



لجان الدفعات

DISPENSING



MORPHINE ACADEMY

MORPHINE
ACADEMY

Colloidal Dispersion: Gel and Magma

Colloidal Dispersion

- A *colloidal dispersion* is a system in which particles of colloidal size of any nature (e.g. solid, liquid or gas) are dispersed in a *continuous phase* of a different composition (or state).
- Dispersion containing particles in the colloidal range (falling between 1.0 nm and 0.5 μm), are termed *colloidal dispersions* such as *Magnas* and *gels*.
يطلق عليها
- If the disperse phase interacts appreciably with the dispersion medium, it is said to be *lyophilic*, meaning *solvent loving*. If the degree of attraction is small, the colloid is termed *lyophobic*, or *solvent hating*.
إذا في تفاعل بيناتهم ويحبوا بعض يعني يكون (lyophilic)
أما إذا التفاعل بيناتهم ضعيف وبكرهوا بعض يكون (lyophobic) زي لما تحكي عندي فوييا من شيء يعني ما بحبوا وبخاف منه نفس الأشي هون
- lyophilic colloidal systems are easier to prepare and have greater stability.
- These terms are more suitably used when reference is made to the specific dispersion medium, for a single substance may be lyophobic with respect to one dispersion medium and lyophilic with respect to another.
- For instance, starch is lyophilic in water but lyophobic in alcohol.

Colloidal Dispersion

- Lyophobic colloids are generally composed of inorganic particles. When these are added to the dispersing phase, there is little if any interaction between the two phases.
- Unlike lyophilic colloids, lyophobic materials do not spontaneously disperse but must be encouraged to do so by special individualized procedures. Their addition to the dispersion medium does not greatly affect the viscosity of the vehicle

وبحسبك انه اذا تمت اضافة lyophobic ما يؤثر على اللزوجة عكس lyophilic بأثر

Colloidal Dispersion

هون حددنا انه بنحكي dispersion medium عبارة عن ماء
وَمُحِب أو كاره للماء

- Terms such as *hydrophilic* and *hydrophobic*, which are more *descriptive* of the nature of the colloidal property, have therefore been developed to refer to the attraction or lack of attraction of the substance specifically to water

Classification of colloidal system

Hydrophilic colloid

وتترطب

- Molecules have affinity for water and become hydrated when they are dispersed in water
- Hydrated colloids swell and increase the viscosity of the system →
 1. improve stability by reducing interaction between particles and their tendency to settle يزيد الاستقرار عن طريق يقلل التفاعل بين الجزيئات ويقلل الترسيب
 2. If they possess a net surface electrical charge (that depend on chemical properties & pH of the system) they will repel other charged particles and thus reduces the likelihood that particles will adhere to one another and settle وإذا كان عليها شحنة التي يعتمد على الخصائص الكيميائية و pH ورح تتنافر مع الجزيئات الثانية المشحونة ورح يقل الالتصاق بيناتهم وترسيبهم

