INTERNATIONAL COLLEGE OF PHARMACEUTICAL INNOVATION
国际创新药学院

Compaction

Course BSc (Pharm) or BSc (ATT)

Year 2024-2025 II

Module Medicines: Pharmaceutics 2 (MP2)

Lecturer Dr. Shi Du

Learning Outcomes

1. Explain the stages of tablet manufacture from the compaction of solid powders

2. List and describe the major components of a tablet rotary press

3. List common types of tablet defects and how they can be avoided in tabletting

4. Revise compaction theory and the factors affecting tablet strength

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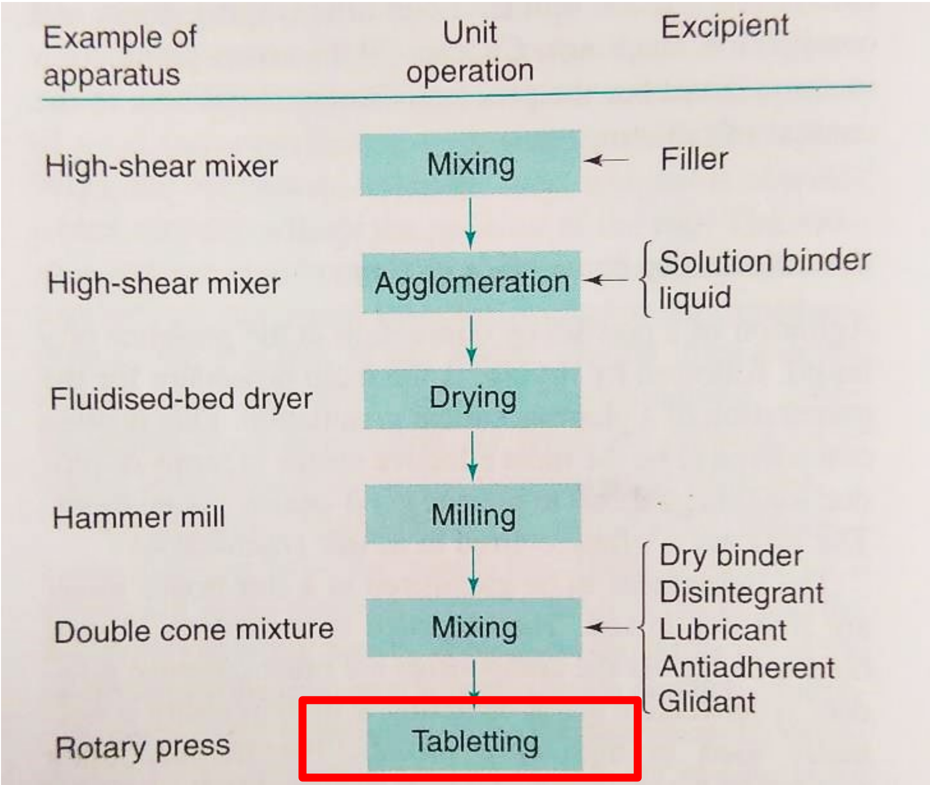
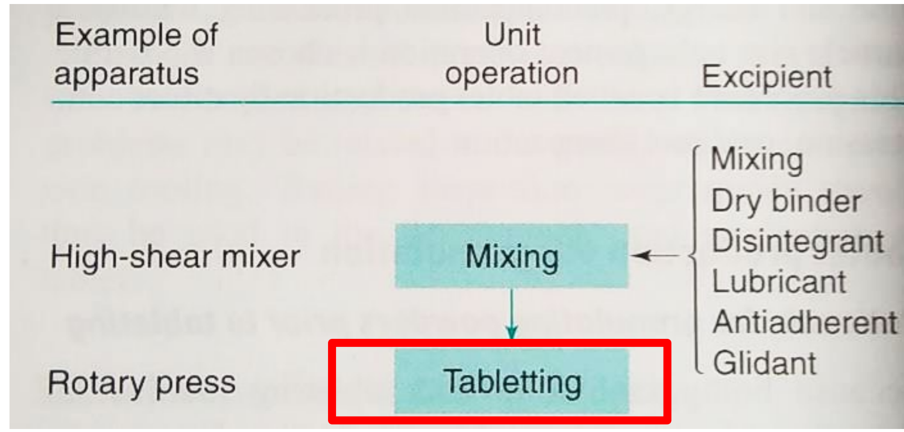
Unit Operations in Tabletting

Tablet Production with Granulation



Tablet Production with Direct Compression



Tablets are solid preparations containing a single dose of one or more active ingredients and are usually obtained by compressing uniform volumes of particles (Ph. Eur.).

- Most tablets are made by compression of granules
- Direct compression: Relatively soluble drugs which can be processed as coarse particles or potent drugs mixed with coarse excipients

