TABLET

Narin Kakarum

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INTRODUCTION

- Tablets are compressed solid unit dosage forms containing one or more medicaments, usually circular in shape and flat or biconvex. They are the most popular dosage form and account for 70% of all dispensed medications. Tablets are prepared by compressing drugs or a mixture of drugs with or without diluents, and may contain excipients.

ADVANTAGES & DISADVANTAGES

- Advantages of tablets:

Tablets offer several advantages as a dosage form, including ease of administration, dispensing, and storage. They are typically more stable than other dosage forms, and provide accurate dosing. Tablets also allow for the easy administration of bitter or nauseous substances. They are light and compact, making them convenient for patients to carry and use. Additionally, sustained-release products can be achieved through enteric coating. Finally, tablets are often more economical than other dosage forms.

- Disadvantages of tablets:

Despite their advantages, tablets also have some limitations. Compression of crystalline drugs can be challenging, and hygroscopic drugs may not be suitable for compressed tablets. Formulating drugs with low solubility or slow dissolution rates can also be difficult. Additionally, coating and encapsulation to mask bitter or unpleasant tastes can increase production costs. Finally, tablets can be difficult to swallow, particularly for children and ill or unconscious patients.

TYPES OF TABLET

(A) Tablets ingested orally

1. Compressed tablet, e.g. Paracetamol tablet
2. Multiple compressed tablets,
3. Delayed release tablet, e.g. Enteric coated Bisacodyl tablet
4. Sugar coated tablet, e.g. Multivitamin tablet

(B) Tablets used in oral cavity

1. Buccal tablet, e.g. Vitamin-c tablet
2. Sublingual tablet, e.g. Vicks Menthol tablet
3. Troches or lozenges
4. Dental cone

(c) Tablets administered by other route

1. Implantation tablet, e.g. Testosterone tablet
2. Vaginal tablet, e.g. Clotrimazole tablet
3. Hypodermic tablet

(D) Tablets used to prepare solution:

1. Effervescent tablet, e.g. Disprin tablet (Aspirin)
2. Dispensing tablet, e.g. Enzyme tablet (Digiplex)
4. Tablet triturates e.g. Enzyme tablet (Digiplex)

TABLETS INGESTED ORALLY

1. Compressed tablets are made by compressing granules, and provide rapid disintegration and drug release
2. Multiple compressed tablets are used to separate incompatible ingredients or produce repeat action products.
3. Sustained action tablets release medication as needed to maintain a consistent concentration of the drug in the blood.
4. Enteric coated tablets dissolve in the intestine, and sugar coated tablets mask bitter tastes and odors.
5. Film coated tablets have a protective film coating, while chewable tablets are easily administered and broken down quickly in the mouth.

ORAL CAVITY TABLETS

- Buccal tablets: placed in buccal pouch or between gum and cheek, dissolve and absorb directly.
- Sublingual tablets: placed under tongue, dissolve quickly and absorbed directly without passing through the digestive tract.
- Lozenge tablets and troches: designed for local effect on mouth or throat, used for sore throat or cough, contain various agents like anaesthetics and antiseptics.
- Dental cones: minor compressed tablets for placing in empty tooth sockets after extraction, containing antibacterial compounds and astringents to prevent growth of bacteria and reduce bleeding.

TABLETS ADMINISTERED BY OTHER ROUTE

1. Implantation tablet:

   Implantation tablets are compressed tablets that are placed below the skin or inserted subcutaneously through a minor surgical operation. They are slowly absorbed and must be sterile. They are made by heavy compression and fusion and are used for drugs like testosterone.

2. Vaginal tablet:

   Vaginal tablets are solid, medicated dosage forms designed to slowly dissolve in the vaginal cavity. They are typically ovoid or pear-shaped and are used to release steroids, antibacterials, antiseptics, and other medications to prevent or treat infections. Examples include clotrimazole tablets.

TABLETS USED TO PREPARE SOLUTIONS

- Effervescent tablet: Dissolve rapidly in water due to chemical reaction, e.g. Disprin tablet (Aspirin)
- Dispensing tablet: Added to water to produce a solution of given concentration, e.g. Enzyme tablet (Digiplex)
- Hypodermic tablet: Composed of one or more drugs, dissolved in sterile water and administered parenterally
- Tablet triturates: Small compressed tablets containing a potent medicament with a diluent, e.g. Enzyme tablet (Digiplex)

