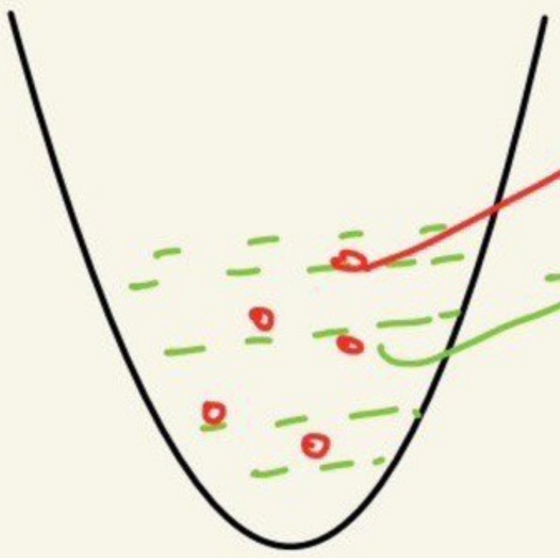
Physical Pharmaceutics Unit-3

UNIT-III **10 Hours**

Coarse dispersion: Suspension, interfacial properties of suspended particles, settling in suspensions, formulation of flocculated and deflocculated suspensions. Emulsions and theories of emulsification, microemulsion and multiple emulsions; Stability of emulsions, preservation of emulsions, rheological properties of emulsions and emulsion formulation by HLB method.

Coarse Dispersion

pharmaceutical suspension is a coarse dispersion in which insoluble solid particles are dispersed in a liquid medium (usually water or water-based vehicle). Generally, the particles have diameters greater than 0.5μm. The concentration of dispersed phase may exceed 20%.



Insoluble (solid particle) → diameter >0.5 µm.

Therapeutically Active Ingredients.

⇓

Dispersed Uniformly in Internal Phase.

Liq. medium

External phase.

Aqous

May be oily or Organic Liq. for Non-Oral Use.

☆ It is Biphasic System.

☆ Heterogenous.

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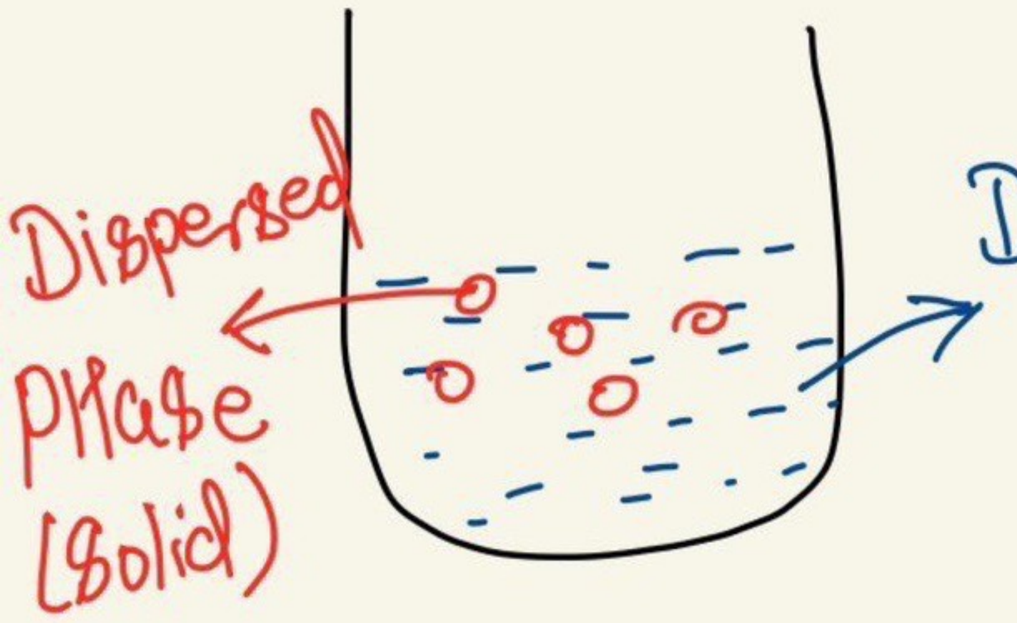
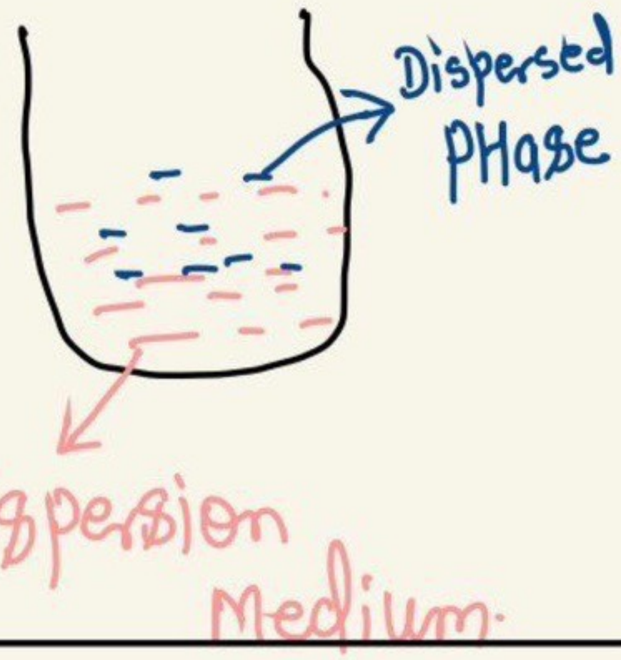
Coarse Dispersion

Suspension

Emulsion
- Oil in water
- H_2O in Oil.

⇒ Liq. in Liq.





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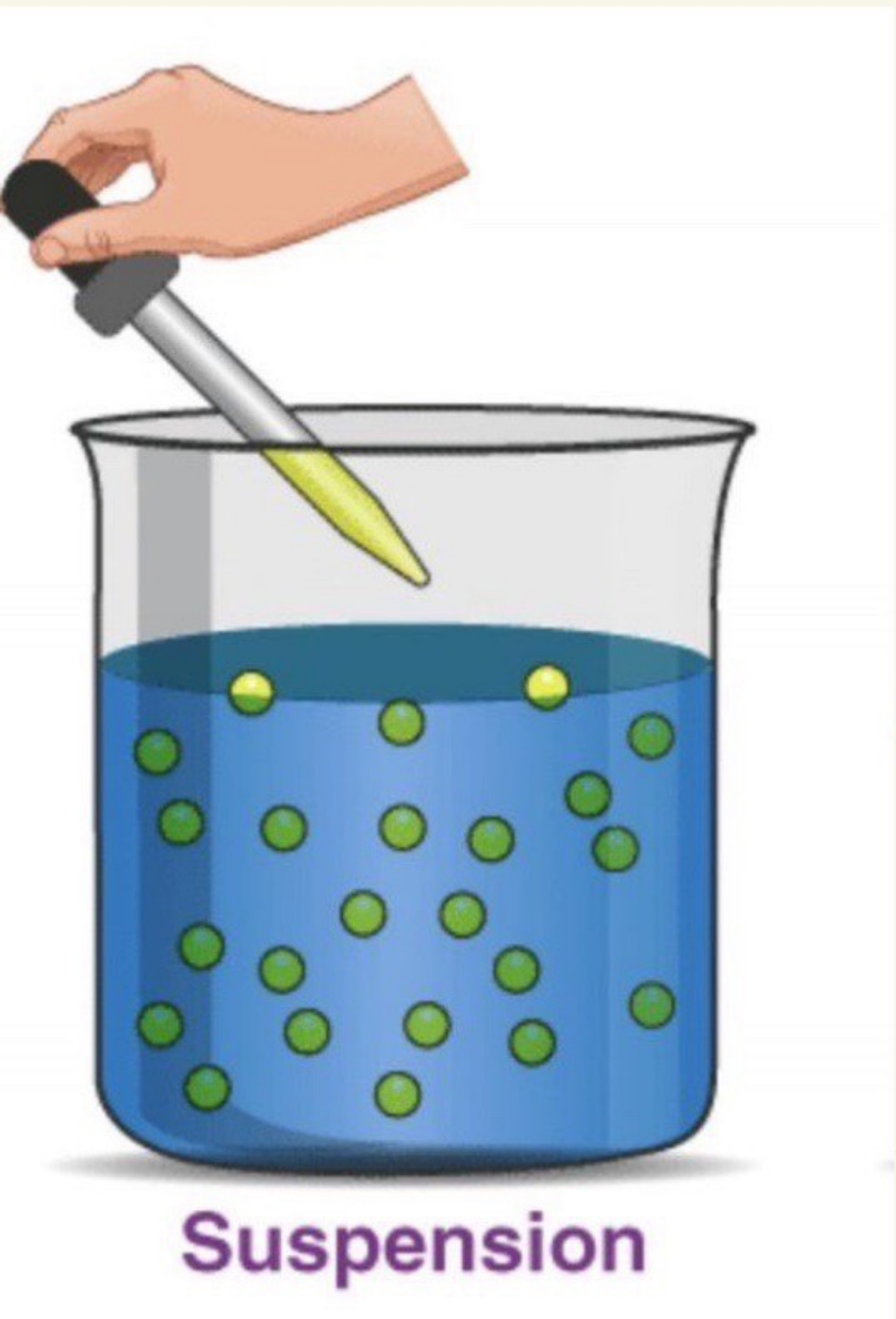
1. Suspension

Particle size small

- Generally taken Orally.
- Also by Parentrally.



