



لجان الرُفَعَات

# DISPENSING



MORPHINE ACADEMY

MORPHINE  
ACADEMY

# Suspensions

# Dispersed system:

- **Dispersed system:** contain an un-dissolved or immiscible drug distributed throughout a vehicle  
لا يذوب لا يمتزج
- Dispersed particles and dispersed medium
- A dispersed system could be a colloid, gel, suspension, emulsion, lotion, cream, ointment, suppository, troche, or medication stick
- Important factors that determine which type:
  - Size of the dispersed particles: e.g. colloids and gels have the smallest size particles

# Dispersed system:

- The particles of the dispersed phase vary widely in size, from large particles visible to the naked eye down to particles of colloidal dimension, falling between 1.0 nm and 0.5  $\mu\text{m}$ :  
تختلف المعلمات حسب الجزيئات الغير زائفة

1. Dispersions containing coarse particles, usually 10 to 50  $\mu\text{m}$ , are referred to as *coarse dispersions*; they include the suspensions and *emulsions*.
2. Dispersions containing particles of smaller size are termed *fine dispersions* (0.5 to 10  $\mu\text{m}$ ),
3. Dispersion containing particles in the colloidal range (falling between 1.0 nm and 0.5  $\mu\text{m}$ ), are termed *colloidal dispersions* such as *Magmas* and *gels*.

# Dispersed system:

- The particles of the dispersed phase are either:
  - solid materials that are insoluble in the dispersion medium as in the case of suspension. → جزيئات صلبة في سائل
  - Or, in the case of *emulsions*, the dispersed phase is a liquid that is neither soluble nor miscible with the liquid of the dispersing phase. ← جزيئات سائلة في سائل
  - Or, In the case of an aerosol, the dispersed phase may be small air bubbles throughout a solution or an emulsion.
  - Or, droplets of a liquid in air.

# Dispersed systems:

| Dispersing medium | Dispersed phase                           |                            |                                  |
|-------------------|---|----------------------------|----------------------------------|
|                   | Solid                                     | Liquid                     | Gas                              |
| Liquid (L)        | Colloidal system (sol),<br>Suspension S/L | Emulsion L/L               | Foam G/L                         |
| Solid (S)         | Alloys, minerals S/S                      | Solid emulsion, gel<br>L/S | Porous bodies, solid<br>foam G/S |
| Gas (G)           | Smoke (aerosols), dust<br>(S/G)           | Fog, mist (aerosol)<br>L/G | -                                |

# COLLOIDS

## Examples of colloidal systems from daily life



Foams



Milk



Fog, smoke



Detergents



Aerogel



Blood



Paints



Cosmetics

# Colloids

**Colloid**-- A mixture of two phases of matter

*emulsions*

*aerosols*

*smoke*

*fog*

*foams*

*gels*

*milk*

*clouds*



**Gel & Foam**



**Clouds**



**Milk**

# Dispersed systems: Suspensions

# Suspensions:

- Suspensions are dispersions of a finely divided insoluble solid that is evenly dispersed (suspended) in a liquid (the dispersing medium)
- A suspension is classified according to particle size to:
  1. **Colloidal suspension:** Suspension containing particles between 1 nm to 0.5  $\mu\text{m}$ .
  2. **Coarse suspension:** Suspension containing particles between 1 to 100  $\mu\text{m}$ ,.

**Most of the pharmaceutical suspensions are coarse suspension.**

# Suspensions

Usage:

1. Oral administration (sweetened, flavored)
2. Topical application
3. Parenteral routes (non-sweetened, non-flavored): **عابزبظ ١٧ لائنه**  
intramuscular, intradermal, SC) **بببببب البببببب وبببببب بببببب**
4. Intraoculr and intranasal suspensions (non-sweetened,  
**بالبببب** non-flavored) **بالبببب**

# When they are used?

- When the active drug is not soluble in a solvent
- When the active drug is not stable in a solution. In this instance, the suspension ensures chemical stability while permitting liquid therapy.

# Advantages of suspensions

1. An ideal dosage form for insoluble drugs for patients who have difficulty swallowing tablets or capsules (i.e. children, elderly). the liquid form is preferred to the solid form of the same drug because of the ease of swallowing liquids and the flexibility in administration of a range of doses. **الدواء يكونا من ذائب زي الحلو فاطعم بيكون اخف**
2. Mask the undesirable tastes of drugs: The disadvantage of a disagreeable taste of certain drugs in solution form is overcome when the drug is administered as un-dissolved particles of an oral suspension. In fact, chemical forms of certain poor-tasting drugs have been specifically developed for their insolubility in a desired vehicle for the sole purpose of preparing a **palatable** liquid dosage.
3. Drugs are chemically more stable compared to solution
4. Oral suspensions can be given for both local or systemic therapeutic effects

# Desirable properties :

## الخصائص المطلوبة

1. A properly prepared pharmaceutical suspension should settle slowly and should be readily redispersed upon gentle shaking of the container. أن يترسب بشكل بطيء أن يرجع لموزع الدواء بسهولة بالهز
2. Of correct viscosity to pour freely from bottles and or to flow through an administration needle بدي انخلي حجم الجرعات نفسه
3. The particle size of the suspension should remain fairly constant throughout long periods of undisturbed standing.
4. الأمراض الجلدية In dermatology, the suspension must be sufficiently fluid to spread over the skin with no resistance and adhere to skin after application. قطرات العين
5. In ophthalmic suspension, the particle size must be kept to a minimum to prevent irritation of the eye.

# Disadvantages of suspensions: سلبيات

*Chemically* ديروا بالكم عندى لها يترسب راح يغير في اخلاطه *Doses* لا

1. Physical instability → settle over time → lack of uniformity of dose → shake before administering each dose الحل ←

2. Texture may be unpleasant to patients القوام ما بيعجب كل المرضى

Chemically instable: Solutions: لأنه الدواء بتأين فيتغير  
هيئته الكيمائية

Physically instable: Suspensions: لأنه الدواء هو نفسه بس  
معلقا ممكن يغير بعدين ممكن بعدين راح نغير

سككع ءءءء ءءءءء (ءءءءءء)

## Sedimentation (settling properties):



- Sedimentation means settling of particle or floccules that occur under gravitational force in liquid dosage form.

