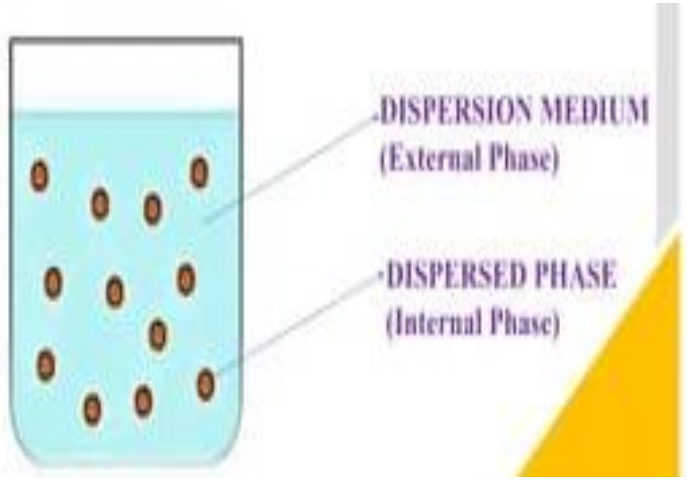
# LEC 4
# PHARMACEUTICAL TECHNOLOGY
## SUSPENSIONS 1

3rd / 1st course

Dr. Ameer S. Sahib

# DEFINITION OF SUSPENSION

- Suspensions are dispersion systems consisting of two phases: dispersion (continuous or external) phase and dispersed (internal) phase.
- The external phase is generally a liquid or semisolid phase, mostly aqueous for oral preparations and may be oily or organic for non-oral preparations, and the internal phase is particulate matter (solid).
- The internal phase is insoluble or slightly soluble solid materials but dispersed throughout the external phase.



# PARTICLE SIZE

◉ Particle size of dispersed systems:

- Molecular dispersion: < 1nm.
- Colloidal dispersion: 1 nm – 0.5 µm.
- Fine dispersion: 0.5 µm – 10 µm.
- Coarse dispersion: 10 µm – 50 µm (Suspensions).

◉ Suspensions can be used orally (metronidazole), parenterally (betamethasone ), topically (calamine lotion), rectally (mesalazine), ophthalmically (prednisolone acetate), etc.

◉ Some suspensions are available in ready to use form (e.g. metronidazole (Flagyl®)) and others are available as dry powders intended for suspension in liquid vehicles, most often purified water (e.g. amoxicillin (Amoxil®)).


2 ml Ampoule
2ml
2mg + 5mg/ml
Diprofos* Injection
BETAMETHASONE SODIUM PHOSPHATE
and BETAMETHASONE DIPROPIONATE
Manufactured by: MEDICAL UNION PHARMACEUTICALS
Abu Sultan - Ismailia - Egypt
Under Authority of
SCHERING-PLOUGH CORPORATION/U.S.A.
Schering-Plough


Flagyl®
(Benzoyl
Metronidazole)
Anti-amoebic and
Anti-infective
120ml
Suspension
Flagyl®
(Benzoyl
Metronidazole)
Anti-amoebic and
Anti-infective
120ml Suspension
SANOFI
Shake well before use.
Flagyl® Suspension
AA100
APR 2022
MAR 2024
103.51


calamine
lotion
calamine topical
suspension USP
up&up
skin protectant
poison ivy, poison oak
and sumac drying lotion
6 FL OZ (177 mL)


KIT
Mesalamine
Rectal Suspension,
USP Enema
4g/60 mL
Unit-Dose
For Rectal Use Only
Perrigo

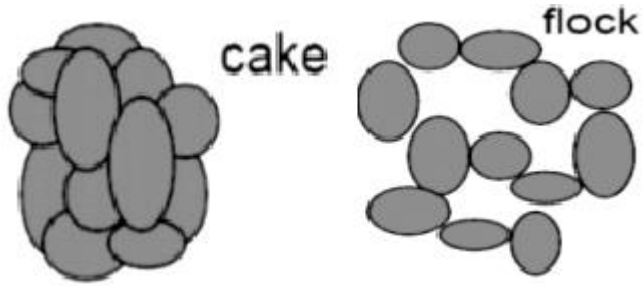

PRED FORTE™
EYE DROPS
SUSPENSION
ALLERGAN
PRED FORTE™
(prednisolone acetate
USP 1%)
EYE DROPS
SUSPENSION
STERILE
5 ml

# PARTICLE SIZE CONTROL:

❑ Particle size of any **suspension is critical and must be reduced within the range .**

❑ Too large or too small particles should be avoided.