Suspension

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

Suspension → Biphasic Liq. dosage form.

- Also used in External application (Topical).
- Both phases are visible.

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Ideal properties of Suspension.

Qualities of Good Suspension

1. Dispersed particle settled slowly.
2. Should be Chemically Inert → Non reactive.
3. Not form Cake.
4. Free from Large Particle.
   - → Because Large particle Spoil it's apperance.
   - → Large particle Cause Irritation.
5. Readily redispersed on Gentle Shaking.

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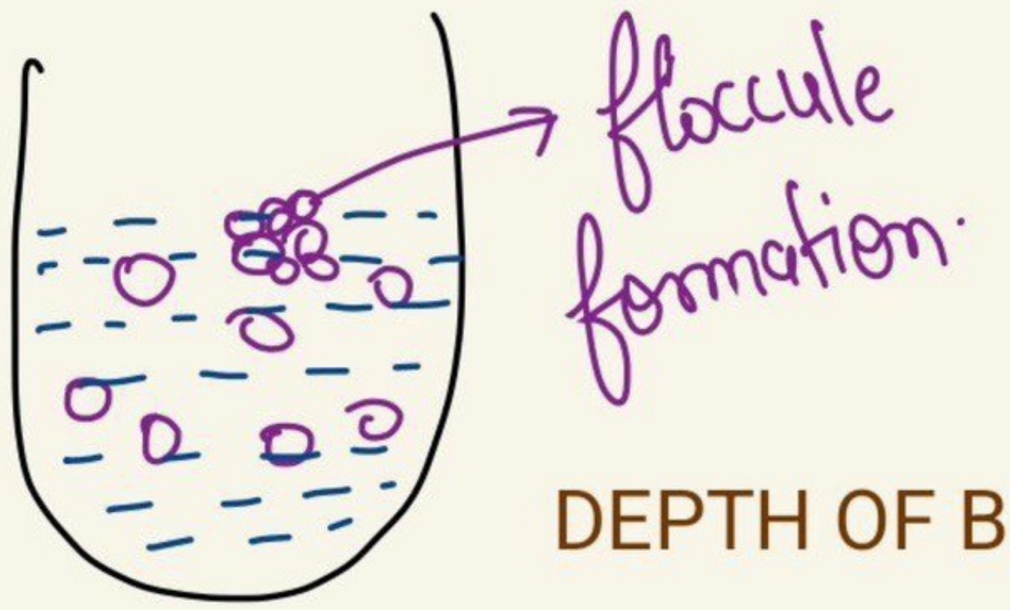
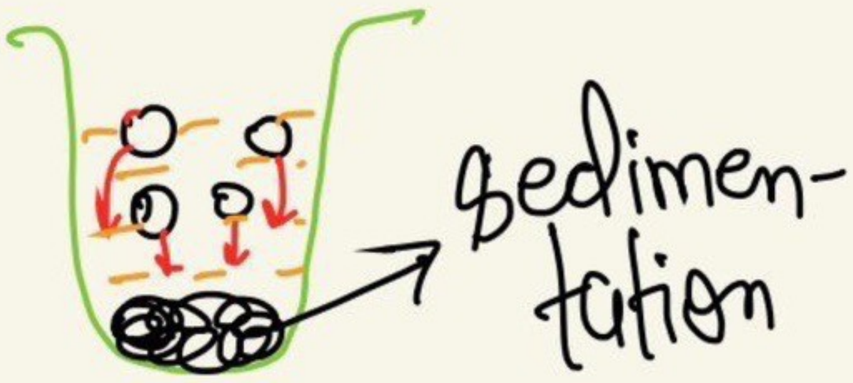
Types of Suspension

Flocullated

① Individual particle are in Come Contact with each other & form a Network Like Structure



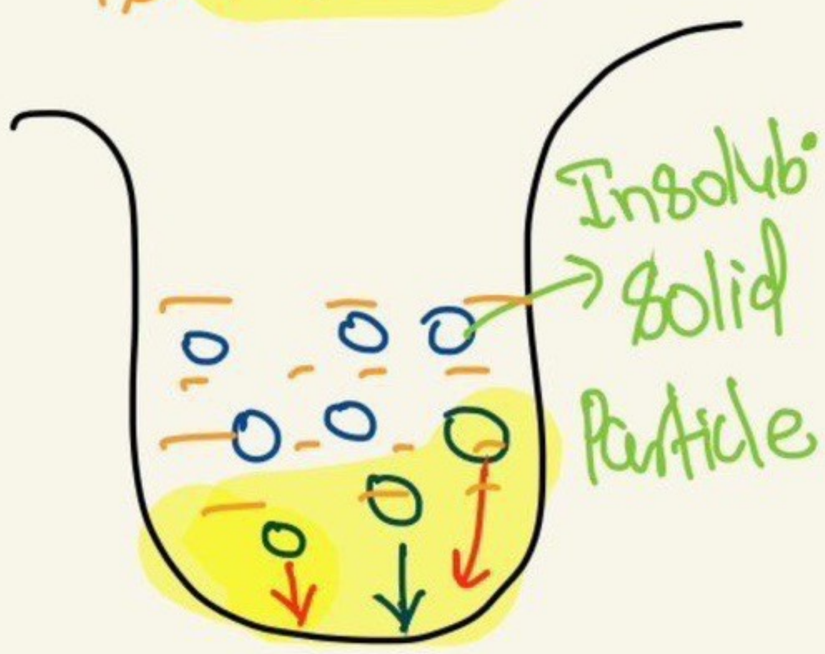
② Rate of Sedimentation is High.



Deflocullated

① Individual particle Exist as a Separate Entity.

② Rate of Sedimentation is low.



Flocculated suspension	Deflocculated suspension
1. Particles exist as loose aggregates.	1. Particles exist as a separate entities.
2. Rate of sedimentation is high.	2. Rate of sedimentation is low.
3. Sediment formed rapidly.	3. Sediment formed slowly.
4. Consist of loosely packed particles possessing a Scaffolding structure a hard dense cake does not form and the sedimentation can easily be redispersed.	4. Sediment becomes very closely packed as the repulsive forces between the particles are overcome a hard cake is formed which is difficult to redisperse.
5. Elegant preparation is obtained due to the uniform distribution of loosely bonded flocs.	5. Unsightly preparation results due to the formation of sedimentation.

⇒ Floccule Stick on the Side of Bottles. (Cap Locking)

6. Stable↑

6. Stable↓

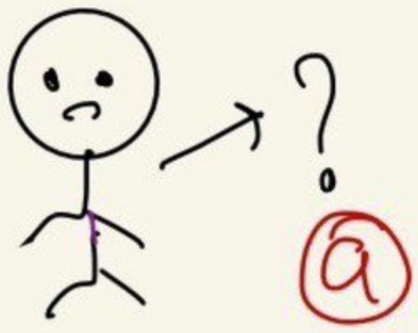
In Suspension Interface is formed b/w Two Phases which Influence the Stab. of Suspension.

Interfacial property of suspended particle

Suspension form → Small Particle Size req. → Surface Area ↑ → Surface free Energy ↑

Because it form Hard Cake

→ Thermodynamically Unstable.



⇒ So, we Use Wetting Agent / Surfactant.

