Tablet Compression operation

Part 6

Industrial pharmacy

5th class

1st semester

Tablet Compression Machines

Tablets are made by compressing a formulation containing a drug or drugs with excipients on stamping machines called presses.

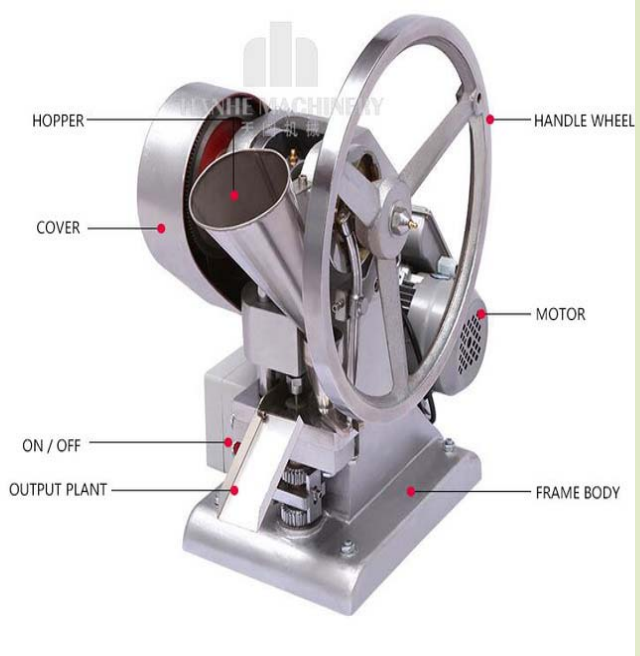
- **Tablet compression machines or tablet presses are designed with the following basic components:**

1. Hopper(s) for holding and feeding granulation to be compressed.
2. Dies that define the size and shape of the tablet.
3. Punches for compressing the granulation within the dies.
4. Cam tracks for guiding the movement of the punches.
5. A feeding mechanism for moving granulation from the hopper into the dies.

Tablet presses are classified as either single punch or multi-station rotary presses:

1. **All of the compression is applied by the upper punch, making the single punch machine a "stamping press".**

2. **Multi-station presses are termed *rotary* because the head of the tablet machine that holds the upper punches, dies, and lower punches in place rotates.**



Note:

i. As the head rotates, the punches are guided up and down by fixed cam tracks (control the sequence of filling, compression, and ejection).

ii. The portions of the head that hold the upper and lower punches are called the upper and lower turrets respectively.

iii. The portion holding the dies is called the die table.

Cam

Compression cycle

A. Granulation stored in a hopper that empties into the feed-frame which has several interconnected compartments.

B. These compartments spread the granulation over a wide area to provide time for the dies to fill.

C. The pull-down cam guides the lower punches to the bottom of their vertical travel, allowing the dies to overfill.

D. The punches then pass over a weight control cam, which reduces the fill in the dies to the desired amount.

E. A wipe-off blade at the end of the feed-frame removes the excess granulation and directs it around the turret and back into the front of the feed-frame.

F. Next, the lower punches travel over the lower compression roll.

G. while simultaneously the upper punches ride beneath the upper compression roll. The upper punches enter a fixed distance into the dies, while the lower punches are raised to squeeze and compact the granulation within the dies.

