Powders

- Powder = dry substance of finely divided particles ranging roughly **1.25 µm – 1.7 mm**.
- **Medicated powder uses**
  - **Internal (oral)**
  - **External (topical)**

Main dosage-form categories

Category	Key features	Critical points to remember
Bulk powders	Mixed ingredients packed in one container.	Example: magnesium-trisilicate + chalk oral powder.
Divided powders	Same formulation as bulk but **pre-portioned single doses**, individually wrapped.	
Effervescent powders	Contain sodium bicarbonate + citric acid; fizz when added to water to make a draught.	
Dusting powders	External application for therapeutic, prophylactic, or lubricant purposes.	• **Sterile** if applied to open wounds (e.g., chlorhexidine). • Non-sterile but pathogen-free for intact skin (e.g., purified talc). • Used for fungal infections such as athlete's foot.
Insufflations	Powder blown or inhaled into ear, nose, throat, or lungs via an insufflator/DPI.	Dose often supplied in pierced gelatin capsules with lactose diluent. **Particle size must be controlled** for lung deposition.
Oral antibiotic "dry syrups"	Drugs unstable in solution supplied as powder/granules in bottle; pharmacist adds a measured volume of water on dispensing.	Examples: ampicillin (Penbritin), penicillin V.
Powders for injection	Sterile powder in ampoule when drug unstable in solution; diluent (e.g., Water for Injection) added immediately before use.	May include excipients to render final solution isotonic; use immediately after reconstitution.

granules

- **Granule = aggregated powder particles** about **2 – 4 mm** in diameter
- **Granulation** = the process of binding fine powders together to create these larger, free-flowing particles.

How we measure particle size

- **Sieving**: mechanical shaking through progressively finer metal sieves; records the fraction retained or passed on each mesh (practical range ≈ 40 µm – 9.5 mm).

***Why* we granulate**

1. **Prevent segregation** of mixed ingredients.
2. **Improve flow**—fine powders stick and bridge; granules flow freely.
3. **Enhance compressibility** for any later tableting.
4. **Reduce caking** in slightly hygroscopic materials (granules absorb a little moisture yet stay free-flowing).
5. **Save space**—granules are denser, so the same weight occupies less volume for storage/shipping.

Granulation methods

Method	Key points
Dry granulation	No liquid; powders are compacted under high pressure and then milled to size.
Wet granulation	Powder wetted with a **volatile, non-toxic solvent** (water, ethanol, isopropanol). Wet mass is sieved → dried. • Water is safe but can cause hydrolysis & needs longer drying. • Organics are used for water-sensitive drugs or faster drying.

Dosage-form variants of medicated granules

Form	Defining feature	Example/Note
Bulk granules	Large single container; suitable for high doses (e.g., methyl-cellulose laxative 1–4 g).	Patient measures dose.
Divided granules	One-dose sachets or wraps.	Same handling rules as divided powders.
Effervescent granules	Contain drug + $NaHCO_3$ + citric & tartaric acids; fizz on water contact.	Formulated exactly like effervescent powders.

Advantages of powders & granules (vs. liquids/tablets)

1. **Greater chemical stability** in dry state (e.g., antibiotic "dry syrups" last 2–3 yrs dry but 1–2 weeks after reconstitution).
2. **Convenient for large doses**—easier to swallow a dispersed powder than many big tablets (e.g., 1–5 g Mg trisilicate).
3. **Faster dissolution** than tablets/capsules because no disintegration step.
4. **faster drug absorption** orally for the same reason.

Disadvantages

1. **Bulky to carry** compared with a small bottle of tablets or capsules (though unit-dose sachets help).
2. **Taste masking** is harder; effervescence can help, but solid-dosage coating is often better.
3. **Unsuitable for low-dose drugs**—tablets/capsules are more accurate below a few milligrams.
4. **Not appropriate for acid-labile drugs**—need enteric-coated tablets instead.

Capsules

- A **capsule** is a solid dosage form in which drug and/or inert ingredients are enclosed in a gelatin shell.
- Two shell types are used: **hard** (two-piece) and **soft** (one-piece, elastic).