Surface free Energy ↓ → Stab. ↑

(b) → Particle form floccule → Surface Area ↓

Surface free Energy ↓ → Stab. ↑

① Surface free Energy.

$$\Delta G = \gamma_{SL} \cdot \Delta A$$

- ΔG → Surface free energy
- γ_{SL} → Interfacial tension b/w solid & liq.
- ΔA → Change in surface Area

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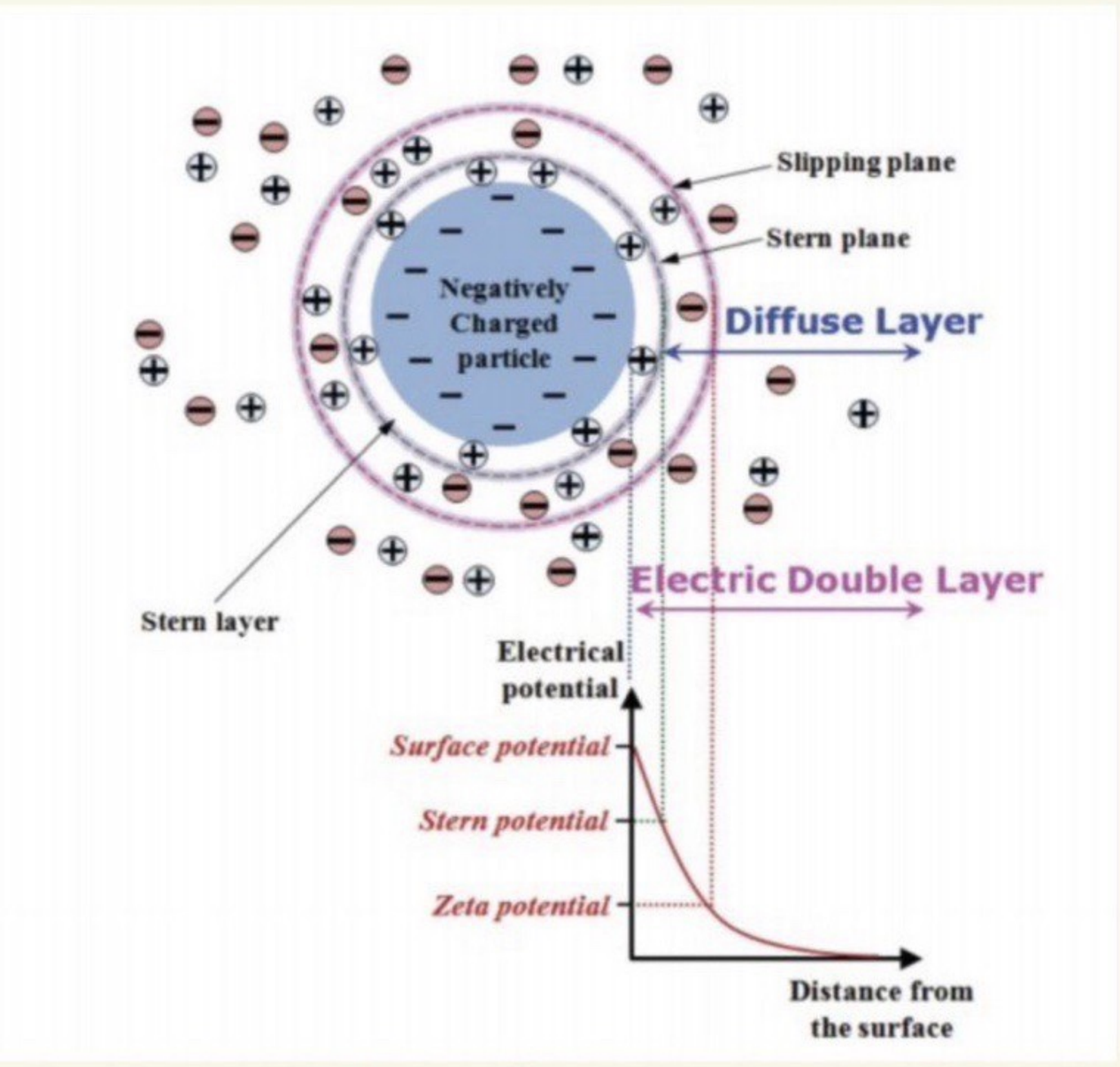
Examples of wetting agents include propylene glycol, sodium lauryl sulphate, polysorbate, docusate sodium, sorbitan fatty acid esters, and glycerin.

② Formation of Electrical double Layer.

The electric double layer consists of two layers. The first, called the Stern layer, results from accumulating the counterions on electrode surface. Then the diffusion layer extends outward from the Stern surface; this second layer is called the Gouy-Chapman layer.



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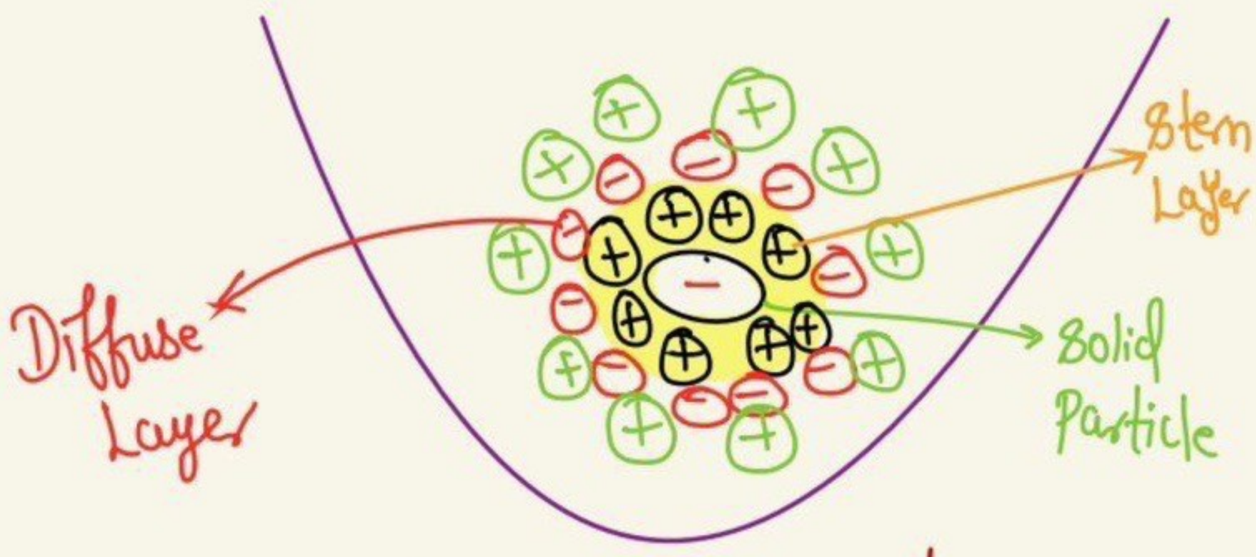

It Looks Like floccule.

So → High electrolyte Concn.

flocculated.

Interaction b/w particle ↑

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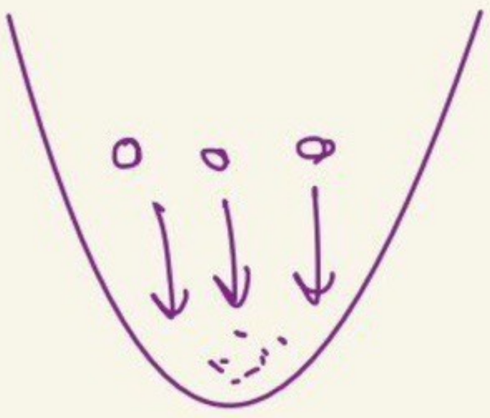
Interaction b/w Particle ↓

Low electrolyte Conc. → Non flocullated.

Settling of suspension

↳ Sedimentation rate.



Settling ≠ Sedimentation (Unstable).

It is explained by Stoke's Law ⇒

$$V = \frac{d^2 (\delta_1 - \delta_2) g}{18\eta}$$

- V → Rate of Sedimentation Or Rate of Settling.
- d → diameter of particle
- δ_1 → density of suspended particle
- δ_2 → density of solvent
- g → gravity
- η → Viscosity of dispersion Medium.

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(a) Diameter of particle ↓

(b) Viscosity of dispersion Medium ↑ → Good suspension.

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Formation of flocculated & deflocculated Suspension.

Methods → ⓐ Wetting Agent ⓑ Controlled flocculation.

