# PHYSICAL PHARMACEUTICS-II

## UNIT 3 NOTES

- COARSE DISPERSION
  - EMULSION
  - SUSPENSION

# COARSE DISPERSION

- A coarse dispersion is a type of heterogeneous system in which the dispersed phase particles are larger than 0·5 microns (500 nm) in diameter.
- These particles are clearly visible under an optical microscope and tend to settle under the influence of gravity due to their size.

## CHARECTERISTICS OF COARSE DISPERSION

| PROPERTY | DESCRIPTION |
|---|---|
| Particle size | Greater than 0·5 μm (micrometers) |
| Visibility | Visible under a light microscope; sometimes to the naked eye. |
| Settling | Readily settles under gravity |
| Separation | Requires agigating (shaking or stirring) to redisperse. |
| Stability | Thermodynamically unstable; requires stabilizers. |
| Example | Suspensions, Emulsions, Foams, aerosols (solid in gas), and some dusts. |

# EMULSIONS

- An Emulsions is a thermodynamically unstable system consisting of at least two immiscible liquids, where one liquid (the dispersed phase) is dispersed in the form of small droplets within the other (the continuous phase) with the help of an emulsifying agent.

## COMPONENTS OF EMULSIONS

① Dispersed Phase (Internal Phase):

- The phase that is present in small droplets.
- Also known as ~~Dispersion~~ ~~Medium~~.

② Continuous Phase (External Phase):

- The medium in which the droplets are dispersed.

③ Emulsifying Agent (Emulsifier / Surfactant):

- A surface-active agent that stabilizes the emulsion by reducing interfacial tension and forming a film around the dispersed droplets.

# Classification Of Emulsions

Emulsions can be classified into the following major types based on the phase nature, droplet size and structure:

1. Oil in water (O/W) Emulsion
2. Water in oil (W/O) Emulsion
3. Multiple Emulsion
4. Microemulsion

## 1. Oil in Water (O/W) Emulsion

Oil droplets are dispersed in a continuous water phase.

- Dispersed phase: Oil
- Continuous phase: Water
- Emulsifier: Hydrophillic (HLB > 10), e.g. Tween 80
- Properties:
  - Can be diluted with water.
  - Conducts electricity.
  - Non-greasy and washable.
- Example:
  - Milk (natural O/W) emulsion
  - Oral emulsions (e.g. castor oil emulsion)
  - Moistorizing lotions.

## ② Water-in-Oil (W/O) Emulsions

Water droplets are dispersed in a continuous oil phase.

- Dispersed phase: Water
- Continuos phase: Oil
- Emulsifier: Lipophilic ( HLB < 10), e.g. Span 80
- Properties:
  - Can be diluted with oil.
  - Doesn't conduct electricity.
  - Greasy, occlusive, provides moistorizing effect.

- Examples:
  - Cold creams
  - Water-resistant sunscreens
  - Ointment for dry skin

## ③ Multiple Emulsions

These are emulsions of emulsions — i.e, droplets within droplets.

- Types: (a) W/O/W - Water droplets inside oil products, further dispersed in water.
  (b) O/W/O - Oil droplets inside water droplets, further dispersed in oil.

- Purpose:
  - Controlled or sustained drug release.
  - Protection of active ingredients.
  - Taste masking.

- **Emulsifiers:** Requires a combination of lipophilic and hydrophilic surfactants.

- **Properties:**
  - Thermodynamically unstable.
  - Requires high formulation precision.

- **Examples:**
  - Advanced topical drug delivery system.
  - Cosmetic formulations for long-lasting effects.

## ④ Microemulsions

Clear, thermodynamically stable emulsions with nanometer-sized droplets.

- **Droplet size:** 10 - 100 nm
- **Appearance:** Transparent or translucent
- **Stability:** Thermodynamically stable
- **Types:**
  - O/W microemulsion
  - W/O microemulsion
- **Uses:**
  - Enhanced bioavailability of poorly soluble drugs.
  - Transdermal and oral drug delivery system.
  - Cosmetic serums and perfumes.
- **Examples:** Cyclosporine ophthalmic emulsion (Restasis).

