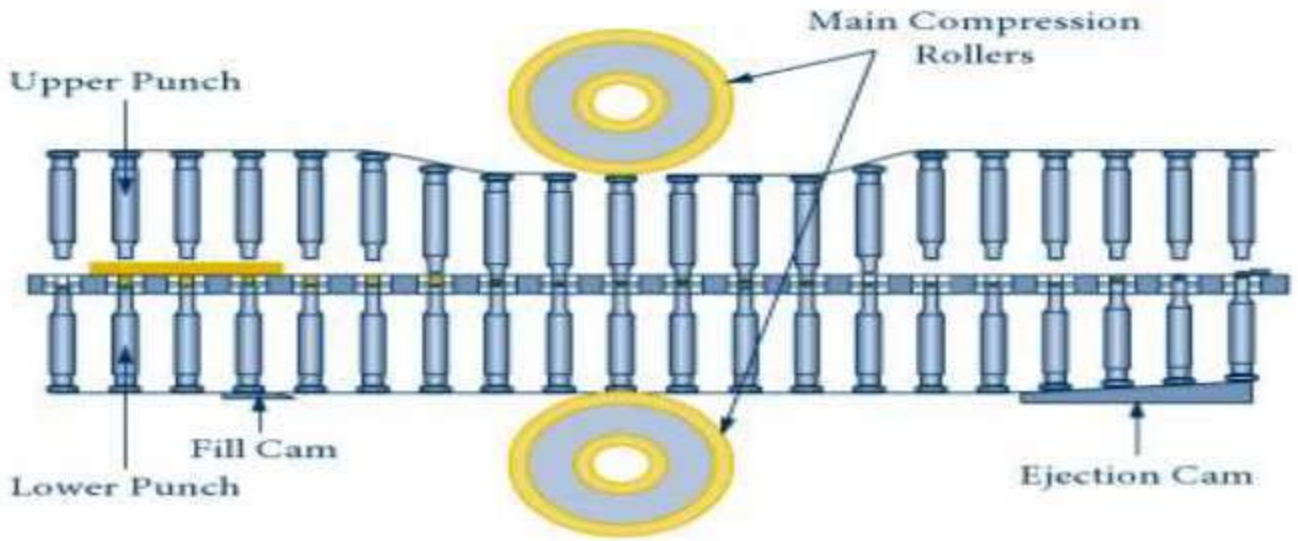
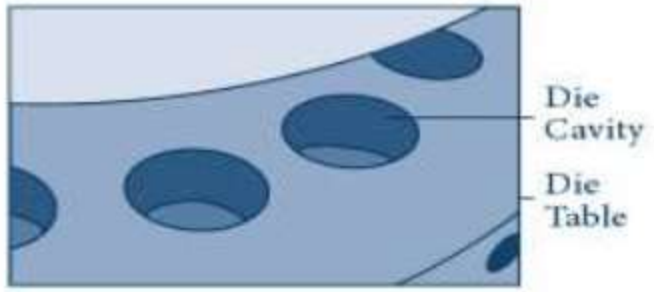
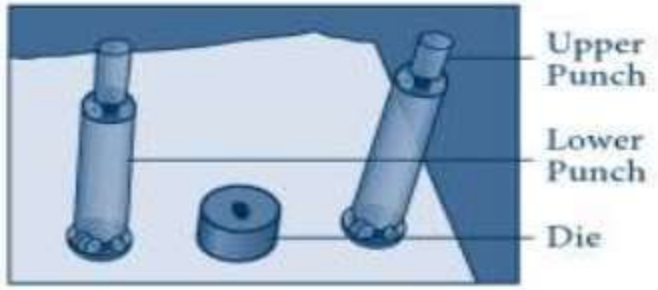
Tableting machine



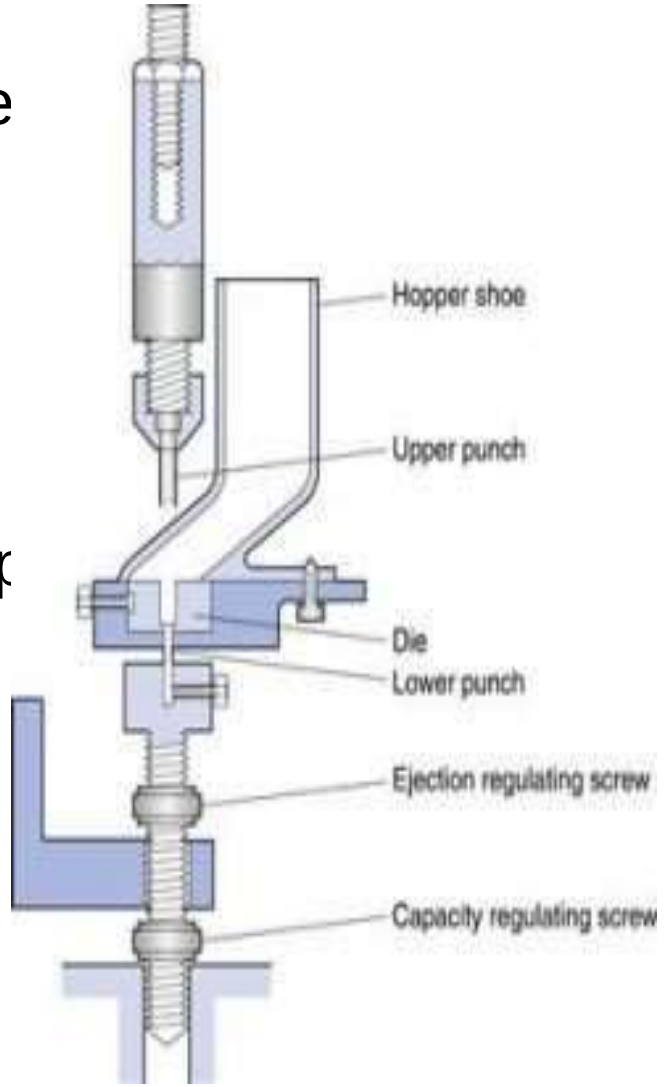




Tablet compression machines

- **Hopper** for holding and feeding granulation to be compresse
- **Dies** that define the size and shape of the tablet.
- **Punches** for compressing the granulation within the dies.
- **Cam tracks** for guiding the movement of the punches.
- **Feeding mechanisms** for moving granulation from the hopp

into the dies.



Round Shapes Dies

Caplet Shape Dies

Star Shapes Dies

Oval Shapes Dies

Stages in tablet formation
“Compaction cycle”

Compaction: The process of consolidating and compaction of powder or granule material to form a tablet is complex.

- Compression means reduction in the bulk volume of the material as a result of displacement of the gaseous phase .
- Consolidation: an increase in the mechanical strength of the material resulting from particle/particle interaction .

1- **Die filling:**

This is normally accomplished by gravitational flow of the powder from a hopper via the die table into the die

•The die is closed at its lower end by the lower punch.

2- Tablet formation:

The upper punch descends and enters the die and the powder is compressed until a tablet is formed.

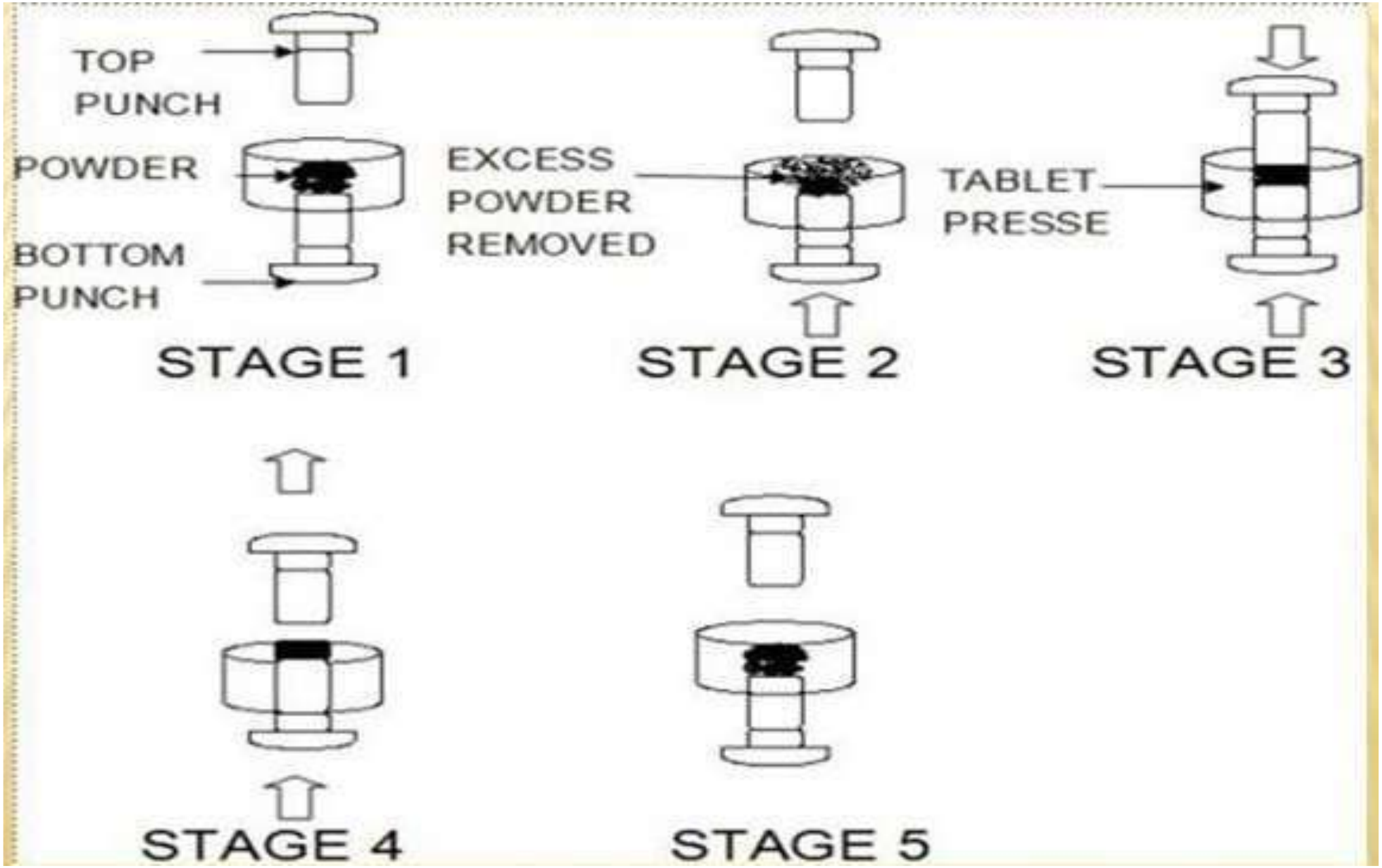
- During the compression phase, the lower punch can be stationary or can move upwards in the die.

•After maximum applied force is reached, the upper punch leaves the powder, i.e. the decompression phase.

3- **Tablet ejection:**

During this phase the lower punch rises until its tip reaches the level of the top of the die.

•The tablet is subsequently removed from the die and die table by a pushing device.