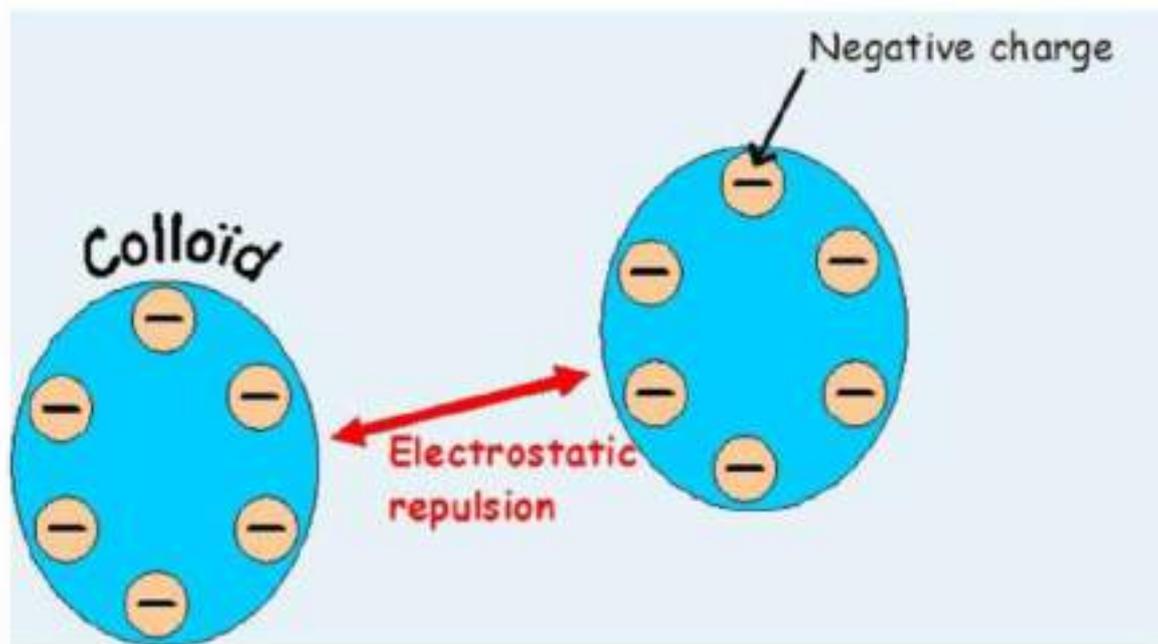
Classification of colloidal system

Hydrophilic colloid

- Examples:
 - acacia
 - Methylcellulose
 - Proteins (gelatin & albumin)

Hydrophobic colloid

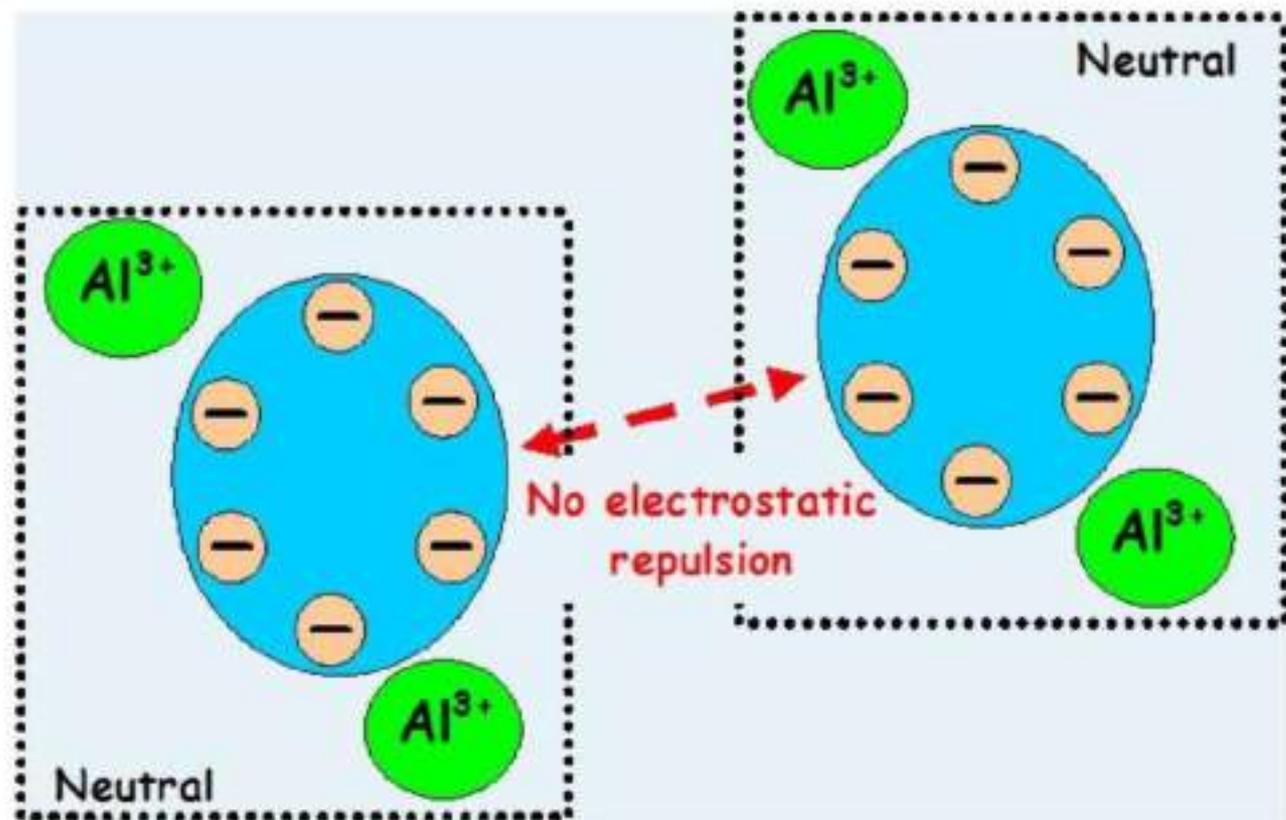
- Has little or no affinity for water molecules
- Produces no change in system viscosity
- The particles may carry a charge
- They maintain their dispersion in the medium as a result of mutual repulsion of like charges and Brownian movement
نتيجة التنافر المتبادل الشحنات المتشابهة الحركة البراونية
- E.g. of hydrophobic colloids:
 - Silver iodide
 - Sulfur
 - Gold



