Pills & Python

Pharmacy · Data · AI · Healthcare

BP504T

Pharmaceutical Dosage Forms II

Unit II — Suspensions

B.Pharm · Semester V · Theory notes

Syllabus coverage: UNIT II (6 hours).

From-zero teaching standard: every technical term is defined before use.

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CHAPTER 3 — SUSPENSIONS: FORMULATION, MANUFACTURING, QC & ADVANCES

Chapter 3 · Suspensions: Formulation, Manufacturing, QC & Advances

Learning Objectives

1. Define suspension and explain when it is preferred over a solution.
2. List formulation additives and classify suspending agents.
3. Describe IPQC and QC tests for suspensions.
4. Explain the instabilities of suspensions and how they are controlled.
5. Describe packaging and advances: nanosuspensions, dry powders for reconstitution, raft-forming systems.

Key definitions

- Suspension: a biphasic liquid dosage form in which finely divided, undissolved solid drug particles are dispersed in a liquid vehicle.
- Suspending agent: an additive that increases the viscosity of the vehicle and keeps particles suspended longer (reduces settling rate).
- Flocculated suspension: particles loosely joined into flocs (clusters) that settle fast but redisperse easily on shaking.
- Deflocculated suspension: particles settle individually and slowly, but pack into a hard cake that is difficult to redisperse.
- Sedimentation volume: ratio of the settled volume to the total volume — a measure of how well the suspension stays dispersed.

Terminology at a glance

Term	Simple meaning
Dispersed phase	The solid drug particles
Continuous phase (dispersion medium)	The liquid vehicle
Stokes' law	Equation linking settling speed to particle size, density difference and viscosity
Caking	Formation of a hard, non-redispersible sediment
Redispersibility	Ability of the sediment to go back into suspension on shaking
Nanosuspension	Suspension with drug particles in the nanometre range
Raft-forming system	Liquid that forms a floating gel "raft" on stomach contents

Explanations

3.4.1 Why suspensions?

Used when the drug is insoluble or unstable in solution, when a sustained/prolonged effect is desired (slowly dissolving particles), to mask bitter taste (drug stays undissolved), and for drugs that need high doses that cannot dissolve fully.

3.4.2 Formulation additives

1. Suspending/viscosity agents: keep particles suspended.
2. Wetting agents: help hydrophobic drug particles get wetted by water (surfactants like polysorbates).
3. Flocculating agents: electrolytes that create loose flocs for easy redispersion.
4. Sweeteners, flavours, colours: palatability and appearance.
5. Preservatives: prevent microbial growth.
6. Buffers: pH control for stability.

3.4.3 Classification of suspending agents

1. Natural polysaccharides: acacia, tragacanth, xanthan gum.
2. Semisynthetic celluloses: methylcellulose, carboxymethylcellulose (CMC), hydroxypropyl methylcellulose (HPMC).
3. Synthetic polymers: carbomers (Carbopol), polyvinylpyrrolidone (PVP).
4. Clays: bentonite, kaolin (also act by forming a gel network).
5. Sugars/polyols: sucrose, sorbitol at high concentration increase viscosity.

3.4.4 Stokes' law — the science of settling

Settling velocity increases with: larger particle size (squared effect — most powerful), bigger density difference between particle and liquid, and decreases with higher viscosity. Simple words: small particles + thick liquid = slow settling. This is why we micronize the drug (small particles) and add suspending agents (thicker vehicle).

Worked numerical:

A suspension has particles of 10 μm settling at 2 mm/hour. If the particles are milled to 5 μm (half the size), what is the new settling rate? Since settling speed is proportional to (diameter)^2, halving the diameter reduces speed to one-quarter: 2 ÷ 4 = 0.5 mm/hour. Every step: v d^2 -> $v_2 = v_1 \times (d_2/d_1)^2 = 2 \times (5/10)^2 = 2 \times 0.25 = 0.5$ mm/hour.