EXCIPIENTS IN TABLET FORMULATION

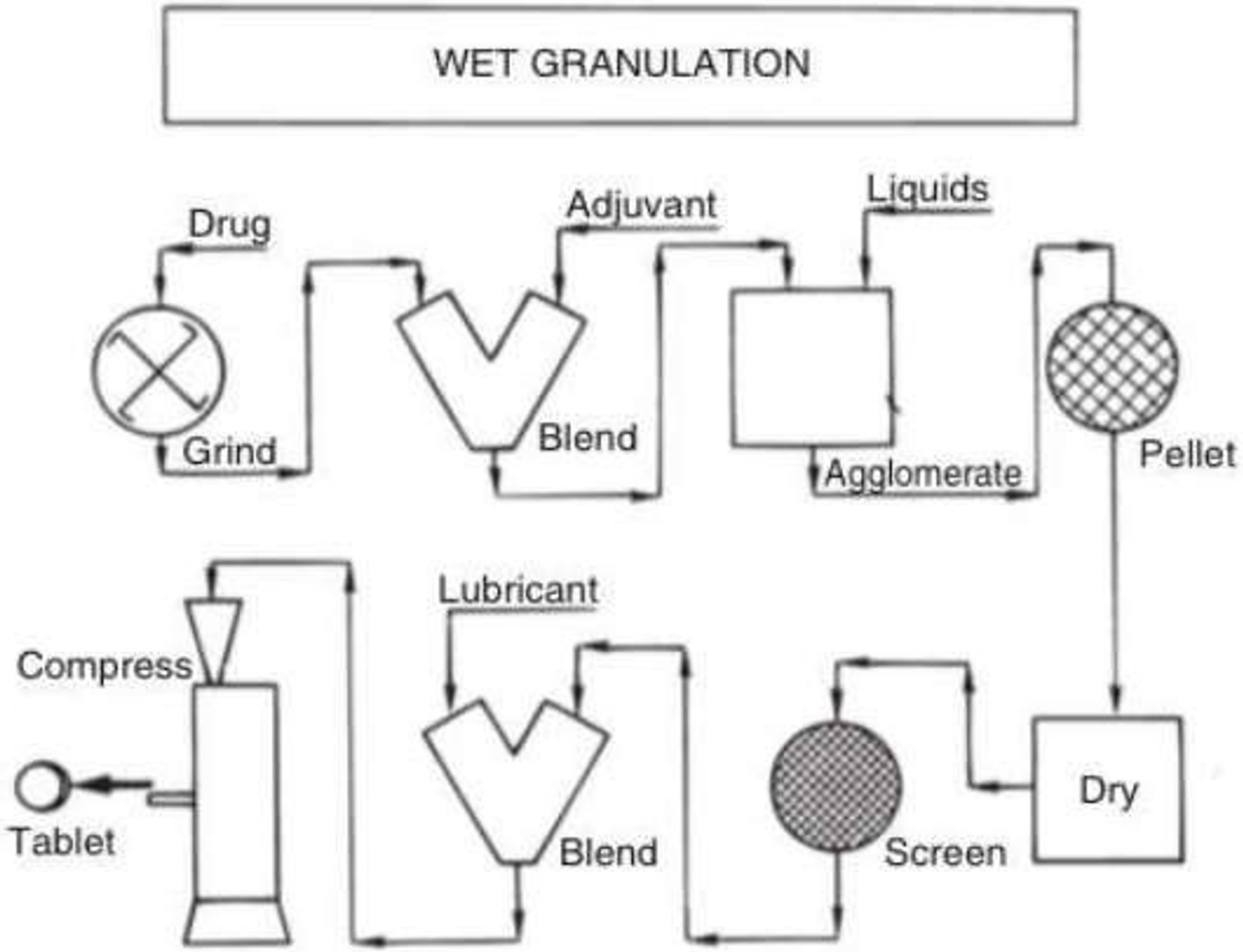
1. Diluents: Increase the bulk of tablets when the quantity of medicament is small. Examples include lactose, sucrose, sodium chloride, dextrose, and starch.
2. Disintegrating agents: Break tablets into smaller particles when swallowed. They can work by swelling, producing effervescence, or melting at body temperature. Some are mixed with other excipients before granules formation, and others are mixed with dry granules before compression. Examples include potato, maize, and wheat starch.
3. Granulating agents: Provide moisture to convert fine powder into a damp mass that forms granules after passing through a sieve. Examples include starch paste, acacia, tragacanth, gelatin solution, and isopropyl alcohol.
4. Glidants: Improve the flow properties of granules. Examples include magnesium stearate and talc.

5. Lubricants: reduce friction during compression and ejection of the tablet
6. Binding agents: provide strength to keep the tablet intact
7. Adsorbing agents: prevent sticking of ingredients
8. Colors, flavors, and sweeteners: added for aesthetic and palatability purposes. All colors used in tablets must be FDA-approved.