Hard gelatin capsules (HGCs)

Key point	Details from your text
Structure	Two parts: *body* (longer) + *cap* (shorter) that locks over the body.
Advantages	– Mask unpleasant taste – Deliver powders without compression → faster dissolution/absorption – Sometimes easier to swallow than tablets
Limitations	- Sensitive to humidity & microbial growth - Hard for some patients to swallow - more expensive
Raw materials	Gelatin solution (demineralized water ± glycerol) + colorants, preservatives, process aids.
Gelatin facts	– Non-toxic, soluble at body T°, film-forming. – Obtained by collagen hydrolysis: *Type A* (acid) from skins, *Type B* (alkaline) from bones. – Critical specs: **bloom strength** (rigidity) & **viscosity**. High-bloom grades used for HGCs.
Plasticizer	Hard shells are essentially non-plasticised (rigid).
Colorants	Soluble dyes or pigments (TiO_2 for white opacity; iron oxides for black/red/yellow). Recent trend toward pigments.
Preservatives	Added mainly during processing; final moisture is too low to support growth.
Sizes	Eight standard sizes 000 (largest) → 5 (smallest); sizes 0-4 most common. Self-locking designs prevent separation.
Fill-weight rule	*Fill weight* = (tapped bulk density) × (capsule volume). Choose size so calculated volume ≈ published capsule volume; add diluent if needed.
Filling materials	Powders, granules, pellets, tablets, or thermo-softening semisolids that do **not** react with or soften gelatin.

Soft gelatin capsules (softgels)

Key point	Details from your text
Description	One-piece, hermetically sealed shell formed, filled, and sealed in a single step; surrounds liquid/semi-solid fill.
Advantages	- Portable liquid dosage - Lower gastric irritation vs. some tablets - Excellent dose uniformity (volumetric fill) - Protect oxidation/hydrolysis-sensitive drugs (low water, low O_2 diffusion) - Often superior bioavailability (drug already dissolved/dispersed).
Shell formulation	Gelatin + **plasticizer** (usually glycerol 0.3–1 part per part gelatin) + water (0.7–1.3 parts) ± preservatives, dyes, opacifier (TiO_2), flavor, drugs. Plasticizer level controls flexibility (higher for water-miscible fills & chewables).
Fill possibilities	Non-aqueous liquids, suspensions, pastes, self-emulsifying oils; insoluble drugs dispersed with suspending agents/surfactants.
Fill limitations	Avoid: high-water excipients, true emulsions, high surfactant content, extreme pH (< 2.5 or > 7.5), aldehydes.
Liquid vehicles	• *Water-immiscible*: volatile/non-volatile oils, hydrocarbons, ethers, esters. • *Water-miscible*: low-MW PEG 400–600, isopropyl alcohol, propylene glycol, glycerol (≤ 10 %).
Suspensions	Use beeswax/paraffin + oil for oily bases or PEG 4000/6000 for non-oily; Tween 80 as wetting agent.
Optional shell treatments	Enteric protection by external coating (e.g., 4 % cellulose acetate phthalate).

- **Shell rigidity**: Hard = rigid, Soft = elastic (high plasticizer).
- **Primary fills**: Hard = dry solids (powders/granules) - Soft = liquids, pastes, suspensions.

TABLETS

Why tablets matter

- Represent ≈ **70 %** of modern pharmaceutical dosage forms.
- Permit precise dosing, high stability, low production cost, uniform weight/appearance, and easy transport.

Core advantages of compressed tablets

1. Accurate, simple dosing.
2. Portable for patient and in bulk.
3. Product uniformity.
4. Typically more chemically stable than liquids; drug-release rate can be engineered.
5. Mass-production is fast and inexpensive.

Main oral tablet categories (all from the text)

Category	Key features & typical uses
Sugar-coated	Masks unpleasant taste; swallowed whole (e.g., metronidazole).
Film-coated	Thin polymer film for protection/taste-masking.
Enteric-coated	Withstands stomach acid; releases drug in intestine.
Effervescent	Contain carbonate + acid; release CO_2 in water for rapid dissolution & palatability.
Sublingual / Buccal	Small, soft, no disintegrant; rapid systemic absorption via oral mucosa (e.g., glyceryl trinitrate).
Lozenges	Large tablets dissolved slowly in mouth; local antiseptic or systemic vitamin delivery.
Chewable	Mannitol base; no disintegrant; ideal for children or quick antacid action.
Multilayer	Separate incompatible drugs in stacked layers.
Controlled-release (SR / MR)	Designed for slow, prolonged drug release.
Implant tablets	2–3 mm sterile pellets of pure drug inserted surgically for months-long release.

