

CONTROLLED FLOCCULATION

- Assuming that the powder is properly wetted and dispersed, we can now consider the various means by which controlled flocculation can be produced so as to prevent formation of a compact sediment that is difficult to redisperse.
- *Electrolytes act as flocculating agents by reducing the electric barrier between the particles, as evidenced by a decrease in the zeta potential and the formation of a bridge between adjacent particles so as to link them together in a loosely arranged structure.*

- If we disperse particles of bismuth subnitrate in water, we find that, they possess a large positive charge, or zeta potential.
- Because of the strong forces of repulsion between adjacent particles, the system is deflocculated.
- By preparing a series of bismuth subnitrate suspensions containing increasing concentrations of monobasic potassium phosphate, it gives a correlation between apparent zeta potential and sedimentation volume, caking, and flocculation.

- The addition of monobasic potassium phosphate to the suspended bismuth subnitrate particles causes the positive zeta potential to decrease owing to the adsorption of the negatively charged phosphate anion.
- With the continued addition of the electrolyte, the zeta potential eventually falls to zero and then increases in the negative direction, as shown in Figure.
- Microscopic examination of the various suspensions shows that at a certain positive zeta potential, maximum flocculation occurs and will persist until the zeta potential has become sufficiently negative for deflocculation to occur once again.
- The onset of flocculation coincides with the maximum sedimentation volume determined.

- Surfactants, both ionic and nonionic, have been used to bring about flocculation of suspended particles.
- The concentration necessary to achieve this effect would appear to be critical because these compounds can also act as wetting and deflocculating agents to achieve dispersion.

FLOCCULATION IN STRUCTURED VEHICLES

- Although the controlled flocculation approach is capable of fulfilling the desired physical chemical requisites of a pharmaceutical suspension, the product can look unsightly if F , *the sedimentation volume*, is not close or equal to 1.
- Consequently, in practice, a suspending agent is frequently added to retard sedimentation of the flocs.
- Such agents as carboxymethylcellulose, Carbopol 934, Veegum, tragacanth, and bentonite have been employed, either alone or in combination.
- This can lead to incompatibilities, depending on the initial particle charge and the charge carried by the flocculating agent and the suspending agent.

- For example, suppose we prepare a dispersion of positively charged particles that is then flocculated by the addition of the correct concentration of an anionic electrolyte such as monobasic potassium phosphate.
- We can improve the physical stability of this system by adding a minimal amount of one of the hydrocolloids .
- No physical incompatibility will be observed because the majority of hydrophilic colloids are themselves negatively charged and are thus compatible with anionic flocculating agents.

- If, however, we flocculate a suspension of negatively charged particles with a cationic electrolyte (aluminum chloride), the subsequent addition of a hydrocolloid may result in an incompatible product, as evidenced by the formation of an unsightly stringy mass that has little or no suspending action and itself settles rapidly.
- Under these circumstances, it becomes necessary to use a protective colloid to change the sign on the particle from negative to positive.

- This is achieved by the adsorption onto the particle surface of a fatty acid amine (which has been checked to ensure its nontoxicity) or a material such as gelatin, which is positively charged below its isoelectric point.
- We are then able to use an anionic electrolyte to produce flocs that are compatible with the negatively charged suspending agent.