MANUFACTURING OF COMPRESSED TABLETS

- PREPARATION OF GRANULES FOR COMPRESSION:
- Methods includes:
- WET GRANULATION

Wet granulation is a common method for producing compressed tablets. The process involves weighing and blending ingredients, creating a damp mass, screening the mass into granules, drying the granules, sizing them, adding lubricant, and then compressing them into tablets.

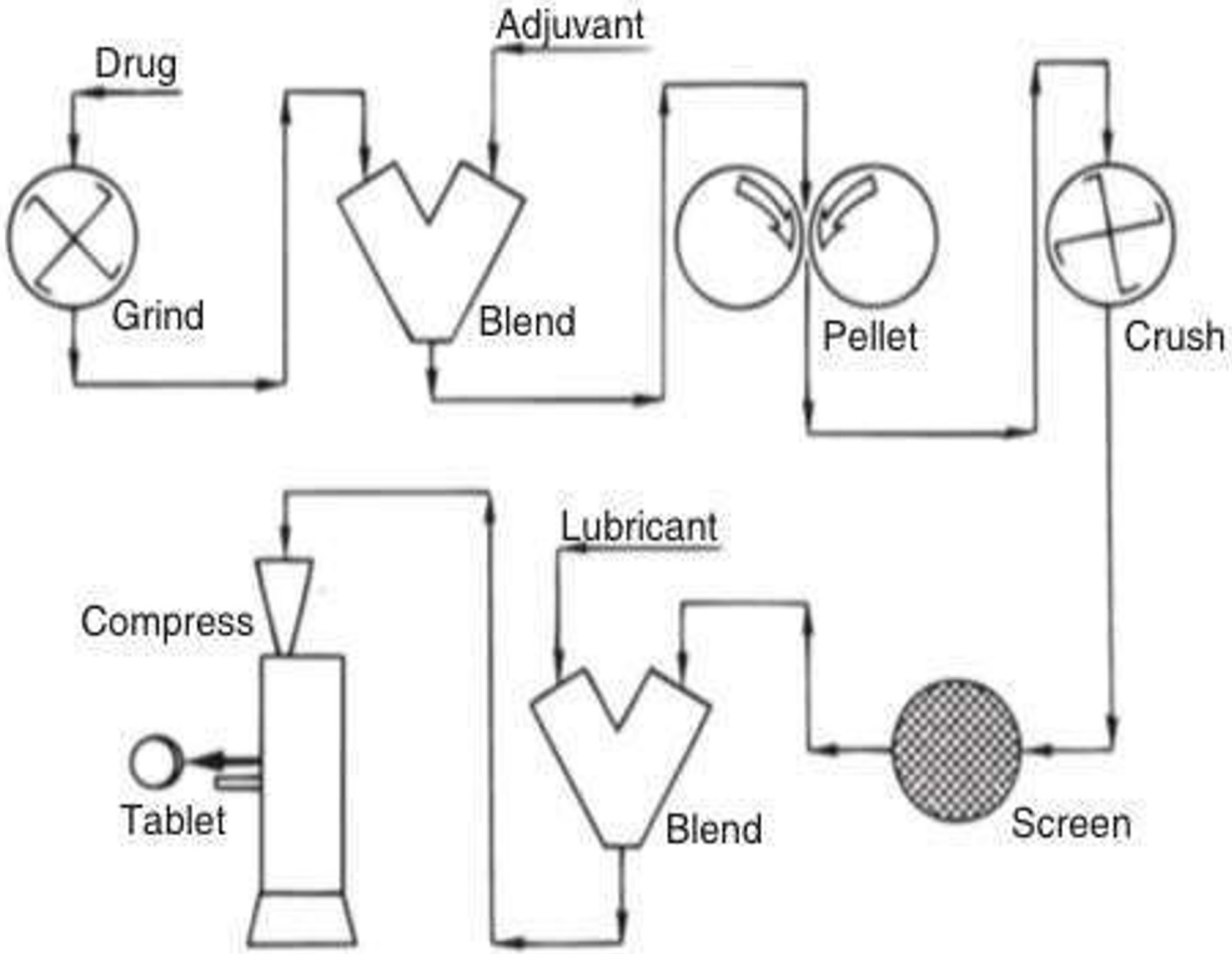

WET GRANULATION
Drug
Adjuvant
Liquids
Grind
Blend
Agglomerate
Pellet
Lubricant
Compress
Tablet
Blend
Screen
Dry

Wet granulation is a widely used method for producing compressed tablets, with advantages such as reduced segregation and the ability to accommodate low and high concentrations of the active ingredient using conventional excipients. However, it requires multiple processing steps and the use of solvents, which can lead to concerns such as drug degradation in the presence of the solvent, drug solubility in the granulation fluid, and the need for heat to remove the solvent.

