Pharmaceutical Technology

Sedimentation parameters

(Index of flocculation)

Sedimentation parameters (Index of flocculation)

- Sedimentation parameters are:

1. Sedimentation volume (F)
2. Degree of flocculation (β)

- These parameters are used as semi quantitative measure of flocculation in suspension.
- Sedimentation volume (F) for flocculated suspension = V_u/V_o

➢ Where

- V_u the ultimate volume of the sediment.
- V_o the the original volume of suspension, before settling.
- For deflocculated suspension:

$F_\infty = V_\infty / V_o$

- F may have one the following values:

1. $F < 1$
2. $F > 1$
3. $F = 1$

- F less than 1 is ordinary case, when the suspension settle to a certain volume of sediment less than the volume of suspension.
- F greater than 1, it is a rare case, when the ultimate volume of sediment become greater than original volume of the suspension. This occurs when the particles form a loose fluffy network in the vehicle so the final volume of the sediment is greater than original volume.
- F equal to 1 when the product shows no clear supernatant when the both volumes are equal i.e., Vu =Vo. It is in state of flocculation equilibrium, it is an acceptable product.

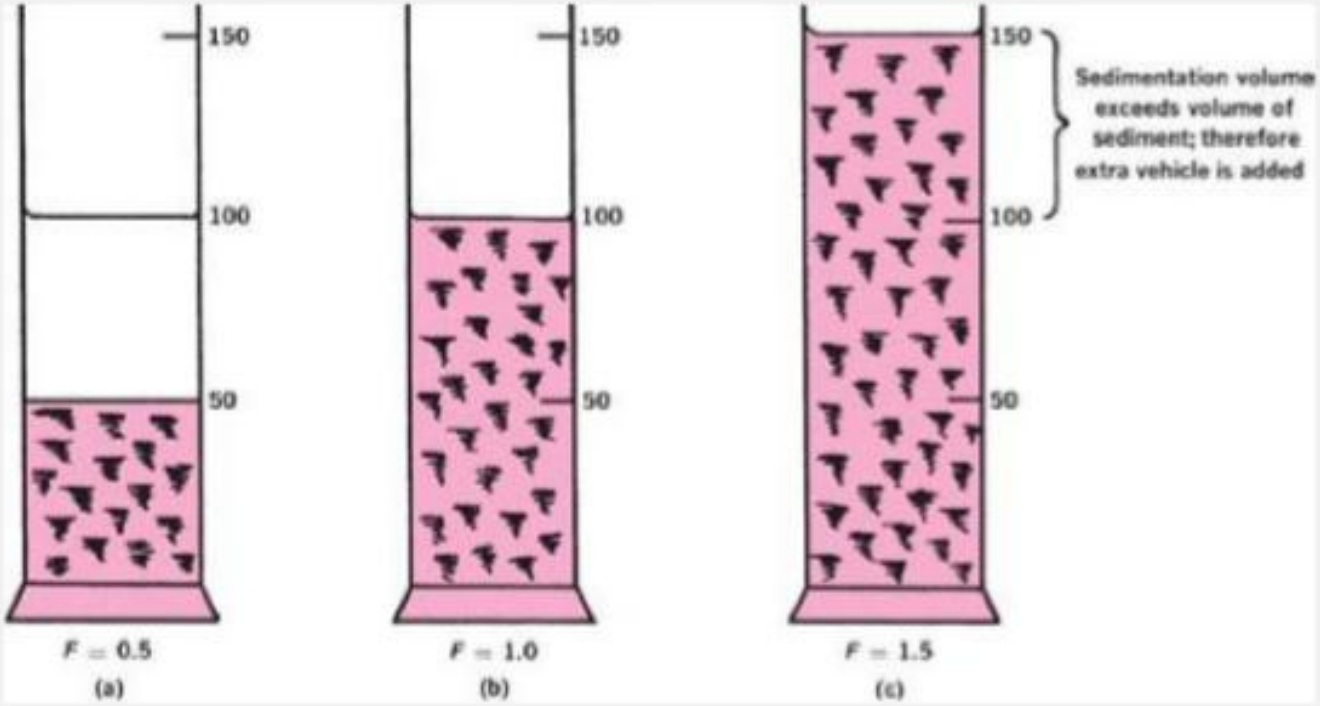


Fig. 17-2. Sedimentation volumes produced by adding varying amounts of flocculating agent. Examples (*b*) and (*c*) are pharmaceutically acceptable.

