BP206T · B.PHARM THEORY

BP206T Physical Pharmaceutics

Unit V — Micromeritics

Final Unit Notes

B.Pharm Semester II · Unit V · 8 Hours

Particle Size · Surface Area · Powder Flow

PILLS & PYTHON

Pharmacy · Data · AI · Healthcare

UNIT V — MICROMERITICS

Chapter 5 — Micromeritics: Particle Size, Surface Area and Powder Flow

5.1 Learning objectives

After studying this chapter, you will be able to:

1. Define micromeritics and explain why particle size matters in pharmacy.
2. Name methods for determining particle size, shape, and surface area, with their size ranges.
3. Explain the significance of particle size and surface area with examples.
4. Determine powder flow properties (angle of repose, Carr's index, Hausner ratio) and interpret the results.
5. List methods of enhancing powder flow.
6. Describe advanced flow measurement using the powder flow tester.

5.2 The basic idea — what is micromeritics?

> **Definition — Micromeritics:** The science of **small particles** — their size, size distribution, shape, surface area, and how powders flow.

Why should a pharmacist care? The same drug in coarse vs fine powder can behave like two different drugs:

- Fine powder → larger surface area → dissolves faster → faster absorption (important for poorly soluble drugs).
- But fine powder also flows badly → tablets vary in weight → dose varies.

So micromeritics is the balancing act between **dissolution** and **manufacturing**.

> **Analogy:** Sugar cubes vs powdered sugar in tea. Same sugar, but the powder dissolves almost instantly because it exposes far more surface to the water. Particle size works the same way for drugs.

5.3 Particle size and size distribution

- **Particle size:** Usually expressed as a diameter (for spheres) or an **equivalent diameter** (for irregular particles — the diameter of a sphere that behaves the same way).
- **Size distribution:** A real powder is never one size — it is a *range*. The distribution (how many particles at each size) matters as much as the average: a few oversized particles can block a tablet die; too many fines ruin flow.
- **Significance:** Dissolution rate and bioavailability (finer = faster), content uniformity of tablets, suspension settling rate (Stokes' law, Chapter 2), stability of emulsions.

5.4 Methods for determining particle size

Method	Principle	Approx. size range	Remarks
Optical microscopy	Direct measurement of particles	0.2 µm and up	Sees shape too; slow, small sample
Sieving	Particles pass through standard mesh screens	Above ~40 µm	Simple, cheap; weight distribution
Sedimentation (Andreasen pipette)	Stokes' law settling rate	1–200 µm	Gives Stokes diameter
Coulter counter (electrical sensing zone)	Particle passing through an orifice changes electrical resistance	0.5–500 µm	Counts number of particles
Laser diffraction	Scattering pattern of laser light	0.1–1000 µm	Fast, modern QC instrument

Diagram to sketch: A sieve stack — sieves of decreasing mesh size stacked vertically, powder on top, shaken; label "coarse stays on top, fines fall through; weigh each fraction → size distribution".

Common confusion: Each method gives a *different kind* of diameter (microscope = geometric, sedimentation = Stokes, Coulter = volume-equivalent). So "particle size" always depends on the method — never compare numbers from two different methods directly.

5.5 Particle shape and surface area

5.5.1 Shape

- Described by terms like spherical, needle-like (acicular), plate-like, irregular; quantified by **sphericity** or aspect ratio.
- **Significance:** Needle-shaped crystals flow poorly and pack badly; spherical granules flow beautifully. Shape also affects dissolution and suspension behaviour.

5.5.2 Surface area and its determination

- **Specific surface area** = surface area per unit mass (m^2/g) or per unit volume.
- **Methods:**
- **Gas adsorption (BET method):** Nitrogen gas adsorbs as a monolayer on the particle surface; from the gas volume, surface area is calculated. The standard for true surface area.
- **Air permeability (Fisher subsieve sizer):** Measures resistance to air flowing through a packed powder bed — fast, popular in QC.
- **Significance:** Dissolution rate is proportional to surface area (Noyes–Whitney equation) — doubling the surface area roughly doubles the dissolution rate. Also affects adsorption of moisture, chemical degradation, and drug-excipient interactions.

Worked numerical 1 — specific surface area (all steps): Question: Spherical drug particles have density 1.25 g/cm^3 and diameter 20 µm. Calculate the specific surface area. What happens if the diameter is reduced to 5 µm?

