

CHAPTERWISE NOTES

Tablets

PHARMACEUTICAL TECHNOLOGY & MODERN PHARMACEUTICS

Tablets

Pharmaceutical tablets are **solid, flat, or biconvex dishes, unit dosage form**, prepared by compressing a drugs or a mixture of drugs, with or without diluents.

➤ **Types of Tablets:**

I. Oral Tablets for Ingestion: (*Swallowed whole with water, designed for systemic effects*)

Type of Tablet	Description & Examples	
Compressed Tablets (CT)		Standard solid dosage forms prepared by compression of drugs and excipients. Example: Paracetamol tablets,
Multiple Compressed Tablets (MCT)		Tablets subjected to more than one compression, leading to multiple-layer or core-shell structures . Used for separating incompatible drugs, controlling release , or aesthetic purposes. Example: Norgesic Tablets.
Sugar-Coated Tablets (SCT)		Coated with a water-soluble sugar layer that protects the drug, masks unpleasant taste, and enhances appearance . Example: Vitamin B-complex tablets.
Film-Coated Tablets (FCT)		Coated with a thin polymer film. Example: Ibuprofen film-coated tablets.
Gelatin-Coated Tablets (Gelcaps)		Capsule-shaped compressed tablets with a gelatin coating. Provides better tamper resistance. Example: Extra Strength Tylenol PM Gelcaps (McNeil-CPC)
Enteric-Coated Tablets (ECT)		Delayed-release , designed to pass through the stomach and dissolve in the intestines. Example: Ecotrin (Aspirin) enteric-coated tablets
Immediate- Release Tablets (IR)		Designed to disintegrate and release the drug immediately with no special rate-controlling mechanisms. Example: Paracetamol IR tablets
Extended- Release Tablets (ER/SR/CR)		Designed to release the drug slowly over time to maintain drug levels in the body. Example: Metformin SR, Propranolol CR

II. Tablets Used in the Oral Cavity: (*Dissolve in mouth for local or systemic absorption*)

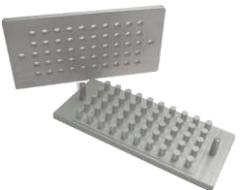
Type of Tablet		Description & Examples
Buccal Tablets		Flat, oval tablets that dissolve slowly in the buccal pouch, allowing absorption through the oral mucosa. Example: Testosterone buccal tablets
Sublingual Tablets		Designed to dissolve rapidly under the tongue for quick absorption and to bypass first-pass metabolism. Example: Nitroglycerin sublingual tablets
Troches and Lozenges		Disc-shaped, hard-candy-like dosage forms intended to dissolve slowly in the mouth. Example: Mycelex Troches (Bayer) for fungal infections
Chewable Tablets		Designed for chewing before swallowing; Ideal for children and those who have difficulty swallowing pills. Example: Pepcid Chewable, Rolaids Chewable
Dental Cones		Dental cones are small, medicated devices inserted into empty tooth sockets after extraction to reduce bleeding and prevent infection. They are designed to dissolve within 20-40 minutes, utilizing a vehicle of sodium bicarbonate, sodium chloride, and amino acids.

III. Tablets Administered by Other Routes: (*Not swallowed or used in the oral cavity, but delivered through other routes*)

Type of Tablet		Description & Examples
Implantable Tablets		Designed for implantation under the skin, providing slow and prolonged drug release. Used in hormone therapy and chronic disease management. Example: Leuprorelin implant tablets
Vaginal Tablets		Inserted into the vagina for localized drug delivery, commonly used for infections or hormone therapy. Example: Clotrimazole vaginal tablets

IV. Tablets Used to Prepare Solutions: (*Dissolved in liquid before administration*)

Type of Tablet		Description & Examples
Effervescent Tablets		Contain effervescent salts that release gas when in contact with water, aiding tablet breakup and enhancing dissolution. Example: Alka-Seltzer, Zantac EFFERdose
Molded Tablets		Very soft, rapidly soluble tablets designed for quick dissolution. Example: Extemporaneous compounding formulations

Tablet Triturates		Small, cylindrical molded or compressed tablets containing potent drugs. Example: Nitroglycerin tablet triturates
Hypodermic Tablets (Obsolete)		Previously used for preparing injectable solutions extemporaneously. Eliminated due to sterility concerns.
Dispensing Tablets (Obsolete)		Previously used by pharmacists to obtain pre-measured amounts of potent drugs for compounding multiple dosage units. Discontinued due to risk of direct dispensing to patients.

TABLET DESIGN AND FORMULATION: FORMULATION COMPONENTS

Tablets = Solid dosage form = Drug (Active) + Excipients (Inactive)

1. Diluents (Fillers in Tablets):

- Diluents, also known as **fillers**, are **inactive** ingredients added to tablets to increase their bulk.
- To facilitate tablet handling during manufacture and to achieve targeted content uniformity, the tablet size should be kept above 2-3 mm and weight of tablet above 50 mg.

Commonly Used Diluents and Their Properties

A. Lactose: Lactose is one of the most widely used tablet diluents.

- **Lactose** = Common filler/diluent in tablets
- **⚠ Reacts with:** Amine drugs + alkaline lubricants (e.g. Mg stearate) → Forms **furaldehyde** → Causes **brown discoloration** over time → **Maillard Reaction**
- **Lactose Monohydrate:** Used in wet granulation.
- **Anhydrous Lactose:** Preferred in direct compression and has the advantage of **not** undergoing the **Maillard reaction** with amine drugs.
- **Spray-Dried Lactose:** Excellent for direct compression due to its superior flowability and compressibility.
- **Grades Available:**
 - Coarse (60 to 80 mesh)
 - Regular (80 to 100 mesh)

B. Microcrystalline Cellulose (MCC): tradename **Avicel**.

- Provides excellent direct compression characteristics and acts as a **disintegrant**.
- Available in two grades:
 - **pH 101:** Fine powder form
 - **pH 102:** Granular form with improved flow properties

Excipients in Tablets

Characteristic	Excipient
 Manufacturing	Binders, lubricants, glidants
 Drug Release	Disintegrants, polymers
 Stability	Antioxidants
 Patient Acceptance	Flavors, sweeteners
 Product Identification	Colorants

C. Starch and Modified Starches

- **Regular USP starch** has poor flow properties and high moisture content (11-14%).
- **Modified Starches:**
 - **Pregelatinized Starch (Starch 1500, Starx 1500)**: Provides better compressibility and flow properties.
 - **Sta-Rx 1500**: Free-flowing, self-lubricating starch with 10% moisture content.
 - **Emdex and Celutab**: Hydrolyzed starches (90-92% dextrose, 3-5% maltose), used for chewable tablets due to their sweetness.

D. Sugars and Sugar Alcohols

- **Sucrose-Based Diluents:**
 - **Sugartab**: 90-93% sucrose, 7-10% invert sugar.
 - **DiPac**: 97% sucrose, 3% modified dextrans.
 - **Nu-Tab**: 95% sucrose, 4% invert sugar, with a small amount of corn starch and magnesium stearate.
 - **Limitation**: Hygroscopic and may not be suitable for diabetics.
- **Mannitol**:
 - It is expensive but because of its negative heat of solution, its slow solubility, and its pleasant feeling in the mouth, it is widely used in chewable tablets.
 - Poor flow properties and requires high lubricant levels.
- **Sorbitol**:
 - Used to reduce cost in combination with Mannitol.
 - Hygroscopic at humidities above 65%.
- **Dextrose (Cerelose)**:
 - Available in two forms: hydrate and anhydrous.
 - Anhydrous form is preferred when low moisture content is required.

E. Calcium Salts and Inorganic Diluents

- **Calcium Carbonate (Cal-Carb, Millicarb, Sturcal)**
- **Dibasic Calcium Phosphate (Cyfos, Calipharm, Emcompress)**
 - Non-hygroscopic, chemically stable, and used in direct compression.
- **Tricalcium Phosphate (Tri-Cal, Tri-Tab)**
 - Provides better flow properties.
- **Calcium Sulfate (Cal-Tab, Compactrol)**
 - Contains bound water that does not release below 80°C, making it stable for moisture-sensitive drugs.

F. Other Diluents

- **Xylitol (Xylifin, Xylitab)**: Used in chewable tablets and sugar-free formulations.
- **Maltodextrin (Glycidex, Maltrin, Lycatab)**: Improves tablet compactness.
- **Dextrates (Emdex)**: Used in chewable tablets due to sweetness.
- **Lactitol (Finlac)**: Alternative for lactose-sensitive patients.

TRADE NAME	DESCRIPTION
Fast Flo lactose	It is spray processed lactose which is a mixture of crystalline α-lactose monohydrate and amorphous lactose.
Microcellac	75% lactose and 25% MCC (MicroCrystalline Cellulose)
Ludipress	93% α-lactose monohydrate, 3.5% polyvinylpyrrolidone, and 3.5% crospovidone.
Nu-Tab	Sucrose 95-97%, invert sugar 3-4% and magnesium stearate 0.5%
Di-Pac	Sucrose 97% and modified dextrans 3
Sugartab	Sucrose 90-93% and invert sugar 7-10%.
Emdex	Dextrose 93-99% and maltose 1-7%
Cal-Tab	Calcium sulfate 93% and vegetable gum 7%
Cal-Carb	Calcium carbonate 95% and maltodextrins 5%
Calcium 90	Calcium carbonate (minimum) 90% and Starch, NF (maximum) 9%

- **Special Considerations in Selecting a Diluent:**

- **Bioavailability**
 - Some diluents ↓ drug absorption
 - e.g. Tetracycline + calcium salts (e.g. Ca phosphate) → **Insoluble complex** → ↓ bioavailability
- **Chemical Incompatibility**
 - Lactose + amine drugs + Mg stearate → **Maillard reaction** → Discoloration
 - Diluents forming **eutectic mixtures** → Soft, unstable tablets
- **Moisture Sensitivity**
 - **Anhydrous diluents**: May absorb moisture → Stability issues
 - **Hydrated diluents** (e.g. dibasic Ca phosphate hydrate): Stable if water is tightly bound
- **Tablet Size and Shape:**
 - Round tablets: 120-700 mg (standard range)
 - Oval tablets: Easier to swallow, up to 800 mg

2. Binders and Adhesives:

- **Function:** Help particles **stick together**, Form **granules** in wet granulation, provide **mechanical strength** to final tablets, ensure **uniformity** and **cohesion** in blend.

A. Natural Binders

1. Acacia and Tragacanth:

- Natural gums used in solution (10–25%).
- They are more effective in wet granulation than in direct compression.
- **Disadvantages:**
 - Prone to bacterial contamination.
 - Wet granulations prepared with these gums should be dried quickly above 37°C to minimize microbial growth.

2. Gelatin

- A **natural protein-based** binder, often used in combination with acacia.

3. Starch Paste

- Prepared by dispersing starch in water followed by heating, heating causes **partial hydrolysis** to dextrin and glucose.

4. Liquid Glucose and Sucrose Solutions

- **Liquid glucose** (50% solution in water) is a common wet granulating agent.
- **Sucrose solutions** are widely used in concentrations between **50% and 74%**.
- **Challenges:** Low-concentration sugar solutions encourage bacterial growth, highly concentrated solutions may cause excessively hard tablets.

