

# Suspensions

خليطاً و لكن ليسوا ذائبات

في رجهن

## Dispersed system:

يعتوي على مواد غير ذائبة و معلول

- **Dispersed system:** contain an **un-dissolved** or **immiscible** drug distributed throughout a vehicle
- Dispersed particles and dispersed medium حجم صغير
- 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 الحجم الجاه

كوال  
مؤثره

# Dispersed system:

تختلف حجم الجسيمات بشكل واسع

- 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  $\mu\text{m}$ :

1. Dispersions containing coarse particles, usually 10 to 50  $\mu\text{m}$ , are referred to as *coarse dispersions*; they include the *suspensions* and *emulsions*.  
مثال  
هي الأكبر
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*.  
هي الأصغر

# Dispersed system:

- The particles of the dispersed phase are either:

• بصفتها  
تكون صلبة solid materials that are insoluble in the dispersion medium as in the case of suspension.

• Two ←  
liquids 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.

• في  
غاز Or, In the case of an aerosol, the dispersed phase may be small air bubbles throughout a solution or an emulsion.

• قطرات Or, droplets of a liquid in air.

أنظمة متناثرة

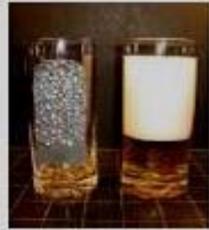
# Dispersed systems:

الألمع  
لبس  
الذرات  
المتنقل

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

# COLLOIDS

## Examples of colloidal systems from daily life



Foams



Milk



Fog, smoke



Detergents



Aerogel



Blood



Paints



Cosmetics

حجم  
الجزيئات  
مغیر جدا

$0.5 \mu\text{g} - 1 \mu\text{g}$

Aerogel

Dispersed لا یعنی آنکل المواد ذائبة / بعضه المواد ذائبة و بعضه

۸

# Colloids

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

*emulsions*

*aerosols*

*smoke*

*fog*

*foams*

*gels*

*milk*

*clouds*



**Gel & Foam**



**Clouds**



**Milk**

# Dispersed systems: Suspensions

العلق



# Suspensions

Usage:

1. Oral administration (sweetened, flavored) له مالح
2. Topical application ( أكيد الحقنة بدون مالح )
3. Parenteral routes (non-sweetened, non-flavored):  
intramuscular, intradermal, SC) فقط بالعضلات  
تحقن الخضرو في أو اللعونة  
العين الأنف
4. Intraocular and intranasal suspensions (non-sweetened, non-flavored)

متى يستخدم suspension?

# When they are used?

الدواء لا يذوب في المذيب

1)

- When the active drug is not soluble in a solvent

2)

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

يزداد ولكن  
لا تكون مستقر  
وغير قابل  
للإستخدام

إذا كانت المادة الفعالة

غير مستقرة في المحلول (يفقد تأثيره لاحقاً)

فيحضره بشكل غير ذائب (معلق)

chemical stability + liquid therapy = ثابته

suspension

الشكل المثالي  
للأشياء  
الذي يجرده  
محبوبة لمبلغ  
الاجوب

# Advantages of suspensions

شكل مثالي

للأدوية غير الذائبة

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.

الشكل السائل  
مفضل أكثر  
لأنه يقدّر

يغطي على طعم الدواء السيء

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.

اتحكم  
بحجم  
الجرعة

مستحلب

مستقر أكثر من المحلول

3. Drugs are chemically more stable compared to solution  
4. Oral suspensions can be given for both local or systemic therapeutic effects

كما دواء

مكان محدد  
مخصص

يعني يعمل إما بشكل عام أو محدد بشكل خاص بالجمع

الخصائص المرغوبة لهذا الشكل

# Desirable properties

أن يكون استقراره

1. أو ترتيبه  
بصلي

A properly prepared pharmaceutical suspension should settle slowly and should be readily redispersed upon gentle shaking of the container

و أن يكون سهل التفتت عند التحريك

2. Of correct viscosity to pour freely from bottles and or to flow through an administration needle

ذو لزوجة مناسبة قابلة للسكب  
تجري من الزجاجات أو عند حقن الإبر

أن يظل

3. حجم الجسيمات  
ثابتاً طوال فترة  
التعليق

The particle size of the suspension should remain fairly constant throughout long periods of undisturbed standing.

4.

