 	<ul style="list-style-type: none"> <li>- <b>Anionic:</b> Potassium stearate, Sodium lauryl sulfate (SLS)</li> <li>- <b>Cationic:</b> Cetrimide (Cetyltrimethylammonium bromide)</li> <li>- <b>Ampholytic:</b> N-dodecyl alanine</li> <li>- <b>Non-ionic:</b> Sorbitan monooleate (Span 80), Polyoxyethylene sorbitan monooleate (Tween 80)</li> </ul>	<ul style="list-style-type: none"> <li>- Reduce interfacial tension and form a <b>monomolecular film.</b></li> <li>- Ionic surfactants impart charge → increase zeta potential, causing repulsion and stability</li> </ul>	<ul style="list-style-type: none"> <li>- Sodium dioctyl sulfosuccinate</li> <li>- Benzalkonium chloride</li> <li>- Lecithin (natural phospholipid)</li> </ul>

<b>Finely Divided Solid Particles (Solid Particle Emulsifiers)</b> 	<ul style="list-style-type: none"> <li>- Bentonite (<i>hydrated aluminum silicate</i>)</li> <li>- Veegum (<i>magnesium aluminum silicate</i>)</li> <li>- Colloidal silica</li> <li>- Aluminum hydroxide</li> </ul>	<ul style="list-style-type: none"> <li>- Adsorb at oil-water interface forming thick, impenetrable film</li> <li>- Stabilize droplets mechanically</li> <li>- May increase viscosity of aqueous phase</li> </ul>	<ul style="list-style-type: none"> <li>- Magnesium stearate</li> <li>- Kaolin</li> </ul>
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It also explains different **methods to determine the type of emulsion**, summarized in **Table**:

Test	Observation
<b>Dilution test</b>	Emulsion dilutes only with its external phase. Useful for liquid emulsions only.
<b>Dye test</b>	Water-soluble dye will dissolve in the aqueous phase whereas oil-soluble dye will dissolve in the oil phase. For example: Amaranth (o/w Emulsion), Scarlet/Sudan (w/o Emulsion). Microscopic observation is helpful.
<b>CoCl<sub>2</sub> filter paper test</b>	Cobalt chloride paper (blue) turns pink with <b>o/w</b> emulsions. May fail if emulsion is unstable or breaks in the presence of electrolytes.
<b>Fluorescence test</b>	Under UV light, <b>o/w</b> emulsions show a dot pattern, while <b>w/o</b> emulsions fluoresce throughout. Not always applicable.
<b>Conductivity test</b>	When current is passed through an emulsion connected to a voltage bulb, the bulb glows if it is an oil-in-water (o/w) emulsion, as water is a good conductor of electricity. Conversely, the bulb does not glow if it is a water-in-oil (w/o) emulsion, because oil is a non-conductor of electricity. i.e. <b>o/w = current flow</b> <b>w/o = current do not flow</b> o/w = current not flow (when purified water instead of potable water is taken)

 <p style="text-align: center; color: red;"><b>Dilution test</b></p>	 <p style="text-align: center; color: red;"><b>Dye test</b></p>	 <p style="text-align: center; color: red;"><b>Fluorescence test</b></p> <p style="font-size: small;">Oils give fluorescence under UV light, while water does not. Therefore, O/W emulsion shows a spotty pattern while W/O emulsion fluoresces.</p>
 <p style="text-align: center; color: red;"><b>Conductivity test</b></p>		 <p style="text-align: center; color: red;"><b>CoCl<sub>2</sub> filter paper test</b></p>

### Gibbs Free Energy in an Emulsion

- **Gibbs free energy (G)** determines the stability of emulsions and suspensions.
- Emulsions contain **two insoluble phases** where internal phase droplets can undergo:
  - **Creaming** (reversible separation)
  - **Cracking** (irreversible merging of droplets to reduce G)

### Gibbs Free Energy Equation: $G = A\Delta\gamma$

Where:

- **G** = Gibbs free energy
- **A** = Total surface area of dispersed particles
- **$\gamma$**  = Interfacial tension (repulsion between phases)

### Key Principles

- **Large G** → **Unstable system** → Causes droplets to merge and reduce surface area (A).
- To create a **stable emulsion**, we need:
  - **Large surface area (A)** for uniform dosing.
  - **Small interfacial tension ( $\gamma$ )** to lower free energy (G).

