Settling in suspensions

- One aspect of physical stability in pharmaceutical suspensions is concerned with keeping the particles uniformly distributed throughout the dispersion.
- It possible to prevent settling completely over a prolonged period of time, it is necessary to consider the factors that influence the velocity of sedimentation.
- ***Theory of Sedimentation***
- ***Particle size***
- ***Effect of Brownian Movement***
- ***Sedimentation of Flocculated Particles***
- ***Sedimentation Parameters***

Theory of Sedimentation

- The velocity of sedimentation is expressed by Stokes's law:

$$v = \frac{d^2(\rho_s - \rho_o)g}{18\eta_o}$$

- where
- v = terminal velocity in cm/sec,
- d = diameter of the particle in cm,
- ρs and ρo = the densities of the dispersed phase and dispersion medium, respectively,
- g = acceleration due to gravity,
- ηo = viscosity of the dispersion medium in poise.

STOKES LAW IS APPLICABLE IN FOLLOWING CONDITION

1. The particle should be spherical, but in suspensions particle are largely irregular.

2. The particles do not interfere with one another during sedimentation, and free settling occurs. In most pharmaceutical suspensions that contain dispersed particles in concentrations of 5%, 10%, or higher percentages, the particles exhibit hindered settling. The particles interfere with one another as they fall, and Stokes's law no longer applies.

- The physical stability can be obtained by diluting the suspension so that it contains about 0.5% to 2.0% w/v of dispersed phase.
- This is not always recommended,
- As the addition of a diluent may affect the degree of flocculation (or deflocculation) of the system, thereby effectively changing the particle-size distribution.

PARTICLE SIZE

- Particle size determines the packing arrangement and influence the settling behavior.
- They also effect the re-suspendability and stability.
- Symmetrical particle (barrel shaped particles of calcium carbonate) produces stable suspension without cracking.
- Asymmetrical particle (needle shaped) forms hard cake, which cannot be re-disperesible.

EFFECT OF BROWNIAN MOVEMENT

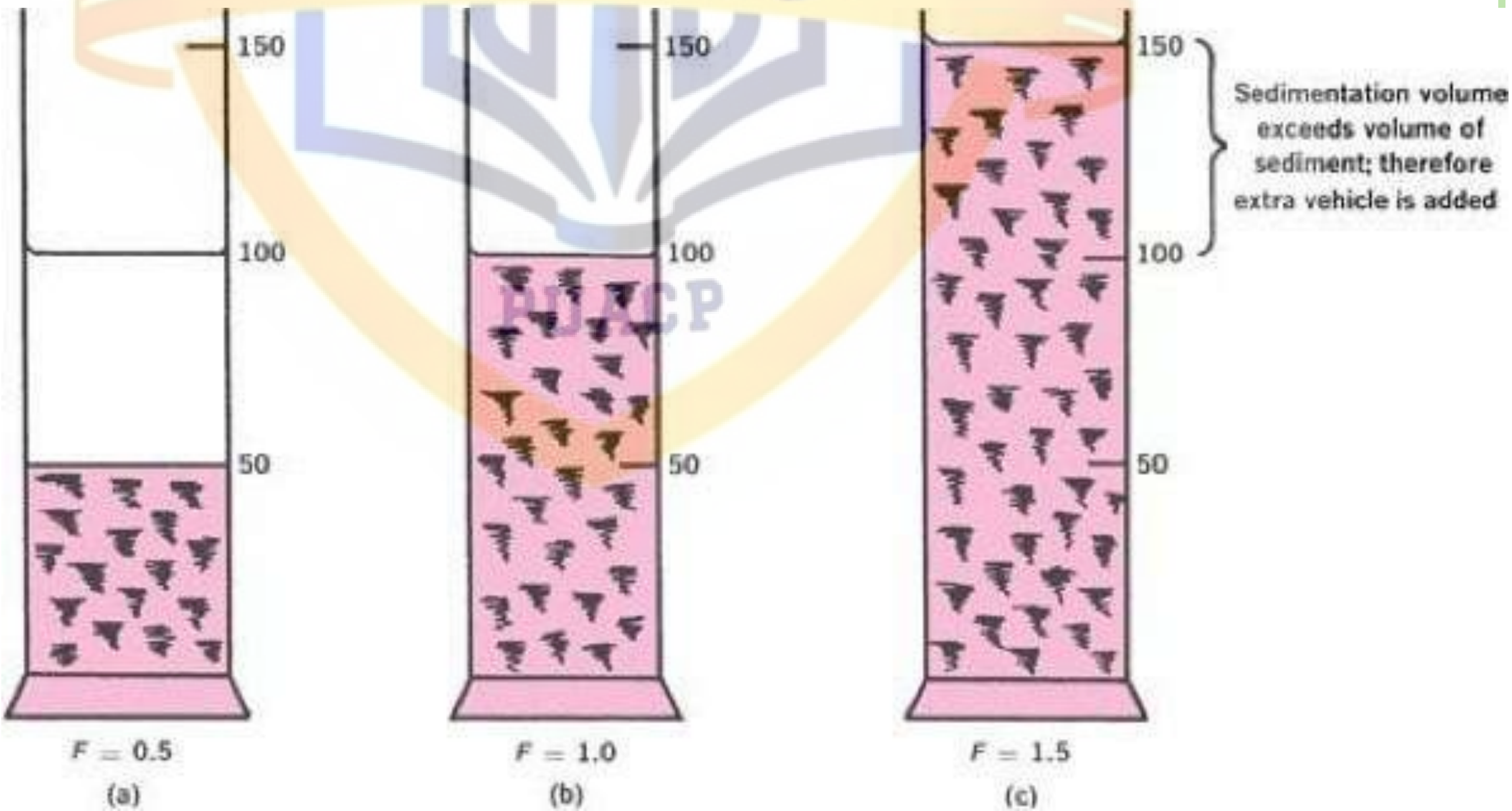
- For particles having a diameter of about 2 to 5 µm (depending on the density of the particles and the density and viscosity of the suspending medium), Brownian movement counteracts sedimentation to a measurable extent at room temperature by keeping the dispersed material in random motion.
- The *critical radius, r, below which particles will be kept in suspension by kinetic bombardment of the* particles by the molecules of the suspending medium (Brownian movement) was worked out by Burton.

