BP206T · B.PHARM THEORY

BP206T Physical Pharmaceutics

Unit III — Colloidal & Coarse Dispersions

Pills & Python Notes

Final unit-wise study notes.

Syllabus coverage: Unit III (12 hours).

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Chapter 1 — Colloidal Dispersions: Types, Properties, Stability and Applications

1.1 Learning objectives

After studying this chapter, you will be able to:

1. Define a colloidal dispersion and state the colloidal size range.
2. Classify colloids as lyophobic, lyophilic, or association colloids with examples.
3. Describe the optical, kinetic, and electrical properties of colloids.
4. Explain peptization and protective action with examples.
5. List pharmaceutical applications of colloidal systems.

1.2 The basic idea — what is a dispersion?

A **dispersion** is a system in which tiny particles of one substance (the **dispersed phase**) are distributed throughout another substance (the **dispersion medium** or continuous phase).

> **Analogy:** Think of making sharbat. Sugar dissolved in water disappears completely — that is a true solution. Sand stirred into water sinks quickly — that is a coarse suspension. Milk, in between, looks uniform but is not a true solution — tiny fat droplets are dispersed through water. Milk is close to what a colloid looks like.

Pharmaceutical dispersions are classified by particle size:

System	Particle size	Example
True (molecular) solution	Less than 1 nm (nanometre)	Sugar in water, saline drip
Colloidal dispersion	1 nm to 0.5 µm (micrometre)	Gum acacia mucilage, colloidal silver
Coarse dispersion	Greater than 0.5 µm	Chalk mixture, milk of magnesia, emulsions

> **Definition — Colloid:** A dispersion in which the dispersed-phase particles are between about **1 nm and 0.5 µm** in size — too small to see, too big to be single molecules.

Key takeaway: Colloids sit between true solutions and coarse suspensions. Their special properties come from their huge total surface area relative to their tiny size.

1.3 Types of colloidal dispersions

1.3.1 Lyophobic colloids ("solvent-hating")

- **Meaning:** *Lyo* = solvent, *phobic* = fearing. These particles **dislike** the dispersion medium and would rather stick to each other than to the solvent.
- **Nature:** Irreversible — once they clump and settle, shaking will not bring them back. Thermodynamically **unstable**.
- **Examples:** Colloidal gold, colloidal silver, ferric hydroxide sol.
- **Stability trick:** They need a protective electric charge or a protective colloid (see Section 1.7) to stop them clumping.

1.3.2 Lyophilic colloids ("solvent-loving")

- **Meaning:** These particles **love** the solvent; they attract solvent molecules and surround themselves with a solvent shell.
- **Nature:** Reversible — dry them to a powder, add solvent again, and the colloid reforms. Thermodynamically **stable**.
- **Examples:** Gelatin, starch, gum acacia, albumin, agar.
- **Stability trick:** They are self-stabilizing because of their strong attraction to the solvent.

1.3.3 Association colloids (amphiphilic colloids)

- **Meaning:** Made of **amphiphilic** molecules — each molecule has a water-loving (hydrophilic) head and a water-hating (hydrophobic) tail.
- At low concentration they behave like ordinary dissolved molecules. Above a certain concentration called the **Critical Micelle Concentration (CMC)**, they gather into clusters called **micelles** — tails hidden inside, heads facing the water.
- **Examples:** Surfactants like sodium lauryl sulphate, Tween 80, bile salts.
- **Pharmacy link:** Micelles can trap poorly soluble drugs inside them and carry them in water — the basis of micellar drug solubilisation.

Feature	Lyophobic	Lyophilic	Association
Affinity for solvent	Hates it	Loves it	Mixed (head loves, tail hates)
Stability	Unstable, needs protection	Stable, self-protected	Stable above CMC
Reversibility	Irreversible	Reversible	Reversible
Example	Colloidal silver	Gum acacia	Tween 80 micelles
Charge	Usually charged	May be neutral	Charged at head groups

Mnemonic — "Phoebe Loves Association Meetings": Phobic = hates solvent, **L**yophilic = loves solvent, **A**ssociation = amphiphiles forming micelles.

> **Common confusion:** Lyophobic does NOT mean "fears water" specifically — it means fearing the *solvent*, which could be water (hydrophobic) or an organic liquid. In pharmacy the solvent is usually water, so lyophobic ≈ hydrophobic in practice.

1.4 Optical properties of colloids

Because colloidal particles are roughly the size of the wavelength of visible light, they **scatter light** — this gives two famous effects.

1.4.1 The Tyndall effect

- **What happens:** When a beam of light passes through a colloidal dispersion, the path of the beam becomes visible as a glowing cone, because the particles scatter the light sideways.
- **True solutions** do not show it (particles too small to scatter); **coarse suspensions** show ordinary reflection.
- **Worked example:** Shine a torch through (a) sugar solution, (b) starch solution, (c) muddy water. Only (b), the colloid, shows a bright visible beam. This is the classic test to identify a colloid.
- **Analogy:** Dust particles in a cinema projector beam — you see the beam only because dust scatters the light.