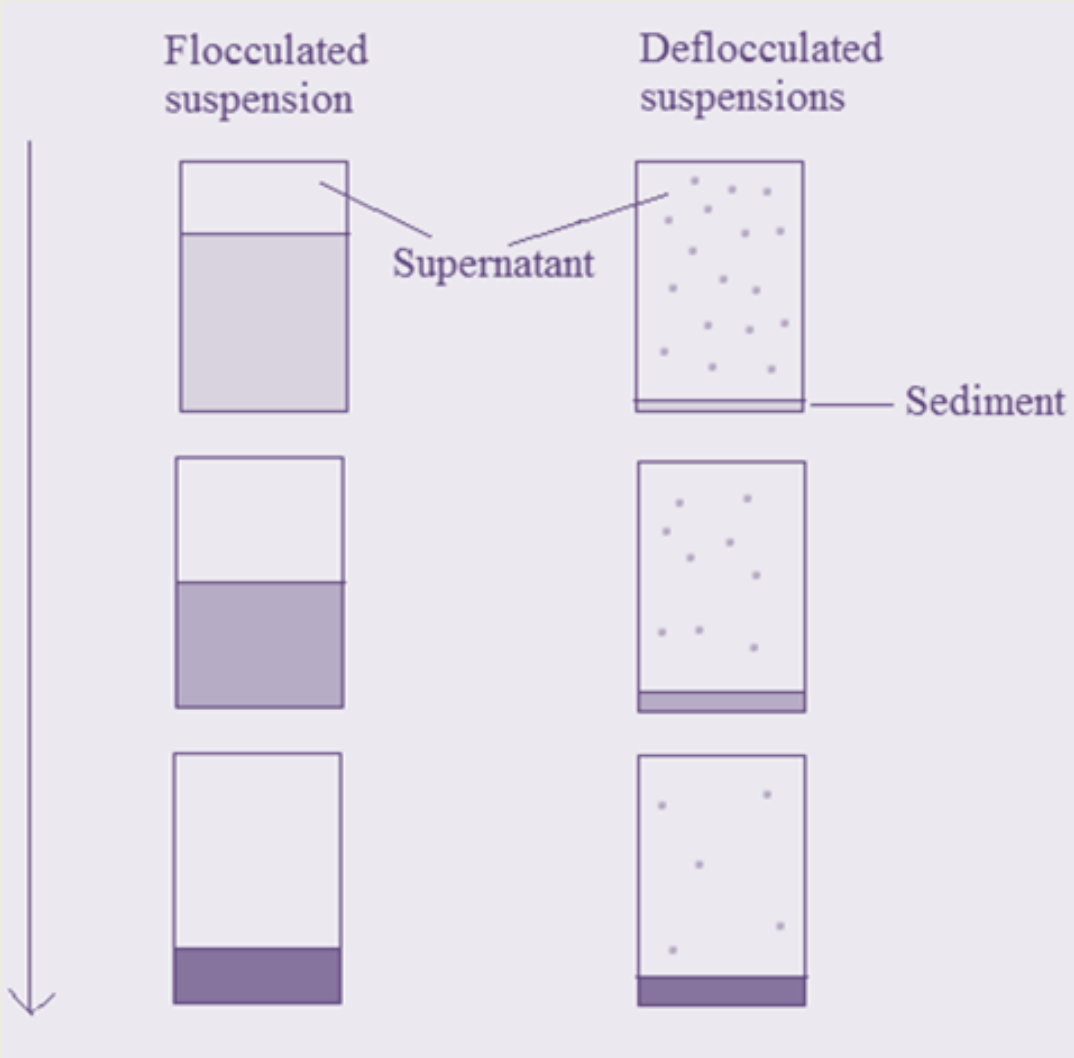
Sedimentation parameter
(Degree of flocculation)

- The second parameter is degree of flocculation(β). It is a better parameter for evaluating flocculation in a suspension, it describes the relationship between the sedimentation volume of the flocculated suspension (F) to the sedimentation volume of the same suspension when deflocculated (F_∞).
- The following equation is used to calculate β

$$\beta = \frac{F}{F_\infty} = \frac{v_u/v_0}{v_\infty/v_0} = \frac{v_u}{v_\infty}$$

- Where,
  - v_u is the ultimate volume of flocculated suspension
  - v_∞ is the ultimate volume of deflocculated suspension

- A suspension consisting of floccules held together loosely will have large β, while suspension containing sediment has small β.
- The lower limit of β is equal to 1; which means there is no flocculation, i.e., $v_u = v_\infty$