ⓒ Structure Vehicle.

ⓐ Wetting Agent →

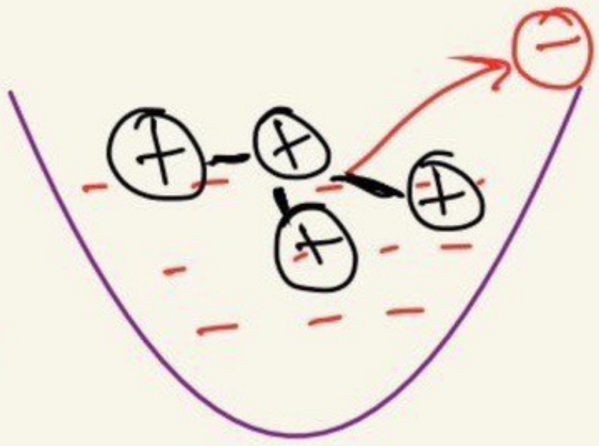
Surface Energy ↓ → Stab ↑

ⓑ Controlled flocculation →

In this method we add electrolyte to the suspension.

Charge Genrate on both phase but opposite.

& opp. Charge of Solvent attract Insoluble Solid particle



Particle repel each other

⇓

flocculation Controlled

Leads to More Stable Suspension.

(3) Structure Vehicle ↗

Here we (↑)se Viscosity of dispersion Medium

⇓

Solid particle Not Settle Easily. (does not Sediment early).

⇓

Remain Dispersed.

eg→ Acacia, Tragacanth.

EMULSION

UNIT-III **10 Hours**

Coarse dispersion: Suspension, interfacial properties of suspended particles, settling in suspensions, formulation of flocculated and deflocculated suspensions. Emulsions and theories of emulsification, microemulsion and multiple emulsions; Stability of emulsions, preservation of emulsions, rheological properties of emulsions and emulsion formulation by HLB method.

Lecture - 2

PHysical PHarma.

Unit - 3

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Emulsion → Biphasic Liq. dosage form.

→ Here 2 Immiscible Liq. are Mixed. → With the Help of Emulsifying Agent.

- Here both phase

Dispersed PHase

Dispersion Medium.

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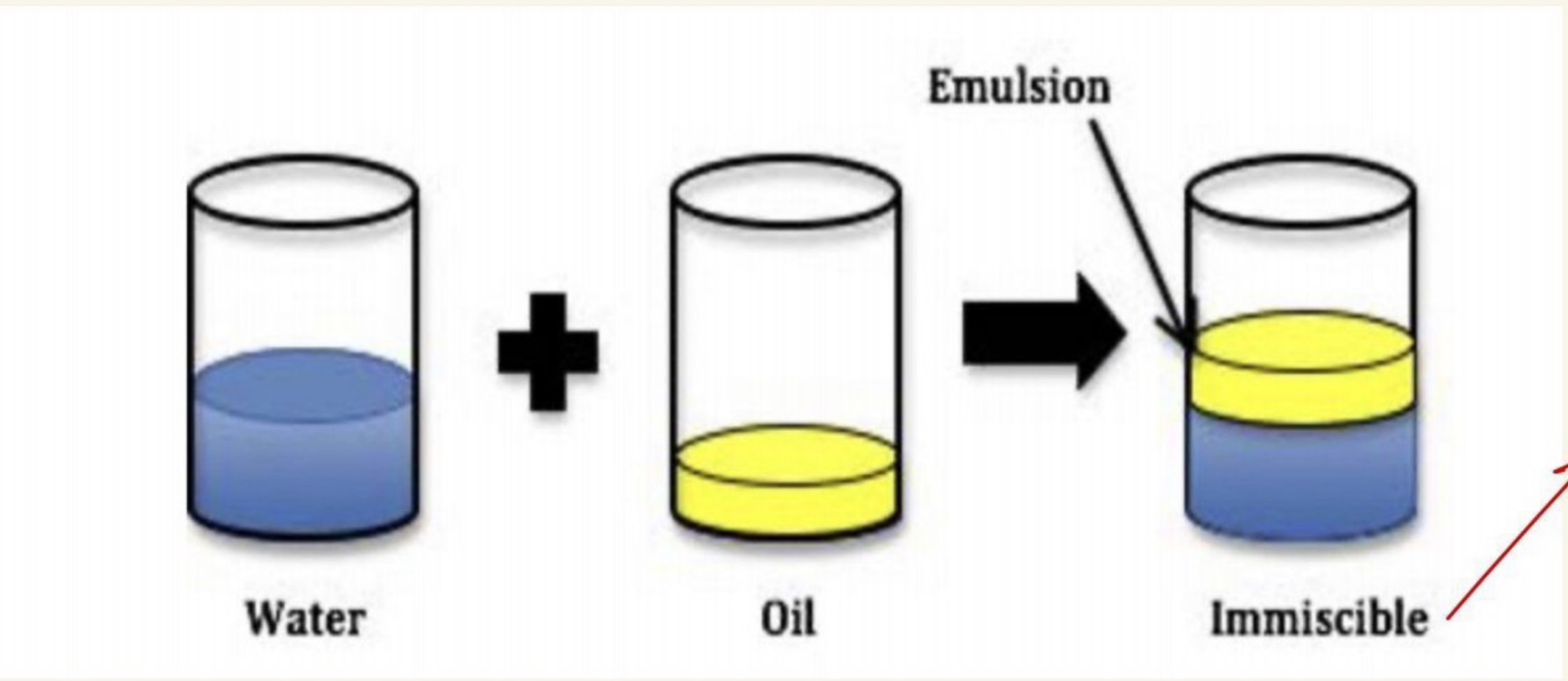
Both are in Liq. PHase.



Miscible with the Help of Emulsifying Agent.

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Some examples of emulsifiers are lecithin, soy lecithin, diacetyl tartaric acid ester of monoglyceride, Mustard, sodium stearoyl lactylate, and sodium phosphates.

Types of Emulsions

Emulsions can be classified on the basis of the properties of the dispersed phase and the dispersion medium.

1) Oil in water (O/W): Aqueous Emulsion

In this type of emulsion, the oil will be the dispersed phase, and water will be the dispersion medium. The best example of o/w emulsion is milk. In milk, the fat globules (which act as the dispersed phase) are suspended in water (which acts as the dispersion medium).

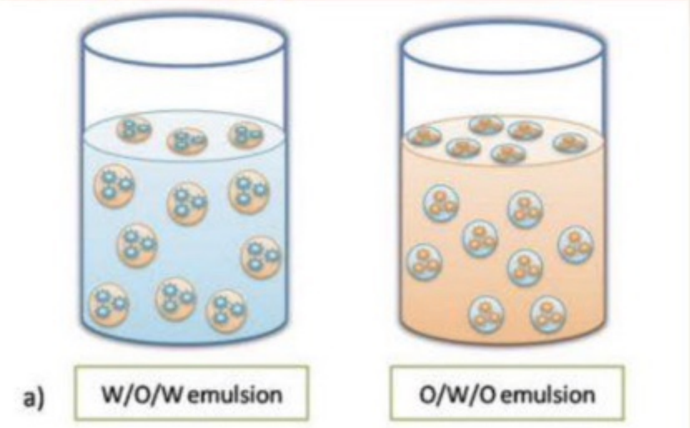
2) Water in oil (w/o): Oil Emulsion

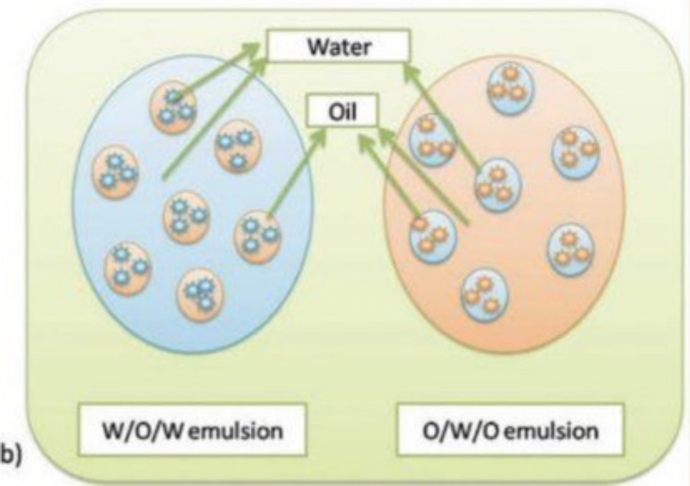
In this type, water will be the dispersed phase, and oil will be the dispersion medium.