1.4.2 Ultramicroscope and turbidity

- **Ultramicroscope:** A microscope that looks at scattered light (not transmitted light), so individual colloidal particles appear as bright dancing points against a dark background — used to *see* what cannot be seen directly.
- **Turbidity:** The cloudiness of a colloidal dispersion, caused by light scattering. Measured with a **nephelometer/turbidimeter** — used in pharmacy to check the clarity of injections and eye drops.

Key takeaway: Light scattering (Tyndall effect, turbidity) is the fingerprint of a colloid — true solutions are optically clear in this test.

1.5 Kinetic properties of colloids

Kinetic = related to movement. Colloidal particles are in constant random motion.

1.5.1 Brownian movement

- **What:** The zigzag, never-stopping random dance of colloidal particles, caused by constant bombardment from solvent molecules.
- **Effect on stability:** It keeps particles suspended and opposes settling — the smaller the particle, the stronger the Brownian movement.
- **Analogy:** A football being kicked randomly by a crowd of small children running around it — the ball jiggles in every direction. The children are solvent molecules, the football is the colloidal particle.
- **Pharmacy link:** Brownian movement is why particles smaller than about 1 μm hardly settle at all — it fights gravity (more on this in Chapter 2, Stokes' law).

1.5.2 Diffusion

- Colloidal particles slowly spread from high to low concentration, but **much more slowly** than dissolved molecules because they are bigger.
- Used in the lab to separate colloids from true solutions (dialysis).

1.5.3 Sedimentation and osmotic pressure

- Colloids settle very slowly under gravity and can be forced to settle in an **ultracentrifuge** — the rate of settling tells us the particle size and shape.
- They exert a small osmotic pressure (used historically to estimate molecular weights of polymers).

Key takeaway: Brownian movement is the colloid's built-in anti-settling engine — it is strongest for the smallest particles.

1.6 Electrical properties of colloids

1.6.1 Why colloidal particles carry a charge

Lyophobic particles usually carry an electric charge — for example, ferric hydroxide particles adsorb Fe^{3+} ions and become positively charged. Particles with the **same charge repel each other**, and this repulsion stops them clumping.

1.6.2 The electrical double layer and zeta potential

- Around each charged particle, oppositely charged ions gather in two layers: a tightly held inner layer and a loose outer (diffuse) layer — together called the **electrical double layer**.
- The **zeta potential (ζ)** is the measurable electric potential at the boundary of the tightly held layer. It is a number (in millivolts) that tells us how strongly particles repel each other.
- **Rule of thumb used in pharmacy:** A zeta potential more positive than +30 mV or more negative than −30 mV usually means a stable dispersion; near zero, particles clump quickly. (This is a practical guideline, not a law of nature.)

1.6.3 Electrophoresis

- **Definition:** The movement of charged colloidal particles toward the oppositely charged electrode when an electric field is applied.
- **Use:** Measuring zeta potential, and in analysis (gel electrophoresis separates proteins by charge and size).

> **Analogy:** Like fans of two rival teams wearing different coloured shirts — as long as everyone keeps their distance (repulsion), there is no fight (no clumping). Remove the shirts (neutralise the charge with an electrolyte) and they mix and clash.

1.7 Size and shape of colloidal systems

- **Size:** 1 nm to 0.5 µm, as defined above.
- **Shape matters:** Spherical particles (gold sol) flow and settle differently from rod-shaped (some viruses, fibrin) or plate-like particles. Shape affects viscosity, light scattering, and how particles pack when they settle.
- **How size is measured:** Ultramicroscope counting, light scattering, ultracentrifugation, electron microscopy — the method is chosen by the size range and the sample.

1.8 Stability of colloidal systems: peptization and protective action

1.8.1 Peptization

- **Definition:** Converting a freshly formed **precipitate** back into a colloidal dispersion by adding a small amount of electrolyte, called a **peptizing agent**.
- **Worked example:** Add ferric chloride solution to water → a reddish-brown precipitate of ferric hydroxide forms. Now add a few drops of ferric chloride (the peptizing agent) → the precipitate disperses into a clear reddish-brown **colloidal** sol. The Fe^{3+} ions adsorb on the particles, giving them a positive charge, so they repel and separate.
- **Analogy:** A crowd blocking a road (precipitate). A traffic policeman (peptizing agent) gives everyone the same instruction — "keep moving apart" — and the crowd breaks into individuals flowing freely (colloid).
- **Key takeaway:** Peptization = precipitate → colloid, using a little electrolyte to give particles a separating charge.

1.8.2 Protective action and the gold number

- **Definition:** Lyophilic colloids (gelatin, gum acacia) can **protect** lyophobic colloids from being clumped by electrolytes — they coat the particles like a shield. This is called **protective action**.
- **Gold number:** A measure of protective power. It is the **minimum weight (in milligrams) of the protective colloid that prevents the colour change of 10 mL of a standard gold sol when 1 mL of 10% sodium chloride solution is added**. Smaller gold number = stronger protection.
- **Worked example:** Gelatin has a gold number of about 0.005–0.01 mg (a tiny amount protects the gold sol — excellent protector). Starch has a gold number of about 10–15 mg (needs much more — weak protector). So gelatin is roughly a thousand times better a protector than starch.

Protective colloid	Approx. gold number (mg)	Protective power
Gelatin	0.005–0.01	Excellent
Gum acacia	0.1–0.2	Good
Starch	10–15	Poor

- **Pharmacy link:** Protective colloids are used to stabilise colloidal silver and gold preparations, and the same principle (polymers coating drug particles) stabilises nanosuspensions and many modern formulations.