TOP
PUNCH
POWDER
BOTTOM
PUNCH
STAGE 1
EXCESS
POWDER
REMOVED
STAGE 2
TABLET
PRESSE
STAGE 3
STAGE 4
STAGE 5

Tableting machine

- **Single Punch Machine:**

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

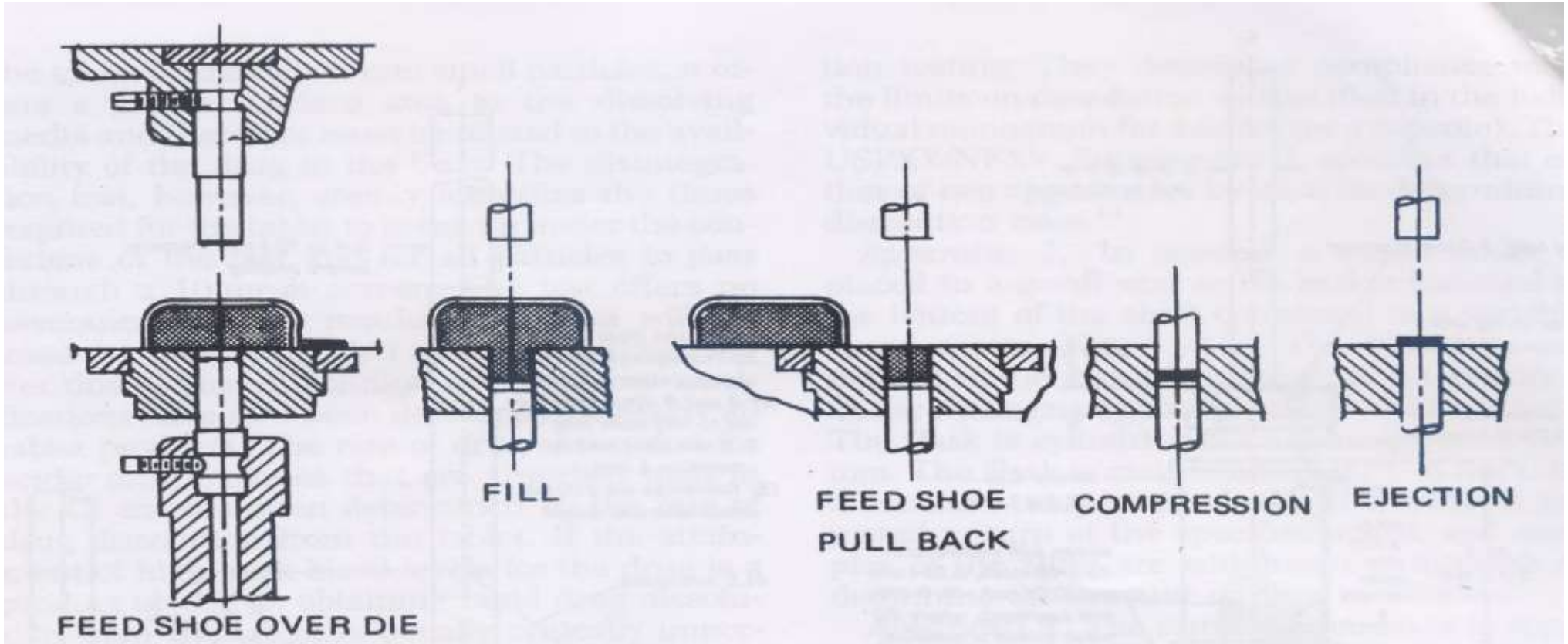


FIG. 11-5. *The compression cycle of a single-punch tablet press. (Courtesy of Vector Corporation, Marion, IA.)*

Multi-station rotary presses:

- ✓ The head of the tablet machine holds the upper punches, dies and lower punches in place rotates
- ✓ As the head rotates, the punches are guided up and down by fixed cam tracks, which control the sequence of filling, compression and ejection.
- ✓ The portions of the head that hold the upper and lower punches are called the upper and lower turrets.
- ✓ The portion holding the dies is called the die table
- ✓ The pull down cam (C) guides the lower punches to the bottom, allowing the dies to overfill.
- ✓ The punches then pass over a weight-control cam (E), which reduces the fill in the dies to the desired amount.

- ✓ A swipe off blade (D) 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.
- ✓ The lower punches travel over the lower compression roll (F) while simultaneously the upper punches ride beneath the upper compression roll (G).
- ✓ 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.
- ✓ After the moment of compression, the upper punches are withdrawn as they follow the upper punch raising cam (H).
- ✓ The lower punches ride up the cam (I) which brings the tablets flush with or slightly above the surface of the dies.

- ✓ 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 pull down cam (C) and the cycle is repeated.

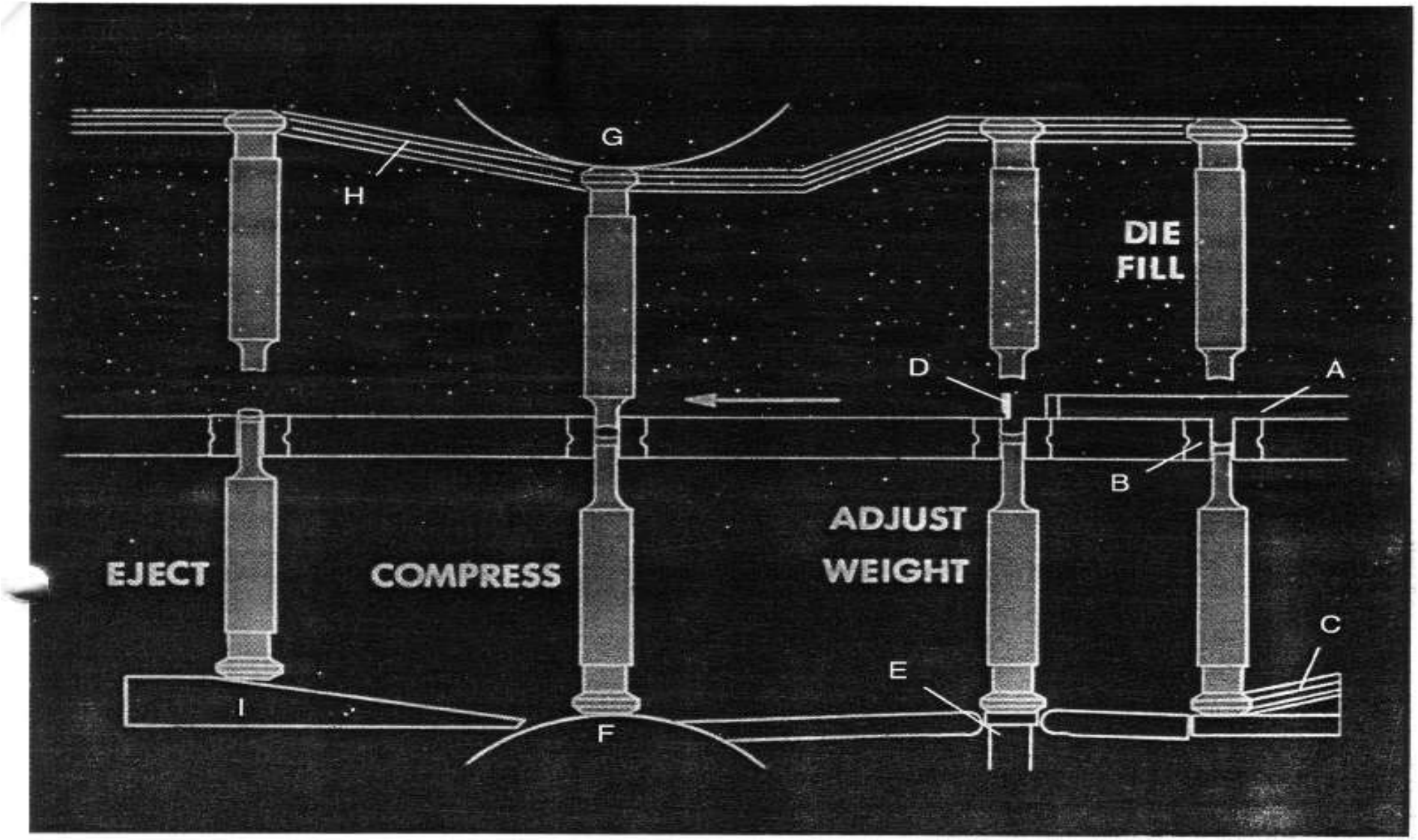
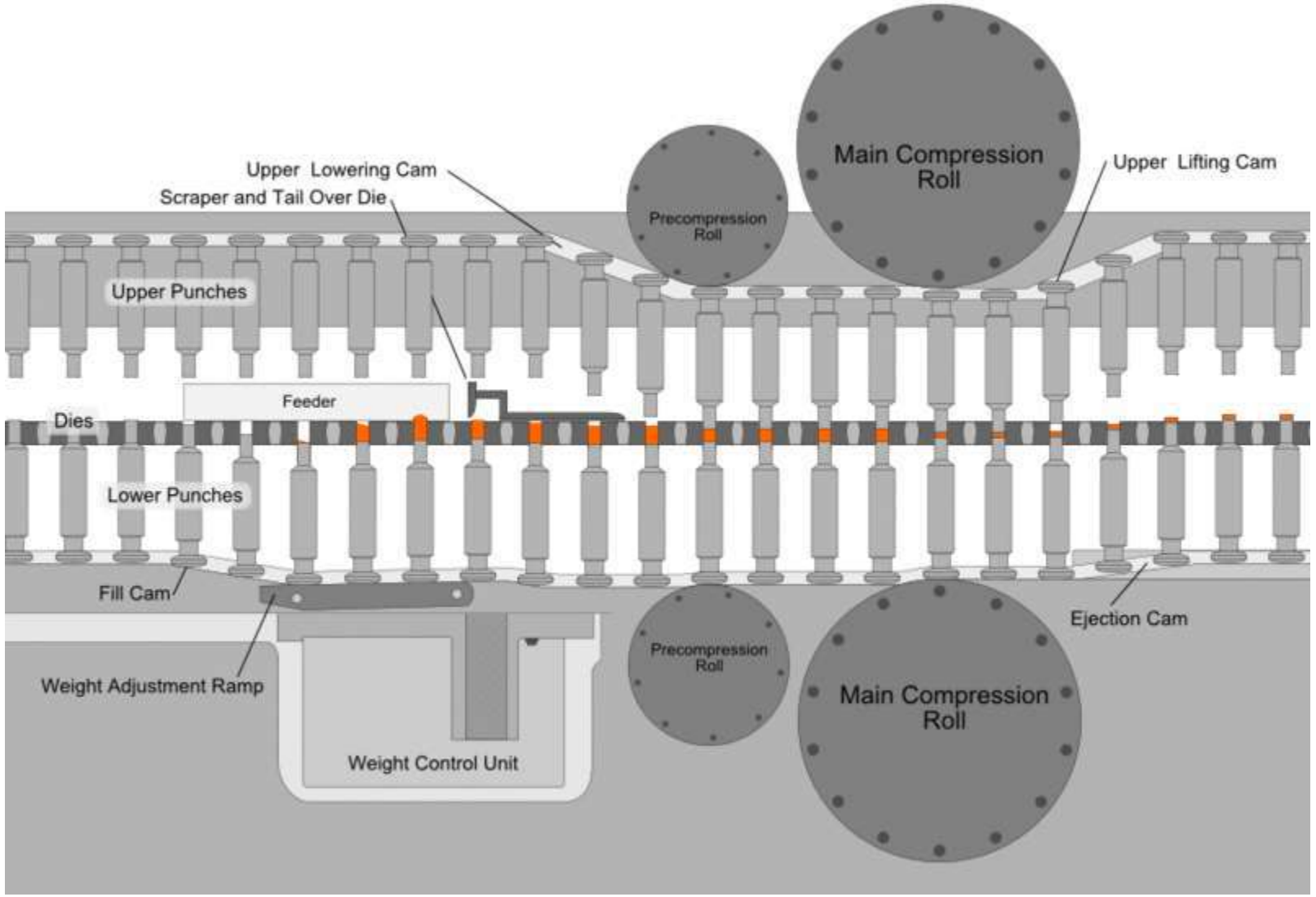


FIG. 11-6. *The compression cycle of a rotary tablet press. (See text for explanation of lettered labels.) (Courtesy of Thomas Engineering, Hoffman Estates, IL.)*

THE COMPRESSION CYCLE OF A ROTARY TABLET PRESS



TABLET COATING

- Tablet coating is the last critical step in the tablet production cycle.
- It is the phenomenon of application of coating to the tablet.