- DRY GRANULATION

Dry granulation is a method where the powder mixture is compressed into large pieces and then broken down or sized into granules. It is useful for materials that cannot be prepared by wet granulation due to their sensitivity to moisture or high temperatures required for drying the granules. One of the key requirements for this method is that either the active ingredient or the diluent must have cohesive properties. Dry granulation is particularly suited for the manufacture of tablets with low-dose APIs, where the use of large amounts of excipients is not practical or desirable. However, this method typically involves several processing steps and may require higher compression forces compared to wet granulation.

DRY GRANULATION



- Advantages
  1. These methods are not generally associated with alterations in drug morphology during processing.
  2. No heat or solvents are required.
- Disadvantages
  1. Specialist equipment is required for granulation by roller compaction.
  2. Segregation of components may occur mixing.
  3. There may be issues regarding powder flow.
  4. The final tablets produced by dry granulation tend to be softer than those produced by wet granulation
  5. Slugging and roller compaction lead to the generation of considerable dust.

- SLUGGING
- After weighing and mixing the ingredients, the powder mixture is compressed into large, flat tablets or pellets known as slugs.
- The slugs are then broken up by hand or by a mill and passed through a screen of desired mesh size for sizing. Lubricant is added, and tablets are prepared by compression.
- This process is called slugging. It is often used for materials that are sensitive to moisture or heat and cannot be prepared using wet granulation.
- Aspirin, for example, can be prepared into tablets after slugging.

- COMPRESSION OF GRANULES INTO TABLET:
- Tablet compression machine consist of:
    1. Hopper 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. Feeding mechanisms for moving granulation from the hopper into the die
    6. Tablet ejector for removing compressed tablets from the die.

- Types of compression machine:

A. Single punch machine

- The compression is applied by the upper punch making the single punch machine a “stamping press.”

