Pharmaceutical Technology
& Modern Pharmaceutics

CHAPTERWISE NOTES

Powders and Granules

PHARMA

PHARMACEUTICAL TECHNOLOGY & MODERN PHARMACEUTICS

Powders and Granules

➤ POWDER AND GRANULES

- ✴ Powders are mixtures of **finely divided drugs and/or chemicals** intended for **internal or external use**.
- ✴ Granules are prepared **agglomerates of powdered materials**. They may be used directly for their medicinal effects or in pharmaceutical processes, such as tablet manufacturing.

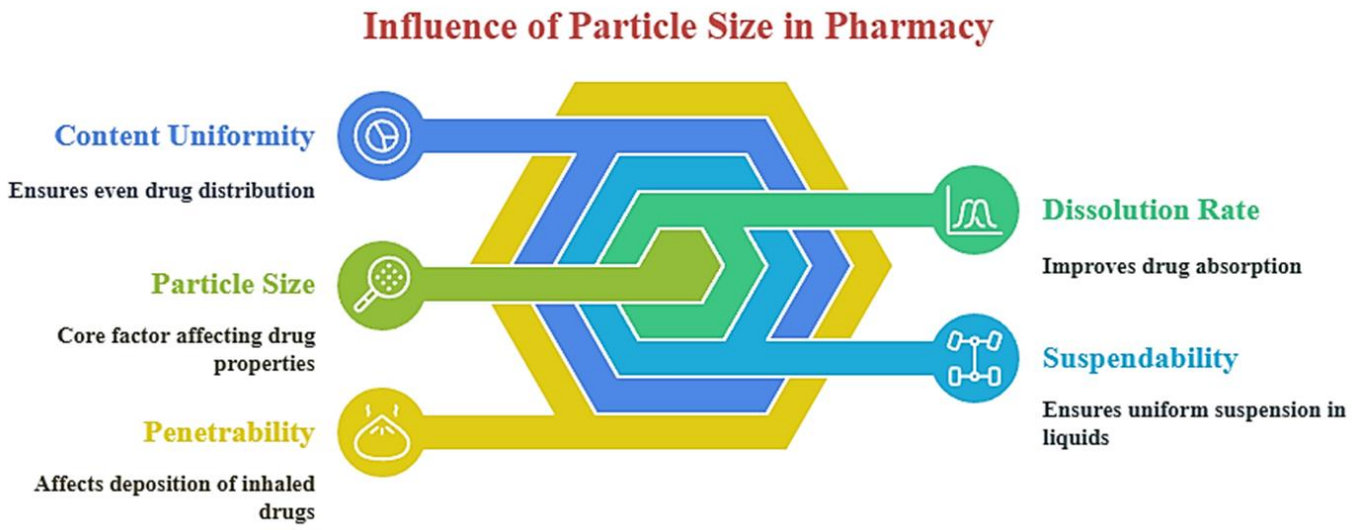
◆ Particle Size and Analysis

- ✴ Pharmaceutical powders and granules vary in size from extremely coarse (10 mm) to very fine (1 µm or less).

◆ Official Standard Pharmaceutical Powders (IP)

Grade of Powder	All particles must pass through Sieve No. *(100%)*	Sieve through which 40% of the particles pass *(40%)*
Coarse powder	10 / (1.70 mm)	44 / (355 µm)
Moderately coarse powder	22 / (710 µm)	60 / (250 µm)
Moderately fine powder	44 / (355 µm)	85 / (180 µm)
Fine powder	85 / (180 µm)	Not specified
Very fine powder	120 / (125 µm)	Not specified

- ✴ Granules generally fall within the 4- to 12-sieve range but sometimes extend to the 12- to 20-sieve range in tablet making.



COMMINUTION OF DRUGS

- Comminution refers to the **process of reducing the particle size** of a substance.
- It is an essential step in pharmaceutical formulation to enhance drug dissolution, absorption, and uniformity in dosage forms.