Mnemonic — "Gelatin Guards Gold": the **G**old number of **G**elatin is tiny — the best **g**uard.

> **Common confusion:** Peptization makes a colloid *from* a precipitate; protective action *keeps* an existing colloid from clumping. Different jobs, both about stability.

1.9 Applications of colloidal systems in pharmacy

1. **Drug delivery:** Colloidal carriers (liposomes, nanoparticles, micelles) carry poorly soluble drugs through the body.
2. **Antimicrobials:** Colloidal silver preparations used as antiseptics.
3. **Formulation aids:** Gum acacia and gelatin as emulsifiers, suspending agents, and tablet binders.
4. **Diagnostics:** Gold colloids in rapid diagnostic kits (the red line on a pregnancy test strip is colloidal gold).
5. **Water purification:** Alum coagulates colloidal impurities in drinking water (the reverse of protection — deliberate clumping).
6. **Eye preparations and injections:** Colloidal clarity/turbidity checks are quality tests.

India context: India is one of the world's largest producers of gum acacia alternatives and natural gums (gum karaya, gum ghatti) used as pharmaceutical excipients; many Indian pharmacopoeial monographs include colloidal and mucilage-based preparations, and gold-colloid-based rapid test kits are manufactured in India for large public-health programmes.

1.10 One-minute revision — Chapter 1

- Colloid = 1 nm to 0.5 µm; between true solution and coarse suspension.
- Three types: lyophobic (hates solvent, irreversible), lyophilic (loves solvent, reversible), association (amphiphiles → micelles above CMC).
- Optical: Tyndall effect, ultramicroscope, turbidity.
- Kinetic: Brownian movement (anti-settling engine), diffusion, slow sedimentation.
- Electrical: double layer, zeta potential (±30 mV rule of thumb), electrophoresis.
- Stability: peptization (precipitate → colloid via electrolyte); protective action measured by gold number (smaller = better; gelatin best).
- Uses: drug delivery, colloidal silver, emulsifiers, diagnostic kits.

1.11 Practice questions — Chapter 1

MCQs

1. The particle size range of a colloidal dispersion is: (a) <1 nm (b) 1 nm–0.5 µm (c) >0.5 µm (d) >1 mm
2. Which colloid is irreversible? (a) Gelatin sol (b) Starch sol (c) Gold sol (d) Gum acacia mucilage
3. Micelles form above the: (a) gold number (b) CMC (c) zeta potential (d) HLB value
4. The Tyndall effect is due to: (a) absorption of light (b) scattering of light (c) refraction of light (d) polarisation of light
5. The gold number of gelatin is approximately: (a) 0.005–0.01 mg (b) 1–2 mg (c) 10–15 mg (d) 100 mg

Short answers

1. Define lyophobic and lyophilic colloids with one example each.
2. What is Brownian movement? How does it help colloidal stability?
3. Define zeta potential and state its practical significance.
4. What is peptization? Give one example.
5. Define gold number. Which is a better protective colloid — gelatin or starch? Why?

Long answers

1. Classify colloidal dispersions with examples, and compare lyophobic, lyophilic, and association colloids.
2. Describe the optical, kinetic, and electrical properties of colloids.
3. Explain peptization and protective action. How is protective power measured?

Application-based

1. A pharmacist notices a colloidal silver preparation has turned from brown to grey and settled. Using your knowledge of protective action, suggest what may have gone wrong and how the formulation could be protected.

Viva

1. Why does a true solution not show the Tyndall effect?
2. What does a zeta potential of −5 mV tell you about a dispersion?

Chapter 2 — Suspensions: Stokes' Law, Sedimentation and Flocculation

2.1 Learning objectives

After studying this chapter, you will be able to:

1. Define a suspension and state how it differs from a colloid.
2. State Stokes' law and identify every symbol in it.
3. Calculate the sedimentation rate of particles using Stokes' law, showing every step.
4. Explain the effect of Brownian movement on sedimentation.
5. Compare sedimentation of flocculated and deflocculated particles.
6. Define sedimentation volume and degree of flocculation.
7. Explain controlled flocculation and its advantages.

2.2 What is a suspension?

> **Definition — Suspension:** A coarse dispersion in which **solid particles larger than about 0.5 µm** are distributed through a liquid. The particles settle on standing but can be redispersed by shaking.

> **Worked example:** Milk of magnesia (magnesium hydroxide mixture) and calamine lotion are classic pharmaceutical suspensions. The label says "shake well before use" — that instruction exists because the solid settles.

> **Analogy:** Muddy river water. Stir it and it looks uniform; leave the glass still and the mud sinks to the bottom. A suspension behaves exactly the same way.

Feature	Colloidal dispersion (Ch. 1)	Suspension (this chapter)
Particle size	1 nm – 0.5 µm	Greater than 0.5 µm
Settling	Very slow; Brownian motion wins	Settles visibly on standing
Appearance	Clear-ish, shows Tyndall effect	Cloudy, opaque
Example	Starch solution	Milk of magnesia

2.3 Stokes' law — the theory of sedimentation

2.3.1 The concept

When a solid particle sinks through a liquid, three forces act on it:

1. **Gravity** pulling it down (depends on the particle's density).
2. **Buoyancy** pushing it up (depends on the liquid's density).
3. **Drag (friction)** opposing the motion (depends on the liquid's viscosity and the particle's size).