- **Coating** is a process by which an essentially dry, outer layer of coating material is applied to the surface of a dosage form in order to confer specific benefits over uncoated variety.
- Coating may be applied to a wide range of oral solid dosage form, such as particles, powders, granules, crystals, pellets and tablets.
- A coating is a covering that is applied to the surface of an object, usually referred to as the substrate.

PURPOSE OF COATING:

1. Providing a means of protecting the drug substance (active pharmaceutical ingredient) from the environment, particularly light and moisture, and thus potentially improving product stability.
2. To mask the disagreeable odor, color or taste of the tablet.
3. To control and sustain the release of the drug from the dosage form.
4. To incorporate another drug which create incompatibility problems.
5. Enabling the coated product (especially tablets) to be more easily handled on high-speed automatic filling and packaging equipment. In this respect the coating often improves product flow, increases the mechanical strength of the product and reduces the risk of cross-contamination by minimizing ‘dusting’ problems.

6. To prevent color migration from core i.e. if the active substance is colored and migrates easily to stain hands and clothes.
7. To protect an acid-labile drug from the gastric environment.
8. To make easier to swallow.
9. For product identification.
10. To improve the pharmaceutical elegance by use of special colors.

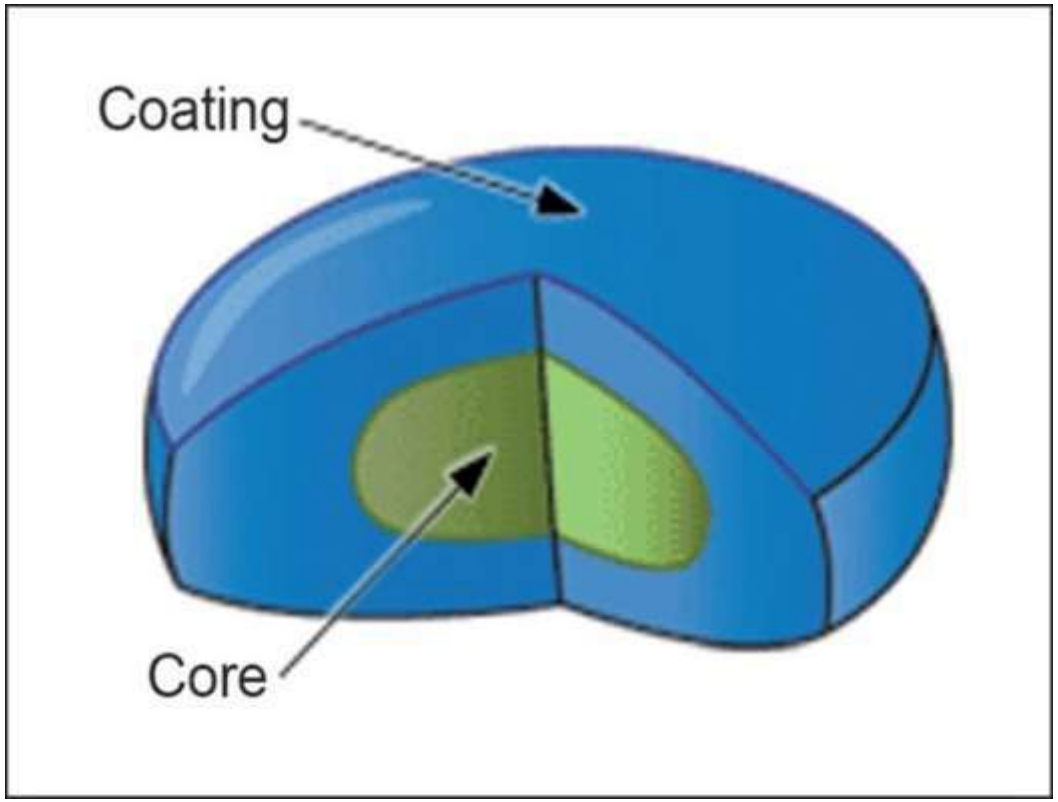
TABLET PROPERTIES

- Tablet to be coated must posses the proper physical characteristics like spherical shape and uniform surface.
- To tolerate attrition of tablets during coating process they must be resistant to abrasion and chipping.
- As the tablet surfaces that are brittle and soften in presence of heat or effected by coating composition and tend to become rough in the early stages of coating process are unacceptable for film coating.

TABLET COATING PROCESS

Three main types of process are used in the pharmaceutical industry:

- ✓ Sugar coating.
- ✓ Film coating.
- ✓ Compression coating.

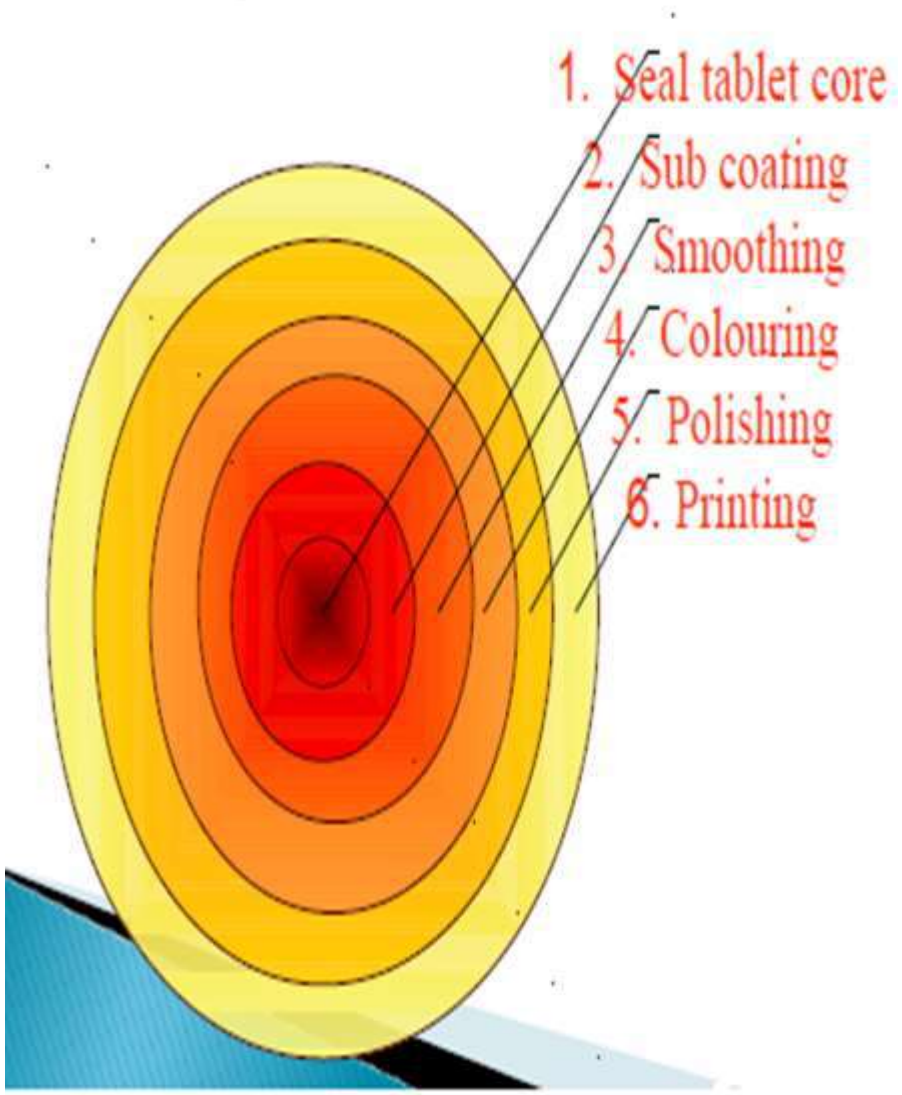


Sugar coating

- Sugar coating as the name suggests is the process which involves application of sugar (sucrose) based coating solution for the tablets.

The act or process of covering tablets with sugar/sucrose solution is called Sugar Coating.

- Compressed tablets may be coated with coloured or uncoloured sugar layer.
- **Multistage Process involving 6 separate operations**.



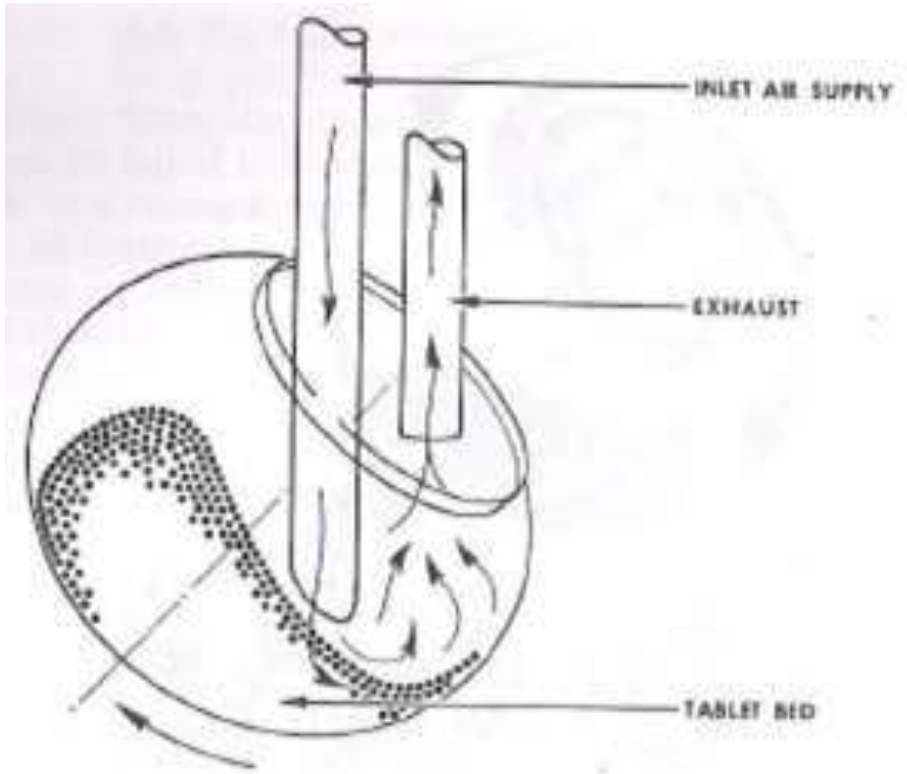
- Sugar coatings are composed of ingredients that are readily soluble, or disintegrate rapidly, in water. In general, sugar-coated tablets are intended to exhibit immediate-release attributes.

However, one of the stages of the sugar-coating process, the sealing step, involves the deposition of a polymer-based coating on the surface of the uncoated tablets. At this stage, it is possible to use some of the speciality polymers that are either partially or completely insoluble in water, thus enabling the sugar-coated product to exhibit delayed (gastro-resistant)-release or extended-release characteristics.

•During operation, the pan is mechanically rotated at moderate speeds, allowing the tablets to tumble over each other while making contact with the coating solutions, which are gently poured or sprayed onto the tablets.

•To allow gradual buildup of the coatings, the solutions are added in portions, with warm air blown in to hasten drying. Each coat is applied only after the previous coat has dried.

•Tablets intended to be coated are manufactured to be thin edged and highly convex to allow the coatings to form rounded rather than angular edges.



1- Sealing (Waterproofing):

- Sealing is done by applying a polymer based water impermeable coating solution by either ladling or spray techniques.
- The waterproofing solution (usually alcoholic) is gently poured or sprayed on the compressed tablets rotating in the coating pans. Warm air is blown into the pan during the coating to hasten the drying and to prevent tablets from sticking together.
- The polymers used are natural gums like shellac, acacia or derivatives of cellulose like cellulose acetate pthalate (CAP), PVAP, HPMC.