H. To regulate the upward movement of the lower punches, the height of the lower pressure roll is changed.

I. After the moment of compression, the upper punches are withdrawn as they follow the upper punch raising cam.

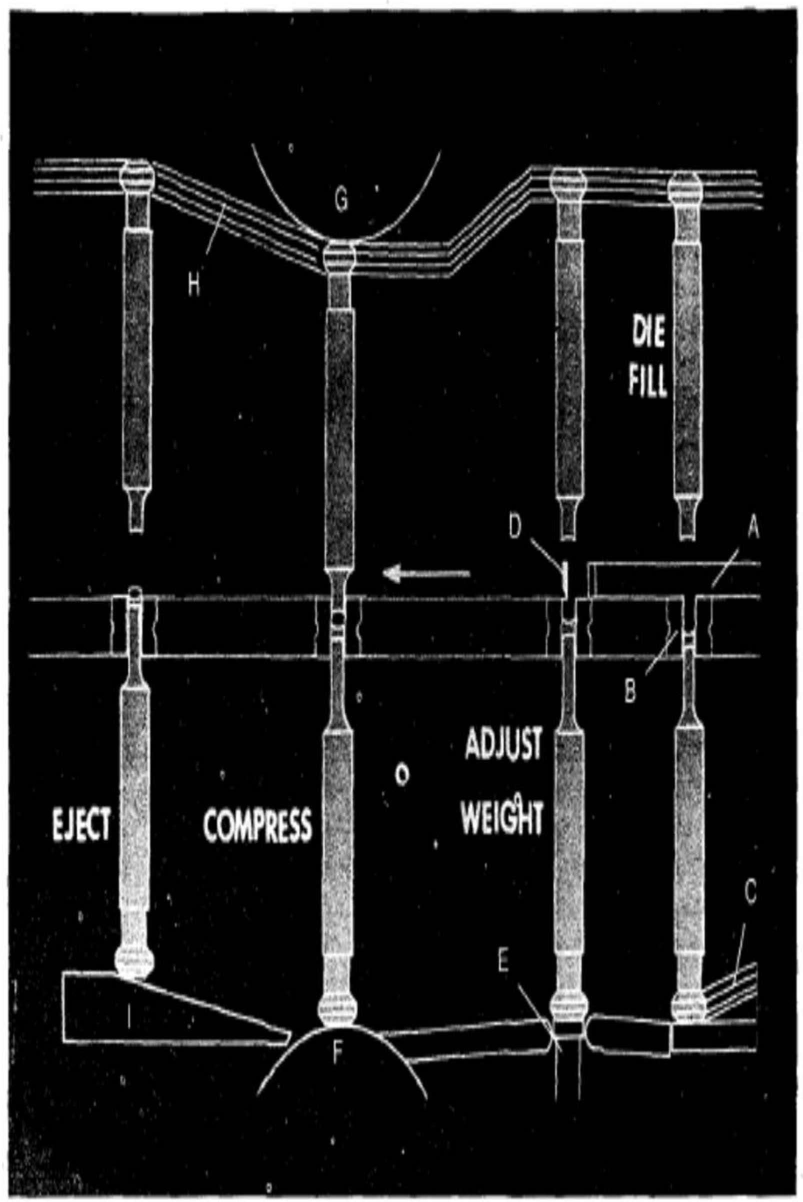


FIG. 11-6. The compression cycle of a rotary tablet press. (See text for explanation of lettered labels.) (Courtesy of Thomas Engineering, Hoffman Estates, IL.)

G. The lower punches ride up the cam, which brings the tablets flush with or slightly above the surface of the dies. **The exact position is determined by a threaded bolt called the *ejector knob*.**

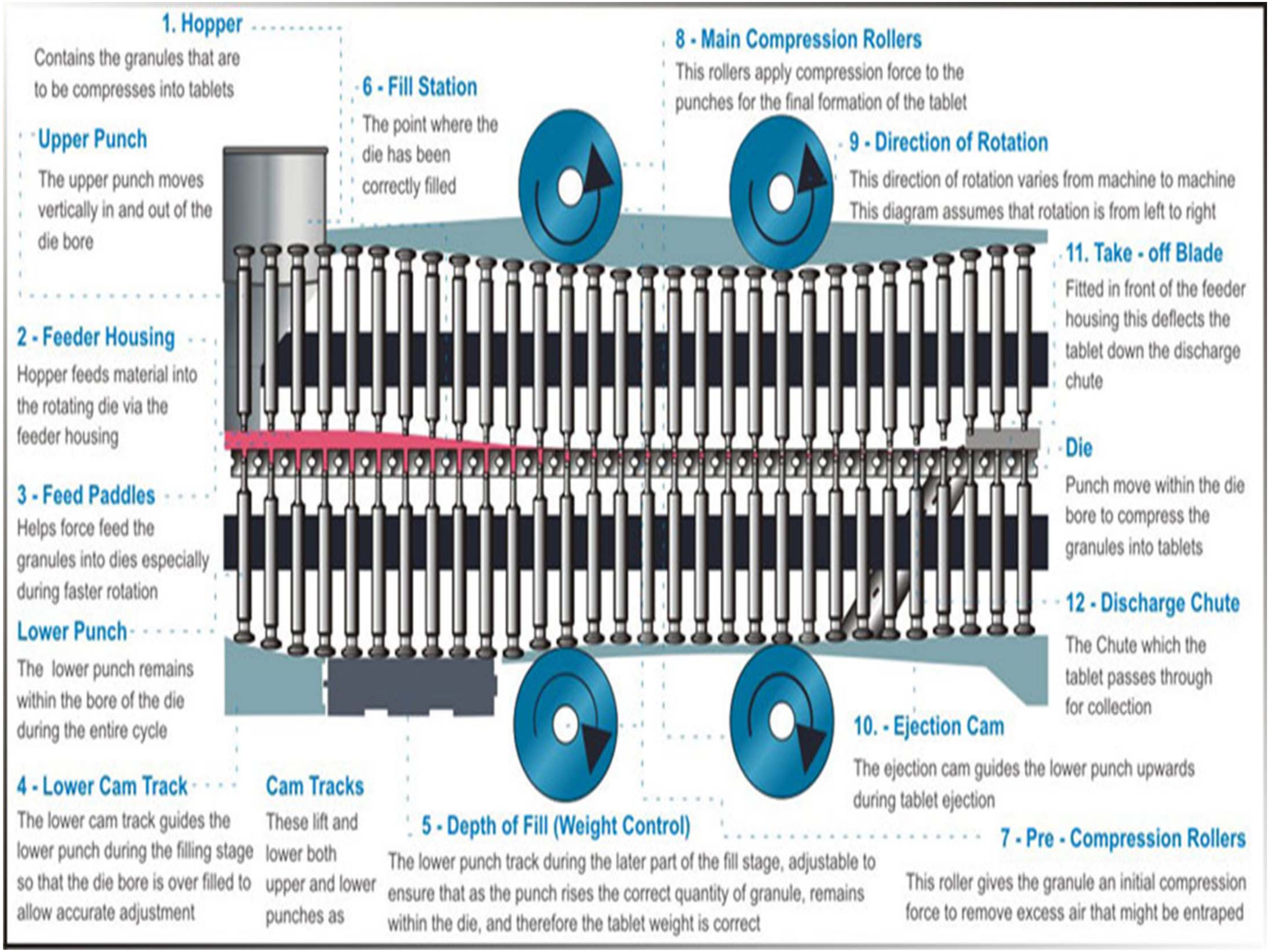
H. The tablets strike a sweep-off blade affixed to the front of the feed-frame (A) and slide down a chute into a receptacle. At the same time, the lower punches re-enter the pulldown cam (C), and the cycle is repeated.

