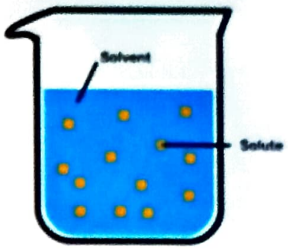
UNIT- III COARSE DISPERSION

Points to be covered in this topic

- INTRODUCTION
- SUSPENSION
- INTERFACIAL PROPERTIES OF SUSPENDED PARTICLES
- SETTLING IN SUSPENSIONS
- FORMULATION OF FLOCCULATED AND DEFLOCCULATED SUSPENSIONS
- EMULSIONS AND THEORIES OF EMULSIFICATION
- STABILITY OF EMULSIFICATION
- PRESERVATION OF EMULSIONS
- RHEOLOGICAL PROPERTIES OF EMULSIONS
- PREPARATION OF EMULSION
- EMULSION FORMULATION BY HLB METHOD

INTRODUCTION



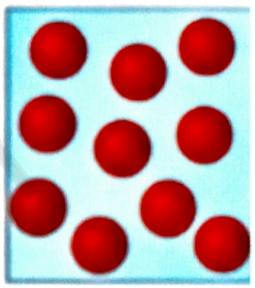
✓ **Solution**

- A **solution** is a **homogeneous mixture** of one or more solutes dissolved in a solvent.

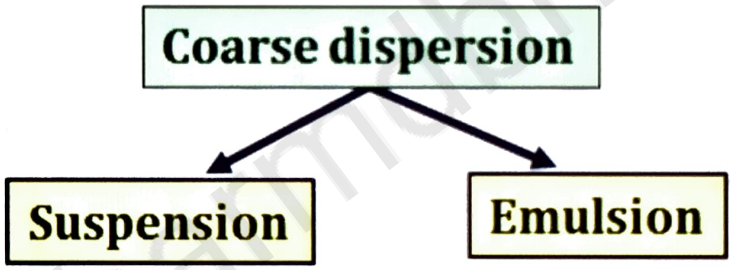
✓ **Dispersion**

- Dispersed phase (solute) **dispersed** into a **dispersion medium** (solvent) also known as continuous system.

➢ COARSE DISPERSION

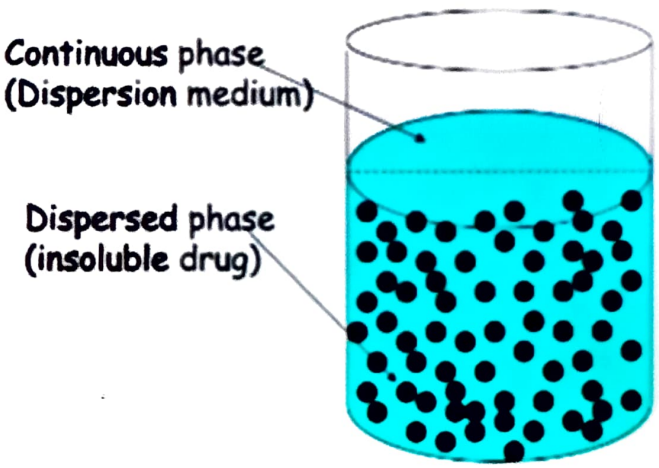


- **Coarse dispersion** is a **heterogenous dispersion** system in which the size of **dispersed particles** ranges from **1µm to 100 µm.**
- Particles more size more than **1000 nanometer** so it can be **easily visible with eyes.**



SUSPENSION

- A **suspension** is defined as a **heterogeneous mixture** in which the **solid particles** are spread throughout the liquid without **dissolving in it.**



➢ PROPERTIES OF SUSPENSION

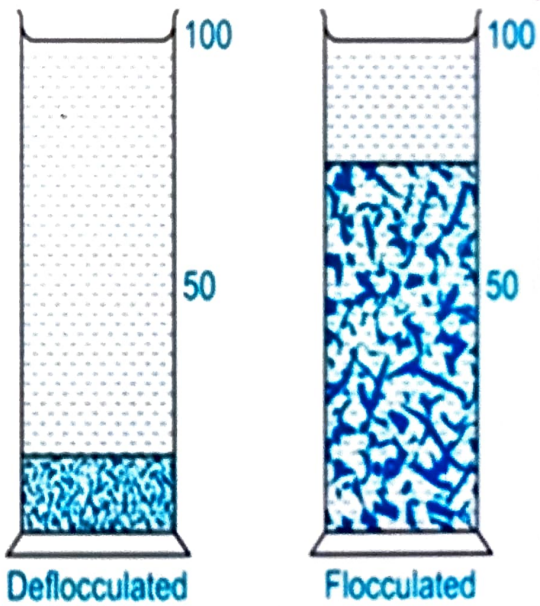
- The **suspended molecules** should not settle rapidly
- The particles which **settle down** should **not deposit** at the bottom as hard cake. They must be **easily re-suspended** by moderate shaking.
- It should be **easy to pour**
- It should be **free from grittiness.**
- The suspension should have **pleasant odour, colour** and **palatability.**
- It should be stable in case of **physical, chemical** and **microbial attack.**
- It should be easily **flow out from syringe needle.**
- The **suspended material** should be stable in the medium.