Hydrophobic colloids

Charged particles

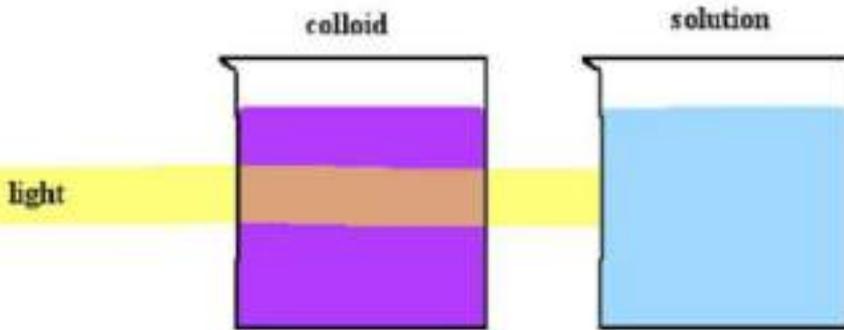
- Charged particles may be neutralized by adding ions of the opposite charges to the dispersion medium عن طريق إضافة أيونات بشحنة معاكسة للوسط
- The neutralized particles cling together تتجمع مع بعض وتترسب → larger particles aggregate → may precipitate



Properties of Colloids

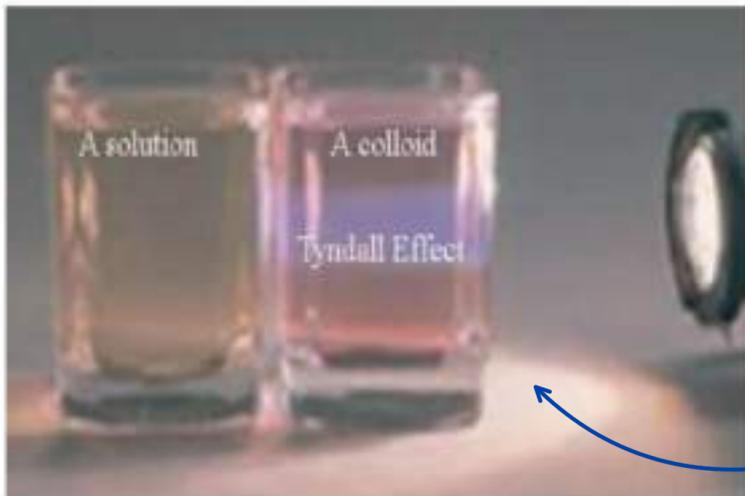
1. **Scattering of a light beam directed through the medium (Tyndall effect):** colloidal بيكون واضح بيسار أما اذا كان في مسار واضح بيكون solution بيكون المسار بوضوح وما توضح المادة اذا تشتتت وما توضح المسار بيكون solution بيكون واضح بيسار
 - a. its magnitude is a result of the size and number of particles present
 - b. Can be used to determine the molecular weight, size, and shape of the colloids
الحركة العشوائية
2. **Brownian movement:** result from bombardment of the colloidal particles by molecules of the dispersion medium (< 5 microns) وهذه الجزيئات الصغيرة الي حجمها
3. The **presence of a charge** on the colloidal particles gives them electrical properties: thus when exposed to an electrical potential colloids can be forced to migrate toward the electrode of opposite charge (electrophoresis) → can be used to separate a mixture of colloidal substances such as proteins

