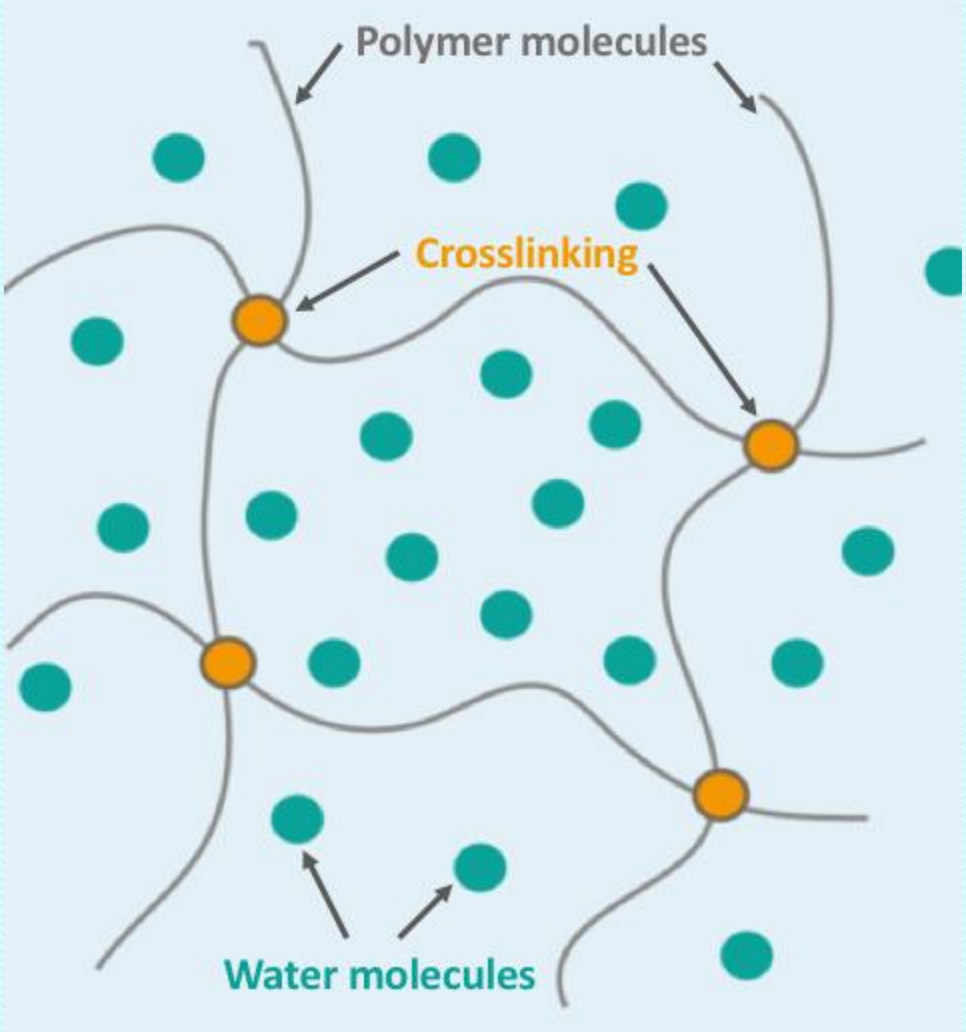
Pharmaceutical Technology-I

Colloid-Part II

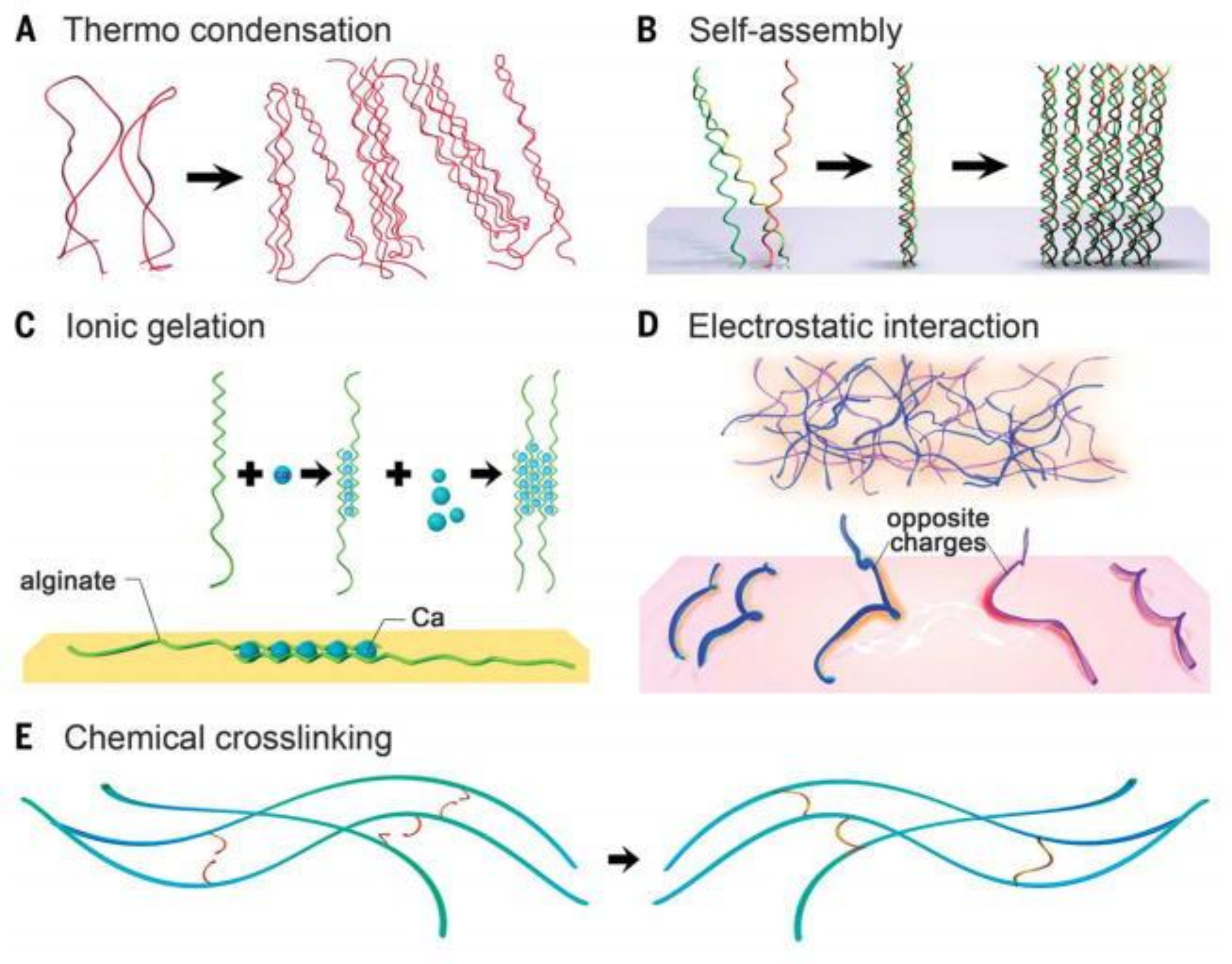
Gels

- 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.
- Gels are also defined as sem-irigid 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.
- A high degree of physical or chemical cross-linking may be involved.



Chemical cross linking

- Where chemical cross-links are covalent bonds, physical cross-links are formed by weak interactions. For example, sodium alginate gels upon exposure to calcium ion, which allows it to form ionic bonds that bridge between alginate chains.