Flocculated suspension
Deflocculated suspensions
Supernatant
Sediment
Time elapsed

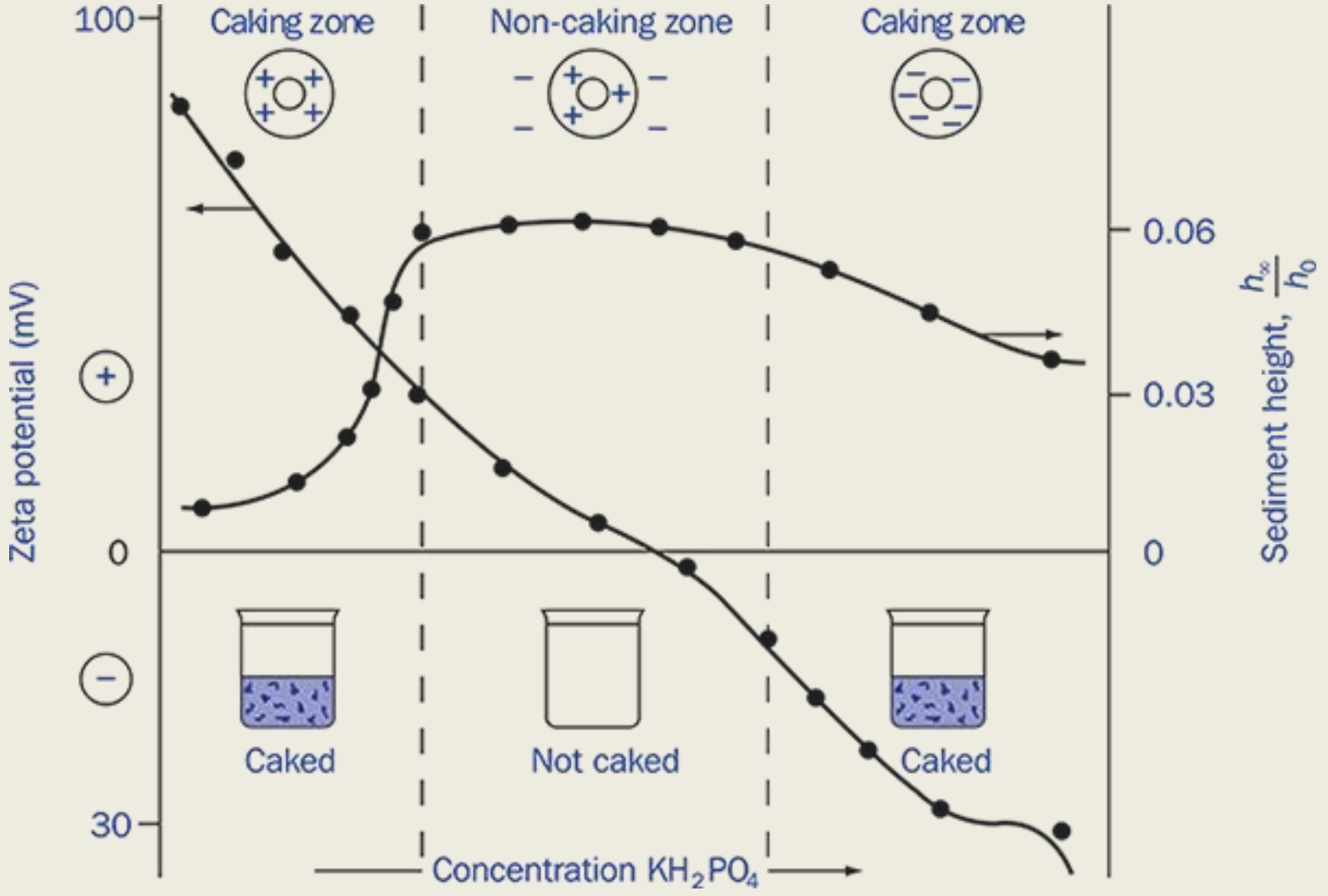
- How can you induce flocculation?
- You can do that by use of flocculating agents, such as

1. Electrolytes
2. Surfactants and
3. Polymers.

- Flocculating agents are agents that are added to the medium to promote flocculation by counter acting the effect of protective layer the thus decrease zeta potential.

1. Electrolytes: they are used to obtain a product of large sedimentation volume. The ions will reduce the electrical barrier between the particles and link them together by forming a bridge between the particles, so the particles are held loosely in the suspension, but these large aggregates although settles rapidly they are easily redispersed by agitation.