A. Multi-station rotary presses

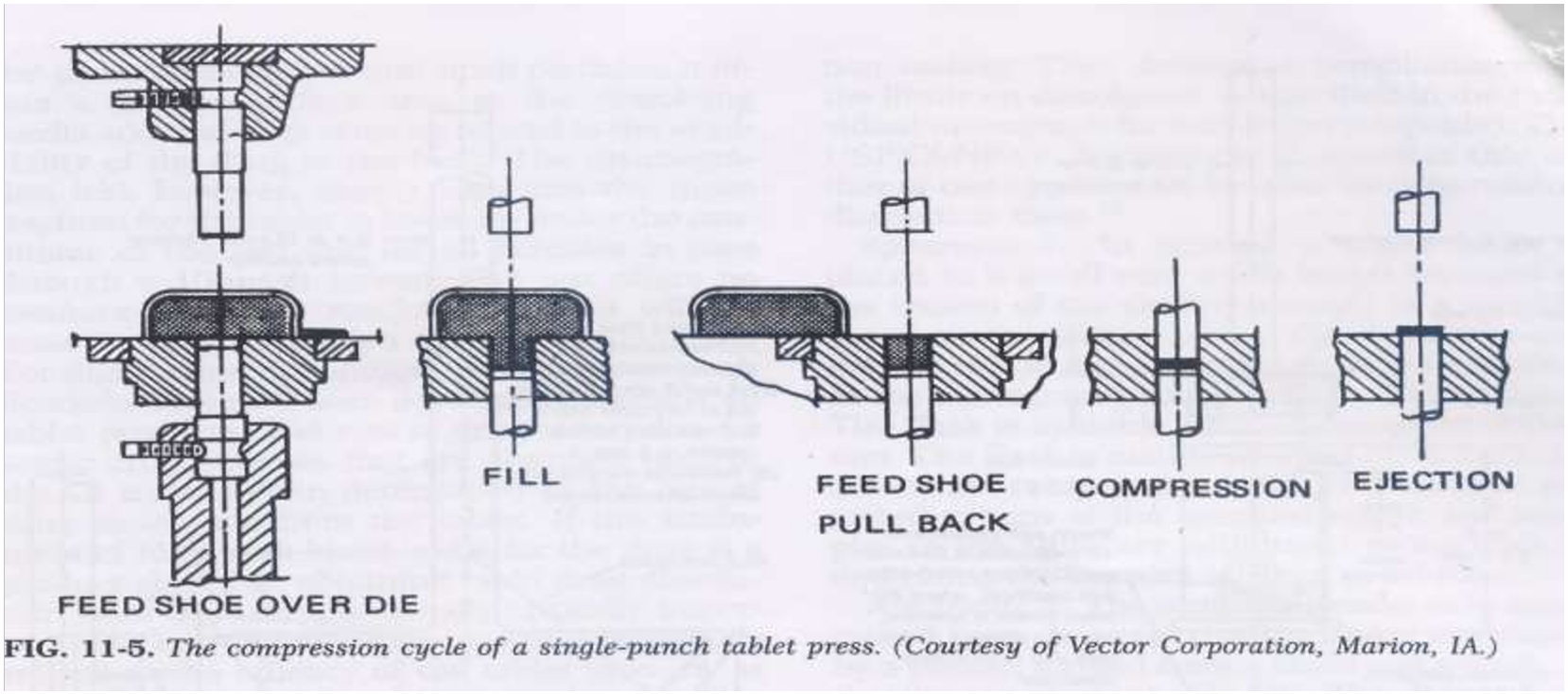
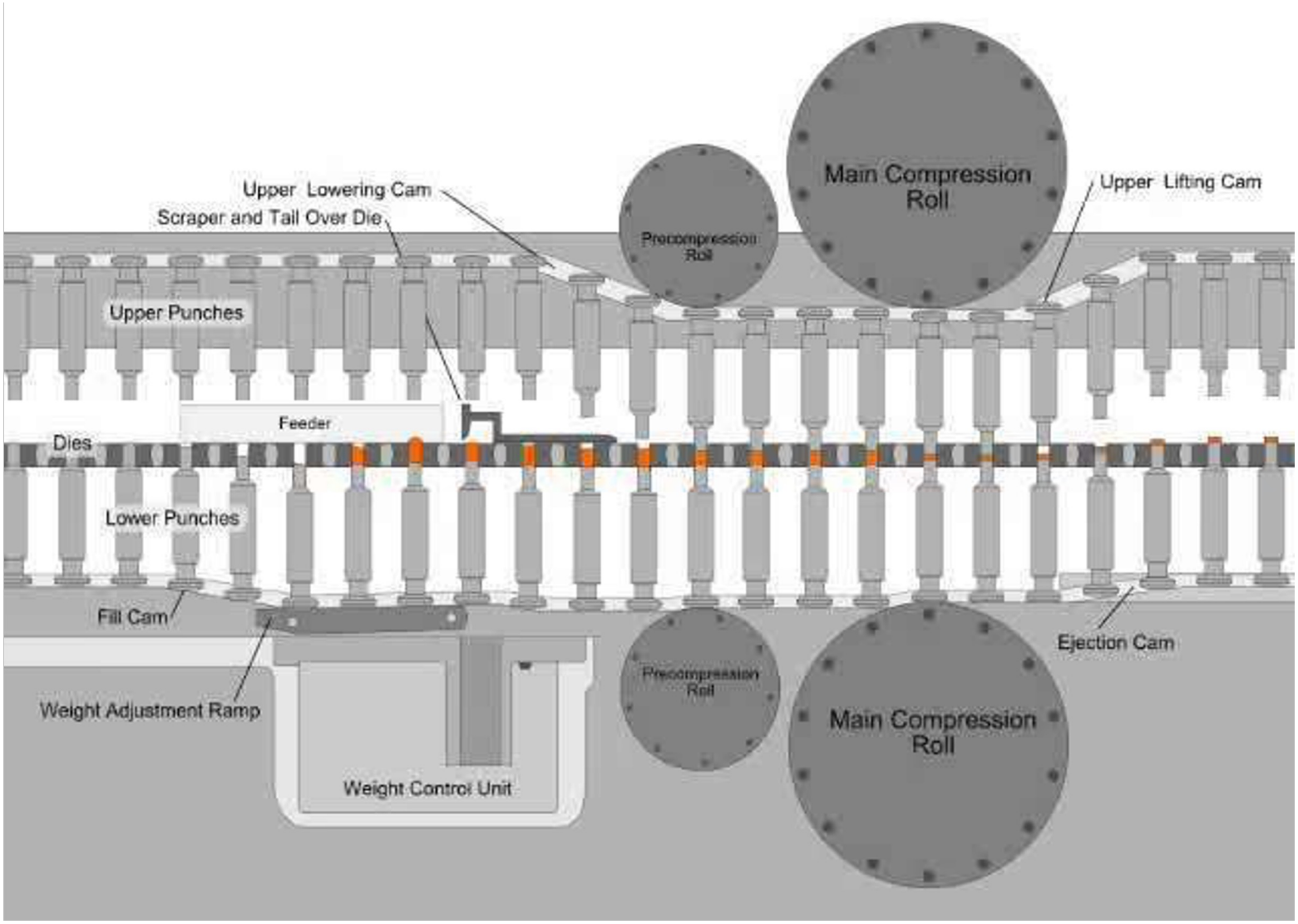


FIG. 11-5. *The compression cycle of a single-punch tablet press. (Courtesy of Vector Corporation, Marion, IA.)*