- Polyvinyl alcohol gels upon the addition of borax through hydrogen bonding between boric acid and the polymer's alcohol groups.
- Other examples of materials which form physically cross-linked gels include gelatin, collagen, agarose, and agar agar



Cross-linking of hydrogels(**A** to **D**) Physical cross-linking. (A) Thermally induced entanglement of polymer chains. (B) Molecular self-assembly. (C) Ionic gelation. (D) Electrostatic interaction. (**E**) Chemical cross-linking.

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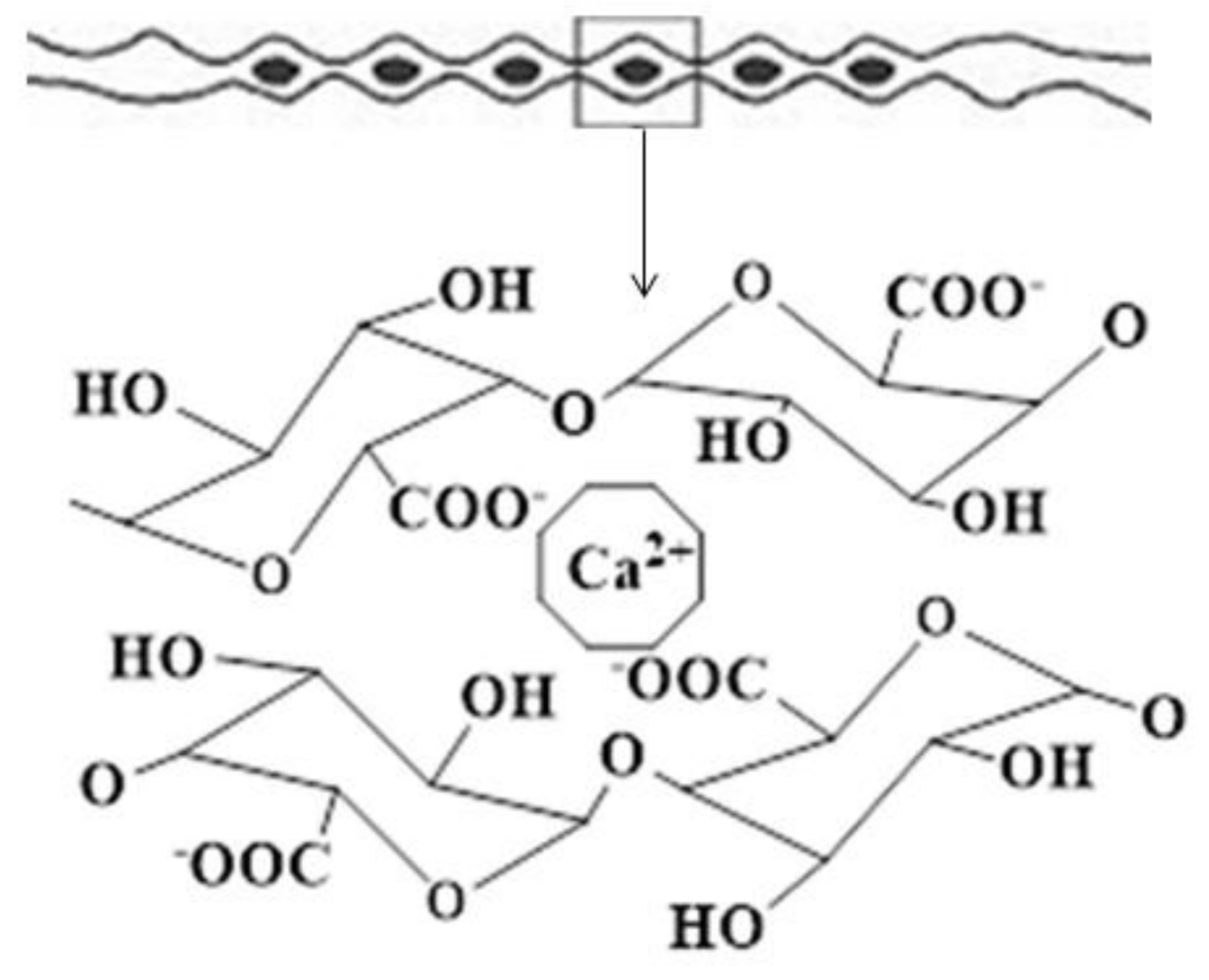