In dermatology, the suspension must be sufficiently fluid to spread over the skin with no resistance and adhere to skin after application

الأمراض الجلدية

يجب أن يكون سائلاً بما يكفي

لكي ينتشر على الجلد

يبقى ثابتاً على الجلد

5.

In ophthalmic suspension, the particle size must be kept to a minimum to prevent irritation of the eye.

قطرات العين

تصليح

# Disadvantages of suspensions:

1. **Physical instability** → **settle over time** → **lack of uniformity of dose** → **shake before administering each dose**  
*اختلاف في تراكيز المادة الفعالة  
تتطلب إعادة الفحالة  
تغير مستقر فيزيائياً  
لازم ترحب العبوة قبل الاستخدام*
2. **Texture may be unpleasant to patients**  
*ليكن يتكلم ويكون مزعج للمريض  
وتختلف التراكيز*

# Sedimentation (settling properties):

كريمة الحبيبات



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

قوة الجاذبية

كيف نتحكم بخصائص الاستقرار

# How to control the settling properties?

الرسوبية (الصورة الى غوة)

رغبتهم

- 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:

نفس الحجم والشكل

والمسافة بعيدة بين الجزيئات

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

التحكم بهم

التحكم بهم

صحيح

- where  $V$  is the sedimentation rate (cm/sec),  $d$  the diameter of the suspended particles (cm),  $\rho_1$  its density and  $\rho_2$  is the density of the medium ( $\text{g/cm}^3$ ),  $g$  is the acceleration of gravity ( $980.7 \text{ cm/sec}^2$ ) and  $\eta_0$  is the viscosity of the external phase in poises ( $\text{g/cm sec}$ ).

قطر

particles

vehicle dispersed phase

اللزوجة

suspended media

# 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.

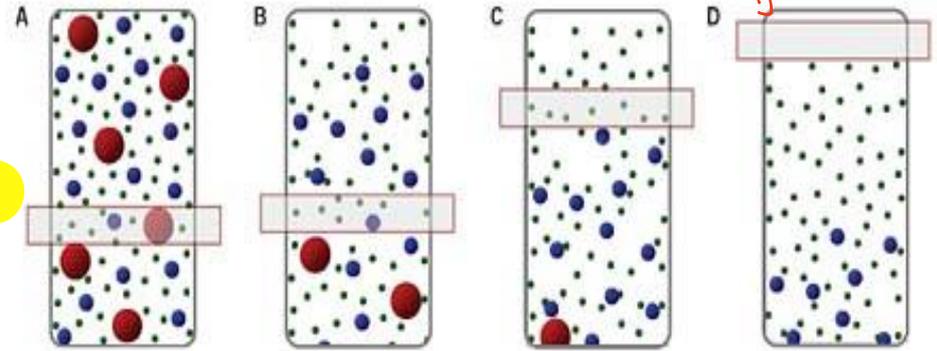
أنا بدى أقل سرعة الركود فلابزم يا إما : (1) أمغر حجم الجباج  
(2) أزيد لزوجة وكثافة السائل

# 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.

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

بخافى ان نصل لهذا # التجانس



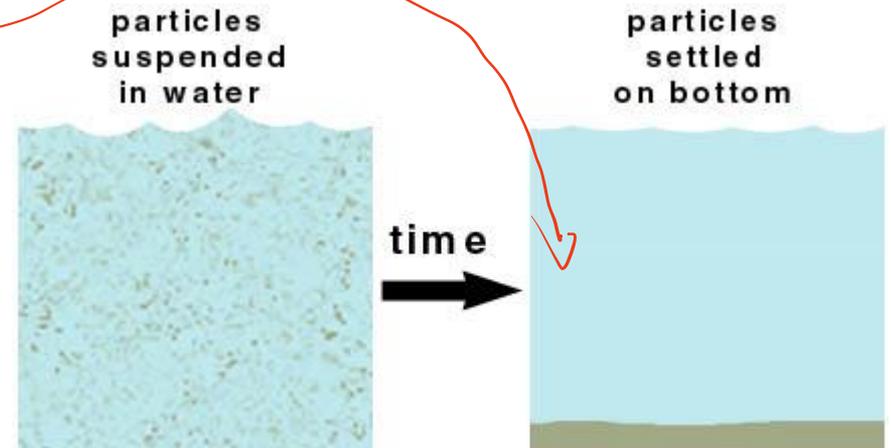
ما لازم  
أهمغرة

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.