Margarine (a spread used for flavouring, baking and working) is an example of water in oil emulsion.

(3) Multiple Emulsion (Double Emulsion)

Multiple emulsions are complex polydispersed systems where both oil in water and water in oil emulsion exists simultaneously which are stabilized by lipophillic and hydrophilic surfactants respectively.





(4) Microemulsion

A microemulsion is **a thermodynamically stable fluid that differs from kinetically stable emulsions, which will separate into oil and water over time**. The particle size of microemulsions ranges from about 10–300 nm. Because of this small particle size, microemulsions appear as clear or translucent solutions.

Some Instab. occur during Storage & formulation of Emulsion ⇒

(a) Creaming.

(b) Coalescence

(c) Breaking -

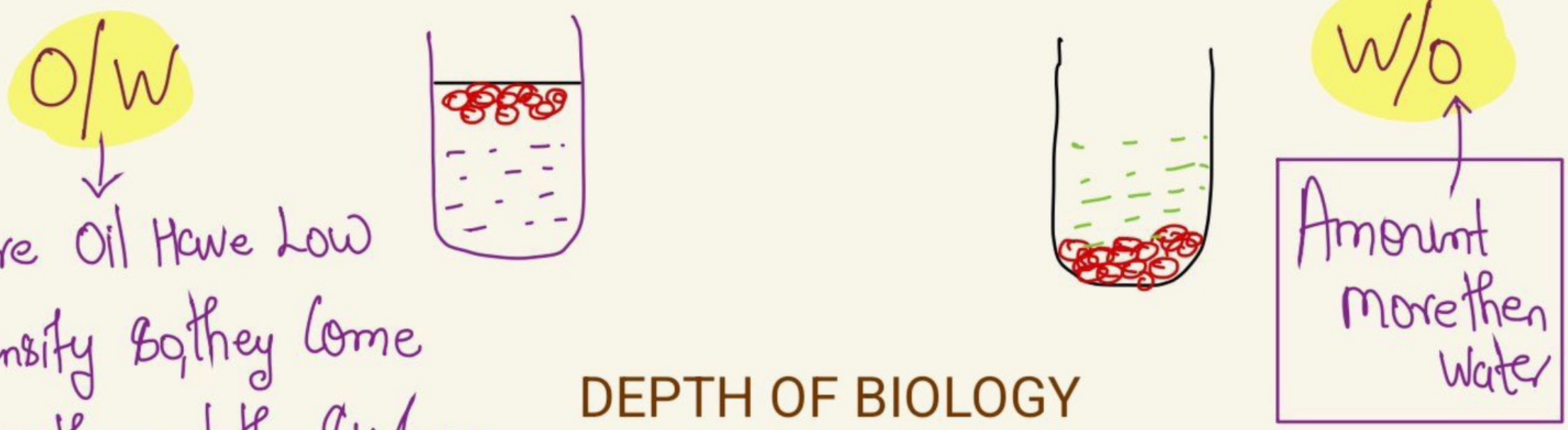
(d) flocculation

(e) Phase Inversion

(f) Physical & Chemical prop.

(a) Creaming ⇒

The rise of dispersed particles to the surface of an emulsion is referred to as creaming, which occurs due to density differences between the dispersed particles and the serum phase. The creaming rate (Cr) of particles in a dilute system follows Stokes's law and is given by.
Creaming rate



Here Oil Have Low density So, they Come Together at the Surface of Emulsion

☆ Upward Creaming.

☆ Downward Creaming.

(b) Coalescence →

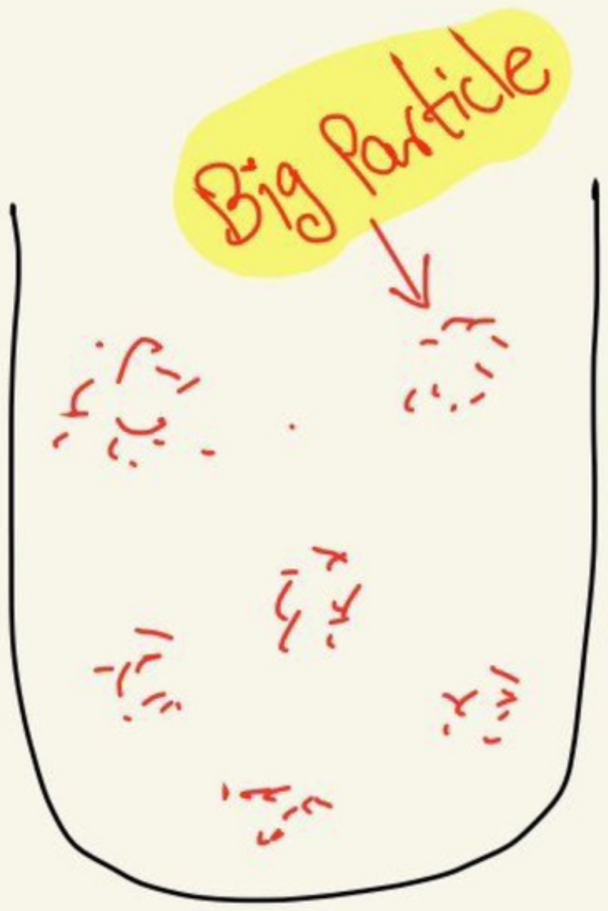
Dispersed Phase (oil particle)

↓

Sticky In Nature attract each other

↓

form Aggregate & Make Big Particle

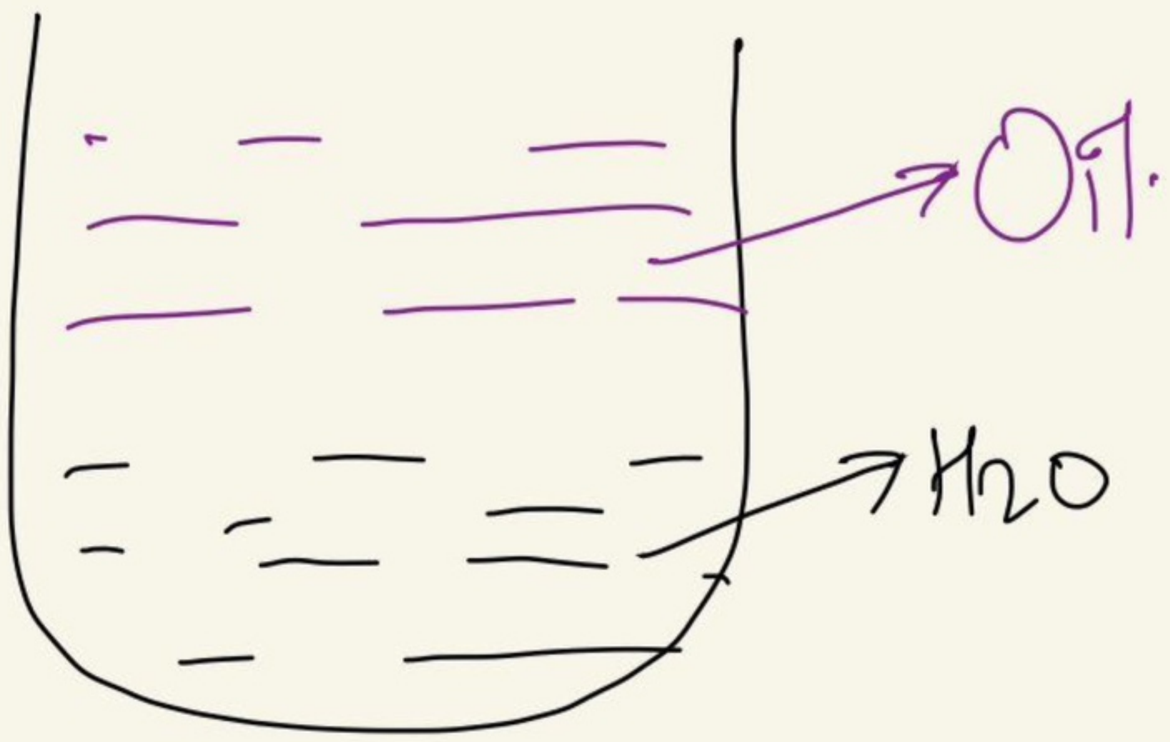


(3) Breaking / Cracking → (Because of Improper ratio of oil & H2O Mixed)

