Subject Name: Physical Pharmaceutics –II Module -III

Subject Code: BP 403T

Objectives of the course

- Demonstrate use of physicochemical properties in the formulation development and evaluation of dosage forms.

Learning outcomes

- Students learnt about the properties, nature and general characteristics of coarse particles like emulsion and suspension.

Structure of Module –III BP 403T

Learning Material

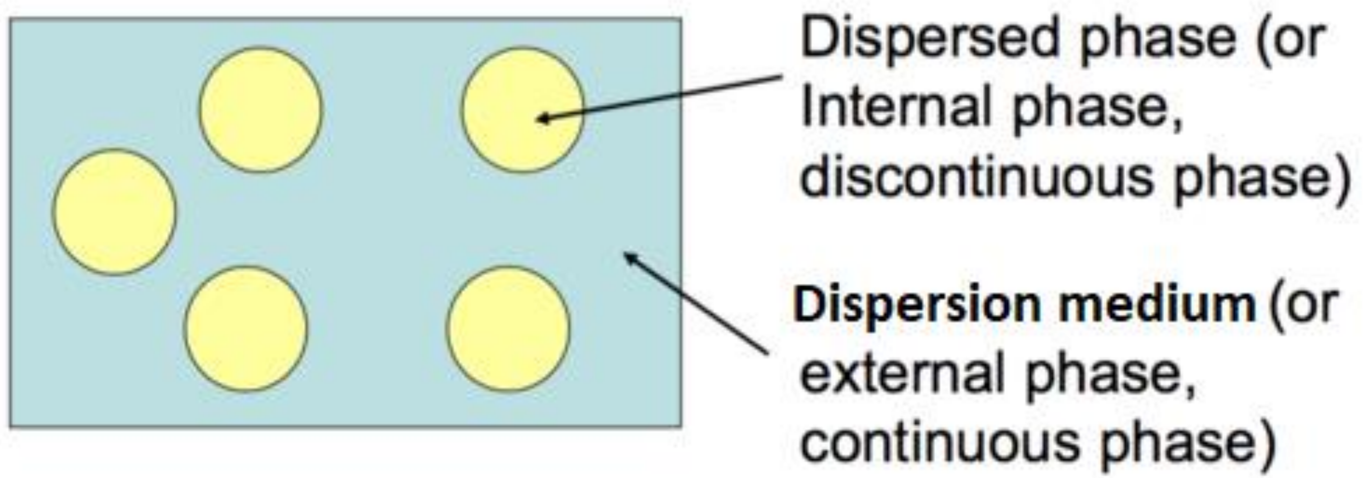
Coarse dispersion-

- 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.

Suspension

Definition

- Suspension is heterogeneous system and Suspension is biphasic liquid dosage form.
- Dispersion medium is liquid and dispersion medium is solid (suspension)



Features desired in Pharmaceutical Suspension

- Particles should settle slowly and should be readily re-dispersed upon shaking of the container.
- The particle size of the suspensoid should remain fairly constant throughout long periods of undisturbed standing.
- The suspension should pour readily and evenly from its container.

Applications of suspensions

- Drugs which degrade in aqueous solution may be suspended in a **non-aqueous** phase. eg. Tetracycline hydrochloride is suspended in a fractionated coconut oil for ophthalmic use.
- Lotions containing insoluble solids are formulated to leave a **thin coating** of medicament on the skin. As the vehicle evaporates, it gives a cooling effect and leaves the solid behind.eg calamine lotion and sulphur lotion compound.
- Bulky, **insoluble powders** can be formulated as a suspension so that they are easier to take eg Kaolin or chalk.

Advantages of suspensions

- Suspension can improve chemical stability of certain drug. E.g. Procaine penicillin G
- Drug in suspension exhibits higher rate of bioavailability than other dosage forms. bioavailability is in following order,
- **Solution > Suspension > Capsule > Compressed Tablet > Coated tablet**

- Duration and onset of action can be controlled. E.g. Protamine Zinc-Insulin suspension
- Suspension can mask the unpleasant/ bitter taste of drug. E.g. Chloramphenicol palmitate

Disadvantages of suspension

- Physical stability, sedimentation and compaction can causes problems.
- It is bulky, therefore sufficient care must be taken during handling and transport.
- It is difficult to formulate
- Uniform and accurate dose can not be achieved unless suspension are packed in unit dosage form

Diffusible / in diffusible solid

1. DIFFUSIBLE SOLIDS– these **sediment sufficiently slowly** to enable satisfactory dose removal after redispersion. eg. <u>Light kaoline</u>, magnesium tricilicate

2. INDIFFUSIBLE SOLIDS- eg. sulphadimidine and <u>chalk</u>. These **sediment too rapidly** and require the addition of other materials to reduce sedimentation rate to an acceptable level.

Content

- Wetting phenomenon,
- Particle-particle interactions, DLVO theory,
- Flocculated and deflocculated systems,
- Schulze Hardy rule,
- Sedimentation in suspensions,
- Ostwald ripening and crystal factors,
- Rheology

Wetting phenomenon

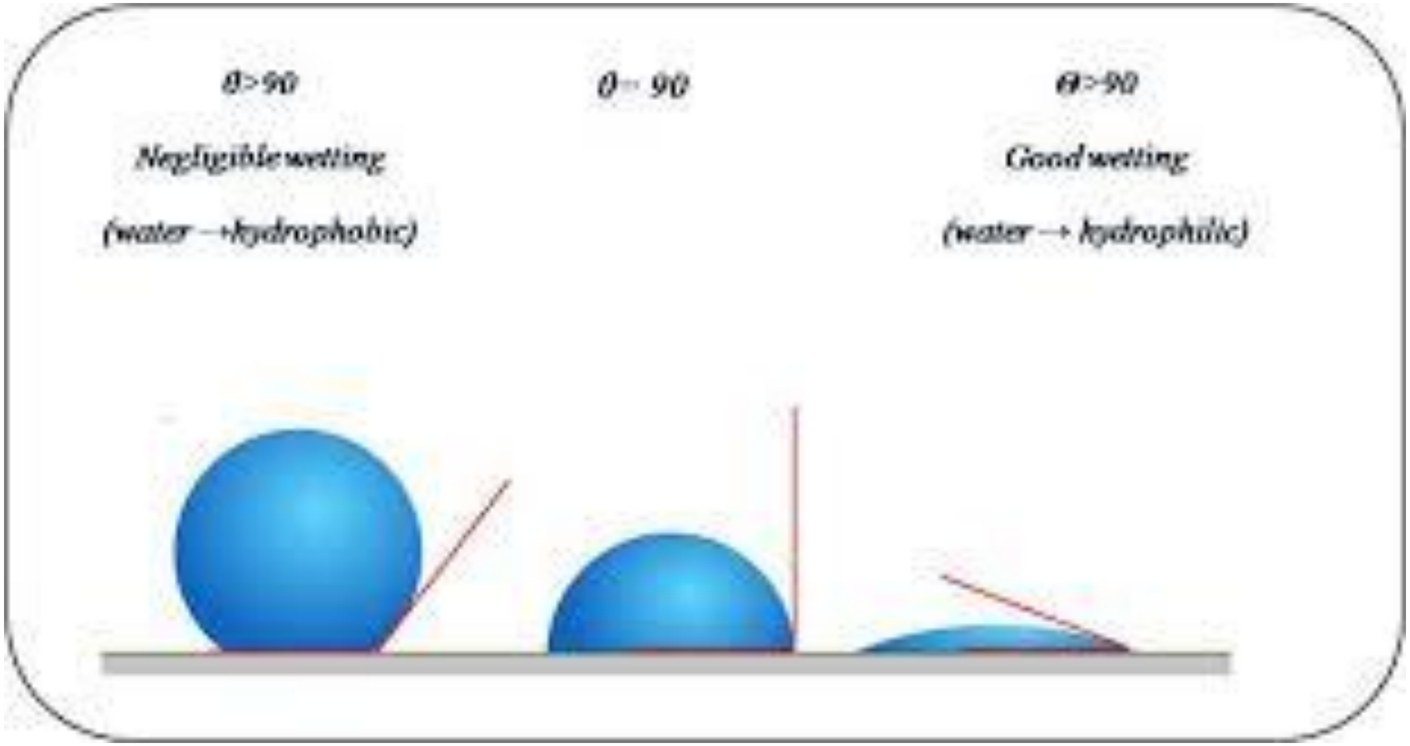
- Hydrophilic solid
- Hydrophobic solid

Wetting phenomenon

Lyophilic (wetting)	**Lyophobic (non-wetting)**
• Not sensitive to electrolytes in medium	• Sensitive to electrolytes in medium
• Readily wetable	• No aggregation

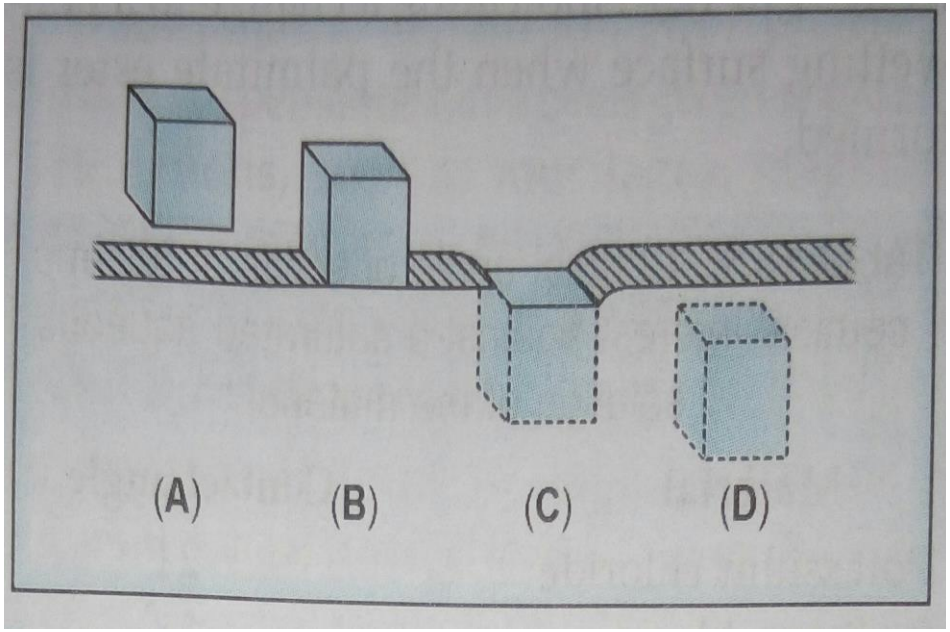
Wetting phenomenon

- Contact Angle.



Steps of wetting

- Adhesional Wetting
- Immersional
- Spreading



Strategies for wetting of hydrophobic solids

- Surfactant
- Hydrophilic polymers
- Water insoluble hydrophilic material (bentonite)

Methods to estimate wetting property of wetting agent

- **Wet point method**
  - Amount of vehicle needed to just wet given amount of solid powder
- **Flow point method**
  - Amount of liquid needed to produce pourability
  - Unit (mL/100gm)

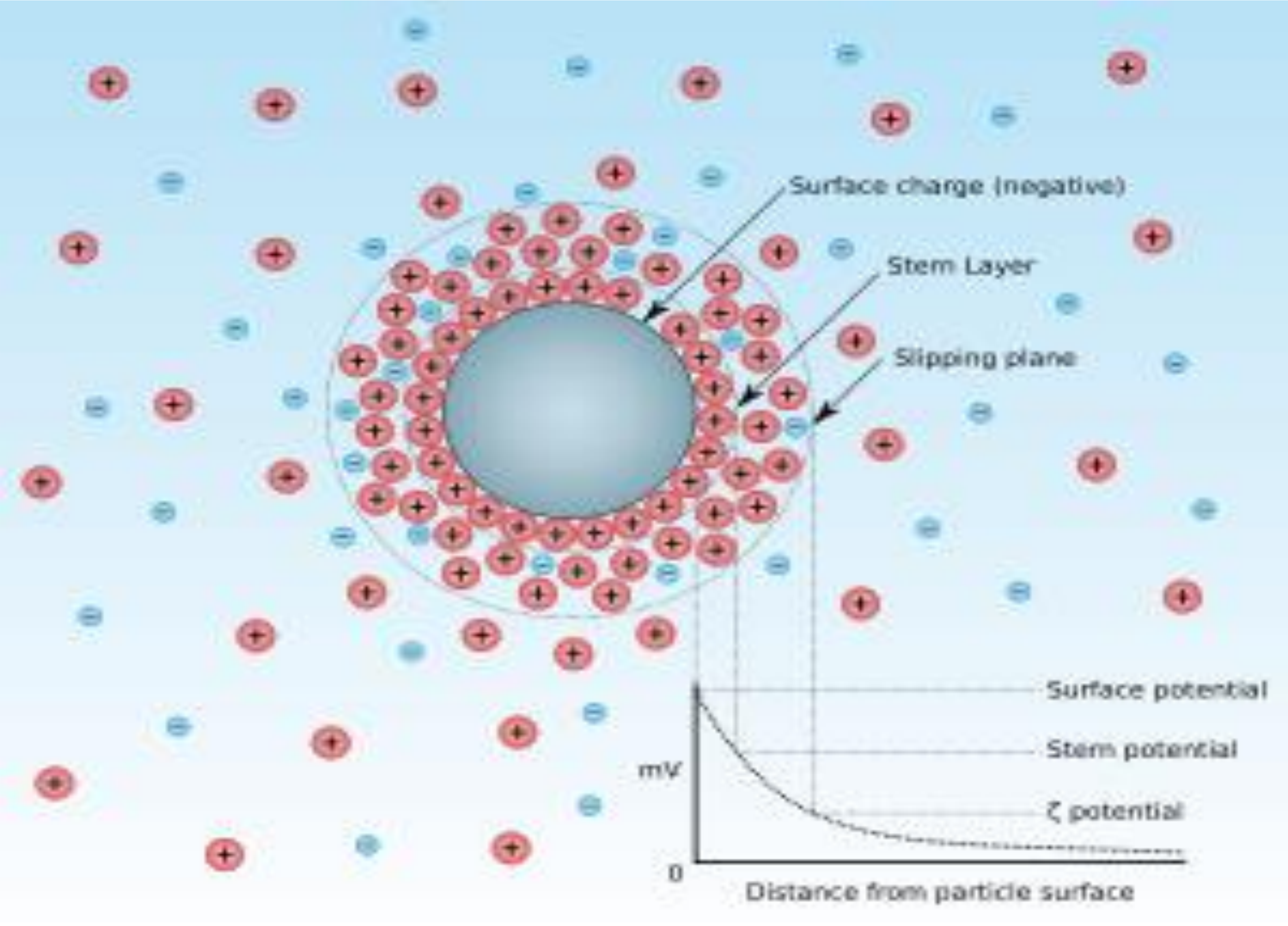
Particle-particle interactions (DLVO Theory)