# How to control the settling properties?

- The rate of sedimentation of a suspended phase depends on several factors which may be controlled by pharmaceutical manipulation.
- Assuming that all dispersed particles are of uniform shape and size and that the particles are sufficiently far apart so that the movement of one does not affect the neighboring particles, the rate of sedimentation can be estimated by Stoke's equation:

لا تخاصوا حتى صوفي بس افهموها

$$V = \frac{d^2 (\rho_1 - \rho_2) g}{18 \eta_0}$$

- where **V** is the sedimentation rate (cm/sec), **d** the diameter of the suspended particles (cm), **p<sub>1</sub>** its density and **p<sub>2</sub>** is the density of the medium (g/cm<sup>3</sup>), **g** is the acceleration of gravity (980.7 cm/sec<sup>2</sup>) and **n<sub>o</sub>** is the viscosity of the external phase in poises (g/cm sec).

# How to control the settling properties?

- Stokes' equation gives an approximation of the settling rate and an appreciation of the variables governing the sedimentation process
- For example, by reducing the particle size or by increasing the viscosity and density of the external phase, the rate of sedimentation can be retarded.

أهلاً برون ، لعافون بتقدروا تجاوبوا بالمنطق :

∴ إذا قلنا حجم الجزيئات ← يقل معدل الترسيب

∴ إذا زدنا لزوجة السائل ← يقل المعدل للترسيب

∴ إذا زدنا كثافة السائل ← يزيد معدل الترسيب

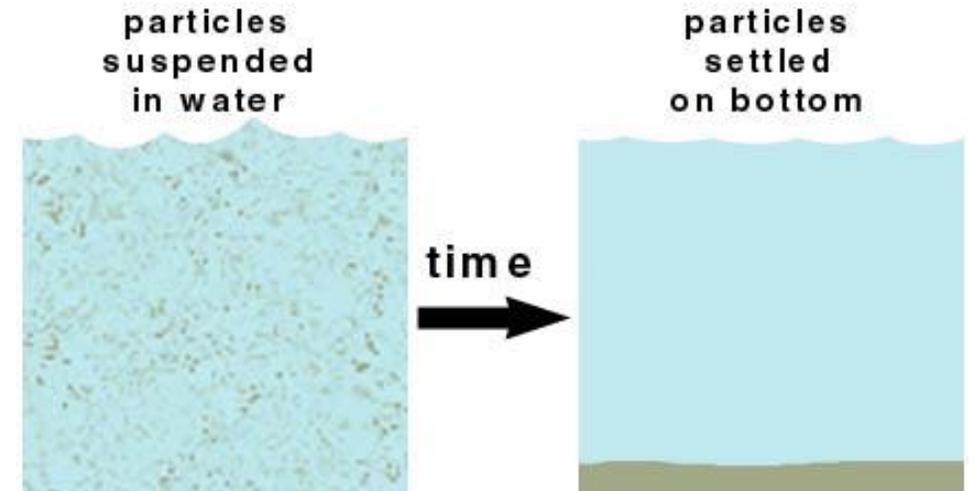
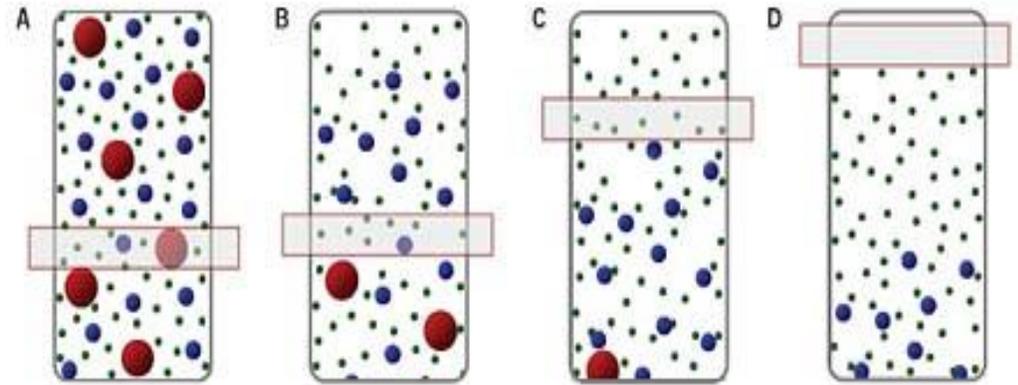
لأنه إذا زدت الفرق بين كثافة السائل واللب فوافق  $\rho$  يطبع ووافق ينزل

# How to control the settling properties?

1. By reducing the particle size of the dispersed phase produces a slower rate of sedimentation of the particles. The velocity of fall of a suspended particle is greater for larger particles than it is for smaller particles.

$$V = \frac{d^2 (\rho_1 - \rho_2) g}{18 \eta_0}$$

- However, one should avoid reducing the particle size too much, because fine particles have a tendency to form a compact cake upon settling to the bottom of the container. The result may be that the cake resists breakup with shaking and forms rigid aggregates of particles that are larger and less suspendable.



هصیح بدنا نضغ الحجم للهلب  
 به صس كتر لانه ح يحل  
 كع

بعض زي هيلك ، ح بتجمع و يصير هعب اني احد توزيره  
 Saja Hamed, Ph.D

# How to control the settling properties?

شرحناها فوق

2. Also, the greater the density of the particles, the greater the *rate of sedimentation*, provided the density of the vehicle is not altered.

$$V = \frac{d^2(\rho_1 - \rho_2)g}{18\eta_0}$$

- Because aqueous vehicles are used in pharmaceutical oral suspensions, the density of the particles is generally greater than that of the vehicle, which is a desirable feature.
- If the particles were less dense than the vehicle, they would tend to float and floating particles would be quite difficult to distribute uniformly in the vehicle.