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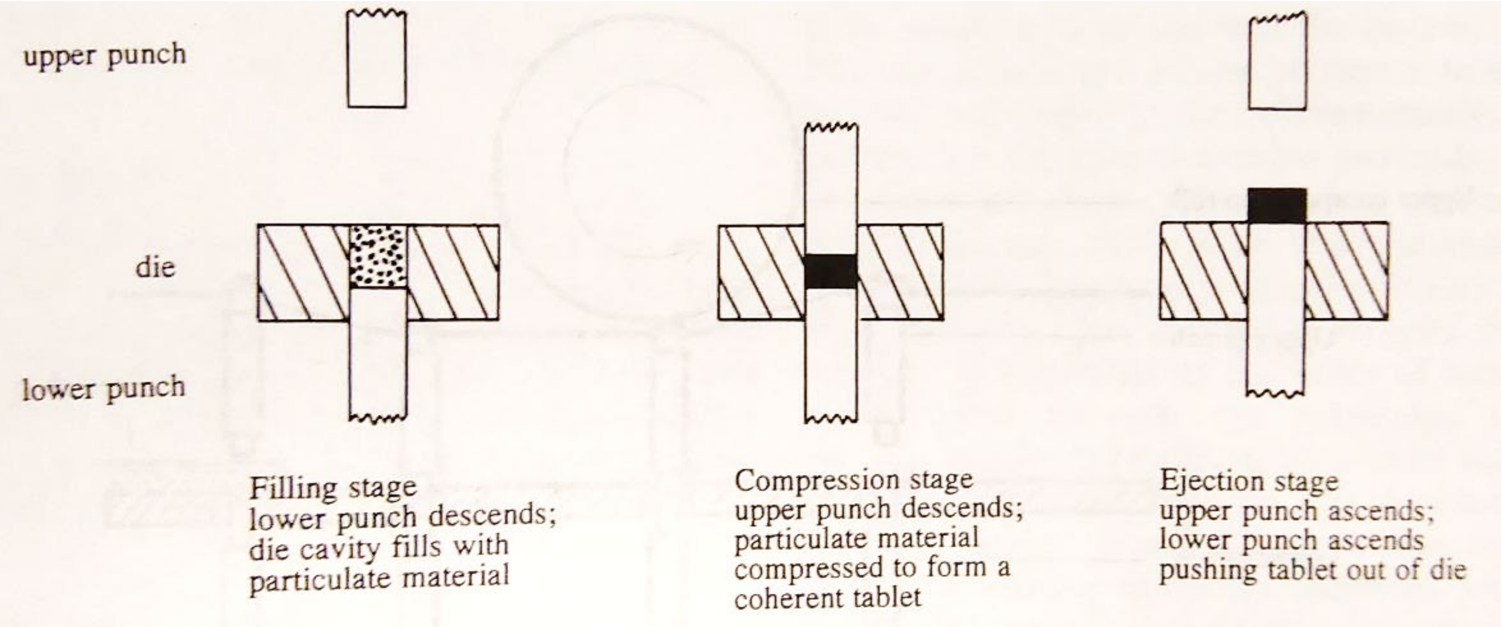
Powder Compression & Compaction



- Compression
  - The reduction in volume when loaded in a confined space
  - Enables powder particles to cohere
  - Volume reduction by application of force

Process of tabletting broadly involves three stages- the "compaction cycle"

- Compaction
  - The propensity of a powder to form a coherent tablet ("compact")
  - Fundamentally a bonding process between particles
  - High compactability means the resultant tablet will have high resistance towards fracture
  - Plastic deformation and brittle fracture produce strong compacts

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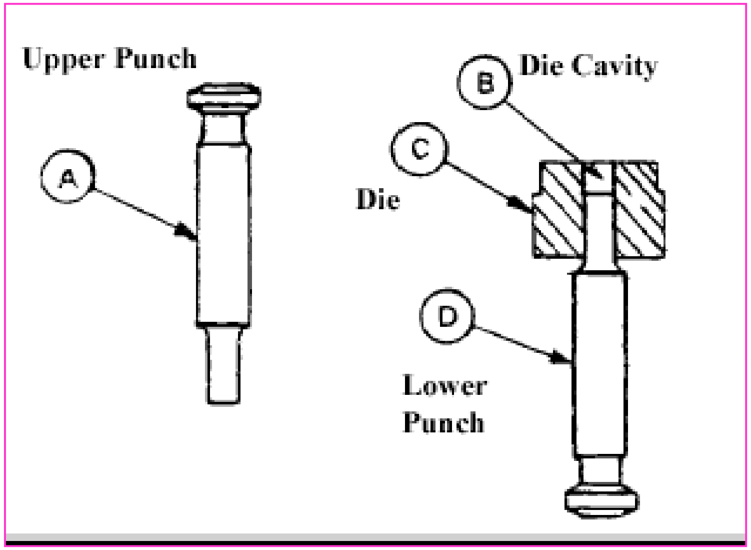
Stages in Tablet Formation: The Compaction Cycle

1. Filling stage
   - Die cavity filled with standardised volume of powder
   - Powder filling normally by gravitational flow via a hopper

2. Compression stage
   - Upper punch descends and enters die
   - Volume powder occupies is reduced: Compression occurs between punches
   - Lower punch can be stationary or can also move upwards
   - After compression of programmed force, upper punch leaves: Decompression