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- Some gel systems are as clear as water, and others are turbid because the ingredients may not be completely molecularly dispersed (soluble or insoluble), or they may form aggregates, which disperse light.
- The concentration of the gelling agents is mostly <10%, usually in 0.5% to 2% range, with some exceptions.
- Gels in which the macromolecules are distributed so that no apparent boundaries exist between them and the liquids are called single-phase gels.

- 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.
- Gels and magmas are considered colloidal dispersions because they contain particles of colloidal dimension.

Terminology Related to Gels

- A number of terms are commonly used in discussing some of the characteristics of gels, including imbibition, swelling, syneresis, thixotropy, and xerogel.
- **Imbibition** is the taking up of a certain amount of liquid without a measurable increase in volume.
- **Swelling** is the taking up of a liquid by a gel with an increase in volume. Only liquids that solvate a gel can cause swelling.
- The swelling of protein gels is influenced by pH and the presence of electrolytes.

- **Syneresis** occurs when the interaction between particles of the dispersed phase becomes so great that on standing, the dispersing medium is squeezed out in droplets and the gel shrinks.
- Syneresis is a form of instability in aqueous and nonaqueous gels.
- Separation of a solvent phase is thought to occur because of the elastic contraction of the polymeric molecules; in the swelling process during gel formation, the macromolecules become stretched, and the elastic forces increase as swelling proceeds.

- **Thixotropy** is a reversible gel–sol formation with no change in volume or temperature, a type of non Newtonian flow.
- **A xerogel** is formed when the liquid is removed from a gel and only the framework remains.
- Examples include gelatin sheets, tragacanth ribbons, and acacia tears.

Classification and Types of Gels

- Table 14.4 is a general classification of gels listing two classification schemes.
- The first scheme divides gels into inorganic and organic. Most inorganic hydrogels are two phase systems, such as aluminum hydroxide gel and bentonite magma.
- Most organic gels are single-phase systems and may include such gelling agents as carbomer and tragacanth and those that contain an organic liquid, such as Plastibase.

- The second classification scheme divides gels into hydrogels and organogels with some additional subcategories.
- Hydrogels include ingredients that are dispersible as colloidals or soluble in water; they include organic hydrogels, natural and synthetic gums, and inorganic hydrogels.
- Examples include hydrophilic colloids such as silica, bentonite, tragacanth, pectin, sodium alginate, methylcellulose, sodium CMC, and alumina, which, in high concentration, form semisolid gels.