➢ TYPES OF SUSPENSION

1. **Flocculated suspension**
2. **Deflocculated suspension**

❖ FLOCCULATED SUSPENSION

- **Flocculation** is a process whereby **small particles** in suspension are caused to **aggregate, giving large clusters** (flocs) that are much more easily separated than the **original particles.**



❖ DEFLOCCULATED SUSPENSION

- These are those in which particles of **dispersed phase** remain apart from each other and **remain dispersed** in the **dispersion medium.**

❖ DIFFERENT BETWEEN FLOCCULATED SUSPENSION AND DEFLOCCULATED SUSPENSION

FLOCCULATED SUSPENSION	DEFLOCCULATED SUSPENSION
Particle exist as loose aggregates	Particles exist as a separate entities
Rate of sedimentation is high	Rate of sedimentation is low
Sediment formed rapidly	Sediment formed slowly
Consist of loosely packed particles possessing a scaffolding structure a hard dense cake does not form and the sedimentation can easily be redispersed.	Sediment become very closely packed as the repulsive forces between the particles are overcome a hard cake is formed which is difficult to redispersed.
Elegant preparation is obtained due to the uniform distribution of loosely bonded flocs	Unslightly preparation results due to the formation sedimentation.

INTERFACIAL PROPERTIES OF SUSPENDED PARTICLES

- In suspension the solid particles is uniformly dispersed in liquid medium.
- The interface is formed in between the two phases, which influence the stability of suspension.
- In the formulation of suspension, the solid is reduced to fine particles and disperse them in a continuous medium.
- The system with very fine particles is thermodynamically unstable because of large surface area.
- The large surface area of the particles is associated with a excess of surface free energy.
- Due to this the particles become highly energetic and tend to regroup in such a way as to decrease the total area and reduce the surface free energy.

- The **equation** that describe the relation between the **surface free energy** and the **surface area** can be expressed by
- $\Delta G = \gamma \Delta A$

✓ **Where**

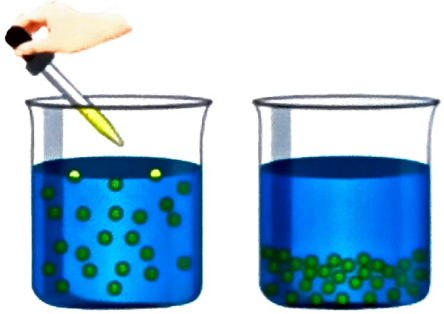
- ΔG = Surface free energy
- γ = Interfacial tension between solid particles and liquid medium
- ΔA = Total surface area

SETTLING IN SUSPENSIONS

- Also known as **Rate of sedimentation**, because Settling of suspension is depend on **sedimentation rate.**
- The settling down of **suspended particles** of suspension at bottom is known as **settling of suspension** or also sedimentation.

Rate of sedimentation ↑ = Rate of settling ↑

- The more **rate of sedimentation**, faster the particles **settle down** and **faster** the formation of **cake.**
- The **rate of settling** of suspended particles is explained by stokes law.



$$v = \frac{d^2 (\rho_1 - \rho_2)}{18\eta}$$

✓ **Where**

- V = rate of sedimentation / rate of settling
- d^2 = diameter of particle
- ρ_1 = density od suspended particle (dispersed phase)
- ρ_2 = density of solvent (dispersion medium)
- g = gravity
- η = viscosity of dispersion medium

Rate of settling ↑ = stability ↓

❖ TO MAKE SUSPENSION STABLE :-

- **Increase viscosity** to dispersion medium by using some agents such as **methylcellulose, natural gums, acacia, trgacanth** etc.
- **Stokes law** is valid for those suspension which does not contain more than **2% solid.**

FORMULATION OF FLOCCULATED AND DEFLOCCULATED SUSPENSIONS

- Three approaches are **commonly involved** in the formulation of **flocculated or deflocculated** suspension.
  1. Use of **structured vehicle**
  2. **Wetting of particles**
  3. Use of **controlled flocculation**
  4. **Flocculation** in structured vehicle

1. USE OF STRUCTURED VEHICLE

- They are the **aqueous solution** of **natural or synthetic gum.**
- Example: methyl cellulose, sodium carboxy methyl cellulose, acacia, gelatin and tragacanth.
- They are also called as **suspending or thickening agent.**

2. WETTING OF PARTICLES

- The dispersion of **insoluble powder** in a vehicle is major step during the **formulation of suspension.**
- Powders those are **not easily wetted** by water such as **sulfur, charcoal and magnesium stearate** are called as hydrophobic while the powders those are readily wetted by water are called **hydrophilic**. e.g. zinc oxide, talc, magnesium carbonate etc.