- Regardless of the specific mechanism, the particles will bear either positive or negative charges.
- Source of the charge on particle may arise from

  - ionizable groups on the surfaces or
  - adsorption of ions from the surrounding solution

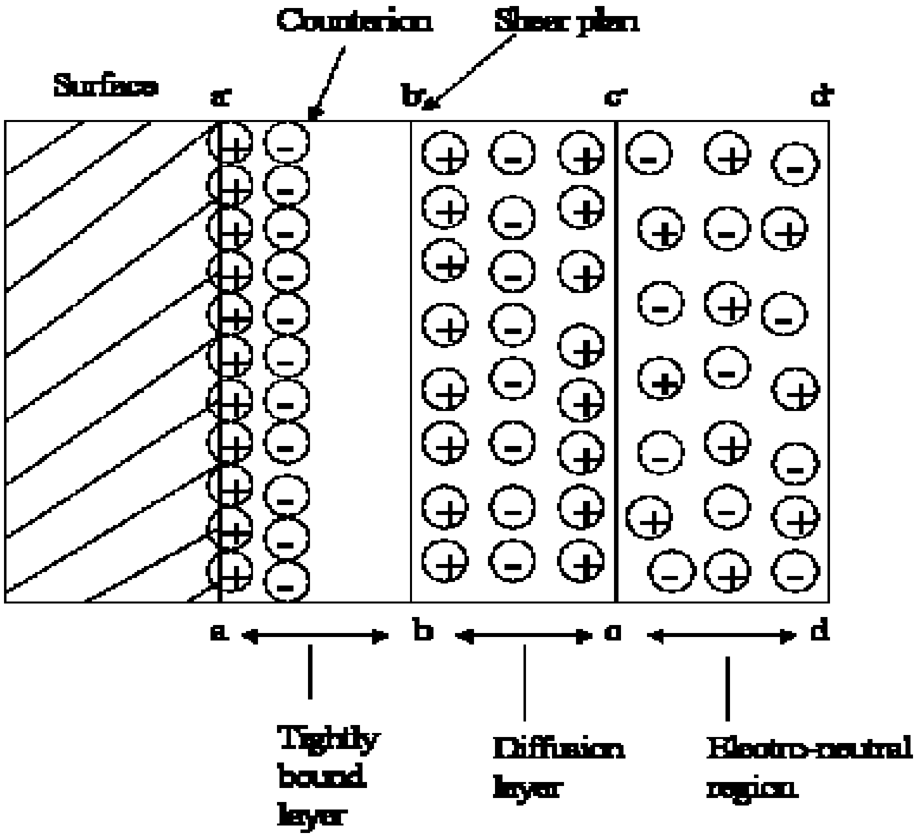
Particle-particle interactions (Interparticle forces)

- Van der Waals attractive forces
- Electrostatic repulsive force → *Overlapping of diffusion layer.*
- Repulsive forces due to hydration → *Structuring of water at interface (Physical barrier)*
- Steric repulsive force → *Because of adsorbent (Physical barrier)*


Surface charge (negative)
Stem Layer
Slipping plane
Surface potential
Stem potential
mV
ζ potential
0
Distance from particle surface

Particle-particle interactions (Zeta Potential)

Zeta potential is defined as the difference in potential between the surface of the tightly bound layer (shear plane) and electroneutral region of the solution.

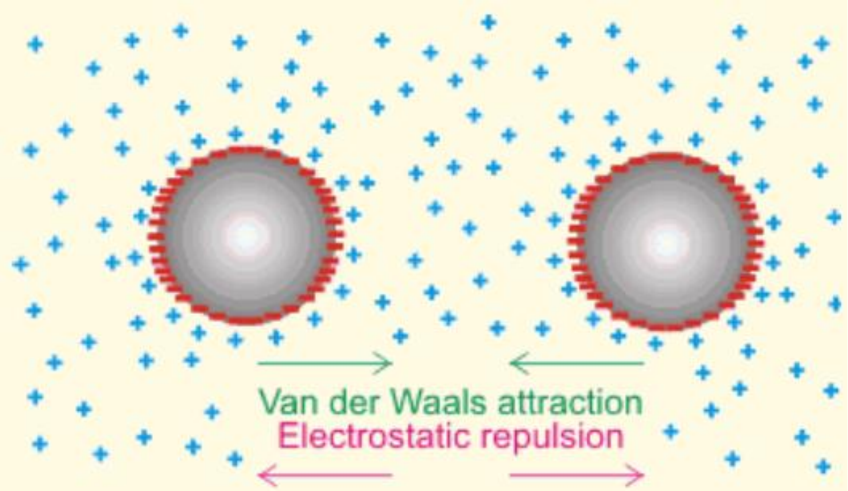


Particle-particle interactions

- Thus electrostatic repulsion set up between adjacent particles preventing them from adhering to one another.
- Accordingly deflocculation occurs.
- Solvation of particle surfaces also helps to prevent particles coming together (Physical Barrier)
- Flocculation and deflocculation mechanism dependent on the presence of surface electrical charges and the distribution of ions around the particles

Particle-particle interactions
(Attractive forces vs Repulsive forces)

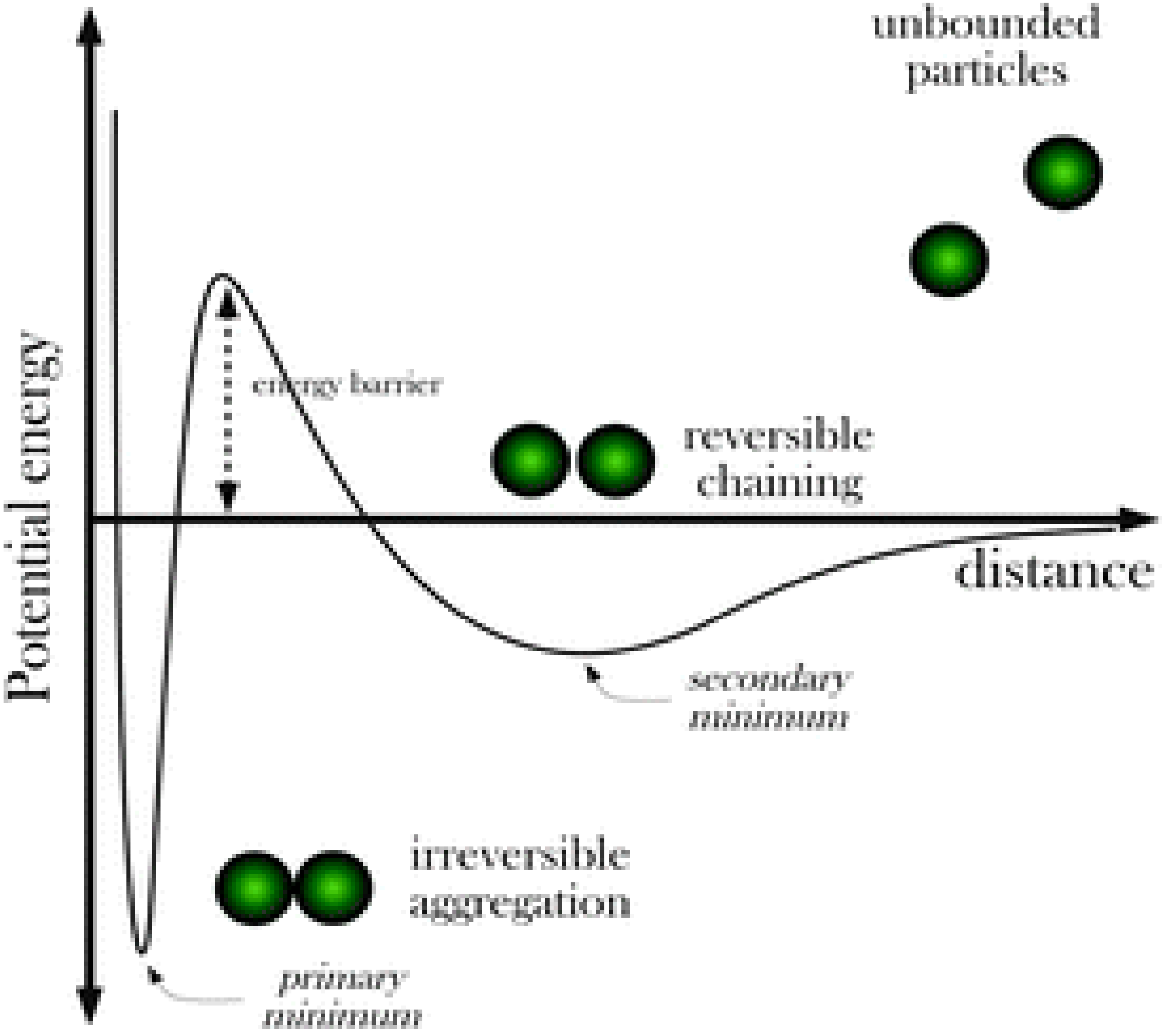
- At high electrolyte conc → Attractive force predominate and cause *coagulation*



- At low electrolyte conc → Repulsive force predominate

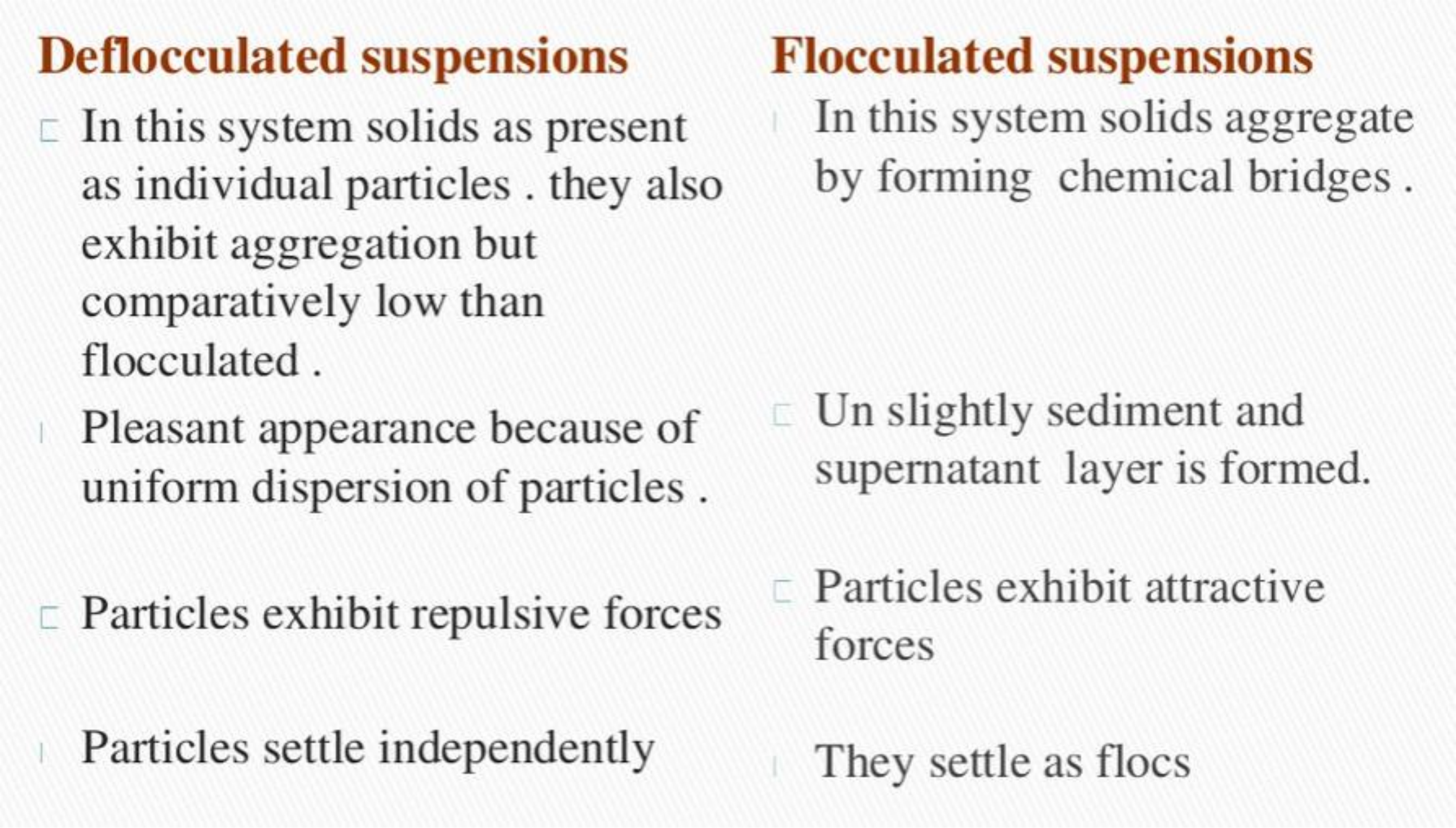
Flocculation curve/Secondary minimum
DLVO theory