The importance of Sealing:

• Sugar-coatings are aqueous formulations which allow water to penetrate directly into the tablet core and thus potentially affecting product stability and possibly causing premature tablet disintegration. To protect the tablet core from adverse effect of moisture

2. Subcoating:

- Large quantities of sugar-coatings are usually applied to the tablet core for increasing the tablet weight by 50- 100%.
- After the tablets are waterproofed if needed, three to five subcoats of a sugar-based syrup are applied. This bonds the sugar coating to the tablet and provides rounding.
- The sucrose and water syrup also contains gelatin, acacia, or PVP to enhance coating.
- Much of this material build-up occurs during the subcoating stage and is achieved by adding bulking agents such as calcium carbonate to the sucrose solutions. In addition, antiadherents such as talc may be used to prevent tablets sticking together, and polysaccharide gums, such as gum acacia, may also be added as a binder in order to reduce brittleness.

- Warm air is applied to the rolling tablets, and when they are dry, the process is repeated until the tablets are of the desired shape and size.

- The subcoated tablets are then scooped out of the coating pan, and the excess powder is removed.

FIGURE 8.32 Gauge used to measure coated tablets. (Courtesy of Eli Lilly and Company.)

3- Smoothing:

- The sub coating stage results in tablets with rough surfaces.
- To facilitate the color application (which requires smooth surface), sub coated tablets are smoothed out by a thick sucrose syrup coating.

➢After the tablets are subcoated, 5 to 10 additional coatings of a thick syrup are applied to complete the rounding and smooth the coatings. This syrup is sucrose based, with or without additional components such as starch and calcium carbonate.

➢ As the syrup is applied, the operator moves his or her hand through the rolling tablets to distribute the syrup and to prevent the tablets from sticking to one another. A dusting powder is often used between syrup applications. Warm air is applied to hasten the drying time of each coat.

4- Coloring:

Color coatings usually consist of thin sucrose syrup containing the requisite coloring materials (water-soluble dyes or water-insoluble pigments may be used).

- To attain final smoothness and the appropriate color to the tablets, several coats of a thin syrup containing the desired colorant are applied in the usual manner. This step is performed in a clean pan, free from previous coating materials.

5- Polishing:

After the colour coating, the tablet surfaces show a dull or matt appearance. To achieve glossy finish, application of waxes (beeswax- carnauba wax) are employed.

➢ Special drum-shaped pans or ordinary coating pans lined with canvas or other cloth impregnated with carnauba wax and/or beeswax may be used to polish tablets as they tumble in the pan.

➢ Or, pieces of wax may be placed in a polishing pan, and the tablets allowed to tumble over the wax until the desired sheen is attained.

➢ A third method is light spraying of the tablets with wax dissolved in a nonaqueous solvent.

• Two or three coats of wax may be applied, depending upon the desired gloss.

• After each coat has been applied, the addition of a small amount of talc to the tumbling tablets contributes to their high luster

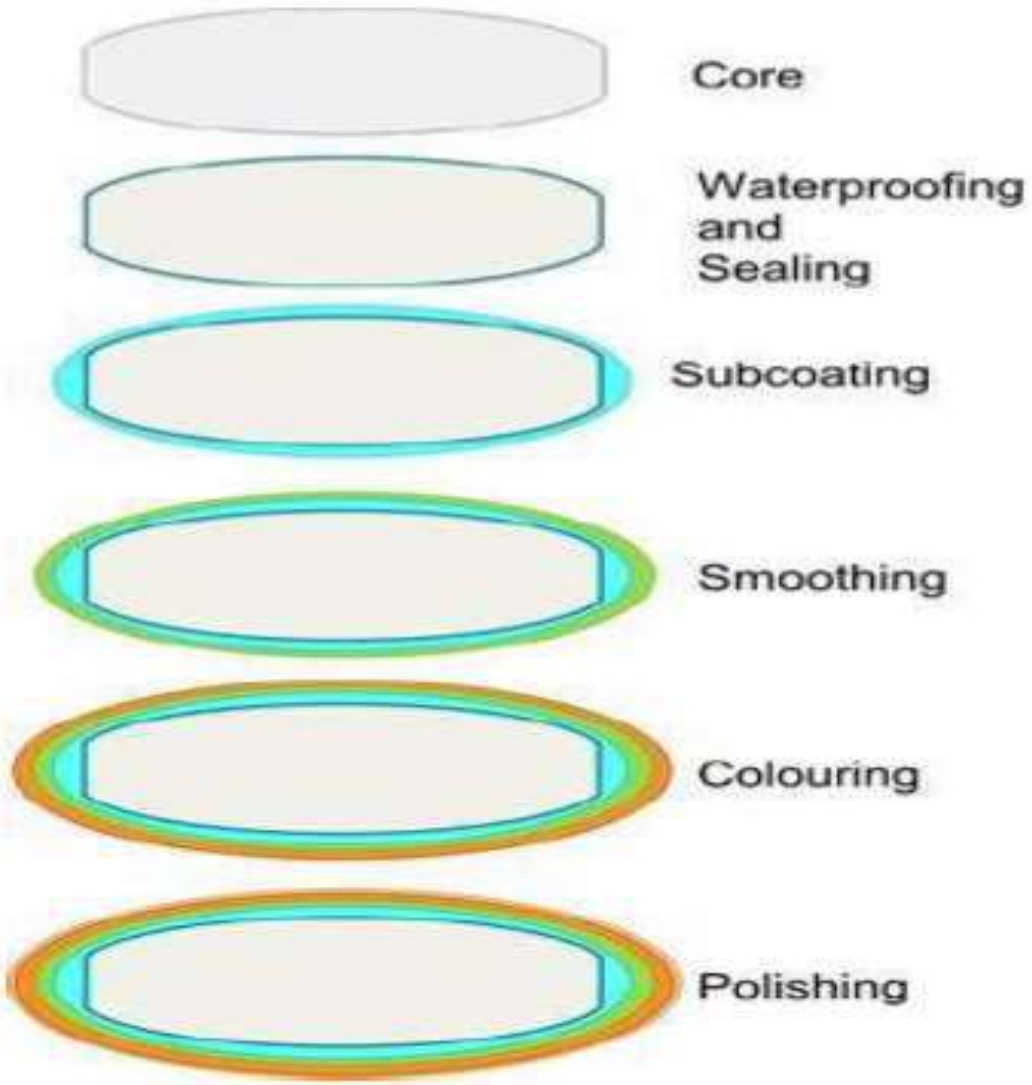
6- Printing (Imprinting):

- Solid dosage forms may be passed through a special imprinting machine to impart identification codes and other distinctive symbols. By FDA regulation, effective in 1995, all solid dosage forms for human consumption, including both prescriptiononly and over-the-counter drug products, must be imprinted with product-specific identification codes.

➢ Some exemptions to this requirement are allowed: those used in clinical investigations, those that are extemporaneously compounded in the course of pharmacy practice, radiopharmaceutical drug products, because of their size, shape, texture, or other physical characteristics, make imprinting technologically not feasible.

- Technically, the imprint may be debossed, embossed, or printed on the surface with ink. Debossed means imprinted with a mark below the surface, embossed means imprinted with a mark raised above the surface.

STEPS OF SUGAR COATING



Disadvantages of sugar coating:

1- The sugarcoating process is tedious, time-consuming.

2- Specialized, requiring the expertise of highly skilled technicians.

3- Coated tablets may be twice the size and weight of the original uncoated tablets.

4- Sugarcoated tablets may vary slightly in size from batch to batch and within a batch.

5- From a patient's point of view, large tablets are not as easily swallowed as are small tablets.

II. Film coating

➢ Film coating involves application and deposition of a thin film of polymer solution around the tablet core.

- A film coating is a thin polymer-based coat applied to a solid dosage form such as a tablet, granule or other particle.
- Film coating is the process whereby a tablet, capsule, or pellet is surrounded by a thin layer of polymeric material.

▪ The thickness of such a coating is usually between 20 and 100 μm.

Advantages of film coating:

1- Film coated tablets having the same weight, shape, and size as the originally compressed tablet.

2- The coating is thin enough to reveal any identifying monograms embossed in the tablet during compression by the tablet punches.

3- Film coating gives a tablet with less weight and small size (The film formed is very thin) than sugar coated tablet.

4- More resistant to destruction by abrasion than are sugarcoated tablets.

5- The cost of the film coated tablets is less.

6- Ability to be applied to a wide range of pharmaceutical products “e.g., tablets, capsules, granules, non-pareils, powders, drug crystals”.

7- Faster processing times.

Types of film coatings:

- **Immediate-release film coatings**: also known as ‘nonfunctional’ coatings or conventional film coating, is used to describe film coatings that are designed to improve product appearance, perhaps improve handling and stability of the dosage form, but has no measurable effect on biopharmaceutical properties of the dosage form.
- **Modified-release film coatings:** also known as ‘functional’ coatings. These may be further categorized as either delayed-release (e.g. gastro-resistant) or extended-release coatings.

Note that the newer term ‘gastro-resistant’ coating is replacing the older term ‘enteric’ coating in pharmacopoeias.

Immediate-release coatings are usually readily soluble in water, while gastro-resistant coatings are only soluble in water at pH values in excess of 5–6

- **Ingredients used in film coating:**

A typical formulation of film coating contains:

1. Polymer (Film former).
2. Plasticizer.
3. Colorant.
4. Solvent (vehicle).

IDEAL CHARACTERISTICS A FLIM

COATING POLYMER

➢ **Solubility:**

Polymer solubility is important for two reasons:

• It determines the behaviour of the coated product in the gastrointestinal tract.

• It determines the solubility of the coating in a chosen solvent system

✓ For conventional film coating the polymer should have good solubility in aqueous fluids to facilitate the dissolution of the active ingredient from the finished dosage form. However, where a modified-release action is required then a polymer system of low water solubility or permeability will be chosen.

- **Viscosity:** is very much a limiting factor with regard to the ease with which a film coating can be applied.

- High viscosity (typically that exceeding approximately 500 mPa s) complicates transfer of the coating liquid from the storage vessel to the spray guns, and subsequent atomization of that coating liquid into fine droplets.
- Ideally, therefore, polymers applied as solutions in a selected solvent should exhibit relatively low viscosities (ideally less than 300 mPa s) at the preferred concentration. This will help to facilitate easy, trouble-free spray application of the coating solution in industrial film coating equipment.

➢ **Permeability:**

- Film coating can be used to optimize the shelf-life of a tablet preparation, as some polymers are efficient barriers against the permeability of water vapour or other atmospheric gases.
- Modify the rate at which the active ingredient will be released from the dosage form.
- These properties vary widely between the individual polymers.

❑ **Film-coating polymers should possess suitable characteristics with respect to:**

• Film strength: which greatly affects the ability of the coating to resist the mechanical stresses to which it will be exposed during the coating process and during subsequent handling of the coated product.

- Film flexibility: which imparts benefits similar to those of film strength and minimizes film cracking during handling or subsequent storage.
- Film adhesion: which is necessary to ensure that the coating remains adherent to the surface of the dosage form right up to the point of being taken by the patient.

Types of film-coating polymers

➢ Immediate-release coating polymers:

1- Cellulose derivatives:

Most cellulosic polymers used in film-coating formulations are substituted ethers of cellulose.

- Hydroxypropyl methylcellulose (HPMC) is the most widely used of the cellulosic polymers. It is readily soluble in aqueous media and forms films that have suitable mechanical properties and coatings that are relatively easy to apply.
- Other cellulosic derivatives used in film coatings which have properties similar to those of hydroxypropyl methylcellulose include methylcellulose and hydroxypropyl cellulose.

2- Vinyl derivatives

The most commonly used vinyl polymer in pharmaceutical applications is polyvinylpyrrolidone. Unfortunately this polymer has limited use in film-coating formulations because of its inherent tackiness.

- ✓ A copolymer of **vinylpyrrolidone and vinyl acetate**, **copovidone**, is considered a better film former than polyvinylpyrrolidone.
- ✓ Another useful vinyl polymer is **poly(vinyl alcohol) (PVA),** a partial hydrolysate of poly(vinyl acetate), which can be used to produce film coatings that have suitable mechanical properties and are highly adherent to pharmaceutical tablets.