### Factors Affecting Stability

- **High  $\gamma$  and High G** → Leads to aggregation of droplets (instability).
- **Reducing  $\gamma$  (using emulsifiers/surfactants)** → Lowers G, preventing droplet merging and ensuring stability.
- **Stable emulsions and suspensions** require **large A with low G** for uniform and consistent dosing.

## FORMULATION COMPONENTS

### I. Lipid Phase in Emulsions

- The **oil portion** of an emulsion, which can be natural or synthetic.
- **Phase Ratio:**
  - Depends on **drug solubility** and required **dosage form consistency**.
  - **Low internal phase** → More **fluid emulsions**.
  - **High internal phase** → **Thicker emulsions**, requiring **more emulsifier**.

### II. Emulsifying Agents: Three major classes:

1. **Surfactants (Surface Active Agents)** → Primary emulsifiers
2. **Hydrophilic Colloids** → Used as auxiliary emulsifiers
3. **Finely Divided Solids** → Act as stabilizers

### 1. Surfactants (Surface Active Agents)

- Molecules with **hydrophilic** (water-loving) and **hydrophobic** (oil-loving) regions.
- **Function:**
  - Reduce **interfacial tension**, making emulsification easier.
  - Form **monomolecular layers** at the oil-water interface.
- **Classification Based on Charge:**

### 1. Anionic Surfactants (Negatively Charged)

- **Example: Sodium Lauryl Sulfate (SLS)** (Used for o/w emulsions).
- **Alkali Metal Soaps:**
  - **Sodium oleate** ( $\text{Na}^+$  form) → o/w emulsions.
  - **Calcium oleate** ( $\text{Ca}^{2+}$  form) → w/o emulsions (low water solubility).
- **Triethanolamine Stearate** → Produces o/w emulsions (e.g., vanishing cream).
- **pH Sensitivity:** Effectiveness varies with pH and electrolytes.

### 2. Cationic Surfactants (Positively Charged)

- **Examples: Quaternary Ammonium Compounds, Pyridinium Salts.**
- **Uses:**
  - Less common in emulsions due to **high cost**.
  - **Antimicrobial properties** → Used in **preservatives and sterilizers**.

### 3. Non-Ionic Surfactants (Neutral Charge)

- **Examples:**
  - **Spans (Sorbitan Esters)** → w/o emulsions (Water-insoluble).
  - **Tweens (Polysorbates)** → o/w emulsions (Water-soluble).
- **Advantages:**
  - **Low toxicity** → Suitable for oral and parenteral formulations.
  - **Stable in varying pH and electrolytes.**
  - **HLB balancing:** Often combined (Span + Tween) for optimal emulsion stability.

### 4. Ampholytic (Zwitterionic) Surfactants

- **Contain both positive and negative charges** depending on pH.
- **Example: Lecithin** (Used in parenteral emulsions).

#### Hydrophilic-Lipophilic Balance (HLB):

- Emulsifiers are selected based on their **hydrophilic (water-attracting)** and **lipophilic (oil-attracting)** nature.
- HLB values help classify surfactants based on their **affinity for oil or water**, making emulsifier selection easier.

#### HLB Calculation Methods

1. **For polyhydric alcohol fatty acid esters:** 
$$\text{HLB} = 20 \left[ 1 - \frac{S}{A} \right]$$

Where,

- **S** = Saponification number of the ester
- **A** = Acid number of the fatty acid

2. **For emulsifiers without saponification numbers (e.g., beeswax, lanolin derivatives):**

$$\text{HLB} = \frac{E + P}{5}$$



Where,

- **E** = Weight percent of oxyethylene chains
- **P** = Weight percent of polyhydric alcohol groups

3. **For emulsifiers with polyoxyethylene chains:**  $HLB = \frac{E}{5}$

where, **E** is the weight percent of oxyethylene groups.

### Application of Surfactants Based on HLB Value

HLB Value	Application
1–3	Antifoaming agents
3–6	w/o (water-in-oil) emulsifiers
7–9	Wetting agents
8–16	o/w (oil-in-water) emulsifiers
13–15	Detergents
15–18	Solubilizing agents

### Phase Inversion Temperature (PIT)

- At **PIT**, the surfactant **shifts between oil and water phases** due to temperature changes, affecting stability and particle size.
- **Key points about PIT:**
  - **Maximum particle size reduction** occurs near PIT.
  - Surfactants that are **water-soluble** at room temperature may become **oil-soluble** near PIT.
  - During cooling, emulsifiers **relocate** to different phases, affecting **emulsion stability**.
  - If the temperature **exceeds PIT during emulsification**, a stable emulsion is formed.