- The addition of electrolytes may be illustrated by the addition of monobasic potassium phosphate (KH_2PO_4) as a negative flocculating agent to a suspension of bismuth subnitrate (the particles of which are positively charged).


100
Caking zone
Non-caking zone
Caking zone
Zeta potential (mV)
+
0
−
30
0.06
0.03
0
Sediment height, $\frac{h_\infty}{h_0}$
Caked
Not caked
Caked
Concentration KH_2PO_4

- Initially, the bismuth subnitrate particles have a large positive charge with the addition of (KH_2PO_4) the apparent zeta potential will decrease to a point where the system have maximal flocculating.
- sedimentation study on bismuth subnitrate with increasing concentrations of flocculating agent have shown that:

1. The sedimentation volume is low initially, a condition that suggests a close-packed sediment of bismuth subnitrate particles.
2. Flocculation by KH_2PO_4 will increase the sediment volume relative to the initial value; until it reaches a maximum value. This is known as noncaking zone.
3. Additional flocculating agent will neutralize the charge on the particles and finely it will reverse the charge from +ve to –ve and again we get a caked suspension.

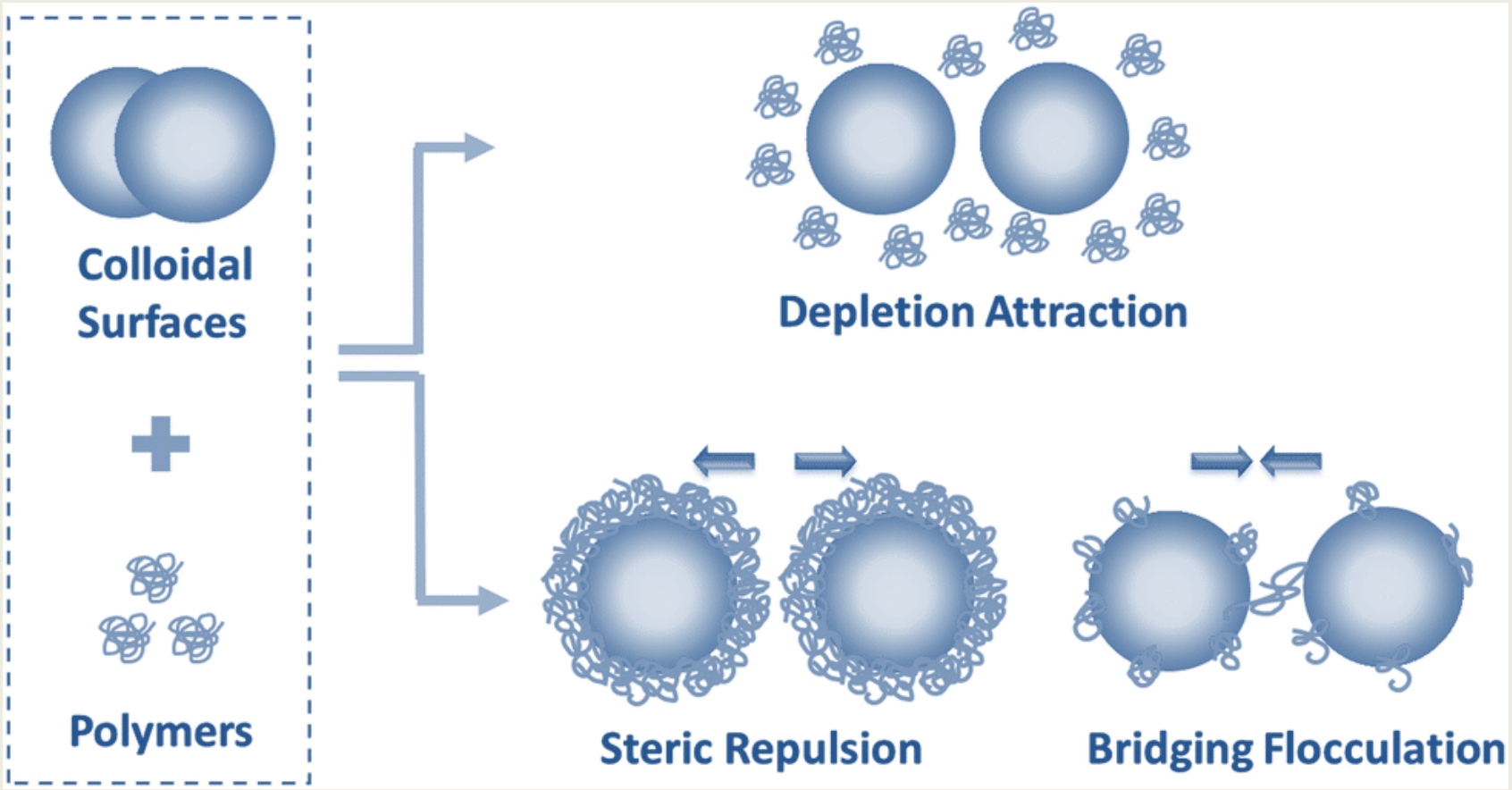
- The bridging action of the flocculated agent is more important than the neutralization of surface charge on the particles.