Note:

Such features as capacity, speed, maximum weight, and pressure vary with the design of the equipment, but the basic elements remain essentially the same.

A tablet machine's output is regulated by three basic characteristics of its design:

1. **Number of tooling sets (dies, upper and lower punches)**
2. **Number of compression stations**
3. **Rotational speed of the press**


1. Hopper
Contains the granules that are to be compresses into tablets
Upper Punch
The upper punch moves vertically in and out of the die bore
2 - Feeder Housing
Hopper feeds material into the rotating die via the feeder housing
3 - Feed Paddles
Helps force feed the granules into dies especially during faster rotation
Lower Punch
The lower punch remains within the bore of the die during the entire cycle
4 - Lower Cam Track
The lower cam track guides the lower punch during the filling stage so that the die bore is over filled to allow accurate adjustment
Cam Tracks
These lift and lower both upper and lower punches as
5 - Depth of Fill (Weight Control)
The lower punch track during the later part of the fill stage, adjustable to ensure that as the punch rises the correct quantity of granule, remains within the die, and therefore the tablet weight is correct
6 - Fill Station
The point where the die has been correctly filled
7 - Pre - Compression Rollers
This roller gives the granule an initial compression force to remove excess air that might be entraped
8 - Main Compression Rollers
This rollers apply compression force to the punches for the final formation of the tablet
9 - Direction of Rotation
This direction of rotation varies from machine to machine
This diagram assumes that rotation is from left to right
10. - Ejection Cam
The ejection cam guides the lower punch upwards during tablet ejection
11. Take - off Blade
Fitted in front of the feeder housing this deflects the tablet down the discharge chute
Die
Punch move within the die bore to compress the granules into tablets
12 - Discharge Chute
The Chute which the tablet passes through for collection

Notes:

I. **In general, all rotary presses are engineered for fast and economical production of all kinds of tablets.** (Larger machines can readily produce several million tablets each in a working day, and their performance can be geared to continuous low-maintenance operation).

II. **Many modifications and options can be obtained from various manufacturers.**

(One modification, which is found on most modern high-speed tablet presses, **use of hydraulic or pneumatic pressure to control the pressure rolls in place of the older spring type pressure).**

- A smoother pressure or compressive load force over a longer period of time.
- More accurate and can be set with closer tolerances, which do not change with time or fatigue.

Compression Machine Tooling

The size and shape of a tablet as well as certain identification markings are determined by compression machine tooling set.

The tooling must meet many requirements:

1. Satisfy the needs of dosage uniformity

2. Production efficiency

3. Esthetic appearance.

Tooling sets

- **BB tooling** (5.25 inches in length, nominal barrel diameter of 0.75 inches and 1-inch head diameter).
- **B tooling** (identical to the BB type except that the lower punch is only $3^{9}/_{16}$ inches long).
- **D tooling** is popular for large tablets, (1-inch barrel diameter, $1^{1}/_{4}$-inch head diameter, and 5.25-inch length).

- The dies that are used with the above punches are either:

a) 0.945-inch outside diameter (OD) die capable of making a $^{7}/_{16}$-inch round tablet or $^{9}/_{16}$-inch capsule-shaped tablet.

b) 1 $^{3}/_{16}$-inch OD die capable of handling a $^{9}/_{16}$-inch round or $^{3}/_{4}$-inch capsule shaped tablet.

