1.1.13. Instability of Colloids

In pharmaceutical formulations, buffer salts are added to maintain the produ pH, and thus, its stability. However, sometimes certain buffers form insolub salts with metallic ions, thus, making the product unstable. **For examp** phosphate buffers can result in instability of a product as most of the heavy me phosphates form insoluble salts.

When a colloidal dispersion precipitates an insoluble phosphate salt, it may c precipitate the colloidal particles along with it. This phenomenon can prevented by adding chelating agents in the formulation which form complex with metal ions and these complexes prevent the reaction of phosphate with th metal ions. Another method which can be employed for preventing instabili involves the usage of non-phosphate buffers.

Instability in colloidal dispersions can be easily detected with respect to phas separation or aggregation. Instability of lyophilic colloids can be due to th addition of oppositely charged colloids, electrolytes, or non-solvents. Similarly i lyophobic colloids, instability can be due to the addition of oppositely charge electrolytes or colloids, or addition or removal of excess electrolytes.

1.1.13.1. Effect of Electrolytes on Lyophilic Colloids

Thermodynamically, the lyophilic colloids are stable systems. Electrical charge an hydration help in determining the stability of a lyophilic colloid in water. Howeve particles might also undergo **precipitation**, **coagulation**, or **aggregatio** Coagulation of lyophilic dispersed phase can occur due to the following reasons:

1) **Addition of Excess Electrolytes:** The zeta potential decreases when sma quantities of electrolytes are added to the sol. This hinders the coagulation particles. However, when increased quantities of electrolytes are adde coagulation is observed. Normally, the stability of lyophilic colloids is due the presence of a solvent sheath around the particles. In hydrophilic colloi hydration of particles can be seen. When higher concentrations electrolytes are added to the sol, the ions get hydrated due to the exce amount of water present for hydration of particles (**figure 1.15**).

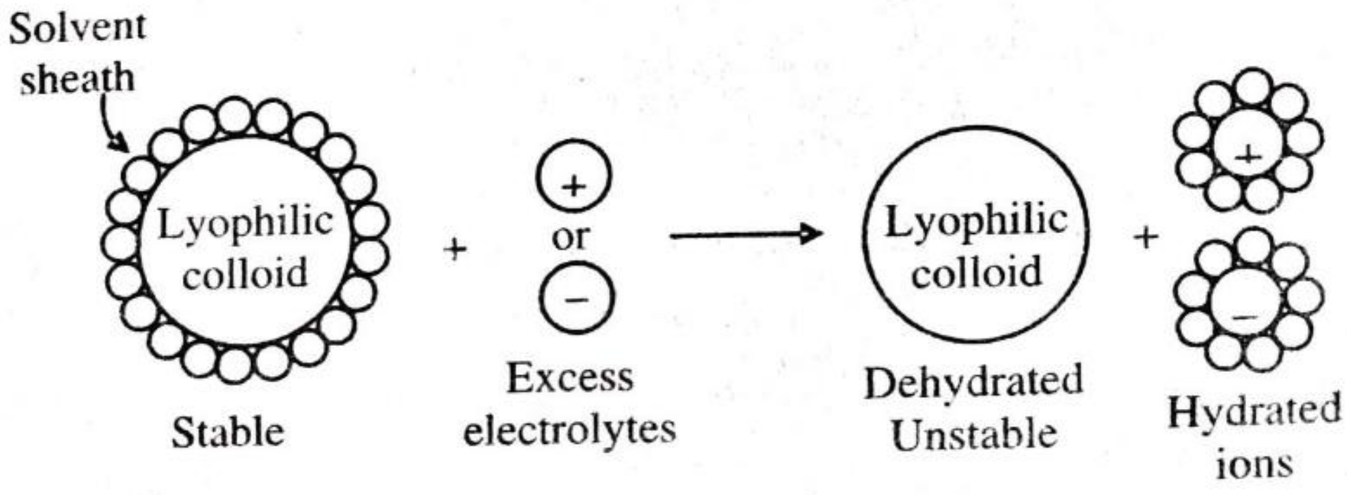


Figure 1.15: Addition of Excess Electrolytes

2) **Addition of Oppositely Charged Colloids:** When lyophilic colloids a mixed with oppositely charged colloidal particles, flocculation occur However, it is thought that the tightly bound water molecule's shell th surrounds the particles prevents them from combining together, but are sti combined together to form floccules as they are held together by th electrostatic attractions of their opposite charges. In such a case, th

dispersion contains colloid-rich aggregates which settle at the bottom imparting greater viscosity. The upper layer is poor in colloid. **For example,** acacia mixed with gelatin; in which gelatin possesses a positive charge and acacia a negative charge below its isoelectric point, i.e., below pH 4.7. Mixing of these dispersions together results in the formation of coacervates **(figure 1.16)**.