- **For large particles:**
  - Too large particles settle faster at the bottom of the container
  - particles > 5 µm impart a gritty texture to the product and also cause irritation if injected or instilled to the eye
  - particles > 25 µm may block the needle




- **For small particles**:
  - Too fine particles will easily form hard cake at the bottom of the container.

# THE REASONS TO FORMULATE SUSPENSION


- When the drug is **insoluble** in the delivery vehicle, e.g. prednisolone suspension.
- To mask the **bitter taste** of the drug, e.g. chloramphenicol palmitate and metronidazole suspensions.


- To increase drug **stability**, e.g. oxytetracycline suspension.
- To achieve **controlled/sustained** drug release, e.g. penicillin procaine suspension.

# DESIRED PROPERTIES IN THE PHARMACEUTICAL SUSPENSION

- **Settle down slowly (remain suspended long enough to withdraw an accurate dose).**
- **Readily redispersed upon gentle shaking of the container.**
- **The particle size should remain fairly constant throughout long periods of storage (with no caking).**
- **Easily pourable from its container (not highly viscous).**
- **Suitable odour, colour, and taste.**
- **Stable and not decompose or support growth of moulds.**
- **Should be free from gritting particles (external, intramuscular, and ophthalmic use)**
- **Should be pleasant & palatable (orally)**

# Some Disadvantages of Suspensions

- They must be well shaken prior to measuring a dose.
- The accuracy of the dose is likely to be less than with the equivalent solution.
- Conditions of storage may adversely affect the disperse system which might lead to aggregation and caking.

# *Storage of suspension*

The physical stability of suspension is adversely affected by extreme variation in temperature, suspension should be stored in cool place but not refrigeration. Freezing and very low temperature may cause the suspended particles to reaggregate.

Stored in room temperature if it is dry powder (25 $^{0}$C).

Also should be stored in a wide mouth container that have a space to allow a good agitation before use. Label: "**Shake Before Use**" to ensure uniform distribution of solid particles and thereby uniform and proper dosage.

# THEORY OF SEDIMENTATION

**The velocity of sedimentation is expressed by *Stoke's law.***

$$V = \frac{d^2 g(\rho_p - \rho_s)}{18\eta}$$

***V*** **= sedimentation velocity**

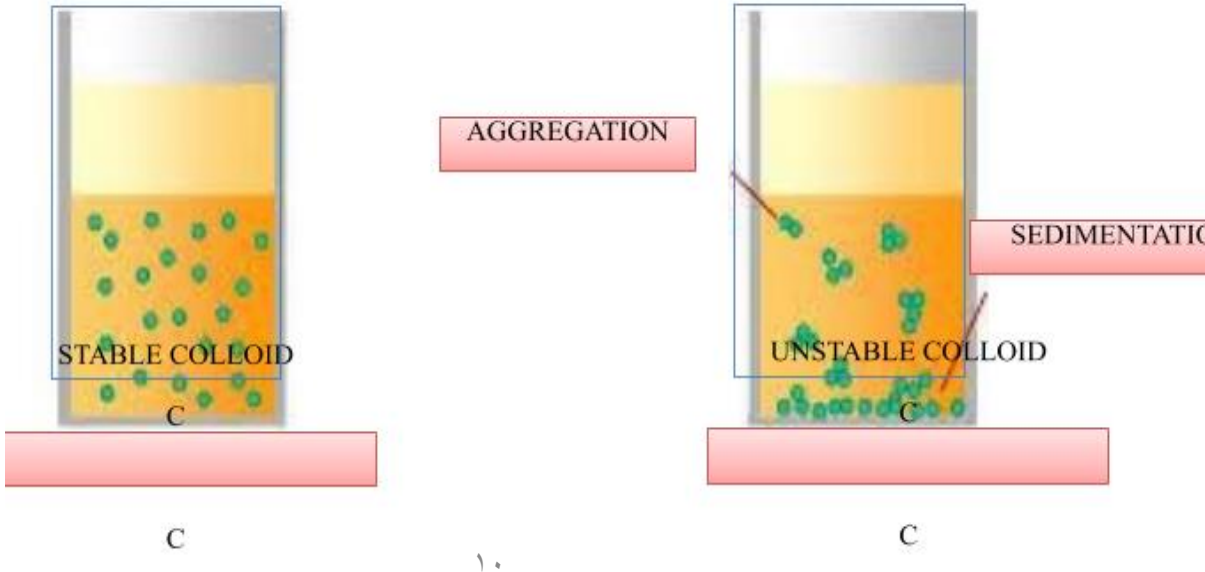
***d*** **= diameter of the particle in cm.**