- It can be seen in the microscope that Brownian movement of the smallest particles in a field of particles of a pharmaceutical suspension is usually eliminated when the sample is dispersed in a 50% glycerin solution, having a viscosity of about 5 centipoise.
- Hence, it is unlikely that the particles in an ordinary pharmaceutical suspension containing suspending agents are in a state of vigorous Brownian motion

Sedimentation of Flocculated Particles

- When sedimentation is studied in flocculated systems, it is observed that the flocs tend to fall together, producing a distinct boundary between the sediment and the supernatant liquid.
- The liquid above the sediment is clear because even the small particles present in the system are associated with the flocs.
- Such is not the case in deflocculated suspensions having a range of particle sizes, in which, in accordance with Stokes's law, the larger particles settle more rapidly than the smaller particles.

- No clear boundary is formed (unless only one size of particle is present), and the supernatant remains turbid for a considerably longer period of time.
- Whether the supernatant liquid is clear or turbid during the initial stages of settling is a good indication of whether the system is flocculated or deflocculated, respectively.
- The initial rate of settling of flocculated particles is determined by the floc size and the porosity of the aggregated mass.
- Subsequently, the rate depends on compaction and rearrangement processes within the sediment.
- The term *subsidence is sometimes used to describe* settling in flocculated systems.


150
100
50
150
100
50
150
100
50
Sedimentation volume exceeds volume of sediment; therefore extra vehicle is added
F = 0.5
(a)
F = 1.0
(b)
F = 1.5
(c)

SEDIMENTATION PARAMETERS

- Two useful parameters that can be derived from sedimentation (or, more correctly, subsidence) studies are sedimentation volume, V, or height, H, and degree of flocculation.
- The sedimentation volume, F, is defined as the ratio of the final, or ultimate, volume of the sediment, Vu, to the original volume of the suspension, Vo, before settling. Thus,

$$F = V_u / V_o$$

- The sedimentation volume can have values ranging from less than 1 to greater than 1.
- *F is normally less* than 1, and in this case, the ultimate volume of sediment is smaller than the original volume of suspension. Figure a, in which $F = 0.5$.
- *If the volume of sediment in a flocculated* suspension equals the original volume of suspension, then $F = 1$ Figure b.
- Such a product is said to be in flocculation equilibrium and shows no clear supernatant on standing.
- It is therefore pharmaceutically acceptable.

- It is possible for *F to have values greater than 1, meaning that the final* volume of sediment is greater than the original suspension volume.
- This comes about because the network of flocs formed in the suspension is so loose and fluffy that the volume they are able to encompass is greater than the original volume of suspension.
- This situation is illustrated in Figure c, in which sufficient extra vehicles have been added to contain the sediment($F = 1.5$).

- The sedimentation volume gives only a qualitative account of flocculation .
- A more useful parameter for flocculation is β, *the degree of flocculation.*
- If we consider a suspension that is completely deflocculated, the ultimate volume of the sediment will be relatively small.
- Writing this volume as $V\infty$, *based on equation* $F\infty = V\infty / V_o$

Where

F = *sedimentation volume of the deflocculated, or peptized, suspension.*

- The degree of flocculation, *β, is therefore defined as the ratio of F to F∞,*

$\beta = F / F_\infty$

- Substituting equations

$$\beta = \frac{V_u / V_o}{V_\infty / V_o}$$

$\beta = V_u / V_\infty$

- The degree of flocculation is a more fundamental parameter than *F because it relates the volume of* flocculated sediment to that in a deflocculated system.

We can therefore say that

$$\beta = \frac{\text{ultimate sediment volume of flocculated suspension}}{\text{ultimate sediment volume of deflocculated suspension}}$$