- Multi-station rotary presses

1. The tablet machine consists of a head that rotates to hold the upper punches, dies, and lower punches in place.
2. Fixed cam tracks guide the punches up and down to control the sequence of filling, compression, and ejection.
3. The upper and lower turrets hold the punches, while the die table holds the dies.
4. The pull-down cam guides the lower punches to the bottom, allowing the dies to overfill.
5. The weight-control cam reduces the fill in the dies to the desired amount.
6. A swipe-off blade removes excess granulation and directs it back to the front of the feed frame.
7. The lower punches compact the granulation within the dies as they ride up the lower compression roll.
8. Simultaneously, the upper punches enter a fixed distance into the dies and ride beneath the upper compression roll.
9. After compression, the upper punches follow the upper punch raising cam, and the lower punches ride up the cam, bringing the tablets flush with or slightly above the surface of the dies.
10. The tablets strike a sweep-off blade and slide down a chute into a receptacle.
11. The lower punches re-enter the pull-down cam, and the cycle is repeated.



Multi-station rotary press

- TABLET COATING:
- Reasons for coating:
    1. To mask unpleasant taste and odour.
    2. To improve the appearance of tablets.
    3. To prevent the medicament from atmospheric effects.
    4. To control the site of action of drugs.
    5. To produce the sustained release product.
- Methods of tablet coating :
    1. Sugar coating:
    2. Film coating
    3. Enteric coating.

- # SUGAR COATING:

- Steps of sugar coating of tablet:

1. Sieving: The tablets to be coated are shaken in a sieve to remove fine powder or broken pieces.
2. Sealing: A thin layer of water-proof material like shellac or cellulose acid phthalate is deposited on the surface of the tablets to protect them from atmospheric effects.
3. Sub-coating: Several coats of sugar and other materials like acacia or gelatin are given to round off the tablet and build it up to the desired size. Dusting powder is added after each addition of syrup.
4. Syrup coating: This is done to give colour, opacity and sugar coats to the tablets. Colouring materials and opacity agents are added to the syrup and several coats are applied until uniform coloured tablets are obtained.
5. Finishing: Three to four coats of sugar are applied in rapid succession without dusting powder and cold air is circulated to dry each coat. This forms a hard, smooth coat.
6. Polishing: Beeswax is dissolved in an organic solvent and applied in a few coats. The finished tablets are transferred to a polishing pan, which is rotated to rub the wax-coated tablets on a canvas cloth, giving them a proper shine.

Tablet coating is an art that requires precision and attention to detail. It is done to mask unpleasant taste and odour, improve the appearance of tablets, prevent medicaments from atmospheric effects, control the site of action of drugs, and produce sustained-release products.

- FILM COATING:

- Film coating is a method of coating tablets with a single or mixture of film-forming polymers, such as Hydroxypropyl methylcellulose, Hydroxyethyl methylcellulose, methylcellulose, Carbowax, PEG 400, etc. The polymer is dissolved in a volatile organic solvent and sprayed over the tablets in a rotating pan. Film coating may be enteric or non-enteric and is also used to make tablets waterproof before sugar coating.
- Advantages of film coating include being a less time-consuming technique, requiring minimal labor, having no adverse effect on tablet disintegration, and being cost-effective. It also protects the drug from atmospheric changes such as light, air, and moisture, and the coating is resistant to cracking and chipping. Furthermore, it does not increase the weight of the tablet, and there is no need for waterproofing before actual film coating.

- # ENTERIC COATING:

Enteric Coated tablet:

Enteric coated tablets are coated with a material that does not disintegrate in the stomach but passes through intact and dissolve in the intestine. This type of coating is made of enteric polymer, such as hydroxypropyl methyl cellulose phthalate. Enteric coated tablets are site-specific, which means they are designed to release their active ingredient in a specific part of the digestive system. These tablets protect the drug from the acidic environment of the stomach, and prevent gastric irritation or inactivation of the drug by stomach acid. Enteric coated tablets are used to deliver drugs that are acid-sensitive or need to be absorbed in the small intestine.

Enteric coating is given to the tablets when:

Enteric-coated tablets are used in situations where the medicament produces severe irritation in the stomach, but its action is required in the intestine. In some cases, the medicament may decompose or be destroyed by the acidic environment of the stomach. Additionally, drug absorption may be better in the intestine. Enteric-coated tablets are designed to pass through the stomach intact and dissolve in the intestine where they can exert their action. They may also be used for delayed release, providing a time-controlled release of the medicament.

- MICROENCAPSULATION:
- Microencapsulation is a process where small particles or droplets are coated to create tiny capsules. The material inside is the core, and the wall is the shell. This technique has many useful properties.
- Microencapsulation techniques:

  The methods are based on:

  1. Chemical Processess
  2. Mechanical Processess
- The following techniques are commonly used:

  1. Pan coating
  2. Fluidised bed coating
  3. Coacervation
  4. Electrostatic deposition
  5. Polymerisation
  6. Multi-orifice centrifugal process

- Most microcapsules have diameters between a few micrometers and a few millimeters.