Very quickly the particle reaches a constant sinking speed called the **terminal (sedimentation) velocity**. Stokes' law gives this speed:

> **Stokes' law:** $v = d^2(\rho s - \rho)\, g \,/\, 18\eta$

Where:

- **v** = sedimentation velocity (m/s) — how fast the particle sinks
- **d** = diameter of the particle (m) — **v is proportional to d^2**, the most powerful factor
- **ρs** = density of the solid particle (kg/m^3)
- **ρ** = density of the liquid (kg/m^3) — bigger density difference = faster settling
- **g** = acceleration due to gravity (9.81 m/s^2)
- **η** = viscosity of the liquid (Pa·s) — thicker liquid = slower settling

Assumptions of Stokes' law (exam favourite): particles are spherical, smooth, and rigid; they settle one at a time (dilute suspension, no particle-particle interference); the liquid is still; flow around the particle is slow and smooth (laminar); no slipping at the particle surface.

> **Analogy:** Dropping a cricket ball and a table-tennis ball into a swimming pool vs into a tank of honey. The heavy, big ball sinks fast; in honey (high viscosity) everything sinks slowly. Stokes' law is the maths behind this everyday observation.

Key takeaway: Sedimentation velocity grows with the **square** of particle diameter — halving the particle size cuts the settling rate to one-quarter. Viscosity of the vehicle is the formulator's main brake pedal.

2.3.2 Worked numerical 1 — sedimentation rate (all steps shown)

Question: A suspension contains spherical drug particles of diameter **5 µm**. Density of drug = **1.5 g/cm^3**, density of the liquid = **1.0 g/cm^3**, viscosity of the liquid = **1 cP**. Calculate the sedimentation velocity. (g = 9.81 m/s^2)

Step 1 — Convert everything to SI units.

- d = 5 µm = 5 × 10^{-6} m
- ρs = 1.5 g/cm^3 = 1500 kg/m^3
- ρ = 1.0 g/cm^3 = 1000 kg/m^3
- η = 1 cP = 0.001 Pa·s

Step 2 — Write Stokes' law: $v = d^2(\rho s - \rho)g / 18\eta$

Step 3 — Substitute:

- $d^2 = (5 \times 10^{-6})^2 = 25 \times 10^{-12} = 2.5 \times 10^{-11}$ m^2
- $(\rho s - \rho) = 1500 - 1000 = 500$ kg/m^3
- Numerator = $2.5 \times 10^{-11} \times 500 \times 9.81 = 1.22625 \times 10^{-7}$
- Denominator = 18 × 0.001 = 0.018

Step 4 — Divide: v = 1.22625 × 10^{-7} / 0.018 = **6.81 × 10^{-6} m/s** (about 6.8 µm per second)

Step 5 — Make it meaningful: In one hour the particle sinks 6.81 × 10^{-6} × 3600 = 0.0245 m ≈ **2.5 cm per hour**. In a day, about 59 cm — so a 10 cm bottle would fully settle in well under a day. Hence "shake well before use".

(Double-checked: 2.5e-11 × 500 = 1.25e-8; × 9.81 = 1.22625e-7; ÷ 0.018 = 6.8125e-6 m/s ✓; × 3600 = 0.024525 m ✓.)

2.3.3 Worked numerical 2 — why particle size matters most

Question: If the same drug is milled from 10 µm to 5 µm, by what factor does the sedimentation rate fall?

Solution: Stokes' law says $v \propto d^2$. Halving the diameter (10 → 5 µm) reduces d^2 to $(1/2)^2 = 1/4$. **The settling rate falls to one-quarter.** (Check with numbers: at 10 µm, v = 2.73 × 10^{-5} m/s; at 5 µm, v = 6.81 × 10^{-6} m/s; ratio = 4.0 ✓.)

Practical lesson: Fine milling is the most powerful way to slow settling — but particles that are too fine may cake (see flocculation below), so formulators balance size against redispersibility.

2.3.4 Worked numerical 3 — creaming (negative sedimentation)

Question: An o/w emulsion has oil droplets of diameter **2 µm**. Oil density = 920 kg/m^3, water density = 1000 kg/m^3, viscosity = 1 cP. Find the velocity and state the direction of movement.

Solution:

- $d^2 = (2 \times 10^{-6})^2 = 4 \times 10^{-12}$ m^2; $(\rho s - \rho) = 920 - 1000 =$ **−80 kg/m^3**
- $v = 4 \times 10^{-12} \times (-80) \times 9.81 / 0.018 = -1.74 \times 10^{-7}$ m/s
- The **negative sign means upward movement** — the oil droplets rise: this is **creaming** (Chapter 3). Speed ≈ 0.17 µm/s ≈ 1.5 cm per day.

Common mistake: Forgetting unit conversion — micrometres to metres (×10^{-6}) and cP to Pa·s (×0.001). Almost every wrong Stokes' answer in exams comes from skipping this step.