كثير  
تشتت  
caking

لما يصير compact cake  
محبب تر حجه لما كان  
قبل حتى لو رجيتيه



# How to control the settling properties?

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. سرعة فيه
- 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. إذا كانت كثافة

الجزيئات أقل من المذيب، فإنها ستطفو

# How to control the settling properties?

## 3. Flocculating agents

Floccule  
فراغات

- flocculation refers to process which leads to aggregates that are loose or open

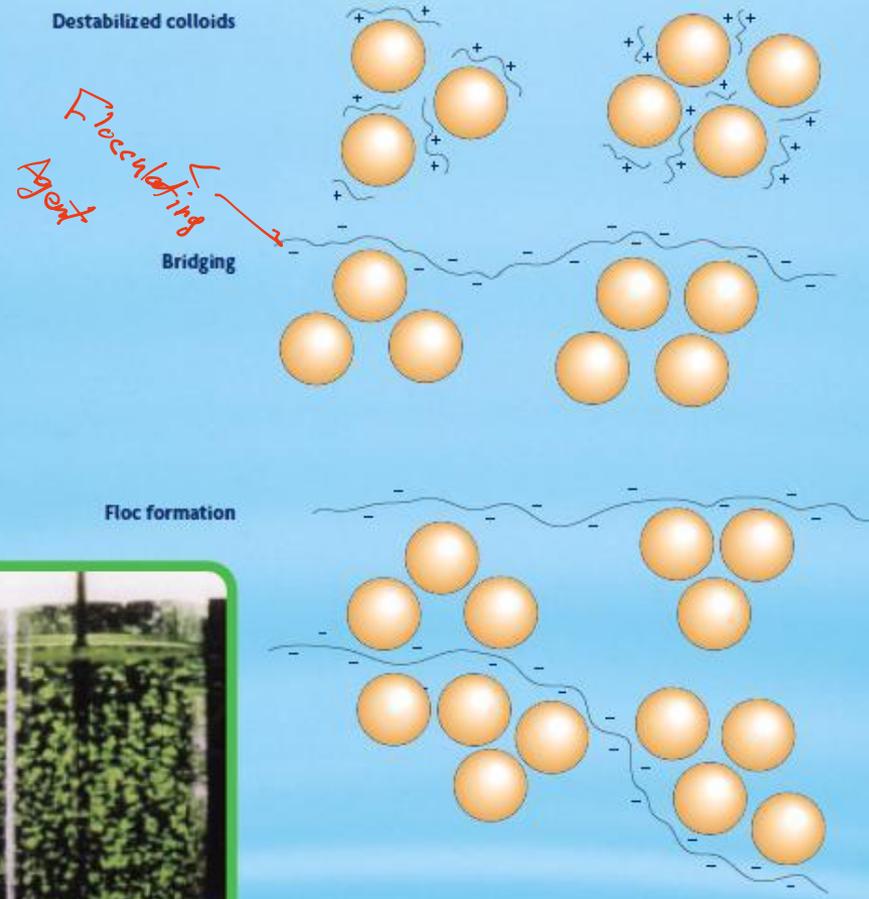
• Flocculating agents are electrolytes that carry an electrical charge opposite from that of the net charge on the suspended particles

• 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.

• 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.