3. USE OF CONTROLLED FLOCCULATION

- **Controlled flocculation** of particles is obtained by **adding flocculating** agents such as **electrolytes, surfactants** and **polymers.**
- The flocs are advantageous because they do not form **hard cake** and **easily redisperse.**

✓ **Electrolytes**

- They act as **flocculating agents.**
- They lessen the **electric barrier** between the particles and form a bridge between **adjacent particles.**

✓ **Surfactants**

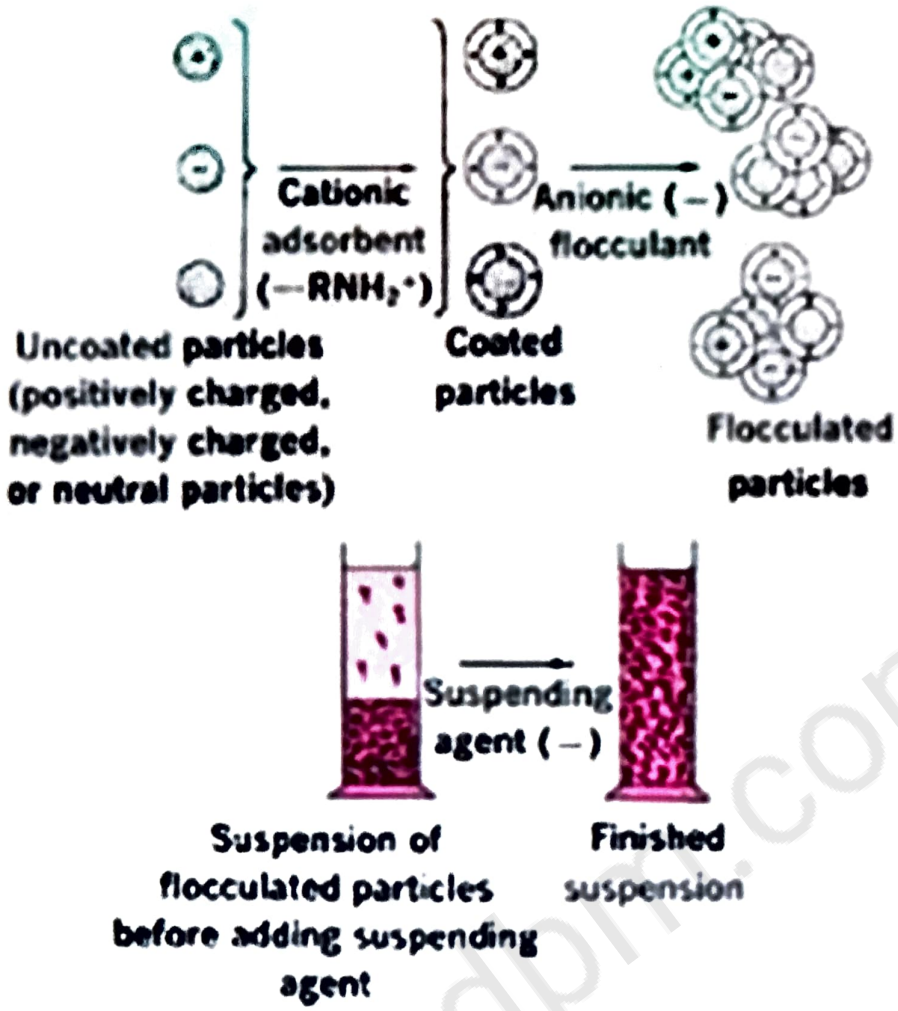
- They are also used for **flocculation of suspended particles.**
- They also act as **wetting agents** to achieve dispersion.
- Both **ionic surfactants (sodium lauryl sulfate)** and non ionic surfactants (Tweens) are used.

✓ **Polymers**

- They are **high molecular** weight compounds.
- These agents also act as **flocculating agents.**
- In polymers, part of the **chain is adsorbed** on the particle surface while remaining parts extruding into the **dispersion medium.**
- This lead to **formation of flocs.**

4. FLOCCULATION IN STRUCTURED VEHICLE

- The **controlled flocculation** approach is essential in the formulation of **pharmaceutical suspension.**
- But the product are not so elegant if **sedimentation volume** is not close to or equal to 1.
- Therefore a **suspending agent** is added to prevent the sedimentation or settling of the flocs.
- The **suspending agents** such as **carboxymethylcellulose (CMC),** Carbopol 934, **Veegum, tragacanth** or bentonite are used.