3.4.5 Manufacturing

1. Prepare the structured vehicle: hydrate/dissolve the suspending agent in purified water (allow full hydration time).
2. Wet and mill the drug (wetting agent + milling for fine particles).
3. Add the drug slurry to the vehicle with stirring.
4. Add flavours, sweeteners, preservatives, colours; make up to volume.
5. Homogenise if needed; IPQC; fill into bottles; label "Shake well before use".

3.4.6 IPQC & QC tests

- Appearance: uniform, no large lumps.
- pH, viscosity: within specification.
- Particle-size distribution: within limits.
- Sedimentation volume: measure after standing; higher is better.
- Redispersibility: number of shakes/inversions needed to redisperse (fewer is better).

- Assay: drug content per volume.
- Pourability: flows easily from the bottle.
- Microbial limits; fill volume; resuspendability after storage.

3.4.7 Instabilities and control

1. Sedimentation/caking: controlled by small particle size, optimum viscosity, flocculation.
2. Crystal growth (Ostwald ripening): small crystals dissolve and redeposit on big ones; controlled by narrow particle-size distribution and temperature control.
3. Caking: prevented by flocculated systems and proper suspending agents.
4. Microbial growth: controlled by preservatives.
5. Chemical degradation: controlled by pH, antioxidants, packaging.

3.4.8 Packaging

Wide-mouth amber bottles (easy pouring and redispersion), with a measuring cup; label must say "Shake well before use" and storage conditions.

3.4.9 Advances

1. Nanosuspensions: drug particles reduced to nanometre size — huge surface area, faster dissolution, better bioavailability for poorly soluble drugs; made by media milling or high-pressure homogenisation.
2. Dry powder for reconstitution as suspensions: antibiotic powders reconstituted at dispensing — combines dry stability with liquid convenience.
3. Raft-forming systems: liquid containing alginate that, on contact with stomach acid, forms a floating gel raft which carries antacid/anti-reflux drug and sits on top of stomach contents, blocking reflux. Example: alginate-based anti-reflux preparations.

Classifications

- Suspensions by use: oral, parenteral (injectable), topical.
- By particle arrangement: flocculated vs deflocculated.
- Suspending agents: natural, semisynthetic, synthetic, clays.

Mechanism / how it works

- Flocculation mechanism: added electrolytes reduce the repulsive charge between particles, letting them form loose, fluffy flocs that settle as a high-volume, easily redispersed sediment.
- Raft formation: sodium alginate + stomach acid -> alginic acid gel; carbonates release CO_2 which gets trapped, making the gel float.

Diagram to draw

1. Flocculated vs deflocculated settling: two cylinders — fluffy high sediment vs compact low cake.
2. Raft system: stomach with floating gel layer on top of contents.
3. Nanosuspension particle: drug nanocrystal surrounded by stabiliser layer.

Process flow

Suspension manufacture:

Hydrate suspending agent -> mill/wet drug -> add drug slurry to vehicle -> add flavours, sweeteners, preservatives -> make up to volume -> homogenise -> IPQC (pH, viscosity, sedimentation volume, redispersibility, assay) -> fill -> label "shake well" -> QC -> pack.

One-glance summary

One-glance summary

SUSPENSIONS — one glance

- [EXP] Solid particles in liquid · TWO phases · cloudy · SHAKE WELL
- [INFO] Stokes' law: small particles + thick liquid = slow settling
- [SALT] Suspending agents: acacia · tragacanth · CMC · HPMC · carbomer · bentonite
- [!] Enemies: caking · crystal growth · microbes
- [QC] QC: sedimentation volume · redispersibility · viscosity · particle size · assay
- Advances: nanosuspensions · dry powder for reconstitution · raft-forming alginate systems

Tables

Suspending agent	Type	Notes
Acacia, tragacanth	Natural	Classic, variable quality
Xanthan gum	Natural (fermentation)	Good suspending, pourable
CMC, HPMC, MC	Semisynthetic	Reliable, widely used
Carbomer	Synthetic	High viscosity at low concentration
Bentonite	Clay	Forms gel network

Examples

1. Antacid suspension: neutralises stomach acid; must be shaken so each spoonful has uniform drug.
2. Paracetamol suspension for children: for children who need a liquid but the dose cannot fully dissolve.
3. Alginate raft preparation: floats on stomach contents to block acid reflux.