## 2. Hydrophilic Colloids

- These are **water-sensitive polymers** that act as:
  - **Primary emulsifiers**
  - **Emulsion stabilizers**
  - **Thickening agents**

### Types of Hydrophilic Colloids

#### 1. Natural and Synthetic Clays

- **Smectite clays (e.g., Bentonite, Montmorillonite)**
  - Swell in water and increase viscosity.
  - Require **pH ≥ 6** to thicken solutions.
- **Amphibole clays (e.g., Attapulgit)**
  - Thicken by **particle interaction** rather than swelling.
  - Used in **makeup formulations and suspensions**.



## 2. Natural Gums and Synthetic Polymers

- **Natural gums:** Mostly **polysaccharides** (e.g., gum arabic, acacia, tragacanth).
- **Synthetic hydrocolloids:** Include **cellulose derivatives** (e.g., carboxymethyl cellulose, hydroxypropyl methylcellulose).
- **Carboxyl vinyl polymers:** Provide **yield value** (ability to resist flow), improving emulsion **thickness and stability**.

## 3. Finely Divided Solids:

- **Finely divided solid particles** can act as emulsifiers, particularly when used with **surfactants** or **macromolecules** that increase viscosity.
- These solids help **stabilize emulsions** by forming a **physical barrier** around the dispersed droplets, preventing coalescence.

### Types of Finely Divided Solids:

#### 1. Polar Inorganic Solids

- These are **solid particles with high water-wetting ability**.
- They promote **oil-in-water (o/w) emulsions**, where water is the **continuous phase**.
- Examples:
  - **Heavy metal hydroxides** (e.g., aluminum hydroxide, magnesium hydroxide)
  - **Certain non-swelling clays** (e.g., kaolin, bentonite)
  - **Pigments** (e.g., titanium dioxide, zinc oxide)

#### 2. Non-Polar Solids

- These are **solid particles that are more oil-wettable**.
- They promote **water-in-oil (w/o) emulsions**, where oil is the **continuous phase**.
- Examples:
  - **Carbon** (e.g., activated charcoal)
  - **Glyceryl tristearate** (a fat-based compound)

## III. Antimicrobial Preservatives in Emulsions

- Emulsions contain **water, lipids, carbohydrates, proteins, sterols, and phosphatides**, which can **support microbial growth**. To prevent contamination, **antimicrobial preservatives** are added to emulsions.

### Types of Antimicrobial Preservatives

Different types of preservatives are used in emulsions. The following table lists **common preservative groups and examples**:

Type	Example
<b>Acids and acids derivatives</b>	Benzoic acid and salts, Propionic acid and salts, Dehydroacetic acid
<b>Alcohols</b>	Chlorobutanol, Phenoxy-2-ethanol
<b>Aldehydes</b>	Formaldehyde, Glutaraldehyde
<b>Formaldehyde donors</b>	Hexamethylenetetramine, Mono (and di-) methylol dimethyl hydantoin
<b>Phenolics</b>	Phenol, Cresol, $\alpha$ -Chlorometaxyleneol
<b>Quaternaries</b>	Methyl p-hydroxybenzoate, Propyl p-hydroxybenzoate, Butyl p-hydroxybenzoate
	Chlorhexidine salt, Benzalkonium chloride, Cetyl trimethyl ammonium bromide
<b>Mercurials</b>	Phenylmercuric acetate, Sodium ethylmercurithiosalicylate

#### IV. Antioxidants in Emulsions

- Many organic compounds are prone to **autoxidation** when exposed to air, and emulsified lipids are particularly vulnerable. Several drugs incorporated into emulsions are also susceptible to oxidation, leading to decomposition.

##### Effects of Autoxidation

- Unsaturated oils (e.g., vegetable oils) undergo rancidity, resulting in **unpleasant odour, taste, and appearance**.
- Mineral oils and saturated hydrocarbons are **less prone** to oxidation.
- Autoxidation is a free-radical chain reaction**, and it can be controlled by:
  - Removing oxygen.
  - Using **free radical chain breakers**.
  - Using **reducing agents**.