B. Modified Natural Polymers

1. Alginates and Cellulose Derivatives

- Types: **Methylcellulose, Hydroxypropyl Methylcellulose (HPMC), Hydroxypropyl Cellulose (HPC)**.
- Used as **dry binders** for direct compression and as **adhesives** when applied in solution form.
- **Hydroxypropyl cellulose (HPC)** is soluble in both water and alcohol.

2. Ethylcellulose

- Used **only in alcoholic solutions**.
- Tends to **retard drug disintegration and dissolution**, making it suitable for sustained-release formulations.

C. Synthetic Binders:

Polyvinylpyrrolidone (PVP)

- A **synthetic polymer** used as a binder in both aqueous and alcoholic solutions, also functions as a **dry binder**.

Sugar	Natural Binder	Synthetic/Semisynthetic Polymer
Sucrose	Acacia	Methyl Cellulose
Liquid glucose	Tragacanth Gelatin Starch Paste Pregelatinized Starch Alginic Acid Cellulose	Ethyl Cellulose Hydroxy Propyl Methyl Cellulose (HPMC) Hydroxy Propyl Cellulose Sodium Carboxy Methyl Cellulose Polyvinyl Pyrrolidone (PVP) Polyethylene Glycol (PEG) Polyvinyl Alcohols Polymethacrylates

3. Disintegrants:

- Disintegrants are excipients added to tablets to induce **breakup (disintegration)** when in contact with an aqueous medium.

Mechanisms of Tablet Disintegration



Methods of Adding Disintegrants:

1. **Intragranular Addition (Before Granulation):**
 - Produces fine particles upon disintegration.
2. **Extrgranular Addition (Before Compression):**
 - Helps in tablet breakup into granules.
3. **Both Intragranular and Extrgranular:**
 - Used for optimized disintegration.

Types of Disintegrants:

1. Starch-Based Disintegrants:

- **Starch:** Absorbs water and swells, breaking the tablet. Suggested concentration: **5-15%**.
- **Pregelatinized Starch:** Hydrolyzed starch, **directly compressible**. Mechanism: **Swelling** (Optimum: **5-10%**).
- **Modified Starch (Sodium Starch Glycolate - Explotab, Primojel):** Chemically modified to enhance swelling. High efficiency at **low concentrations (4-6%)**.

2. Cellulose-Based Disintegrants:

- **Sodium Carboxymethylcellulose (NaCMC) & Crosslinked Cellulose (Crosscarmellose Sodium):** Highly hydrophilic, rapidly swells 4-8 times its original volume. Crosslinking makes it **nearly insoluble** but enhances disintegration.
- **Microcrystalline Cellulose (MCC):** Acts by **wicking** (absorbing water and breaking the tablet).

3. Ion-Exchange Resins: Examples: Amberlite resins, highest water uptake capacity among disintegrants.

4. Alginates: Hydrophilic colloidal substances with high sorption capacity. Do not **retard flow** and work well with multivitamin formulations.

5. Miscellaneous Disintegrants

- Surfactants
- Gas-producing agents (Effervescent disintegrants)
- Hydrous aluminum silicate

Superdisintegrants: Effective at low concentrations and work intragranularly.

- **Mechanism:**
 - Swelling and pressure generation → bursts the tablet.
 - Rapid water absorption → increases tablet volume, leading to breakup.
- **Drawback:** Hygroscopic (not suitable for moisture-sensitive drugs).

4. Tablet Lubricants, Antiadherents, and Glidants

Objectives:

- Prevent adhesion of tablet material to die and punch surfaces.
- Reduce inter-particulate friction and improve flow rate of granules.
- Facilitate easy ejection of tablets from the die cavity.

Lubricants: Lubricants reduce friction by forming an intermediate layer between tablet constituents and the die wall during compression and ejection.

Mechanisms of Lubrication: Boundary Lubrication: Solid lubricants adhere to metal surfaces and reduce friction. Example: **Magnesium stearate** (widely used boundary lubricant).

Types of Lubricants

Water-Insoluble Lubricants

- More effective at lower concentrations than water-soluble lubricants.
 - Function by coating granules; their effectiveness depends on surface area, Particle size reduction, Mixing procedure and time

Insoluble Lubricants	Concentration
Stearates (Magnesium Stearate, Calcium Stearate, Sodium stearate)	0.25 - 1
Talc	1 - 2
Sterotex	0.25 - 1
Waxes	1 - 5
Stearowet	1 - 5
Glyceryl behapate	1 - 5
Liquid paraffin	Up to 5

Water-Soluble Lubricants

- Used when a tablet requires complete solubility or fast disintegration/dissolution.
- Higher dissolution rate than water-insoluble lubricants.

Water Soluble Lubricants	Concentration Range (%W/W)
Boric acid	1
Sodium chloride	5
Sodium benzoate	5
Sodium oleate	5
Sodium acetate	5
Sodium Lauryl sulfate (SLS)	1 – 5
Magnesium lauryl sulfate (MLS)	1 – 2
PEG 4000, 600	1 – 4

Method of Lubricant Addition:

- Bolting the Lubricant:**
 - Finely divide lubricant by passing it through a **60–100 mesh nylon cloth**.
- Mixing:**
 - Granulation is **tumbled/mixed gently** to distribute lubricant.
 - Avoid over-mixing**, which can:
 - Coat all particles and reduce dissolution.
 - Break granules and create excess fines.

Antiadherents: Prevent sticking of tablet material to punches and die walls. Examples: **Talc, Magnesium stearate, Corn starch.**

Glidants:

- Improve **flow properties** of tablet granules.
- Help in **particle rearrangement** within the die during compression.
- Always added **dry**, just before compression (during lubrication step).
- Mechanism of Action:**
 - Glidant particles interpose between granules, reducing **inter-particulate friction** and improving flow.

Glidant	Proprietary Name	Concentration Used (%)
Calcium silicate		0.5–2
Cellulose, powdered	Elcema, Solka, Floc	1–2
Magnesium carbonate		1–3
Magnesium oxide		1–3
Magnesium silicate		0.5–2
Silicon dioxide, colloidal	Aerosil, Cab-o-Sil	0.05–0.5
Starch		2–10
Talc		1–10

5. Colouring agents:

- Colouring agents are added to tablets for **aesthetic appeal, product identification, patient compliance, brand differentiation, uniformity and recognition.**
- **Types of Colouring Agents**

1. Dyes

- Dyes are **water-soluble colourants**.
- They are dissolved in the binding solution before the granulation process.
- However, during drying, dyes may migrate to the tablet surface, causing **mottling** (uneven colour distribution).
- **Methods to Prevent Colour Migration:**
 - Slow drying at low temperatures.
 - Continuous stirring during drying.
 - Adsorbing the dye onto starch or calcium sulfate before incorporation into the formulation.

Examples of Pharmaceutical Dyes (FD&C and D&C Dyes):

- FD&C Yellow No. 6 (Sunset Yellow)
- FD&C Blue No. 1 (Brilliant Blue)
- FD&C Red No. 40 (Allura Red)
- D&C Green No. 5
- D&C Red No. 7

2. Lakes

- Lakes are **water-insoluble** pigments formed by adsorbing dyes onto an insoluble base, such as **aluminum hydroxide or calcium sulfate**.
- These colourants provide uniform colour distribution and **prevent mottling**.
- They are **more stable** than dyes and are commonly used in dry-blended formulations.

Examples of Common Lakes: Yellow Lake, Red Lake, Blue Lake

6. Flavors and sweeteners:

- They are primarily used in **chewable tablets, effervescent tablets, and orally disintegrating tablets**.
- **Types of Flavors:** Flavors are categorized based on their origin:
 1. **Natural Flavors:** Extracted from fruits, herbs, and spices (e.g., orange, lemon, mint, vanilla, chocolate).
 2. **Synthetic Flavors:** Artificially created to mimic natural flavors (e.g., bubblegum, tutti-frutti, grape, cherry).

Taste	Suitable Flavors
Bitter	Wild Cherry, Walnut, Chocolate, Mint, Anise
Salty	Peach, Butterscotch, Wintergreen Mint, Apricot
Sour	Liquorice, Root Beer, Citrus Flavors, Raspberry
Excessively Sweet	Vanilla, Fruit, Berry

Note: The maximum amount of flavor oil that can be added without affecting tablet properties is **0.5% to 0.75% w/v**.

Sweeteners: Sweeteners are essential for improving the taste of chewable and orally dissolving tablets. They provide a **pleasant sweetness** without affecting the drug's efficacy.

- Sweeteners can be classified into **natural** and **artificial** sweeteners:

A. Natural Sweeteners

Sweetener	Sweetness (Compared to Sucrose)	Key Features
Sucrose	1.0 (Reference)	Standard sweetness but cariogenic (causes tooth decay)
Mannitol	0.7 (70%)	Cooling effect, used in chewable tablets, suitable for diabetics
Xylitol	1.0 (100%)	Natural, prevents tooth decay , cooling effect
Stevia	200-300x	Zero-calorie , enhances palatability

B. Artificial Sweeteners

Sweetener	Sweetness (Compared to Sucrose)	Key Features
Aspartame	200x	Low-calorie , unstable in moisture and heat
Acesulfame-K	200x	Heat-stable, no aftertaste, often combined with other sweeteners
Sucratose	600x	Zero-calorie, highly stable, used in pharmaceuticals
Saccharin	500x	Bitter aftertaste, sometimes combined with other sweeteners
Cyclamate	30x	Banned in many countries due to safety concerns

TABLET MANUFACTURING

1. Direct Compression Method

- Direct compression is a tablet manufacturing process that involves compressing **crystalline substances** (such as sodium chloride, sodium bromide, and potassium chloride) directly into tablets.
- **Directly compressible diluents** are used.
- *Steps involved in the Direct compression method of Tablet.*

Weighing of Drug & Excipients → Screening of Sieving (#20–25) → Mixing → Compression → Tablets

2. Dry or Compression Granulation Method: used in tablet formulation when:

- The drug dose is too high for direct compression.
- The drug is sensitive to heat or moisture, making wet granulation unsuitable.
- The final granules need better flow properties for uniform die filling.
- *Steps involved in the Compression Granulation Method of Tablet.*

Compaction → Milling and Screening → Final Compression → Tablets

1. Compaction:

- The powdered material is compressed using a **tablet press or roller compactor**.
- This creates large compacted masses called **slugs** (if using a tablet press) or **ribbons** (if using a roller compactor).

2. Milling and Screening:

- The slugs or ribbons are broken down into granules using a milling machine or sieve.
- If necessary, the granules are **recompacted** and **remilled** to improve their properties.

3. Final Compression:

- The granules, now having improved flow and compressibility, are compressed into tablets.

Slugging Process

- Involves creating **large tablets (about 2 inches in diameter)** using a heavy-duty tablet press.
- These slugs are then crushed and sieved to produce granules.

Roller Compaction Process

- Uses **two rotating rollers** that compress powder (apply pressure 1 to 6 tons) into a thin ribbon.
- A **screw feeder** pushes powder between the rollers.
- The compacted ribbon is broken down into granules by milling.
- This method is highly efficient, producing up to **500 kg/hour** of granules.