2.4 Effect of Brownian movement on sedimentation

- For particles **smaller than about 1 µm**, random Brownian bombardment (Chapter 1) is strong enough to fight gravity — such particles hardly settle at all, even though Stokes' law predicts a small downward velocity.
- For coarse particles (tens of micrometres), Brownian movement is negligible and Stokes' settling dominates.
- **Key takeaway:** Stokes' law describes the *driving force* of settling; Brownian movement is the *opposing* random force that matters most for fine particles.

2.5 Sedimentation of flocculated vs deflocculated particles

Particles in a suspension exist in two states:

Deflocculated (peptized) suspension:

- Particles stay separate, each carrying the same charge, repelling each other.
- They settle **slowly, one by one**, and pack into a tight, dense sediment at the bottom — a hard **cake** that is very difficult to redisperse.
- Supernatant (the liquid above) stays cloudy for a long time.

Flocculated suspension:

- Particles join into loose, fluffy clusters called **flocs** (like bunches of grapes).
- Flocs are big, so they settle **fast** — but they form a loose, high-volume sediment that is **easy to redisperse** by shaking.
- Supernatant becomes clear quickly.

Property	Deflocculated	Flocculated
Particle arrangement	Separate particles	Loose flocs (clusters)
Rate of settling	Slow	Fast
Sediment	Dense cake, hard to redisperse	Fluffy, easy to redisperse
Supernatant	Cloudy	Clear
Desirability	Poor (caking)	Good (if controlled)

Analogy: Deflocculated settling is like bricks stacked tightly by a mason — strong wall, hard to break. Flocculated settling is like dry leaves piled loosely — a big fluffy heap, but one shake of wind scatters them again.

Common confusion: "Fast settling" sounds bad, but in suspensions it is GOOD when the sediment is fluffy and redispersible. The real enemy is **caking** — slow settling that forms an unshakable cake.

2.6 Sedimentation parameters

Two numbers quantify all this:

2.6.1 Sedimentation volume (F)

F = Hu / Ho — the ratio of the final (ultimate) height of the sediment (Hu) to the original height of the suspension (Ho).

- F ranges from 0 to 1. **F = 1 means no settling at all** (ideal); a flocculated suspension has F close to 1 (fluffy, high sediment); a deflocculated one has a small F (dense cake).
- **Worked example:** A 10 cm column of suspension settles to a sediment 7.5 cm high. F = 7.5 / 10 = **0.75**. A second formulation gives 9.2 cm → F = 0.92 → the second is more flocculated and will redisperse better.

2.6.2 Degree of flocculation (β)

β = F / F∞ — the sedimentation volume of the flocculated suspension (F) divided by that of the fully deflocculated suspension (F∞).

- β = 1 means no flocculation; larger β means stronger flocculation.
- Used in the lab to pick the right amount of flocculating agent.

Diagram to sketch: Two measuring cylinders side by side. Left (deflocculated): thin dense cake at bottom, cloudy liquid above, label "small F, hard cake". Right (flocculated): tall fluffy sediment, clear liquid above, label "F near 1, easy to shake". This single sketch answers many exam questions.

2.7 Flocculation and controlled flocculation

- **Flocculation** is deliberately induced by adding **flocculating agents** — usually electrolytes (e.g., salts) that reduce the zeta potential, so particles stop repelling and form loose flocs.
- **Controlled flocculation** goes one step further: the formulator adds just enough electrolyte to flocculate, plus a **structured vehicle** (a polymer like methylcellulose or Veegum) that thickens the liquid and holds the flocs suspended. Result: an elegant suspension that hardly settles, and redisperses with one shake.
- **Too little** electrolyte → deflocculated → caking. **Too much** → excessive flocculation, coarse flocs, poor appearance and pouring.

Pharmacy relevance: Every "shake well before use" suspension on an Indian pharmacy shelf — antacid mixtures, antibiotic dry syrups after reconstitution, calamine lotion — is designed around these principles: controlled flocculation plus a structured vehicle.

India context: Antibiotic dry syrups (e.g., amoxicillin suspensions reconstituted at the pharmacy) are a huge Indian market; their 7–14 day in-use stability depends on controlled flocculation so that each 5 mL spoonful carries a uniform dose. The Indian Pharmacopoeia includes sedimentation and redispersibility expectations for such preparations.

Mnemonic — "F over F-infinity": β = **F**locculated **F**raction over the deflocculated one. And "**F**luffy = **F** near one".

2.8 One-minute revision — Chapter 2

- Suspension = solid particles > 0.5 µm in liquid; settles, redispersed by shaking.
- Stokes' law: $v = d^2(\rho s - \rho)g/18\eta$; $v \propto d^2$; assumptions: spherical, dilute, laminar, still liquid.
- Brownian movement opposes settling for particles below ~1 µm.
- Deflocculated: slow settling, dense cake, bad. Flocculated: fast settling, fluffy sediment, easy to shake, good.
- F = Hu/Ho (near 1 is good); β = F/F∞ (degree of flocculation).
- Controlled flocculation = right electrolyte + structured vehicle; avoids caking.