$\rho_p$ **=density of the dispersed phase (particles).**

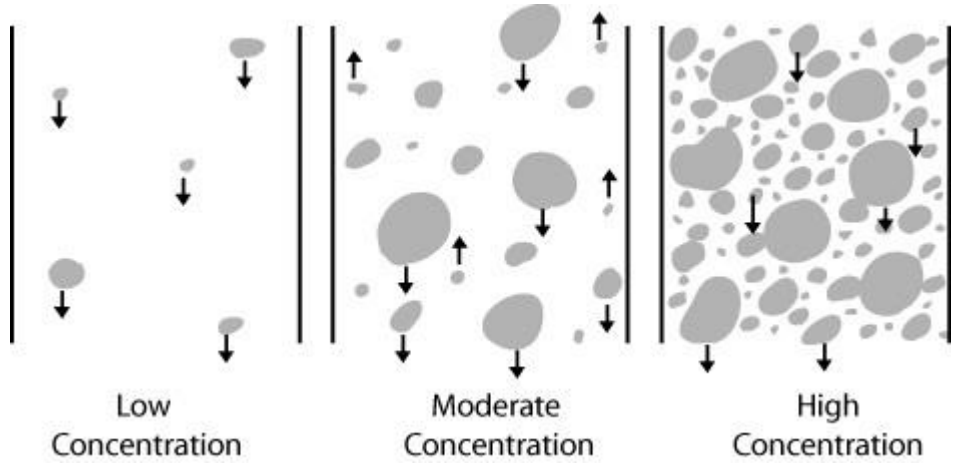
$\rho_s$ **=density of the dispersed medium.**

***g*** **= acceleration due to gravity.**

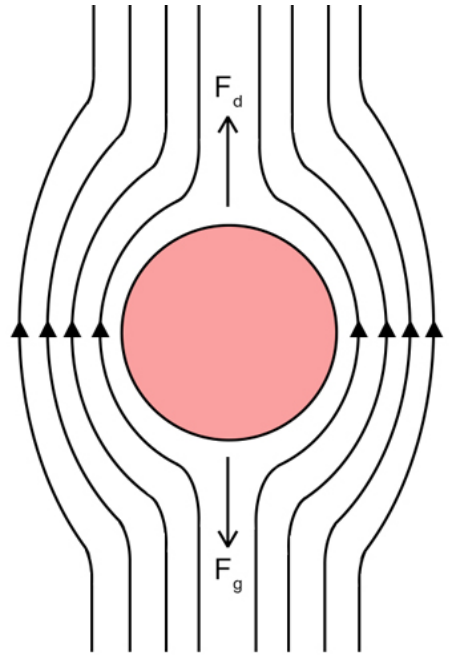
$\eta$ **= viscosity of the dispersion medium in poise.**



- One aspect of physical stability in pharmaceutical suspensions is concerned with keeping the particles uniformly distributed throughout the dispersion.