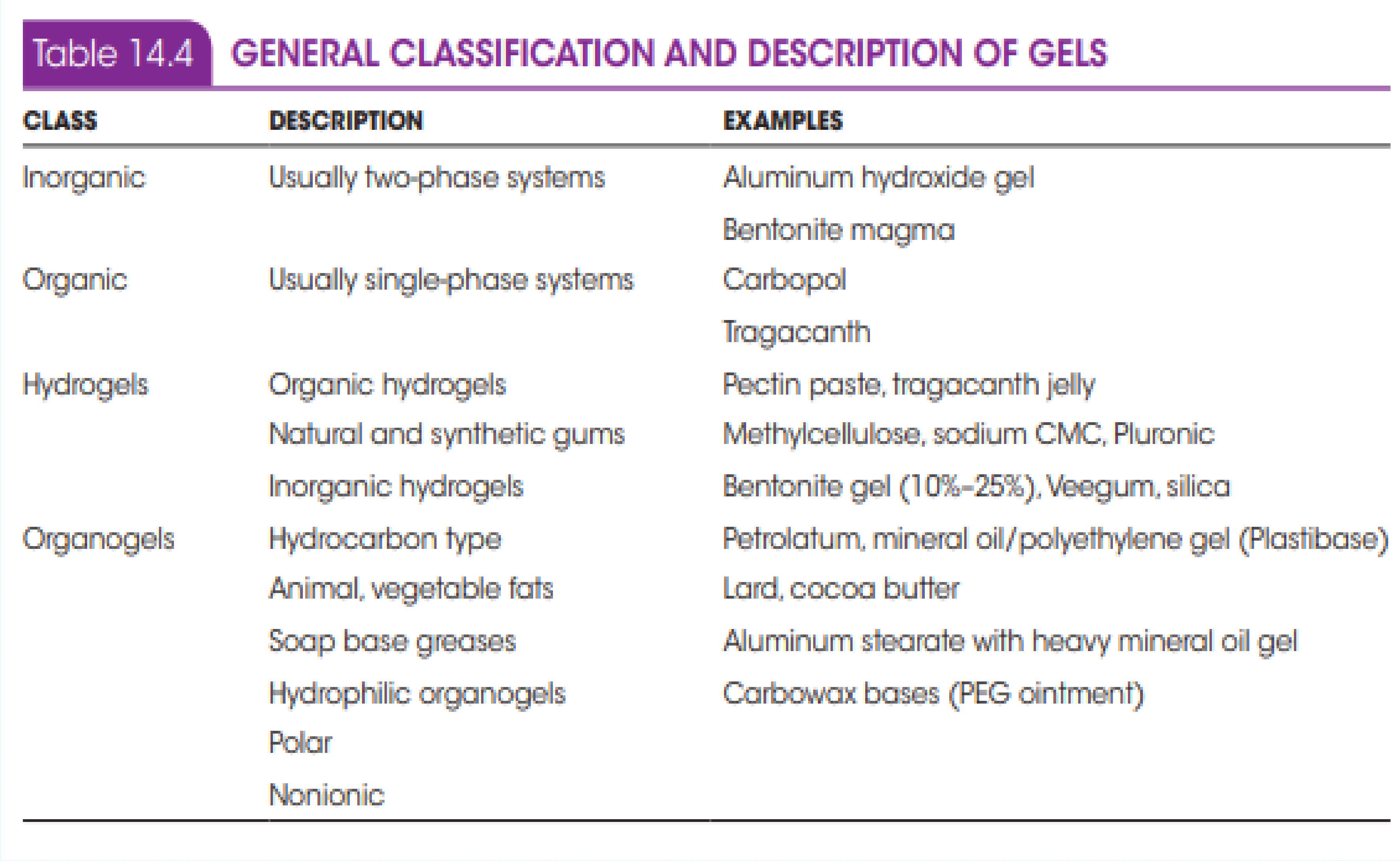
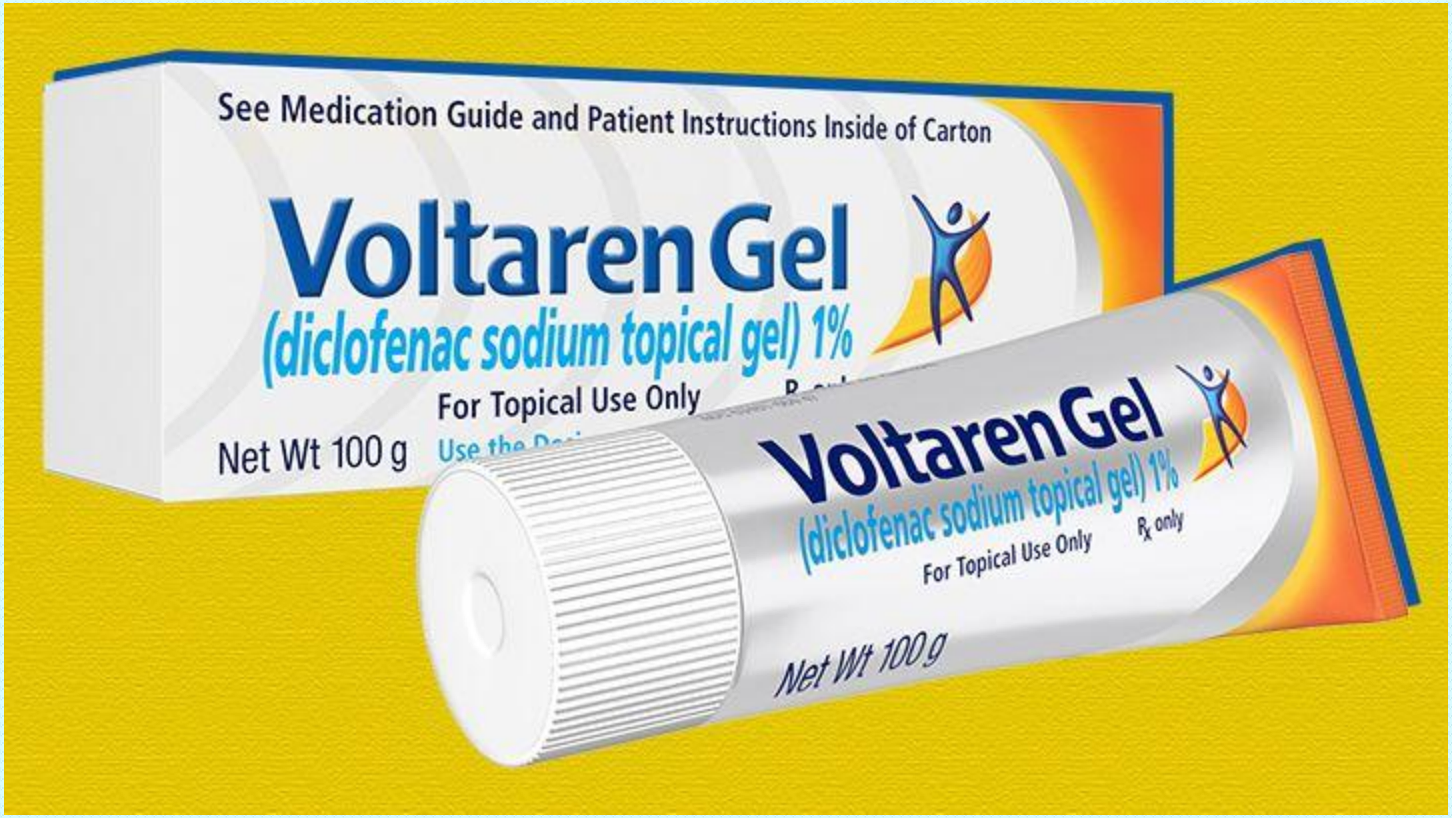