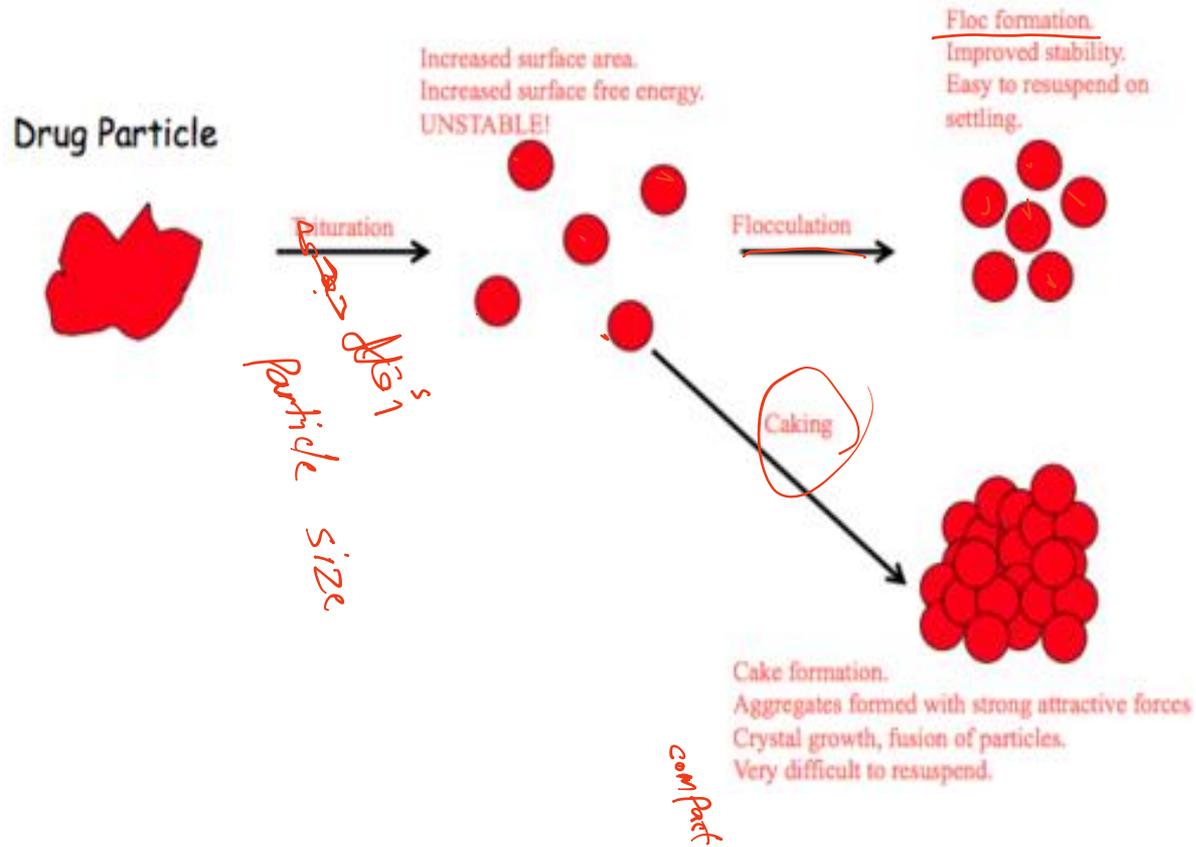
# DIAGRAM OF FLOCCULATION



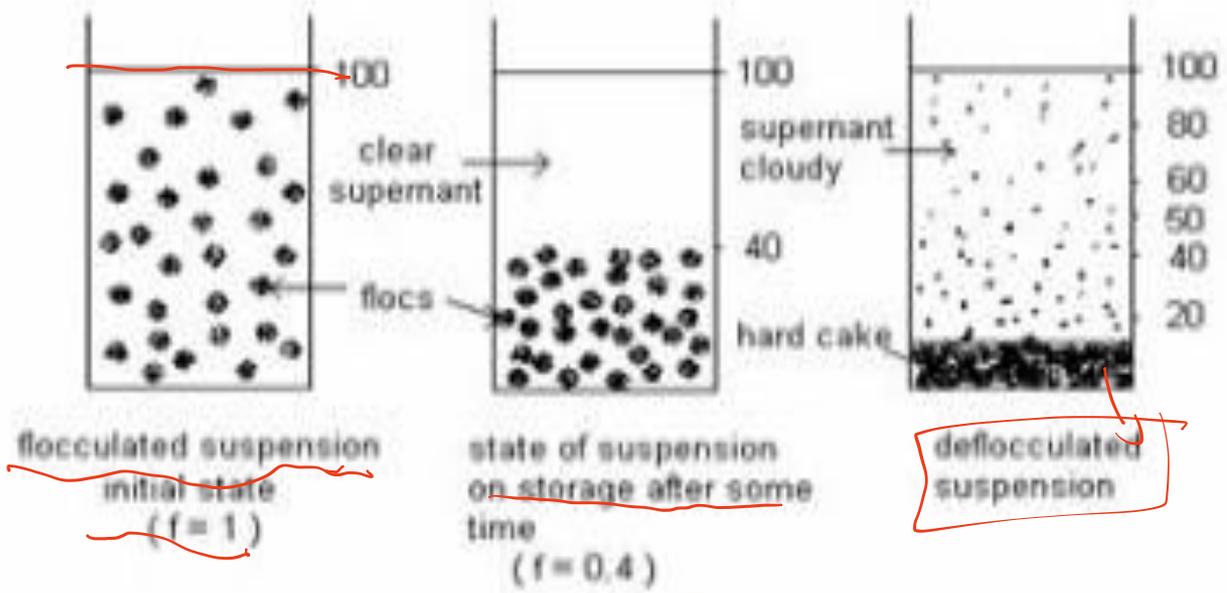
وسعة توضيح  
كيفه تكون  
Floccule

loose  
تكون فراغات



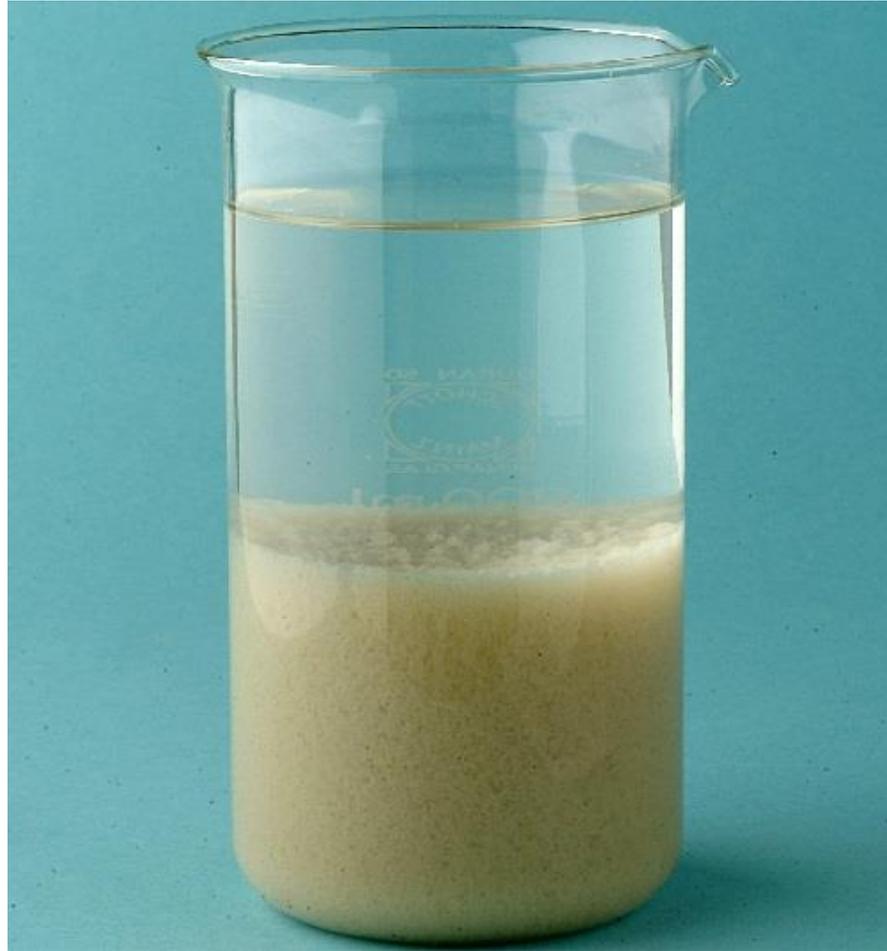


على الحجم الذي يتراكم  
 على الحجم الذي وصله  
 f = 1



(انتشار الصبغة)  
 f: كم صار الحجم الذي وصله  
 على الحجم اية بدائي

اخفض  
 ويمكن ارجاعه  
 بسهولة  
 عن طريق تحريكه



Saja Hamed, Ph.D

# How to control the settling properties?

بالخضار flocculated

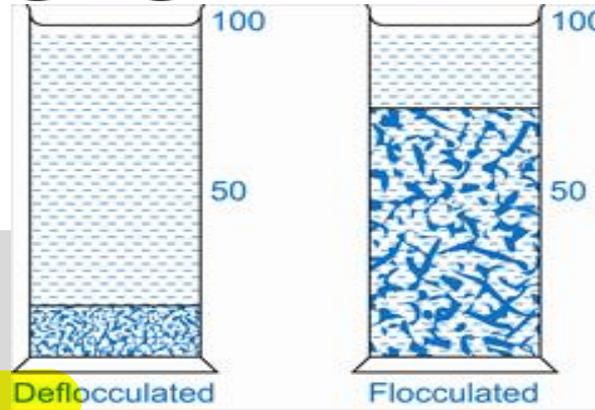
## 3. Flocculating agents

ليس يستخدم لمعالجة

مشكلة caking لكن يقرب

بشكل أسرع ولذا نلجأ

للكثافة



### 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, PhD

ممكن

### 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:

كلهم نفس الـ ايچ اس

## 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)

الحالة التي نريد الوصول إليها

علم الطفو

شبه اللامتناهي

• Ideally, the system should (rheologically) be **pseudoplastic**;   
 *لزوج عند ما لا تستقر فيه* 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).   
 *قليل اللزوجة عند التحريك*

• 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

سرعة  
الهبط  
تقل بزيادة اللزوجة

- 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.