##### Selection and Use of Antioxidants

- The choice of an **antioxidant** depends on **safety, acceptability, and effectiveness**.
- Common concentration range:** 0.001 – 0.1% (w/v).
- Examples of widely used antioxidants in pharmaceuticals and cosmetics:**
  - Butylated hydroxyanisole (**BHA**)
  - Butylated hydroxytoluene (**BHT**)
  - L-Tocopherol
  - Alkyl gallates

Antioxidant	Remarks
Gallic acid	Bitter taste
Propyl gallate	Bitter taste
Ascorbic acid	Commonly used in pharmaceuticals
Ascorbyl palmitate	Suitable for lipophilic formulations
Sulfites	Reducing agents
L-Tocopherol	Well-suited for <b>edible/oral</b> formulations
Butylated hydroxytoluene ( <b>BHT</b> )	Strong antioxidant, <b>pronounced odour</b>
Butylated hydroxyanisole ( <b>BHA</b> )	Strong antioxidant, <b>pronounced odour</b>
4-Hydroxymethyl-2,6-di-tert-butylphenol	Effective antioxidant

## EMULSION FORMATION

- Emulsions are usually made using the **dispersion method**, which involves breaking up the internal phase into small droplets and stabilizing them in the external phase.
- The process must be quick enough to prevent the internal phase from merging back (coalescence).
- While droplet breakup happens quickly through physical force, stabilization depends on time and temperature.

### Methods of Emulsion Formation

#### ◆ Small-Scale Production (Manual) – Pestle & Mortar

Method	Sequence of Mixing	Use
<b>Dry Gum / Continental</b>	Oil + Gum → then Water	Common for <b>fixed oils</b>
<b>Wet Gum / English</b>	Water + Gum → then Oil	Forms mucilage first
<b>Bottle / Forbes Method</b>	Oil + Gum → shake, then add Water	Ideal for <b>volatile / low-viscosity oils</b>

#### ◆ Large-Scale Production (Mechanical)

Equipment Used	Function
<b>Homogenizers</b>	Reduces droplet size for stable emulsions
<b>Electric Mixers</b>	Uniform mixing of phases
<b>Colloidal Mills</b>	High shear dispersion of droplets
<b>Ultrasonic Devices</b>	Uses sound waves to break droplets

## Proportions for Emulsion Preparation

### Oil : Water : Gum Ratios (Continental / Dry Gum Method)

Type of Oil/Substance	Example(s)	Ratio (O:W:G)
<b>Fixed Oils</b>	Almond, Arachis, Castor, Cod Liver Oil	<b>4 : 2 : 1</b>
<b>Mineral Oils</b>	Liquid Paraffin	<b>3 : 2 : 1</b>
<b>Volatile Oils</b>	Turpentine, Cinnamon, Peppermint	<b>2 : 2 : 1</b>
<b>Oleoresins</b>	Male Fern Extract	<b>1 : 2 : 1</b>

### Special Emulsion Type: Multiple Emulsions (w/o/w)

- Made in **two steps**:
- w/o emulsion** is formed using a **low HLB emulsifier**.
- This w/o emulsion is mixed into **water** containing a **high HLB emulsifier (HLB 12-14)**.

### STABILITY OF EMULSIONS

- The **stability** of an emulsion depends on its **physical properties** and how they change over time. An emulsion may become unstable due to temperature changes, time, or external forces.
- When an emulsion becomes unstable, the following problems can occur:

Type	Description	Reversibility	Phase Separation?
<b>Creaming</b>	Droplets <b>rise</b> (↑) or <b>settle</b> (↓) due to density difference; no merging	✓ Reversible	✗ No
<b>Flocculation</b>	Droplets form <b>loose clusters</b> without merging	✓ Reversible	✗ No
<b>Coalescence</b>	Droplets <b>merge into larger ones</b> → leads to breaking	✗ Irreversible	✓ Yes

### Flocculation

- Flocculation** happens when small droplets of the dispersed phase come together to form clusters.
- It **does not** lead to droplet merging (coalescence) as long as the **interfacial film** remains intact.
- Causes of Flocculation:**
  - Low emulsifier concentration** – If there is not enough emulsifier, droplets come together easily.
  - Electrolytes (Salts)** – Some salts reduce droplet repulsion, promoting flocculation.
  - High internal phase volume** – More dispersed phase means droplets are packed closely, increasing flocculation.
- Flocculation affects viscosity:**
  - More flocculation increases viscosity because droplets cannot move freely.
  - Stirring reduces flocculation, lowering viscosity (shear thinning).