Table 14.4 **GENERAL CLASSIFICATION AND DESCRIPTION OF GELS**

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

- Sodium alginate has been used to produce gels that can be employed as ointment bases. In concentrations >2.5% and in the presence of soluble calcium salts, a firm gel, stable between pH 5 and 10, is formed.
- Methylcellulose, hydroxy ethylcellulose, and sodium CMC are among the commercial cellulose products used in ointments. They are available in various viscosity types, usually high, medium, and low.


See Medication Guide and Patient Instructions Inside of Carton
Voltaren Gel
(diclofenac sodium topical gel) 1%
For Topical Use Only
Net Wt 100 g
Voltaren Gel
(diclofenac sodium topical gel) 1%
Rx only
For Topical Use Only
Net Wt 100 g

Jellies

- Jellies are a class of gels in which the structural coherent matrix contains a high proportion of liquid, usually water. They usually are formed by adding a thickening agent such as tragacanth or carboxymethyl cellulose to an aqueous solution of a drug substance.
- The resultant product is usually clear and uniformly semisolid.
- Jellies are subject to bacterial contamination and growth, so most are preserved with antimicrobials.
- Jellies should be stored with tight closure because water may evaporate, drying out the product.

Examples of Magmas and Gels

- One official magma, Bentonite Magma, NF, used as a suspending agent, finds application in the extemporaneous compounding of prescriptions.
- Sodium Fluoride and Phosphoric Acid Gel, USP, is applied topically to the teeth as a dental care prophylactic.
- Other official gels applied topically include Fluocinonide Gel, USP, an anti-inflammatory corticosteroid, and Tretinoin Gel, USP, an irritant that stimulates epidermal cell turnover, causes peeling, and is effective in the treatment of acne.

- Examples of such drugs and drug products are erythromycin and benzoyl peroxide topical gel (Benzamycin Topical Gel, Dermik Laboratories),
- clindamycin topical gel (Cleocin T Topical Gel, Pfizer), clindamycin and benzoyl peroxide topical gel (BenzaClin, Dermik), and benzoyl peroxide gel (Desquam-X 10 Gel, Westwood-Squibb) used in the control and treatment of acne vulgaris;
- hydroquinone gel (Solaquin Forte Gel, ICN), a bleach for hyperpigmented skin;
- salicylic acid gel (Compound W Gel, Medtech), a keratolytic; and desoximetasone gel (Topicort Gel, Taro) and augmented betamethasone dipropionate topical gel (Diprolene, Schering-Plough), anti-inflammatory and antipruritic agents.

- Other official magmas and gels are employed as antacids: Aluminum Phosphate Gel, USP; Aluminum Hydroxide Gel, USP; and Dihydroxyaluminum Aminoacetate Magma, USP.