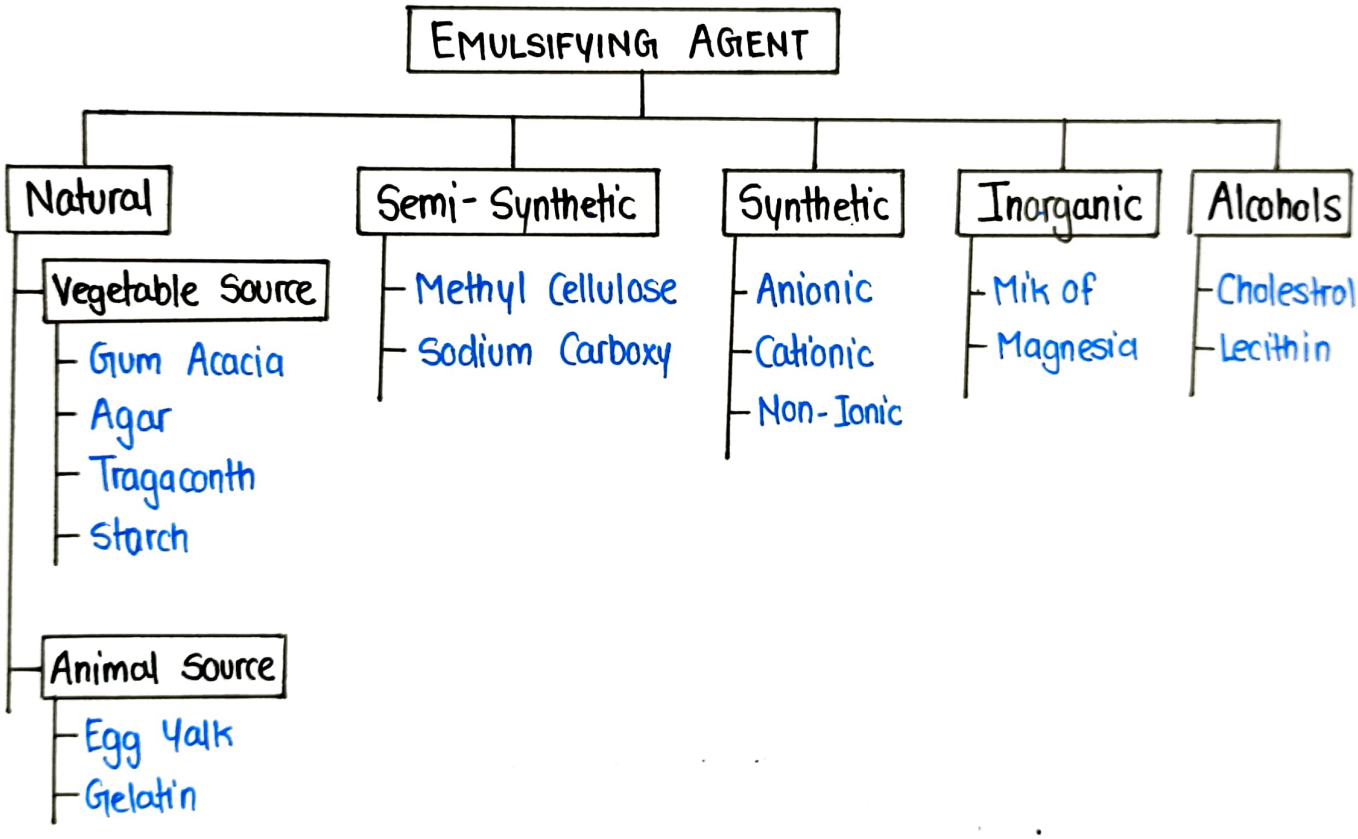
O/W Emulsion

W/O Emulsion

# EMULSIFYING AGENTS

Emulsifying agents are those chemical compounds which reduces the interfacial tension between two immiscible liquids (oil and water) and make them miscible to form a stable emulsion.
Emulsifying Agents are also known as 'Emulsifiers'

## Classification




## Properties of Emulsifying Agents :

- It should be chemically stable.
- It should be compatible with other ingredients of the emulsion
- It should be Non-toxic
- It must be capable of reducing interfacial tension.