Methods of Comminution

Small-Scale Comminution

- **Trituration: Grinding a drug in a mortar and pestle** to reduce its particle size.
  - A **porcelain mortar** (rough surface) provides finer grinding.
  - A **glass mortar** (smooth surface) is preferred when simple mixing is required.
- **Levigation:** Used in the preparation of ointments and suspensions.
  - **A paste is formed** by mixing the powder with a levigating agent (e.g., mineral oil, glycerin) in which the powder is insoluble.
  - The paste is then triturated to reduce the particle size.
  - The levigated paste is incorporated into the ointment base for a smooth texture.

Large-Scale Comminution

- **Milling and Pulverization:** Various types of mills and pulverizers are used to reduce particle size efficiently.
  - **FitzMill Comminuting Machine:** Uses rapidly moving blades to grind particles and pass them through a screen of desired size.

Blending of Powders

Spatulation:

- Mixing small amounts of powders using a spatula on an ointment tile or paper.
- Suitable for substances prone to forming **eutectic mixtures** (e.g., phenol, camphor, menthol).

Trituration:

- Used for both mixing and comminution.
- Preferred when mixing potent substances with diluents using **geometric dilution** to ensure uniform distribution.
- Geometric dilution involves stepwise addition and mixing of diluent in equal proportions to the potent drug.

Sifting:

- Powders are passed through sifters to achieve a **light, fluffy texture**.
- Not suitable for potent drugs requiring precise blending.

Tumbling:

- Powders are mixed in a rotating chamber.
- Used in both **small-scale** and **large-scale** blending.
- Though effective, it is a time-consuming process.

Segregation of Powders

- **Sifting or percolation:** Fine particles settle at the bottom, pushing larger particles upward.
- **Air entrapment (fluidization):** Fine particles remain suspended in air, creating uneven distribution.
- **Dusting:** Fine particles stay airborne longer than heavier particles.

Geometric Dilution – Powder Mixing

- Used when **potent drug** is mixed with a **large quantity of diluent**.
- Ensures **uniform distribution** of drug in the mixture.

Example:

- **100 mg potent drug + 900 mg lactose**

Steps:

1. Mix **100 mg drug + 100 mg lactose → 200 mg mixture**
2. Add **200 mg lactose** to 200 mg mixture → **400 mg mixture**
3. Add **400 mg lactose** to 400 mg mixture → **800 mg mixture**
4. Add **remaining lactose (200 mg) → 1000 mg final mixture**

Key Point:

Always **double the mixture weight** by adding an equal weight of diluent at each step.

➢ CLASSIFICATION OF POWDERS

1. Bulk Powders for Internal Use

- ✷ Dispensed when **accuracy of dosage is not critical**.
- ✷ Contains multiple doses and is supplied in **wide-mouthed containers** for easy access.
- ✷ Suitable for **non-potent substances** like antacids and laxatives.

Examples:

- ✷ **Compound Rhubarb Powder B.P.C.** (Gregory's Powder): Contains rhubarb, magnesium carbonate, and ginger.
- ✷ **Compound Bismuth Powder:** Contains calcium carbonate, magnesium carbonate, sodium bicarbonate, and bismuth carbonate.

2. Bulk Powders for External Use

- ✷ These are non-potent substances used for external applications, supplied in containers designed for specific usage.

Types of Bulk Powders for External Use:	
	✷ **Dusting Powders** ○ **Medical** → For superficial skin conditions, pathogen-free ■ Example: Clotrimazole dusting powder ○ **Surgical** → For wounds/body cavities; sterile ■ Example: Sterile talc for pleurodesis
	✷ **Insufflations** ○ Medicated powders introduced into body cavities (nose, ear, throat, vagina) via insufflator ■ Example: Boric acid insufflation powder
	✷ **Snuffs** ○ Finely divided powders inhaled into nostrils for antiseptic/decongestant action

	✶ **Dentifrices (Tooth Powders)** ○ Used with toothbrush for teeth cleaning ○ Contains abrasives ($CaCO_3$, NaCl) and flavors ■ Example: Tooth powder with $CaSO_4$, NaCl, peppermint oil

3. Simple and Compound Powders for Internal Use

- ✶ **Simple Powders:** Contain **only one ingredient** (either crystalline or amorphous) divided into doses.
- ✶ **Compound Powders:** Contain **two or more ingredients**, mixed and divided into single-dose portions.