In addition, PVA exhibits good barrier properties with regard to environmental gases and water vapour.

- ✓ Recently, film coatings based on a **copolymer of vinyl alcohol and ethylene glycol** have become available. These coatings are less tacky than traditional PVA coatings and have the additional benefit of being extremely flexible, thus improving film robustness and allowing greater expansion capabilities should the tablet cores expand slightly during the coating process.

- ➢ **Modified-release coating polymers:**

1- Cellulose derivatives:

As is the case with cellulosic polymers used in immediate-release applications, cellulosic polymers used for modified-release purposes are typically substituted ethers of cellulose.

However, the level of substitution in this case is usually much higher, thus rendering the polymer insoluble in water.

A typical example of such a cellulosic polymer is ethylcellulose (EC), which is preferred for many extended-release applications. Ethylcellulose has been applied as solutions in organic solvents, although aqueous polymer dispersions are commercially available.

2- Methylmethacrylate copolymers:

Acrylic ester polymers are typically insoluble in water but can be prepared with varying degrees of permeability to render them suitable for a variety of extended-release applications.

3- Methacrylic acid copolymers

The special functionality conferred by the presence of carboxylic acid groups enables this class of polymer to function as gastro-resistant coatings.

This is because the polymer is insoluble in water at the low pH that typifies conditions in the stomach but gradually becomes soluble as the pH rises towards neutrality, a condition that is more typical of the upper part of the small intestine.

4- Phthalate esters:

Phthalate ester polymers exhibit properties similar to those of methacrylic acid copolymers in that they are most suited to delayed-release applications.

Thus some common examples of phthalate ester polymers are hydroxypropyl methylcellulose phthalate (HPMCP), cellulose acetate phthalate (CAP), and poly(vinyl acetate phthalate (PVAP).

2- Plasticizer:

- Plasticizers are generally added to film coating formulations to modify the physical properties of the polymer to make it more usable.
- One important property is that their ability to decrease film brittleness.
- It is generally accepted that the mechanism by which plasticizers exert their effect is for plasticizer molecules to interpose themselves between the polymer molecules, thus increasing free volume and facilitating increased polymer chain motion within the structure of the coating.

The positive benefits of this interaction include:

✓ Increased film flexibility; and

✓ Reduced residual stresses within the coating as it shrinks around the core during drying.

Examples of plasticizers are:

- **Polyols:** such as polyethylene glycol 400 .
- **Organic esters:** such as diethyl phthalate.
- **Oils/glycerides:** such as fractionated coconut oil**.**
- In general, only water-miscible plasticizers can be used for aqueous based spray systems.

3.Colourants:

Colourants are used to improve the aesthetic value of the final product as well as helps in identifying the product.

Pharmaceutically acceptable colourants are available in both water-soluble form (known as dyes) and water-insoluble form (known as pigments).

The insoluble form is preferred in film-coating formulations, because pigments:

- ✓ tend to be more chemically stable towards light,
- ✓ provide better opacity and covering power,
- ✓ and provide a means of optimizing the permeability properties of the applied film coating.

✓ In addition, water-insoluble pigments will not suffer from the disadvantageous phenomenon of mottling (caused by solute migration) that can be observed with water-soluble dyes.

Examples of colourants are:

- Iron oxide pigments
- Titanium dioxide
- Aluminum Lakes.

4.Solvents:

Solvents play an important role in formulation of coating solution. They serve as a vehicle for dissolving and dispersing the constituents of coating solutions and helps in the applications of the coating to the tablet surface.

- Initially, film-coating processes were very much dependent on the use of organic solvents (such as methanol–dichloromethane combinations or acetone) in order to achieve the rapid drying characteristics demanded by the process.

Unfortunately, organic solvents possess many disadvantages that are related to the following factors:

1. Environmental issues: The venting of untreated organic solvent vapour into the atmosphere is ecologically unacceptable, and efficient solvent vapour removal from gaseous effluent of coating processes is expensive.

2. Safety issues: Organic solvents may be flammable (and thus explosive hazards) or expose plant operators to toxic hazards.

3. Financial issues: Potentially unacceptable cost factors associated with the use of organic solvents are related to the need to build explosion-proof processing areas and provide suitable storage areas for hazardous materials. In addition, the relative expense of organic solvents as a raw material has to be considered.

4. Solvent residue issues: For a given process, the amount of organic solvent retained in the film coat must be investigated, especially since there is increasing regulatory pressure to quantify and limit the residue levels.

- Such disadvantages have provided the momentum for the current utilization of aqueous coating formulations as the preferred option.

Film-coating solutions may be nonaqueous or aqueous:

❖The **nonaqueous solutions** contain the following types of materials to provide the desired coating to the tablets:

1. A film former :capable of producing smooth, thin films reproducible under conventional coating conditions and applicable to a variety of tablet shapes. Example: cellulose acetate phthalate.

2. An alloying substance: providing water solubility or permeability to the film to ensure penetration by body fluids and therapeutic availability of the drug. Example: polyethylene glycol.

3. A plasticizer :to produce flexibility and elasticity of the coating and thus provide durability.

Example: castor oil.

4. A surfactant: to enhance spreadability of the film during application.

Example: polyoxyethylene sorbitan derivatives.

5. Opaquants and colorants: to make the appearance of the coated tablets handsome and distinctive.

Examples: Opaquant, titanium dioxide; colorant, FD&C or D&C dyes.

6. Sweeteners, flavors, and aromas: to enhance the acceptability of the tablet by the patient.

Examples: sweeteners, saccharin; flavors and aromas, vanillin.

7. A glossant: to provide luster to the tablets without a separate polishing operation.

Example: beeswax.

8. A volatile solvent: to allow the spread of the other components over the tablets while allowing rapid evaporation to permit an effective yet speedy operation.

Example: alcohol mixed with acetone.

- Tablets are film coated by application or spraying of the coating solution on the tablets in ordinary coating pans. The volatility of the solvent enables the film to adhere quickly to the surface of the tablets.

➢One commercial water-based colloidal coating dispersion called **Aquacoat** (FMC Corporation) contains a 30% ethyl cellulose pseudolatex. Pseudolatex dispersions have a high solid content for greater coating ability and a relatively low viscosity.

- The low viscosity allows less water to be used in the coating dispersion, requiring less evaporation and reducing the likelihood that water will interfere with tablet formulation.

A typical aqueous film-coating :

formulation contains the following :

1. Film-forming polymer (7% to 18%). Examples: cellulose ether polymers such as hydroxypropyl methylcellulose, hydroxypropylcellulose, and methylcellulose
2. Plasticizer (0.5% to 2.0%). Examples: glycerin, propylene glycol, polyethylene glycol, diethyl phthalate, and dibutyl subacetate
3. Colorant and opacifier (2.5% to 8%). Examples: FD&C or D&C lakes and iron oxide pigments
4. Vehicle (water, to make 100%)

THE PROCESS OF FILM COATING:

- Tablets are placed inside the coating drum which is then set to rotate, to mix the tablets.
- Ambient air is heated and passes through perforations in base of the rotating drum to warm up the tablets. Air is circulated through the tablets as the drum rotates and exhausted through a vent system at the top or side of the drum.
- A solution or suspension of the coating material is sprayed as fine droplets through the bed of tablets. To achieve uniform coating across the bed, the distance between the spray gun and tablet bed is measured and adjusted accordingly.
- Once the droplets hit the surfaces of the tablets, it spreads into film on the surface before solvent is removed rapidly by the hot air.
- The coating thickness on each tablet is increased as the tablets pass underneath the spray gun by the rotating drum.

Table 32.1 Major differences between sugar coating and film coating

Features	Sugar coating	Film coating
Tablets		
Appearance	Rounded with high degree of polish	Retains contour of original core Usually not as shiny as sugar coat types
Weight increase due to coating materials	30% to 50%	2% to 3%
Logo or 'break lines'	Not possible	Possible
Other solid dosage forms	Coating possible but little industrial importance	Coating of multiparticulates very important in modified-release forms
Process		
Stages	Multistage process	Usually single stage
Typical batch coating time	8 h, but easily longer	1.5 h to 2 h
Functional coatings	Not usually possible apart from gastro-resistant (enteric) coating	Easily adaptable for controlled release

STANDARD COATING PAN:

- It is also known as conventional pan system
- Circular metal pan(mounted angularly on a stand)
- 8-60 inches in diameter
- Rotated on its horizontal axis by a motor
- Heated air is directed into the pan & on to the tablet bed

surface and is exhausted by means of ducts through the front of the pan.

➢**Coating solution are applied to the tablets by ladling or spraying the material on to the rotating tablet bed.**

Use of spraying systems:

✓ Produces a faster, more even distribution of the solution or suspension.

✓ Reduces drying time between solution application in sugar coating .

✓Allows continuous application of the solution in film coating.

Standard coating pan

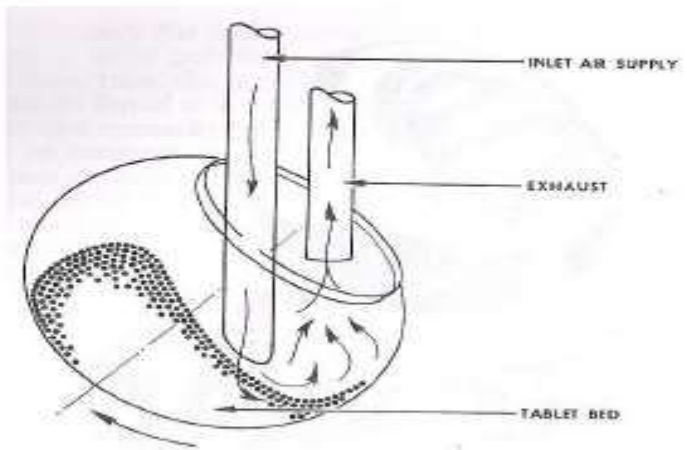
e.g., Pellegrino pan system

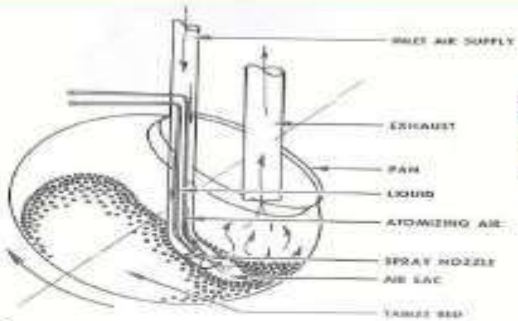
Immersion sword system

Immersion tube system

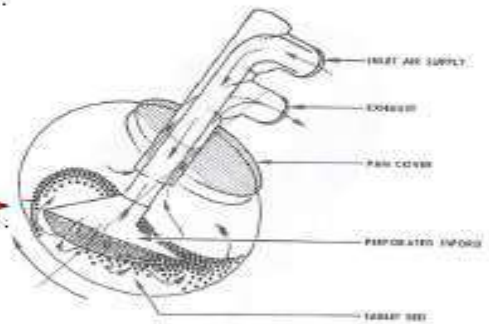
STANDARD COATING PAN

Standard Coating Pan

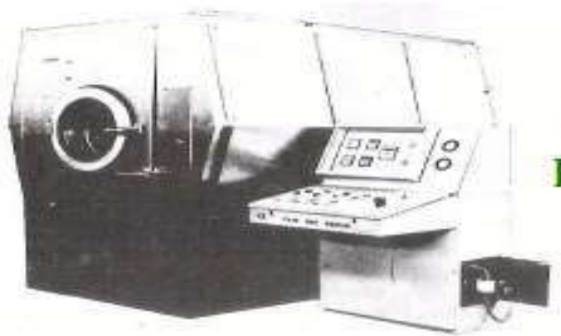




Immersion-tube system



Glatt Immersion sword system



Pellegrini pan system

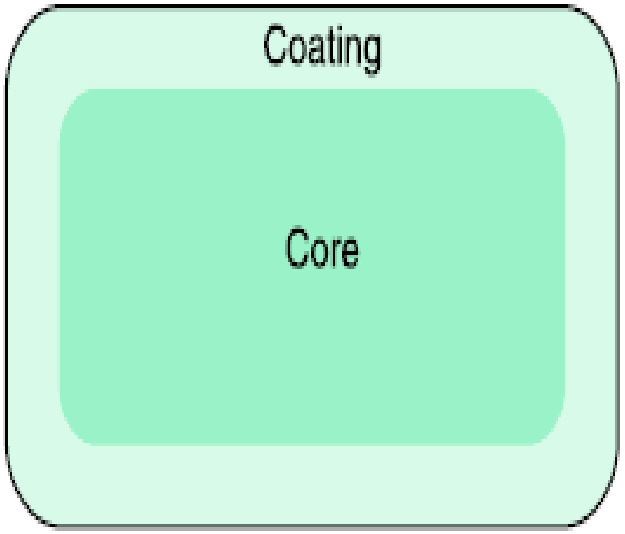
Compression Coating

Compression coating is based on a modification of the traditional tableting process.