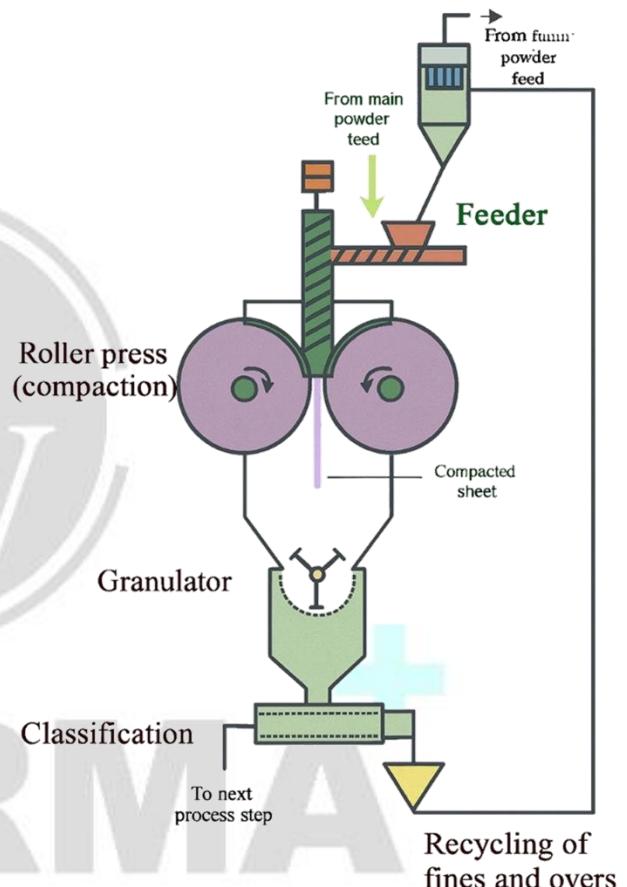
Advantages of Compression Granulation

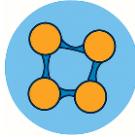
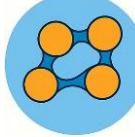
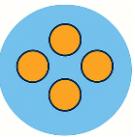
- No need for **heat or moisture**, suitable for sensitive drugs.
- Requires **less equipment and space** than wet granulation.
- Produces **stronger granules** that flow well and compress into tablets with good uniformity.
- This method is commonly used for drugs like **aspirin and vitamins**, where wet granulation is not feasible.

3. Wet Granulation Method

- Wet granulation forms granules by binding powder particles together using a liquid adhesive, rather than by compaction.
- A binder solution or slurry is added to the powder mixture.
- The binder can be added **dry** and activated by liquid, or **dissolved** in the liquid before addition.
- **Granule Formation Stages**

Pendular State → Funicular State → Capillary State → Droplet Formation



			
(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 eliminated.	(D) Droplet formation Excess liquid weakens granules by reducing intragranular forces

Granulation Properties:

Property	Key Points
Particle Size/Shape	Affects: ↓ Tablet wt variation, ↓ Disintegration, ↓ Friability, ↑ Flowability, ↑ Drying rate
Surface Area	↑ Surface area → ↑ Dissolution; Measured by: (a) Gas adsorption → Monolayer gas, (b) Air permeability → Air flow
Density	Particle density via pycnometer; Accuracy ↑ if intrusion fluid enters pores
Compressibility	↓ Compressible material → ↑ Flowability
Strength/Friability	Van der Waals forces needed for granule cohesion
Flow Forces	Types: Frictional, Cohesive (VDW), Electrostatic, Mechanical interlocking, Surface tension
Fine Powder (<150 µm)	Dominated by: Frictional + Van der Waals forces
Coarse Powder (>150 µm)	Dominated by: Frictional forces > Van der Waals

Flow Measurement Methods:

Property	Measurement Methods	Value Range	Flowability
Angle of Repose (°)	Funnel method Tilting box Cylinder method	< 25	Excellent
		25 – 30	Good
		30 – 40	Passable/Satisfactory
		40 – 50	Poor
		> 50	Very poor/Damp

Carr's Index (%)	$CI = \frac{\text{Tap Density} - \text{Bulk Density}}{\text{Tap Density}} \times 100$	5 – 15	Excellent
		12 – 16	Good
		18 – 21	Fair
		23 – 31	Poor
		32 – 37	Very Poor
		> 40	Very, Very Poor
Hausner Ratio	$\text{Hausner Ratio} = \frac{\text{Tap Density}}{\text{Bulk Density}}$	1.05 – 1.18	Excellent
		1.12 – 1.20	Good
		1.24 – 1.26	Fair
		1.30 – 1.34	Poor
		1.35 – 1.60	Very Poor
		> 1.61	Very, Very Poor

Process of Wet Granulation

Steps involved in the Wet Granulation Method of Tablet.

Weighing and Blending → Preparing the Damp Mass → Screening the Damp Mass into Granules → Drying the Granulation → Sizing the Granulation by Dry Screening → Adding Lubrication and Blending → Forming Tablets by Compression → Tablets

1. Weighing and Blending

- Active ingredients, diluents (fillers), and disintegrants are mixed uniformly using a mechanical blender.
- **Common fillers:**
 - Lactose (soluble, compatible)
 - Microcrystalline cellulose (good compaction and uniformity)
 - Starch, powdered sucrose, calcium phosphate
- **Common disintegrants:**
 - Croscarmellose (2%), Sodium starch glycolate (5%) – absorb water rapidly
 - Starches (5-10%, up to 20%) – promote tablet breakup
- **Double disintegration:** A portion of the disintegrant is added before granulation, and the rest is added later to enhance breakdown in the gastrointestinal tract.

2. Preparing the Damp Mass

- A **liquid binder** is added to the powder mix to promote adhesion between particles.
- The mixture forms either **granules** or a **dough-like damp mass**.



- **Common binders:**
 - Povidone solution
 - Cornstarch (10-20%)
 - Glucose solution (25-50%)
 - Methylcellulose (3%), Carboxymethylcellulose
 - Microcrystalline cellulose
- If water-sensitive drugs are used, **nonaqueous binders** may be used instead.
- **Key considerations:**
 - **Overwetting** → Hard granules, difficult compression
 - **Underwetting** → Soft granules, tablet crumbling
- **Colorants or flavorants** can be added to the binder for aesthetic purposes.

3. Screening the Damp Mass into Granules

- The **wet mass is passed through a mesh screen (typically 6 or 8 mesh)** to form granules manually or using granulation equipment.
- The granules are spread evenly on trays for **drying** to a consistent moisture content.

4. Drying the Granulation

- Granules are dried in thermostatically controlled ovens, where time, temperature, and humidity are closely monitored to achieve the desired moisture content.

5. Sizing the Granulation by Dry Screening

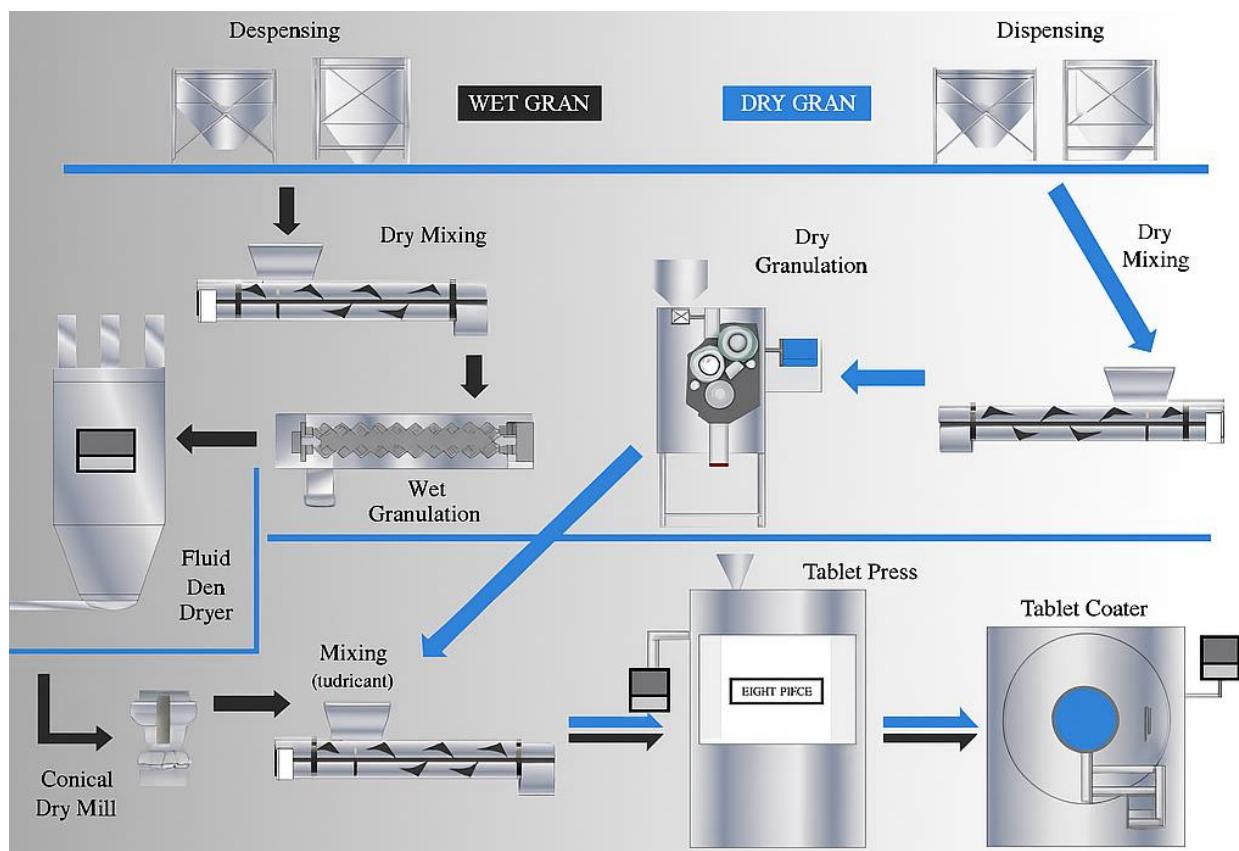
- After drying, granules are passed through a finer **mesh screen (12 to 20 mesh)**.

6. Adding Lubrication and Blending

- A dry lubricant is added to prevent the granules from sticking to tablet punches and dies during compression.
- **Common Lubricants:** Magnesium stearate (most common), calcium stearate, stearic acid, talc, sodium stearyl fumarate.
- The lubricant is added in small quantities (0.1% to 5% by weight of granulation).

7. Forming Tablets by Compression:

The granules are compacted into tablets.