3. Ejection stage
   - Lower punch rises to level of top of die
   - Tablet pushed away from die



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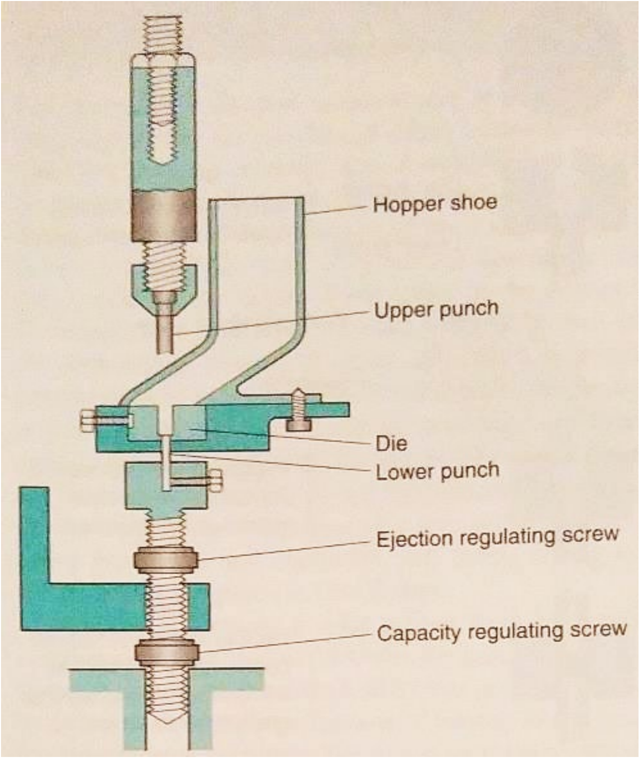
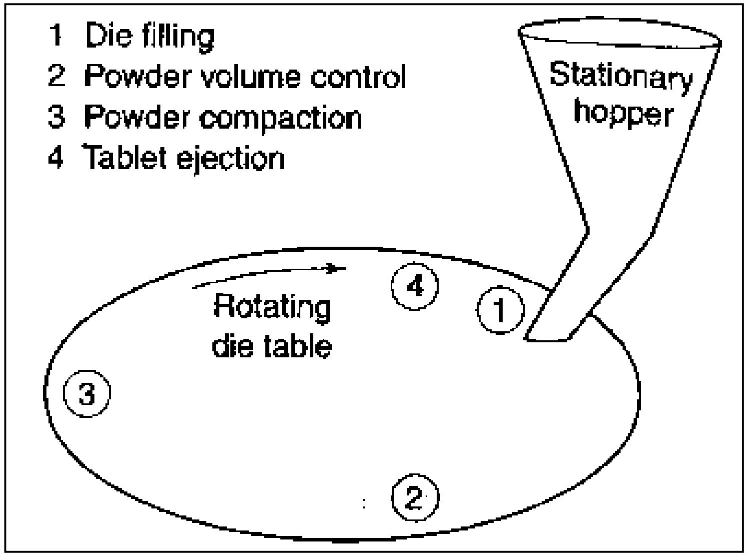
Stages in Tablet Formation: Tablet Presses

1. Single punch press
   - One pair of punches and a die
   - Max output ~200 tablets per minute
   - Lower punch controls volume of powder fill
   - Upper punch controls pressure
   - Normally for research or small-scale clinical trials

2. Rotary press
   - Multiple sets of presses and dies
   - Max output >10,000 tablets per minute
   - Sets of punches and dies rotate during machine operation
   - Force feeders ensure reproducible filling
   - Both punches move in compression
   - Ejected tablet pushed away by feed frame

- Rotary presses can be automated and instrumented
  - Save time and personnel input
  - Greater output
  - In process monitoring





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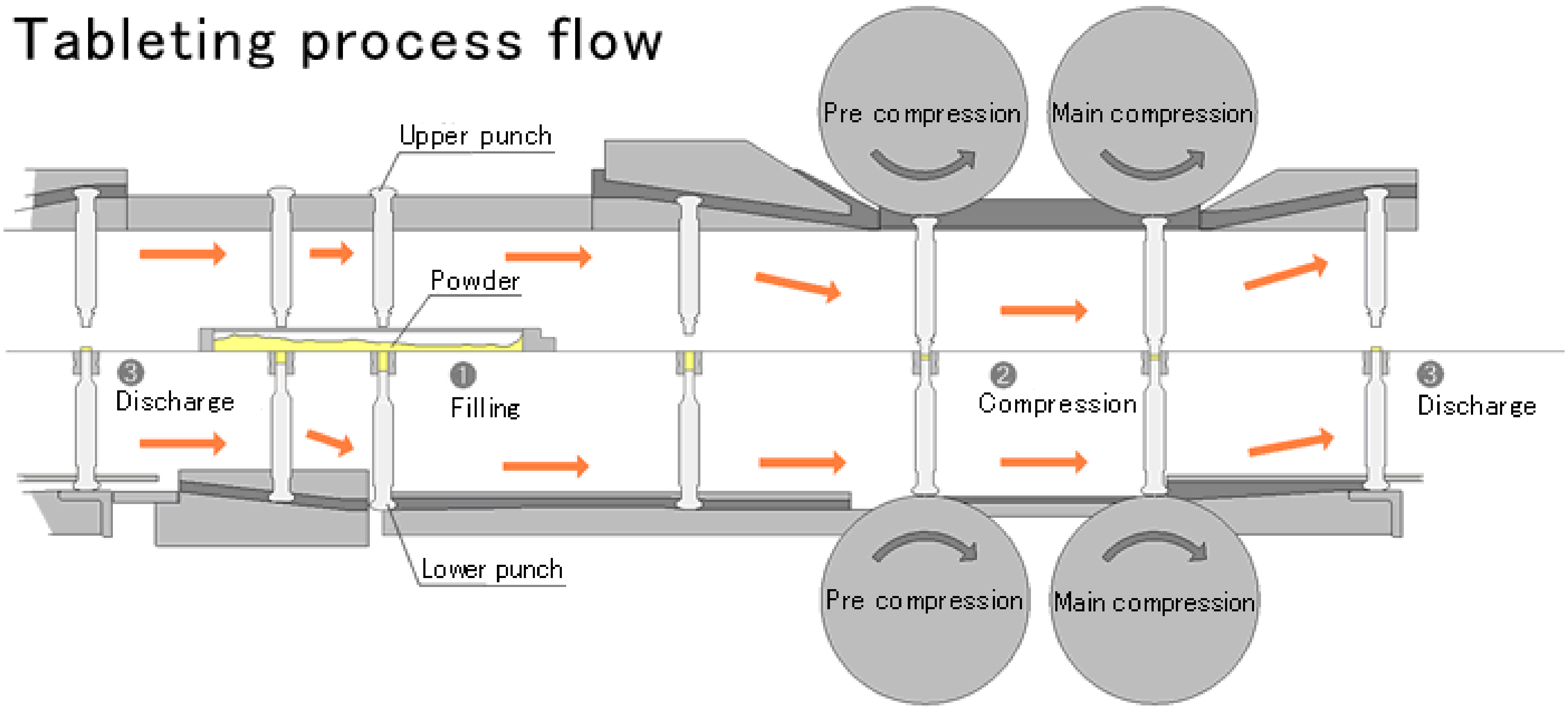
Rotary Tablet Press: Operation