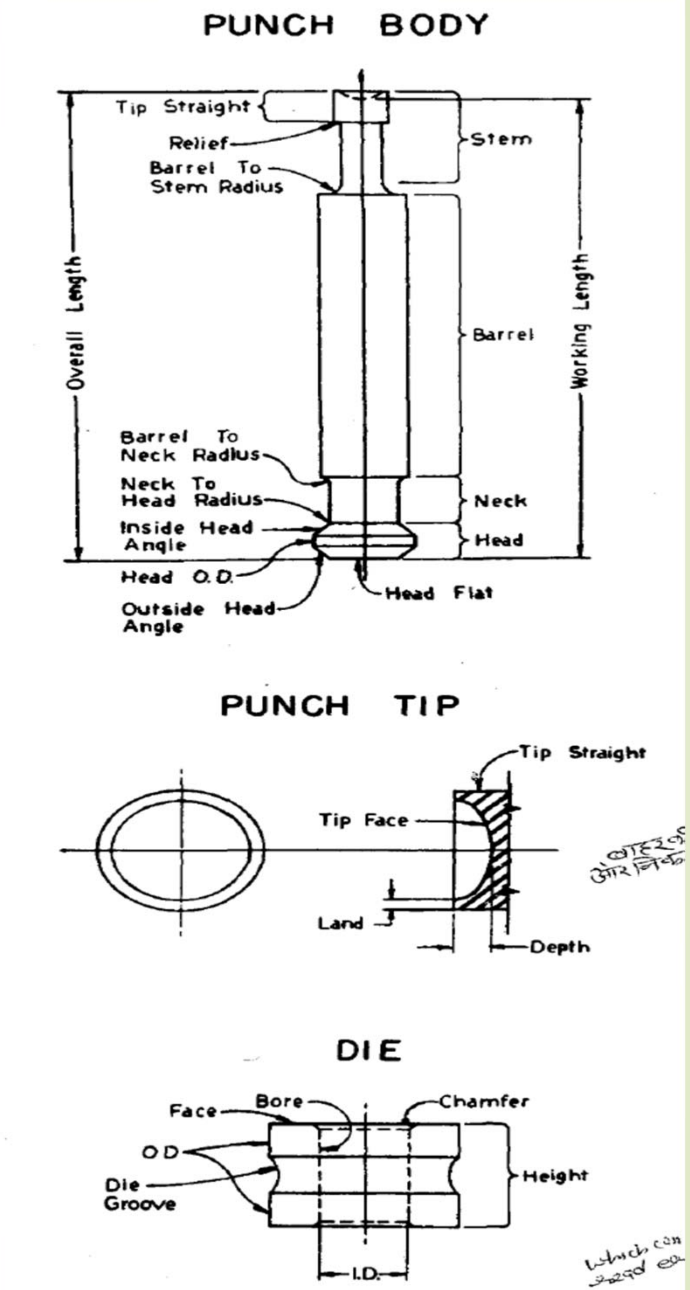


FIG. 11-9. Tablet press tooling nomenclature. (Courtesy of Thomas Engineering, Hoffman Estates, IL.)

Important notes:

I. **Several types of steel are normally used in the manufacture of compression tooling that differ in:** (toughness to withstand the cyclic compacting forces, ductility (elasticity), and in wear resistance).

II. No single steel type has a high resistance to abrasive wear and a high ductility.

III. **Selection of the best steel for a specific application must be based on:**

a. Experience and an accumulated history of the product being tabletted

b. Selection of the proper steel for a specific use

c. Shape of the punch tip, whether or not debossing is to be employed on the tooling

d. The expected compression forces

e. Materials to be processed are abrasive or corrosive.

IV. Tooling can be made with certain information (aid in producing a visibly unique tablet product).

Ex: Company names or symbols, trade names, dosage strength, or National Drug Code (NDC) numbers can be cut or engraved into a punch face, or the punches may be scored, to produce uniquely embossed or engraved tablets.

V. Even though tooling design would appear to be limitless, certain practical aspects do limit design implementation.

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Because of the movement of tooling during a compression operation, certain tablet shapes or contour configurations perform better than others.

Ex1: Round tablets perform better than irregularly shaped tooling since they do not require "keying" to maintain the proper upper punch orientation with the die.

Ex2: When the tip on an upper punch is not round, it must not rotate, or it will strike the edge of the die hole as it for compression. (To prevent this, a slot is cut longitudinally into the barrel of the punch and a key is inserted).

key protrudes a short distance so that it engages a similar slot cut into the upper punch guides on the tablet press.

VI. Lower punches do not need keys (because their tips remain within the die bore, which controls the axial movement of the punch).

VII. Because keyed punches cannot rotate, wear is distributed unevenly, and punch life is shortened.

How to put tools?

When a press is set up with keyed punches, the upper punches are inserted first to determine the placement of the dies.

Once the dies are properly aligned and seated, they are locked in place, and the lower punches are inserted.

Notes:

i. The more curvature that is built into a tablet contour, the more difficult it is to compress, especially if the tablet tends to laminate or cap.

ii. The engraving or embossing on a tablet must be designed to be legible, must not add to compression problems, must fit on the tablet surface.

Tools problems:

Because of its hard steel structure, tablet tooling may appear to be indestructible.

a. <u>During normal use, the punches and dies become worn</u>, and the cyclic application of stress can cause the steel to fatigue and break.

b. <u>Improper storage and handling can readily result in damage</u> that necessitates discarding of an entire tooling set.

c. <u>The punch tips are especially delicate and susceptible to damage if the tips make contact with each other, the dies, or the press turret</u> upon insertion or removal of the tools from the tablet machine.

Solving tool problems

- To avoid tooling damage, compressive loads or pressures at the pressure rolls must be translated into a calculation of pressure at the punch tips.

- As tablet punch diameter decreases, less force is required to produce the same pressure at the punch face, since the face represents a smaller fraction of a unit area (square inch).

Auxiliary Equipment

Problem 1: the speed of the die table is such that the dwell time of a die under the feed frame is too short to allow for adequate or consistent gravity filling of the die with granulation.