2.9 Practice questions — Chapter 2

MCQs

1. Stokes' law assumes the particles are: (a) cubes (b) spheres (c) rods (d) plates
2. If particle diameter is doubled, sedimentation velocity becomes: (a) double (b) half (c) four times (d) one-fourth
3. A flocculated suspension ideally has sedimentation volume F: (a) near 0 (b) near 1 (c) exactly 0.5 (d) greater than 1
4. Caking is a problem of: (a) flocculated suspensions (b) deflocculated suspensions (c) emulsions (d) colloids
5. Degree of flocculation β is defined as: (a) Hu/Ho (b) F/F∞ (c) Ho/Hu (d) η/ρ

Short answers

1. State Stokes' law and name each symbol.
2. Why is a flocculated suspension preferred over a deflocculated one?
3. Define sedimentation volume and degree of flocculation.
4. What is controlled flocculation?
5. How does Brownian movement affect sedimentation?

Long answers

1. Derive and explain Stokes' law. Discuss its assumptions and the factors affecting the rate of sedimentation.
2. Compare flocculated and deflocculated suspensions under: rate of settling, nature of sediment, supernatant, and redispersibility.

Numericals

1. Calculate the sedimentation velocity of 8 µm drug particles (density 1.4 g/cm^3) in a vehicle of density 1.0 g/cm^3 and viscosity 2 cP. (Answer: ≈ 6.98 × 10^{-6} m/s — show all steps.)
2. A suspension column of 12 cm settles to 10.8 cm (flocculated) and to 3.0 cm (deflocculated). Calculate F and β, and comment on the formulation.
3. An oil droplet of diameter 1 µm (oil density 900 kg/m^3) in water (1000 kg/m^3, 1 cP) — calculate the creaming velocity and direction.

Application-based

1. A pharmacist receives a complaint that an antacid suspension forms a hard cake that will not redisperse even after vigorous shaking. Diagnose the problem in Stokes/flocculation terms and suggest two formulation fixes.

Viva

1. Why does the label of a suspension say "shake well before use"?
2. What happens to settling rate if you double the vehicle's viscosity?

Chapter 3 — Emulsions: Theories of Stabilisation and Physical Instabilities

3.1 Learning objectives

After studying this chapter, you will be able to:

1. Define an emulsion and name its two main types.
2. Explain the five theories of emulsification and stabilisation in the syllabus (DLVO, monomolecular adsorption, multimolecular adsorption, film formation, solid particle adsorption).
3. Describe the physical instabilities of emulsions: creaming, coalescence/breaking, and phase inversion.
4. Distinguish reversible from irreversible instabilities.
5. Suggest how each instability can be minimised in formulation.

3.2 What is an emulsion?

> **Definition — Emulsion:** A coarse dispersion of **two immiscible liquids** — tiny droplets of one liquid (dispersed phase) distributed through the other (continuous phase). Because oil and water do not mix, an **emulsifying agent** is needed to keep the droplets apart.

Two main types:

- **o/w (oil-in-water):** Oil droplets in water — e.g., milk (natural o/w emulsion), vanishing cream. Feels non-greasy, washes off with water.
- **w/o (water-in-oil):** Water droplets in oil — e.g., cold cream, butter. Feels greasy, moisturising.

> **Analogy:** A salad dressing of oil and vinegar separates within minutes — that is an *unstable* emulsion. Mayonnaise (oil + water + egg yolk as emulsifier) stays creamy for weeks — the egg yolk is the emulsifying agent doing the stabilising job.

Key takeaway: Emulsions are thermodynamically unstable by nature — oil and water *want* to separate. Every theory below is a different trick for stopping them.

3.3 Theories of emulsification and stabilisation

The syllabus names five theories. Learn each as: *what it says → example → limitation*.

3.3.1 DLVO theory (electrical barrier theory)

- **Named after** Derjaguin, Landau, Verwey, and Overbeek.
- **Core idea:** Every droplet is surrounded by an electrical double layer (Chapter 1). When two droplets approach, two forces fight: **van der Waals attraction** (pulls them together) and **electrical double-layer repulsion** (pushes them apart).
- If repulsion wins, an **energy barrier** keeps droplets apart → stable emulsion. If droplets collide with enough energy to cross the barrier, they fall into the attraction zone and **flocculate or coalesce**.
- **Analogy:** Two people wearing strongly repelling magnets on their chests trying to shake hands — they can only touch if they push very hard. The magnet strength is the zeta potential; adding salt weakens the magnets (compresses the double layer) and they can finally touch.
- **Limitation:** Works well for dilute, charged systems; less useful for non-ionic surfactant or polymer-stabilised emulsions.

3.3.2 Monomolecular adsorption

- **Core idea:** Surfactant molecules (e.g., sodium lauryl sulphate, Tweens, Spans) adsorb at the oil–water interface as a **single-molecule-thick layer (monolayer)**, with heads in water and tails in oil. This sharply **lowers interfacial tension**, so less energy is needed to make small droplets, and the charged/packed monolayer stops droplets merging.
- **Example:** Tween 80 (HLB ~15) stabilising an o/w emulsion.
- **Limitation:** A single molecular layer is thin — it lowers tension well but gives only modest mechanical strength against coalescence.