# Preparation Of Emulsions

Emulsions are usually prepared by using three methods :

- Dry Gum Method
- Wet Gum Method
- Bottle Method

## Dry Gum Method

- The ratio of Oil : Water : Gum is 4 : 2 : 1
- It requires Mortar and Pestle
- First Oil is mixed with Gum and triturated
- Little amount of water is added and trituration continued till a 'clicking' sound is heard and thick cream is formed.
- Once primary emulsion is formed, remaining water is added to form the final emulsion.

## Wet Gum Method

- The Ratio of Oil : Water : Gum is 4 : 2 : 1
- It also requires mortar and pestle
- First water is mixed with Gum and triturated
- Required amount of oil is added and trituration continues to form the primary emulsion
- Once primary emulsion is formed, remaining water is added to form the final emulsion.

## Bottle Method

- The ratio of Oil : water : Gum is 2 : 2 : 1
- The method is basically used for volatile and Non - viscous oils
- First oil is mixed with gum and shaken throughly
- Required amount of water is added and shaking continued to form a primary emulsion
- Once the primary emulsion has been formed remaining quantity of water is added slowly to form the final emulsion.

# Stability Of Emulsions

The following changes usually occurs which affects the stability of emulsions.

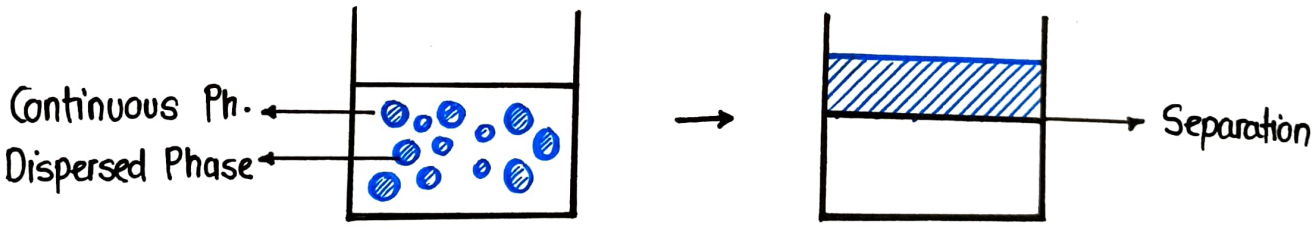
- Cracking
- Creaming
- Phase Inversion
- Coalescence

## Cracking

Cracking means the separation of two layers / phases of the emulsion (dispersed phase and continuous phase

Cracking may be occur due to :

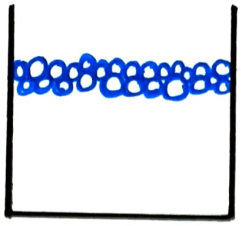
- Addition of wrong emulsifying agent
- Growth of microorganism
- Change in Temperature



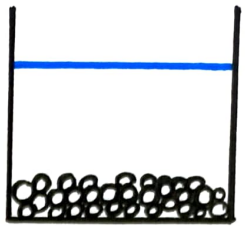

## Creaming

Creaming can be defined as upward or downward movement of dispersed phase (dispersed globules) to form a thick layer at surface or bottom of the emulsion.

- O/w Emulsion → Upward Creaming
- w/o Emulsion → Downward Creaming



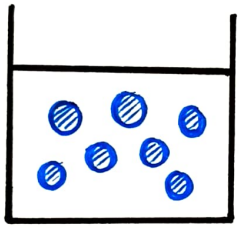
Upward Creaming
(o/w Emulsion)



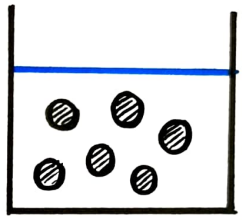
Downward Creaming
(w/o Emulsion)

## Phase Inversion

Phase inversion is simply defined as conversion of o/w Emulsion into w/o Emulsion, or vice versa (w/o Emulsion into o/w)



(o/w Emulsion)



(w/o Emulsion)

## Coalescence

Coalescence is the process in which two or more droplets merge together to form a single large droplet.

## Methods To Overcome the Stability Problems

- Selection of proper emulsifying agent.
- By increasing the viscosity of the emulsion
- By proper storage of the emulsion
- Maintaining appropriate temperature
- By maintaining minimum density difference
- By reducing size of dispersed globules.