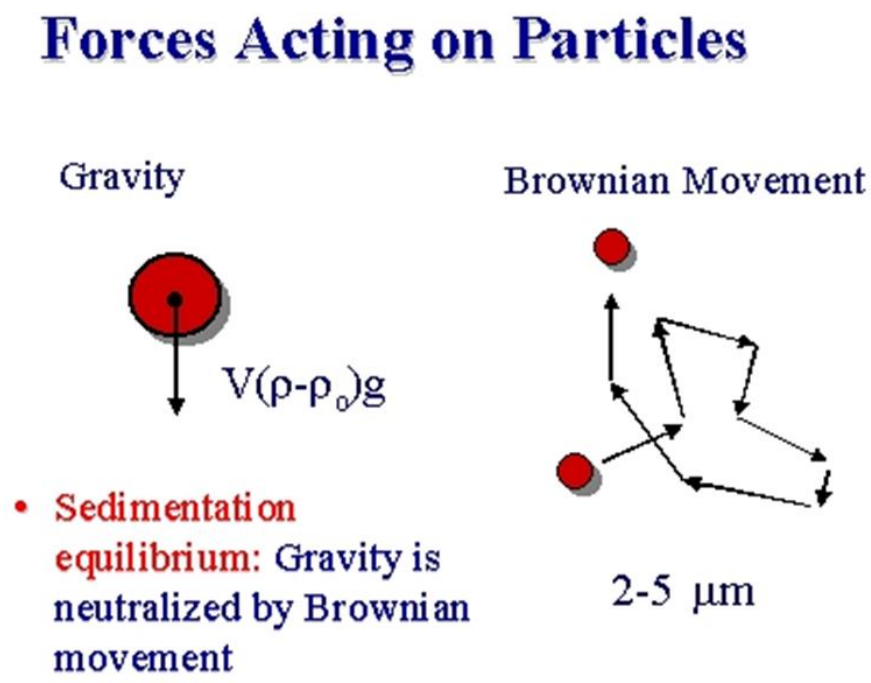

- While it is seldom possible to prevent settling completely over a prolonged period of time, it is necessary to consider the factors which influence the velocity of sedimentation.
- Particle size of any suspension is critical.
- Larger particles will settle faster at the bottom of the container.
- The particle size can be reduced by using mortar and pastel
- But very fine particles will easily form hard cake at the bottom of the container.



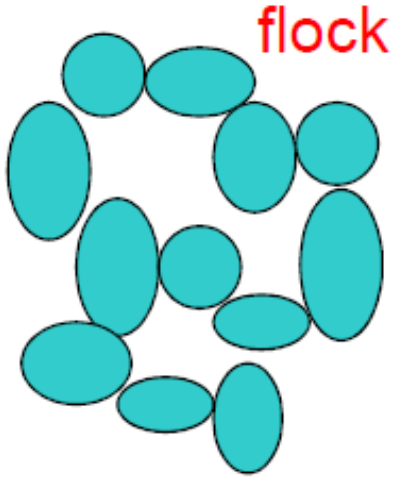
# BROWNIAN MOVEMENT

For particles having a diameter of about 2-5 μm, Brownian movement counteracts sedimentation to a measurable extent at room temperature by keeping the dispersed material in random motion.

Brownian movement depends on the particle size, density of dispersed phase and the density and viscosity of the disperse medium.