واللزوجة  
تكون  
محدودة  
بحيث يمكن  
ذكي

- 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

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

### 2. Semisynthetic hydrocolloids

Methylcellulose, sodium carboxymethylcellulose

### 3. Synthetic hydrocolloids

Carbopol®

### 4. Clays

Bentonite, Veegum®

## The particle shape can also affect caking and product stability:

مقاله علمی  
آنالیز روایتی  
توضیحی  
caking و پایداری

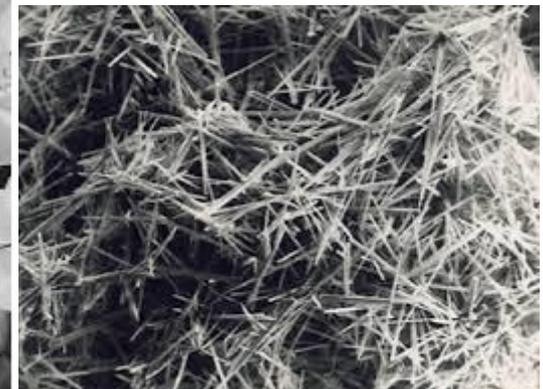
- It has been shown that symmetrical barrel-shaped particles of calcium carbonate produced more stable suspensions than did asymmetrical needle-shaped particles of the same agent.

اکثر پایداری

- 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



اذا صار cake تدخل ایبریشن  
و کاتسویج ارجاعه



فنا یقین ارجاعه مچه لو کاز  
cake

# Preparation of suspension:

## wetting agents

أحياناً رغبة العلاقات سهل دخولها في المعادله

ولكنه فضائل محاليله تسفر مع المحلول

• 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.

• **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.