Equipment	Key Features / Functions
Littleford Lodige	High-shear blender; mixes & blends wet mass
Littleford MGT	Forms agglomerated granules → ready for fluid bed drying
Diosna Mixer	High-speed vertical bowl; mixer + vacuum dryer; handles various batch sizes
Gral Mixer	High-shear granulator; conical/cylindrical bowl; impeller + chopper + motor + discharge pot
Sigma Blade Mixer	High shear via intermeshing sigma blades; mass mixing & kneading
Nauta Mixer	Conical screw mixer; used for free-flowing, segregative powders/pastes

TABLET COMPRESSION OPERATION

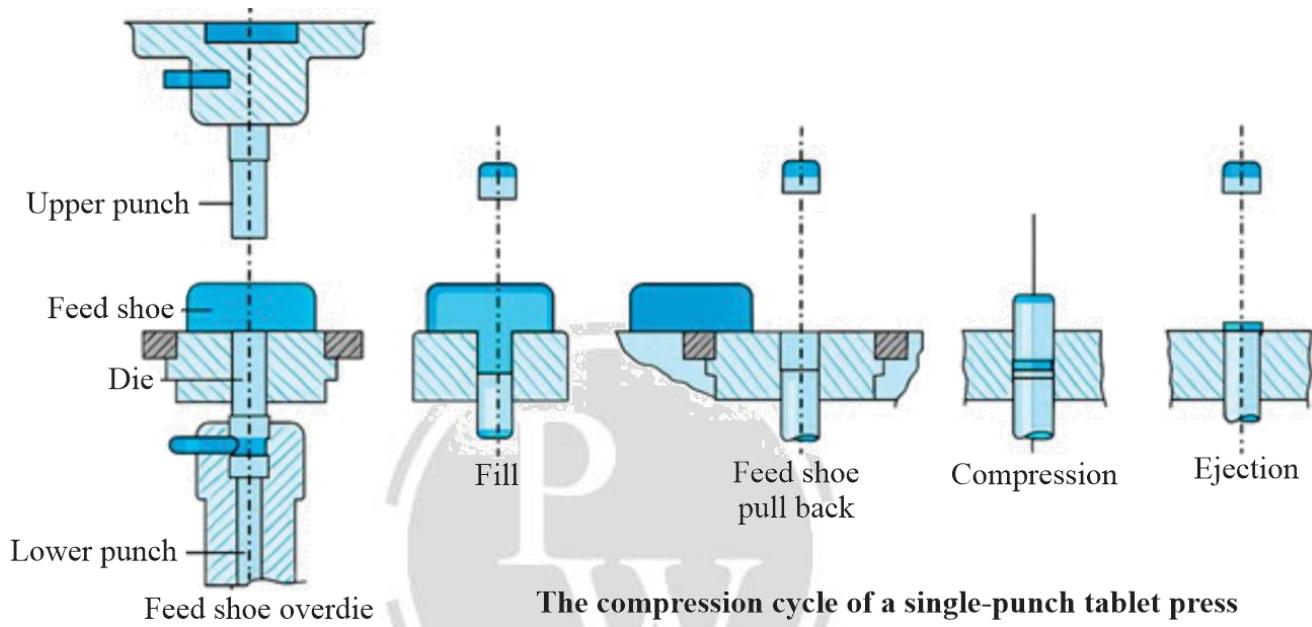
- The machine applies mechanical force to compress the powder into tablets of uniform size, shape, and weight.

Tablet Compression Machines: Basic components:

Component	Function
Hopper	Holds & feeds powder mix; ensures continuous supply
Dies	Defines tablet size, shape, thickness ; acts as compression cavity
Punches	Upper punch ↓ compresses; lower punch ↑ supports & ejects tablet
Cam Tracks	Controls punch movement → filling, compression, ejection
Feeding Mechanism	Transfers powder from hopper → die cavity; ensures uniform fill & consistent weight

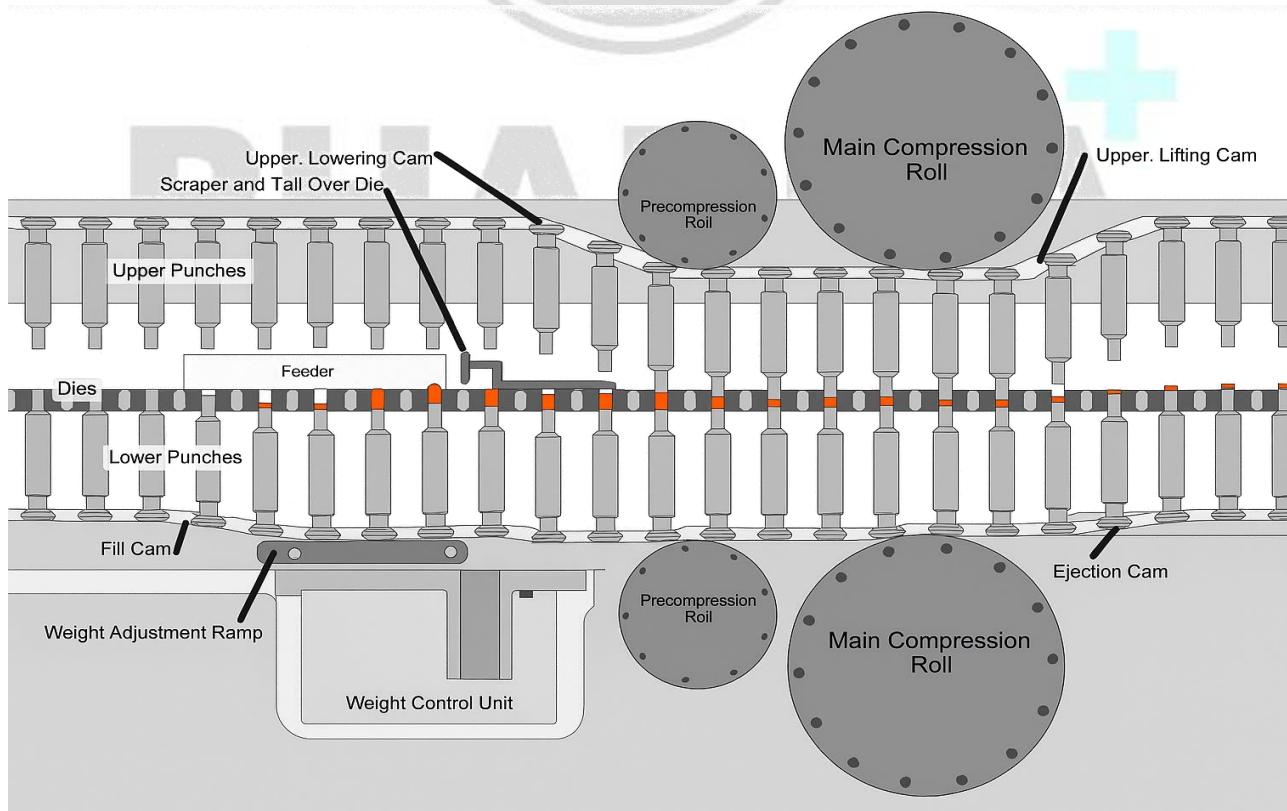
Tablet Compression Process

1. **Filling:** Lower punch drops to create cavity in die. Hopper releases granulation, and die cavity is filled.
2. **Metering:** Excess powder is scraped off to ensure uniform fill weight.
3. **Compression:** The upper punch descends, compressing the powder under high pressure to form a tablet.
4. **Ejection:** Upper punch retracts, and lower punch rises to push the tablet out

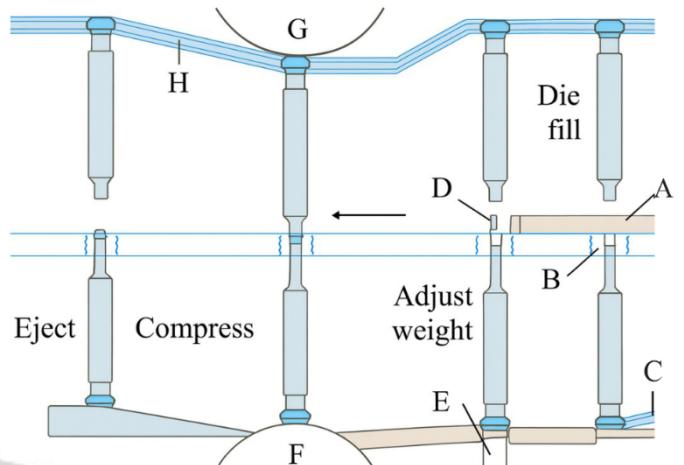


The compression cycle of a single-punch tablet press

Multi-Station Rotary Tablet Press:



- **Upper and Lower Turrets:** Hold the **upper and lower punches** in place, moving in synchronization during tablet compression.
- **Die Table:** Holds the dies that define the **size and shape** of the tablets. Rotates along with the turrets for continuous production.
- **Feed-Frame (A):** Ensures that the dies fill properly.
- **Die (B):** Cavity where the powder is compacted into tablets. Receives powder from the feed-frame.
- **Pull-Down Cam (C):** Guides **lower punches** to the bottom to allow **overfilling** of die.
- **Weight-Control Cam (E):** Adjusts the **amount of granulation** in die by controlling the fill height.
- **Wipe-Off Blade (D):** Scrapes excess powder off the die table.
- **Compression Rolls:**
 - **Lower Compression Roll (F):** Raises lower punches for compression.
 - **Upper Compression Roll (G):** Guides upper punches to press the powder.
- **Upper Punch Raising Cam (H):** Lifts **upper punches** after compression.
- **Lower Punch Ejection Cam (I):** Raises **lower punches** to bring tablets to die surface for ejection.
- **Ejector Knob:** Adjusts the exact position of the **tablet ejection** height.
- **Sweep-Off Blade:** Pushes the **formed tablets** into a collection chute.



The compression cycle of a rotary tablet press.

Rotary Tablet Press Operation:



1. **Filling:**
 - Powder flows from the hopper into the die.
 - The die is slightly overfilled, and extra powder is removed.
 2. **Compression:**
 - The lower punch moves up while the upper punch comes down.
 - The powder is squeezed tightly into a tablet under high pressure.
 3. **Ejection:**
 - The upper punch moves up, and the lower punch pushes the tablet out.
 - A blade guides the tablet into a chute for collection.
 4. **Cycle Repeats:**
 - The machine continuously makes tablets as the turret rotates.
- A **tablet machine's output** is regulated by three basic characteristics of its design:
 - Number of tooling sets
 - Number of compression stations
 - Rotational speed of the press

Compression Machine Tooling:

Tablet presses use different types of punches and dies to shape tablets. The most common types are:

1. BB Tooling:

- Punch length: **5.25 inches**
- Barrel diameter: **0.75 inches**
- Head diameter: **1 inch**



2. B Tooling:

- Same as BB, but **lower punch is shorter**

3. D Tooling:

- Used for **large tablets**
- Barrel diameter: **1 inch**
- Head diameter: **3.25 inches**
- Length: **5.25 inches**

4. Dies:

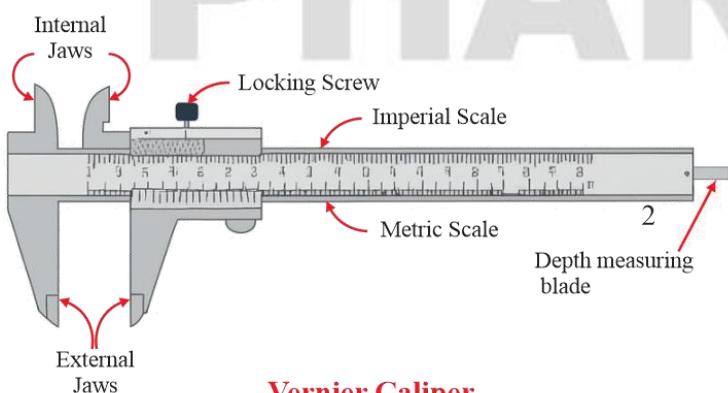
- **0.945-inch OD die:** Makes **round or capsule-shaped tablets**
- **Larger dies make bigger tablets**

These tools help determine the **size and shape** of the tablets produced.