Solution:

- For spheres, specific surface Sw = 6 / (ρ × d).
- Convert: ρ = 1.25 g/cm^3 = 1250 kg/m^3; d = 20 μm = 2 × 10^{-5} m.
- Sw = 6 / (1250 × 2 × 10^{-5}) = 6 / 0.025 = **240 m²/kg**.
- At d = 5 μm: Sw = 6 / (1250 × 5 × 10^{-6}) = 6 / 0.00625 = **960 m²/kg** — exactly 4× larger (halving the diameter twice multiplies surface area by 4).
- **Meaning:** The finer powder exposes 4× the surface → dissolves much faster → but also picks up moisture faster and flows worse.

> *(Double-checked: 1250 × 2e-5 = 0.025; 6/0.025 = 240 ✓; 1250 × 5e-6 = 0.00625; 6/0.00625 = 960 ✓.)*

5.6 Flow properties of powders

> Good flow = uniform tablet weight = uniform dose. Poor flow = weight variation = failed QC. Three standard tests:

5.6.1 Angle of repose (θ)

- **Method:** Let powder flow through a funnel onto a flat surface; it forms a cone (heap). Measure the heap's height (h) and base radius (r).
- **Formula:** tan θ = h / r.
- **Interpretation:** Smaller angle = better flow. Rough guide: below 30° excellent, 30–40° fair/passable, above 40° poor.
- **Worked numerical 2 (all steps):** A powder heap is 3.5 cm high with base radius 7 cm. tan θ = 3.5/7 = 0.5 → θ = arctan(0.5) = **26.6°** → excellent flow.
- **Analogy:** Dry sand poured on the floor makes a low flat cone (good flow); wet sticky mud makes a tall steep heap (poor flow).

5.6.2 Carr's compressibility index (CI)

- **Method:** Measure the **bulk density** (poured, ρb) and the **tapped density** (after tapping the cylinder, ρt).
- **Formula:** CI = (ρt − ρb) / ρt × 100%.
- **Interpretation:** A powder that compresses a lot on tapping was full of air gaps → poor flow. Rough guide: 5–15% excellent, 16–20% good/fair, 21–25% passable, above ~25% poor.
- **Worked numerical 3 (all steps):** Bulk density 0.62 g/mL, tapped density 0.76 g/mL. CI = (0.76 − 0.62)/0.76 × 100 = 0.14/0.76 × 100 = **18.4%** → fair flow.

5.6.3 Hausner ratio (HR)

- **Formula:** HR = ρt / ρb (tapped ÷ bulk).
- **Interpretation:** Below 1.25 good flow; 1.25–1.5 fair/passable; above 1.5 poor.
- **Worked numerical 4 (all steps):** Same powder: HR = 0.76 / 0.62 = **1.23** → good-to-fair flow, consistent with the Carr's result above.

> *(Double-checked: 0.14/0.76 = 0.1842 → 18.42% ✓; 0.76/0.62 = 1.2258 ✓.)*

Test	Formula	Good flow	Poor flow
Angle of repose	tan θ = h/r	< 30°	> 40°
Carr's index	(ρt−ρb)/ρt × 100	5–15%	> 25%
Hausner ratio	ρt/ρb	< 1.25	> 1.5

Key takeaway: All three tests measure the same thing — interparticle friction. Report them together; if they disagree, repeat the test.

5.7 Methods of enhancing powder flow

1. **Glidants:** Tiny particles (e.g., **colloidal silicon dioxide**, talc) that sit between drug particles like ball bearings, reducing friction. Added at 0.1–1%.
2. **Granulation:** Converting fine powder into larger, spherical **granules** (wet or dry granulation) — bigger spheres flow far better than fine irregular powder.
3. **Spray drying:** Produces uniform spherical particles with excellent flow.
4. **Controlling particle shape and size:** Recrystallisation to get compact crystals instead of needles.
5. **Reducing moisture:** Drying the powder; moisture creates liquid bridges between particles that kill flow (a real problem in humid Indian monsoons).
6. **Vibration-assisted filling** and proper hopper design in manufacturing.

Analogy: Glidants are like putting marbles between sticky floor tiles — the tiles (drug particles) can now slide over each other instead of gripping.