Causes: Improper filling of the dies with granulation results in unsatisfactory weight variation and content uniformity of the resulting tablets. A similar result can occur with a poorly flowing granulation.

Solution: mechanized feeders can be employed to force granulation into the dies

Problem 2: The high tablet output rates of modem presses demand that the granulation hoppers be refilled at frequent intervals; the larger the tablet is, the more frequently the hopper needs to be replenished.

Causes: Allowing a tablet machine to run "dry" results in a series of rapidly degenerating and unacceptable events:

1- low-weight tablets and tablets with poor weight variation are produced.

2- soft granulation is unable to be formed into tablets.

3- tooling is usually ruined, particularly with thin tablets, by the punches being forced together without any granulation between them. Because of the relatively low volume of press hoppers, the filling of hoppers by hand on high-speed presses is inefficient, increases the risk of-punch damage, and can contribute to weight variation problems.

Solution: mechanized equipment has been developed *to* load granulation into the press hoppers.

Problem 3: handling large quantities of material into the hoppers.

Solution: place bulk granulation containers directly above tabletting machines to gravity-feed the granulation into hoppers.

1. Either by placing bulk granulation containers on floors above a tablet machine, and granulation can then be directed through openings in the floor into the hoppers.
2. Or granulation containers can be held on mezzanines above tablet machines. If such overhead room is unavailable, hoists and mechanical lifts can be used to elevate granulation containers or material transfer devices directly in position above the press.
3. Also granulation level sensors can be used to stop the press automatically when the granulation level drops to a critical level in the hopper.

Problem 4: The high rate of tablet output with modem presses calls for a higher frequency or even continuous monitoring of tablet weight.

Solution: Electronic monitoring devices, such as the Thomas Tablet Sentinel, Phannakontroll, and the Kilian Control System-Me:

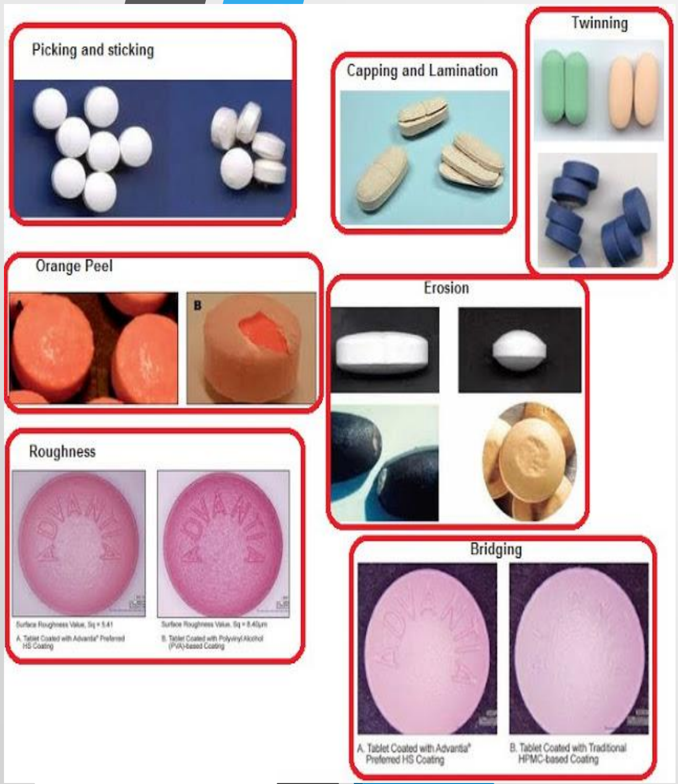
1. Monitor the force at each compression station, which correlates with tablet weight.
2. Monitors are also capable of initiating corrective actions, altering the amount of die fill to maintain a fixed force, ejecting tablets that are out of specification, counting, and documenting the machine operation throughout the run.

Another auxiliary: In almost all cases, tablets coming off a tablet machine bear excess powder and are run through a tablet deduster to remove that excess.

Thomas tablet Sentinel

In Process Quality control

Part 7



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In-Process Quality Control

- **During the compression of tablets, in-process tests are routinely run to monitor the process, including tests:**
  - Tablet weight
  - Weight variation
  - Hardness
  - Thickness
  - Disintegration
  - Various evaulations of elegance.

- **The in-process tests are performed by production and/or quality control (QC)**

Processing Problems

The source of the problem:

1. **Formulation**
2. **Compression equipment**
3. **Combination of the two.**

Capping and Lamination.

Capping: describe the partial or complete separation of the top or bottom *crowns* of a tablet from the main body of the tablet.

Lamination: *is the* separation of a tablet into two or more-distinct layers.

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Appear immediately after compression or occur hours or even days, later.

Detection of these problems: subjecting tablets to friability test.

Causes of the problems:

1. During the compression process, air is entrapped among the particles or granules and does not escape until the compression pressure is released.
2. Capping and lamination are due to the deformational properties of the formulation during and immediately following compression.

MECHANSIM:

I. During compaction, particles undergo sufficient plastic deformation to produce die-wall pressures greater than can be relieved by elastic recovery when the punch pressure is removed.