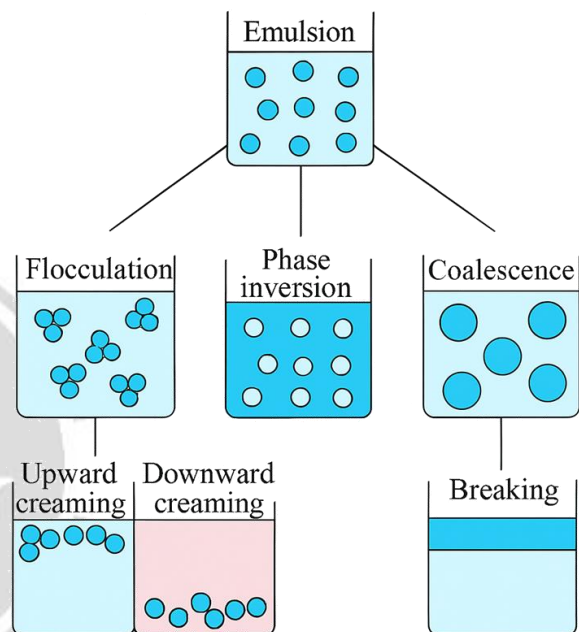
### Creaming

- Creaming** happens when dispersed droplets **rise or settle** due to gravity.
- If droplets remain separate, **shaking can redisperse them**.

- The **Stokes equation** explains creaming, but real emulsions have variations due to different droplet sizes and interactions.
- **Factors affecting creaming:**
  1. **Droplet size** – Larger droplets cream faster.
  2. **Density difference** – If the densities of the two phases are similar, creaming is reduced.
  3. **Viscosity** – Higher viscosity of the continuous phase slows down creaming, improving stability.

### Coalescence (Breaking of the Emulsion)

- **Coalescence occurs when emulsion droplets merge to form larger droplets.**
- If this continues, the emulsion **completely separates into two layers** (breaks).
- **How to prevent coalescence:**
  1. **Use a strong interfacial barrier** – Thick layers of emulsifier or solid particles prevent droplet merging.
  2. **Nonionic surfactants and polymers** – These stabilize emulsions by forming strong protective films around droplets.
  3. **Natural gums and proteins** – These can act as emulsifiers to prevent coalescence at low concentrations and even work as primary emulsifiers at higher levels.






**INSTABILITY PROBLEMS OF EMULSIONS**

### Assessment of Emulsion Shelf-Life

- To evaluate **physical, chemical, and functional stability** of emulsions over time under various stress conditions.
- Used to **predict shelf-life** and ensure **product quality** during storage.

### Factors Affecting Shelf-Life

#### Packaging & Container Interactions


-  **Leaching:** Container extracts plasticizers or other components into emulsion
-  **Absorption:** Drug/emulsifier loss by absorption into container wall
-  **Loss of volatiles:** Water or oil may evaporate via closures → destabilization

### Stress Testing Conditions

#### A. Aging & Temperature Cycling

- Standard test: **Cycle between 4°C ↔ 45°C**
- Detects:
  - **Creaming**
  - **Coalescence**
  - **Viscosity shifts**
- **Freezing danger:** Ice crystal formation + emulsifier insolubility → emulsion breakdown

## B. Centrifugation

- Mimics **long-term gravitational separation**
- Standard: **3,750 rpm × 5 hrs**  $\approx$  1 year of storage
-  **>25,000 rpm**: Causes **artificial separation**

## C. Agitation

- Mild shaking: simulates transport & handling
- Excessive agitation: may induce **coalescence**  
(e.g., butter from cream under heavy churning)

## Chemical Stability Considerations


Compound	Stability Risk
PEG-based emulsifiers	Oxidation → foul odor & degradation products
Non-ionic esters	Hydrolysis in aqueous environment → ↓ emulsifying power

## Physical Stability Parameters

### 1. Phase Separation

- Distinguish:
  - **Creaming** = Reversible
  - **Coalescence** = Irreversible
- Evaluate by sampling **top, middle, bottom** layers

### 2. Viscosity Changes

- **O/W Emulsions**: ↑ Viscosity due to **flocculation**
- **W/O Emulsions**: ↓ Viscosity initially
-  **Non-linear changes** suggest **instability**

### 3. Electrophoretic Properties

- **Zeta Potential**: Indicates surface charge stability  
(↓ zeta potential = ↑ flocculation risk)
- **Conductivity Changes**: Signal **aggregation** or **phase leakage**

### 4. Particle Size Monitoring

- ↑ in droplet size = early sign of **coalescence**
- Use **light scattering or microscopy** for routine checks.