بدى اذلى كئامة  
الصعب اكبر من السائل

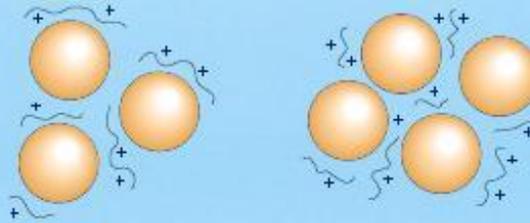
# How to control the settling properties?

## 3. Flocculating agents ركزوا عليّ معي

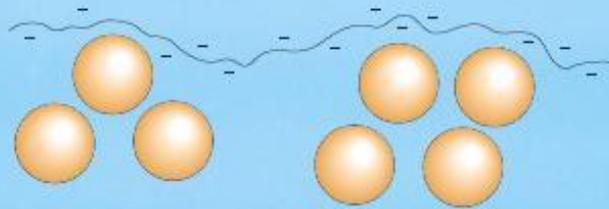
- flocculation refers to process which leads to aggregates that are loose or open. *flocculation* عرات حجم الصلب يكون هيفي كثير فبجمعه عن هيرص
- Flocculating agents are electrolytes that carry an electrical charge opposite from that of the net charge on the suspended particles
- Electrolytes act as flocculating agents, apparently by reducing the electrical barrier between the particles of the suspensoid and forming a bridge so as to link them together. الصلب
- The addition of the flocculating agent, at some critical concentration, reduce the surface charge on the suspended particles and allows the formation of floccules or clusters.
- Floccules will **not cake** and may be **easily redispersed** by shaking the suspension.