https://www.youtube.com/watch?v=oXEKVuucxbg

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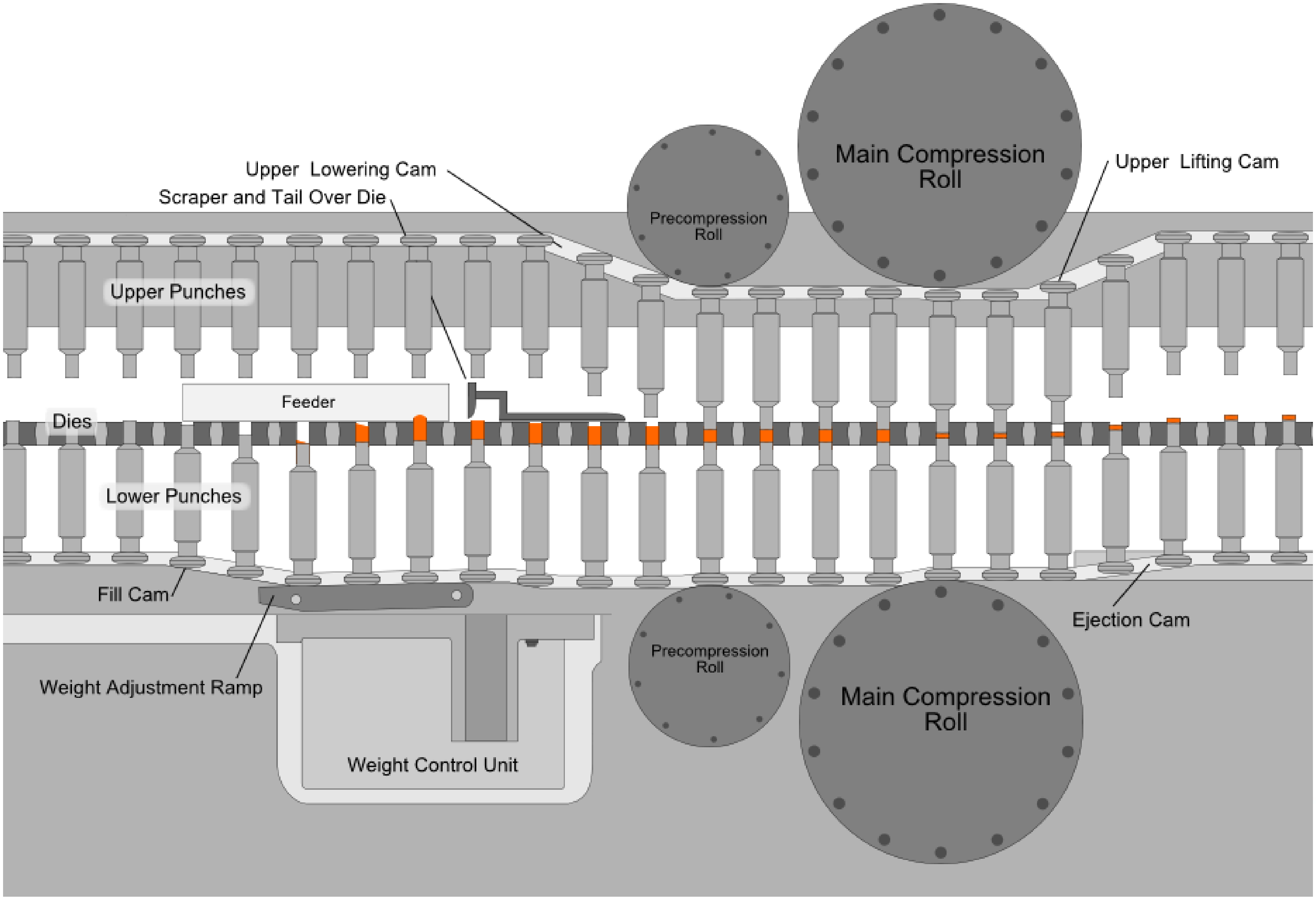
Rotary Tablet Press: Operation



Factors affecting Compression with Tablet Press

1. Speed of tablet press
   - The faster the press, the less time the die cavity spends under the feed frame
   - Can increase variable filling and reduced volume fill
   - Need to alter weight adjustment cam to compensate for drop in volume fill
   - Feeder speeds also need to be adjusted

2. Dwell time
   - Dwell time: Time that a set of punches are held under pressure by compression rollers
   - Will affect compaction and tablet strength
   - Need to adjust with speed of tablet press

3. Tablet press maintenance
   - Account for wear and tear of punches, cams, blades and other components
   - Mechanical forces wear down equipment too!
   - Regular maintenance and quality of machinery important

4. Powder (granule) quality
   - Flow and compressibility properties critical

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Tablet Tooling (Punch & Die Design)

- Tablets come in a variety of shaped and sizes
  - Tooling determines tablet features after compaction
  - Shape: Circular, oblong, flat, convex
  - Embossed and debossed: Logo, dose
  - Size: Different doses of drug
  - Scores: Splitting tablets

- Punch and die design
  - Punches: Head, neck, barrel, stem, tip
  - Die: Face, chamfer, bore
  - Material: Stainless steel
  - Tooling inspection very important

- Importance of tooling
  - Compression properties
  - Correct tablet dose
  - Tablet identification and market brand