# DEFLOCCULATION AND FLOCCULATION




## Flocculated Suspensions

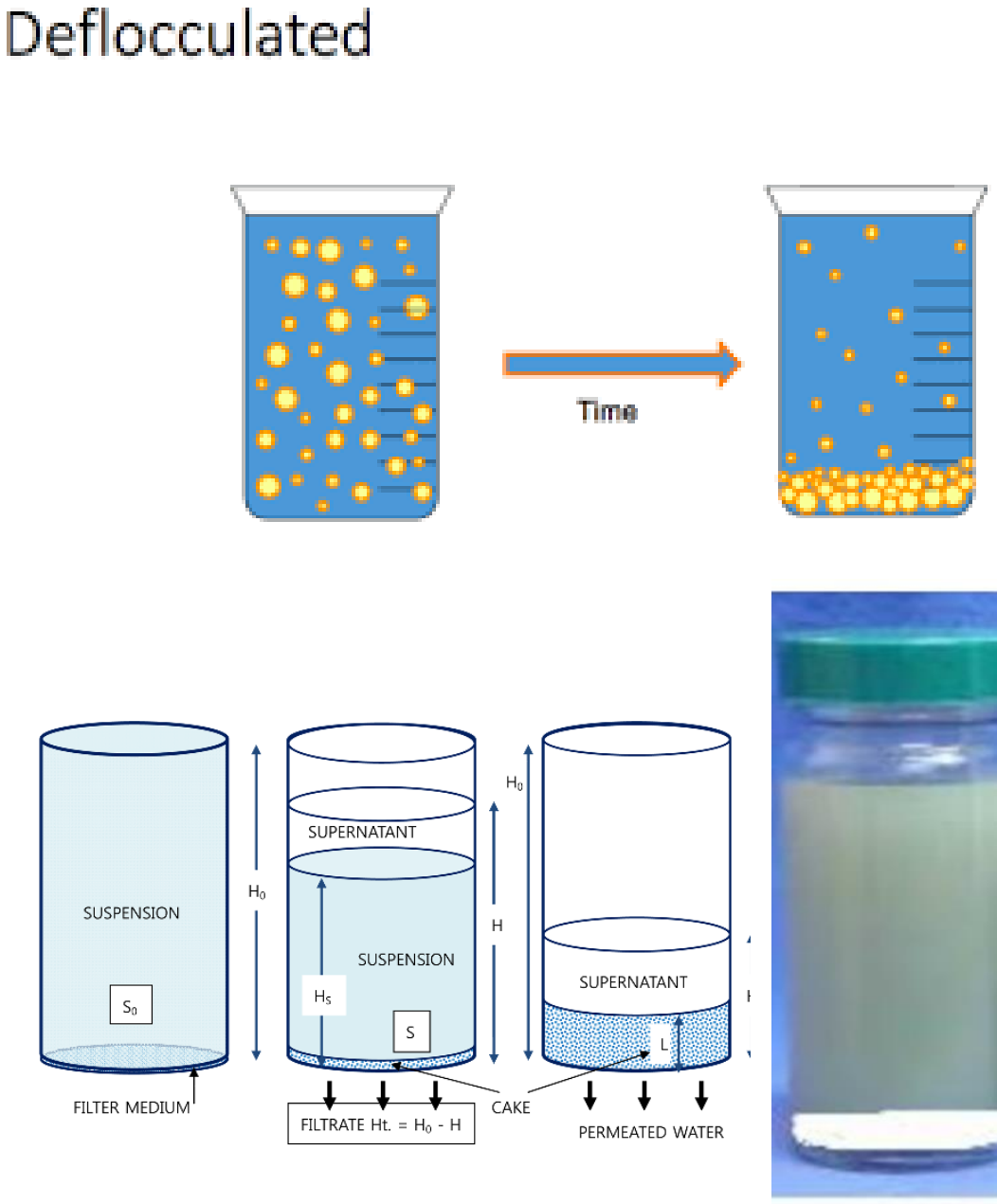
- In flocculated suspension, **formed flocs** (**loose aggregates**) will cause increase in sedimentation rate due to increase in size of sedimenting particles. Hence, flocculated suspensions sediment more rapidly.

- Here, the sedimentation depends **not only on the size** of the flocs but also on the porosity of the flocs.

# Deflocculated suspensions

- In deflocculated suspension, individual particles are settling through time.

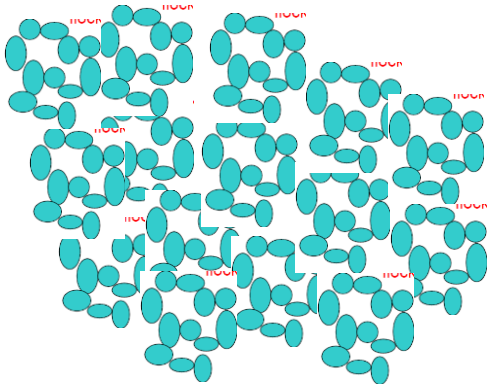
- Rate of sedimentation is slow, hence the sediment prevents entrapping of liquid medium which makes it difficult to re-disperse by agitation.
- This phenomenon called ‘caking’ or ‘claying’.
- In deflocculated suspension larger particles settle fast and smaller remain in supernatant liquid so supernatant appears cloudy.