# Theories Of Emulsification

1. Monomolecular Theory
2. Multimolecular Theory
3. Solid Adsorption Theory

## 1. Monomolecular Film Theory

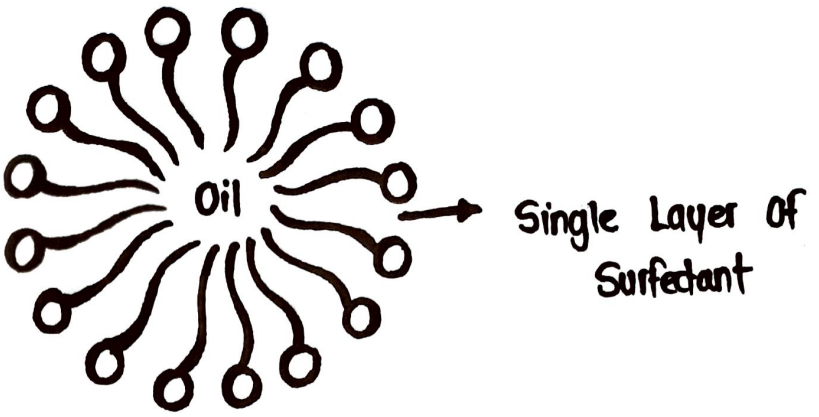
- In this theory, surfactants molecules (emulsifiers) form a single-molecule-thick film around oil droplets.
- This thin film prevents the droplets from coming together (coalescing).

Mechanism:

- Surfactants have two parts:
  - Hydrophilic head (Water-loving)
  - Lipophilic tail (Oil-loving).
- They align at the oil-water interface: Head in water, tail in oil.
- This forms a stable monolayer that protects each droplet.

Example of Emulsifiers:
- Tween 80
- Span 20
- Sodium Lauryl Sulphate (SLS)

Key Points:
- Film = Only one molecule thick
- Works well with low molecular weight surfactants
- Helps in reducing surface tension




## ② Multimolecular Film Theory

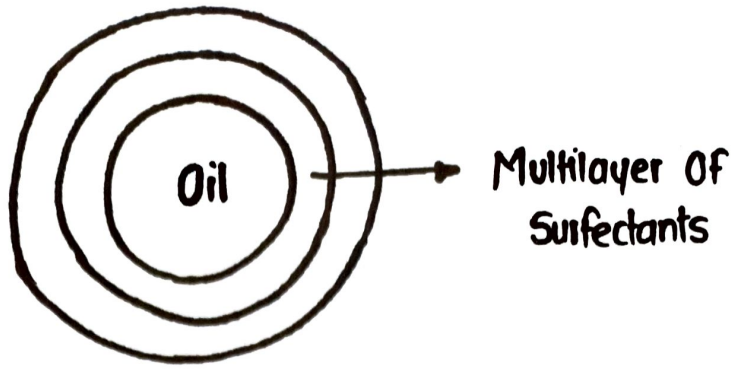
- Uses natural colloids or polymers that form a thick film (which many molecules) around each droplet.
- This film acts as a physical barrier to prevent droplet fusion.

Mechanism:

- Emulsifiers like gum acacia, gelatin or casein adsorb on the droplet surface.
- They form a strong, multilayered coating.
- Also increase viscosity of the emulsion, slowing down droplet movement.

Example of Emulsifiers:
- Gum acacia
- Gelatin
- Tragacanth
- Sodium alginate

Key points:
- Film = thick and viscous
- Provides good stability
- Increases viscosity of the system




## ③ Solid Particle Adsorption Theory

- Usses very fine solid particles to stabilizes emulsions.
- These particles adsorb on the oil-water interface and form a rigid protective film around droplets.

Mechanism:

- Solid particles collect at the interface of oil & water.
- They form a machenical barrier to prevent coalescence.
- Depends on whether particles are more wettable by water or oil:
  - More wettable by water - O/W Emulsion
  - More wettable by oil - W/O Emulsion

Key points:

- No chemical surfactant required
- Film = rigid and strong
- Long-term physical stability

Examples of Solid Emulsifiers:

- Bentonite
- Kaolin
- Magnesium hydroxide
- Aluminium hydroxide

# Preservation Of Emulsions

- Emulsions contain water, oil and emulsifiers – all of which can support:
  - Microbial growth (especially in aqueous phase)
  - Oxidation (especially in oil phase)
- To prevent spoilage, discoloration, rancidity and loss of potency, preservatives and antioxidants are added.