➢ PREPARATION OF THE SUSPENSION

Grinding of insoluble material with vehicle containing wetting agent to get smooth paste

↓

Dissolve soluble ingredients in some portion of vehicle and add into above step to get slurry

↓

Transfer the slurry to graduated cylinder

↓

Rinse mortar with some part of vehicle

↓

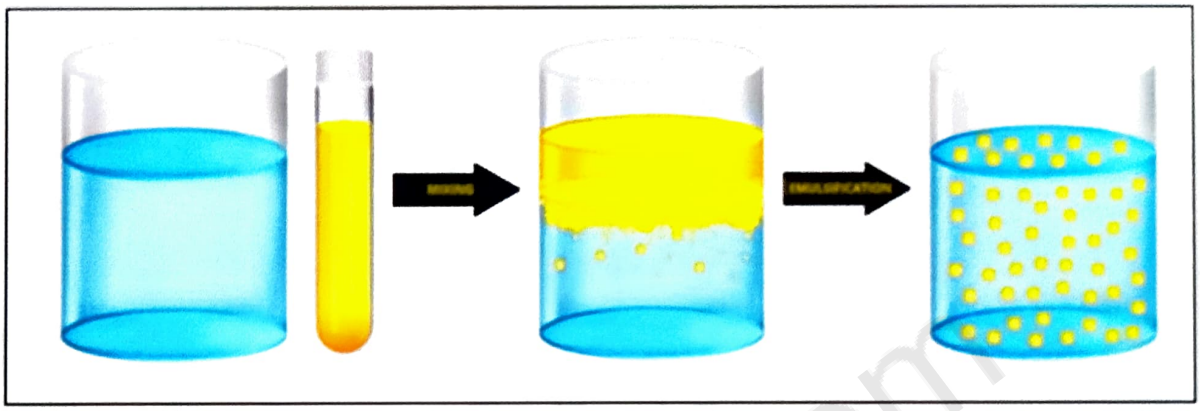
Add suspending agent of flocculating agent if any by mixing into vehicle

↓

Finally adjust the volume by vehicle

EMULSIONS

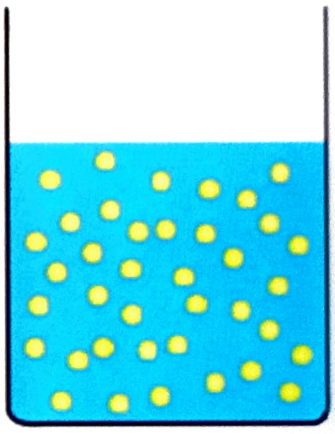
- It is Liquid a where **biphasic system** of **two immiscible** one Liquid (dispersed phase) is another Liquid (dispersion medium).
- **Dispersed** into with the help of any **emulsifying agent**. eg. Vanishing cream



Water + oil | Immiscible liquid | Emulsion

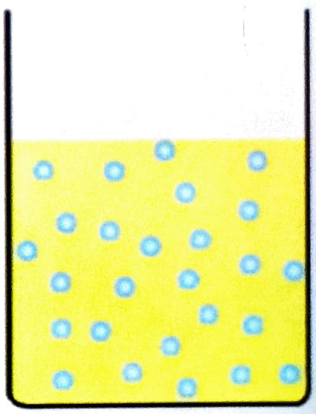
➢ CLASSIFICATION OF EMULSION (TYPES)

- It can be classified into four types
  1. **Oil-in-water (O/W) emulsion**
  2. **Water-in-oil (W/O) emulsion**
  3. **Multiple emulsion**
  4. **Microemulsion**



1. OIL-IN-WATER EMULSION

- This are **those emulsion** in which dispersed phase is **oil** and **continuous phase** is water.
- Example :- **milk, lotions, liniments** etc
- **Non-greasy nature** (easily remove from body).

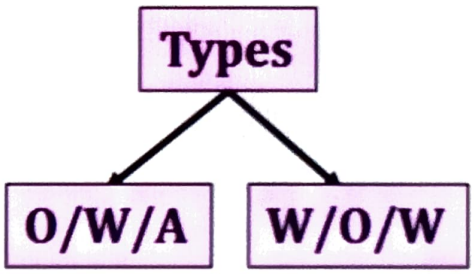


2. WATER-IN-OIL EMULSION

- This are those emulsion in which dispersed phase is **water and continuous phase is oil.**
- Examples – **butter and cold cream** etc.
- **Greasy in nature** (oily nature, not easily removed from body)