II. In some materials, this die-wall pressure causes enough internal stress to cause a crack to propagate and initiate fracture of the compact in the die.

III. If the excess stresses do not initiate fracture upon decompression in the die, the compact may laminate or cap upon ejection from the die.

IV. The emerging portion of the compact expands while the confined portion cannot, thus concentrating shear stresses at the edge of the die and causing a break to develop.

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Rapid decompression results in tablets that fracture.

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While tablets that do not fracture have the ability to relieve shear stress (stress relaxation) which is time-dependent; therefore, the occurrence of tablet fracture is also time dependent.

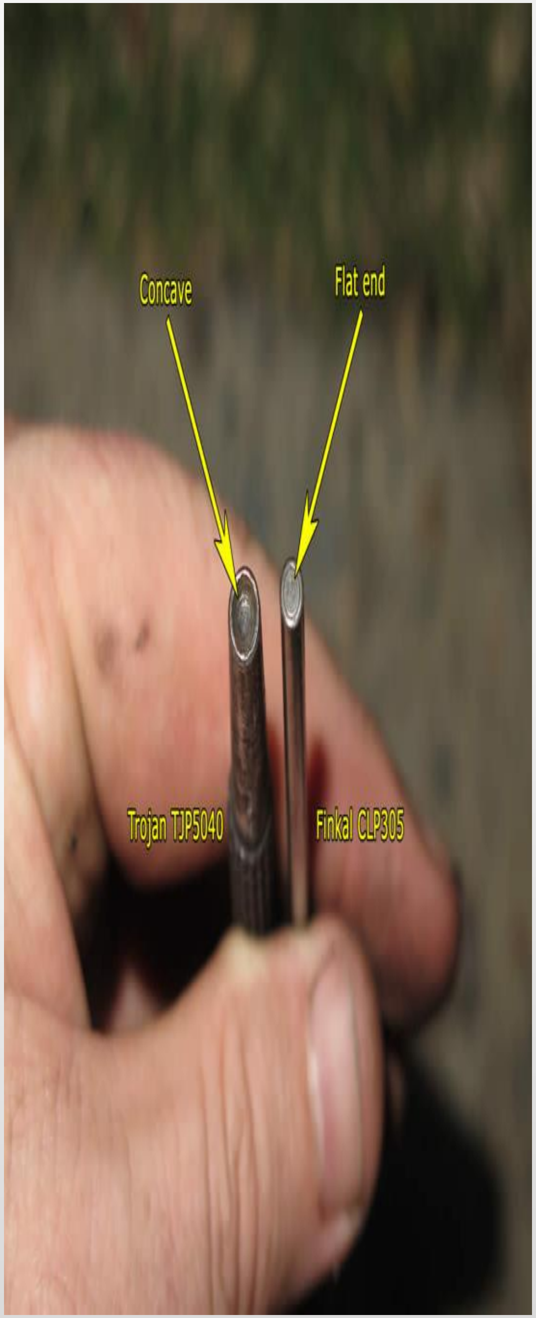
ELIMINATION OF CAPPING AND LAMINATION:

1. Precompression
2. Slowing the tabletting rate
3. Reducing the final compression pressure.

I. As the stress relaxation time is increased
II. The amount of stress needing to be relieved is reduced
III. Allowing an intact compact to be formed.

PROBLEM: deep concave punches produce tablets that cap (curved part of such tablets expands radially while the body of the tablet cannot, which establishes a shear stress that produces the fracture).

Solution: Flat punches may eliminate this additional shear stress.



PROBLEM: A granulation that is too dry tends to cap or laminate for lack of cohesion.

Solution: A certain percentage of moisture is often essential for good compaction (in moisture-critical granulations, the addition of a hygroscopic substance, e.g., sorbitol, methylcellulose, or PEG 4000, can help to maintain a proper moisture level).

PROBLEM: Capping and lamination in direct compression product (powder or fine particulate materials may not be compressible or may have poor compression properties).

Solution: Relative compressibility of various materials may be reflected by their degree of consolidation (crown thickness) when compressed in standard tooling under identical compression conditions.

PROBLEM: Tablet tooling is a cause of capping.

Causes:

1. The concave or beveled edge faces of punches (gradually curve inward with use and form a "claw" that can pull off the crowns of a tablet).
2. Wear in the upper punch (accelerates this claw formation by permitting the punch tips to strike the edges of the die hole).
3. The greater the radius of curvature of the punch face (greater is the force exerted on the edges and the less on the center of the tablet at the moment of compression).

PROBLEM: Dies develop a wear "ring" in the area of compression.

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As the ring develops, and enlarges, the tablets that are compressed in the rings have a diameter that is too large to pass easily through the narrower portion of the die above the ring.

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Upon ejection, this constriction causes the tablet to cap or laminate.

Cause:

Wear on tablet tooling increases as the hardness of the material being compressed increases (most organic materials are soft; certain inorganic materials such as magnesium trisilicate are relatively hard and abrasive).