Tablet cores are first prepared and then mechanically transferred, on the same machine, to another, slightly larger die that has been partially filled with the coating powder.

The tablet core is positioned centrally into this partially filled die, more coating powder is added on top of the core and the whole composite mass undergoes a second compaction event.

Compression coating is an anhydrous operation and thus may be safely employed in the coating of tablets containing a drug that is labile to moisture.



- Compared to sugarcoating using pans, compression coating is more uniform and uses less coating material, resulting in tablets that are lighter, smaller, and easier to swallow and less expensive to package and ship.
- Compression coating has been used to separate incompatible materials (one contained in the tablet core and the second contained in the coating).
- Also may provide dual release patterns.

FLUIDIZED BED SYSTEM

- In this system fluidization of the tablet mass is achieved in a columnar chamber by the upward flow of drying air.
- The air flow is controlled, so that more air enters the center of the column, causing the tablets to rise in the center.
- The movement of tablets is upward trough the center of the chamber.
- It has a vertical cylinder.
- A column of drying air flows upwards suspending all the tablets. This causes the tablets to move upwards, outwards and then downwards, a process we refer to as fluidization.

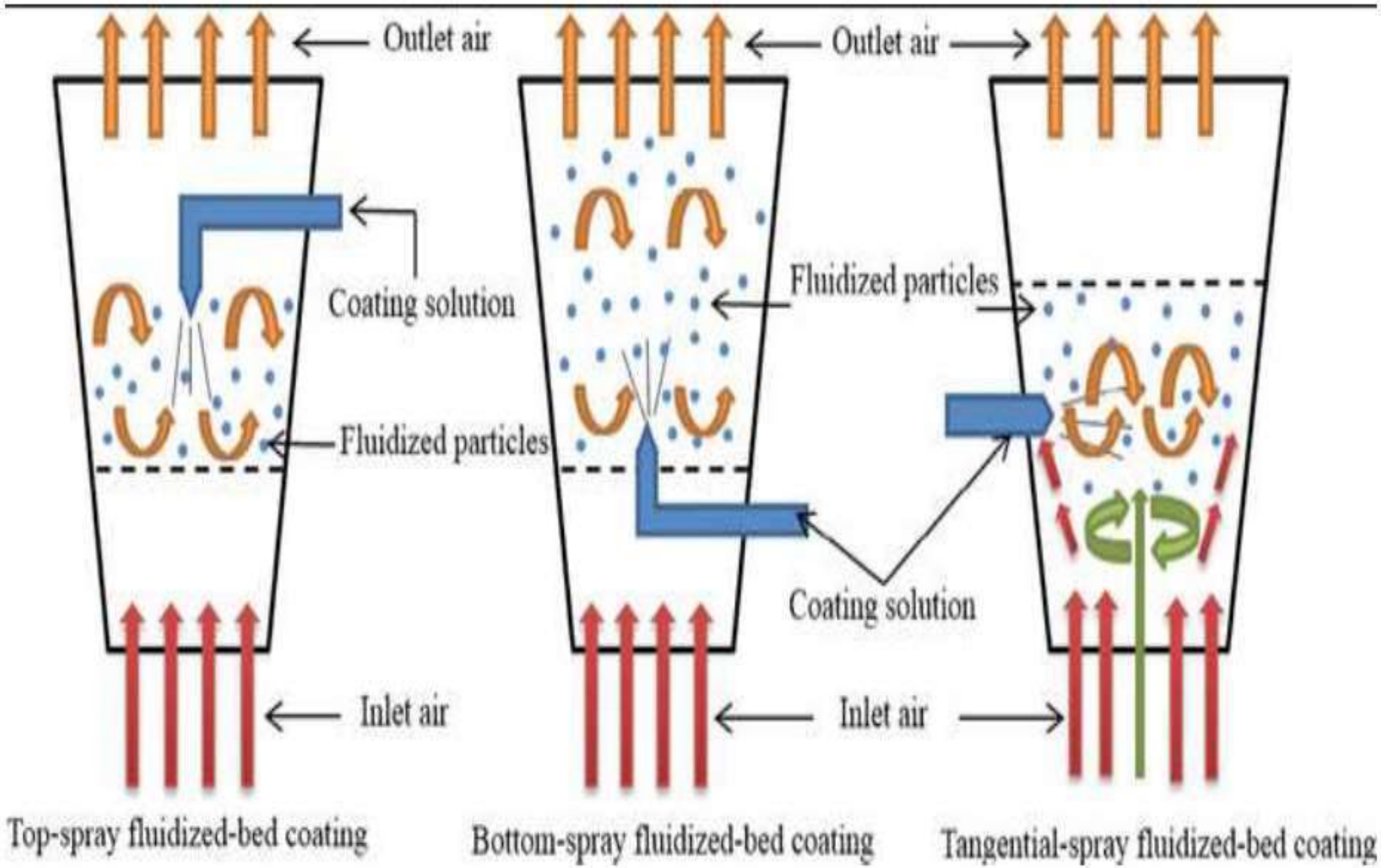
- Spray nozzle atomizes and introduces the coating fluid into a fluidized bed. The nozzle’s position can either be at the top mid or bottom of the fluidized bed coater.
- This process will continue until you achieve the right coating on your tablets.
- Basically, we can choose any of the three types of tablet coating machines.
- The degree of coating fluid atomization in any of these machines will depend on,

i. Type, design and size of the nozzle

ii. Fluid pressure

iii. Orifice size

FLUIDIZED BED COATER



TABLET PROCESSING PROBLEMS AND ITS REMEDIES

- The imperfections known as: VISUAL DEFECTS are either related to imperfections in any one or more of the following factors:

I. Formulation design.

II. Tableting process.

III. Machine.

Tablet defects

1- Capping

- The upper or lower segment of the tablet separates horizontally, either partially or completely from the main body and comes off as a cap, during ejection from the tablet press, or during subsequent handling.

Reason:

- Due to the air–entrapment in a compact during compression, and subsequent expansion of tablet on ejection of a tablet from a die.

The Causes and Remedies of Capping related to **Formulation**

	Causes	Remedies
1-	Large amount of fines in the granulation	Remove some or all fines through 100 to 200 mesh screen.
2-	Too dry or very low moisture content (leading to loss of proper binding action).	Moisten the granules suitably. Add hygroscopic substance e.g.: sorbitol, methyl- cellulose or PEG-4000
3-	Not thoroughly dried granules	Dry the granules properly
4-	Insufficient amount of binder or improper binder	Increasing the amount of binder Adding dry binder such as pre-gelatinized starch, gum acacia, powdered sorbitol, PVP, hydrophilic silica or powdered sugar.
5-	Insufficient or improper lubricant	Increase the amount of lubricant or change the type of lubricant
6-	Granular mass too cold	Compress at room temperature

The Causes and Remedies Of Capping Related To **Machine**

	Causes	Remedies
1-	Poorly finished dies	Polish dies properly. Investigate other steels or other materials
2-	Deep concave punches or beveled-edge faces of punches	Use flat punches.
3-	Lower punch remains below the face of die during ejection	Make proper setting of lower punch during ejection
4-	Incorrect adjustment of sweep-off blade.	Adjust sweep-off blade correctly to facilitate proper ejection.
5-	High turret speed	Reduce speed of turret (Increase dwell time).

2-Lamination:

- Separation of a tablet into two or more distinct horizontal layers.

Reason:

- Air–entrapment during compression and subsequent release on ejection.
- The condition is exaggerated by higher speed of turret.

The Causes and Remedies of Lamination related to ‘**Formulation**’

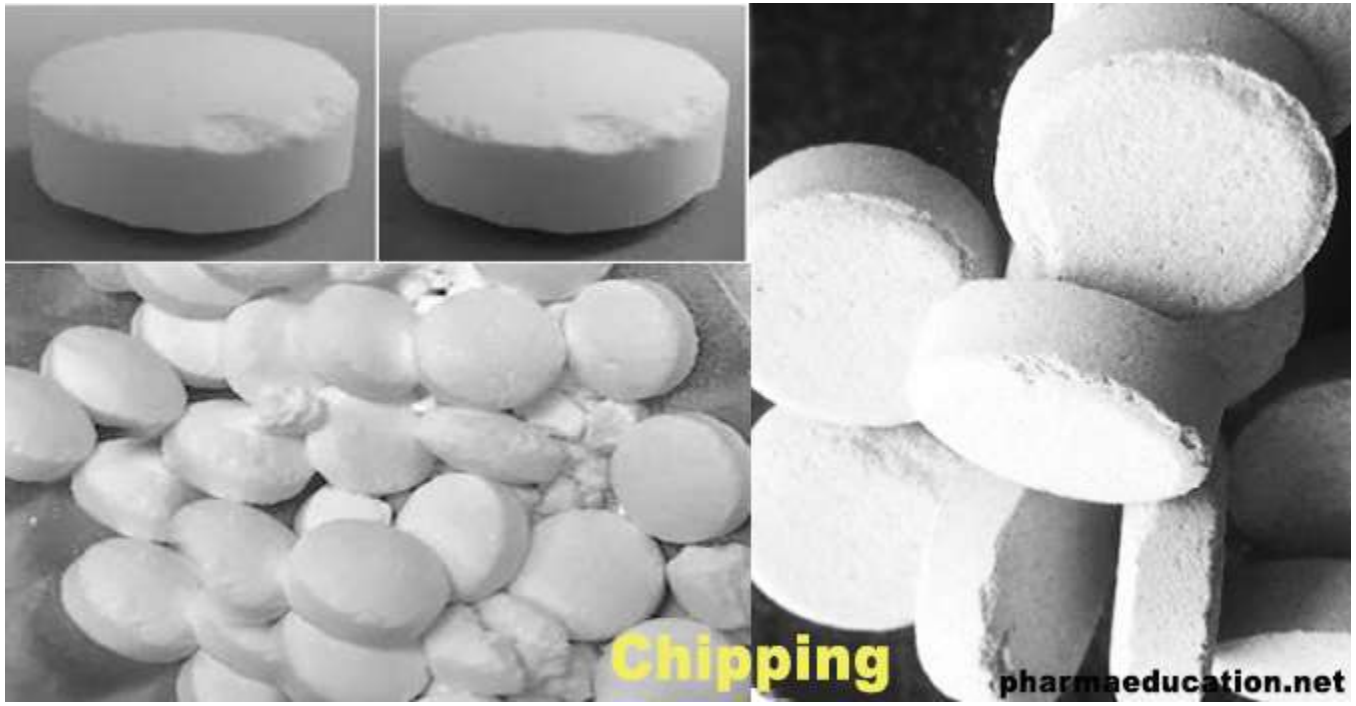
	Causes	Remedies
1-	Oily or waxy materials in granules.	Modify mixing process. Add adsorbent or absorbent.
2-	Too much of hydrophobic lubricant. e.g. Magnesium-stearate.	Use a less amount of lubricant or change the type of lubricant.