Applications of microencapsulation include:

1. Masking the bitter taste of drugs like Paracetamol and Nitrofurantoin
2. Reducing gastrointestinal (GI) irritations and providing sustained release for drugs
3. Converting liquids to solids for easy handling and storage
4. Reducing the hygroscopic properties of core materials
5. Providing protection against external environment
6. Protecting the core materials
7. Separating incompatible substances

DEFECTS IN TABLETS

1. Capping:

- "Tablet capping" refers to the partial or complete separation of the top or bottom portion of a tablet from the main body. This defect can occur due to reasons such as excessive fine, defective punch die, high speed of machine, or granules that are too dried. To address this issue, steps such as properly setting the die and punch, reducing the percentage of fine, polishing punches, maintaining the desired moisture in granules, regulating the speed and pressure of punches, can be taken to remove the defect.

2. Picking and sticking:

- In this defect, material is either removed or picked up by the upper punch from the upper surface of the tablet, or it sticks to the wall of the die cavity during compression. Some common reasons for this defect are the use of worn-out die and punch, small quantity of lubricants, presence of excess moisture in the granules, scratches on the surface of the face of the punches, and formulation defects. To resolve this issue, it is recommended to use a new set of die and add the proper quantity of lubricants in the granules. The granules should also be dried properly to remove excess moisture.

3. Mottling:

- Mottling is the uneven distribution of color on the surface of a colored tablet, which can affect its appearance and lead to quality issues. The main reasons for mottling are the migration of dye during drying of granules, and the use of different coloration of medicaments and excipients. To avoid mottling, it is recommended to dry the granules at a low temperature and to use a dye that can mask the color of all medicaments.

4. Weight variation:

- Weight variation in tablets can occur due to several reasons during the compression process, resulting in tablets of non-uniform weight. These reasons include non-uniform granule size, excess powder in the granules, inadequate mixing of lubricants and non-uniform flow of granules, changes in die capacity during compression, and variation in the speed of the tablet machine. To avoid this defect, steps such as ensuring uniform granule size, proper mixing of lubricants, and regulating the speed of the tablet machine can be taken.

5. Hardness variation:

The tablet hardness is not uniform when the weight of the material and the distance between the punches during compression varies. The volume of the material can cause this variation, leading to differences in hardness.

6. Double impression:

Double impression on a tablet is caused by the lower punch having an engraving on it. During compression, the tablet receives an imprint of the punch. If the punch moves slightly upward before ejection, a second impression can occur. This can be controlled by managing the punch movement.

EVALUATION OF TABLET

- The official tests for tablets include the evaluation of size, shape, and appearance, content of active ingredient, uniformity of weight (weight variation test), uniformity of content, disintegration, and dissolution.
- In addition to these, there are also unofficial tests such as the hardness test and the friability test that are commonly performed to assess the strength and durability of the tablet.

Official tests

1. Size, shape & appearance:

Tablets are evaluated for their size, shape, and appearance to ensure lot-to-lot and tablet-to-tablet uniformity, as well as consumer acceptance. Size and shape can be measured dimensionally and controlled within a ±5% variation of the standard value. Unique identification markings, such as company name or product name, are used. Color distribution should be uniform with no mottling, and the tablet should have a consistent odor and taste.

2. Content of active ingredient

- Procedure:
- Perform the assay of 20 tablets as per monograph
- The result should lie within the range for the content of active ingredient stated in the monograph.
- If small no. of tablets (min 5) are used then the limits specified in the monograph may be relaxed to the extent indicated in the table.

Weight of medicament in each tablet	Subtract from the lower limit for sample of			Add to the upper limit for sample of		
	15	10	05	15	10	05
0.12 g or less	0.2	0.7	1.6	0.3	0.8	1.8
>0.12 g &< 0.3 g	0.2	0.5	1.2	0.3	0.6	1.5
0.3 g or more	0.1	0.2	0.8	0.2	0.4	1.0

3. Uniformity of weight:

The uniformity of weight test involves weighing 20 tablets selected at random and calculating their average weight. The individual weights should not deviate from the average weight by more than the percentage deviation allowed as per the table, and no tablet should deviate by more than twice that percentage. This test is important for ensuring consistent dosing and avoiding underdosing or overdosing of the active ingredient.