Sustained-release tablets (SRT)

Advantages

- ☞ Improved compliance (once-daily dosing).
- ☞ Night-time coverage without waking.
- ☞ Useful for forgetful or psychiatric patients; saves nursing time.
- ☞ Can lower side-effect incidence (e.g., less gastric bleeding with SR aspirin).
- ☞ Produces steadier plasma drug levels.

Disadvantages

- ☞ Higher unit cost.
- ☞ Ineffective for drugs absorbed only in specific GI regions.
- ☞ Overdose management is difficult; slower body clearance.
- ☞ Possible local ulceration (e.g., KCl), variable absorption, or dose "dumping" from poor design.

Tablet formulation

Property needed	How it is achieved
Powder fluidity	Vibrators, glidants (e.g., fumed silica < 0.01 %), spheronisation, **granulation**.
Compressibility	Choice of excipients or granulation; poorly compressible drugs (e.g., paracetamol) often require granulating.

Ideal granules for compression: withstand high pressure, contain uniform drug distribution, have narrow size range, near-spherical shape, minimal dust.

Tableting methods

1. **Dry techniques**
   - **Direct compression** (mix drug with a *direct-compression vehicle*).
   - *Slugging* or *roller compaction*.
2. **Wet granulation** (powder → wet mass → granulate → dry → compress).

Direct-compression vehicles (three groups):

1. Disintegrating but poor-flow (e.g., microcrystalline cellulose, MCC).
2. Free-flow, non-disintegrating (dibasic calcium phosphate).
3. Free-flow, dissolve to disintegrate (anhydrous lactose, sucrose, dextrose, mannitol).

MCC is widely used, chemically inert, yet hygroscopic; can sometimes stabilize moisture-sensitive drugs.

Tablets Excipients

Diluents (bulking agents)

- **Purpose** : Raise tablet weight to a practical ≥ 50 mg when drug dose is tiny.
- **Characters**: Chemically inert, inexpensive, non-hygroscopic, neutral, hydrophilic, good taste & flow/compression properties.
- **Examples:**
  - Lactose (most used, compressible)
  - Dicalcium phosphate (insoluble, for hygroscopic drugs)
  - Starches (also binders)
  - Microcrystalline cellulose (flows, disintegrates)
  - Dextrose (soft, moisture-absorbing)
  - Sucrose (sweet, very hygroscopic)
  - Mannitol (rapidly soluble, cooling taste for chewables)

Binders / Adhesives

- **Purpose** : Glue powder particles together during wet granulation to give strong granules/tablets.
- **Characters**: More effective in solution than dry form; choice depends on process.
- **Examples:**
  - Traditional: starch paste, gelatin, sugars (glucose, lactose), natural gums (acacia, alginate), cellulose gums (methyl- & carboxymethylcellulose).
  - Modern: polyvinyl-pyrrolidone (PVP), hydroxypropyl-methylcellulose (HPMC), dry binders like MCC, cross-linked PVP.

Glidants

- **Purpose** : Improve powder/granule flow by reducing inter-particle friction.
- **Characters**: Added in very small amounts (< 0.1 %).
- **Examples:** Fumed (colloidal) silica (most effective), starch (also disintegrant).

Lubricants & Antiadherents

- **Purpose** : Prevent sticking to punches/dies and ensure smooth ejection.
- **Characters**: Must be present when tooling carries logos/markings.
- **Examples:**
  - Magnesium stearate, calcium stearate, stearic acid (hydrophobic, may slow disintegration).
  - Talc (also glidant, not hydrophobic).
  - Polyethylene glycol (water-soluble).
  - Liquid paraffin (dispersion issues).
  - Sodium lauryl sulphate (adds wetting).

Disintegrants

- **Purpose** : Promote tablet breakup when exposed to aqueous fluids to enable drug release.
- **Characters**: Always included; choice influences disintegration speed.