Think of it this way

- A suspension is like a snow globe — shake it and the snow (drug) swirls evenly; leave it and it settles.
- Caking is like wet sand drying into a brick at the bottom of the bucket.

Pharmacy relevance

Counsel every suspension patient: shake well, use the measuring cup, note storage and discard dates for reconstituted antibiotics.

India context

Antacid and anti-diarrhoeal suspensions are household medicines across India; correct shaking and measuring directly affect dose accuracy.

Key points

1. Suspension = undissolved solid particles in liquid; shake before use.
2. Stokes' law: settling $\propto$ (particle size)^2 × density difference ÷ viscosity.
3. Suspending agents: natural, semisynthetic, synthetic, clays.
4. QC: sedimentation volume, redispersibility, viscosity, particle size, assay.
5. Instabilities: sedimentation, caking, crystal growth, microbial, chemical.
6. Advances: nanosuspensions, reconstitutable dry powders, raft systems.

Common confusions

- Flocculated vs deflocculated: flocculated settles fast but redisperses easily (good); deflocculated settles slowly but cakes badly (bad).
- Solution vs suspension: solution needs no shaking; suspension must be shaken.

Common mistakes

1. Dispensing a suspension without the "shake well" instruction.
2. Using too much suspending agent — product becomes too thick to pour.
3. Storing reconstituted antibiotic suspensions beyond the discard date.

Mnemonics

- "Small Thick Slow" — small particles + thick liquid = slow settling (Stokes).
- Suspending agents: "NaSeSyCl" — Natural, Semisynthetic, Synthetic, Clay.

Exam summary

Suspensions are biphasic liquids with solid drug dispersed in a vehicle, used for insoluble/unstable/high-dose drugs. Formulation needs suspending agents, wetting agents, flocculating agents, sweeteners and preservatives. Stokes' law guides stability: small particles and viscous vehicles slow settling. QC covers sedimentation volume, redispersibility, viscosity, particle size and assay. Advances include nanosuspensions, dry powders for reconstitution and raft-forming systems.

One-minute revision

Two phases, shake well. Stokes: small + thick = slow. Agents: natural/semisynthetic/synthetic/clay. QC: sedimentation, redispersibility, viscosity. Advances: nano, dry powder, raft.

Exam questions

Short answers:

1. Define suspension. When is it preferred over a solution?
2. Classify suspending agents with two examples each.
3. State Stokes' law and its significance in suspension stability.
4. What is caking? How is it prevented?
5. Write a note on raft-forming systems.

Long answers:

1. Describe the formulation and manufacturing of suspensions, including the role of additives.
2. Discuss the instabilities of suspensions and the QC tests performed on them.

MCQs:

1. "Shake well before use" appears on: (a) Solutions (b) Suspensions (c) Elixirs (d) Syrups — Answer: (b)
2. According to Stokes' law, settling rate is proportional to: (a) Diameter (b) Diameter^2 (c) 1/diameter (d) Viscosity — Answer: (b)
3. Bentonite is a: (a) Sweetener (b) Clay suspending agent (c) Preservative (d) Flavour — Answer: (b)
4. Nanosuspensions improve: (a) Colour (b) Dissolution/bioavailability (c) Taste only (d) Weight — Answer: (b)
5. Raft-forming systems contain: (a) Alginate (b) Alcohol (c) Sugar (d) Oil — Answer: (a)

Viva:

1. Why is a flocculated suspension preferred over a deflocculated one?
2. How does particle-size reduction help both dissolution and suspension stability?

Application-based:

1. A suspension cakes within a week. Analyse the probable causes and suggest reformulation steps.

References