Cracking is occur due to Improper Mixing of oil & water in Emulsion

↓

Emulsion Get Separated Into two Layer → Oil, H2O



④ flocculation → Particle Size ↓ → Surface Area ↑

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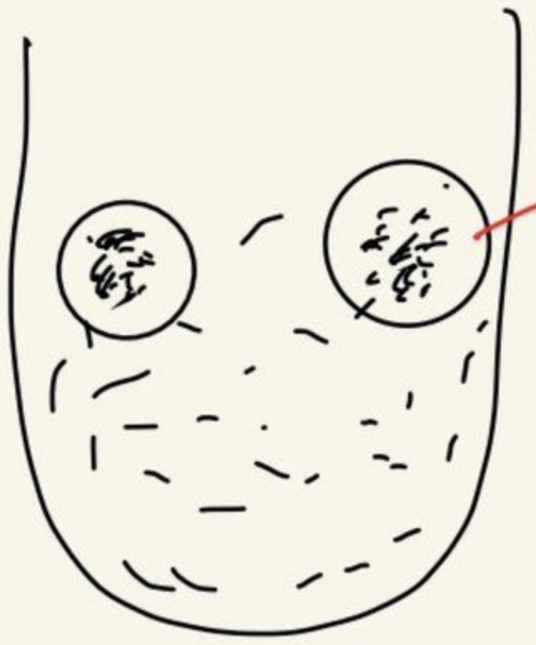
Surface free Energy ↑ → Stab ↓↓



→ floccule → Surfacea Area ↓ → SFE ↓

Stab ↑

But due to floccule formation It is Unstable

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⑤ PHase Inversion → PHase of Emulsion get Changed during formulation

o/w → w/o

w/o → o/w.

It is due to Mixing Problem or by adding Wrong dispersed PHase.

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⑥ Physical & Chemical Prop. Change → DEPTH OF BIOLOGY

Emulsifying Agent is req. to formulate Emulsion.

↓

Make More Stable Emulsion.

Sometime this Emulsifying Agent Lead to Change in property Like pH, odour, Taste.

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Theories of Emulsion

↓↓

Theories.

- Monomolecular Theory
- Multimolecular Theory
- Solid particle Theory.

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⑨ Monomolecular → DEPTH OF BIOLOGY

As We Know in Emulsion particle Size is too small

⇓

Due to Small particle Size More will be the Surface Area.

⇓

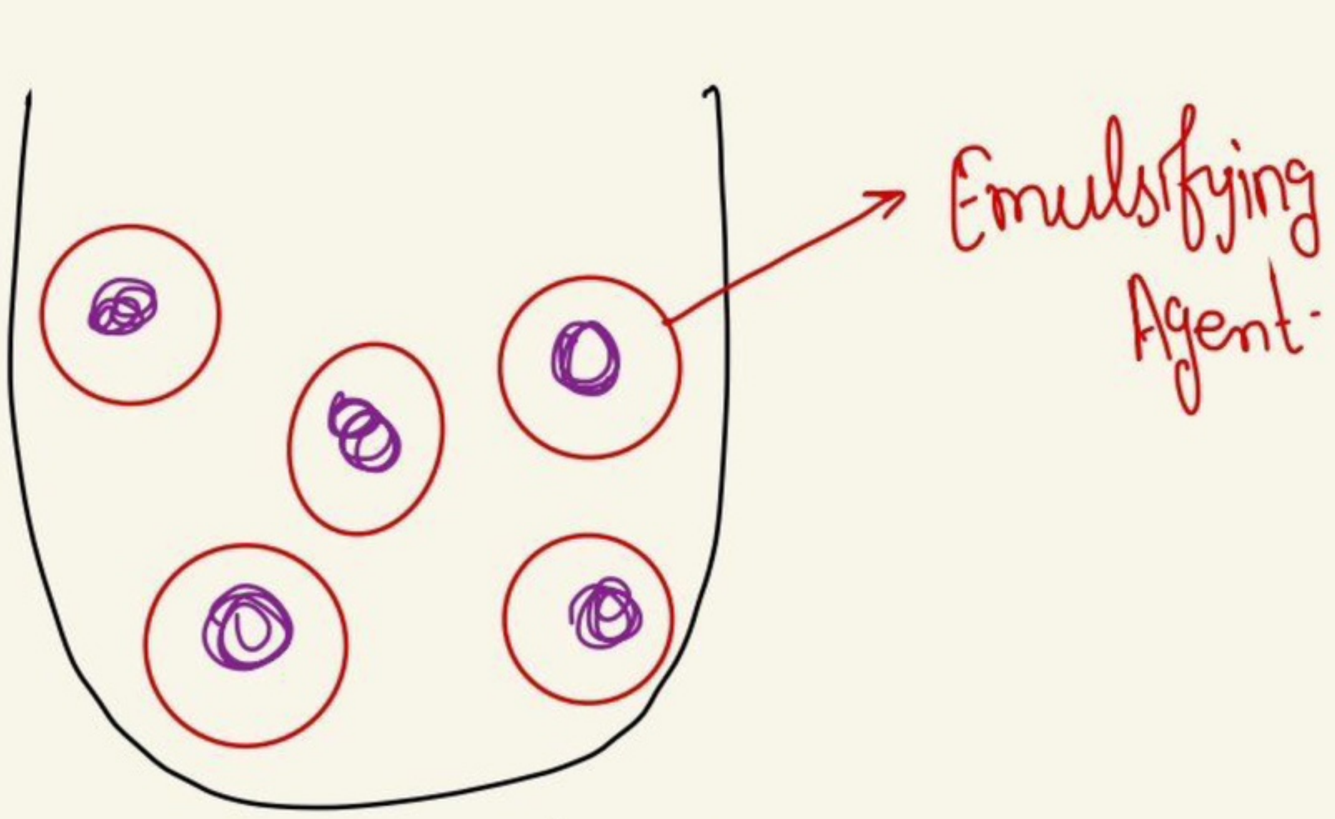
If Surface Area ↑ then Surface free Energy ↑

↓

Lead to ↓se in Thermodynamic Stability.

⇓ DEPTH OF BIOLOGY

We Have to add Surfactant to Make it More Stable.



Mono Molecular.

(Single Layer formed Or Single E.Agent Particle is Used.

(b) Multimolecular Theory.

Here we Have to Make More Stable Emulsion.

We Have to Mix Dispersed PHase & dispersion Medium Properly.

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Oil & H_2O Mixed by Emulsifying Agent / Surfactant / Wetting Agents.

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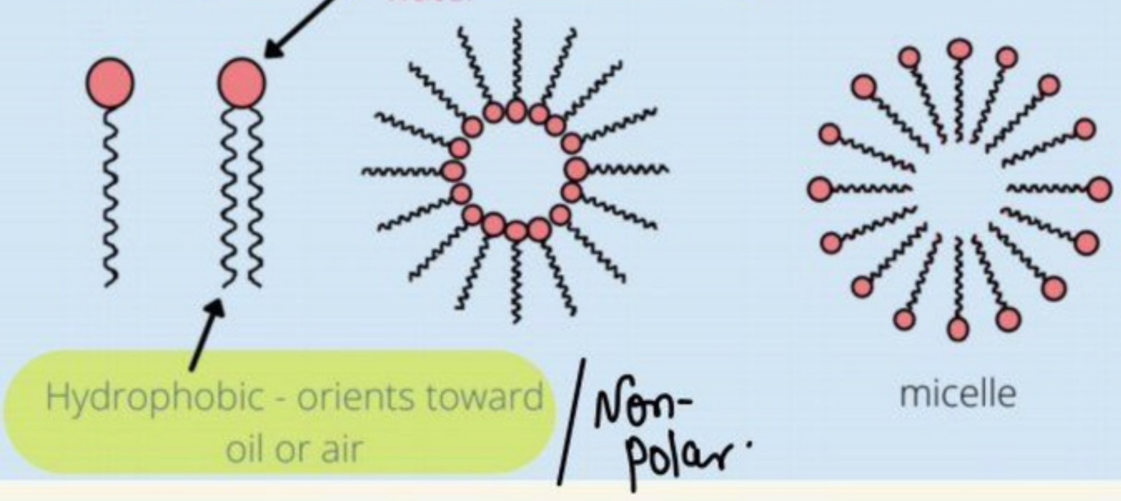
What Is a Surfactant?