Sr. No.	Average Wt. of a tablet deviation	Percentage (%)
1	80 mg or less	10
2	More than 80 mg and less than 250 mg	7.5
3	250 mg or More	5

4. Uniformity of content:

The content uniformity test is a critical measure of ensuring that each tablet contains the intended amount of drug substance with minimal variation. In this test, 10 tablets are assayed, and 9 of them should have a percentage limit of 85-115%. If more than one tablet deviates from this range, 20 tablets are assayed, and not more than one tablet should have a percentage limit of 75-125%. This test is crucial in ensuring the efficacy and safety of the medication.

5. Disintegration test:

- The disintegration test measures the time required for a tablet to break down into smaller particles after swallowing.
- The test apparatus consists of a basket-rack assembly with 6 glass tubes held vertically by two plastic plates.
- The assembly is moved up and down in a liquid medium at 37°C. Tablets are placed in the tubes and guided discs keep them immersed in the liquid.
- The test is generally conducted for 15 minutes, and tablets pass if all of them disintegrate. If 1 or 2 tablets fail, 12 additional tablets are tested, and at least 16 of the total 18 tablets must disintegrate to pass the test.

- For Uncoated tablets:

The disintegration test is used to assess the ability of tablets to break down into smaller particles after ingestion. For uncoated tablets, start the test with 6 tablets and observe whether they completely disintegrate within 30 minutes. If one or two tablets fail to disintegrate, repeat the test on another 12 tablets. In total, at least 16 of the 18 tablets tested should disintegrate within the time frame. If more than two tablets fail to disintegrate, the batch should be rejected.

- For Coated tablets:

1.The disintegration test is used to determine whether tablets dissolve properly in the digestive tract.

2.To perform the test on uncoated tablets, immerse 6 tablets in distilled water for 5 minutes. Then, place the tablets in the disintegration apparatus in water or 0.1 N HCl for 30 minutes at 37°C (according to the U.S.P).

3. If any of the tablets fail to disintegrate completely, repeat the test on an additional 12 tablets. At least 16 out of the 18 total tablets tested must disintegrate completely within the specified time.

4. If two or more tablets fail to disintegrate, the batch is rejected. If the tablets have a coating, they should be immersed in distilled water for 5 minutes prior to the disintegration test. If they still do not disintegrate, the test should be repeated in intestinal fluid.

- For Enteric coated tablets:

Immerse the tablet in water to dissolve the coat. Test in simulated gastric fluid for two hours and then in phosphate buffer for one hour. If one or two tablets fail to disintegrate, repeat on 12 tablets. 16 tablets should disintegrate, and if more than two fail to do so, reject the batch.

6. Dissolution test:

- Dissolution testing is a method used to measure the rate at which a drug dissolves in a specific media. It involves a cylindrical vessel with 1000 ml capacity, an electric motor, a stainless steel basket with aperture size of 425 µm, and a device for sample withdrawal. The method is used to determine the time required for a given percentage of the drug substance in a tablet to dissolve under specified conditions.

- Method:
- In dissolution testing, tablets are placed in a vessel containing a specified amount of water and stirred at a specific temperature and speed. Samples are withdrawn at set time intervals, filtered, and the amount of active ingredient is determined using the method provided in the monograph. The apparatus consists of a vessel with a lid having holes for a stirrer shaft, thermometer, and sample removal, and a stainless steel basket attached to a driving shaft. The temperature and rotation speed are set according to the monograph.
- Acceptance criteria:

1. S1= 6 tablets are taken Acceptable: If all of the tablets are not less than Q ±5%
1. If S1 fails, S2=S1+6 tablets are taken Acceptable: If average of 12 tablets is ≥Q and no tablet is less than Q-15%
2. If S2 fails, S3= 12+12 tablets are taken Average of 24 ≥ Q% not more than 2 tablets should be less than Q-15% and None should be less than Q-25%

Unofficial tests

1. Hardness test:

- Hardness is the force required to break a tablet in a compression test. Tablets need to have a certain level of hardness to withstand mechanical shocks during handling, packaging and shipping. There are different types of hardness testers available, including the Monsanto, Strong Cobb and Pfizer testers. The ideal range of tablet hardness depends on the type of tablet, with conventional tablets having a hardness of 2.5-5 kg/sq cm, dispersible/chewable tablets having a hardness of 2.25-2.5 kg/sq cm, and extended release tablets having a hardness of 5-7.5 kg/sq cm.

2. Friability test :

- The friability test evaluates a tablet's ability to withstand wear and tear during transportation, handling, and packaging. The test is conducted using a device called a "Friabilator," which consists of a plastic chamber divided into two parts that revolve at 25 rpm.
- Twenty tablets are weighed and placed inside the chamber, which rotates for 4 minutes or 100 revolutions. During each revolution, the tablet falls from a distance of 6 inches. After 100 revolutions, the tablets are removed and weighed, and the loss in weight indicates the friability. A loss of less than 0.8% is considered acceptable and indicative of good tablet quality.

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