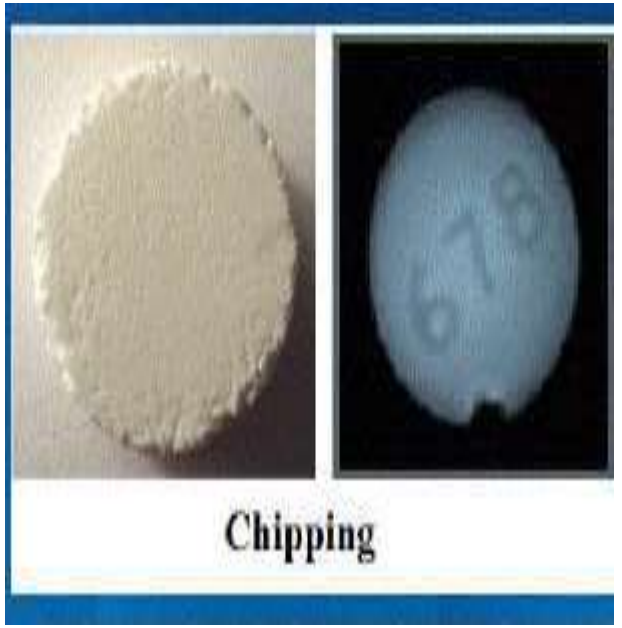
The Causes and Remedies of Lamination related to **Machine**

	Causes	Remedies
1-	Rapid relaxation of the peripheral regions of a tablet, on ejection from a die.	Use tapered dies, i.e. upper part of the die bore has an outward taper of 3° to 5°.
2-	Rapid decompression	Use pre-compression step. Reduce turret speed and reduce the final compression pressure.

3- Chipping:

Breaking of tablet edges, while the tablet leaves the press or during subsequent handling and coating operations.





The Causes and Remedies of Chipping related to ‘**Formulation**’

	Causes	Remedies
1-	Sticking on punch faces	Dry the granules properly or increase lubrication.
2-	Too dry granules.	Moisten the granules to plasticize. Add hygroscopic substances.
3-	Too much binding causes chipping at bottom	Optimize binding, or use dry binders

The Causes and Remedies of Chipping related to **Machine**

	Causes	Remedies
1-	Groove of die worn at compression point	Polish to open end, reverse or replace the die.
2-	Barreled die (center of the die wider than ends)	Polish the die to make it cylindrical
3-	Edge of punch face turned inside/inward	Polish the punch edges
4-	Concavity too deep to compress properly.	Reduce concavity of punch faces. Use flat punches.

4-Cracking:

Small, fine cracks observed on the upper and lower central surface of tablets, or very rarely on the sidewall are referred to as 'Cracks'.

Reason:It is observed as a result of rapid expansion of tablets, especially when deep concave punches are used.

THE CAUSES AND REMEDIES OF CRACKING RELATED TO 'MACHINE'

	Causes	Remedies
1-	Tablet expands on ejection due to air entrapment	Use tapered die
2-	Deep concavities cause cracking while removing tablets	Use special take-off.


Cracking

The Causes and Remedies of Cracking related to **Formulation**’

	Causes	**Remedies**
1-	Large size of granules.	Reduce granule size. Add fines.
2-	Too dry granules	Moisten the granules properly and add proper amount of binder.
3-	Tablets expand	Improve granulation. Add dry binders.
4-	Granulation too cold.	Compress at room temperature.

5- Sticking:

➢Sticking is a defect of the tablet where the tablet surface sticks to the punch face or adhesion of tablet material to the die wall during compression. Simply, sticking is the adherence of material to the faces of tablet press punches or dies after compression

Reason*:*

• Improperly dried or improperly lubricated granules.

The Causes and Remedies of Sticking related to Formulation

	Causes	Remedies
1-	Granules not dried properly	Dry the granules properly. Make moisture analysis to determine limits
2-	Too little or improper lubrication	Increase or change lubricant.
3-	Too much binder	Reduce the amount of binder or use a different type of binder
4-	Hygroscopic granular material	Modify granulation and compress under controlled humidity.
5-	Oily or way materials	Modify mixing process. Add an absorbent
6-	Too soft or weak granules.	Optimize the amount of binder and granulation technique.

The Causes and Remedies of Sticking related to Machine

	Causes	Remedies
1-	Concavity too deep for granulation	Reduce concavity to optimum
2-	Too little pressure	Increase pressure
3-	Compressing too fast	Reduce speed.

6- Picking:

- Small amount of material from a tablet is sticking to and being removed off from the tablet-surface by a punch face.
- The problem is more prevalent on the upper punch faces than on the lower ones.
- Picking is a specific type of sticking that refers to particles getting stuck in or around the logo/characters embossed on the punch face.
- Sticking occurs when granules attach themselves to the faces of tablet press punches. Picking is a more specific term that describes product sticking only within the letters, logos, or designs on the punch faces

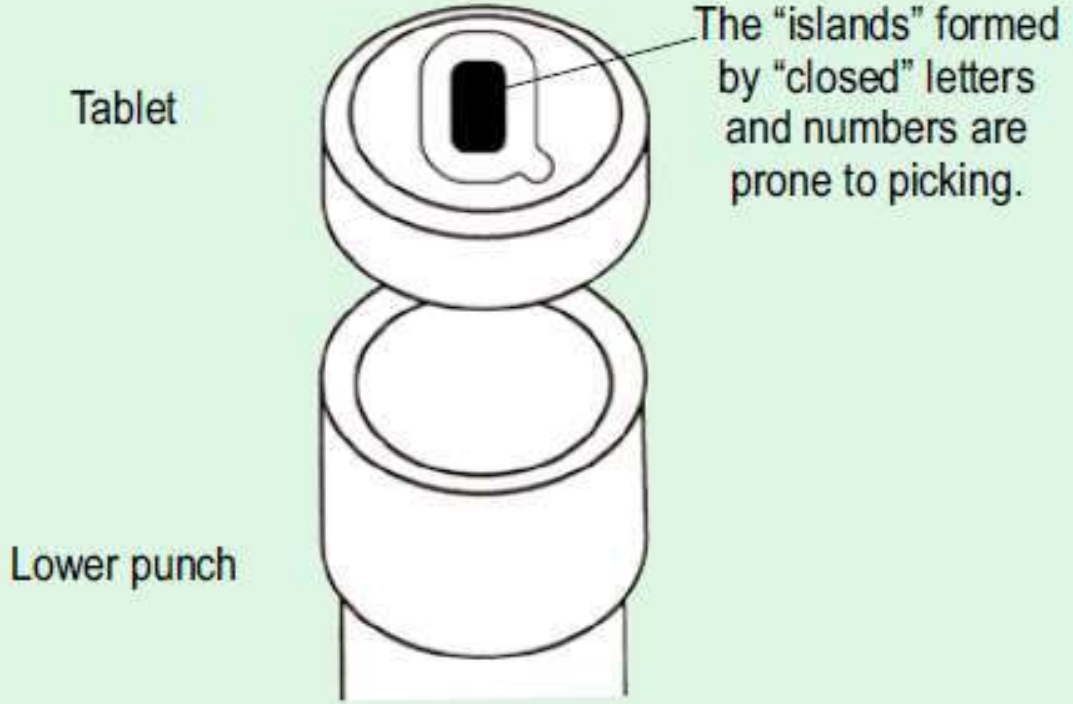
- Figure 1 shows the face of an upper punch with sticking product.
- Where figure 2 shows the particles stick within the letters and logos that are embossed or debossed on the faces of the compression tooling (Picking).

FIGURE 1

Product sticking to the face of an upper punch

FIGURE 2

An example of picking



- **Reason**:
  - Picking is of particular concern when punch tips have engraving or embossing letters.
  - Granular material is improperly dried.

The Causes and Remedies of Picking related to Formulation

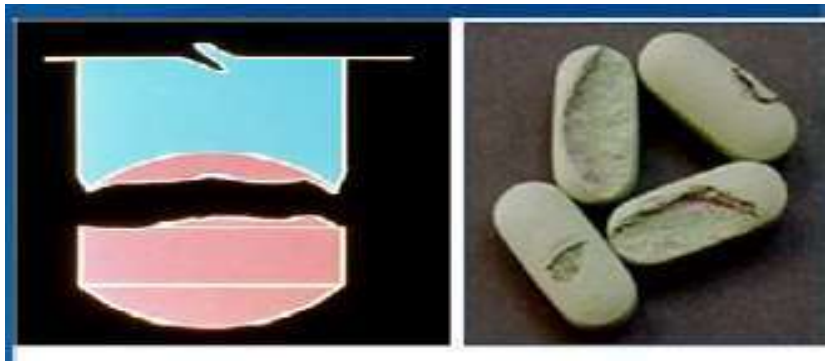
	Causes	Remedies
1-	Excessive moisture in granules	Dry properly the granules, determine optimum limit.
2-	Too little or improper lubrication	Increase lubrication; use colloidal silica as a polishing agent, so that material does not cling to punch faces.
3-	Low melting point substances, may soften from the heat of compression and lead to picking	Add high melting-point materials. Use high meting point lubricants
4-	Low melting point medicament in high concentration	Refrigerate granules and the entire tablet press
5-	Too warm granules when compressing	Compress at room temperature. Cool sufficiently before compression
6-	Too much amount of binder	Reduce the amount of binder, change the type or use dry binders

The Causes and Remedies of Picking related to Machine

	Causes	Remedies
1-	Rough or scratched punch faces.	Polish faces to high luster.
2-	Bevels or dividing lines too deep	Design lettering as large as possible.
3-	Pressure applied is not enough; too soft tablets	Plate the punch faces with chromium to produce a smooth and non-adherent face
4-		Reduce depths and sharpness
5-		Increase pressure to optimum.

Sticking & Picking

7- Binding:



- Sticking of the tablet to the die and does Not eject properly out of the die.
- Tablets adhere, seize or tear in the die.
- A film is formed in the die and ejection of tablet is hindered.
- With excessive binding, the tablet sides are cracked and it may crumble apart.

Reason*:* Usually due to excessive amount of moisture in granules, lack of lubrication and/or use of worn dies.

The Causes and Remedies of Binding related to Formulation

1-	Too moist granules and extrudes around lower punch.	Dry the granules properly
2-	Insufficient or improper lubricant.	Increase the amount of lubricant or use a more effective lubricant
3-	Too coarse granules	Reduce granular size, add more fines, and increase the quantity of lubricant
4-	Too hard granules for the lubricant to be effective	Modify granulation. Reduce granular size
5-	Granular material very abrasive and cutting into dies.	If coarse granules, reduce its size. Use wear-resistant dies.
6-	Granular material too warm sticks to the die	Reduce temperature. Increase clearance if it is extruding.

The Causes and Remedies of Binding related to Machine

	Causes	Remedies
1-	Poorly finished dies	Polish the dies properly.
2-	Rough dies due to abrasion, corrosion.	Investigate other steels or other materials or modify granulation
3-	Undersized dies. Too little clearance	Rework to proper size. Increase clearance
4-	Too much pressure in the tablet press	Reduce pressure. Or Modify granulation

8-Mottling:

Mottling is the term used to describe an unequal distribution of colour on a tablet, with light or dark spots standing out in an otherwise uniform surface.

- Reason: One cause of mottling may be a coloured drug, whose colour differs from the colour of excipients used for granulation of a tablet

The Causes And Remedies Of Mottling

	Causes	Remedies
1-	A coloured drug used along with colourless or white-coloured excipients	Use appropriate colourants
2-	A dye migrates to the surface of granulation while drying.	Change the solvent system, Change the binder, Reduce drying temperature and Use a smaller particle size.
3-	Improperly mixed dye, especially during Direct Compression	Mix properly and reduce size if it is of a larger size to prevent segregation
4-	Improper mixing of a coloured binder solution	Incorporate dry colour additive during powder blending step, then add fine powdered adhesives such as acacia and tragacanth and mix well and finally add granulating liquid

9- Double Impression:

- Involves only those punches, which have a monogram or other engraving on them.
- If the upper punch is uncontrolled, it can rotate during the short travel to the final compression stage and create a double impression.