Force of
repulsion



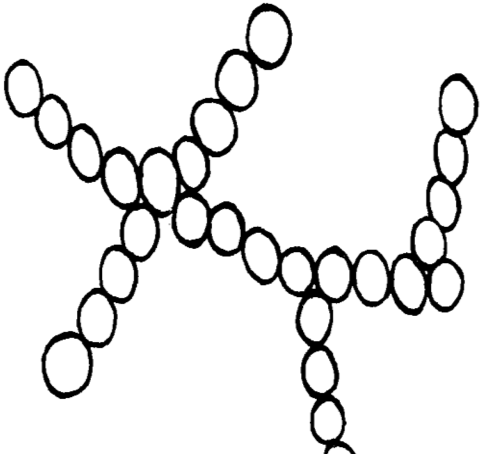
Force of
attraction

Deflocculated vs Flocculated Suspension

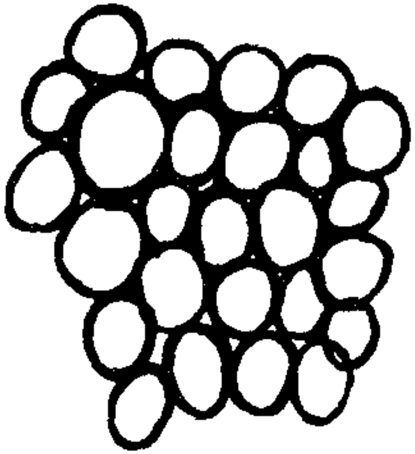


Deflocculated suspensions	**Flocculated suspensions**
In this system solids as present as individual particles . they also exhibit aggregation but comparatively low than flocculated .	In this system solids aggregate by forming chemical bridges .
Pleasant appearance because of uniform dispersion of particles .	Un slightly sediment and supernatant layer is formed.
Particles exhibit repulsive forces	Particles exhibit attractive forces
Particles settle independently	They settle as flocs

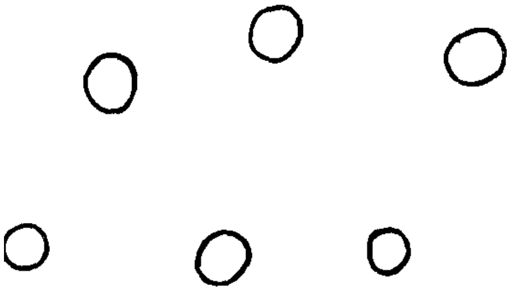
Types of suspension aggregates



Open Network aggregate



Close network aggregate



Deflocculated

Factors affecting repulsion between particles which influences hydration of particles

- Electric (diffuse) double layer and its thickness
- Ionic strength (ionic concentration)
- Valency, size of ion on surface and in electric double layer

Swamping

- Increase in ionic strength (concentration of electrolytes) decreases thickness of electric double layer .. This effect is known as swamping
- Swamping encourage aggregation

Schulze Hardy rule

- Specific adsorption of ion on solid neutralize surface charge and allow aggregation
- Concentration of ion need to attain optimum aggregation of particles depend upon type of interacting ion.
- Addition of more concentration beyond limit causes reversal of charge → aggregation→ causes caking
- This effect is explained by ‘Schulze Hardy rule’

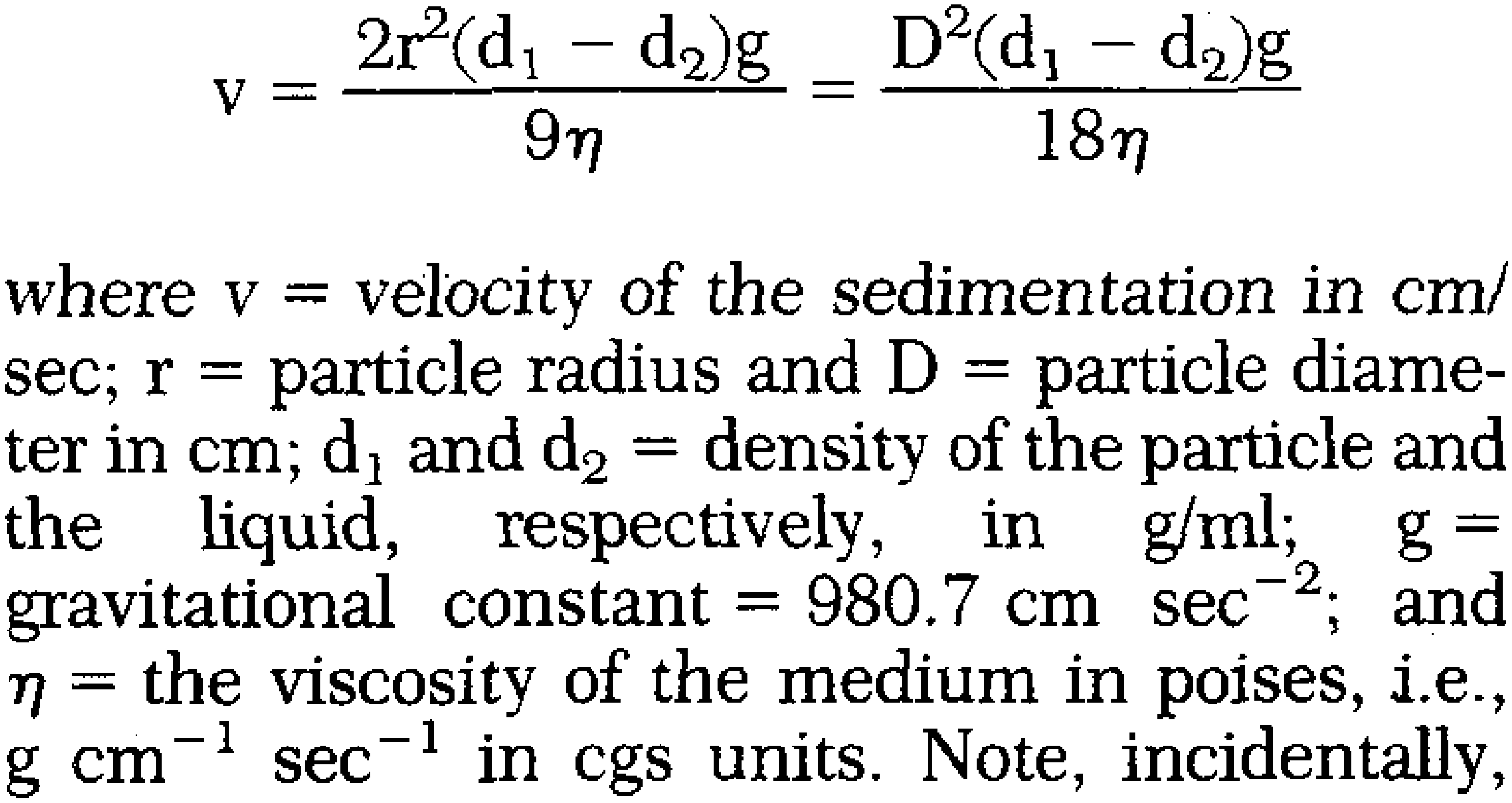
Schulze Hardy Rule

- Statement "valency of ion having charge opposit to that of hydrophobic particle appears to determine the effectiveness of the electrolyte in aggregating the particle"
- Aggregating value of ion increase with valency of ion
- $Al^{+++} >> Fe^{++} >> Na^{+}$
- 1000 >>> 10 >> 1

Schulze Hardy Rule

- This rule is valid only for system in which there is no interaction between electrolyte and ion of double layer of particle surface.
- Influence of valency of ion on aggregation of lyophobic particle can be correlated to → Zeta potential and Sedimentation volume
- *Hofmeister of lyotropic rule* apply to hydrophilic particle

Sedimentation
(Stoke's Law)



$$v = \frac{2r^2(d_1 - d_2)g}{9\eta} = \frac{D^2(d_1 - d_2)g}{18\eta}$$

*where v = velocity of the sedimentation in cm/*sec; r = particle radius and D = particle diameter in cm; d_1 and d_2 = density of the particle and the liquid, respectively, in g/ml; g = gravitational constant = 980.7 cm $\sec^{-2}$; and η = the viscosity of the medium in poises, i.e., g cm^{-1} sec^{-1} in cgs units. Note, incidentally,

Sedimentation

- This is a phenomenon which occurs in dispersed system where the dispersed particles settle to the bottom of the container.
- This occurs because the particles are too large to remain permanently suspended in the vehicle.
- Therefore suitable suspending agents are added to retard this process.

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Sedimentation
(Stoke's Law of sedimentation)

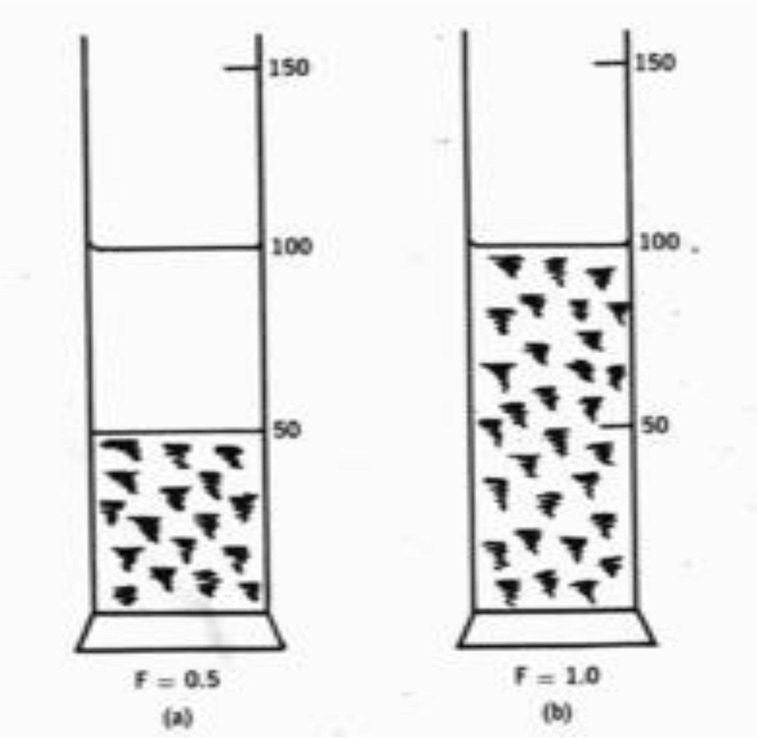
$$\mathbf{V = D^2 (\rho_1 - \rho_2)/18\eta}$$

- V= Velocity of sedimentation
- D= Diameter of particle
- ρ_1 and ρ_2 =Density of particle and liquid
- η = viscosity of liquid

- Pharmaceutical suspension containing less than 2% (w/v) of solid follow Stoke's Law.
- If solid content increase viscosity increases

Sedimentation Volume

- Sedimentation volume is ratio of ultimate height of sediment to total height of suspension when sedimentation occur in standard condition
- $S=H_u/H_o$
- Higher value expected.



Oswald Ripening
&
Crystal effect

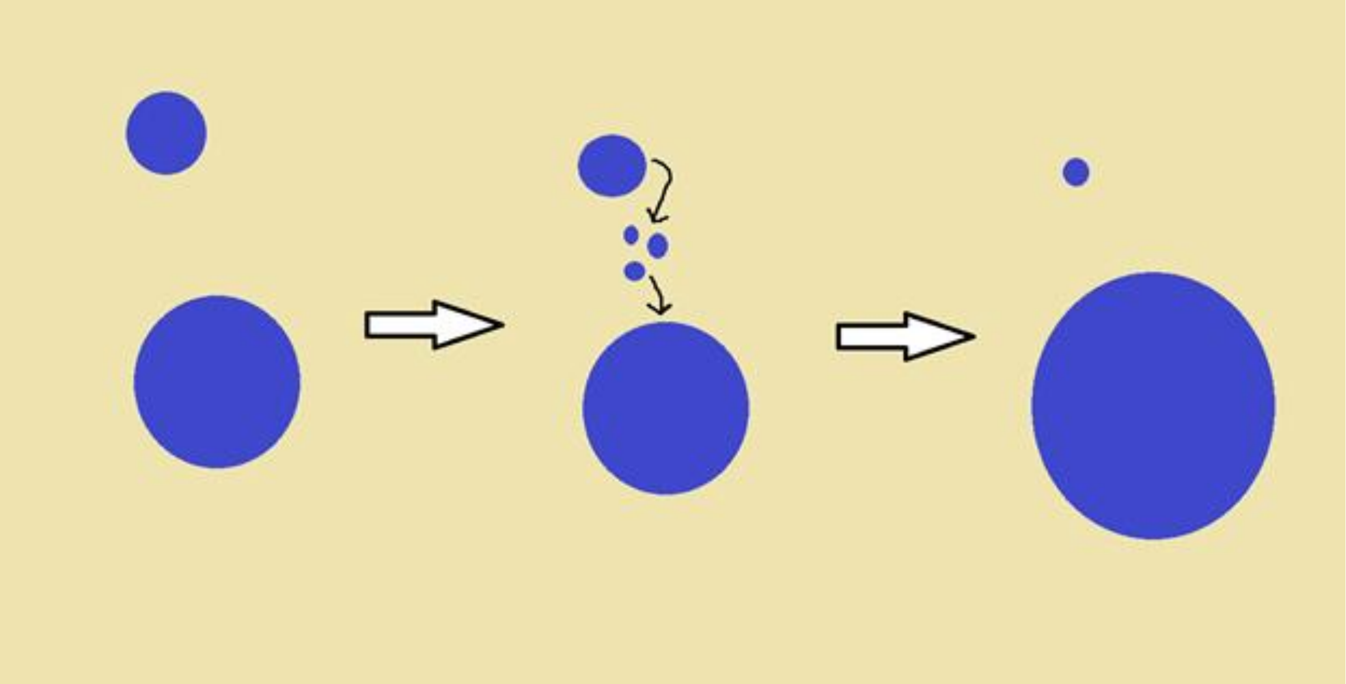
Oswald Ripening

- **Solubility** of large crystal is less than that of smaller crystals
- It is because of **more surface energy** per unit mass on smaller crystals.
- Smaller crystals are in a state of unstable equilibrium in a supersaturated solution.
- As a result **larger crystals grow until the small crystals disappear**.