2. Surfactant: Both ionic and non-ionic surfactants are used to bring about flocculation of suspended particles.

- Ionic surfactant increases sedimentation volume, while non-ionic surfactant may be adsorbed onto suspended particles and produce flocculated system at certain concentration.
- Optimum concentrations of surfactants bring down the surface free energy by reducing the surface tension between liquid medium and solid particles.
- The particles possessing less surface free energy are attracted towards to each other by Van der waals forces and forms loose agglomerates.

3. Polymers: lyophilic polymers are commonly used as suspending agent.

- The polymer molecules contain active groups spaced along molecules may be adsorbed on the particles, leaving extended segments projecting out from the particle for bridging across to adjacent particles and thus producing flocculated system.


Colloidal Surfaces
Polymers
Depletion Attraction
Steric Repulsion
Bridging Flocculation

- A number of hydrocolloids are polyelectrolytes, their flocculating action is dependent on the pH of the medium and the ionic strength, and there is an optimum pH for sedimentation.
- For example, gelatin, which is a natural hydrocolloid may be used to bring about flocculation and prevent caking.

Suspending agents

- Suspending agents are substances that are used to keep finely divided insoluble materials suspended in a liquid media by preventing their agglomeration (coming together) and by imparting viscosity to the dispersion media so that the particles settle more slowly.
- There are various types suspending agents

Types of suspending agents

1. Natural agents: this class consists of
A. Animal source: e.g., gelatin
B. Plant source: e.g., acacia, tragacanth, starch, sea weed.
C. Mineral sources: e.g., bentonite, kaolin.
2. semi-synthetic agents: these consist of substituted cellulose, e.g. methyl cellulose.
3. Synthetic agents: they are synthetic polymer, e.g., carbopol.

- Most suspending agents perform two functions i.e., besides acting as a suspending agents they also imparts viscosity to the solution.
- Suspending agents form film around particle and decrease interparticle attraction.
- A good suspension should have well developed thixotropy:

➢ at rest the solution is sufficient viscous to prevent sedimentation and thus aggregation or caking of the particles.

➢ When agitation is applied the viscosity is reduced and provide good flow characteristic from the mouth of bottle.

- So in the preparation of suspension, the suspending agent act both as protective colloid to keep a settled particles from caking and as flocculating agent to produce loose cell-like structure in the liquid medium; through its rheological properties the suspending agent may provide certain consistency for supporting the particles.

- When polymeric substances and hydrophilic colloids are used as suspending agents, appropriate tests must be performed to show that the agent does not interfere with availability of the drug.
- These materials can bind certain medicinal agents, rendering them unavailable or only slowly available for therapeutic function.
- Also, the amount of the suspending agent must not be such to render the suspension too viscous to agitate (to distribute the suspensoid) or to pour.

- Frequently, the usual adult oral suspension is designed to supply the dose of the particular drug in a convenient measure of 5 mL or 1 teaspoonful. Pediatric suspensions are formulated to deliver the appropriate dose of drug by administering a dose-calibrated number of drops or with the use of a teaspoon.
- The following Figure shows commonly packaged oral suspensions administered as pediatric drops.

FIGURE 14.4 Oral pediatric suspensions showing package designs of a built-in dropper device and a calibrated dropper accompanying the medication container.

- Some are accompanied by a calibrated dropper, whereas other packages have the drop capability built into the container.
- On administration, the drops may be placed directly in the infant's mouth or mixed with a small portion of food.
- Because many of the suspensions of antibiotic drugs intended for pediatric use are prepared in a highly flavored, sweetened, colored base, they are frequently referred to by their manufacturers and also popularly as syrups, even though in fact they are suspensions.