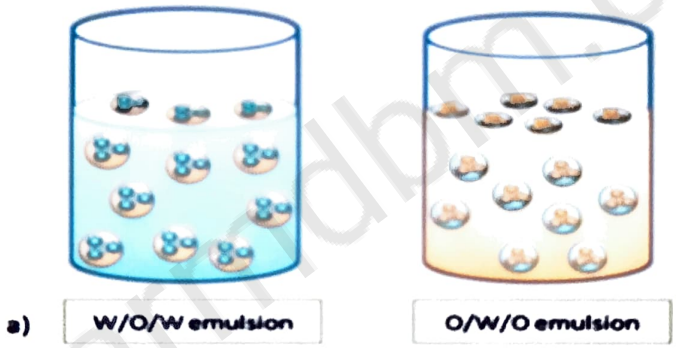
3. MULTIPLE EMULSION

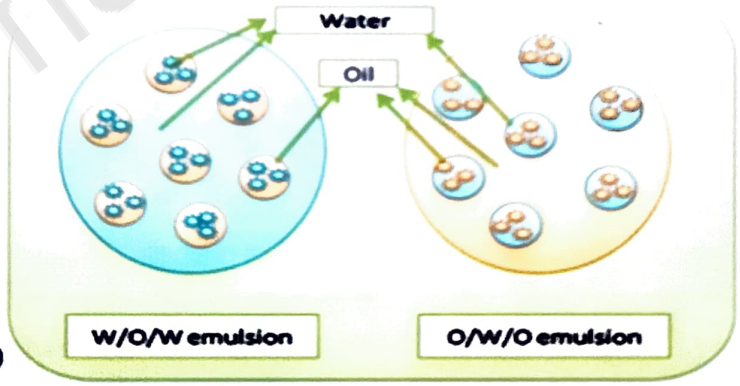
- Those **emulsion** which are made up of more than **two phase.**
- In which the **droplets** of **one liquid** are **dispersed in droplet** of **second liquid**, which is further dispersed in dispersion medium.



Oil-in-water-in-oil
In which o/w emulsion dispersed in another oil phase

Water-in-oil-in water
In which w/o emulsion dispersed in another water phase





4. MICRO-EMULSION

- Those emulsion in which **particle size of dispersed** phase is less than **14micron.**
- It is **clear, transparent** and **thermodynamically** stable as compared to **normal emulsion.**

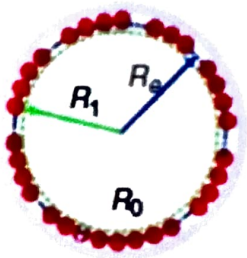
THEORIES OF EMULSIFICATION

- Those theories which make and stay emulsion stable
  1. **Monomolecular theory**
  2. **Multi-molecular theory**
  3. **Solid particle theory**

1. MONOMOLECULAR THEORY

- During **preparation of emulsion**, the **oil/water droplet** get dispersed in **continuous phase**, particle get atomized (reduce particle size).
- Due to **small particles** size surface area increase which further increases the **surface free energy**, therefore system becomes unstable.
- To **resolve this problem** or to make system stable we **add surfactants or emulsifying agents** which reduce the **interfacial tension** or **surface free energy** and make emulsion stable.

❖ MECHANISM

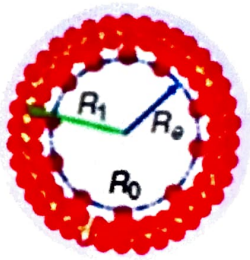


- **Surfactant contain** polar and **non-polar part.**
- **Polar oriented** toward water and non polar oriented toward oil and form a stable **monomolecular film** on the surface of dispersed droplet.

2. MULTI-MOLECULAR ADSORPTION THEORY

- **Mono-molecular** and **multi-molecular theory** both used to stop flocculation, also prevent the **breaking of emulsion.**

❖ MECHANISM



- In this **emulsifying agents** small – small particles join together and cover the **dispersed particles** and make **multi-molecular film.**

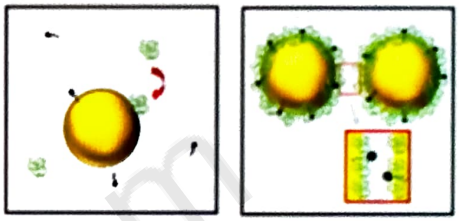
3. SOLID PARTICLE ADSORPTION THEORY

- In this we **add solid emulsifying agent** in emulsion which increase the **viscosity of emulsion.**
- It also **reduce coalescense** of dispersed particles.

4. FORMATION OF ELECTRICAL DOUBLE LAYER

- In **emulsion oil droplets** contain either negative or positive charge.
- Due to **present of charge** they develop **electrical double layer**
- Due to this **oil droplets produce** repulsion force into each other and they **remain suspended.**
- They prevent **coalescence** and **breaking of emulsion.**

STABILITY OF EMULSIFICATION

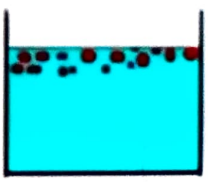


- A **stable emulsion** is one in which the **globules** (dispersed phase) retain their size and as well as remain **uniformly distributed** throughout the continuous phase.
- Some instability occur during storage and formulation of emulsion
  1. **Creaming**
  2. **Coalescence**
  3. **Breaking**
  4. **Flocculation**
  5. **Phase inversion**
  6. **Physical and chemical properties**

1. CREAMING

- It is **reversible phenomenon .**
- In which **droplets of disposed phase** come together or deposite at the surface of the emulsion.