What is Ostwald ripening?

- This is a spontaneous process that occurs because larger crystals are more **energetically (thermodynamically) favored** than smaller crystals.
- Large crystals, have lower energy state.
- While the formation of many small crystals is **kinetically favored.**
- Small crystals have a larger specific surface area (surface area to volume ratio)
- Thus, many **small crystals** will attain a lower energy state by getting transformed into large crystals and this is Ostwald ripening.

Ostwald Ripening



Larger crystals are more stable than smaller crystals – the energy of a system will naturally tend towards the formation of larger crystals at the expense of smaller ones

Classification of suspensions

- **Based On General Classes**
  - Oral suspension
  - Externally applied suspension
  - Parenteral suspension
- **Based On Proportion Of Solid Particles**
  - Dilute suspension (2 to10%w/v solid)
  - Concentrated suspension (50%w/v solid)
- **Based On Electrokinetic Nature Of Solid Particles**
  - Flocculated suspension
  - Deflocculated suspension
- **Based On Size Of Solid Particles**
  - Colloidal suspension (< 1 micron)
  - Coarse suspension (>1 micron)
  - Nano suspension (10 ng)

Rheology

- **Viscosity is a measure of a fluid's resistance to flow**.
- It describes the internal friction of a moving fluid.
- A fluid with large viscosity resists motion because its molecular makeup gives it a lot of **internal friction**.
- A fluid with **low** viscosity **flows easily** because its molecular makeup results in very little friction when it is in motion.

Rheograms

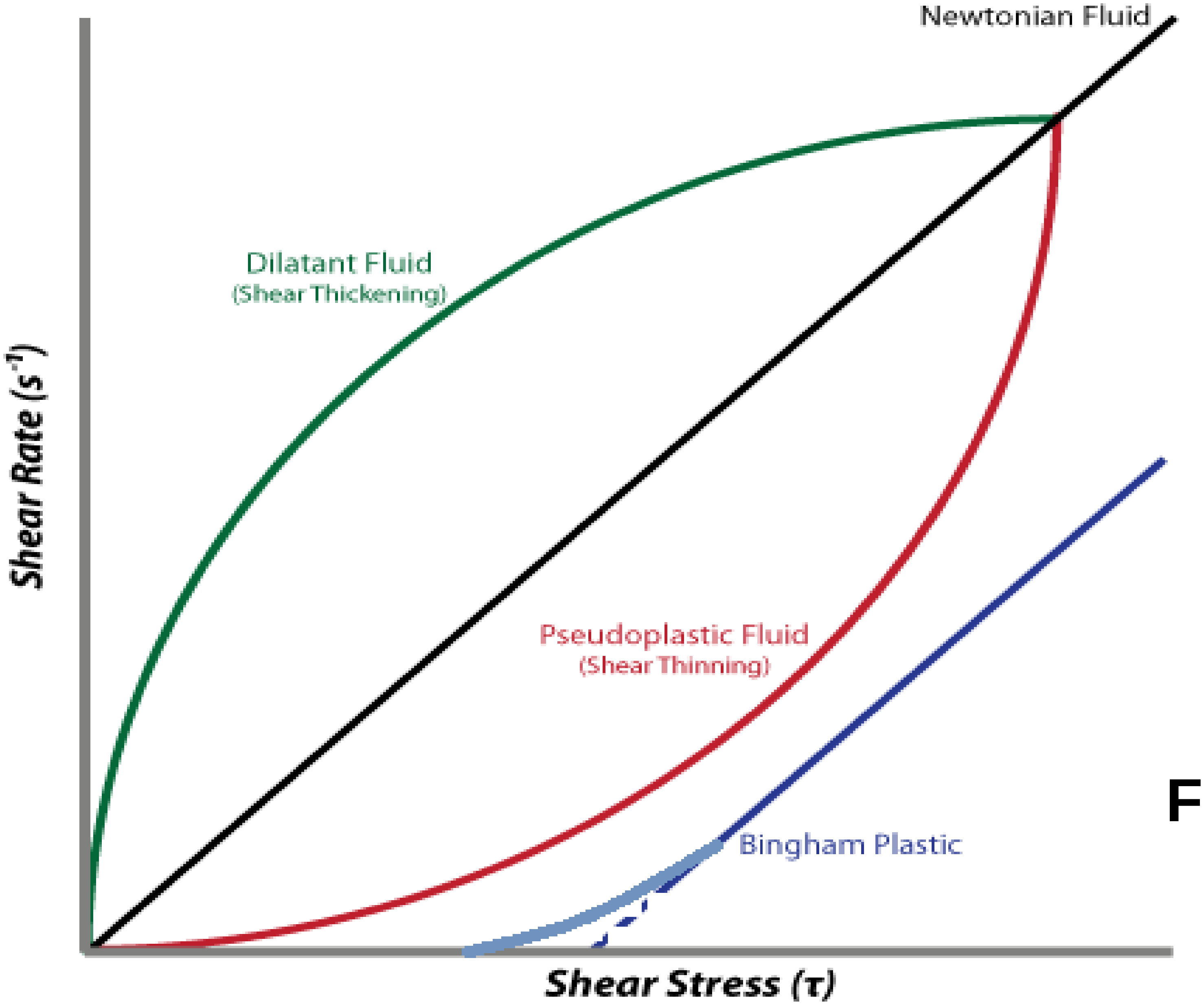


Fig. 2

Rheology

Desirable

- ***Thixotrophy*** is a phenomenon or property exhibited by highly floculated preparation in which a preparation is sem-solid at rest (in the absence of shearing forces) but becomes so fluid when tapped or shaken and resumes its original structure after only a few minutes of rest.
- A thixotropic suspension is the one which is viscous during storage but loses consistency and **become fluid upon shaking.**
- A well-formulated thixotropic suspension would remain fluid long enough for the easy dispense of a dose but would slowly regain its original viscosity within a short time.

Rheology

Undesirable

- Undesirable because of poor stability
- Pseudo plastic (shear thinning with no yield value)
- Dilatant
- Rheopexy (viscosity increases with time)

Rheology method

- To study structure achieved on storage
- T-bar spindle with helipath
- T-bar continually descend to study undisturbed sample
- Dial reading vs no. of turns of spindle

Formulation of suspensions
(Excipients & additives)

- The formulation of a suspension depends on whether the suspension is flocculated or deflocculated.

- Two approaches are commonly involved

  1. Use of structured vehicle
  2. Use of controlled flocculation

1) Suspending agents

(Structured vehicle)

- Suspending agent form film around particle decrease interparticle attraction and reduces the sedimentation of particles
- It is used only for deflocculated suspensions.

- Suspending agent such as **hydrophilic colloids** which form colloidal dispersion with Water and increase the viscosity of the continuous phase.

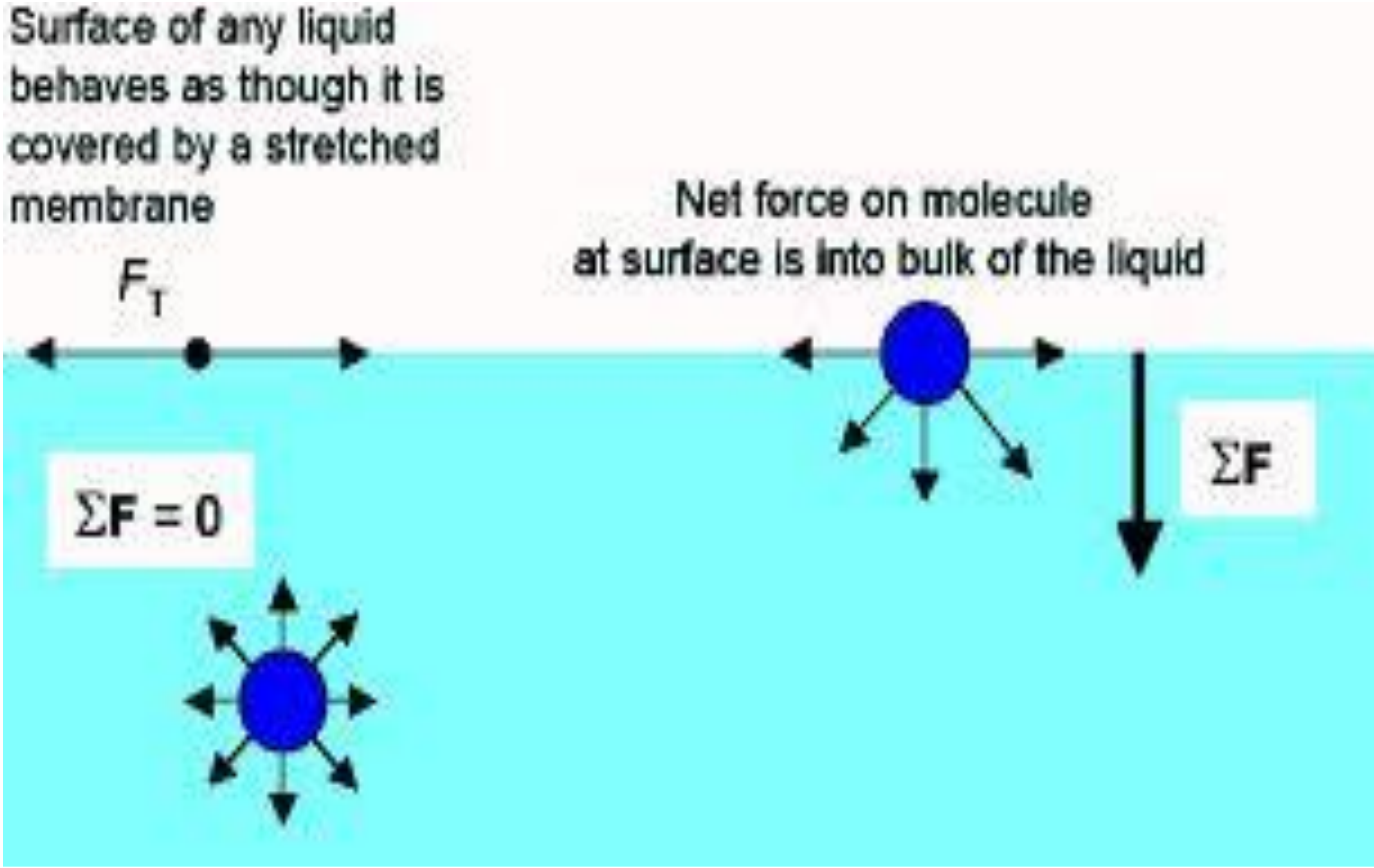
- Most suspending agents perform two functions i.e. besides **acting as a suspending agent** they also **imparts viscosity to the solution.**

- Preferred suspending agents are those that give **thixotropy** to the media such as Xanthan gum, Carageenan

Eg. Methylcellulose, Hydroxyethylcellulose, Carboxymethylcellulose, Microcrystalline cellulose, Acacia, Tragacanth, Carbomer, Gelatin

Surface tension

"Surface tension is a **contractive tendency** of the surface of a fluid that allows it to resist to an external force."



Surface of any liquid behaves as though it is covered by a stretched membrane

Net force on molecule at surface is into bulk of the liquid

2) Wetting Agents

Hydrophilic materials are easily wetted by water while hydrophobic materials are not.

- However hydrophobic materials are not easily wetted by Water (polar liquids)

- The extent of wetting by water is dependent on the **hydrophilicity** of the materials.

- If the material is hydrophobic then it is difficulty to wet by water.

3) Surfactants

Surfactants decrease the interfacial tension between drug particles and liquid thus liquid is penetrated in the pores of drug particle displacing air from them and thus ensures wetting.

- ➢ Generally, we use **non-ionic surfactants**

- ➢**Polysorbate 80** is most widely used due to its following advantages

  - It is non-ionic so no change in pH of medium
  - No toxicity. Safe for internal use.

4) Dispersion medium (Solvents)

The commonly used solvents used are **water , glycerin, polyethylene glycol and polypropylene glycol.**

- The mechanism by which they provide wetting is that they are **miscible with water and reduce liquid air interfacial tension.**

- Liquid penetrates in individual particle and facilitates wetting.

5) Osmotic Agents

They are added to produce **osmotic pressure comparable to biological fluids** when suspension is to be intended for ophthalmic or injectable preparation.

- Most commonly used osmotic agents are

- dextrose,
- mannitol
- sorbitol.
- sodium chloride,
- sodium sulfate
- glycerol.

6) Preservatives

- Naturally occurring suspending agents such as tragacanth, acacia, xanthan gum are susceptible to microbial contamination.