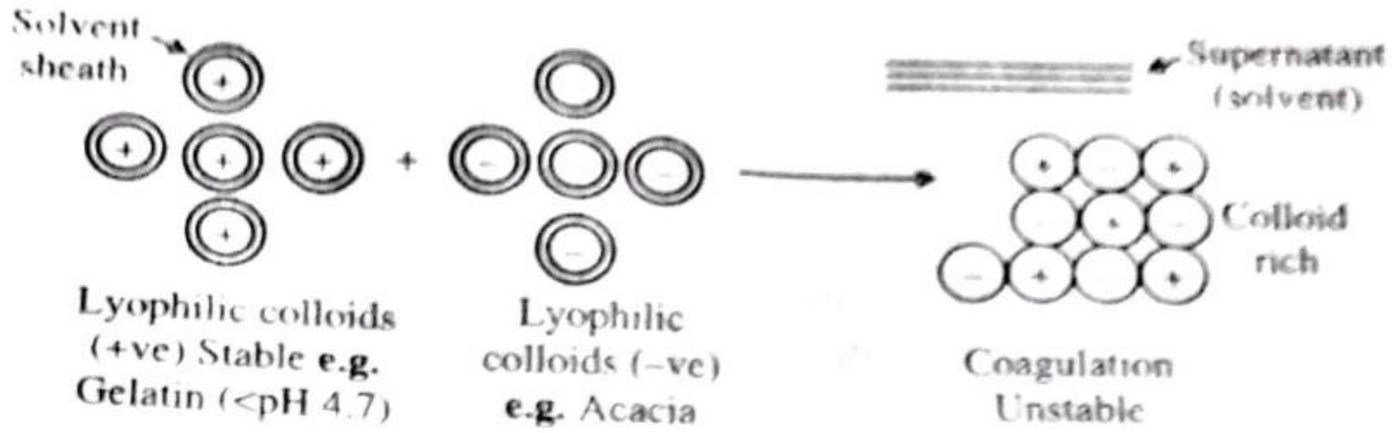


Figure 1.16: Addition of Oppositely Charged Ions

1.1.13.2. Effect of Electrolytes on Lyophobic Colloids

Precipitation of the sol or coagulation can be defined as the state in which settling of the dispersed particles and **aggregation** (**flocculation**) is observed. A colloidal dispersion is said to be unstable if flocculation or coagulation occurs in the dispersion medium.

Coagulation of lyophobic particles can occur due to the following reasons:

1) **Removal of Electrolytes:** A decrease in the inter-particle repulsions can be observed when electrolytes are present in trace amounts. This causes decrease in the electrical double layer below the critical value. The repulsive forces between the particles approaching each other are decreased to such an extent that those colliding with some specific velocity can combine together (**figure 1.17**), thereby, resulting in coagulation. The dispersed solid particles settle down at the bottom of the dispersion.

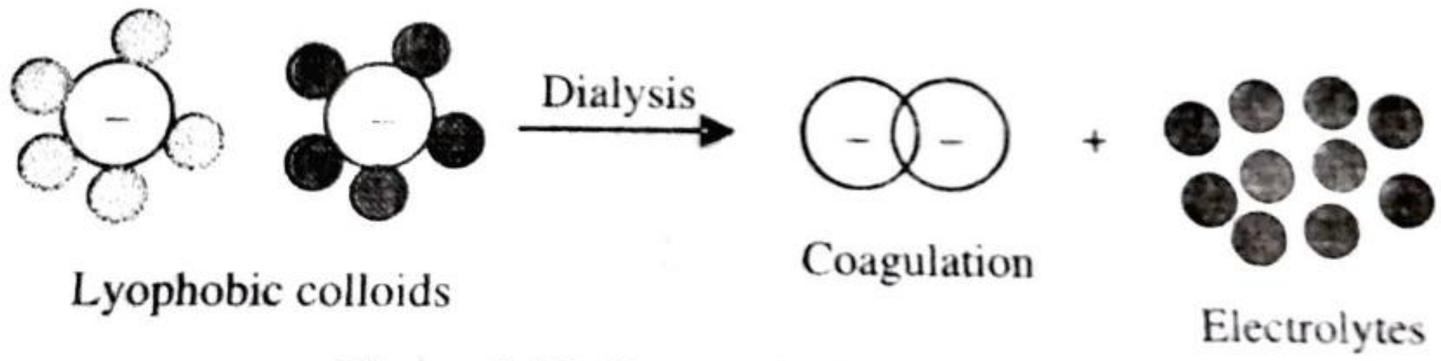
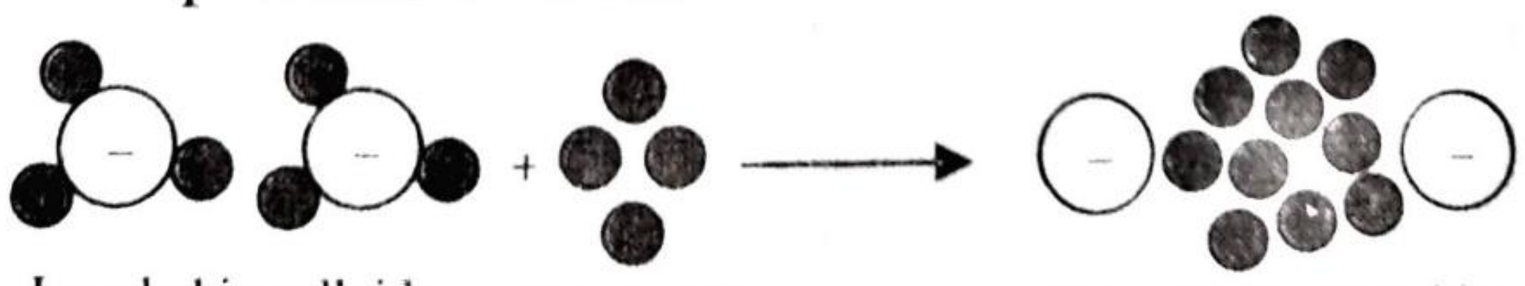