## ① Preservation From Microorganisms

- Microbes like bacteria, molds, fungi can grow in emulsions (especially in water).
- This leads to contamination, odor, degradation, and even infection in pharmaceutical / emulsion products.

- Solution: Add preservatives (Antimicrobial agents)

Ideal properties of Preservatives:

- Effective in low concentration.
- Non-toxic, non-irritant.
- Broad spectrum (active against bacteria, fungi etc.)
- Chemically stable in emulsion
- Soluble in phase where microbial growth occurs (usually water).

Common preservatives:

- Methylparaben
- Propylparaben
- Phenol ~~bacteria~~
- Benzoic Acid

## ② Prevention From Oxidation

- Oils used in emulsions ( like unsaturated fatty acids) are prone to oxidation.
- Oxidation leads to :
  - Rancidity
  - Off- smell
  - Discoloration
  - loss of drug potency

- Solution : Acid antioxidants

Ideal properties of Antioxidants :

- Chemically stable
- Non - toxic
- Effective at low concentrations
- Soluble in the oil phase
- Should not alter emulsion stability.

Common Antioxidants used :

- Butylated Hydroxyanisole
- Butylated Hydroxytoluene
- Tocopherol
- Ascorbic acid

- They often used in oil- soluble phase as oxidation mostly affects oils.

# Rheological Properties Of Emulsion

- Rheology is the study of flow and deformation of matter - basically, how a liquid behaves when force is applied.
- For emulsions, rheology tell us about:
  - Viscosity (thickness)
  - Flow type (Newtonian or Non-Newtonian)
  - How the emulsion will pour, spread or apply on the skin.

## Types Of Flow In Emulsions

### ① Newtonian Flow

- Flow is directly proportional to applied force
- Constant viscosity
- Seen in dilute emulsions

Examples: Simple liquid emulsions with low oil content.

### ② Non-Newtonian Flow

- This type of flow shows by concentrated emulsion.
- Optimum viscosity is desirable for good stability of Emulsion.

Examples: Lotions, Creams etc.

## Factors Affecting Rheological Properties Of Emulsions

① Type of Emulsion - O/W & W/O behave differently.

② Phase ratio - More dispersed phase – higher viscosity.

③ Droplet size - Smaller droplets – smoother & thicker

④ Emulsifier used - Some increase viscosity.

⑤ Temperature - Higher Temperature – Lower viscosity

⑦ Additives - Thickeners or polymers can affect flow

## Importance Of Rheological Properties In Emulsions

① Physical Stability - High viscosity reduces creaming / sedimentation.

② Spreadability - Affect patient compliance.

③ Packaging & Dispensing - Flow must suit container (tube, bottle, pump).

④ Product performance - Controls how the drug is released.