The Tyndall effect, also known as Tyndall scattering, is light scattering by particles in a colloid or particles in a fine suspension. It is named after the 19th-century physicist John Tyndall وطبعًا هذا نسبة للعالم

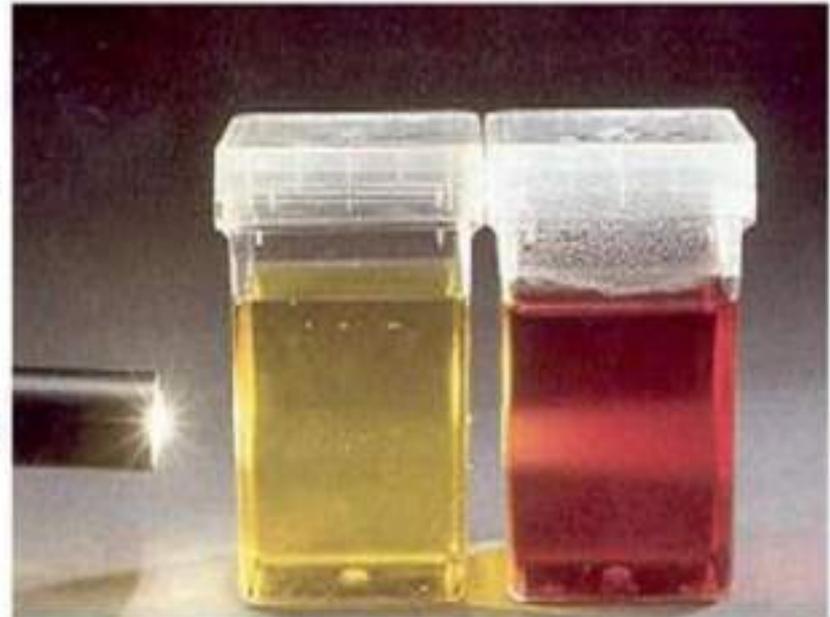


A beam of light shining toward the solution and the colloid. The light particles are suspended when passing through the colloid's large particles, but not when passing through the solution's smaller particles.