A surfactant is a chemical that lowers surface tension.

Each surfactant molecule has a hydrophilic or water-loving component and a hydrophobic or water-fearing component.

Polar / Hydrophilic - orients toward water

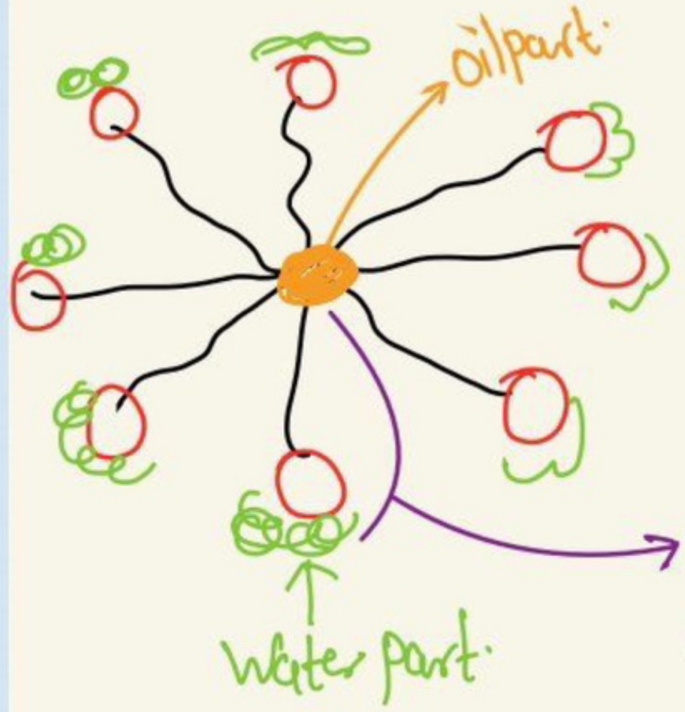


Hydrophobic - orients toward oil or air / Non-polar.

micelle

Examples

- detergent
- emulsifier
- wetting agent
- foaming agent



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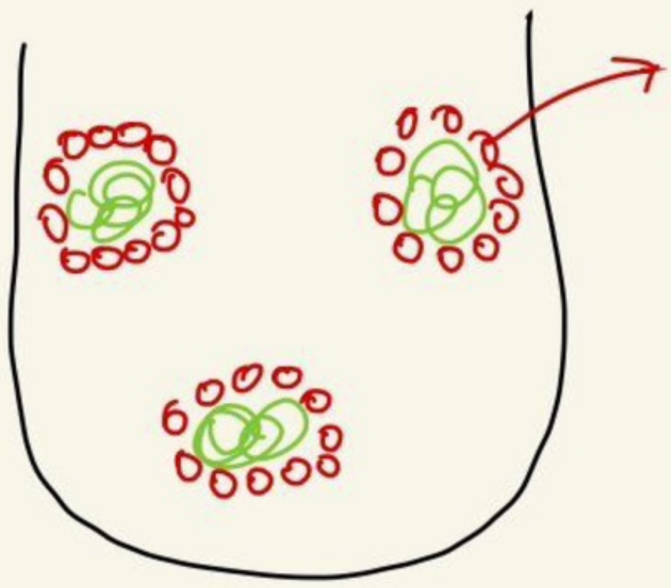


⇒ MultiMolecular.

③ Solid particle Adsorption Theory →

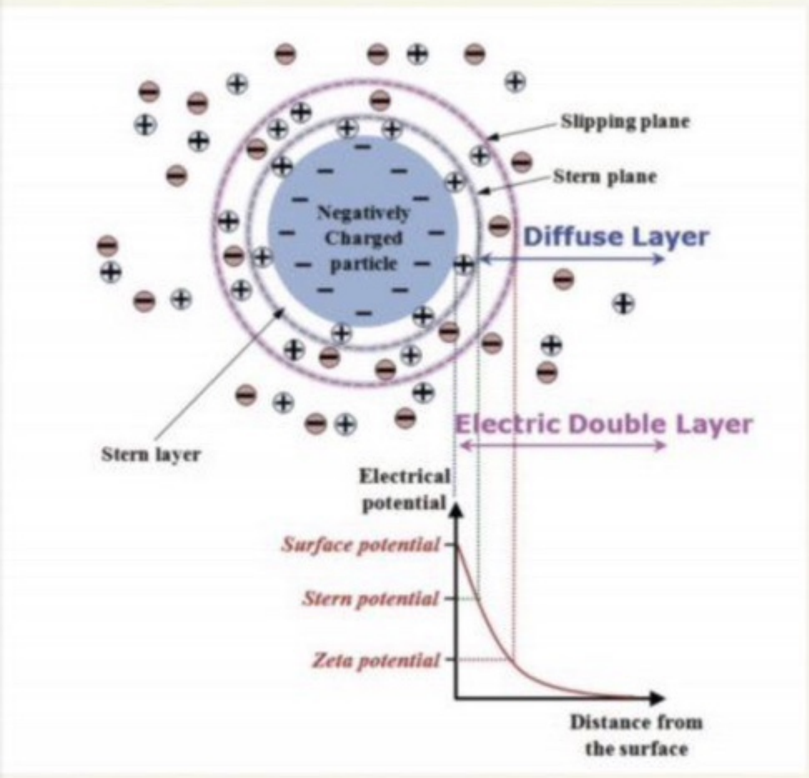
May be dispersed particle (Liq.) ⟶ Settle Down.

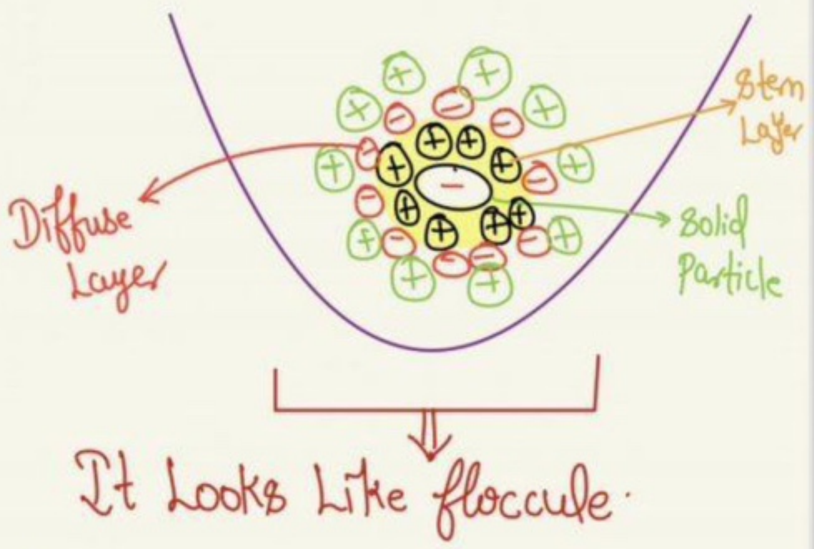
⇩

We Have to ↑se Viscosity of Dispersion Medium.

With the Help of Colloidal Clay We can ↑se Viscosity of dispersion Medium.

④ Formation of Electrical double Layer. ⇒





⇩

It Looks Like floccule.

So ⟶ High electrolyte Concn.

⇩

flocculated.