Solution:

1. Turn the die over so that compression occurs in an unworn area above the ring.
2. On some presses, the depth of penetration of the upper punch can be regulated so that compression may be performed over some range of locations within the die.
3. Using dies with tungsten carbide inserts. The carbide is so durable that the casing wears out before the insert does.

PROBLEM: The punch remains below the face of the die, so sweep-off blade cuts off the tablet, leaving the bottom in the die) and can also result in tablet fracture.

Causes:

1. **Incorrect setup of the press causes a capping (the edge of the tablet catches on the die and chip).**
2. **The blade is adjusted too high (tablets can start to travel under it, become stuck, and break off).**

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The resulting broken pieces of tablets then enter the feed frame; if they are large enough, they can cause a disruption of the granulation feed, as well as affect the weight and hardness of subsequent tablets.

Solution:

Adjust a compressed tablet ejection from the die so the lower punch must rise flush with or protrude slightly above the face of the die at the point where the tablet strikes the sweep-off blade.

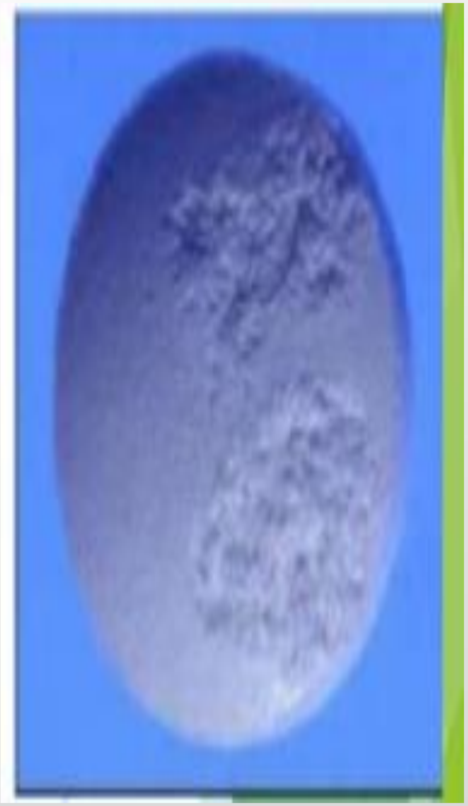
Picking and Sticking.

"Picking": is a term used to describe the surface material from a tablet that is sticking to and being removed *from* the tablet's surface by a punch.

CAUSES: concern when punch tips have engraving or embossing.

Example: *Small* enclosed areas such as those found in the letters "B," "A," and "o" are difficult to manufacture cleanly.

Tablet materials that stick to the punches can accumulate to the point of obliterating the tip design.



STICKING: refers to tablet material adhering to the die wall.

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Additional force is required to overcome the friction between the tablet and the die wall during ejection.

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Serious sticking at ejection can cause chipping of a tablet's edges and can produce a rough edge.

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Also, a sticking problem does not allow the lower punch free movement and therefore can place unusual stress on the cam tracks and punch heads, resulting in their damage.

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Sticking can also apply to the buildup of material on punch faces.

Sticking occurs when particles adhere to the punch face

SOLUTION:

1. Lettering should be designed as large as possible, particularly on punches with small diameters. The tablet can perhaps be reformulated to a larger size.
2. Plating of the punch faces with chromium (produce a smooth, nonadherent face).
3. Colloidal silica added to the formula (acts as a polishing agent and makes the punch faces smooth so that material does not cling to them). Frictional nature of this material may require additional lubrication to facilitate release of the tablet from the die.
4. Additional binder or a change in binder (make granules more cohesive, less adherent than before).

PROBLEM: low-melting-point substances, either active ingredients or additives such as stearic acid and polyethylene glycol, may soften sufficiently from the heat of compression to cause sticking.

Solution:

1. Dilution of the active ingredient with additional higher-melting-point materials → consequent increase in the size of the tablet that may help.
2. The level of low-melting-point lubricants may be reduced, or higher-melting-point replacements may be substituted.
3. When a low-melting-point medicament is present in high concentration, refrigeration of the granulation and the press may be in order.
4. Excessive moisture may be responsible for sticking, and further drying of the granulation is then required.

Mottling.

Mottling is an unequal distribution of color on a tablet, with light or dark areas standing out in an otherwise uniform surface.

Cause of mottling: is a drug whose color differs from the tablet excipients or a drug whose degradation products are colored.

Solution: use of colorants may solve the above problem but can create others.

- A dye can cause mottling by migrating to the surface of a granulation during drying.
- To overcome this difficulty, the formulator may **(change the solvent system, change the binder system, reduce the drying temperature, or grind to a smaller particle size).**

Note: The use of colorants in direct compression formulations can lead to mottling if the dye is not well dispersed or if its particle size is too large.

PROBLEM: Certain colored adhesive gel solutions may not be distributed well because they must be hot when added to much cooler powder mixtures. The adhesive then precipitates from solution and carries most of the color with it.

Temporary solution: Further wetting, even overwetting, is needed to disperse the binder and the color. The additional mixing and increased activation of the binder, however, *may result in tablets with increased disintegration times.*

Permeant solution: Therefore, a better practice may be to:

1- incorporate fine powder adhesives such as acacia and tragacanth into the product before adding the granulating fluid,

2- or disperse a dry color additive during the powder blending step.