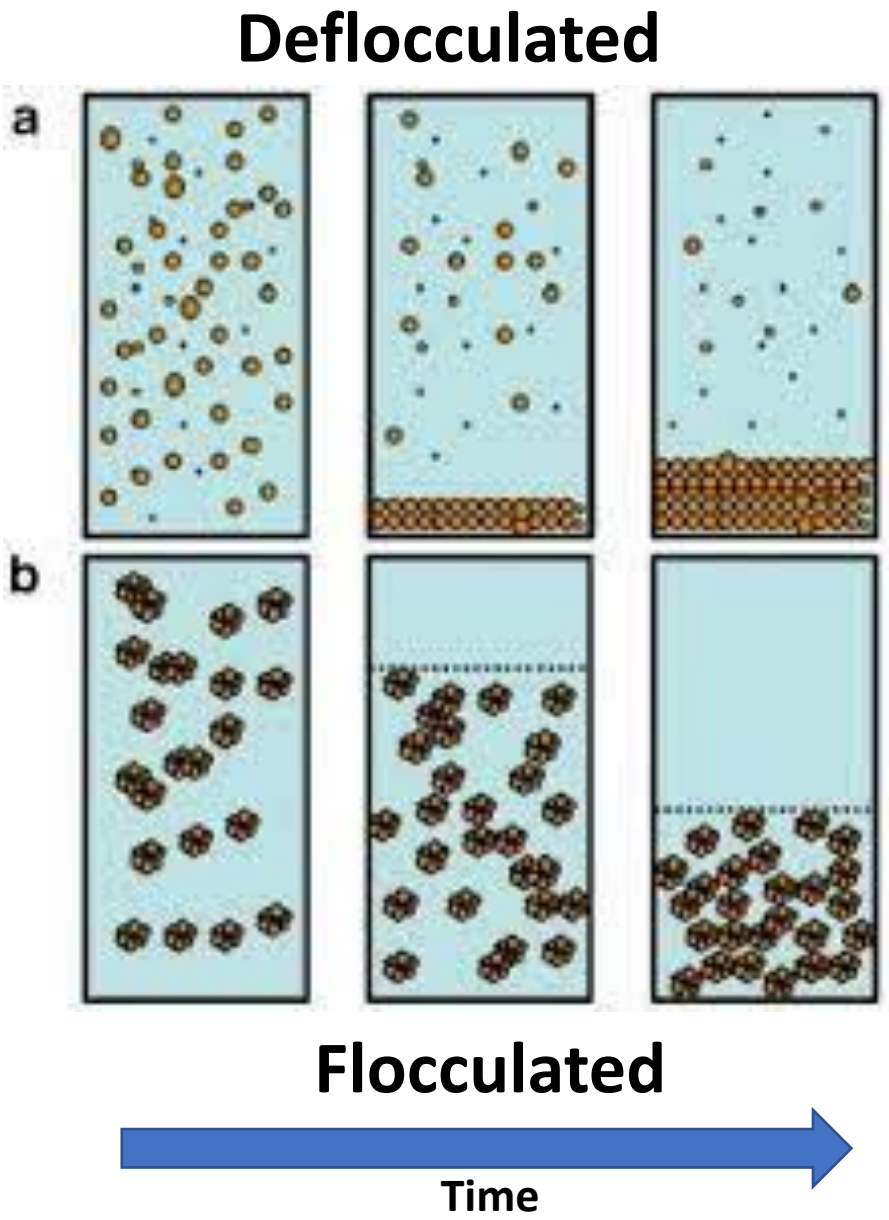


Deflocculated Suspension

flocculated Suspension

Not dense flocks aggregates





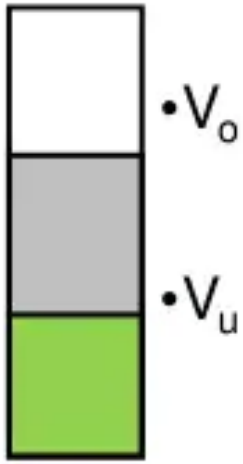
| | Flocculated | Deflocculated |
|---|---|---|
| Sedimented particle | Forms a network like structure | Separate individual particles |
| Velocity of sedimentation | fast<br>fall together | slow<br>fall according to size |
| Boundary | a distinct boundary between sediment and supernatant | no distinct boundary between sediment and supernatant |
| Supernatant | clear | turbid |
| Suspension | Not pleasing in appearance | Pleasing in appearance |
| Viscosity | High | Low |
| Rheology | plastic & pseudoplastic | Dilatent |
| Sediment | Loosely packed and doesn't form a cake | Closely packed and form a hard cake |
| Redispersibility | Easy | Difficult |