- This leads to:
  - loss in suspending activity of suspending agents,
  - loss of color, flavor and odor,
  - change in elegance etc.

Name of preservatives	Concentration range
Propylene glycol	5-10%
Disodium EDTA	**0.1%**
Benzalkonium chloride	**0.01-0.02%**
Benzoic acid	0.1%
Butyl paraben	0.006-0.05% oral suspension 0.02-0.4% topical formulation

7) Flavoring And Coloring Agents

- They are added to increase patient acceptance.

- Only **sweetening agent** are not capable of complete taste masking of unpleasant drugs therefore, a **flavoring agents are incorporated**

- E.g.

Mint
Anise oil
Benzaldehyde
Ginger
Glucose
Glycerin
Sarsaparilla syrup
Spearmint oil
Thyme oil

8) Coloring agents_

Colors are obtained from natural or synthetic sources.

- Plant colors are most widely used for oral suspension.

- The **synthetic dyes should be used within range of(0.0005 % to 0.001%)**
- Color aids in identification of the product.

- Brilliant blue (blue)
- Indigo carmine(blue)
- Amaranth (red)
- **Tartarazine (yellow)**

9) Sweetening Agents

They are used for taste masking of bitter drug particles.

Bulk sweeteners

Sugars such as Sucrose, **xylose, ribose, glucose, mannose.**

Sugar alcohols such as **sorbitol, xylitol, mannitol**

A bulk sweeteners is used at **concentration of 15-70 %**

Artificial sweetening agents

Sodium cyclamate, Sodium saccharin, Aspartame

10) Humectants

Humectants absorb moisture and prevent degradation of API by moisture.

- Examples of humectants most commonly used in suspensions are propylene glycol , glycerol

- Total quantity of humectants should be **between 0-10 % w/w.**

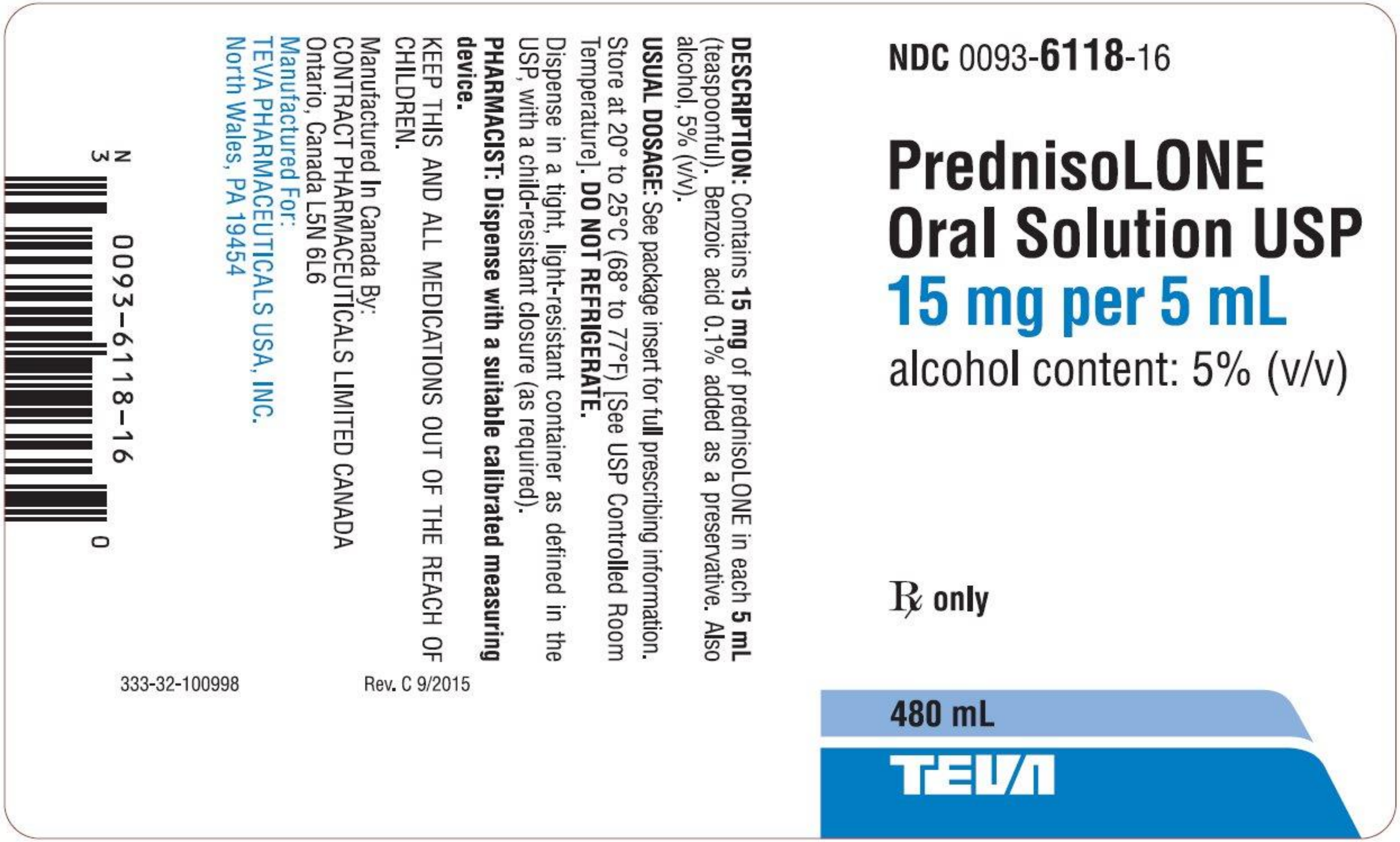
11) Antioxidant

Ascorbic acid derivatives such as **ascorbic acid, erythorbic acid,**

- Thiol derivatives such as **thio glycerol, cytosine, acetylcysteine,**
-
- Tocopherols
- Butylated hydroxy anisole(BHA)
- Butylated hydroxytoluene (BHT)
- Sodium bi sulfite,

Wetting agents	They are added to disperse solids in continuous liquid phase.
Flocculating agents	They are added to floc the drug particles
Thickeners	They are added to increase the viscosity of suspension.
Buffers and pH adjusting agents	They are added to stabilize the suspension to a desired pH range.
Osmotic agents	They are added to adjust osmotic pressure comparable to biological fluid.
Coloring agents	They are added to impart desired color to suspension and improve elegance.
Preservatives	They are added to prevent microbial growth.
External liquid vehicle	They are added to construct structure of the final suspension.

Label



NDC 0093-**6118**-16

PrednisoLONE
Oral Solution USP
15 mg per 5 mL
alcohol content: 5% (v/v)

℞ only

480 mL

TEVA

DESCRIPTION: Contains **15 mg** of prednisoLONE in each **5 mL** (teaspoonful). Benzoic acid 0.1% added as a preservative. Also alcohol, 5% (v/v).

USUAL DOSAGE: See package insert for full prescribing information.

Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature]. **DO NOT REFRIGERATE.**

Dispense in a tight, light-resistant container as defined in the USP, with a child-resistant closure (as required).

PHARMACIST: Dispense with a suitable calibrated measuring device.

KEEP THIS AND ALL MEDICATIONS OUT OF THE REACH OF CHILDREN.

Manufactured In Canada By:
CONTRACT PHARMACEUTICALS LIMITED CANADA
Ontario, Canada L5N 6L6
Manufactured For:
TEVA PHARMACEUTICALS USA, INC.
North Wales, PA 19454

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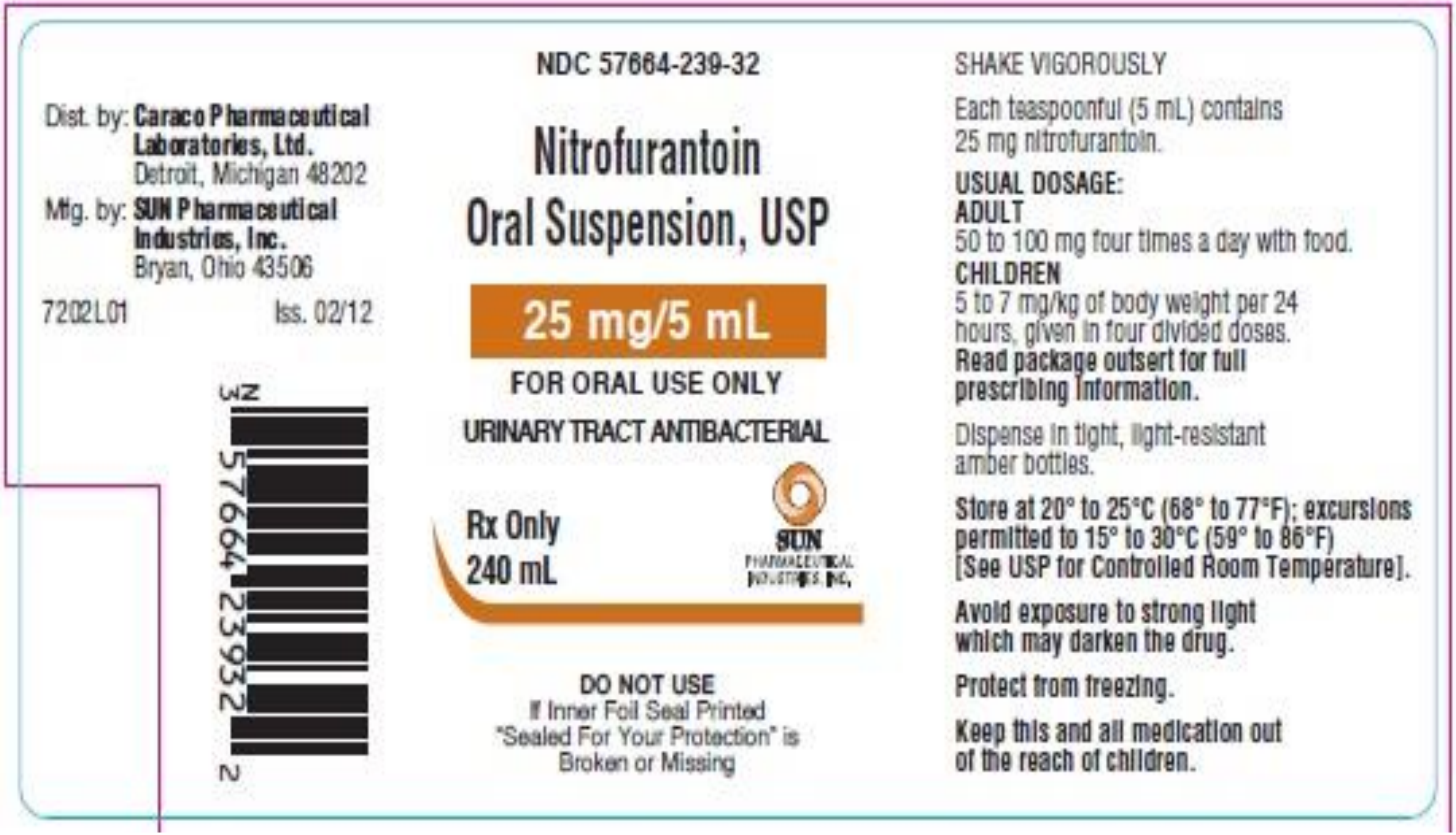
Label



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NDC 57664-239-32

Nitrofurantoin
Oral Suspension, USP

25 mg/5 mL

FOR ORAL USE ONLY

URINARY TRACT ANTIBACTERIAL

Rx Only
240 mL

SUN PHARMACEUTICAL INDUSTRIES, INC.

DO NOT USE
If Inner Foil Seal Printed "Sealed For Your Protection" is Broken or Missing

SHAKE VIGOROUSLY

Each teaspoonful (5 mL) contains 25 mg nitrofurantoin.

USUAL DOSAGE:
ADULT
50 to 100 mg four times a day with food.
CHILDREN
5 to 7 mg/kg of body weight per 24 hours, given in four divided doses.
Read package outsert for full prescribing information.

Dispense in tight, light-resistant amber bottles.

Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [See USP for Controlled Room Temperature].

Avoid exposure to strong light which may darken the drug.

Protect from freezing.

Keep this and all medication out of the reach of children.

EMULSIONS STABILITY

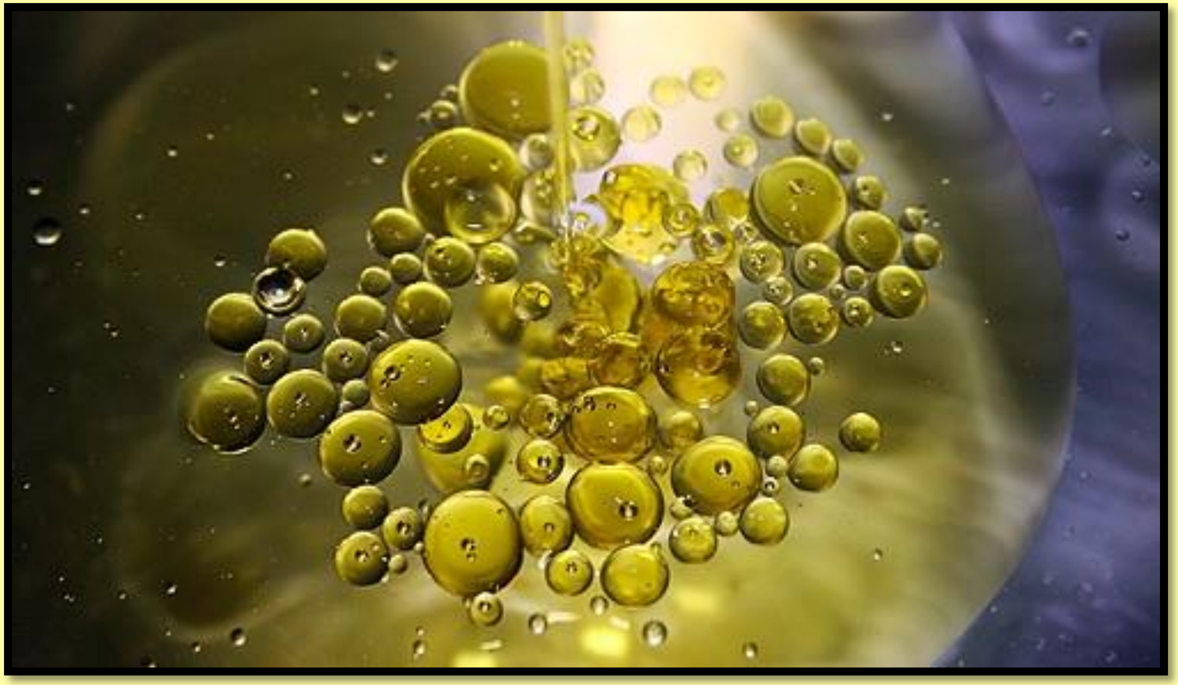


Photo courtesy of Beatriz Bonal on Flickr

Mechanisms of Emulsion Instability

- Emulsion stability – ability to resist changes in its physicochemical properties with time.