جزيئات كبيرة
جزيئات صغيرة



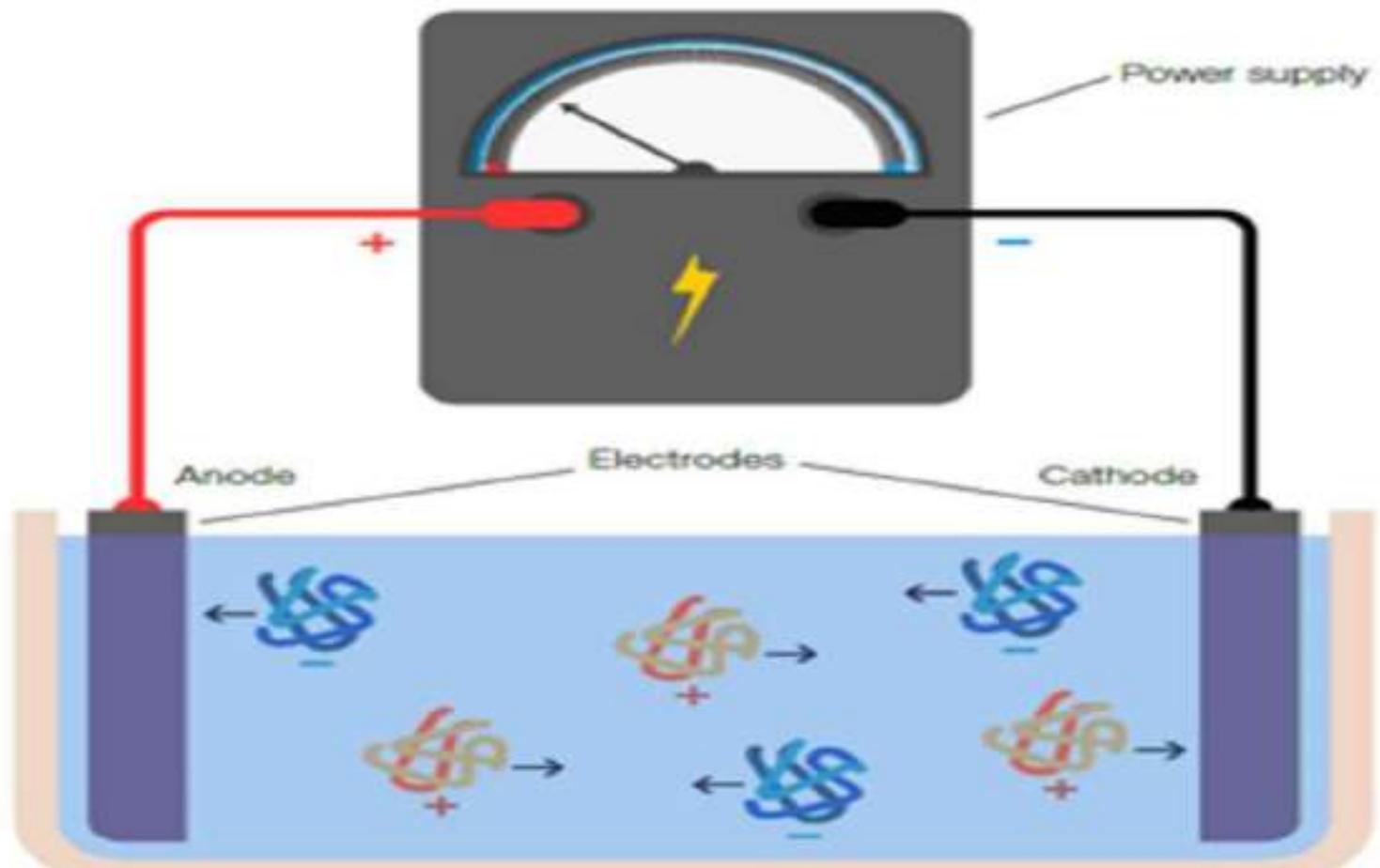
بيخبط الضوء
بالجزيئات
الكبيرة وبيظهر



True solution
(No scattering
of light)

Colloidal sol
(Scattering of
light)

Electrophoresis:



Properties of Colloids

4. Colloids do not pass through a semi-permeable membrane:

إذا حظيناه في كيس من السيلوفان رح ندخل الماء الى الكيس وتخففه

- a. when an albumin dispersion is placed into a cellophane sac and submerged into water, water molecules will enter the sac to dilute the albumin dispersion that cannot diffuse out بس هو ما بقدر يطلع
- b. This principle explains the role of human serum albumin in maintaining the osmotic pressure of blood وهذا يفسر الحفاظ على الضغط الاسموزي في الدم
- c. This principle is in the kidney too: ions and small molecules are filtered while serum protein are retained زي في الكليه

بنعمل فلتره للأيونات والجزيئات الصغيرة ونخلي البروتينات

Gels

- Gels are defined as semisolid systems consisting of dispersions made up of either small inorganic particles or large organic molecules enclosing and interpenetrated by a liquid.
lyophobic colloid Lyophilic colloid
مُحاط ويدور حوله السائل
- Gels are also defined as semi-rigid systems in which the movement of the dispersing medium is restricted by an interlacing three-dimensional network of particles or solvated macromolecules of the dispersed phase.
مقيدة
تشابك
- Gels also are defined as a substantially dilute cross-linked system, which exhibits no flow when in the steady-state.

Gels

- Gels are useful as liquid formulations in oral, ophthalmic, nasal, topical, vaginal, and rectal administration
- Are made by using substances called gelling agent
- Gelling agent undergo extensive cross-linking or enlargement when dissolved or dispersed in the dispersing medium
- This cross linking increases the viscosity of the dispersing medium and also restricts its movement