❖ O/W



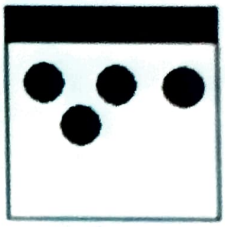
- In this **oil** have **low density** so they come together at the **surface of emulsion.**
- **Upward creaming**

❖ W/O

- In this **density of water** (dispersed phase) is more than **continuous phase.**
- So particles come together at the **bottom of emulsion.**
- **Downward creaming**

2. COALESCENCE

- In **emulsion**, **oily particles** (disperses phase) because of **sticky nature** attract each other and they aggregate to form **bug particles.**



Coalescence

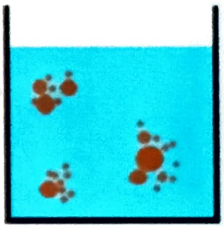
3. BREAKING (CRACKING)

- Due to **improper mixing** of **oil and water** in emulsion.
- Emulsion get **separated into two layer** i.e. oil and water.
- It is also occurred due to **improper ratio** of oil and water.

Breaking

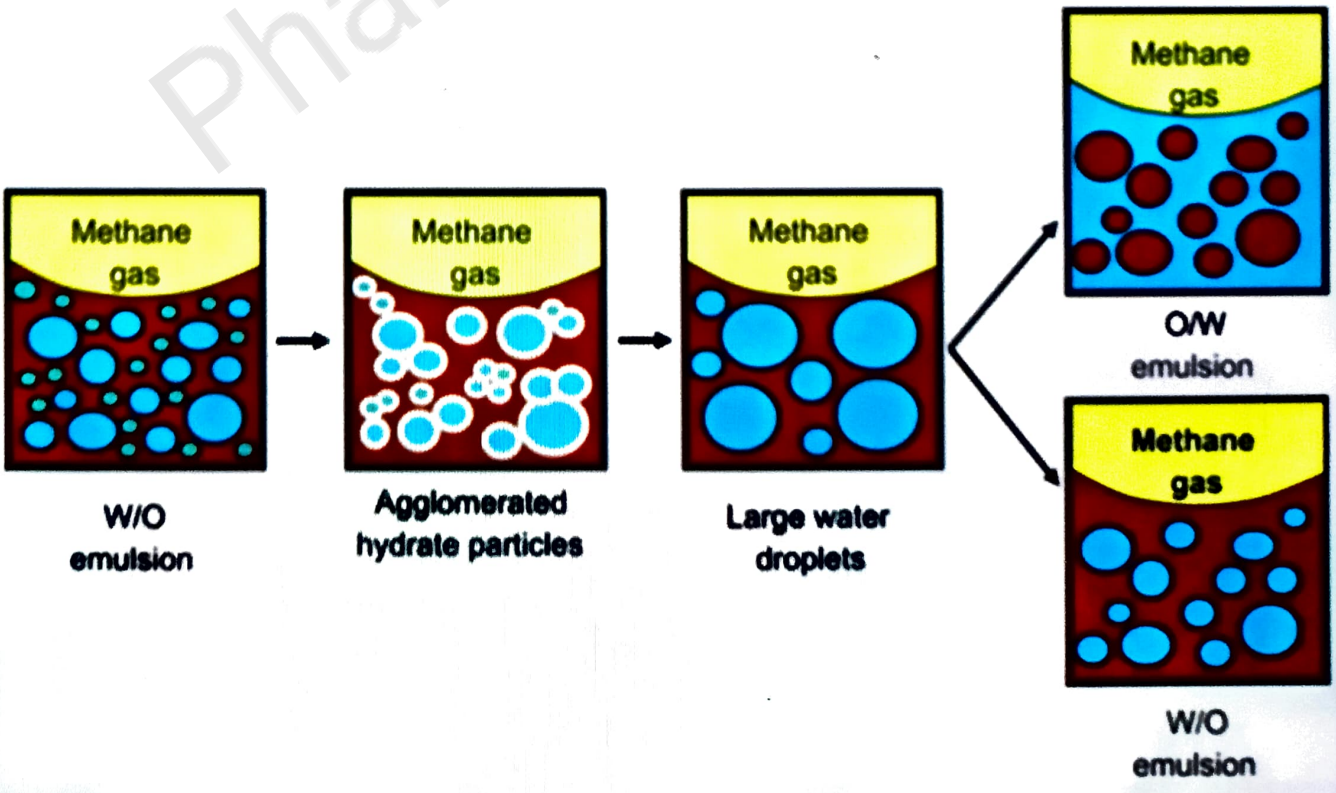
4. FLOCCULATION

- In this due to **increased surface free energy** particles get aggregated to form **floccules to decrease** surface area.