Mechanisms of emulsion breakdown:

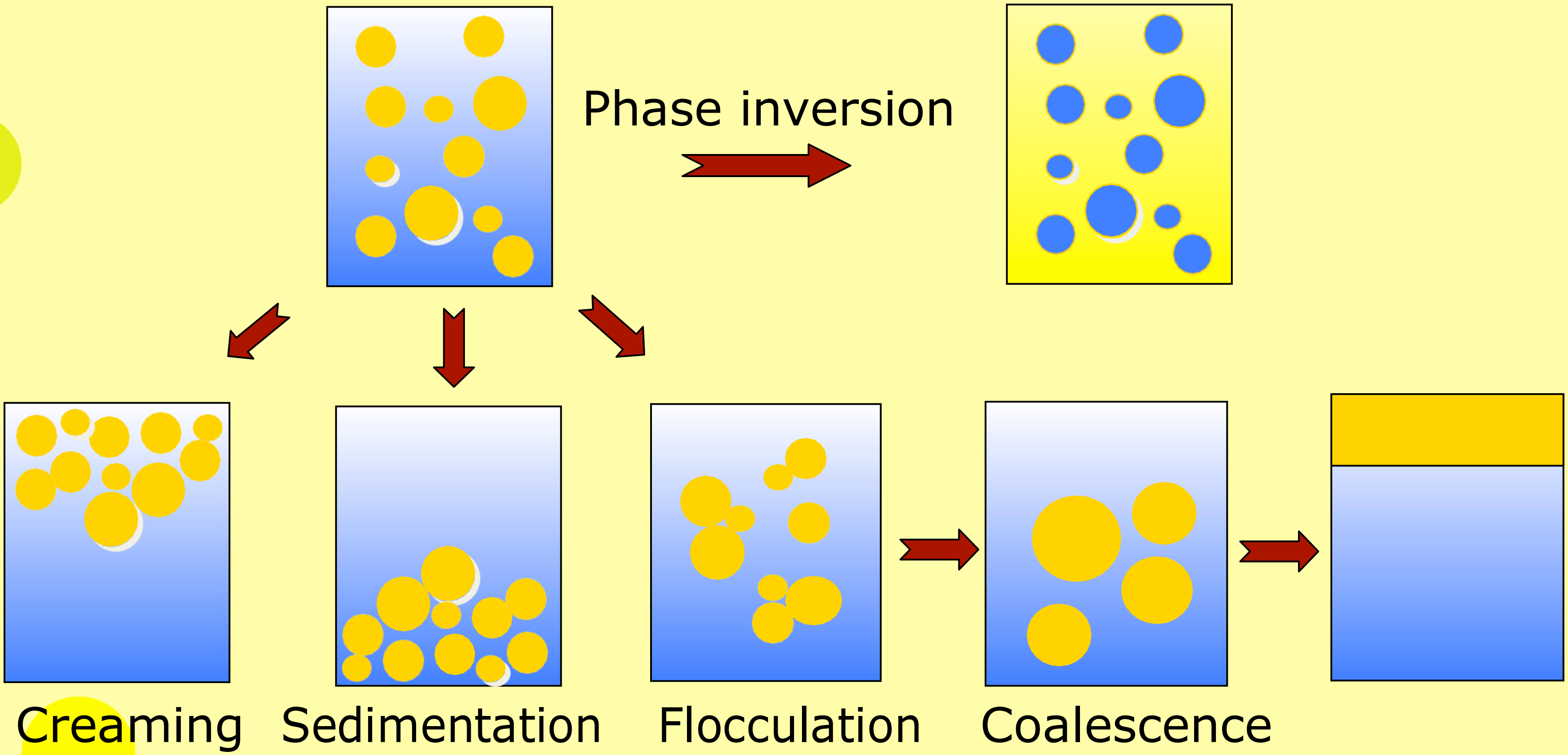
- Creaming – the process in which droplets move upwards (droplets density < density of continuous phase)
- Sedimentation - the process in which droplets move downwards (droplets density > density of continuous phase)

Mechanisms of Emulsion Instability

Mechanisms of emulsion breakdown (..cont'):

- Flocculation – the process in which two or more droplets "stick" together to form an aggregate (but the droplets still retain their individual integrity)
- Coalescence - the process in which two or more droplets merge together to form a single larger droplet.
- Phase inversion – the process in which o/w emulsion changes to w/o emulsion, or vice versa.

Mechanisms of Emulsion Instability



Phase inversion

Creaming

Sedimentation

Flocculation

Coalescence

Forces between colloidal particles

- Types of electrostatic (interactive/repulsive) forces
- DLVO theory
- Electrical double layer
- Zeta potential (what it is, its significance, how to measure)
- Effect of ionic strength & pH

INTERACTIONS BETWEEN DISPERSED DROPLETS

- The effects of the intermolecular forces on the stability of disperse systems can be described in terms of the forces between the colloidal particles determined by the summation of the intermolecular forces over many molecules.

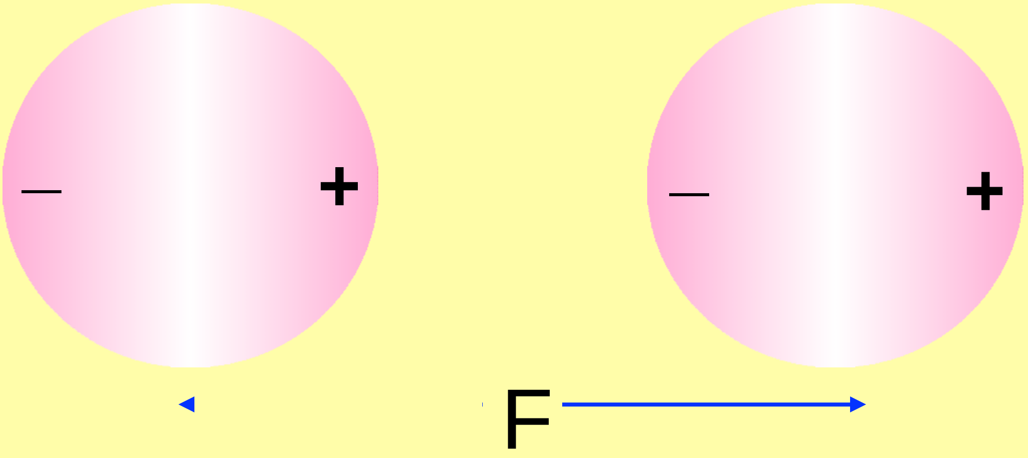
INTERACTIONS BETWEEN DISPERSED DROPLETS

- Two main interacting forces in affecting colloid systems: (1) van der Waals attractive forces and (2) electrostatic repulsive forces.
- Attractive forces tend to destabilise colloids whereas repulsive forces generally impart stability.

van der Waals Interactive Forces

- Originates from the dipole-dipole interactions.
- The force between two droplets arising from van der Waals interactions is always attractive for like droplets.
- The attractive force increases more and more rapidly as the droplets approach.

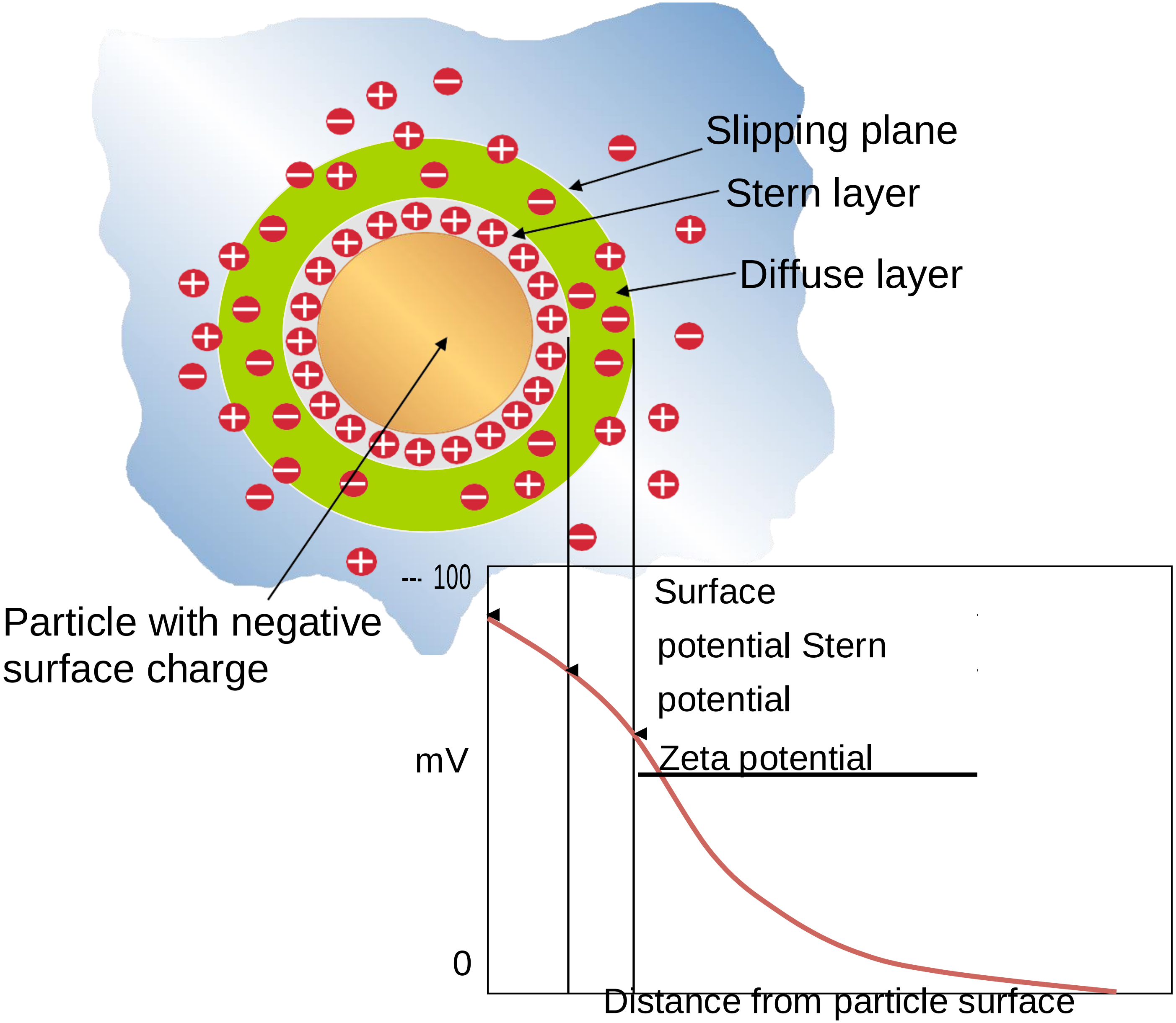
van der Waals Interactive Forces



$$F = -\beta/r^6$$

β = constant; r = distance in between

Electrical Double Layer & Zeta Potential



Slipping plane

Stern layer

Diffuse layer

Particle with negative surface charge

--- 100

mV

0

Surface

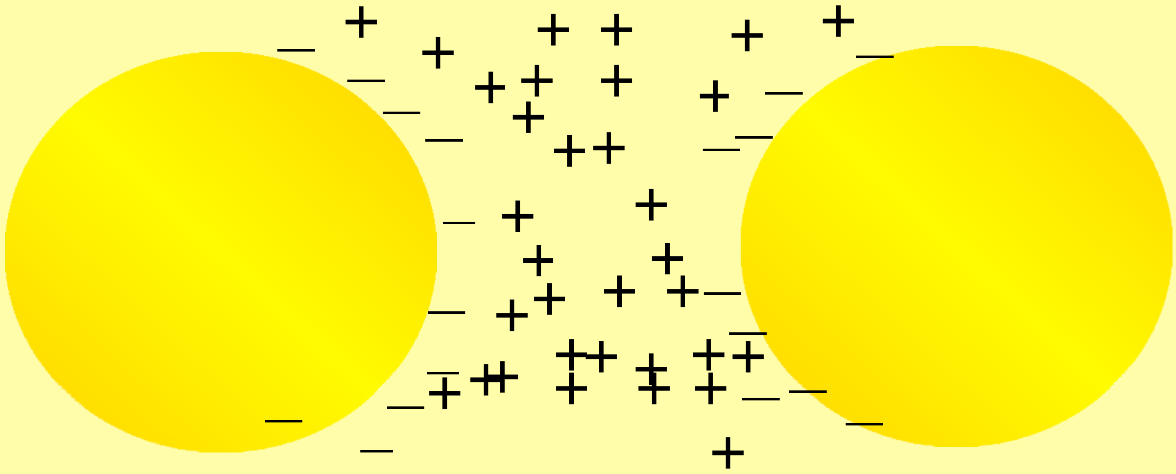
potential Stern

potential

Zeta potential

Distance from particle surface

ELECTRICAL DOUBLE LAYER



- Oppositely charged ions (counterions) are preferentially attracted towards the surface, and ions of the same charge (coions) tend to be repelled away.
- The combination of the charged surface & the unequal distribution of coions & counterions near the surface is called the electrical double layer.