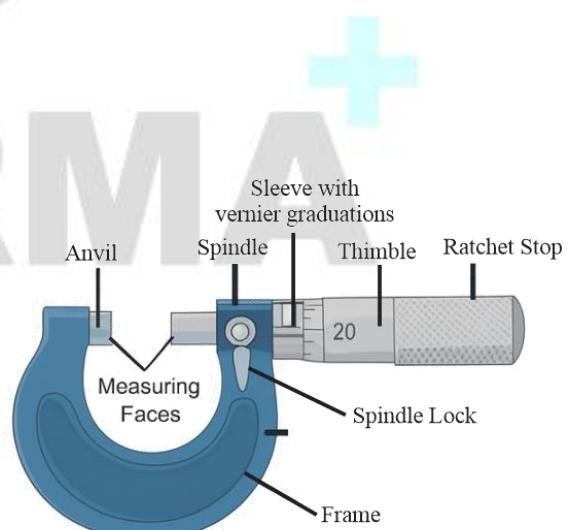
EVALUATION/QUALITY CONTROL TEST

1. General Appearance

- **Size & Shape:** Controlled by compression machine tooling.
 - Thickness is measured using a **micrometer** and **vernier caliper** (should be within $\pm 5\%$ of standard).
- **Color:** Uneven color (mottling) can be tested using:
 - **Reflectance spectrophotometry**
 - **Tristimulus colorimetry**
 - **Micro-reflectance photometry**



Vernier Caliper



Micrometer

2. Tablet Hardness (Crushing Strength)

- Historically tested by breaking the tablet with fingers and thumb (a sharp snap meant good strength).
- Now tested by a **diametric compression test**:

- Tablet is placed between **two anvils**, force is applied, and the strength needed to break it is recorded.
- **Devices used:**
 - **Monsanto Tester** (Strength in kg)
 - **Strong-Cobb, Pfizer, Erweka, and Schleuniger Testers**
- **Standard hardness: Minimum 4 kg**
- Hardness affects **tablet dissolution and handling stability**.



Monsanto Tester



Pfizer



Erweka



Schleuniger Testers



Strong-Cobb

3. Friability (Tablet Strength During Transport)

- Determines tablet loss during transport using Roche friabilator
- USP Official Test (Not official in BP & IP)
- **Test conditions:**
 - **Fall height:** 6 inches
 - **Speed:** 25 rpm
 - **Time:** 4 minutes (100 revolutions)
 - **Sample size:**
 - **Tablet weight \leq 650mg:** Take sample weighing around 6.5 grams.
 - **Tablet weight $>$ 650mg:** Take a sample of 10 whole tablets.
 - **Limit:** Not more than 1% weight loss (IP), 0.5-1% (USP)
- **Friability (f) is calculated as:**

$$\text{Friability} = \frac{w - w_0}{w} \times 100$$
- where **w** = initial weight, **w₀** = final weight.
- If cracked, cleaved, or broken tablets appear, the batch fails.
- If weight loss exceeds the limit, test should be repeated **twice**, and the mean of **three tests** should be calculated.



4. Uniformity of Weight (Weight Variation Test)

- **Total tablets used for the test:** 20
- **Significance:** If weight variation is large, it means the active medicament will also vary considerably.
- Select **20 tablets randomly** and weigh them individually.
- Calculate the **average weight** of the tablets.
- **Acceptance Criteria:**
 - **Not more than two tablets should deviate** from the average weight beyond the percentage shown in the table below

Weight Variation Limits (IP & USP):

Average Weight of Tablet		Maximum % Difference Allowed
IP	USP	
80 mg or less	130 mg or less	± 10%
80 - 250 mg	130 - 324 mg	± 7.5%
More than 250 mg	More than 324 mg	± 5%

5. Uniformity of Content (Content Uniformity Test)

- **Purpose:**
 - Ensures that each tablet contains the **correct drug amount**.
 - **Important for low-dose, highly potent drugs like digitoxin.**
- **To assure uniform potency for tablets of low-dose drugs:**
- **Number of tablets tested:** 30
- **Assay at least 10 tablets** using an analytical method.
- **Passes if:**
 - 9 tablets contain **85-115% of labeled drug**
 - 10th tablet may contain **75-125% of labeled drug**
- **If failed:** Test 20 more tablets; **all must be 85-115%**

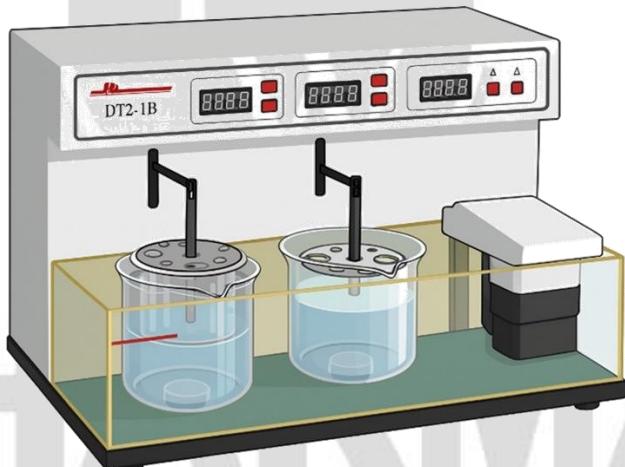
6. Disintegration:

- **Disintegration** is the process where a tablet breaks down into smaller particles or granules.
- **Not applicable to:**
 - **Modified-release tablets**
 - **Mouth dissolving tablets**
- **USP Disintegration Test Apparatus:**
 - Consists of **6 glass tubes** (3 inches long), **Tablet Sample:** 6 tablets.
 - Open at the **top** and held against a **10-mesh screen** at the **bottom** of the **basket rack assembly**.
[**IP: 8 mesh (2 mm)**]
- **Test Conditions:**
 - **Medium:** 1-L beaker containing **water, simulated gastric fluid, or simulated intestinal fluid**
 - **Temperature:** $37^{\circ}\text{C} \pm 2^{\circ}\text{C}$

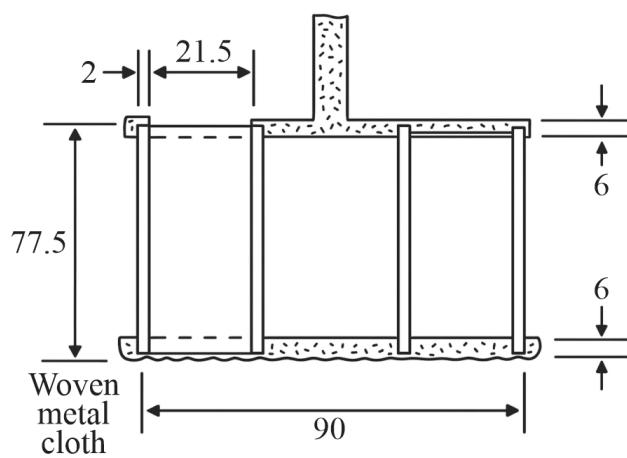
- **Movement:**
- Basket rack moves **up and down** through **5-6 cm**
- Frequency: **28-32 cycles per minute**
 - Perforated plastic discs may be placed on top of tablets to add an **abrasive action**, especially for **floating tablets**
- Tablets must completely disintegrate within the specified time, passing through the **10-mesh screen**
- If any residue remains, it must be a **soft mass with no firm core**.

Disintegration Time Limits (USP):

- Uncoated tablets: ≤ 30 min (Aspirin: ≤ 5 min).
- Film-coated tablets: ≤ 30 min (in water or 0.1 N HCl).
- Sugar-coated tablets: ≤ 60 min.
- Enteric-coated tablets:
 - No disintegration in 1 hour in simulated gastric fluid.
 - Must disintegrate within 2 hours in simulated intestinal fluid.
- Buccal tablets: ≤ 4 hours.
- Sublingual tablets: ≤ 3 minutes.



Disintegration Test Apparatus





7. Dissolution Test:

- It measures **how fast a drug dissolves in a liquid** (usually simulated gastric or intestinal fluid).
- It helps predict **drug absorption and bioavailability**.
- Faster dissolution = **faster drug absorption**.
- Ensures **batch-to-batch consistency** in drug formulations.

Dissolution Testing Apparatus

The USP specifies **two main apparatus** for testing:

Apparatus 1 (Basket Method)

- **Used for:** Capsules, floating tablets, and drugs with low solubility.
- **Setup:**
 - **Tablet placed in a wire mesh basket** attached to a rotating shaft.
 - Basket is dipped in **900 mL of dissolution medium** at **$37 \pm 0.5^{\circ}\text{C}$** .
 - **Speed is controlled** as per USP monograph (e.g., 50-100 rpm).
- **Sampling:** Fluid samples are taken at intervals to measure drug release.

Apparatus 2 (Paddle Method)