5. PHASE INVERSION

- In this, the **phase of emulsion** get inverted i.e. **O/W → W/O / W/O → O/W.**
- It happened **due to mixing problem** or by choosing wrong dispersed phase **during formulation.**



5. PHYSICAL AND CHEMICAL PROPERTY CHANGE

- In **prepare an emulsion**, we use **emulsifying agent** to mix and make stable emulsion.
- Sometime addition of these agents causes changes in properties like **color , pH, odour, taste etc.**

PRESERVATION OF EMULSIONS

➢ PRESERVATION FROM MICROORGANISM

- **Microorganism** may arrise in emulsion due to **carbon content** of emulsion or due to present of **high water content.**
- For this, we **add preservative** like **methyl paraben, propyl paraben, benzoic acid** etc which inhibit the growth of bacteria.
- Preservative should be
  - ✓ **Non – irritant** and **non – toxic.**
  - ✓ **Tasteless, colorless and odourless.**
  - ✓ **Should be stable.**

➢ PRESERVATION FROM OXIDATION

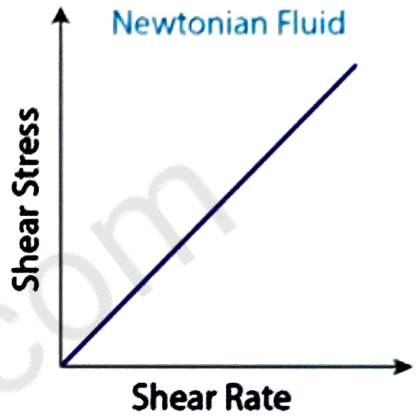
- **Oxygen prevent** in **atmosphere cause oxidative** cause such as **rancidity and spoilage** for this, we use some antioxidant which can prevent the changes occurs due to **atmospheric oxygen.**
- Antioxidant should be
  - ✓ **Non- toxic and non-irritant**
  - ✓ Effective at **low concentration**
  - ✓ E.g. **BHT (butylated hydroxyl toluene), ethyl and propyl gallate etc.**

RHEOLOGICAL PROPERTIES OF EMULSIONS

- These **properties of emulsion** are related to the flow of emulsion.

✓ **Application :-**

- **Spreadibility (for skin)**
- **Removal from container (bottle)**
- **Flow of emulsion** through hypodermic needle
- **Proper mixing** (during manufacturing)
- It can be of two types

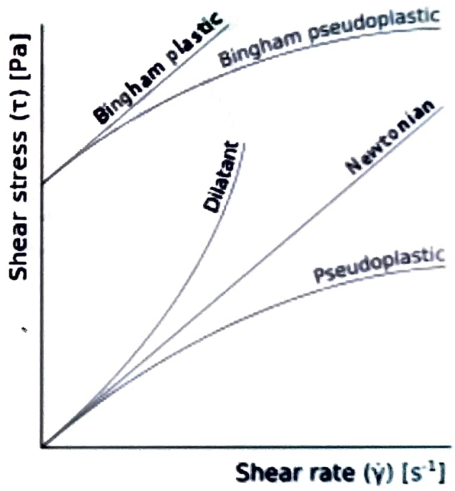


1. Newtonian flow :-

- This type of **flow show** by dilute emulsion.
- **Example – Microemulsion**

2. Non-Newtonian flow

- This type of flow show by **concentrated emulsion**
- Example- **lotions, creams etc**
- **Optimum viscosity** is desirable for **good stability of emulsion.**
- The **increase in the viscosity** of the emulsion reduce the flocculation.



✓ **Rheological property of emulsion can be controlled by :-**

- Concentration of **dispersed phase**
- **Particle size** of dispersed phase
- **Viscosity** of continuous phase
- **Nature and concentration** of emulsifying system.