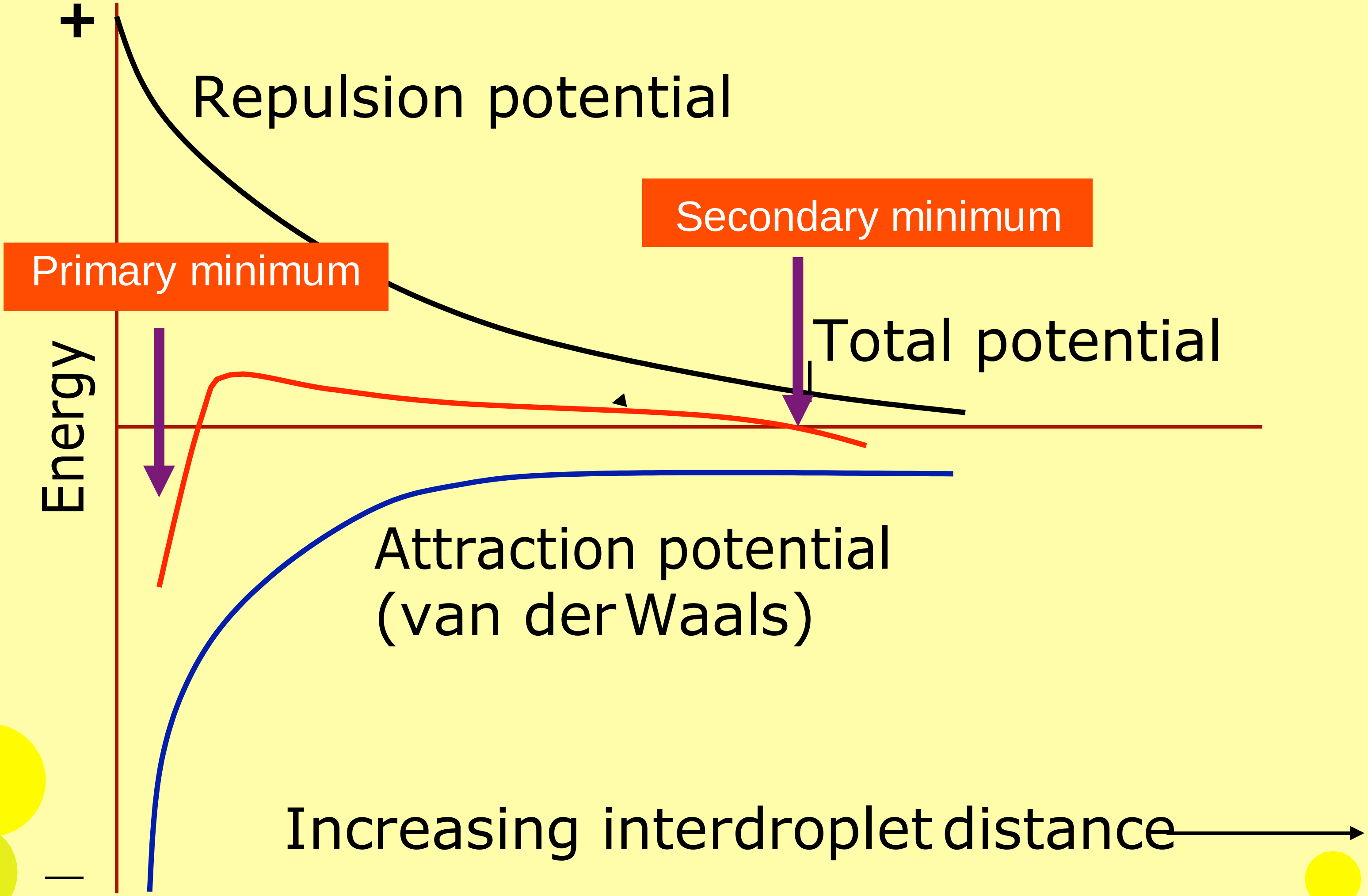
ELECTRICAL DOUBLE LAYER

- The formation of a double layer is very important for the stability of the colloid.
- The double layer is sensitive to electrolytes and also temperature.
- This means that the stability of the colloid may be manipulated by adding electrolytes or changing the temperature.

ELECTROSTATIC FORCES & DLVO THEORY

- DLVO theory — named after four scientists: Derjaguin, Landau, Verwey & Overbeek
- When two charged surfaces approach so that their electrical double-layers begin to overlap, a repulsive force is induced which tends to oppose further approach.
- DLVO theory suggests that electrical double-layer repulsion will stabilize emulsion, when the electrolyte concentration phase is less than a certain value.

ELECTROSTATIC FORCES & DLVO THEORY



ELECTROSTATIC FORCES & DLVO THEORY

- DLVO theory relates the stability of emulsified droplets to two independent potentials that come into action when two droplets approach each other.
- For small distances, the sum of the two energies is always negative (i.e., net attractive) ⇒ cause aggregation.
- When the sum of two energies is +ve ⇒ repulsive force

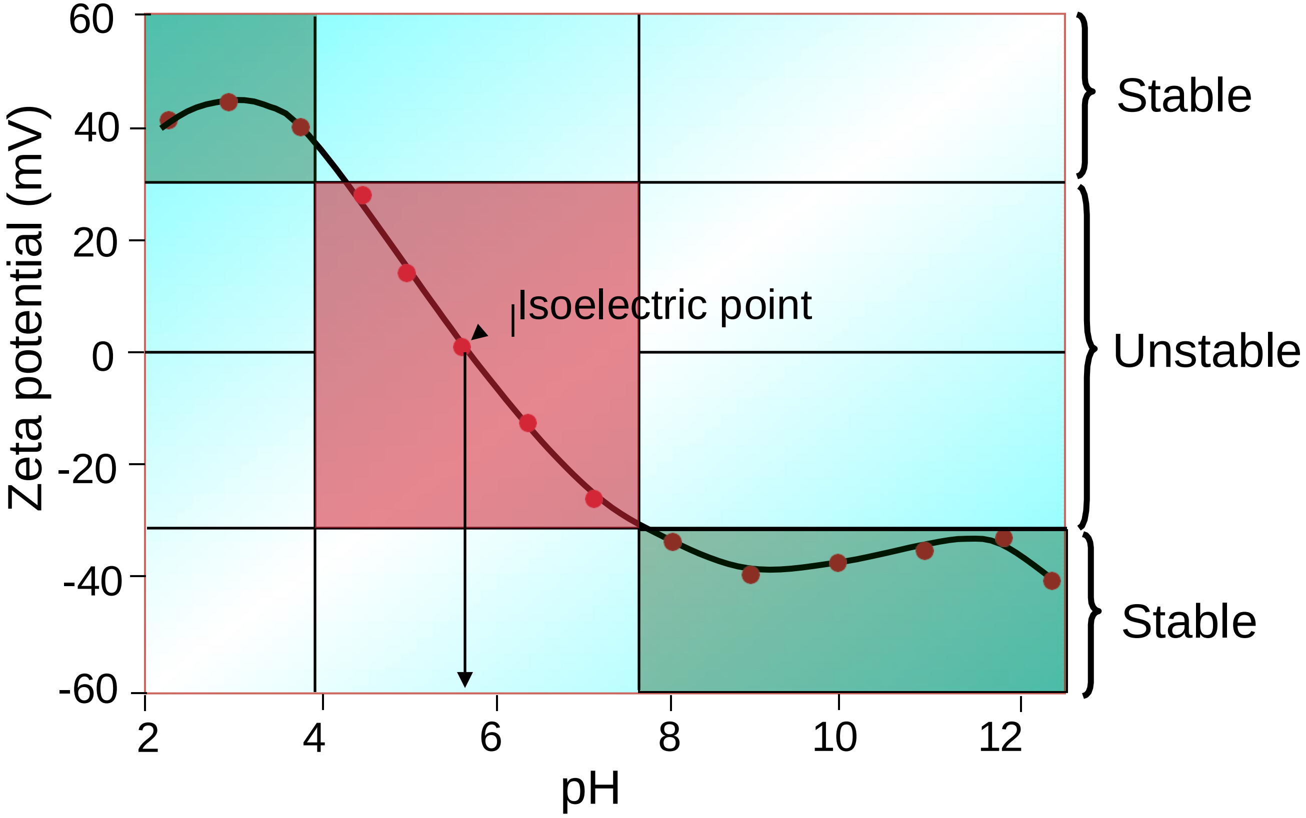
ZETA POTENTIAL

- Zeta potential is the electrical potential at the hydrodynamic plane of shear
- Particles interact according to the magnitude of the zeta potential, not their surface charge
- Zeta potential tells us the effectiveness of the surface charge
- For electrostatically stabilized dispersions, the higher the value of zeta potential, the more stable the dispersion is likely to be

ZETA POTENTIAL

- Stability dividing line is generally considered to be ±30mV
- Particles with zeta potential more positive than +30 mV or more negative than -30 mV are formed a stable dispersion.
- Small changes in the pH or concentration of ions (ionic strength) can lead to dramatic changes in the zeta potential

Effect of pH on Zeta Potential



Emulsion Stabilization

Ionic (Electrostatic) Stabilization

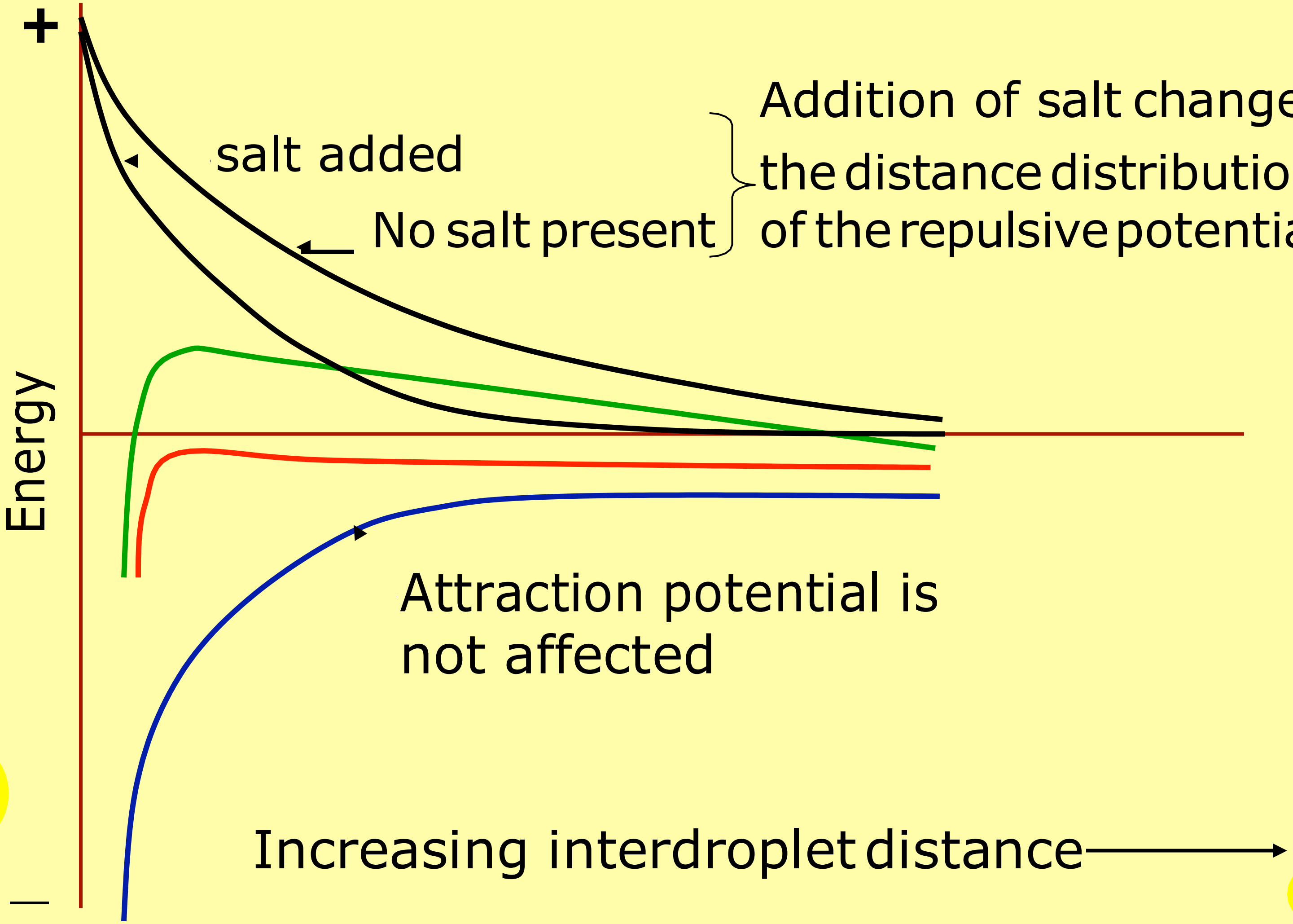
- The introduction of charged groups on the surface of the emulsion droplets increases the repulsive forces.
- Ionic emulsifiers will form an electrically charge double layer in the aqueous solution surrounding each oil droplet.