3.3.3 Multimolecular adsorption

- **Core idea:** Large molecules (e.g., **gum acacia, gelatin, methylcellulose**) adsorb at the interface in **thick, multi-molecule layers**, forming a bulky cushion around each droplet. Droplets cannot get close enough to merge — this is **steric stabilisation**.
- **Example:** Gum acacia in the classic 4:2:1 o/w emulsion method.
- **Limitation:** Needs high concentrations of gum; viscous; sensitive to pH and electrolytes.

3.3.4 Film formation

- **Core idea:** Some agents form a **continuous, flexible, plastic-like film** around each droplet — like wrapping each oil droplet in cling film. The film has mechanical strength: even when two droplets collide, the film does not rupture.
- **Example:** Methylcellulose and other polymers forming tough interfacial films; combinations of surfactant + fatty alcohol (e.g., cetrimide + cetostearyl alcohol) forming strong mixed films.
- **Limitation:** The film must be flexible — a brittle film cracks on collision and the emulsion breaks.

3.3.5 Solid particle adsorption (Pickering stabilisation)

- **Core idea: Finely divided solid particles** (bentonite, aluminium hydroxide, colloidal silica) sit *at* the oil–water interface like tiles on a floor, forming a solid mechanical barrier around droplets.
- **Key rule:** If the solid is preferentially wetted by **water**, it stabilises **o/w** emulsions; if wetted by **oil**, it stabilises **w/o** emulsions.
- **Example:** Bentonite-stabilised o/w emulsions; milk of magnesia-type particles.
- **Limitation:** Needs the right particle size and wetting; too-large particles do not coat well.

Theory	Stabilising mechanism	Typical agent	Weakness
DLVO	Electrical repulsion barrier	Ionic surfactants	Fails with non-ionics, high salt
Monomolecular adsorption	Lowers interfacial tension, monolayer	Tweens, Spans, SLS	Thin, weak film
Multimolecular adsorption	Thick steric cushion	Gum acacia, gelatin	High concentration needed
Film formation	Tough flexible film	Methylcellulose, mixed films	Brittle films crack
Solid particle adsorption	Solid particle barrier at interface	Bentonite, $Al(OH)_3$	Wetting must be right

Mnemonic — "Don't Make Milk Film Sour": **D**LVO, **M**onomolecular, **M**ultimolecular, **F**ilm formation, **S**olid particle adsorption.

> **Common confusion:** Monomolecular vs multimolecular — *mono* = small surfactant molecules, one layer, works by lowering tension; *multi* = big polymer molecules, thick layers, works by steric bulk.

3.4 Bancroft's rule and HLB (supporting concepts)

- **Bancroft's rule:** The liquid in which the emulsifier is **more soluble** becomes the **continuous phase**. A water-soluble emulsifier (high HLB) gives o/w; an oil-soluble one (low HLB) gives w/o.
- **HLB (Hydrophile–Lipophile Balance):** A number 1–20 describing the emulsifier. Rough guide: 3–6 → w/o emulsifier; 8–18 → o/w emulsifier; 13–16 → detergent; 15–18 → solubiliser. (Standard textbook ranges; exact cut-offs vary by source.)

3.5 Physical instabilities of emulsions

Three instabilities are in the syllabus. The golden rule: **creaming is reversible; coalescence and breaking are irreversible; phase inversion changes the emulsion type.**

3.5.1 Creaming

- **What:** Droplets rise to the top (o/w) or sink to the bottom (w/o) under gravity, forming a concentrated layer — but the droplets **do not merge**; each keeps its identity.
- **Cause:** Density difference between oil and water — it is Stokes' law again (Chapter 2, Numerical 3): $v \propto d^2$, and the sign of $(\rho s - \rho)$ decides up vs down.
- **Reversible:** Yes — gentle shaking redisperses the cream.
- **Analogy:** Malai rising on boiled milk left overnight — the cream layer is still milk, just concentrated; stir it back in.
- **Minimised by:** Reducing droplet size (homogenisation), increasing viscosity of the continuous phase, matching densities of the two phases.

3.5.2 Coalescence and breaking (cracking)

- **Coalescence:** The protective film around droplets ruptures and two droplets **merge into one bigger droplet**. Bigger droplets coalesce faster (vicious cycle), until finally...
- **Breaking (cracking):** Complete separation into two distinct liquid layers — the emulsion is destroyed. **Irreversible** — no amount of shaking brings it back.
- **Causes:** Film rupture from temperature changes, pH shifts, addition of incompatible electrolytes, microbial growth, freezing.
- **Analogy:** Soap bubbles in a sink — they sit together for a while (like creamed droplets), but when the thin film between two bubbles pops, they merge into one bigger bubble (coalescence). Pop enough and you are left with flat soapy water (breaking).
- **Minimised by:** Strong interfacial films (right emulsifier blend), adequate emulsifier concentration, avoiding temperature extremes and incompatible additives.

3.5.3 Phase inversion

- **What:** The emulsion **flips type** — o/w becomes w/o, or the reverse. The dispersed phase becomes the continuous phase.
- **Causes:** Changing the **phase volume ratio** (adding too much dispersed phase — beyond ~74% packing, droplets must invert), **temperature** changes (the Phase Inversion Temperature, PIT, for non-ionic surfactants), or changing/adding electrolytes.
- **Analogy:** A crowded local train — normally people (droplets) stand in the coach (continuous phase). If you keep stuffing in more people than the coach holds, the situation inverts: the crowd becomes the "coach" with pockets of empty space. Crossing the critical ratio flips the system.
- **Detection:** Conductivity test — o/w conducts electricity (water continuous), w/o does not; dye test; dilution test (o/w dilutes with water).
- **Minimised by:** Keeping phase volumes well within limits, choosing temperature-stable emulsifiers, controlling electrolyte content.