## DIAGRAM OF FLOCCULATION

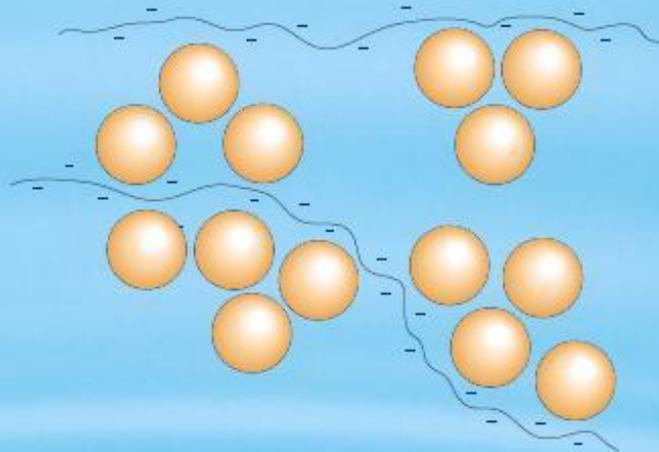
Destabilized colloids

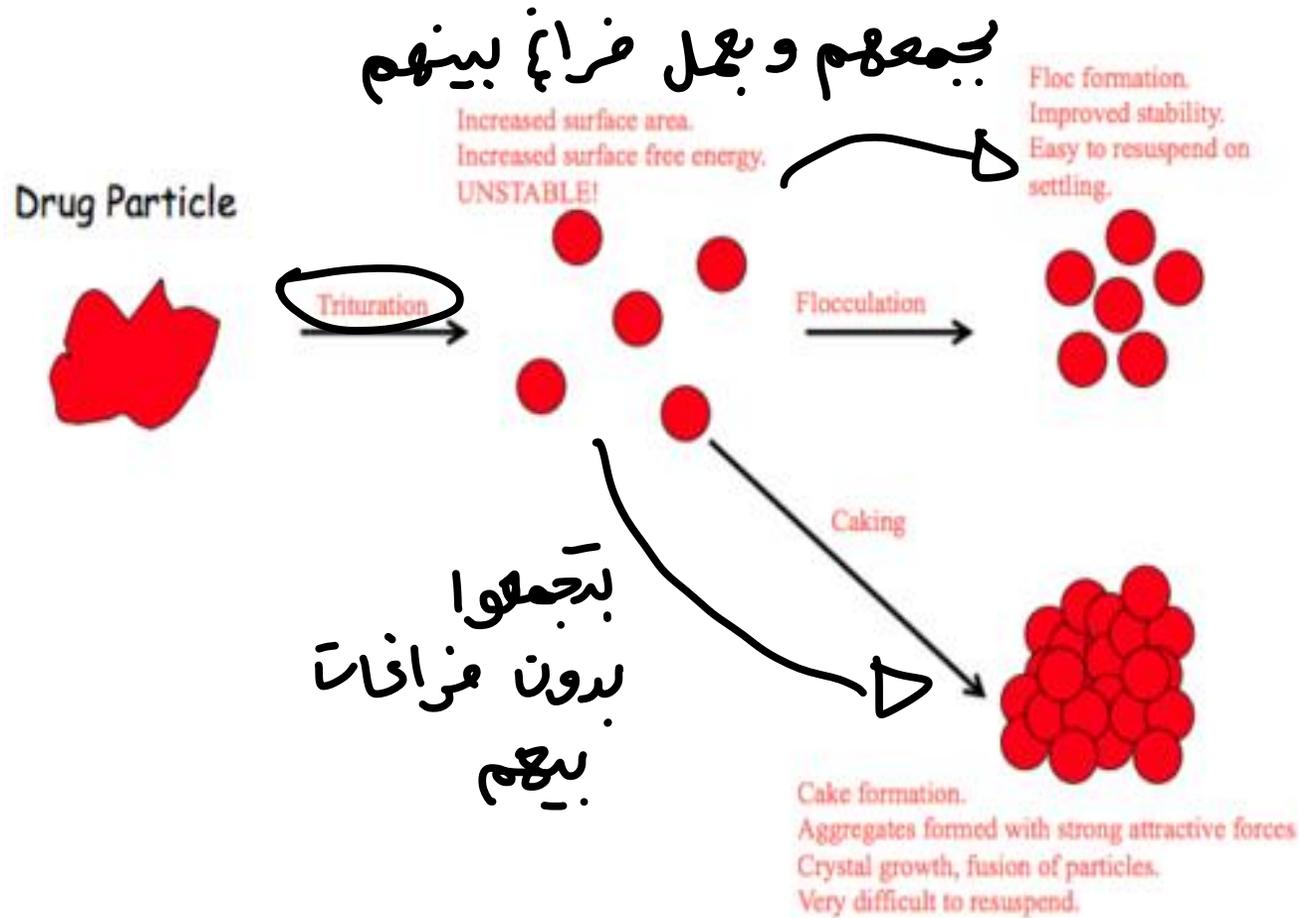


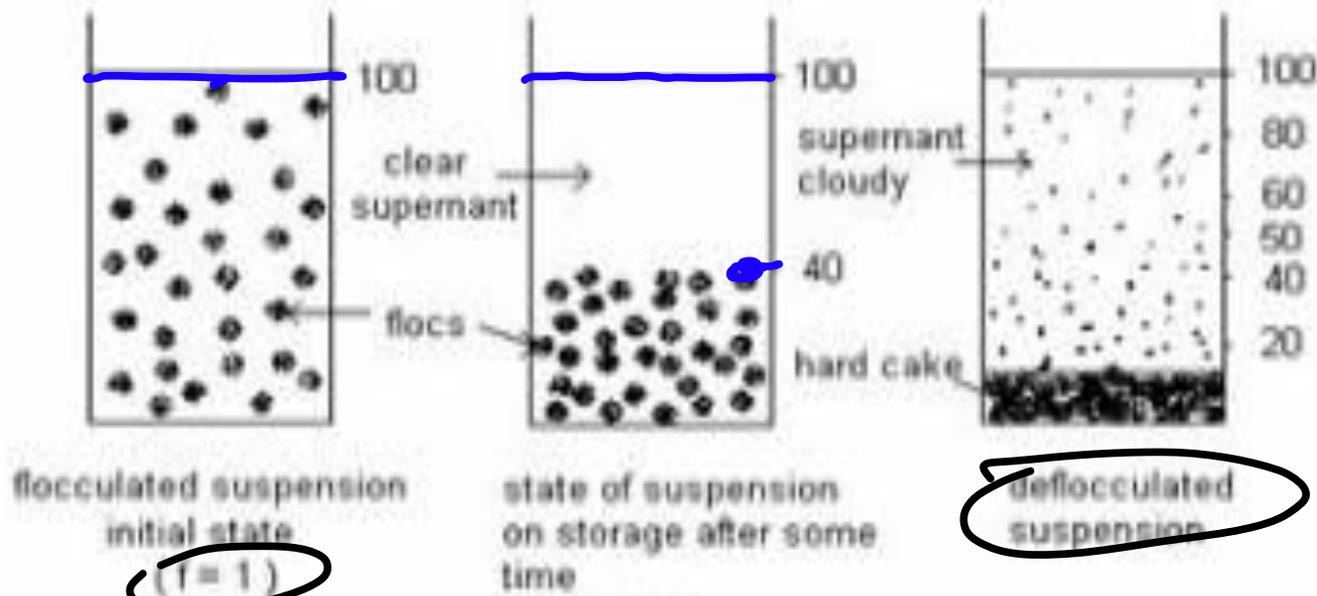
Bridging



Floc formation





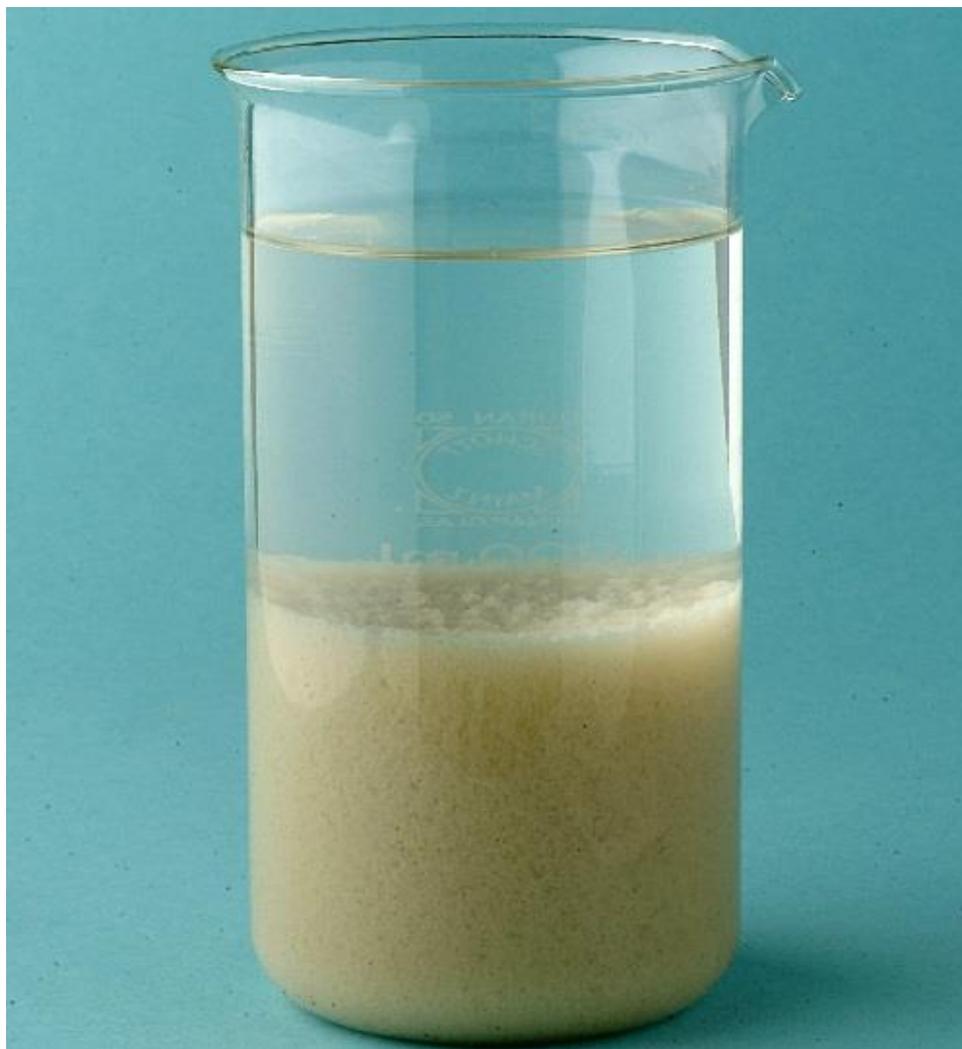


نسبة أعلى نقطة وصلها  
الحزبان إلى حجم المعلق

$$\frac{100}{100}$$

$$\frac{40}{100}$$

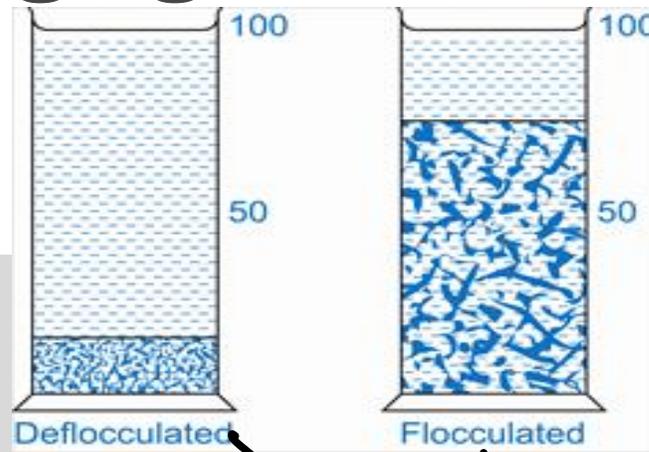
Deflocculated  
يعني طاعلنا  
floculation  
فصل cake



Saja Hamed, Ph.D

# How to control the settling properties?

## 3. Flocculating agents



### Flocculated

- Particles forms loose aggregates and form a network like structure
- Rate of sedimentation is high
- Sediment is rapidly formed
- Sediment is loosely packed and doesn't form a hard cake
- Sediment is easy to redisperse

Saja Hamed, Ph.D

لا تني جمعهم

### Non-flocculated (Deflocculated)

- Particles exist as separate entities
- Rate of sedimentation is slow
- Sediment is slowly formed
- Sediment is very closely packed and a hard cake is formed
- Sediment is difficult to redisperse

# How to control settling properties:

## 4. Viscosity enhancers (suspending agents or thickening agents)

- flocculation as a means of preventing caking will increase the particle diameter, and thus increase the rate of sedimentation.
- **Now we need some means to reduce this rate of settling, so that the suspension can be accurately dosed before it begins to settle.**
- Practically speaking, the viscosity of the dispersion medium is the only other Stoke's variable affecting sedimentation rate over which the pharmacist can exert any control.
- Suspending or thickening agents are added to suspensions to thicken the suspending medium, thereby reducing the movement (sedimentation) of suspended particles and physically stabilizing the product.
- This is particularly important in flocculated systems in which rapid particle settling is the primary factor leading to physical instability and lack of dosage uniformity in the product.