# Preparation of suspension:

## wetting agents

حسب powder نحدد

نخلطهم مع كمية قليلة ثم نضيفهم الى الوسيط

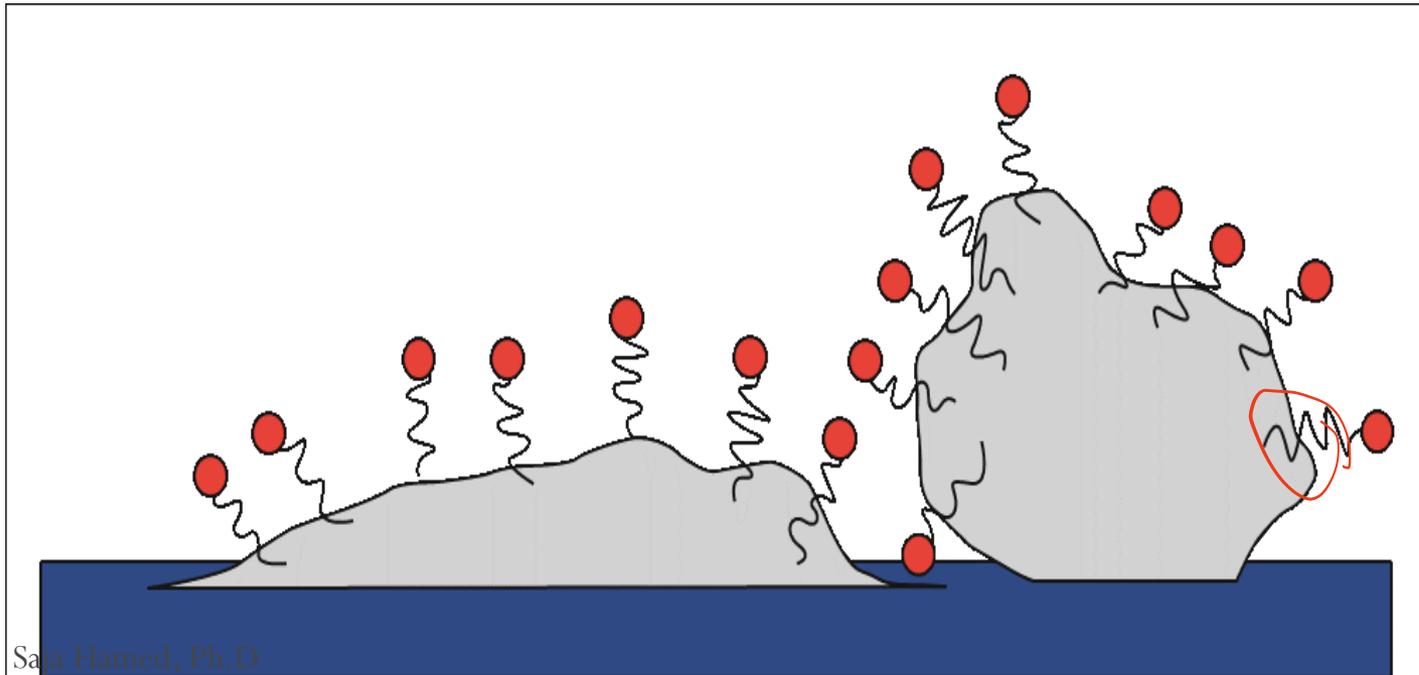
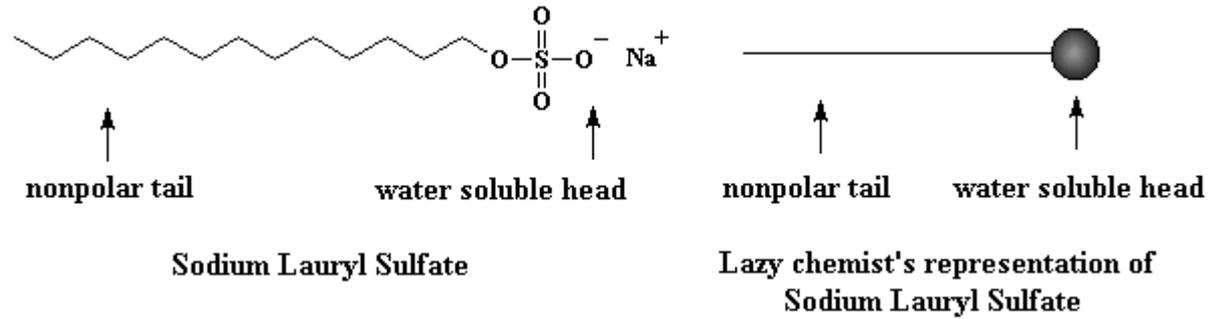
دلائل  
كميات  
قليلة  
منه

- 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
- 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

يمكن نضيفه مع الوسيط

surface agent  
جزء polar  
non-polar

# Preparation of suspension: wetting agents



# 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.

بلون  
معجون  
dispersion  
media

# 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 Saja Hamed, Ph.D	They are added to construct structure of the final suspension.

امداد الحافظة

آسی ایسے فاسی لازم ہونے سے

# 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

API (المادة الفعالة)



Aluminum hydroxide  
compressed gel

326.8g

sweetness

Sorbitol solution

282.0mL



Syrup

93.0mL

Glycerin

25.0mL

Preservative

Methylparaben

0.9g

Propylparaben

0.3g

Flavor

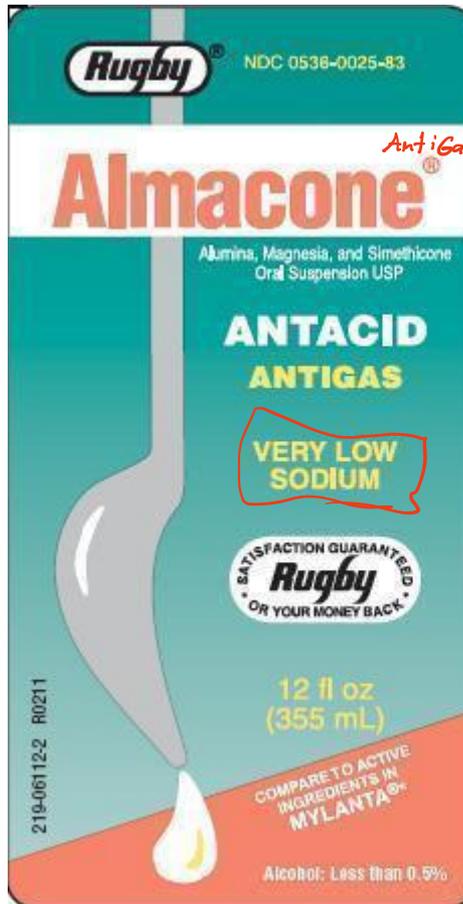
q.s.