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Potential Problems in the Tabletting Process

- Technical problems during tabletting
  1. High weight and dose variation of the tablets
  2. Low mechanical strength of the tablets
  3. Tablet capping and lamination
  4. Tablet picking and sticking to punch tips
  5. Mottling
  6. High friction during tablet ejection

- These problems are related to powder properties, equipment design and condition of press and tooling

- Powder properties contributing to these problems
  1. Segregation tendency
  2. Flowability
  3. Friction and adhesion properties
  4. Compression properties and compactability

- Controlling these powder properties has been outlined in previous lectures

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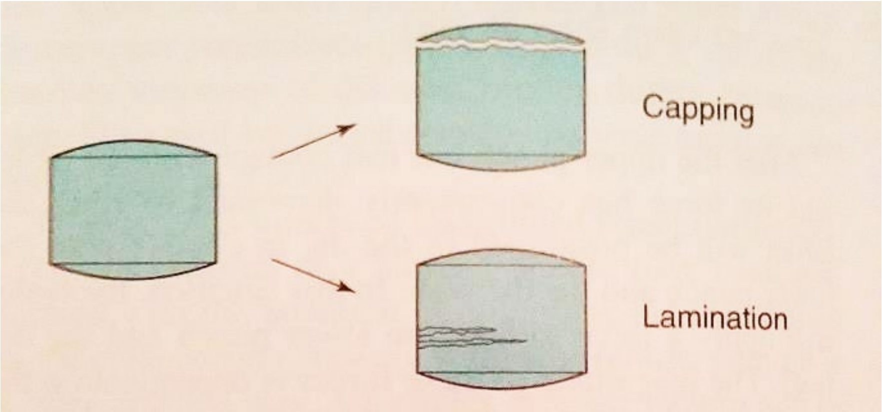
Tablet Defects: Capping & Lamination



- Capping and lamination
  - Capping: Partial or complete separation of the top or bottom crown on ejection of tablet or during handling
  - Lamination: Separation of a tablet into two or more layers

- Reasons
  - Formulation reasons: Inadequate binder, over-drying of granules, elastic material
  - Processing reasons: Air entrapment, concave tools, rapid speed of press

- Solutions
  - Formulation: Binder concentration, adjust granulation and drying steps, mill elastic materials
  - Process: Adjust speed of press, tool maintenance, tool shape design

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Tablet Defects: Picking & Sticking

- Picking and sticking
  - Picking: Slow removal of tablet's surface by the punch
  - Sticking: Adhesion of the tablet material to the die wall/ punch surface

- Reasons
  - Formulation reasons: Insufficient lubricant, excessive moisture, API/excipients with low melting point substances
  - Processing reasons: Damaged or unclean tools, logos, score marks

- Solutions
  - Formulation: Lubricant concentration, adjust granulation and drying steps, temperature-controlled tooling
  - Process: Tool maintenance, tool design

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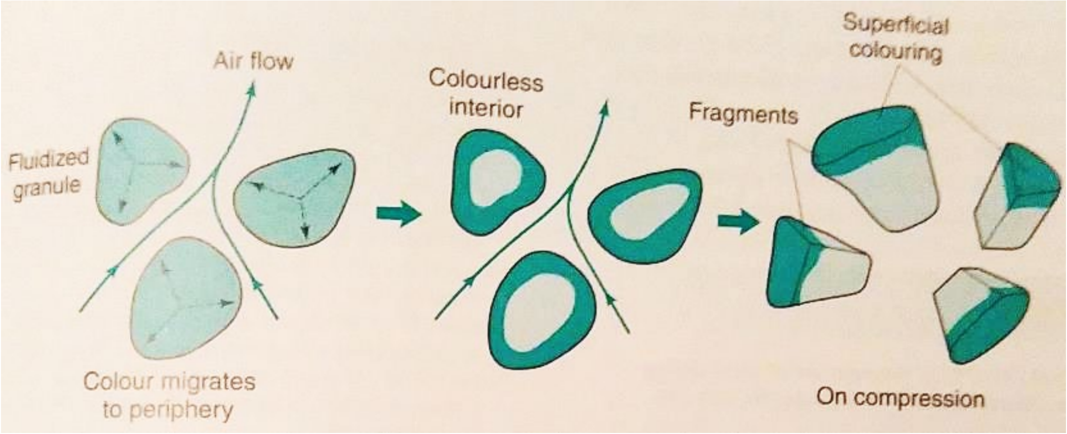
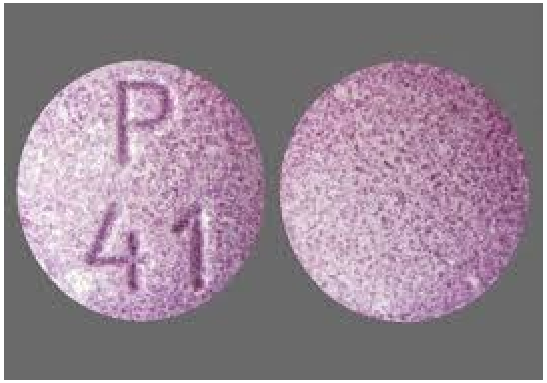
Tablet Defects: Mottling





- Mottling
  - Unequal distribution of colour

- Reasons
  - Solute migration: Colourants with high affinity for granulation fluid
  - Different colours of drug and excipients
  - Inadequate mixing of colour
  - Formation of degradation products

- Solutions
  - Minimise solute migration
  - Improve mixing of API and excipients
  - Tablet coating
  - Minimise degradation in manufacture process

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Time to revisit compression and compaction…