# How to control settling properties:

4. Viscosity enhancers (suspending agents or thickening agents) *يعني بدنا الدواء وهو عارف لزوجة عالية ولعائنه تقلل من قدرنا عند ال Dose*

- Ideally, the system should (rheologically) be pseudoplastic; that is, it should have high viscosity at low shear rates (during storage) and low viscosity at high shear rates (during shaking, pouring, or spreading).
- Thus selecting appropriate viscosity enhancer with desirable rheological properties
- Suspending agents which are pseudoplastic are desirable, since they recover slowly from the deformation that occurs through shearing (i.e. upon shaking, they remain fluid long enough to be poured and spread).

How to control settling properties:

#### 4. Viscosity enhancers (suspending agents or thickening agents)

- The rate of sedimentation may be appreciably reduced by increasing the viscosity of the dispersion medium
- However, a product having too high a viscosity is not generally desirable, because it pours with difficulty and it is equally difficult to redisperse the suspensoid.
- Therefore, if the viscosity of a suspension is increased, it is done so only to a modest extent to avoid these difficulties.

# How to control settling properties:

## 4. Viscosity enhancers (suspending agents or thickening agents):

- Viscosity enhancers include agents from each of the following categories. Typically, the concentrations used range from 0.5% to 5%, but the needed viscosity will depend on the suspended particle's tendency to settle:

### 1. Natural hydrocolloids : طبيعية

Acacia, tragacanth, alginic acid, carrageenan, locust bean gum, guar gum, gelatin.

### 2. Semisynthetic hydrocolloids : شبه صناعية

Methylcellulose, sodium carboxymethylcellulose

### 3. Synthetic hydrocolloids: صناعية

Carbopol®

### 4. Clays : الطين = حصى حارفي جمعها

Bentonite, Veegum®

صالح

أنواع  
ال  
Viscosity  
Enhancers



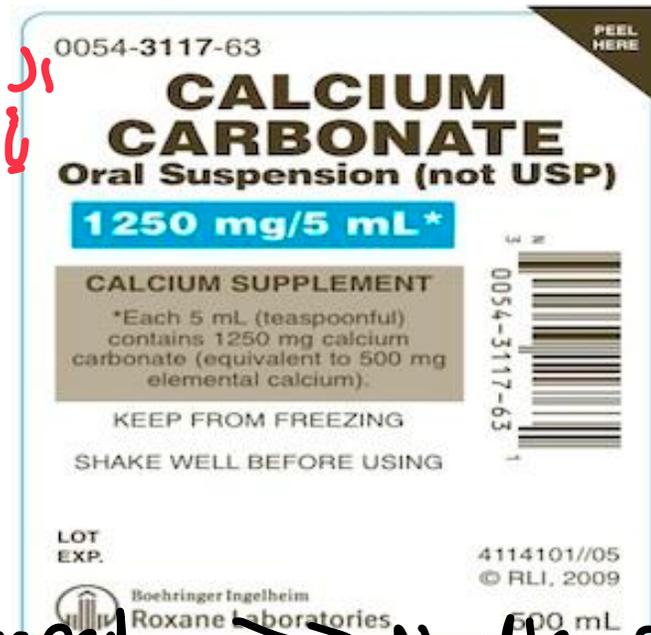
أون جمع طين: طين

The particle shape can also affect caking and product stability:

- It has been shown that symmetrical barrel-shaped particles of calcium carbonate produced more stable suspensions than did asymmetrical needle-shaped particles of the same agent.
- The needle-shaped particles formed a firm sediment cake on standing that could not be redistributed, whereas the barrel-shaped particles did not cake upon standing

Saja Hamed, Ph.D

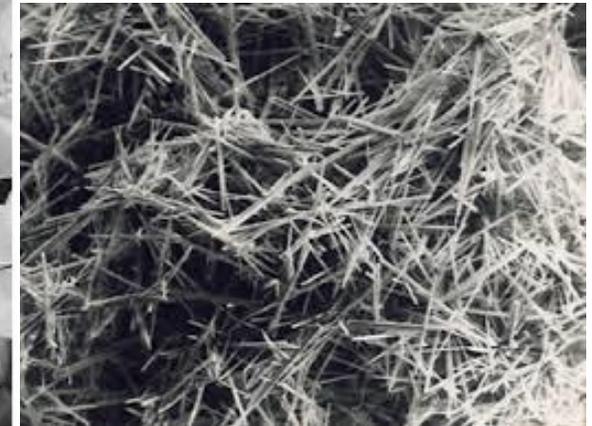
ممكن بشكل  
Suspensoid  
يا انت كمان



Barrel-shaped >> Needle-shaped



اصلا من شكله بقطع الرزق



# Preparation of suspension: wetting agents

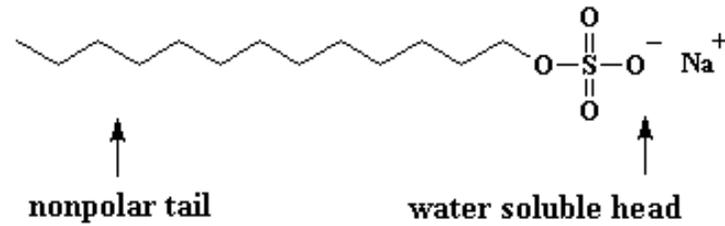
- In some instances, the dispersed phase has an affinity for the vehicle to be employed and is readily wetted by it.
- Other drugs are not penetrated easily by the vehicle and have a tendency to clump together or to float on the vehicle. In this case, the powder must first be wetted to make it more penetrable by the dispersion medium. الكحول والجليسيرين زي كحائي برهم يَدْخَلُوا  
بكل اشئي
- Alcohol, glycerin, propylene glycol, and other hygroscopic liquids are employed as wetting agents when an aqueous vehicle is to be used as the dispersion phase.
- They function by displacing the air in the crevices of the particles, and by allowing penetration of dispersion medium into the powder. ستان نصح لوفان الدواء بي اُفهِفِ wetting agent  
مبدأ عمله أنه يستبدل الهواء بين جزيئات الدواء بال Vehicle

# Preparation of suspension: wetting agents

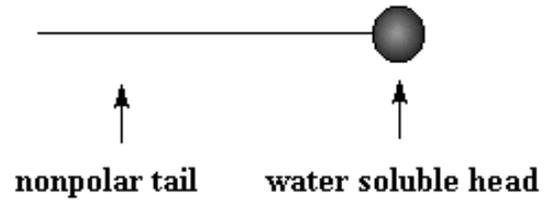
- <sup>عجبة الماء</sup> Hydrophilic powders (e.g. ZnO, MgCO<sub>3</sub>, talc) can be wetted with water or other polar liquids (alcohol, glycerin) using a mortar and pestle
- <sup>كارهة للماء</sup> Hydrophobic powders (sulfur, charcoal) are wetted with alcohol or glycerin or mineral oil
- Only minimal amount used
- Sometimes a surfactant is needed to ensure sufficient wetting
- Surface active agents that induce wettability are called wetting agents