Lyophobic Dispersion (Colloid)

1. A system in which there is little attraction between dispersed phase and dispersion medium. It is called solvent-hating.
2. Unlike lyophilic colloids, lyophobic materials do not spontaneously disperse, but must be encouraged to do so by special individualized procedures.
3. Their addition to the dispersion medium does not greatly affect the viscosity of the vehicle.

- When the dispersion medium is water then the system called hydrophobic and this system consists of a particle which is not hydrated by water, so water molecules attract to each other to solvate particle.
- This system includes aqueous dispersion of

1. Oleophilic materials such as polystyrene, gum rubber, steroids, paraffin wax and
2. Some other organic lipophilic materials like Magnesium stearate
3. There is an exception for materials that are not lipophilic and form hydrophobic dispersion, these are AgCl and gold.

- Lyophobic dispersions are intrinsically unstable because of the lack of attraction between the dispersed phase and continuous phase, and they are irreversible.
- The instability is also due to the large surface area, which gives large surface free energy, which is not lowered by solvation.
- The dispersion process does not take place spontaneously and once the dispersed phase is separated from the dispersion medium the dispersion is not easily reconstituted.

Preparation of lyophobic colloid

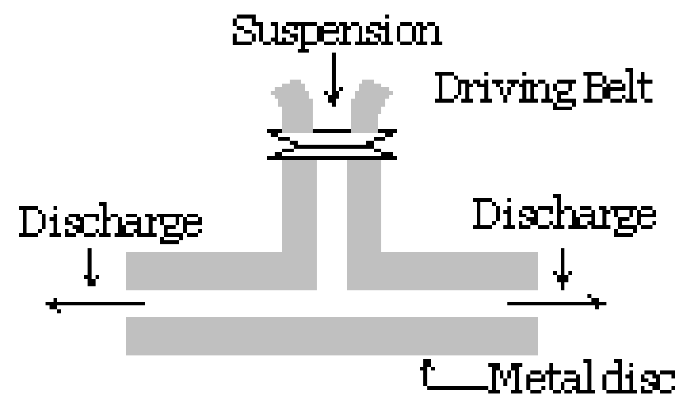
- For preparing lyophobic colloidal sol, the substance in bulk is broken down into particles of colloidal dimensions (Dispersion) or aggregating smaller particles of into particles of colloidal dimensions (condensation).
- To improve the stability of sol creation substances are added to the sol, the substances added are called stabilizers.

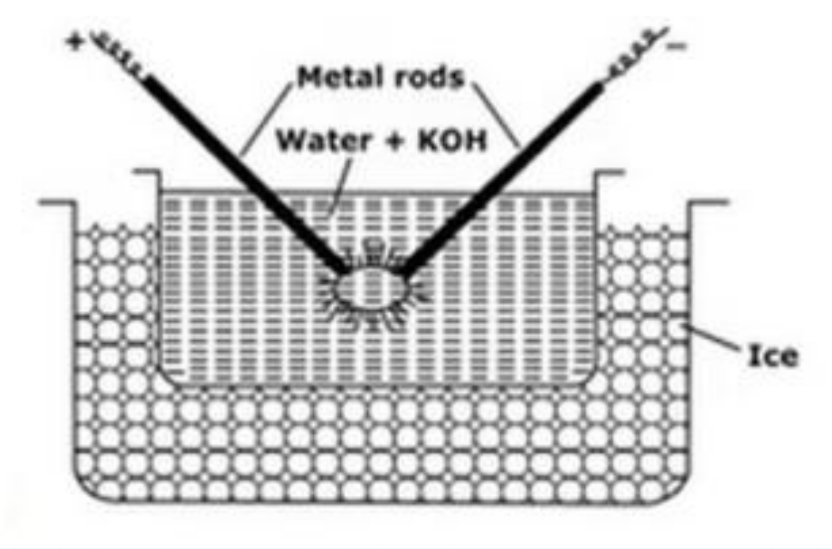
Dispersion methods

- In the dispersion method particle of larger size are broken down to colloidal size in the dispersion medium.
- Starting with the material in massive form, a colloidal dispersion is prepared by using suitable devices to disintegrate it into particles of colloidal size.
- Normally this is carried out by physical methods.

Mechanical dispersion method

- The substance which is to be dispersed is finely ground. It is then mixed with the dispersion medium, protective materials or stabilizer is also added when a coarse suspension is obtained.
- This suspension is then passed through a colloid mill. A colloid mill consists of two heavy metal discs placed one above the other separated by a very small gap from each other. They are rotated in the opposite directions at a very high speed of about 7000 r.p.m.
- The sol results due to the large shearing effect.
- Protective material used prevents particles from coagulation.





https://thefactfactor.com/facts/pure_science/chemistry/physical-chemistry/preparation-of-colloids/11294/

Electrical dispersion or Bredig's Arc method

- This method used to prepared metal sols like platinum, silver, gold, copper in water.
- A dispersion medium (conductivity water) and a trace of sodium hydroxide (the stabilizing agent) is taken in porcelain or glass (non conducting) vessel.
- Metal to be dispersed is dipped in the vessel in the form of electrodes. Electrodes are connected to the high voltage source. The ends of electrodes in the dispersion medium are very near to each other.
- A very high voltage is applied and then an electrical arc is struck between the tips of electrodes. This creates large heat due to which metal rods melt, evaporate and suddenly cooled due to freezing mixture gives rise to the colloidal solution of the metal.