5.8 Advanced flow properties — the powder flow tester

- Basic tests (angle of repose, Carr's) are simple but operator-dependent. Modern QC uses the **powder flow tester** (e.g., the **Schulze ring shear tester**).
- **Principle:** The powder is pressed (consolidated) in a cell and then sheared; the instrument measures the **yield locus** — how much stress is needed to make the powder start flowing.
- **Key output — the flow function (ff_c):** the ratio of consolidation stress to unconfined yield strength. Rough guide: ff_c > 10 free-flowing, 4–10 easy-flowing, 2–4 cohesive, < 2 very cohesive.
- **Why it matters:** It predicts real problems — will the powder **arch or rat-hole in the hopper**? Will the tablet press feed uniformly? It gives numbers that basic tests cannot, and is increasingly used in Indian pharmaceutical plants for scale-up and troubleshooting.

India context: Tablet weight variation is a common audit observation; Indian QC labs routinely run bulk/tapped density and angle of repose, while larger formulation R&D centres now add shear-cell (powder flow tester) data in development reports to prevent hopper-flow failures during technology transfer to production.

5.9 One-minute revision — Chapter 5

- Micromeritics = size, shape, surface area, flow of small particles.
- Size methods: microscopy, sieving (>40 μm), sedimentation/Andreasen (Stokes), Coulter counter, laser diffraction.
- Surface area: BET gas adsorption (standard), air permeability; Sw = 6/(ρd) for spheres; more area = faster dissolution.
- Flow tests: angle of repose (tan θ = h/r, <30° excellent), Carr's index ((ρt−ρb)/ρt ×100, 5–15% excellent), Hausner ratio (ρt/ρb, <1.25 good).
- Improve flow: glidants, granulation, spray drying, drying, better crystal shape.
- Advanced: powder flow tester (ring shear) → yield locus, flow function ff_c; predicts hopper problems.

5.10 Practice questions — Chapter 5

MCQs

1. Micromeritics deals with particles of size: (a) >1 mm (b) colloidal range only (c) small particles, generally micrometre range (d) nanoparticles only
2. The Andreasen pipette works on the principle of: (a) light scattering (b) Stokes' law (c) electrical resistance (d) gas adsorption
3. The BET method determines: (a) particle size (b) surface area (c) density (d) flow rate
4. An angle of repose of 26° indicates: (a) poor flow (b) passable flow (c) excellent flow (d) no flow
5. The flow function ff_c greater than 10 means: (a) very cohesive (b) free-flowing (c) passable (d) flooded

Short answers

1. Define micromeritics. Why is particle size important in pharmacy?
2. Name four methods of particle-size determination with their principles.
3. Define specific surface area. How is it measured by the BET method?
4. Write the formulae for angle of repose, Carr's index, and Hausner ratio.
5. What is a glidant? Give two examples.

Long answers

1. Describe the methods for determination of particle size, indicating the size range and principle of each.
2. Discuss the flow properties of powders: their determination, significance, and methods of enhancement.
3. Write a note on advanced flow measurement using the powder flow tester.

Numericals

1. A powder has bulk density 0.58 g/mL and tapped density 0.81 g/mL. Calculate Carr's index and Hausner ratio, and comment on flow. (Answers: CI ≈ 28.4%, HR ≈ 1.40 → poor flow.)
2. A heap of granules is 4 cm high with a base diameter of 20 cm. Calculate the angle of repose and comment. (Answer: r = 10 cm; tan θ = 0.4; θ ≈ 21.8° → excellent flow.)
3. Spherical particles: density 1.5 g/cm³, diameter 10 µm. Calculate specific surface area. (Answer: 400 m^2/kg.)

Application-based

1. A tablet batch fails weight-variation limits. The granules show Carr's index 29% and angle of repose 44°. Diagnose the problem and propose three corrective actions in order of practicality.

Viva

1. Why can't you compare a "particle size" measured by sieving with one measured by laser diffraction?
2. How does moisture affect powder flow?

UNIT V — INFOGRAPHIC CONCEPT (for the PDF designer): A "Powder Journey" strip titled "From Particle to Tablet". Left: particle-size ladder with method icons (microscope, sieve stack, laser beam). Centre: a sphere with the formula Sw = 6/(ρd) and arrows showing "smaller particle → more surface → faster dissolution". Right: three flow-test icons — powder cone with θ angle, graduated cylinder before/after tapping (Carr's/Hausner), and a shear-cell diagram — each with a green/amber/red traffic-light scale. Bottom: glidant "ball bearing" cartoon between rough particles, captioned "glidants reduce friction".

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).