Emulsions بالترتيب

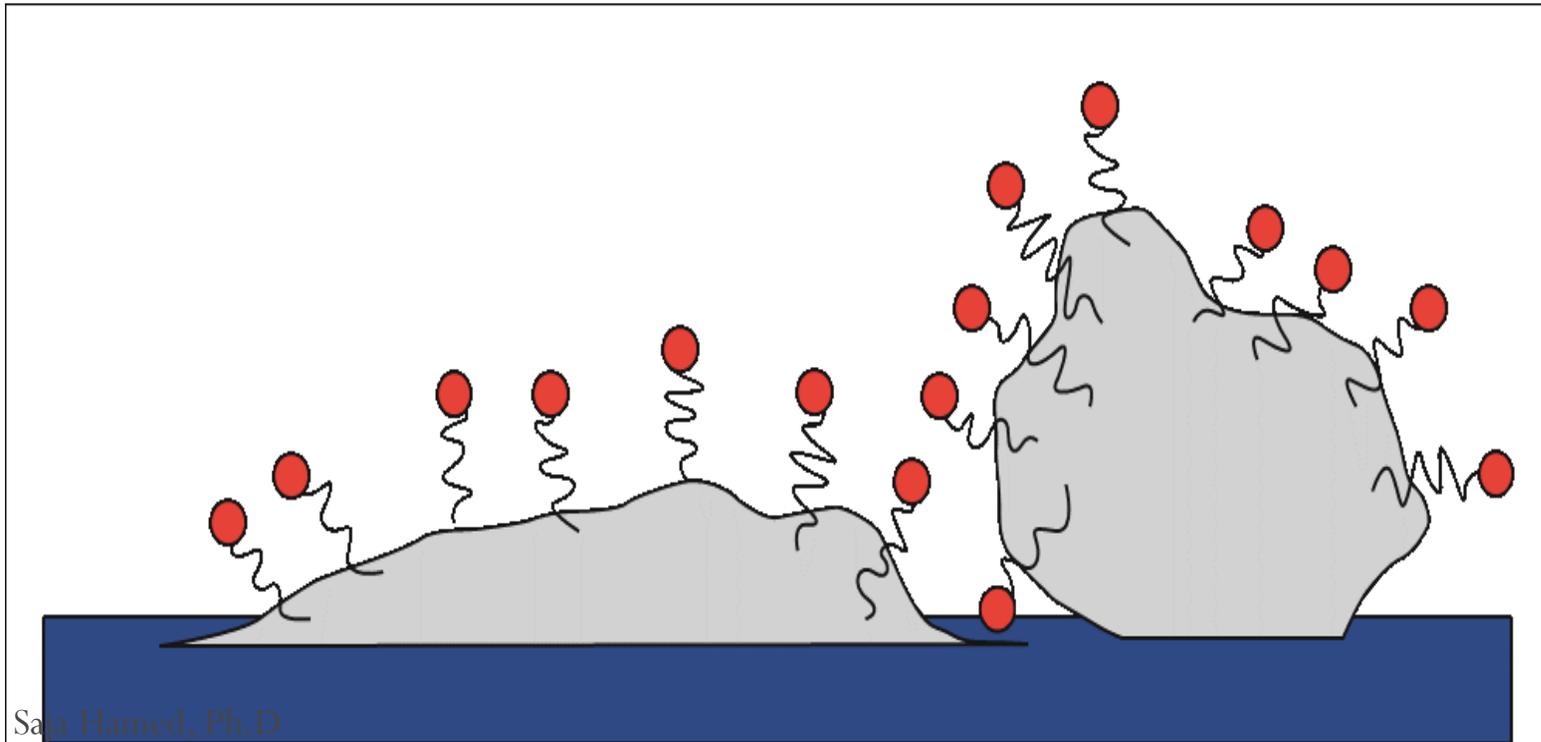
# Preparation of suspension: wetting agents



Sodium Lauryl Sulfate



Lazy chemist's representation of  
Sodium Lauryl Sulfate



# Preparation of suspension: wetting agents

- Wetting agents are mixed with a mortar and pestle.
- Once the powder is wetted, the dispersion medium (to which have been added all of the formulation's soluble components, such as colorants, flavorants, and preservatives) is added in portions to the powder, and the mixture is thoroughly blended before subsequent additions of vehicle.

# The various components, which are used in suspension formulation, are as follows:

| Components                                  | Function   |
|---|--|
| API   | Active drug substances   |
| 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<br>Saja Hamed, Ph.D | They are added to construct structure of the final suspension.             |

# Example

- An example formula for an oral suspension follows.

The suspensoid is the antacid aluminum hydroxide, the preservatives are methylparaben and propylparaben, and syrup and sorbitol solution provide the viscosity and sweetness

|                         |               |           |
|-------------------------|---------------|-----------|
| Aluminum hydroxide      | API           | 326.8g    |
| compressed gel          | wetting agent |           |
| Sorbitol solution       | Sweetener     | 282.0 mL  |
| Syrup                   | Co-solvent    | 93.0 mL   |
| Glycerin                | Co-solvent    | 25.0 mL   |
| Methylparaben           | Preservative  | 0.9g      |
| Propylparaben           | Preservative  | 0.3g      |
| Flavor                  |               | q.s.      |
| Purified water, to make | Co-Solvent    | 1000.0 mL |

# Antacid Oral Suspensions

- Most antacid preparations are composed of water-insoluble materials that act within the المعدة و الأمعاء gastrointestinal tract to counteract the acid and/or soothe the irritated or inflamed linings of the gastrointestinal tract.
- A few water-soluble agents are employed, including **sodium bicarbonate**, but for the most part, **water-insoluble salts of aluminum, calcium, and magnesium are employed**; these include aluminum hydroxide, aluminum phosphate, dihydroxyaluminum aminoacetate, calcium carbonate, calcium phosphate, magaldrate, magnesium carbonate, magnesium oxide, and magnesium hydroxide

**Rugby**® NDC 0536-0025-83

# Almacone®

Alumina, Magnesia, and Simethicone  
Oral Suspension USP

**ANTACID  
ANTIGAS**

**VERY LOW  
SODIUM**

**SATISFACTION GUARANTEED  
Rugby  
OR YOUR MONEY BACK**

12 fl oz  
(355 mL)

COMPARE TO ACTIVE  
INGREDIENTS IN  
MYLANTA®

Alcohol: Less than 0.5%

219-06112-2 R0211

### Drug Facts

**Active ingredients** (in each 5 mL teaspoonful)

|  |         |
|--|---------|
| Aluminum hydroxide 200 mg (equivalent to dried gel, USP) | Antacid |
| Magnesium hydroxide 200 mg                               | Antacid |
| Simethicone 20 mg  | Antigas |

**Purposes**

**Uses** relieves • heartburn • sour stomach • acid indigestion • the symptoms of gas

**Warnings**

Ask a doctor before use if you have • kidney disease • a magnesium-restricted diet

Ask a doctor or pharmacist before use if you are taking a prescription drug. Antacids may interact with certain prescription drugs.

Stop use and ask a doctor if symptoms last more than 2 weeks

Keep out of reach of children.