Instability	What happens	Reversible?	Main cause	Prevention
Creaming	Droplets rise/sink, stay separate	Yes (shake)	Density difference (Stokes)	Small droplets, viscous vehicle
Coalescence	Droplets merge, grow	No	Film rupture	Strong films, enough emulsifier
Breaking	Full separation into 2 layers	No	Severe coalescence	Avoid heat, pH shock, incompatibles
Phase inversion	o/w ↔ w/o flip	Sometimes	Phase ratio, temperature	Control ratio, PIT-aware formulation

Diagram to sketch: One beaker divided into four panels: (1) uniform emulsion — dots evenly spread; (2) creaming — dots crowded at top, clear layer below, arrow "shake → back to (1)"; (3) coalescence — dots merging into bigger blobs; (4) breaking — two flat layers, labelled "irreversible". Underneath, a fifth small panel for phase inversion with a flip arrow o/w ⇄ w/o.

> **Common mistake:** Saying "creaming means the emulsion has broken". Creaming is a *warning sign* — the droplets are still intact. Breaking is the death of the emulsion. Keep them separate in answers.

3.6 Pharmacy relevance and India context

- **Pharmacy relevance:** Creams, lotions, liniments, and many oral liquid formulations are emulsions; intravenous fat emulsions (parenteral nutrition) must never show coalescence — merged oil droplets could block blood vessels, so their manufacture and QC are extremely strict.
- **India context:** India manufactures large volumes of topical emulsions (antifungal creams, emollients) and the classic cod-liver-oil-type o/w products; in hot Indian summers, storage temperature control matters because heat accelerates creaming and can push non-ionic systems toward their phase inversion temperature.

3.7 One-minute revision — Chapter 3

- Emulsion = two immiscible liquids, droplets in a continuous phase; o/w and w/o; needs an emulsifier; Bancroft's rule picks the type.
- Five stabilisation theories: DLVO (electrical barrier), monomolecular (lowers tension), multimolecular (steric cushion), film formation (tough film), solid particle adsorption (Pickering barrier).
- Instabilities: creaming (reversible, Stokes), coalescence → breaking (irreversible, film rupture), phase inversion (type flip; phase ratio, temperature).
- Prevention: small droplets, viscous continuous phase, right emulsifier, temperature control.

3.8 Practice questions — Chapter 3

MCQs

1. Butter is an example of: (a) o/w emulsion (b) w/o emulsion (c) suspension (d) colloid
2. Which theory explains emulsion stability through an electrical energy barrier? (a) Film formation (b) DLVO (c) Multimolecular adsorption (d) Pickering
3. Which instability is reversible by shaking? (a) Breaking (b) Coalescence (c) Creaming (d) Phase inversion
4. A water-wetted solid particle stabilises: (a) w/o emulsion (b) o/w emulsion (c) both equally (d) neither
5. According to Bancroft's rule, a water-soluble emulsifier forms: (a) w/o (b) o/w (c) multiple emulsion (d) microemulsion

Short answers

1. Define emulsion. Name its two types with one example each.
2. State Bancroft's rule.
3. What is the difference between creaming and coalescence?
4. What causes phase inversion? How is it detected?
5. Explain solid particle adsorption with an example.

Long answers

1. Describe the five theories of emulsification and stabilisation with examples.
2. Discuss the physical instabilities of emulsions, their causes, and how each is prevented.

Application-based

1. A pharmacist finds that a lotion stored in a hot warehouse has separated into two clear layers that do not remix on shaking. Identify the instability, explain what happened at the droplet level, and suggest two preventive measures for future batches.

Viva

1. Why can't you make a stable emulsion of oil and water without an emulsifying agent?
2. How would you distinguish creaming from breaking at the counter?

UNIT III — INFOGRAPHIC CONCEPT (for the PDF designer): A vertical flowchart titled "From Colloid to Emulsion — Stability at Every Scale". Top: particle-size ladder (true solution < 1 nm → colloid 1 nm–0.5 µm → coarse > 0.5 µm) with one example each. Middle-left: three colloid-type icons (lyophobic = particles pushing each other away with lightning bolts; lyophilic = particles hugging water drops; association = micelle circle with heads out, tails in). Middle-right: Stokes' law equation $v = d^2(\rho s - \rho)g/18\eta$ with the d^2 term highlighted and a "shake well" suspension bottle. Bottom: emulsion panel — five small icons for the five stabilisation theories, and three instability icons (creaming = upward arrows, reversible; coalescence = merging blobs; phase inversion = flip arrow o/w ⇄ w/o). Colour code: blue = stable/reversible, red = irreversible.

COMBINED REFERENCES — BP206T UNITS III–V

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3. Adejare, A., *Remington: The Science and Practice of Pharmacy* (latest edition).
4. Aulton, M.E. and Taylor, K.M.G., *Aulton Pharmaceutics: The Design and Manufacture of Medicines*, Elsevier (latest edition).