# Sedimentation Volume (F) or Height (H) for Flocculated Suspensions:

**Definition:**

Sedimentation volume is the ratio of the ultimate volume of sediment (Vu) to the original volume of sediment (Vo) before settling.

$$F = V_u / V_O$$




F=0.5

Where,

Vu = final or ultimate volume of sediment

VO = original volume of suspension before settling

F has values ranging from less than one to greater than one.

I- When F < 1 ⟶ Vu < Vo

II- When F =1 ⟶ Vu = Vo

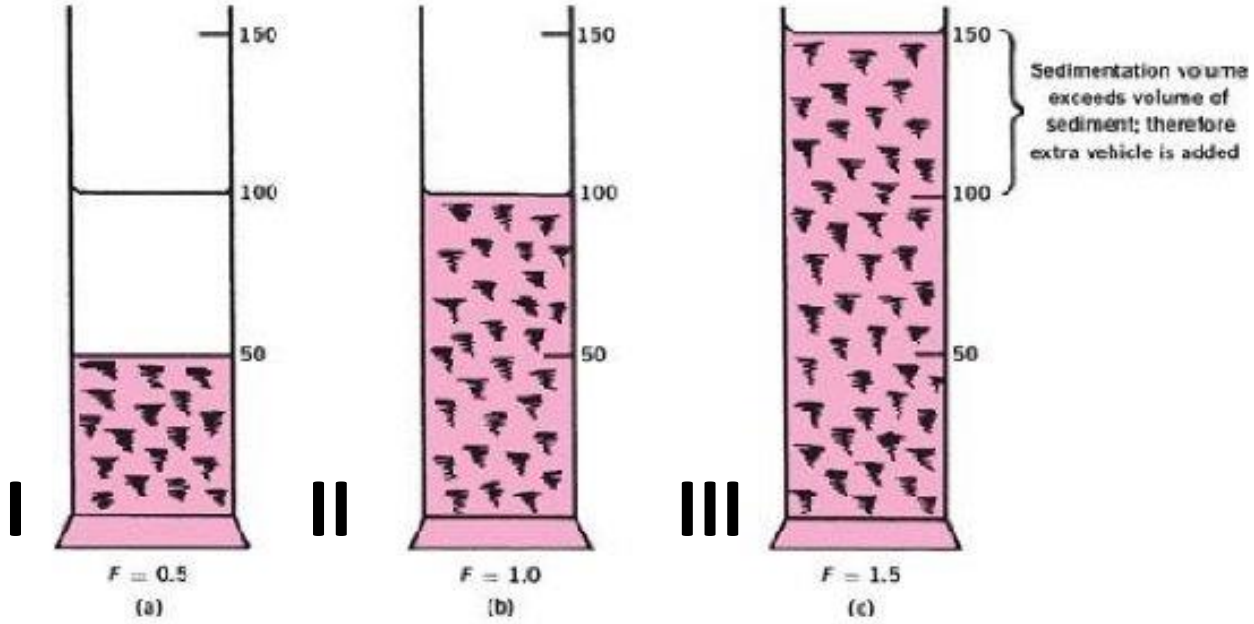
In the second case the system is in flocculated equilibrium and show no clear supernatant on standing.

III- When F > 1 ⟶ Vu > Vo

In this case the sediment volume is greater than the original volume due to the network of flocs formed in the suspension and so loose and fluffy sediment

- 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.




The sedimentation volume gives only a qualitative account of flocculation.

# Degree of flocculation (β)

It is the ratio of the sedimentation volume of the flocculated suspension (F) to the sedimentation volume of the deflocculated suspension (F∞).

$$\beta = F / F\infty$$

$$\beta = \frac{(Vu/Vo)\ \text{flocculated}}{(Vu/Vo)\ \text{deflocculated}}$$

- **The maximum value of ß is 1, when flocculated suspension sedimentation volume is equal to the sedimentation volume of deflocculated suspension.**

# THANK YOU