Gels

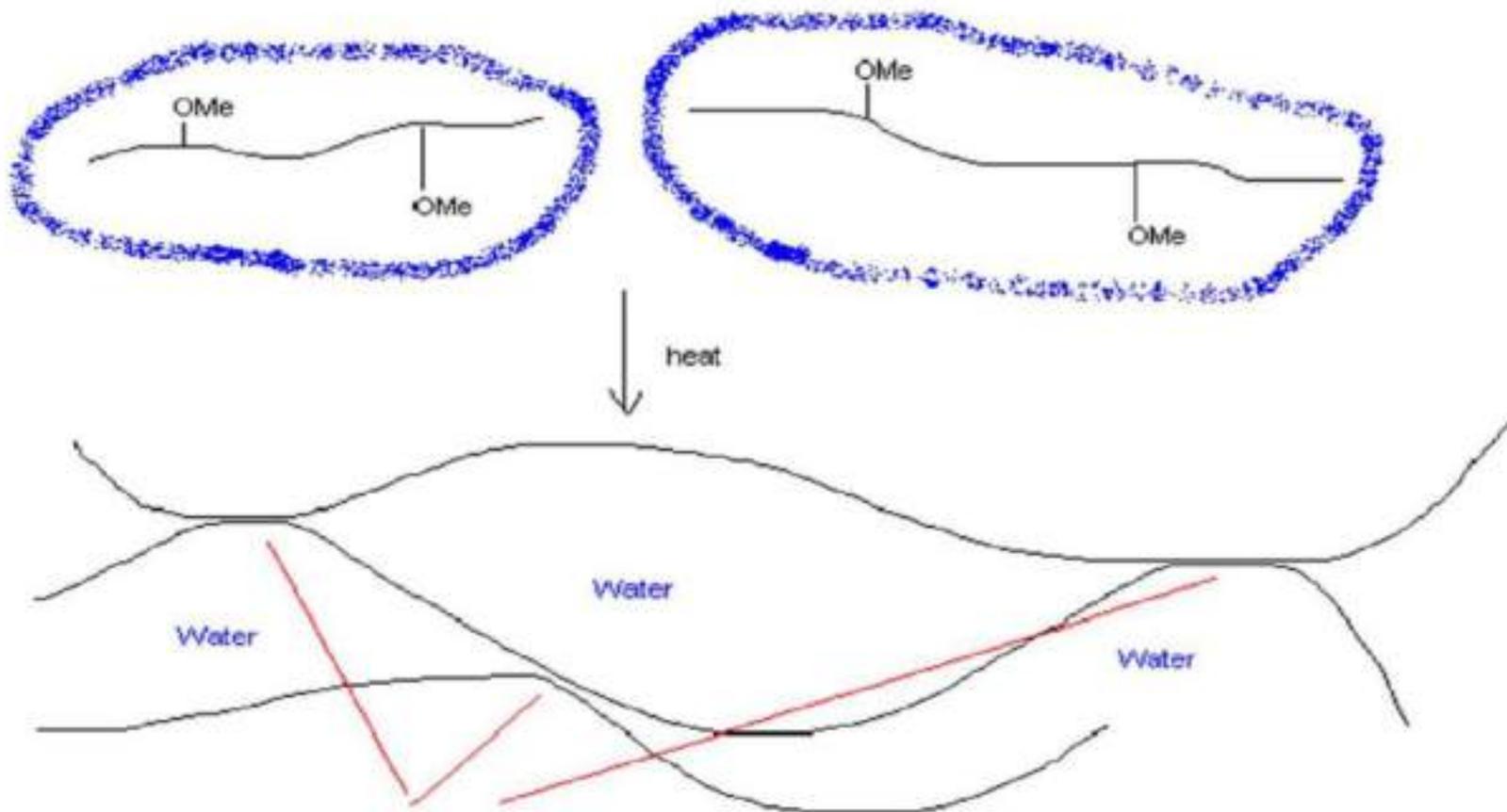
انت بتفكرها من شكلها ثلاثي الابعاء كأنها اشي صلب بس هي أغلبها ماء ويتفرد بكل سهولة

- By weight, gels are mostly liquid, yet they behave like solids due to a three-dimensional cross-linked network within the liquid.