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Compression and Tabletting

- Compression in general
  - Particles initially rearranged in die and porosity is reduced
  - Deformation occurs once no further interparticulate movement is possible
  - Particle-particle bonds can form
  - Fracture can occur
  - Several cycles of fragmentation and deformation can occur

- Compression in granules
  - Compression can induce physical changes to the granules and/or physical changes to the particles making up the granules
  - Granules normally fill a die with low voidage (porosity) due to their improved flow and powder density, so little rearrangement normally occurs
  - Deformation occurs in granules due to elastic and plastic mechanisms of particles and also due to reduction of intragranular voids
  - Granules can also be broken down by attrition or by granule fragmentation into smaller granules, though studies have shown that granules are not usually prone to breaking down into smaller units during compression

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Compression and Tabletting

Table 31.2 Dominating compression mechanisms for dense particles and granules (porous particles)

Dense particles	Granules
Repositioning of particles	Repositioning of granules
Particle deformation	Granule deformation (permanent)
elastic	Granule densification
plastic	Granule fragmentation/attrition
viscous/viscoelastic	Deformation of primary particles
Particle fragmentation	

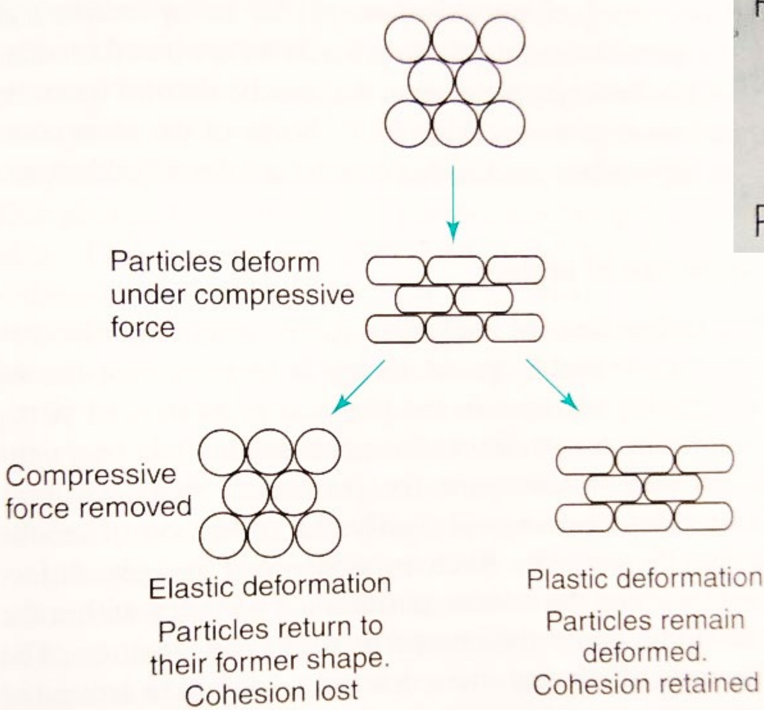

Fig. 31.24 Schematic illustration of particle deformation, elastic and plastic, during compression. (From Armstrong 1982.)

Compaction and Tabletting: Bonding Mechanisms in Tablets

1. Intermolecular forces
   - Referred to as adsorption bonding
   - Solid surfaces brought into intimate contact at an interface
   - They adsorb to each other
   - van der Waals and electrostatic interactions
   - Considered most common mechanism

2. Solid bridges
   - Referred to as the diffusion theory of bonding
   - Solid surfaces brought into intimate contact at an interface
   - Mixing occurs at interface to form a continuous phase region that fuses solids
   - Solid molecules must be capable of mobility during compression
   - Most likely to occur in partially melted or amorphous solids; also considered common

3. Mechanical interlocking
   - Interparticulate hooking due to irregular shape of particles
   - Rod and needle-shaped particles; less common for regular shapes

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Compaction and Tabletting: Bonding Mechanisms in Tablets

4. Binder bridges
   - Excipient forms intergranular bonds during compression in addition to its role in intragranular bonds
   - Binders can interact with binders in other granules or with other powder components in other granules

Table 31.4 Suggested predominant bond types in tablets formed from dense particles (interparticulate bonds) and from granules (intergranular bonds)

Interparticulate bonds	Intergranular bonds
Adsorption bonds (intermolecular forces)	Adsorption bonds of three types: binder–binder binder–substrate substrate–substrate
Solid bridges	Solid binder bridges