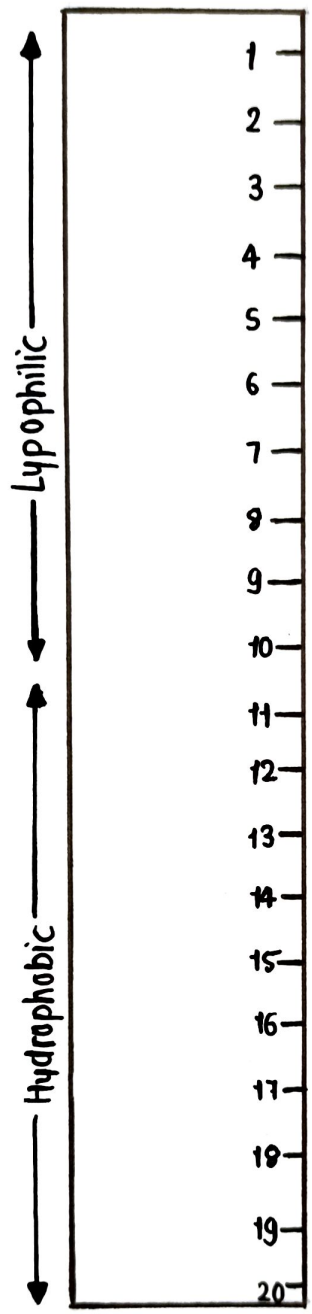
# Emulsion Formulation By HLB Method

① HLB (Hydrophobic 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 (10-18) indicate a hydrophillic molecule, and produce an O/W emulsions.
- Low numbers (3-6) indicate a lipophilic molecule and produce a W/O emulsions.
- Oils and waxy materials have a 'required HLB number' which helps in the selection of appropriate emulsifying agent when formulating emulsions.
- Liquid parafinn, for example, has a required HLB value of 4 to obtain a W/O 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) laury ether | 9.5 |
| Polyoxy ethylene (6) laryl ether | 10.3 |
| Polyoxy ethylene (20) sorbitan tristearate | 10.5 |
| Polyoxyethylene (9) nonyl phenol | 13.0 |
| Sodium Oleate | 18.0 |
| Polyxyethylene (100) stearate | 18.8 |
| Potassium Oleate | 20.0 |




HLB Scale For Emulsion Formulation

# SUSPENSIONS

- A suspension is a biphasic liquid dosage form in which finely divided solid particles dispersed into the liquid.
- In suspensions, Dispersed phase → Solid particles
  Continuous phase → Liquid

- The size of solid particles in the suspension ranges from 0.5 μm to 5 μm.

## Classification of Suspensions

Suspensions can be classified on the basis of 3 categories

① On the basis of general classes
② On the basis of proportion of solid particles
③ On the basis of electrokinetic nature of solid particles

### On the Basis of General classes

- Oral Suspensions
- Topical Suspensions
- Parentral Suspensions
- Opthalmic Suspensions

### Oral Suspensions :

These suspensions are administered orally (by mouth)
example : Paracetamol Suspensions

## Topical Suspensions :

These are suspensions that are used for external purposes. They are mainly applied on the skin.

## Parentral Suspensions :

These suspensions are administered via intravenous or intramuscular routes through injections. Particle size of solid particles in these suspensions should be very less.

## Opthalmic Suspensions :

These are the suspensions in the form of eye drops. Its particle size should be very fine, nor irritating, sterile and isotonic.

## On the basis of proportion of solid Particles

- Dilute Suspensions
- Concentrated Suspensions

## Dilute Suspensions :

The ~~size of solid~~ range of solid particles in dilute suspensions is 2 - 10 % per volume. example : Cortisone Acetate Suspension.

## Concentrated Suspensions :

The range of solid partides in concentrated suspensions is 50 % per volume. example : Zinc oxide suspensions.

## On the basis of electrokinetic nature of solid Particles

- Flocculated Suspension
- Deflocculated Suspension

## Advantages of Suspensions

- Suspension improves the chemical stability of certain drugs such as procaine, penicillin G
- Easy masking of unpleasant taste.
- Used for both internal and external preparations
- Drugs in the suspension form shows higher rate of bioavailibility. (Solution > Suspension > Capsule > tablet)

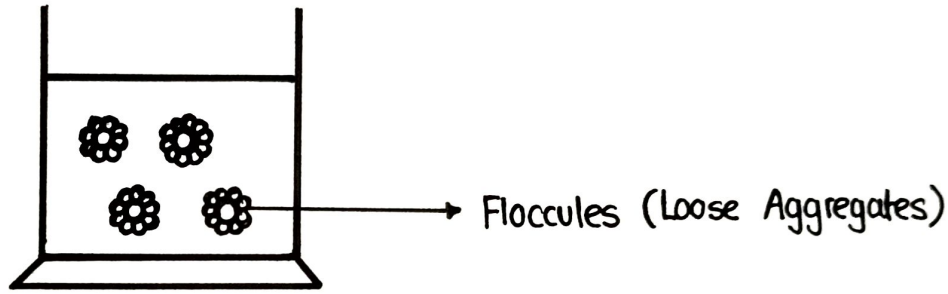
## Disadvantages of Suspensions

- Require shaking before use
- Inaccuracy of dose
- Packing, handling and storage is difficult
- Sedimentation of particles.