4. Powders Enclosed in Cachets

- ✶ Solid unit dosage forms made from rice paper (Enclose measured doses of powders within two rice paper halves).
- ✶ Used to enclose **nauseous or unpleasant-tasting powders**.
- ✶ Available in different sizes (0.2 to 1.5 g capacity).
- ✶ Softened in water before swallowing.

5. Compressed Powders (Tablets)

- ✶ **Powders are compressed** into solid dosage forms for easier administration and dosage control.
- ✶ Common in pharmaceuticals due to **longer shelf life and precise dosing**.

DISPENSING OF POWDERS INVOLVING SPECIAL PROBLEMS

1. Volatile Substances

- ✶ Some vegetable powders contain volatile oils that may be lost during grinding.
- ✶ Substances like **menthol, camphor, and essential oils** may evaporate when incorporated into powders.
- ✶ **Solution:** Use **double wrapping** (inner wax paper, outer thick paper) to minimize volatilization.

2. Hygroscopic and Deliquescent Powders

- ✶ **Hygroscopic powders** absorb moisture from the air.
- ✶ **Deliquescent powders** absorb so much moisture that they dissolve.
- ✶ **Examples:** Ammonium chloride, sodium bromide, zinc chloride.
- ✶ **Solution:**
  - ○ Supplied in **granular form** to reduce surface area exposure.
  - ○ **Double wrapping** is recommended.
  - ○ **Aluminum foil or plastic covers** are advisable in humid weather.

3. Efflorescent Powders

- ✶ Some crystalline substances release **water of crystallization** when exposed to humidity, leading to dampness.
- ✶ **Examples:** Caffeine, citric acid, ferrous sulfate.
- ✶ **Solution:**
  - ○ Use the **anhydrous form** of the substance.
  - ○ Mix with an **inert absorbent** before blending with other ingredients.

4. Eutectic Mixtures

- When two or more substances mix, they liquefy due to forming a compound with a lower melting point.
- **Examples:** Menthol, camphor, phenol, aspirin, chloral hydrate.
- **Solutions:**
  - Dispense as **separate sets of powders**.
  - Mix with an **inert absorbent** (e.g., magnesium carbonate, kaolin, starch).
  - If other ingredients are present, first **triturate eutectic substances**, then incorporate the rest.

AEROSOL POWDERS

- Used in dry-powder inhalers (DPI) for conditions like asthma.
- Micronized particles (**1–6 µm**) allow deep lung penetration.
- Often contain **pharmaceutical diluents** like crystalline alpha-lactose monohydrate to improve flow and stability.

GRANULES

- Granules are **agglomerates** of smaller powder particles. They are irregularly shaped but can also be prepared as **spherical** granules.
- They usually fall within the **4- to 12-mesh sieve** size range, but their size can vary depending on their intended application.

METHODS OF GRANULE PREPARATION

Granules can be prepared using **wet** and **dry** methods.

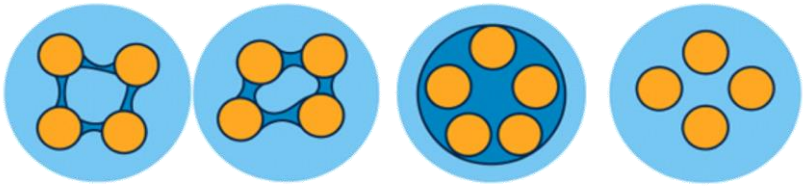
Wet Granulation

1. **Moistening Method:**
   - The powder or powder mixture is moistened.
   - The resulting paste is passed through a screen of desired mesh size.
   - The granules are placed on drying trays and dried by **air** or **heat**.
   - Granules are moved periodically to prevent sticking.
2. **Fluid Bed Processing:**
   - Particles are dispersed in a conical chamber.
   - A liquid excipient is sprayed onto them while they remain suspended.
   - The mixture dries, forming **granules or pellets** of defined particle size.