**Directions** • shake well before use • adults and children 12 years and older: take 2 to 4 teaspoonfuls between meals, at bedtime, or as directed by a doctor • do not take more than 24 teaspoonfuls in 24 hours or use the maximum dosage for more than 2 weeks • children under 12 years: ask a doctor

**Other information** • each 5 mL teaspoonful contains: magnesium 85 mg, sodium 1 mg • store at room temperature • protect from freezing • keep tightly closed • TAMPER-EVIDENT: Do not use if breakaway band on bottle cap is missing or broken.

**Inactive ingredients** benzyl alcohol, butylparaben, carboxymethylcellulose sodium, flavor (contains alcohol), hypromellose, microcrystalline cellulose, propylparaben, purified water, saccharin sodium, sorbitol solution

**Questions or comments?**

Call 1-800-645-2158, 9 am - 5 pm ET, Monday-Friday

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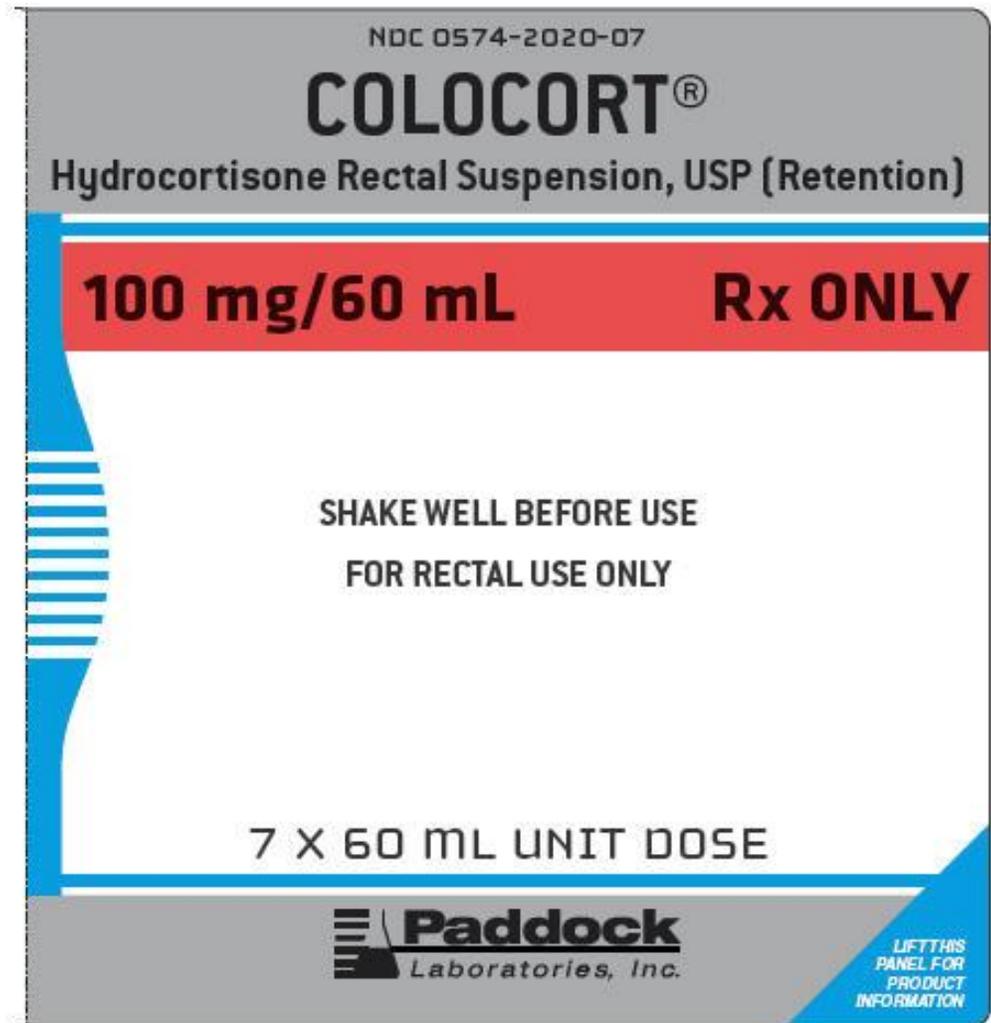
# Antibiotic Oral Suspensions

- Dry powder for reconstitution
- Drugs that are unstable if maintained for extended periods in the presence of an aqueous vehicle (e.g. many antibiotic drugs) are most frequently supplied as dry powder mixtures for reconstitution at the time of dispensing.
- Many antibiotic materials are **unstable** when maintained in solution for an appreciable length of time

كل الالع قديم

# Rectal suspension

- Colocort is a hydrocortisone rectal suspension indicated as adjunctive therapy <sup>صَرَفَ الِغُولُونِ</sup> in the treatment of ulcerative colitis and is packaged in a convenient disposable single-dose enema designed for self-administration.
- It contains hydrocortisone in an aqueous solution that contain carbomer, polysorbate 80, purified water, sodium hydroxide, and methylparaben.



# Packaging and Storage of Suspensions:

- 1) Should be packaged in wide mouth tight containers having adequate air space above the liquid to permit thorough mixing by shaking and an opening large enough to pour a viscous liquid easily.
- 2) Should be stored at room temp or refrigerated protected from: freezing, excessive heat & light
- 3) Label: "Shake Well Before Use" to ensure uniform distribution of solid particles and thereby uniform and proper dosage and label to specify whether the medications are for "external" or "internal use"
- 4) Stored in room temperature if it is dry powder ( $25^{\circ}\text{C}$ ). It should be stored in the refrigerator after opening or reconstitution (freezing should be avoided to prevent aggregation)

# Observing formulations for evidence of instability:

- USP/NF Chapter <1191>
  1. Major sign of suspension instability is a “caked” solid dosage that cannot be re-suspended by a reasonable amount of shaking → no longer flocculated
  2. Presence of relatively large particles → excessive crystal growth
  3. Microbial contamination (discoloration, turbidity, or gas formation)