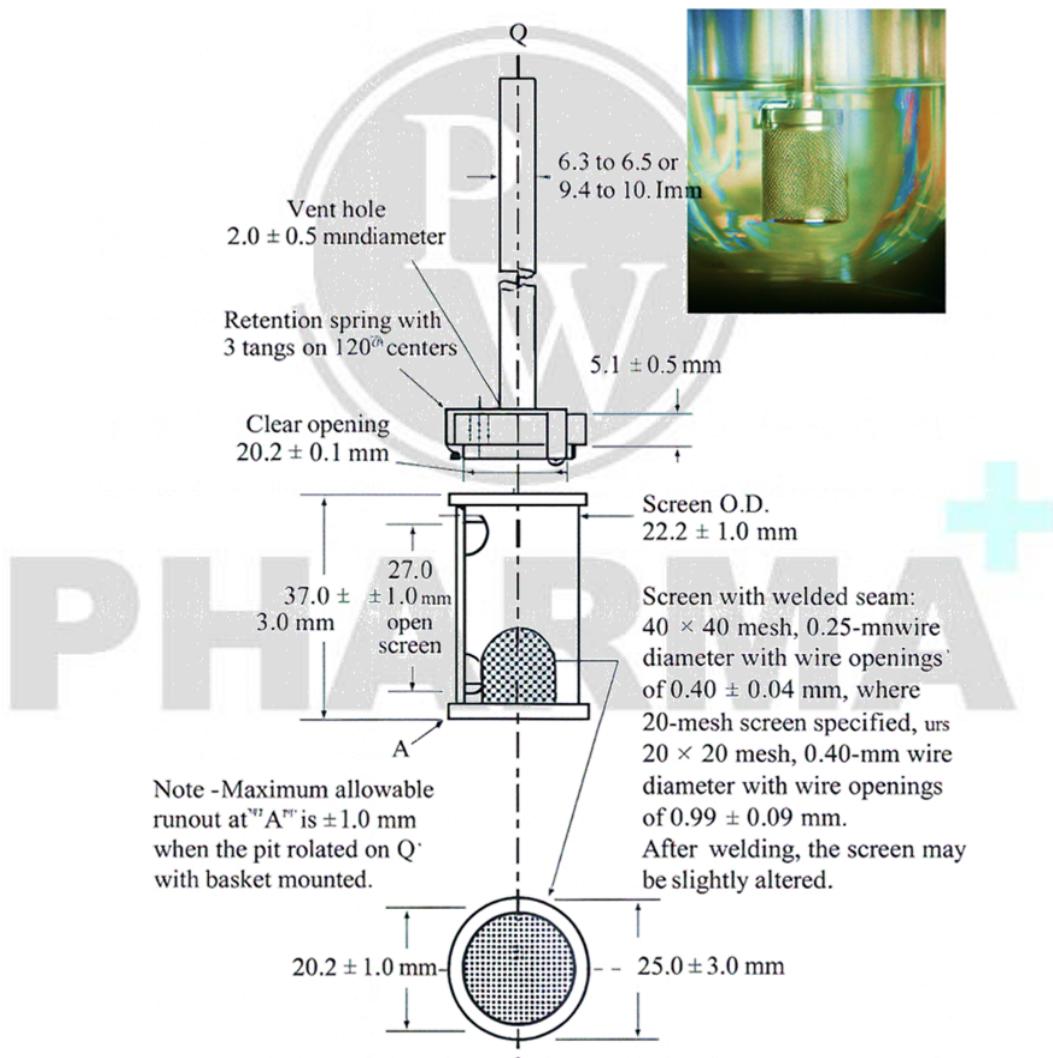
- **Used for:** Tablets and drugs that sink easily.
- **Setup:**
 - **Tablet sinks to the bottom** of the beaker.
 - A **paddle stirs the dissolution medium** at a set speed (e.g., 50-75 rpm).
 - If the tablet **floats**, a **wire helix** can be used to keep it submerged.
- **Acceptance Criteria (Dissolution Limits)**
- Dissolution tests are performed in **three stages (S1, S2, S3)**:

Stage	No. of Tablets Tested	Acceptance Criteria
S1 (Initial)	6 tablets	All must have $\ge (Q + 5\%)$
S2 (If S1 fails)	Additional 6 tablets (Total: 12)	Average of 12 tablets $\ge Q$ & None $< (Q - 15\%)$
S3 (If S2 fails)	Additional 12 tablets (Total: 24)	Average of 24 tablets $\ge Q$ & Not more than 2 tablets $< (Q - 15\%)$

Important Dissolution Parameters

- **t50% (Time for 50% dissolution):** Helps compare different formulations.
- **t90% (Time for 90% dissolution):** Ideal target: ≤ 30 minutes.
- **USP Standard:** Common tolerance is $\ge 75\%$ dissolved in 45 minutes.

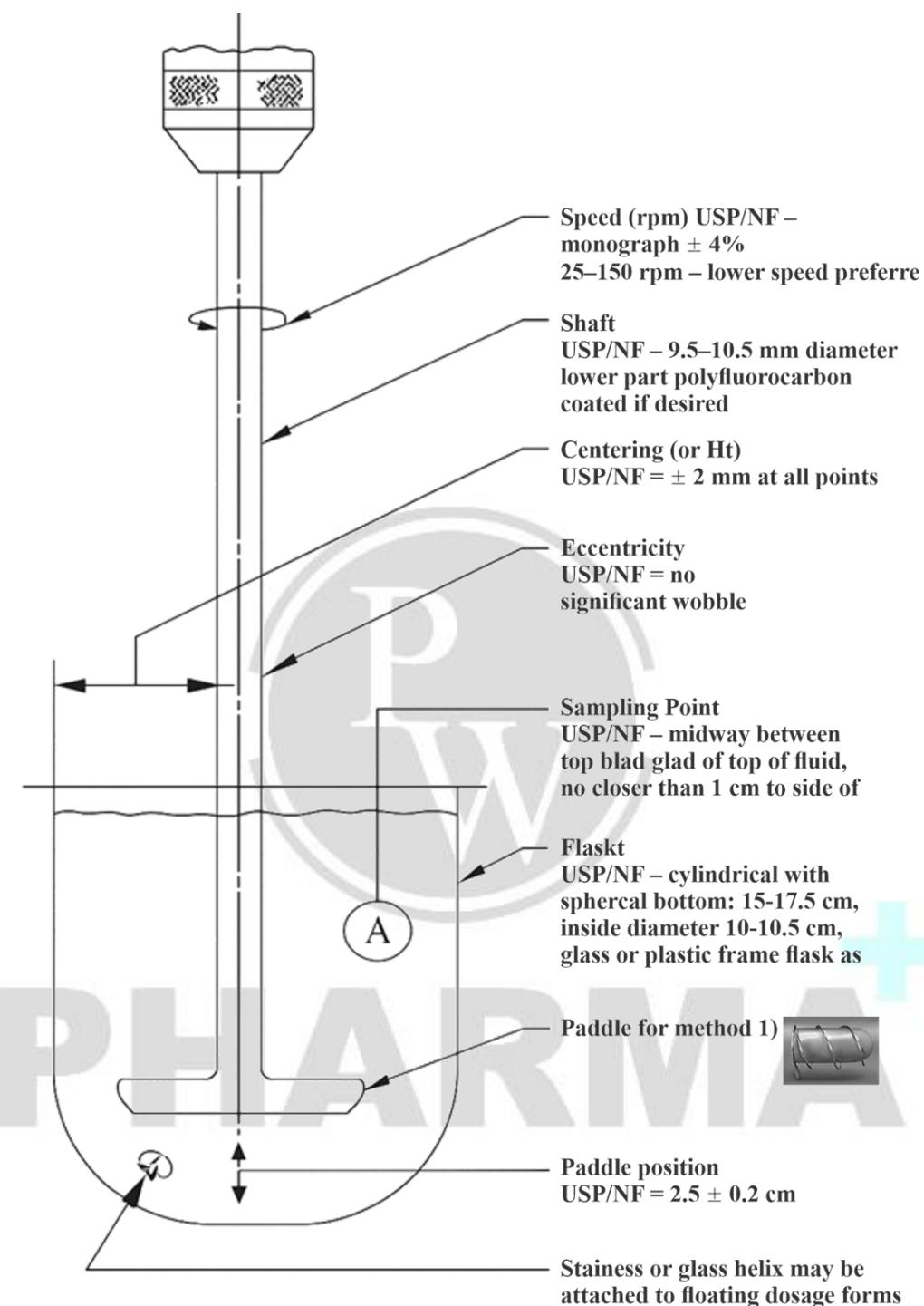
Types of Dissolution Apparatus as per USP		
USP Apparatus	Type	Use
Apparatus I	Rotating Basket	Capsules, Modified release solid dosage forms
Apparatus II	Paddle	Tablets, Modified release solid dosage forms
Apparatus III	Reciprocating Cylinder	Determination of pH profile of modified release solid dosage forms
Apparatus IV	Flow-Through Cell	Rapidly degrading drugs
Apparatus V	Paddle Over Disc	Transdermal patches, Ointments, Emulsions
Apparatus VI	Rotating Cylinder	Transdermal patches
Apparatus VII	Reciprocating Disc	Transdermal patches



USP Apparatus 1 (Basket Apparatus)

USP Apparatus 1.

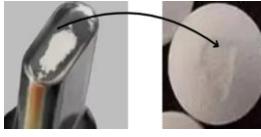
Basket type: Mesh screen-10 mesh (USP), Temperature: $37 \pm 0.5^\circ\text{C}$. 900 ml flask.



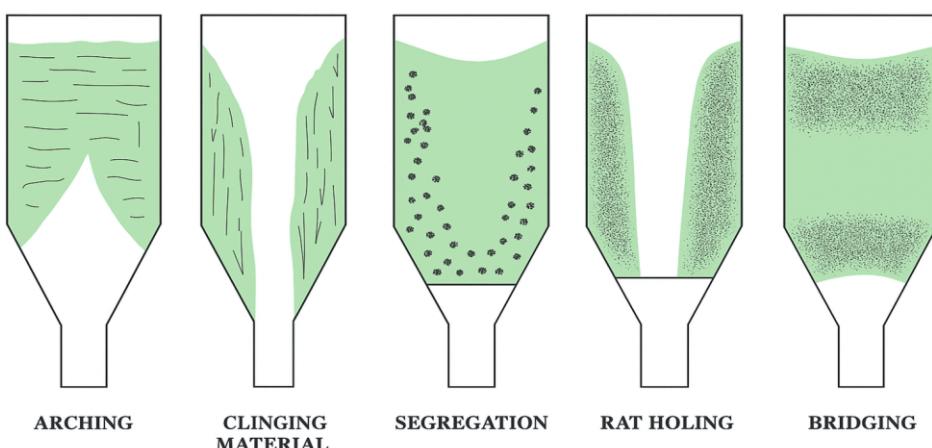
- **USP Apparatus 2 (Paddle type)**

900 ml. Flask. Contains wire helix to prevent tablet from floating. Distance between inside bottom of vessel and basket or paddle - 25 ± 2 mm, Speed - 25 to 150 rpm.

PROCESSING PROBLEMS

Problem	Definition	Causes	Solutions
Capping and Lamination 	Capping: Separation of the top or bottom layer of a tablet. Lamination: Splitting of the tablet into multiple layers.	- Entrapped air in granules - Rapid decompression - Weak interparticle bonding - Overdrying of granules	- Optimize binder concentration - Reduce compression force - Modify granulation moisture content - Use pre-compression step
Picking and Sticking 	Picking: Material sticks to punch tips, especially in engraved areas. Sticking: Material adheres to die walls, causing rough tablet edges.	- Low melting ingredients soften due to compression heat - Excessive moisture in granulation - Poor lubrication - Poor punch surface finish	- Use chromium-plated punches - Add colloidal silica or lubricants - Reformulate with higher melting excipients - Refrigerate granules if needed
Mottling 	Uneven color distribution on tablet surface.	- Difference in color between drug and excipients - Improper dispersion of colorants - Migration of dye during drying	- Use well-dispersed fine powder colorants - Adjust solvent or binder system - Reduce drying temperature - Optimize mixing process
Weight Variation 	Tablets exhibit inconsistent weight due to variations in die filling.	- Poor granule flow - Granule size variation - Uneven mixing of lubricants - Hopper design issues causing flow obstruction	- Add glidants like talc or colloidal silica - Optimize granule size distribution - Use vibrators or modified hoppers - Ensure uniform lubricant mixing
Hardness Variation	Tablets exhibit inconsistent hardness , affecting durability and dissolution.	- Uneven weight variation - Variations in punch movement - Improper granule compression	- Maintain uniform die filling - Standardize compression force - Control punch alignment
Double Impression 	Secondary, unintended imprint on the tablet due to punch movement.	- Rotation of lower punch before ejection - Uncontrolled upper punch rotation in two-stage compression	- Use antiturning devices - Optimize tablet press design - Adjust machine settings

Defects due to improper feeding of hopper



TABLET COATING

Nonenteric Film Formers in Tablet Coating:

Film Former	Properties	Uses
Hydroxypropyl Methylcellulose (HPMC)	<ul style="list-style-type: none"> - Soluble in gastrointestinal fluids and various solvents. - Does not affect tablet disintegration or drug release. 	<ul style="list-style-type: none"> - Used in air suspension and panspray coating. - Combined with plasticizers to prevent bridging or filling of debossed surfaces.
Ethylcellulose	<ul style="list-style-type: none"> - Insoluble in water and gastric fluids. - Requires water-soluble additives (e.g., HPMC) for coating. 	<ul style="list-style-type: none"> - Used in sustained-release coatings. - Available as Aquacoat (pseudolatex system) for aqueous coatings.
Hydroxypropylcellulose (HPC)	<ul style="list-style-type: none"> - Soluble in water below 40°C but insoluble above 45°C. - Produces very flexible films. 	<ul style="list-style-type: none"> - Used in combination with other polymers for better film characteristics.
Povidone (Polyvinylpyrrolidone, PVP)	<ul style="list-style-type: none"> - Available in four viscosity grades (K-15, K-30, K-60, K-90) - Soluble in water and many organic solvents. 	<ul style="list-style-type: none"> - Used as a tablet binder and film former. - Helps in even color dispersion.
Sodium Carboxymethylcellulose (NaCMC)	<ul style="list-style-type: none"> - Easily dispersed in water, forming colloidal solutions. - Insoluble in organic solvents. 	<ul style="list-style-type: none"> - More useful in aqueous-based coatings.
Polyethylene Glycols (PEGs)	<ul style="list-style-type: none"> - Low molecular weight PEGs (200-600) → Liquid at room temperature, used as plasticizers. - High molecular weight PEGs (900-8000) → Solid, waxy, used for film modification. 	<ul style="list-style-type: none"> - Combined with cellulose acetate phthalate for gastric-soluble films. - Sensitive to high temperatures.
Acrylate Polymers (Eudragit)	<ul style="list-style-type: none"> - Eudragit E: Cationic polymer, soluble in stomach acid (pH up to 5). - Eudragit RL & RS: Used for delayed-release formulations. 	<ul style="list-style-type: none"> - Eudragit E: Used for coatings that dissolve in stomach acid. - Eudragit RL & RS: Used for delayed-release formulations.



Enteric Coating:

- A special coating applied to tablets or pills to **prevent them from dissolving in stomach acid.**
 - **Protects acid-sensitive drugs** (e.g., enzymes, some antibiotics).
 - **Prevents stomach irritation** from drugs (e.g., sodium salicylate).
 - **Ensures drugs reach intestines** for local action (e.g., intestinal antiseptics).
 - **Delivers drugs effectively to absorption sites** in the small intestine.
 - **Provides delayed release** for long-lasting effects.

Common Enteric Coating Materials

- **Cellulose Acetate Phthalate (CAP):**
 - Dissolves **above pH 6** → may delay drug absorption. Aquateric® Improved version of CAP.
- **Acrylate Polymers (Eudragit L & S)**
 - **Eudragit L** dissolves at **pH 6**.
 - **Eudragit S** dissolves at **pH 7**.
- **Hydroxypropyl Methylcellulose Phthalate (HPMCP)**
 - Dissolves at **pH 5 to 5.5** → can improve drug absorption.
- **Polyvinyl Acetate Phthalate (PVAP)**

Materials used in Coating Solution:

Solvents:

- A solvent's main job is to dissolve or disperse polymers and other ingredients, making them easy to apply to the surface of tablets.
- **Common solvents used:** Water, ethanol, methanol, isopropanol, chloroform, acetone, methyl-ethyl-ketone, and methylene chloride.

Plasticizers:

- Plasticizers are added to improve the flexibility, strength, and other properties of the polymer film.
- **Common plasticizers:** Castor oil, propylene glycol, glycerin, and polyethylene glycols (e.g., PEG 200 and PEG 400).
- Surfactants like polysorbates (Tweens) and sorbitan esters (Spans) are also used.
- For aqueous coatings, water-soluble plasticizers like PEG and propylene glycol are used.
- For organic-solvent coatings, castor oil and Spans are common.

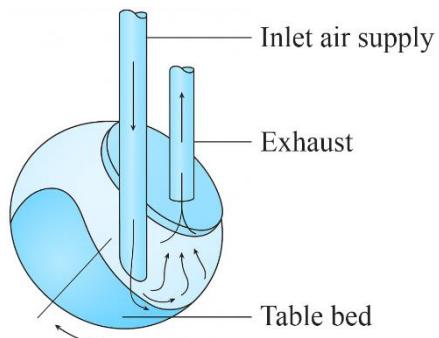
Colorants:

- **Types of colorants:**
- **Dyes:** Water-soluble and provide vibrant colors.
- **Lakes:** Dyes precipitated with carriers like alumina or talc, making them insoluble. Lakes are preferred for coating because they give more stable and consistent colors.

Commercial Colorants:

- **Opalux:** Opaque color concentrate for sugar coating.
- **Opaspray:** Opaque color concentrate for film coating.
- **Opadry:** Complete film coating concentrate that helps reduce lot-to-lot color variation.
- **Opaquant-extenders** are fine **inorganic powders** added to the coating solution to make the film more opaque and give a **pastel color**.
- **Common Opaquants:** Titanium dioxide is the most common, Other materials include **silicates** (like talc), **carbonates** (like magnesium carbonate), **sulfates** (like calcium sulfate), **oxides** (like magnesium oxide), and **hydroxides** (like aluminum hydroxide).

COATING PROCESS



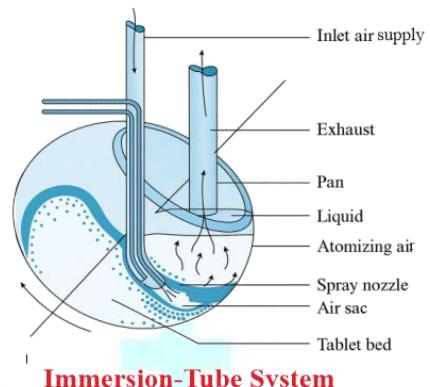
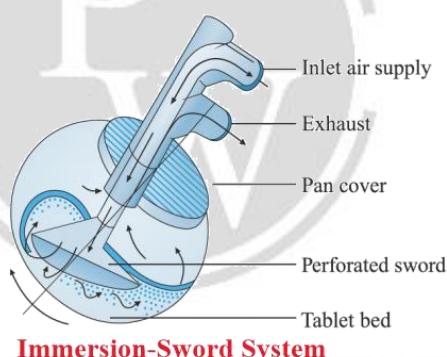
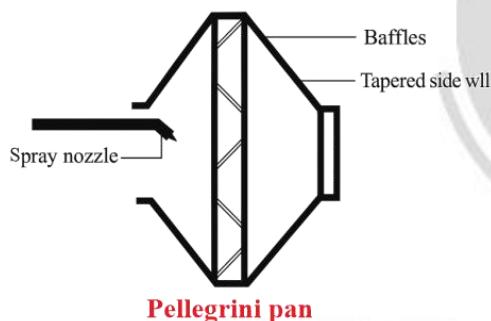
Coating Equipment Types

1. Standard Coating Pan

- A circular metal pan mounted on a stand and rotated on a horizontal axis. The pan can be 8 to 60 inches in diameter.
- Heated air is directed into the pan and onto the tablet bed surface.
- Coating solutions are applied by spraying.

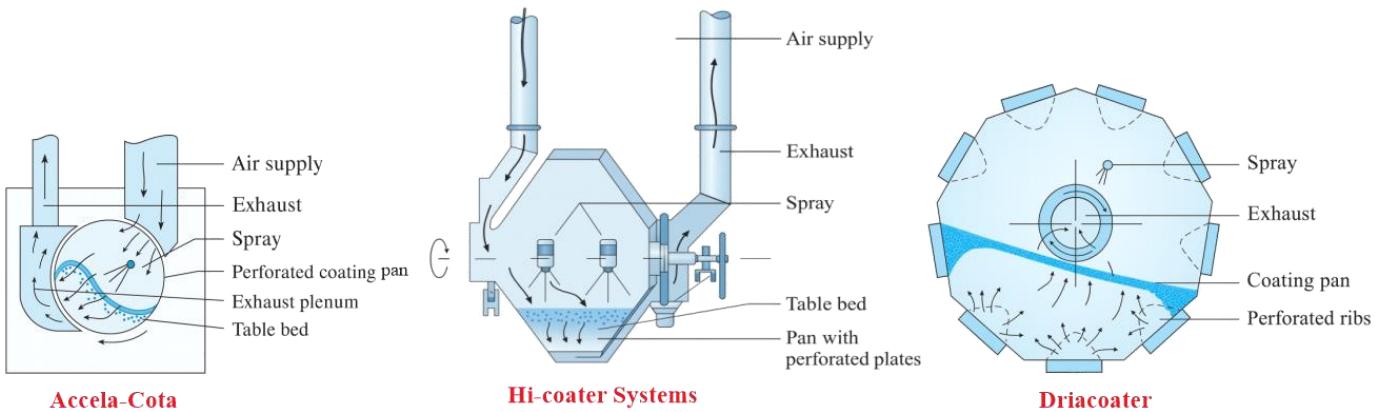
Improvement in Drying Efficiency:

- **Pellegrini Pan:** Includes a baffled pan and a diffuser to distribute drying air uniformly.
- **Immersion-Sword System:** Uses a perforated metal sword immersed in the tablet bed to introduce drying air upward.
- **Immersion-Tube System:** A tube immersed in the tablet bed delivers heated air and applies the coating solution simultaneously.

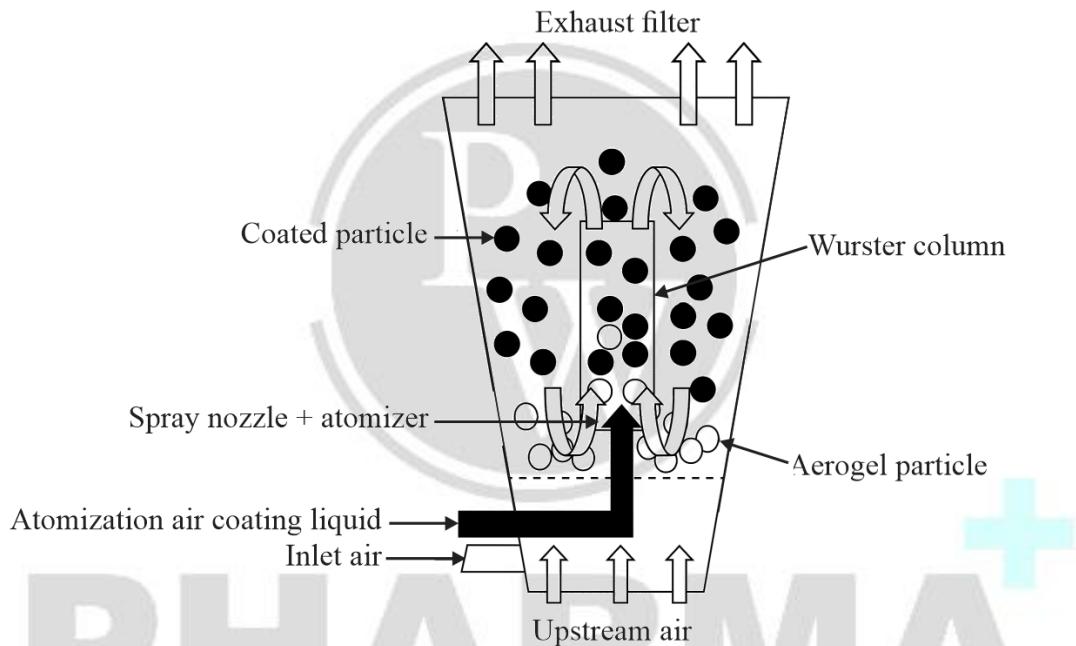


2. Perforated Coating Pan

- Consists of a perforated or partially perforated drum that rotates on its horizontal axis inside an enclosed housing.
- **Accela-Cota and Hi-Coater Systems:** Drying air is directed into the drum, passed through the tablet bed, and exhausted through perforations in the drum.
- **Driacoater:** Drying air is introduced through hollow perforated ribs, which dip into the tablet bed and fluidize it.
- **Glatt Coater:** Allows airflow configurations where drying air can flow through or reverse through the tablet bed.