➢ Function of the freezing mixtures are

1. Freezing mixture helps in condension of metal vapours forming the colloids
2. It prevents vapourisation of water.
3. It prevents coagulation of colloids, by keeping sol cold.

Ultrasonic Dispersion

- Ultrasound is a very effective processing method in the generation and application of colloidal size particles.
- High-intensity ultrasonic waves are used for this purpose.
- During sonicating of liquids the ultrasonic waves that propagate through dispersion medium result in alternating high-pressure (compression) and low-pressure (rarefaction) cycles. This mechanical stress causes Ultrasonic cavitation in liquids. It creates high-speed liquid jets of up to 100km/h.
- Such jets press liquid at high-pressure between the particles and separate them from each other.
- Smaller particles are accelerated with the liquid jets and collide at high speeds.
- Various substances like oils, mercury, sulphur, sulphides and oxides of metal can be dispersed in a colloidal state by this method.

Condensation methods

- These methods involve chemical reactions.
- In these methods factors like temperature, pressure, concentrations, etc. are properly maintained.
- The unwanted ions present in the sol are removed by dialysis, as these ions may eventually coagulate the sol.

Oxidation method

- Preparation of colloidal Sulphur:

  when H_2S in water (aqueous solution) is exposed to air, it slowly gets oxidise to sulphur.

- The sulphur so formed remains in water in the colloidal state and the solution so formed remains in water in the colloidal state and the solution has a slightly milkish appearance.

$$H_2S \; + \; O2 \rightarrow H_2O \; + \; 2S \text{ (colloidal)}$$

- A sol of sulphur can also be prepared when H_2S gas is bubbled through an aqueous solution of SO_2

$$H_2S \; + \; SO_2 \rightarrow 2\,H_2O \; + \; 3S \text{ (colloidal)}$$

Reduction Method

- Preparation of Gold Sol:
- A number of metals like silver, gold, platinum, mercury leas can be obtained in the colloidal state by the reduction of their salt solutions (dilute) using suitable reducing agents like hydrogen sulphide, formuldehyde, stannous chloride, tannic acid etc.
- Gold sol can be obtained when $AuCl_3$ (dil) solution is treated with stannous chloride.

$$2\,AuCl_3 + 3\,SnCl_2 \rightarrow 3\,SnCl_4 + 2\,Au\ (\text{colloidal})$$

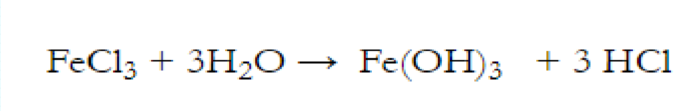
- Similarly, silver, platinum mercury sols are prepared

$$AgNO_3 + \text{Tannic acid} \rightarrow \text{Ag sol}$$

$$AuCl_3 + \text{Tannic acid} \rightarrow \text{Au sol}$$

Hydrolysis method

- Preparation of Ferric hydroxide sol:
- A colloidal solution of ferric hydroxide is obtained by boiling a dilute solution of ferric chloride.



$$FeCl_3 + 3H_2O \rightarrow Fe(OH)_3 + 3\,HCl$$

- Preparation of silicic acid sol:
- By hydrolysis of a dilute solution of sodium silicate with a hydrochloric acid, the colloidal solution of silicic acid is obtained.

- By exchange solvent method:
- There are a number of substances whose colloidal solution can be be prepared by taking a solution of the substance in one solvent and pouring it into another solvent in which is relatively less soluble.
- Preparation of sulphur or phosphorous sol: If a solution of sulphur or phosphorous prepared in alcohol is poured into water, a colloidal solution of sulphur or phosphorus is obtained due to the low solubility of sulphur or phosphours in water
- By change of physical state:
- A colloidal solution of certain elements such as mercury and sulphur are obtained by passing their vapours through cold water containing a stabilizer (an ammonium salt or a citrate).
- Excessive cooling method:
- A colloidal solution of ice in an organic solvent like ether or chloroform can be prepared by freezing a solution of water in the solvent. The molecules of water which can no longer be held in solution, separately combine to form particles of colloidal size.

Amphiphilic or association colloids

- Association colloid is formed by the grouping or association of molecules that exhibit both lyophilic and lyophobic properties.
- Amphiphilic colloids form dispersions in both aqueous and non aqueous media.
- Depending upon their individual character and the nature of the dispersion medium.
- However, they generally cause an increase in the viscosity of the dispersion medium with an increase in concentration.
- Example of association colloids are surfactant micelles (aggregation of surfactant molecules).