Figure 1.17: Removal of Electrolytes

Addition of Excess Electrolytes: In order to maintain the stability of a sol, it is necessary that the particles should possess a minute charge on the surface. When electrolytes are added in excess amount, the particle coagulate beyond a specific concentration. This occurs because the oppositely charged particles get accumulated (**figure 1.18**) and the critic value of zeta potential deviates.



Electrolytes of Opposite Charge: In order to maintain electrost
repulsions among the particles, they require charge. However, additio
oppositely charged substances causes the dispersed particles to coagu
(**figure 1.19**), thereby, making them unstable.

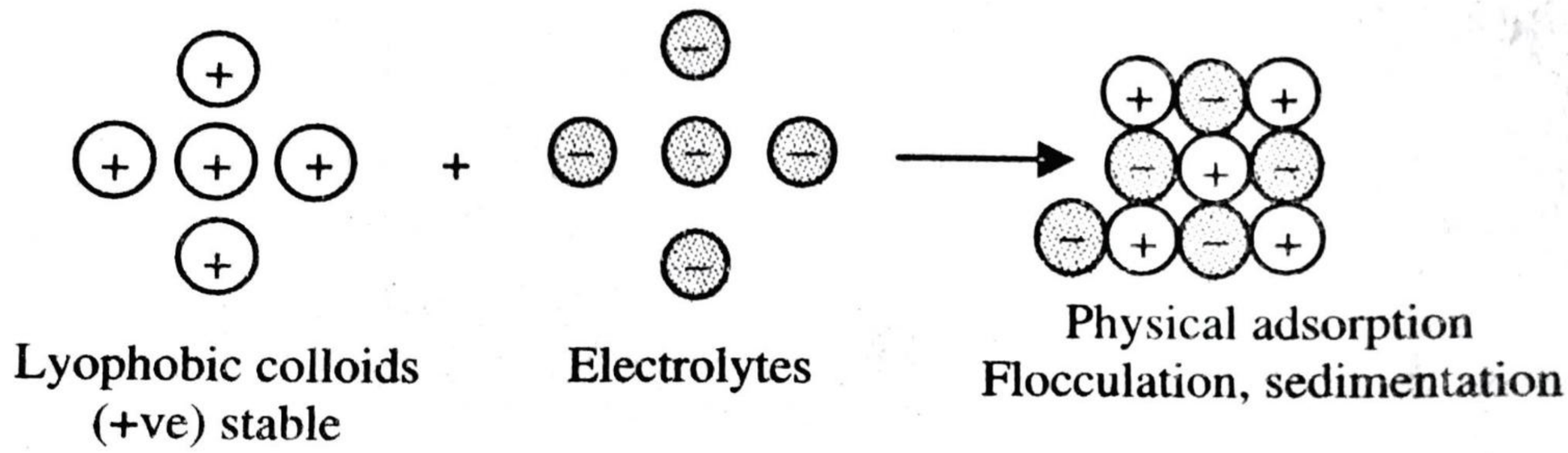


Figure 1.19: Addition of Electrolytes of Opposite Charge to Lyophobic Colloids