Emulsion Stabilization – Functions of Emulsifiers

Ionic Stabilization

- The thickness of the electrical double layer is affected by ionic strength. As long as ionic strength is low, electrical repulsion is > van de Waals attraction ⇒ the droplets remain suspended.
- With ionic emulsifiers, low [salt] enhances stability, while high [salt] conc increase flocculation and/or coalescence.

Emulsion Stabilization – Effect of ionic strength



salt added

No salt present

Addition of salt changes the distance distribution of the repulsive potential

Attraction potential is not affected

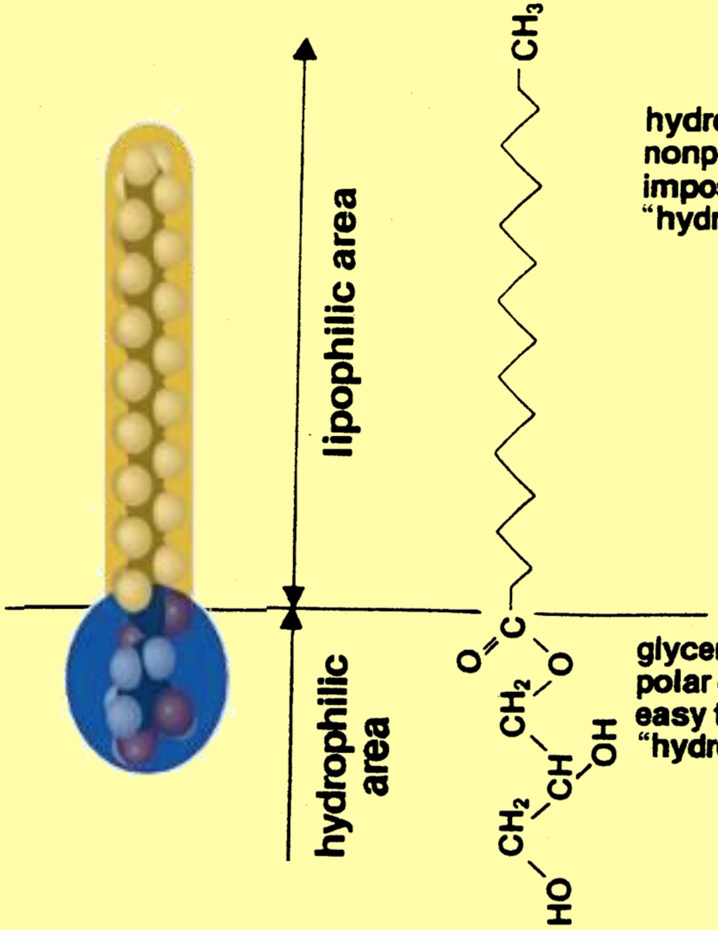
Increasing interdroplet distance

Emulsion Stabilization

Emulsion stability can be achieved by using emulsifiers (surfactants) and/or stabilizers:

- Emulsifiers – compounds that facilitate the formation of emulsion by lowering the oil/ water interfacial tension & imparting short-term stability by forming a protective film around the droplets.
- Stabilizers – compounds that are not (or only slightly) surface active but impart long-term stability to emulsions by restricting interfacial interactions.

Emulsion Stabilization – Functions of Emulsifiers



hydrocarbon chain
nonpolar group
impossible or hard to hydrate
"hydrophobic tail"

glycerol-residue
polar group
easy to hydrate
"hydrophilic head"

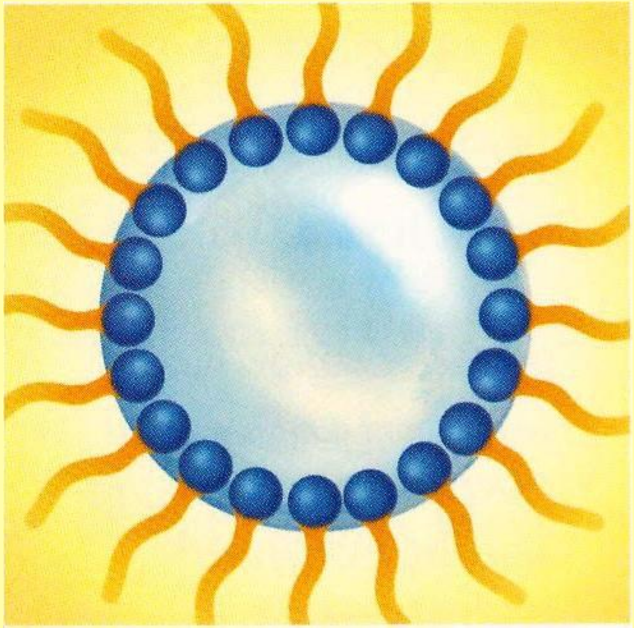
Emulsion Stabilization – Functions of Emulsifiers

Adsorption at Interface

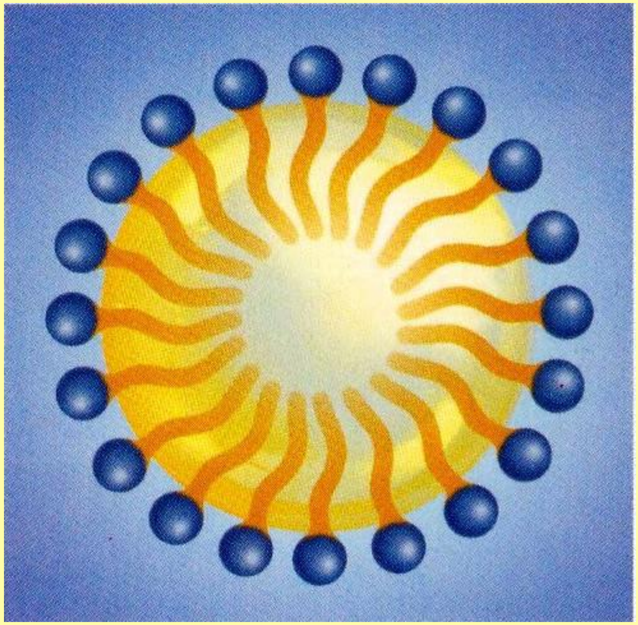
- Emulsifiers, because of their amphiphilic nature, adsorb at the interface between oil & water & form an interfacial film ⇒ reduction of interfacial tension.
- The reduction of interfacial tension through addition of emulsifiers allows emulsion formation with considerably less energy input.

Emulsion Stabilization – Functions of Emulsifiers

W/O emulsion



O/W emulsion



Emulsion Stabilization – Functions of Emulsifiers

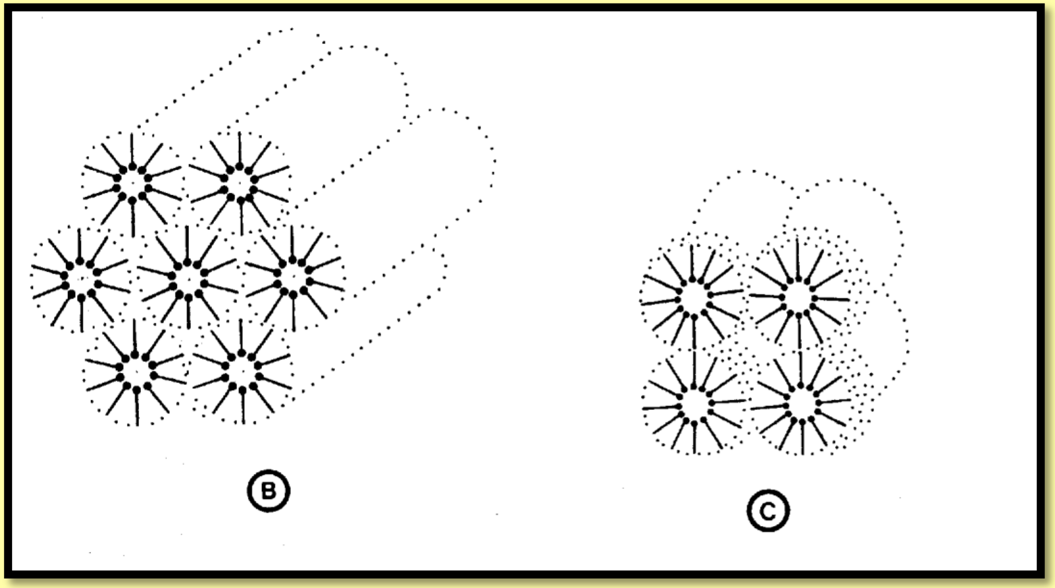
Liquid Crystal Stabilization

- Mixtures of emulsifier & water form a "liquid crystals" or mesophase structures.
- Liquid crystalline phases may form on the surface of oil droplets in o/w emulsions & reduces the rate of coalescence, even if flocculation occurs.

Emulsion Stabilization – Functions of Emulsifiers

Liquid Crystal Stabilization

A micelle is an aggregation of the emulsifier molecules, oriented with the hydrophobic chains to the inside & the hydrophilic groups on the surface.



Some examples of mesophase structures

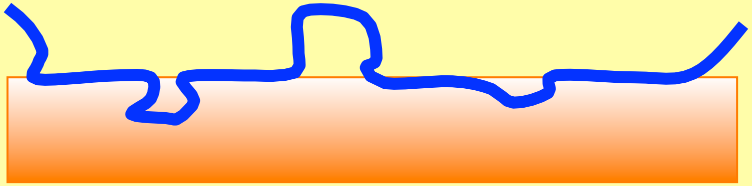
Emulsion Stabilization – Functions of Emulsifiers

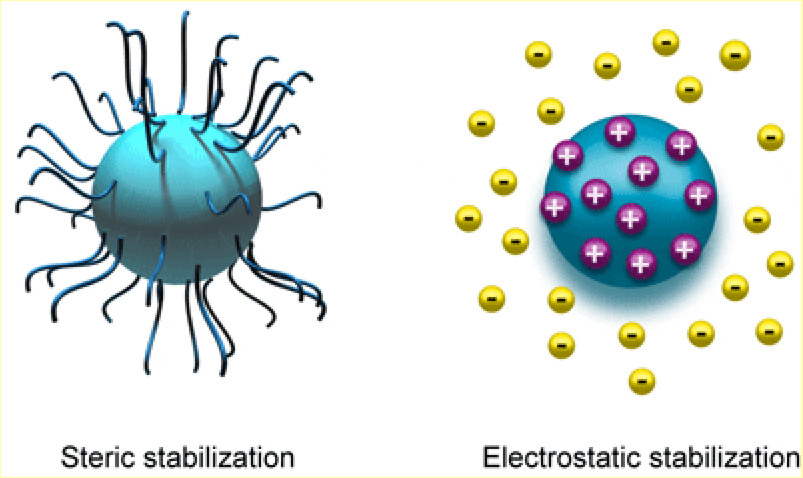
Stabilization via Steric Hindrance (also known as steric stabilization)

- Hydrocolloids such as xanthan gum, arabic gum, CMC, guar gum, etc., significantly increase emulsion stability (function as stabilizers).
- The macromolecules act by either increasing the viscosity or partitioning into the o/w interface as a physical barrier to coalescence.

Emulsion Stabilization

Steric Stabilization





Emulsion Stabilization

Gravitational Separation

- Droplets in an emulsion have a different density to that of liquid which surrounds them ⇒ a net gravitational force acts upon them ⇒ cause creaming or sedimentation.
- Droplets in an o/w emulsion tend to cream (e.g. milk), whereas those in a w/o emulsion tend to sediment.

Emulsion Stabilization

Gravitational Separation

- Creaming rate of an isolated spherical particle can be predicted by Stokes’s equation:

$$\boxed{v_{Stoke} = -\frac{2gr^2(\rho_d -}{9 \quad {}_1}}$$

- In general, if creaming rate < 1 mm/day, the emulsion is considered stable toward creaming.

Emulsion Stabilization

Methods of Controlling Gravitational Separation

(1) Minimize Density Difference

- Matching the densities of the oil & aqueous phases
- Density matching can be achieved by mixing natural oils with brominated vegetable oils (which have a higher density than water).

“Ring” in beverage emulsion

- The driving force for gravitational separation is the density difference between the droplets and the surrounding liquid: Δr = $(r_2 - r_1)$
- Therefore possible to prevent gravitational separation by “matching” the densities of the oil and aqueous phases

“Ring” in beverage emulsion

- This approach is commonly used for stabilizing beverage emulsion whereby the “ring” phenomenon due to creaming of the flavor oil is sometimes observed.
- Density matching can be achieved by mixing natural oils with *brominated vegetable oils* (which have a higher density than water), so that the overall density of the oil droplets is similar to that of aqueous phase.

Emulsion Stabilization

Methods of Controlling Gravitational Separation

(2) Reduce droplet size

- The velocity at which a droplet moves is proportional to r^2 (Stoke's law).
- Stability of an emulsion to gravitational separation will increase by reducing the size of droplets.
- High pressure homogenization

Emulsion Stabilization

Methods of Controlling Gravitational Separation

(2) Modify rheology of continuous phase

- Increasing the viscosity of continuous phase surrounding the droplets decreases the velocity at which droplet moves.

- Add thickening agent, e.g. hydrocolloids such as arabic gum, xanthan gum, etc.

Emulsion Stability Index

- To predict long term stability of an emulsion
- Simple test using centrifuge at a given speed & time – observed degree of creaming.
- Measure the change in particle size distribution (PSD) of an emulsion with time (a good emulsifier does not change PSD with time, and vice versa).

Changes in droplet size distribution