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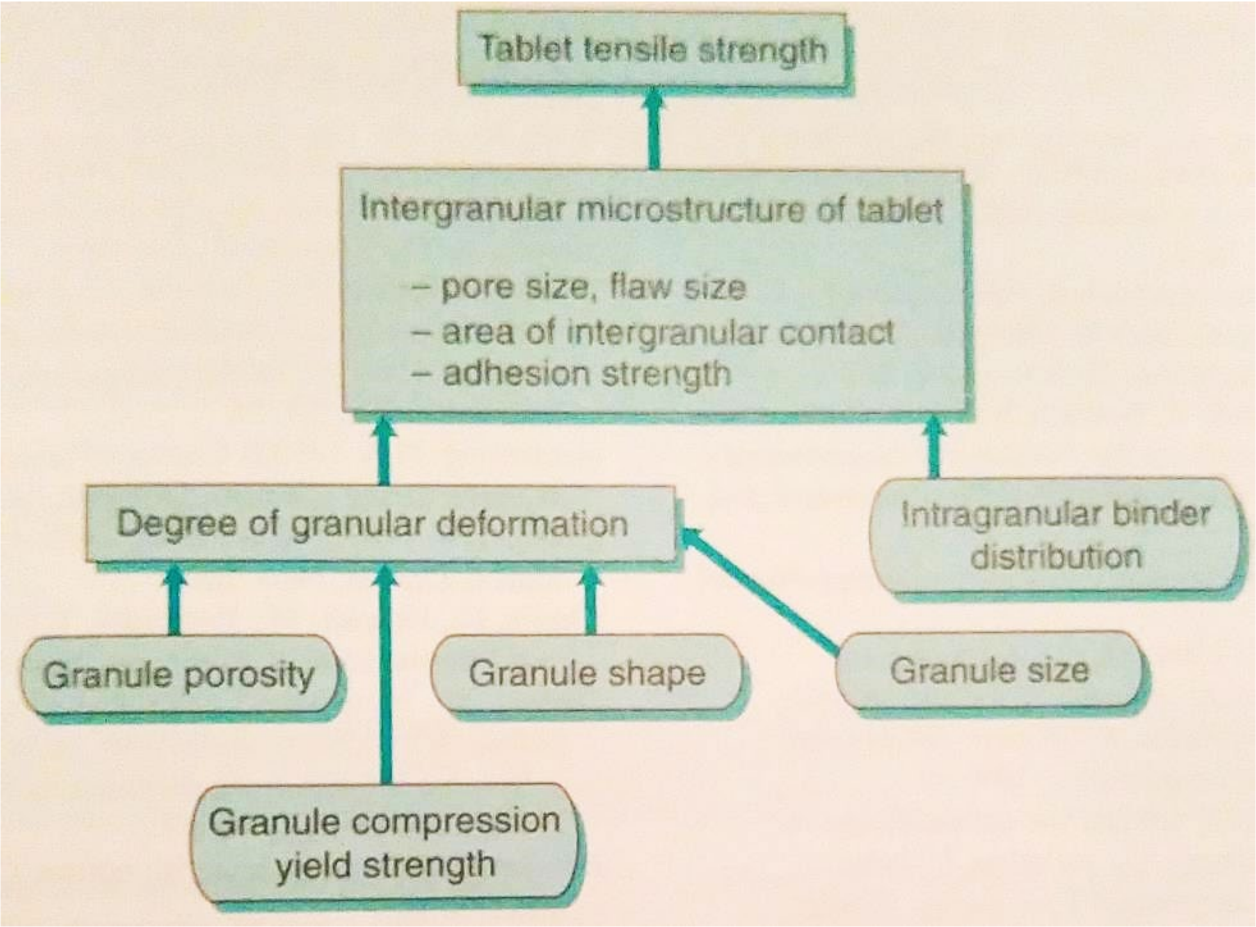
Compaction and Granules

- In general, compactability of granules will increase with:
  - Increased porosity
  - Decreased yield strength
  - Irregular shape
  - Increased binder concentration



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Application of Material Properties to Tablet Formulation

- The relationships between compaction pressure, tensile strength and solid fraction are critical to characterise the compaction process for a given powder mixture during tabletting

- This relationship is described by three parameters:
  1. Compactability-> Relationship b/w tensile strength and solid fraction
  2. Tabletability-> Relationship b/w tensile strength and compression pressure
  3. Compressibility-> Relationship between compaction pressure and solid fraction

- Evaluation of these factors provides valuable information on a tablet formulation
  1. Insight into the compaction process and mechanical properties of a material
  2. Assessment of deformation mechanism, yield pressure and porosity

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Application of Material Properties to Tablet Formulation: Case Studies

- 2001: Sun et al., Pharm. Res.
  - Investigation of properties of two polymorphs of sulphamerazine

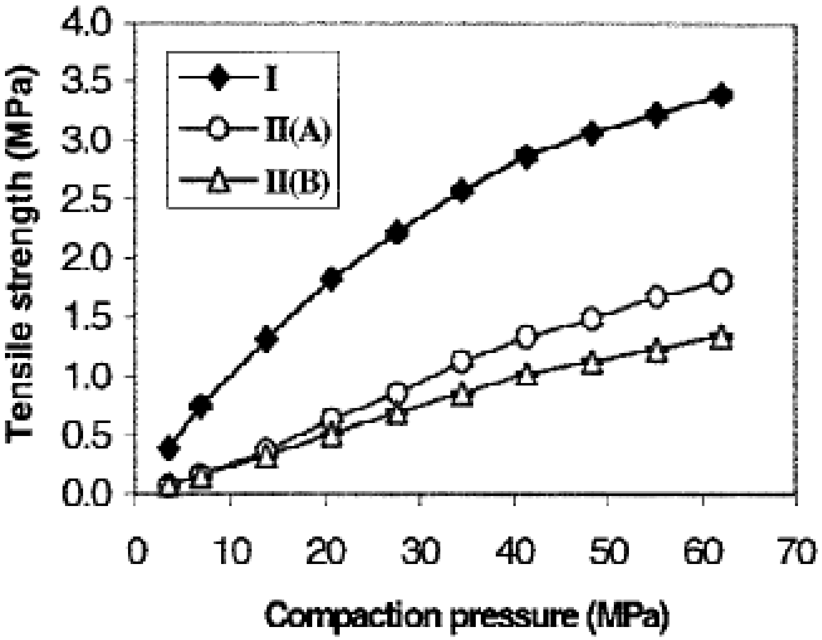

Fig. 3. Plots of tensile strength against compaction pressure, showing the tabletability of three powders of sulfamerazine, **I**, **II(A)**, and **II(B)**. The tabletability follows the order: **I** >> **II(A)** > **II(B)**.