- These aggregates, which may contain 50 or more monomers, are called micelles. Because the diameter of each micelle is of the order of 50 Å, micelles lie within the size range we have designated as colloidal.
- The concentration of monomer at which micelles form is termed the critical micelle concentration(CMC). The number of monomers that aggregate to form a micelle is known as the aggregation number of the micelle. The phenomenon of micelle formation can be explained as follows.
- Below the CMC, the concentration of amphiphile undergoing adsorption at the air–water interface increases as the total concentration of amphiphile is raised.

- Eventually, a point is reached at which both the interface and the bulk phase become saturated with monomers. This is the CMC.
- Any further amphiphile added in excess of this concentration aggregates to form micelles in the bulk phase, and, in this manner, the free energy of the system is reduced.

- The effect of micellization on some of the physical properties of solutions containing surface-active agents as shown in the Figure 16-3. Note particularly that surface tension decreases up to the CMC. From the Gibbs' adsorption equation, this means increasing interfacial adsorption.
- Above the CMC, the surface tension remains essentially constant, showing that the interface is saturated and micelle formation has taken place in the bulk phase.

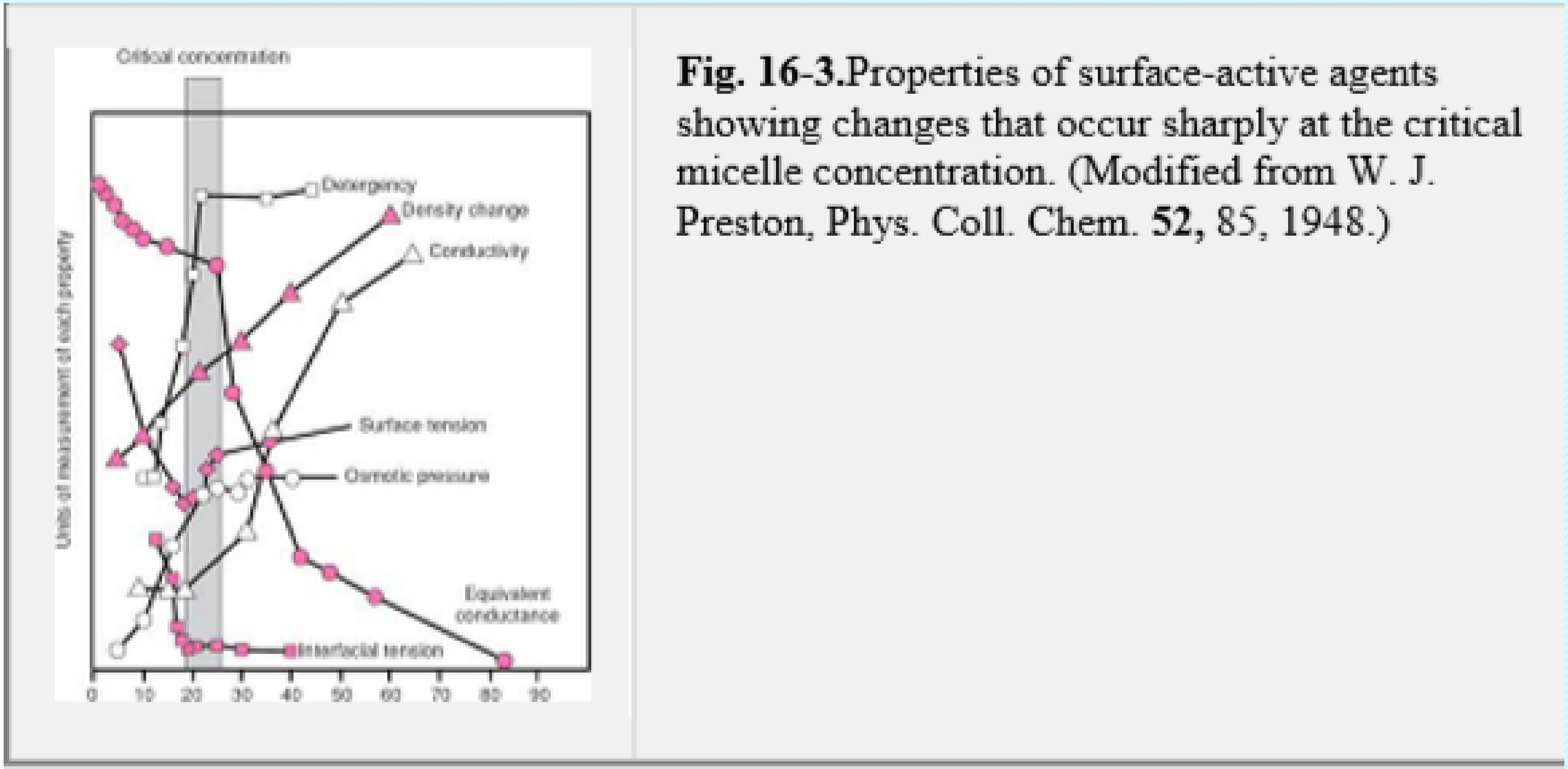


Fig. 16-3. Properties of surface-active agents showing changes that occur sharply at the critical micelle concentration. (Modified from W. J. Preston, Phys. Coll. Chem. **52,** 85, 1948.)