هذا بيعطيها الشكل الصلب

- It is the cross-linking within the fluid that give a gel its structure (hardness) and contribute to the adhesive stick.
- So gels are actually mixtures containing a solid skeletal structure which completely ensnares liquid inside its 3D structure

يحتجز السائل داخل شكله الصلب ثلاثي الابعاد



Hydrophobic interactions are favored at higher temperatures, thus forming junction zones, which produces a gel



Gel's classification

TABLE 14.4 GENERAL CLASSIFICATION AND DESCRIPTION OF GELS

CLASS	DESCRIPTION	EXAMPLES
Inorganic	Usually two-phase systems	Aluminum hydroxide gel Bentonite magma
Organic	Usually single-phase systems	Carbopol Tragacanth
Hydrogels	Organic hydrogels Natural and synthetic gums Inorganic hydrogels	Pectin paste, Tragacanth jelly Methylcellulose, sodium carboxymethylcellulose, Pluronic Bentonite gel (10%–25%), Veegum, silica
Organogels	Hydrocarbon type Animal, vegetable fats Soap base greases Hydrophilic organogels Polar Nonionic	Petrolatum, mineral oil/polyethylene gel (Plastibase) Lard, cocoa butter Aluminum stearate with heavy mineral oil gel Carbowax bases (PEG ointment)

Gel's classification:

1. Two Phase system

- When the gel mass consists of floccules of small, distinct particles, the gel is classified as a two-phase system and frequently called a *magma* or *a milk* (e.g. milk of magnesia, aluminum hydroxide gel, bentonite magma)
- Two phase systems are **thixotropic** (semi solid on standing but liquefy when shaken)

بكون شكله صلب بس هو سائل لما ترجمه

Gel's classification:

2. Single Phase system

- If the gel does not appear to ^{جزينات منفصلة} have discrete particles it is called a one-phase system
- Single phase systems contain ^{خطي} linear or ^{متفرع} branched polymer macromolecules that dissolve in water and have no apparent boundary with the dispensing medium
- Macromolecules are classified as natural polymers (e.g. tragacanth), semisynthetic cellulose derivatives (e.g. methylcellulose), or synthetic polymers (e.g. carbomer polymers)
- Single phase gels made from synthetic or natural macromolecules are called mucilages

mucilage



Bentonite Magma, NF

Two phase system

Bentonite magma is a preparation of 5% bentonite, a native colloidal hydrated aluminum silicate, in purified water. It may be prepared mechanically in a blender with the bentonite added directly to the purified water while the machine is running, or it may be prepared by sprinkling the bentonite, in portions, upon hot purified water, allowing each portion to become thoroughly wetted without stirring before another portion is added. By the latter method, the mixture must be allowed to stand for 24 hours before it may be stirred. The standing period ensures complete hydration and swelling of the bentonite.

Aluminum Hydroxide Gel, USP

Two phase system

- A gelatinous precipitate composed of insoluble aluminum hydroxide and the hydrated aluminum oxide
- To the gel, the USP permits the addition of peppermint oil, glycerin, sorbitol, sucrose, saccharin, or other flavorants and sweeteners as well as suitable antimicrobial agents.
- This antacid preparation is white and viscous.
- It is effective in neutralizing a portion of the gastric hydrochloric acid and by virtue of its gelatinous, viscous, and insoluble character, coats the inflamed and perhaps ulcerated gastric surface, and is useful in the treatment of hyperacidity and peptic ulcers. The main disadvantage to its use is its constipating effects. The usual dose is 10 mL four or more times a day, that is, after meals and at bedtime. The analogous commercial product (Amphojel, Wyeth-Ayerst) at 10 mL has the capacity to neutralize about 13 mEq of acid. The preparation should be stored in a tight container, and freezing should be avoided.

Refer to USP Monographs Aluminum Hydroxide Gel

http://www.pharmacopeia.cn/v29240/usp29nf24s0_m2100.html



Single phase system

- Fluocinonide Gel, USP, an anti-inflammatory corticosteroid,
- Tretinoin Gel, USP, stimulates epidermal cell turnover, causes peeling, and is effective in the treatment of acne.
- Erythromycin and benzoyl peroxide topical gel (Benzamycin Topical Gel, Dermik Laboratories)



Common gelling agents: common properties

1. If the gelling agent is added to the dispersing medium too rapidly the agents tend to clump ^{تكتلات} → layer with a gelled surface that is more difficult for the medium to hydrate

Some compounding techniques to minimize the problem: → Clump

- a. ^{غربلة} Sift the powders into the vortex of the rapidly stirring medium
- b. Levigate the powder with a water miscible non-solvent such as absolute alcohol or propylene glycol ^{← wetting agent نفس مبدأ}
- c. Use a blender to mix the powder and solvent homogenously

Common gelling agents: common properties

2. Some gelling agents are more soluble in cold water than in hot water

e.g.