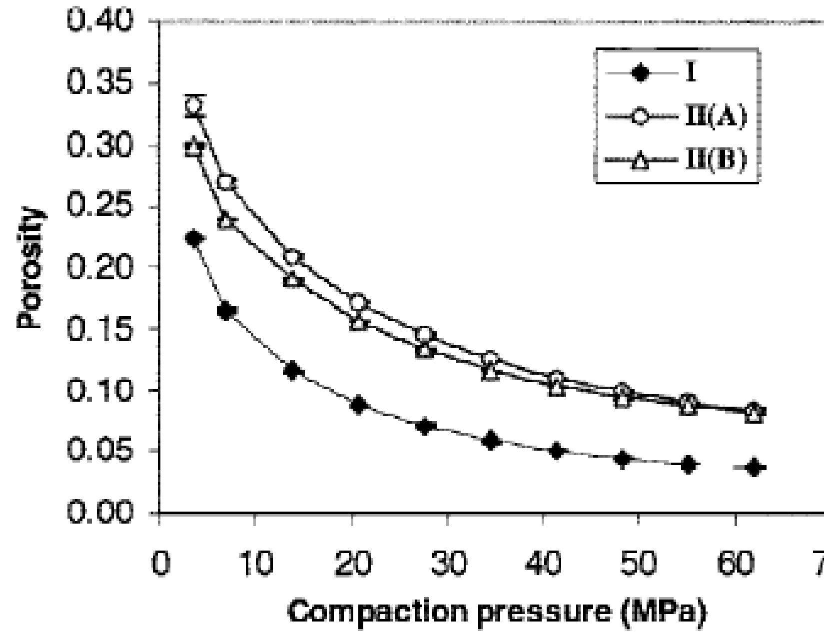

Fig. 4. Plots of tablet porosity against compaction pressure, showing the compressibility of three powders of sulfamerazine, **I**, **II(A)**, and **II(B)**. The compressibility follows the order: **I** >> **II(B)** > **II(A)**.

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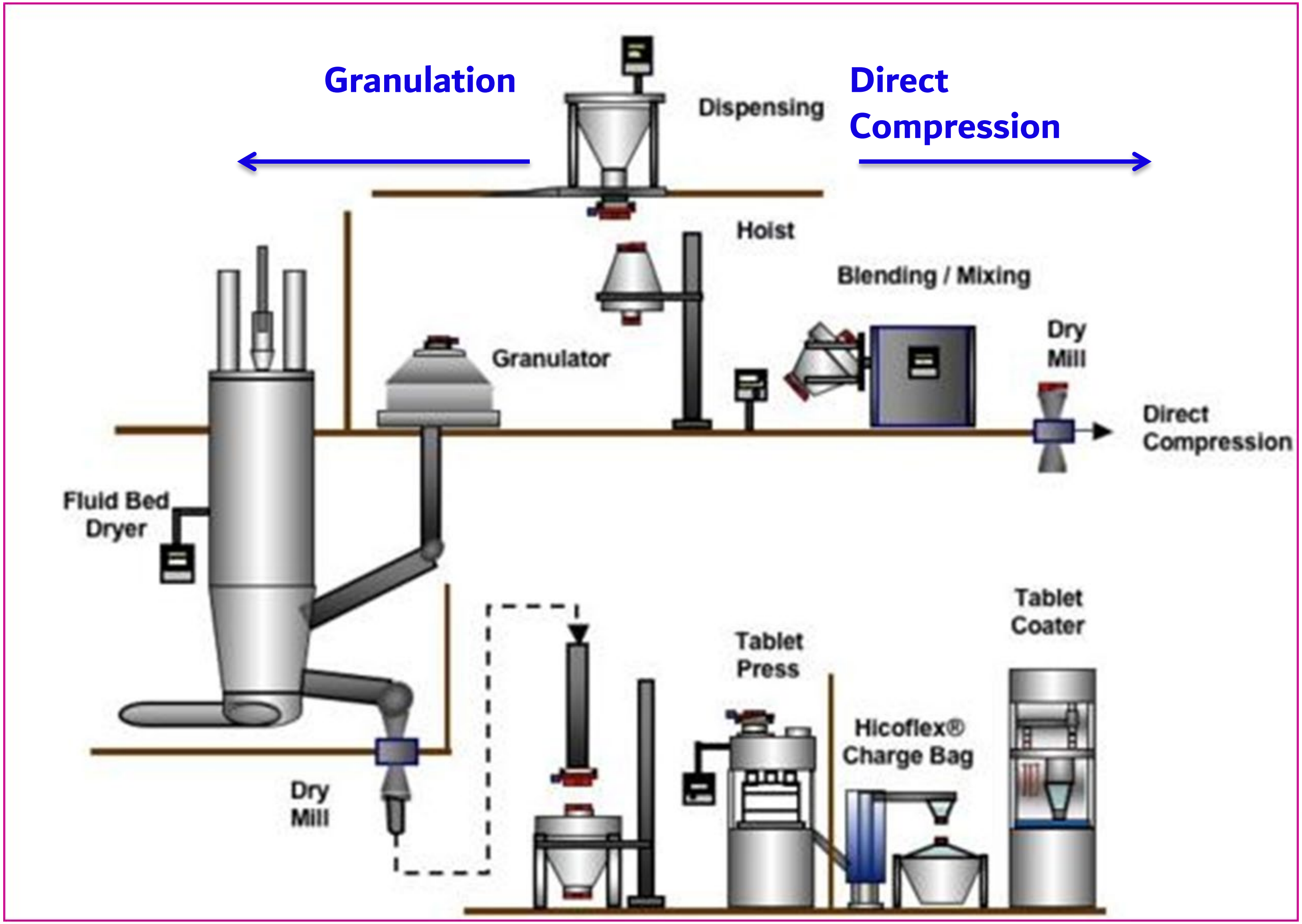
Tablet Manufacture: Summary of Processes



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Further Reading

- Aulton's Pharmaceutics Chapter
  - Tablets and Compaction

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