3. Fluidized Bed (Air Suspension) Coater



- Uses a stream of air to suspend the tablets in a bed while applying the coating solution.

- **Spray Application Systems**

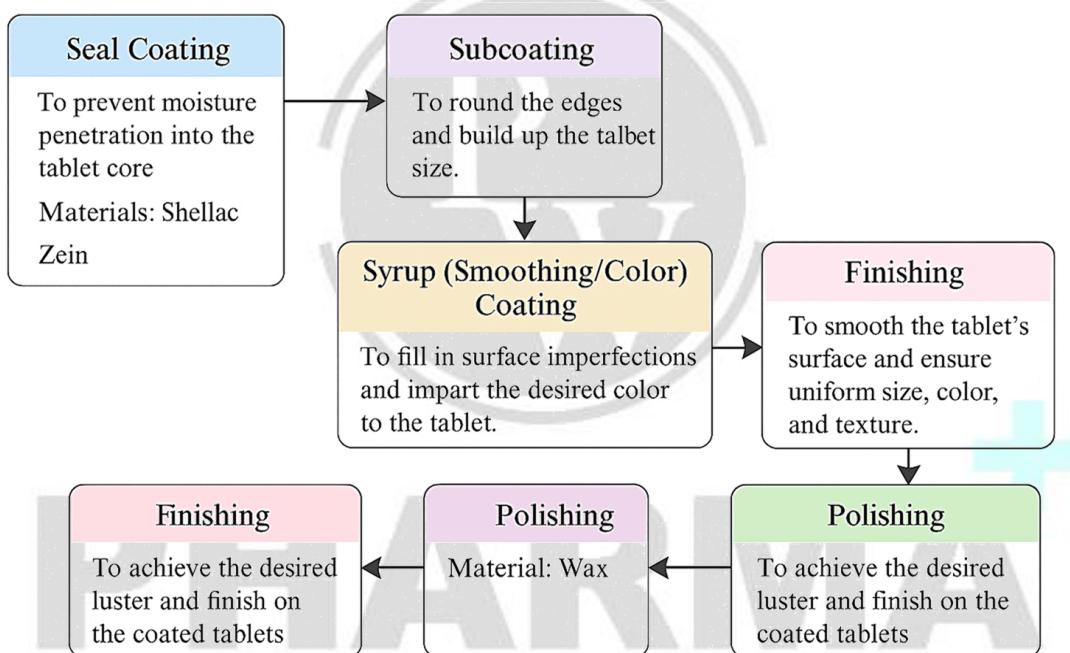
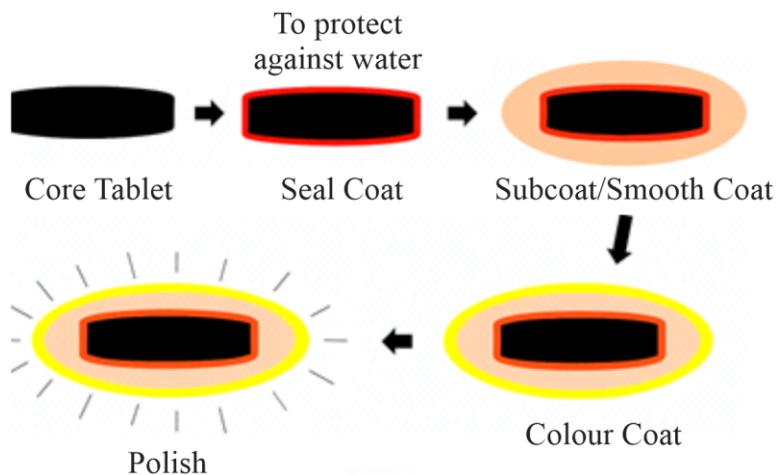
1. **High-Pressure, Airless System:**

- Liquid is pumped at high pressure (250 to 3,000 psig) through a small orifice (0.009 to 0.020 inch in diameter).
- The result is a finely divided spray, with atomization controlled by fluid pressure, orifice size, and the viscosity of the liquid.

2. **Low-Pressure, Air-Atomized System:**

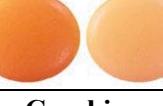
- Liquid is pumped at lower pressures (5 to 50 psig) through a larger orifice (0.020 to 0.060 inch in diameter).
- Low-pressure air (10 to 100 psig) contacts the liquid stream at the tip of the atomizer, resulting in a finely divided spray.

SUGAR COATING PROCESS



Coating Type	Materials
Seal Coating Solutions	Cellulose Acetate Phthalate, Zein, Oleic Acid (USP), Propylene Glycol (USP), Polyethylene Glycol 4000, Methylene Chloride, Alcohol SD 3A 200-proof
Subcoating Solutions	Gelatin, Acacia, Sugar Cane Syrup, Corn Syrup, Syrup USP, Distilled Water
Subcoating Powders	Kaolin, Dextrin, Cocoa Powder, Calcium Carbonate (pptd), Sugar Cane Powder, Acacia Powdered, Corn Starch, Talc (USP), Calcium Sulfate
Syrup Solutions	Colorant (q.s. ad), Subcoating Powder (e.g., Calcium Carbonate Light, Sugar Cane Powder, Starch Corn, Syrup USP, Water Distilled)
Polishing Solutions	Carnauba Wax (Yellow), Beeswax (White), Paraffin Wax, Naphtha

FILM DEFECTS

Defect	Cause	Solution
Sticking and Picking 	Overwetting, excessive tackiness causing tablets to stick to each other or to the coating pan, leading to exposed core .	Reduce liquid application rate, increase drying air temperature.
Roughness 	Rapid drying of droplets before reaching the tablet bed, creating “ spray-dried ” particles. Higher pigment or polymer concentration.	Move nozzle closer, reduce atomization, decrease pigment and polymer concentration in the coating solution.
Orange-Peel Effects 	Inadequate spreading of the coating solution causes a bumpy or “orange-peel” appearance. This is due to too rapid drying or high solution viscosity .	Thin the solution with additional solvent, adjust drying speed.
Bridging and Filling 	The film shrinks and pulls away from sharp corners during drying, leading to a “ bridging ” effect where surface depressions are covered . Excessive solution application can cause filling.	Increase plasticizer content, change plasticizer, monitor fluid application rate, and ensure proper tablet mixing.
Blistering 	Rapid solvent evaporation or high drying temperatures cause high internal stresses on the film, leading to blister formation .	Use milder drying conditions, reduce evaporation speed during drying.
Hazing/Dull Film 	High processing temperatures or exposure to high humidity causes partial solvation of the film, resulting in a dull or hazy appearance.	Avoid high processing temperatures, adjust humidity exposure.
Color Variation 	Improper mixing, uneven spray patterns, or migration of soluble dyes and additives during drying leads to inconsistent color, resulting in mottled or spotted coatings.	Ensure uniform mixing, use lake dyes, improve spraying technique.
Cracking 	Internal stresses in the film exceed its tensile strength, leading to cracks. This occurs when the film cannot withstand the forces acting on it.	Use higher molecular-weight polymers or blends, adjust plasticizer and pigment concentrations.
Twinning 	Tablets stick together , particularly flat-faced or caplet-shaped tablets, due to excessive application of solution, causing cores to stick together.	Minimize overwetting, apply slight curvature to flat surfaces to reduce sticking and twinning.

TABLET PUNCH FORCES:

TABLET FORMATION PROCESS

- **Compaction:** A process where powder is subjected to **mechanical force** to form a solid mass.
- **Compaction occurs in two steps:**
 1. **Compression:**
 - **Reduction in bulk volume** due to displacement of air or gas between particles.
 - **Compressibility:** The ability of powder to reduce in volume under applied pressure.
 2. **Consolidation:**
 - **Increase in mechanical strength** due to **particle-particle interaction**.
 - Strong **bonds** are formed between particles, creating a **coherent compact mass**.

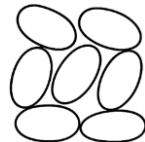
$$\text{Compaction} = \text{Compression} + \text{Consolidation}$$

Mechanism of Tablet Compaction

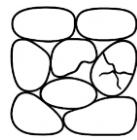
The process of tablet formation occurs in **three major phases**:

1. **Transitional Repacking (Particle Rearrangement)**
 - Initial **rearrangement** of powder particles to fill void spaces.
2. **Deformation**
 - **Elastic deformation:** Particles compress but return to their original shape after removing force.
 - **Plastic deformation:** Permanent change in shape occurs beyond the **elastic limit**.
 - **Brittle fracture:** Hard particles **break** into smaller pieces, filling the gaps between them.
3. **Consolidation (Bonding)**
 - **Formation of strong bonds** between particles.
 - Strength of the tablet depends on **bonding forces**.

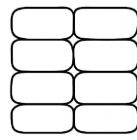
Tablet Punch Force Mechanism	Effects & Considerations
Elastic Deformation: A temporary deformation where the material returns to its original shape once the force is removed.	Leads to limited volume reduction.
Plastic Deformation: A permanent change in shape due to applied force. The material flows into void spaces, similar to modeling clay.	Enhances tablet strength and bonding. Requires sufficient dwell time for proper compaction.
Brittle Fracture: Occurs when the material fractures instead of deforming plastically. Common in hard, brittle particles like sucrose.	Can cause weak tablet structure, leading to chipping or breaking.
Microsquashing: Small particles deform plastically, increasing particle bonding. Fine powders or sheared-off asperities of larger particles exhibit this behavior.	Affects tablet integrity and compaction efficiency.
Dwell Time Effect: The duration a tablet remains under peak compression affects consolidation. Longer dwell times allow continued plastic deformation and prevent expansion during decompression.	Short dwell times may cause tablet expansion, leading to lamination or capping. Adjusting machine speed and compression force helps optimize results.



Transitional Repacking (Particle Rearrangement)
Transitional repacking (Particle rearrangement)



Deformation
Elastic deformation plastic fracture



Consolidation (Bonding)
Formation of strong bonds between particles