Weight Variation.

The weight of a tablet being compressed is determined by the amount of granulation in the die prior to compression.

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Anything that can alter the die-filling process can alter tablet weight and weight variation.

Granule Size and Size Distribution Before Compression.

Variations in the ratio of small to large granules and in the magnitude of difference between granule sizes

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Influence how the void spaces between particles are filled.

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- If large granules are used to fill a small die cavity (relatively few granules are required) → the average may represent a high percentage weight variation.
- If hundreds of granules are required on the average for die fill, (variation of a few granules around the average would produce a minor weight variation, given a narrow particle size range).

Poor Flow.

The die-fill process is based on a continuous and uniform flow of granulation from the hopper through the feed frame.

Problem:

a. When the granulation does not flow readily, it tends to move spasmodically through the feed frame so that some dies are incompletely filled.

b. Similarly, dies are not filled properly when machine speed is in excess of the granulation's flow capabilities.

Solution:

1. Addition of a glidant (talcum or colloidal silica), or an increase in the amount already present, may be helpful.
2. Induced die feeders, which mechanically "force" the granulation down into the die cavities as they pass beneath the feed frame.

Problem: Poor flow through the feed frame (a sign that the granulation is not flowing properly out of the hopper).

As particulate solids move under the force of gravity through progressively smaller openings; they are subjected to uneven pressures from the mass above and alongside.

Depending on the geometry of the hopper, this situation may give rise to one or another of two causes for poor flow: "arching" or "bridging," and "rat-holing.

When poor hopper flow occurs, it may be controllable with vibrators attached to the hopper sides to induce the granulation flow.

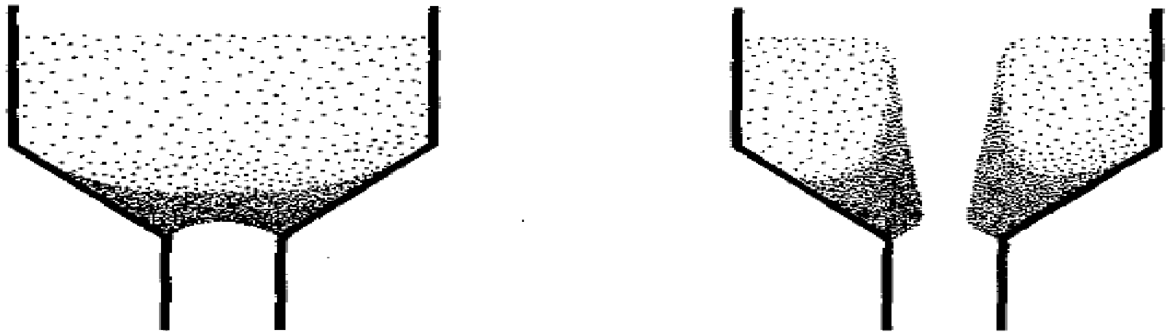

FIG. 11-12. *Bridging (left); rat-holing (right).*

Another problem arise: most tablet granulations consist of materials with a range of particle sizes.

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Vibration or mixing action of the flow promoting devices may induce segregation and stratification of the particles.

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The larger particles tend to drift upward while the smaller particles sift downward.

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Changes in tablet weight and weight variation but it can also lead to poor content uniformity, since drug is often not uniformly distributed between the larger and smaller particles.

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A new feed frame design that accommodated excessive flow from the hopper without compromising uniform weight variation.

Poor Mixing.

Problem 1: lubricants and glidants are not thoroughly distributed.

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The flow of particles is then impaired, and the granules do not move efficiently into the dies.

Problem 2: a tendency to minimize the mixing time during lubricant addition to prevent or reduce granule friability

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Inadequate mixing during this stage can result in unsatisfactory granulation flow.

Punch Variation.

Problem: When lower punches are of unequal lengths-the difference may be only a few thousandths of an inch-the fill in each die varies because the fill is volumetric.

Solution: Only a good punch and die control program can provide tooling of uniform dimensions.

Hardness Variation.

Hardness variation → weight variation.

Hardness depends on:

1. **Weight of material**
2. **Space between the upper and lower punches at the moment of compression.**

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If the volume of material or the distance between punches varies → hardness is inconsistent.

Double Impression.

This involves only punches that have a monogram or other engraving on them.

Problem: At the moment of compression, the tablet receives the imprint of the punch. On some machines, the lower punch is free to drop and then travel uncontrolled for a short distance before it rides up the ejection cam to push the tablet out of the die.

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During its free travel, it rotates.

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At this point, the punch may make a new, although lighter, impression on the bottom of the tablet, resulting in a double imprint.

Problem: Similar problems can be encountered with engraved upper punches and tablet machines that utilize two compression stages to compress a tablet.

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The first stage (*precompression)* uses a lower compaction force than the final compression stage

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But the tablet does receive the imprint of the punch.

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If the upper punch is uncontrolled, it can rotate during the short travel to the final compression stage and thus create a double imprint.

Solution for both problems: The newer presses have anti-turning devices as an integral part of their design and construction.


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