- methylcellulose and poloxamers have better solubility in cold water
- Bentonite, gelatin, and sodium carboxymethylcellulose are more soluble in hot water
- Carbomers, tragacanth, and alginic acid gels are made with tepid water

Common gelling agents: common properties

3. Some gelling agents (e.g. carbomers) require a “neutralizer” or pH adjusting chemical to create the gel after the gelling agent has been wetted in the dispersing medium
4. Most gelling agents require 24 to 48 hours to completely hydrate and reach maximum viscosity and clarity
5. Gelling agents commonly are used in concentrations of 0.5-2% but some may be used up to 10%
6. It is easier to add the active drug before the gel is formed if the drug doesn't interfere with the gel formation

Common gelling agents:

Carbomers

- Carbomer is a generic name for a family of polymers known as Carbopol®
- 1950
- They are dry powders with high bulk density
- Form acidic aqueous solutions (pH around 3)
- Thicken at a higher pH (5 or 6) → swell as much as 1,000 times their original volume
- A neutralizer (e.g sodium hydroxide, triethanolamine) is added to increase the pH

Selected Carbomers:

Polymer Name	Viscosity*	Properties
Carbopol® 910	3,000 - 7,000	Effective in low concentrations and will provide a low viscosity formulation.
Carbopol® 934	30,500 - 39,400	Effective in thick formulations such as emulsions, suspensions, sustained-release formulations, transdermals, and topicals. Forms clear gels with water.
Carbopol® 934P	29,400 - 39,400	Same properties as 934, but intended for pharmaceutical formulations. "P" = highly purified product
Carbopol® 940	40,000 - 60,000	Effective in thick formulations, very good clarity in water or hydroalcoholic topical gels. Forms clear gels with hydroalcoholic systems.
Carbopol® 941	4,000 - 11,000	Produces low viscosity gels, very good clarity.

* 0.5% solution, pH 7.5

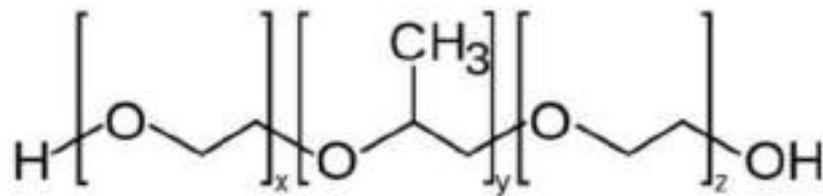
Common gelling agents: Cellulose derivatives

- Methylcellulose, hydroxyethylcellulose, hydroxypropyl cellulose, hydroxypropylmethyl cellulose, and carboxymethyl cellulose)
- All of the cellulose derivatives except ^{CMC} carboxymethyl cellulose maintain the viscosity of the gel over a wide pH range (3-11). CMC can maintain the viscosity between pH 7-9
- The addition of salts to medium reduces the ability of cellulose to hydrate

Common gelling agents:

Poloxamers

- Pluronic®
- Are copolymers of polyoxyethylene and polyoxypropylene
- They forms **reverse thermal gels** in conc. ranging from 15-20%
تتأثر بالحرارة
- Liquids at cool temp and gels at room or body temp.
- PLO gel: look it up



Packaging

- Gels generally are stored in tight containers at refrigerated or room temperature
- Patients prefer gels that appear clear, water washable, sparkle, water soluble, and greaseless
- Tubes, jars, squeeze bottles, pump dispensers

Observing formulations for evidence of instability:

- Gels should be observed for shrinkage, separation of liquid, discoloration, and microbial contamination
- Preservatives are recommended for gels
- Carbomer polymers are quite hygroscopic → store away from moisture

TABLE 11.2: COMMON PRESERVATIVES USED IN GELS

Preservative	Concentration (%)	Appearance
Benzalkonium chloride	0.01–0.1	clear – cloudy
Sodium benzoate	0.01–0.1	clear – cloudy
Methylparaben	0.18	clear
Propylparaben	0.02	clear
Thimerosal	0.01–0.1	clear