Purified water, to make

1000.0mL

# Antacid Oral Suspensions

- Most antacid preparations are composed of water-insoluble materials that act within the 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



**Drug Facts**

Active Ingredients (in each 5 mL teaspoonful)	Purposes
Aluminum hydroxide 200 mg (equivalent to dried gel, USP)	Antacid
Magnesium hydroxide 200 mg	Antacid
Simethicone 20 mg	Antigas

**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 65 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 1-800-845-2158, 9 am - 5 pm ET, Monday-Friday

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2-919-06112-4 R0211



# Antibiotic Oral Suspensions

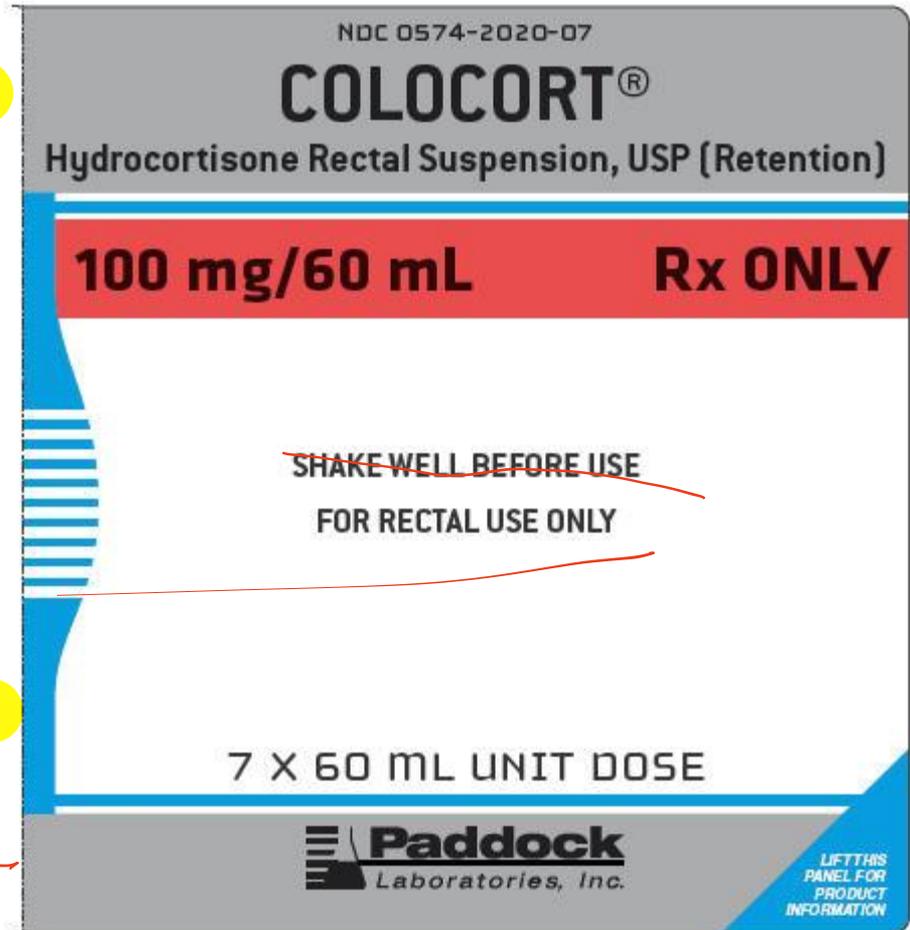
بودرة تم اذوبه ليصير suspension

- 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

أمنحه كبودرة حتى يبقو نعال لأطول فترة ممكنة وعند الإبتداء أضفه للماء

# Rectal suspension

- Colocort is a hydrocortisone rectal suspension indicated as adjunctive therapy 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.



تغليف

# 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.

سواء لازم

يكون مقادير

عشان يقدروا

يعمل shaking

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 °C). It should be stored in the refrigerator after opening or reconstitution (freezing should be avoided to prevent aggregation)

ممنوع تجميد suspension freezing

# 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  
*رج العجوة لا يكون كبير*
2. Presence of relatively large particles → excessive crystal growth  
*حبات كبيرة أعين غير متقرة جدًا*
3. Microbial contamination (discoloration, turbidity, or gas formation)