# Flocculated And Defllocculated Suspensions

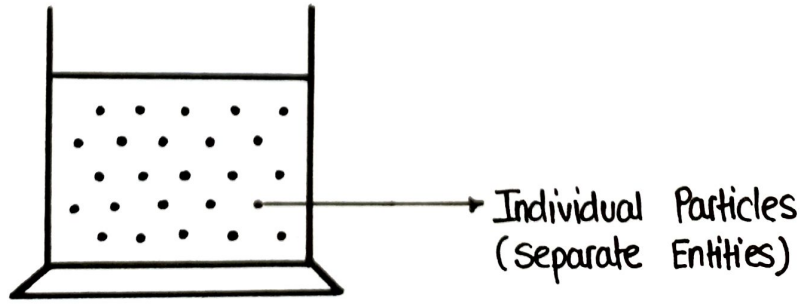
## Flocculated Suspension

- A flocculated suspension is a suspension in which particles of the suspension has undergone flocculation.
- In flocculated suspension solid particles of dispersed phase combine together and make 'floccules'.
- In flocculated suspension rate of sedimentation is very high due to the heavy size of floccules.




## Deflocculated Suspension

- A deflocculated suspension is a suspension in which no flocculation takes place
- In deflocculated suspension solid particles exist as separate entities.
- In deflocculated suspension rate of sedimentation is slow due to smaller size of dispersed solid particles.



## Sedimentation

Sedimentation is the settling down of solid particles of suspension to the bottom of the liquid (suspension)

## Difference between Flocculated and Deflocculated Suspension

| Flocculated Suspensions | Deflocculated Suspensions |
|---|---|
| • Particles form loose aggregates<br>• Rate of sedimentation is high<br>• Sediment form rapidly<br>• Doesn't form hard cake<br>• Sediment easily redispersed<br>• Unpleasant appearance<br>• More stable Pharmaceutical Suspension | • Particles exist as separate entities<br>• Rate of sedimentation is Low<br>• Sediment form slowly<br>• Form hard cake<br>• Sediment difficultly redispersed<br>• Pleasant appearance<br>• Very less stable Pharmaceutical Suspension |

**Colouring Agents** : Tartarazine , Erythrosine

**Flavouring Agents** : Vanila, Strawberry, Orange

**Sweetening Agents** : Sucrose , Saccharin

## Method of Preparation

- First convert the solid particles in fine powder form
- Take insoluble powder in a mortar
- Add sufficient liquid / vehicle to produce smooth paste
- Now add any non-volatile solid ingredient , if required.
- Add any volatile solid ingredient , if required .
- Now add other ingredients and mix well
- Transfer the mixture in a measuring cylinder and make up to the required volume by adding sufficient vehicle.

**Packaging** : Thick container with wide mouth

**Storage** : Store in a cool dry place

# Stability Of Suspension

The following stability problems occurs during storage of a suspension :

- Caking
- Cap Locking
- Colour Change
- pH Change
- Rapid Settling of Particles

## Caking

Caking is the formation of hard sediment in deflocculated suspensions Due to small particle size of solid particles, they come very close to each other which leads to a very hard cake formation.

**Prevention** : By adding flocculating agents which prevents hard cake formation by making Floccules

## Cap Locking

Cap locking problem occurs when particles of dispersed phase spreads over the surface of the bottle cap

**Prevention** : By using different vehicles containing sucrose, glucose sorbital etc.

## Colour Change

Light sensitive colour in solvent (liquid phase) maybe changed in the presence of light.

**Prevention** : Can be prevented by keeping the bottle in a dark place.

## pH Change

During long storage the acidity or basicity of suspension can be increase or decrease which leads to the pH change.

**Prevention** : By adding buffering agents, which helps to maintain pH of the suspension.

## Rapid Settling of Particles

Due to large particle size of flocculated suspension, the particles of the suspension very rapidly settle down at the bottom of liquid (continuous phase)

**Prevention** : By adding viscosity enhancing agents, rapid settling can be prevented.

# THANK YOU

FOR CHOOSING IMPERFECT PHARMACY AS YOUR STUDY PARTNER

IMPERFECT PHARMACY

## JOIN US ON :

IMPERFECT PHARMACY

IMPERFECT PHARMACY

@IMPERFECTPHARMA

IMPERFECT PHARMACY

@IMPERFECTPHARMACY

IMPERFECT PHARMACY

IMPERFECTPHARMACY@GMAIL.COM