Interaction b/w particle ↑ ⟶

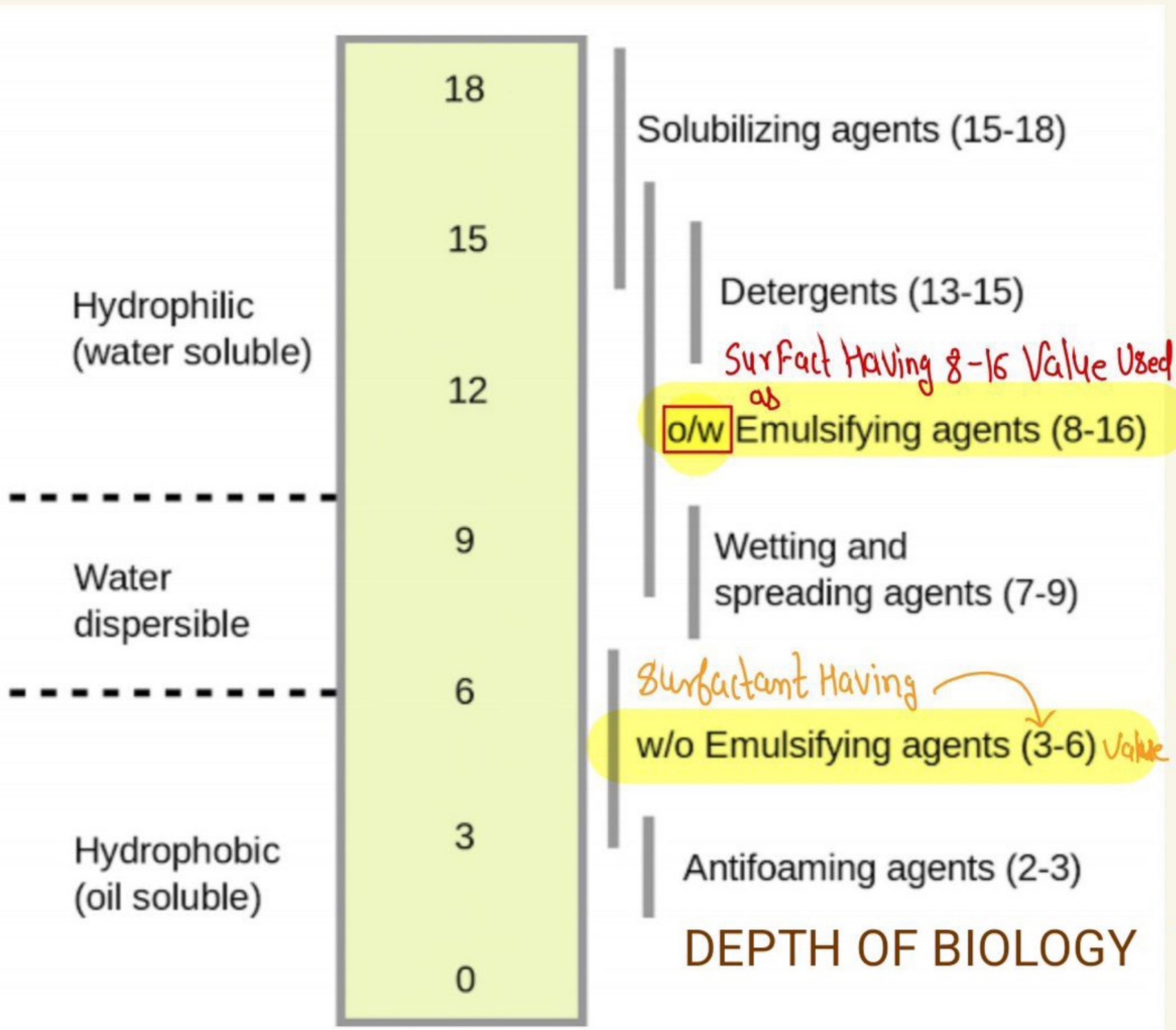
Low electrolyte Conc. ↗ Non flocullated.

Interaction b/w Particle ↓

Formulation of Emulsion

Check Description / Or Search formulation of Emulsion by depth of Biology.

Formulation by HLB Method ⇒ Hydrophilic Lipophilic Balance



With the Help Of this We Can Easily Choose which Emulsifying Agent is Used in Emulsion

Preservation of Emulsion.

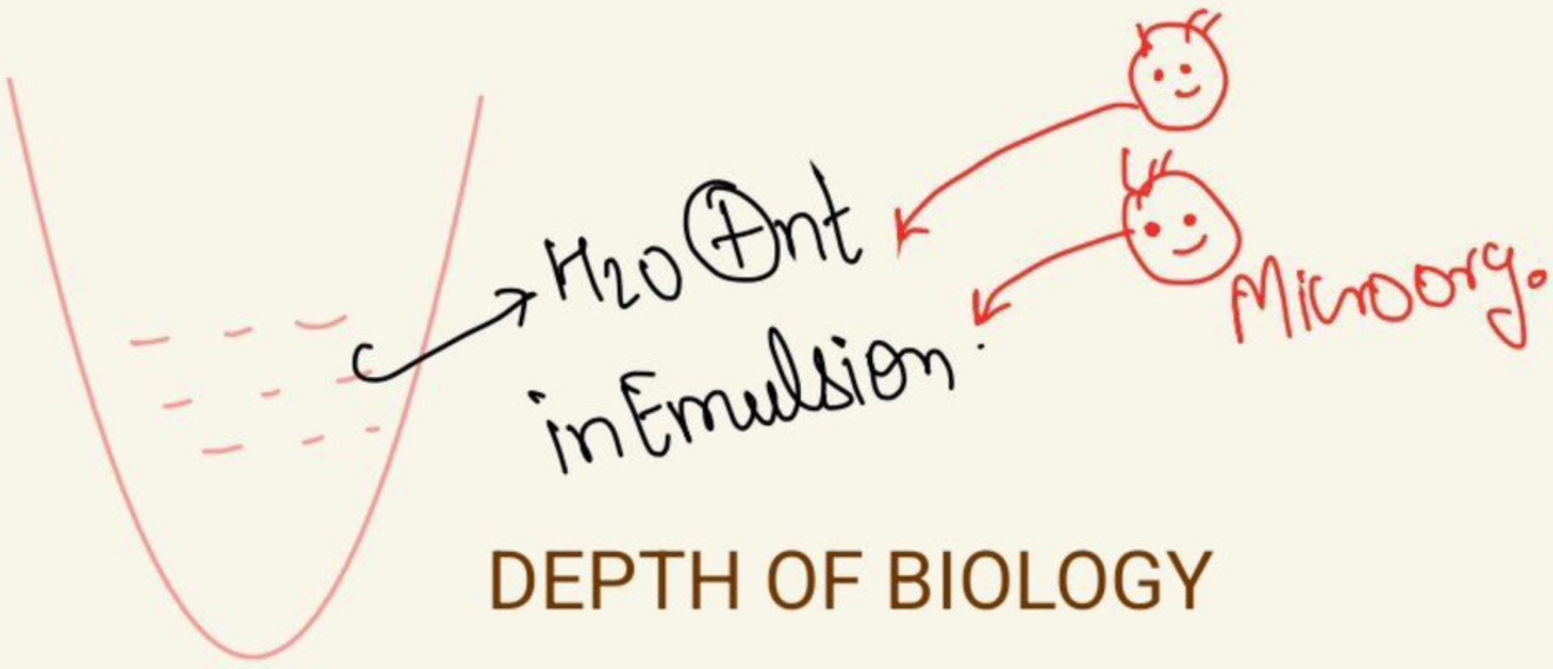
To Keep Emulsion Stable & Effective till Expiry date.

Preservatives.

- Non-Toxic
- Inert.
- Cheap

Stable

(a) Preservation from Microorg. ⇒



We Have to add Methyl Paraben Benzoic Acid Which Inhibit Bacteria Growth.

- Preservative should be → Tasteless, Colourless, odourless

↓

Non-Toxic, Non-Irritant, Stable

(b) Preservation from Oxidation ⇒

Due to Oxidation → Lead to Rancidity & Spoilage of Emulsion.

↓

Add Antioxidant.

(eg → BHT)

↓

Stable, Non-Toxic effective at Low Conc^n.

To prevent Oxidation.

Rheological Properties of Emulsion.

↓

flow Properties.

RHEOLOGICAL PROPERTIES OF AN EMULSION

In order for an emulsion to perform optimally, the following flow-related characteristics are desirable:

- Emulsions are removed from bottles and tubes.
- A hypodermic needle applied to an emulsion.
- Emulsion spreadability on the skin.
- Flow changes during manufacturing under stress.

Emulsions are rheologically similar to suspensions, but they differ in three main ways -

- Interfacial rheology is important when considering the liquid/liquid interface that contains a surfactant or polymer layer.
- Dispersion phase viscosity is dependent on the medium viscosity in determining emulsion rheology.
- A dispersed phase droplet's deformability has an effect on the rheology of an emulsion, particularly a large droplet.

→ Microemulsion.

Dilute emulsions generally exhibit Newtonian flow. As the viscosity of emulsion increases, flocculated globules will diminish because their mobility is restricted. A viscosity of optimum is desirable to ensure a stable emulsion.

Emulsions that are concentrated show non-Newtonian flow.

→ eg → Lotion.

Rheological prop. of Emulsion can be controlled by.

- Conc. of dispersed Phase.
- Particle Size of dispersed Phase.
- Viscosity of continous phase.