PREPARATION OF EMULSION

➢ DRY GUM METHOD

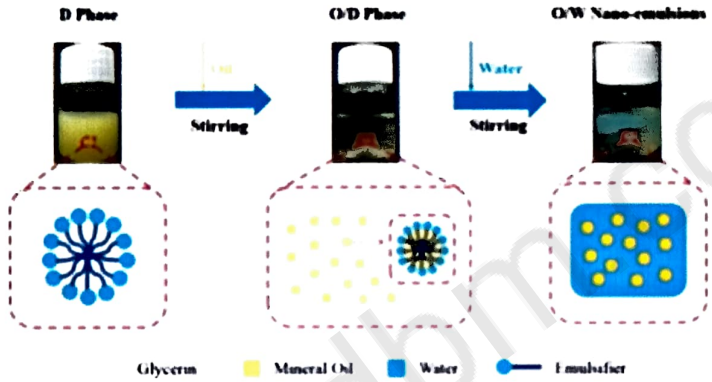
- In this method the **oil is first triturated** with **gum** with a little amount of water to form the **primary emulsion.**
- The **trituration** is continued till a **characteristic 'clicking'** sound is **heard** and a thick **white cream** is formed.
- Once the **primary emulsion** is formed, **the remaining quantity** of water is slowly added to form the **final emulsion.**
- This method consists of
  - ✓ **4:2:1 formula**
  - ✓ **4 parts (volumes) of oil**
  - ✓ **2 parts of water**
  - ✓ **1 part of gum**

➢ WET GUM METHOD

- As the **name implies,** in this method **first gum** and **water** are triturated together to form a mucilage.
- The **required quantity** of oil is then added gradually in **small proportions** with thorough trituration to form the **primary emulsion.**
- Once the **primary emulsion** has been formed remaining quantity of water is added to make the **final emulsion.**
- This method consists of
  - ✓ **4:2:1 formula**
  - ✓ **4 parts (volumes) of oil**
  - ✓ **2 parts of water**
  - ✓ **1 part of gum**

➢ BOTTLE METHOD

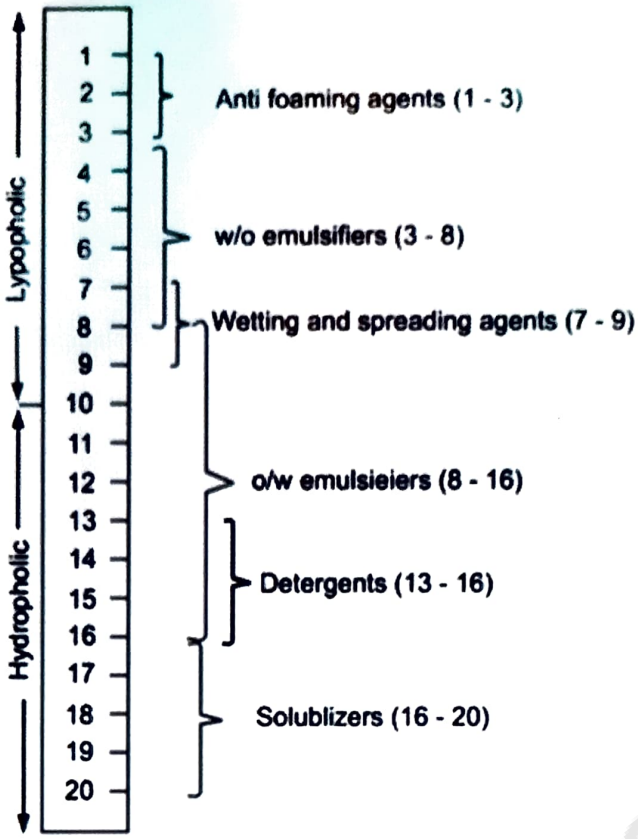
- This method is used to **prepare emulsions** of volatile oils or substance having **very low viscosity.**
- **1 part gum** placed in **dry bottle** then **2 parts of oils** are added, now shake the mixture.
- A **volume of water** (approx. equal to oil) is added in portion then again shake.
- Now dilute it with proper **volume of water.**
- On **large scale** this process is done **inside bottle** with or along with **propeller movement.**



EMULSION FORMULATION BY HLB METHOD

❖ HLB (HYDROPHILIC LIPOPHILIC BALANCE SYSTEM) OF EMULSIFYING AGENTS

- An **HLB number (1-20) represents** the relative proportions of the **lipophilic and hydrophilic parts** of the molecule.
- **High numbers (8-18)** indicate a **hydrophilic molecule**, and produce an **O/W emulsion.**
- **Low numbers (3-6)** indicate a **lipophilic molecule** and produce a w/o emulsion.
- **Oils and waxy materials** have a 'required HLB number' which helps in the selection of appropriate **emulsifying agents** when formulating emulsions.
- **Liquid paraffin**, for example, has a required **HLB value of 4** to obtain a w/o **emulsion and 10.5** for an o/w emulsion.



➢ HLB VALUES OF SELECTED EMULSIFIERS

CHEMICAL DESIGNATION	HLB VALUES
Ethylene glycol distearate	1.5
Sorbitan sesquioleate	3.7
Diethylene glycol monostearate	4.7
Sucrose	7.1
Polyoxyethylene (4) lauryl ether	9.5
Polyoxyethylene (6) lauryl ether	10.3
Polyxyethylene (20) sorbitan tristearate	10.5
Polyxyethylene (9) nonyl phenol	13.0
Sodium oleate	18.0
Polyxyethylene (100) stearate	18.8
Potassium oleate	20.0