Granule Formation Stages

Pendular State → Funicular State → Capillary State → Droplet Formation

Stages in development of moist granules as proportion of liquid



(A) **Pendular State** Initial wetting forms liquid bridges with low mechanical strength.

(B) **Funicular State** More liquid Strengthens the bridges.

(C) **Capillary State** Maximum granule strength is achieved as voids are elimination.

(D) **Droplet Formation** Excess liquid weakness granules by reducing intragranular forces.

Dry Granulation

1. Roll Compaction Method:

- Powder is passed through a **roll compactor**.
- Two mechanically rotating metal rolls press the powder into **dense sheets**.
- The compacted material is granulated into uniform particle size using a **granulating machine**.
- This method is often integrated into a **compactor-granulation system**.

2. Slugging Method:

- The powder is compressed into **large tablets or slugs** using high pressure (8,000–12,000 lb).
- Slugs are then granulated into **desired particle sizes** for tablet production.
- Some fine particles (fines) that do not form granules are collected and reprocessed.

Properties and Advantages of Granules

- **Better Flowability:** Compared to powders, granules flow freely from hoppers into tablet presses, improving the efficiency of tablet production.
- **Improved Stability:** Due to their smaller surface area, granules are **less affected by humidity** and are less likely to cake or harden over time.
- **Enhanced Wettability:** Granules dissolve or suspend more easily in liquids than fine powders, which may float on the surface.

Granulated Pharmaceutical Products

Antibiotic Granules for Oral Suspension:

- Contain the active drug along with **colorants, flavorants, and excipients**.
- Mixed with purified water just before dispensing to create a stable liquid.
- **Examples:**
  - **Biaxin** (Clarithromycin)
  - **Omnicef** (Cefdinir)
  - **Augmentin ES-600** (Amoxicillin/Clavulanate Potassium)
  - **Ceftin** (Cefuroxime Axetil)

Lactinex Granules:

- Contain **Lactobacillus acidophilus** and **Lactobacillus bulgaricus**.

- Used for **diarrhea treatment**, including antibiotic-associated diarrhea.
- Can be mixed with water, sprinkled on food, or eaten directly.

✴ **Effervescent Granules:**

- Dissolve in water before use.
- Can also be compressed into effervescent tablets.
- Example: **Zantac EFFERdose Tablets** (Ranitidine).

EFFERVESCENT GRANULATED SALTS

✴ Effervescent salts are **granules or coarse powders** that contain a medicinal agent in a **dry mixture** of sodium bicarbonate, citric acid, and tartaric acid.

✴ When added to water, these components react to release **carbon dioxide**, creating effervescence.

Role of Citric and Tartaric Acids

✴ **Tartaric Acid Alone:** Results in granules that lose firmness and crumble.

✴ **Citric Acid Alone:** Creates a sticky mixture that is difficult to granulate.

✴ **Combination of Both:** Prevents these issues and ensures a stable granule formulation.

Methods of Preparation

1. Dry or Fusion Method

✴ **Binding Agent:** The water present in citric acid acts as the binding agent.

✴ **Procedure:**

1. **Citric acid crystals** are powdered and mixed with other powders of the same sieve size for uniformity.
2. **Mixing is done quickly** in a low-humidity environment to prevent premature reaction.
3. The mixture is **heated at 34°C to 40°C** in an oven.
4. The released water of crystallization dissolves some powder, triggering a slight reaction and softening the mass.
5. Once a spongy consistency is achieved, the mass is passed through sieves to obtain the desired granule size:
   - **No. 4 sieve** → Large granules
   - **No. 8 sieve** → Medium granules
   - **No. 10 sieve** → Small granules
6. The granules are **dried at ≤54°C** and immediately stored in tightly sealed containers.

2. Wet Method

✴ **Binding Agent:** Water added to alcohol acts as the moistening agent.

✴ **Procedure:**

1. All powders used can be **anhydrous**, unlike the fusion method.
2. Water is added gradually in portions to form a **pliable mass**.
3. Granules are then prepared and dried using the same method as in the fusion process.