Reason*:*

• At the moment of compression, the tablet receives the imprint of the punch.

• The lower punch freely drops and travels uncontrolled for a short distance before riding up the ejection cam to push the tablet out of the die

• Now during this free travel, the punch rotates and at this point, the punch may make a new impression on the bottom of the tablet, resulting in ‘double impression’.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Double Impression
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The Causes and Remedies of Double Impression

	Causes	Remedies
1-	Free rotation of either upper punch or lower punch during ejection of a tablet.	• Use keying in tooling, i.e. inset a key alongside of the punch, so that it fits the punch and prevents punch rotation. • Newer presses have anti-turning devices, which prevent punch rotation

Quality Control tests of Tablets

- Organoleptic properties.
- Thickness and diameter.

Non-pharmacopoeial tests:

- Hardness.
- Friability.

Pharmacopoeial tests:

- Weight variation.
- Drug content.
- Disintegration time.
- In- vitro dissolution.

The quality attributes that a tablet must possess can be summarized as follows:

1. The tablet should include the correct dose of the drug.
2. The appearance of the tablet should be elegant, and its weight, size and appearance should be consistent.
3. The drug should be released from the tablet in a controlled and reproducible way.
4. The tablet should be biocompatible, i.e. not include excipients, contaminants and microorganisms that could cause harm to patients.
5. The tablet should be of sufficient mechanical strength to withstand fracture and erosion during handling at all stages of its lifetime.
6. The tablet should be chemically, physically and microbiologically stable during the lifetime of the product.
7. The tablet should be formulated into a product acceptable to the patient.
8. The tablet should be packed in a safe manner.

➢ Organoleptic properties (color, odor and taste):

Color:

•Many pharmaceutical tablets use color as a vital means of rapid identification and consumer acceptance.

•The color of a product must be uniform within a single tablet (nonuniformity is referred to as ‘mottling’).

•Nonuniformity of coloring not only lacks esthetic appeal but could be associated with poor quality of the product.

For visual color comparison compare the color of

sample against standard color

Odor:

•The presence of odor in a batch of tablets could indicate stability problems, such as the odor of acetic acid in degrading aspirin tablets.

•However, the presence of an odor could be characteristic for the drug (vitamins), added ingredients (flavoring agents) or the dosage form (film-coated tablets).

Taste:

•Taste is important in consumer acceptance of, especially, chewable tablets.

➢ Diameter and shape:

•The diameter and shape depend on the die and punches selected for the compression of the tablet.

•Generally, tablets are discoid in shape, although they may be oval, oblong, round, cylindrical, or triangular.

•Their upper and lower surfaces may be flat, round, concave or convex to various degrees.

•The tablets may be scored in halves or quadrants to facilitate breaking if smaller dose is desired.

•The top or lower surface may be embossed with a symbol or letters which serve as an additional mean of identifying the source of the tablets.

•These characteristics along with the color of the tablets tend to make them distinctive and identifiable with the active ingredient which they contain.

➢Tablet thickness:

Thickness can vary with no change in weight due to:

a- Difference in the density of the granulation.

b- The pressure applied to the tablets.

c- The speed of tablet compression.

•Tablet thickness important in reproducing tablets identical in appearance but also to insure that every production lot will be usable with selected packaging components.

•If the tablets are thicker than specified, a given number no longer may be contained in the volume of a given size bottle.

- Tablet thickness can be measured by micrometer or by other device.
- Tablet thickness should be controlled within a ± 5% variation of standard value.

Why do we measure hardness?

- To determine the need for pressure adjustments on the tableting machine.
- To withstand the mechanical shocks of manufacturing, packaging, and shipping.
- To ensure consumer acceptance.

- Various devices used to test hardness are: Monsanto tester, Pfizer tester, Strong-cobb tester and schleuniger tester, erweka tester.

Factors Affecting the Hardness:

✓ Compression of the tablet and compressive force.

✓ Amount of binder.

✓ Method of granulation in preparing the tablet.

➢**To perform this test**, a tablet is placed between two anvils and the crushing strength that just causes the tablet to break is recorded.

Several **devices** operating in this manner have been used to test tablet hardness, e.g., the Erweka hardness tester.

Make hardness test on 5 tablets and then take the average hardness.

- **Limits:**

Oral tablets have a hardness of 4 to 10kg ; but, hypodermic and chewable tablets have a hardness of 3 kg and sustained release tablets have about 10-20 kg.

Fig-1: Monsanto Hardness tester

Fig-2: Pfizer tester

Fig-3: Erweka tester

➢ HARDNESS (CRUSHING STRENGTH):

Tablets require a certain amount of strength, or hardness to withstand mechanical shocks of handling in manufacture, packaging and shipping.

- Tablet hardness has been defined as the force required to break a tablet in a diametric compression test.
- Hardness of tablets may be defined as the resistance of tablets to capping, abrasion or breakage under conditions of storage, transportation and handling.
- The instrument measures the force required to break the tablet when the force generated by a coil spring is applied diametrically to the tablet.
- Hardness generally measures the tablet crushing strength.

➢ Friability:

- It is may be defined as the excessive breakness of tablets during mechanical shocks of handling in manufacture, packaging, and shipping.

This can affect the elegance appearance, consumer acceptance of the tablet, and also add to tablet's weight variation or content uniformity problems.

- Friability is affected by various external and internal factors like: Punches that are in poor condition or worn at their surface edges, resulting in „whiskering" at the tablet edge and show higher than normal friability values.

- Friability of a tablet can determine in laboratory by Roche friabilator. This consist of a plastic chamber that revolves at 25 rpm, dropping the tablets through a Distance of six inches in the friabilator, which is then operate for 100 revolutions. The tablets are reweighed.

Compress tablet that lose less than 0.1 to 0.5 % of the tablet weigh are consider acceptable

Fig-5: Friability apparatus

Procedure:

1. Weigh 20 tab al together

2. Put these tablets in the friabilator and adjust the instrument at 100 rpm.

3. Weigh the 20 tablets (only the intact ones).

$F = 100 \times (1-w/w0)$

Where w0 = weight of tablets before friability

w = weight of tablets after friability

4. Friability (% loss) = It must be less than or equal to1% but

➢ Some chewable tablets and most effervescent tablets are highly friable and require special unit packaging

➢ Disintegration test for tablet:

• The time required to disintegrate the tablet is called **Disintegration Time.**

❑ The U.S.P. device to test disintegration uses 6 glass tubes that are 3” long; open at the top and 10 mesh screens at the bottom end.

✓ To test for disintegration time, one tablet is placed in each tube and the basket rack is positioned in a 1-L beaker of water, simulated gastric fluid or simulated intestinal fluid at 37 ± 20 C such that the tablet remain 2.5 cm below the surface of liquid on their upward movement and not closer than 2.5 cm from the bottom of the beaker in their downward movement.

✓ Move the basket containing the tablets up and down through a distance of 5-6 cm at a frequency of 28 to 32 cycles per minute.

- ✓ Floating of the tablets can be prevented by placing perforated plastic discs on each tablet. According to the test the tablet must disintegrate and all particles must pass through the 10 mesh screen in the time specified. If any residue remains, it must have a soft mass.

Fig-6: Disintegration apparatus

Disintegration limits for tablets

Tablet type	
Uncoated	15 minutes
Enteric coated tablet	3 hours
Dispersible tablet	3 minutes
Effervescent tablet	< 3 minutes
Sublingual table	4 hours
Buccal tablet	4 hours
Vaginal tablet	60 minutes
Chewable tablet	Not required

➢ Dissolution test:

• The dissolution rate is defined as the amount of drug substance that goes into solution per time under standardized conditions of liquid / solid interface, temperature, and solvent composition .

•Dissolution is considered one of the most important quality control tests performed on pharmaceutical dosage forms and is now developing into a tool for predicting bioavailability, and in some cases, replacing clinical studies to determine bioequivalence.

Fig-9: Dissolution apparatus paddle type

The formulation and manufacturing factors affecting the dissolution of tablet:

1-**Particle size:**

The rate of dissolution is directly proportional to the surface area of the drug. The effective surface area of the particles in the dissolution medium is inversely proportional to the particle size.

- One method of increasing effective surface area is micronization or by reducing the particle size of the drug.

✓ Particle size reduction a successful strategy for enhancing the dissolution rate of water insoluble, hydrophilic drugs (such as nitrofurantoin, chloramphenicol and griseofulvin).

✓ However, in case of water-insoluble, hydrophobic drugs as exemplified by phenobarbital, phenacetin and aspirin, micronization might result in a decreased dissolution rate.

Micronized particles of hydrophobic drug adsorbed more air on their surface, resulting in floating of drug on the dissolution medium.

2- Manufacturing processes:

High compression force during tablet manufacturing decreases the dissolution rate by increasing particle bonding, increasing density and hardness, decreasing permeability of the dissolution medium and by inhibiting the wettability of the tablet due to the formation of a sealing layer by the lubricant under high pressure and temperature.

Of the known granulation procedures, wet granulation is the most accepted procedure to dry or direct compression in terms of achieving higher dissolution rates. Wet granulation imparts hydrophilic properties to the surface of the granules and improves the dissolution rates of poorly soluble drugs.

3- The type and concentration of lubricant, disintegrant, and binder.

Apparatus-1 (Basket Type)

- A single tablet is placed in a small wire mesh basket attached to the bottom of the shaft connected to a variable speed motor.
- The basket is immersed in a dissolution medium contained in a 1000 ml flask.
- The flask is cylindrical with a hemispherical bottom.
- The flask is maintained at 37±0.50C by a constant temperature bath.
- The motor is adjusted to turn at the specified speed and sample of the fluid are withdrawn at intervals to determine the amount of drug in solutions.

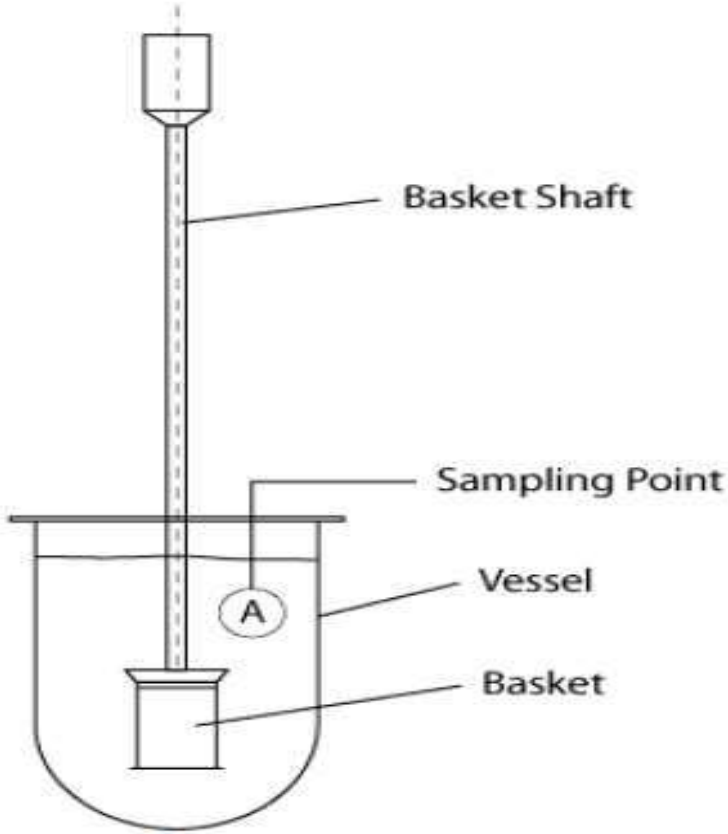
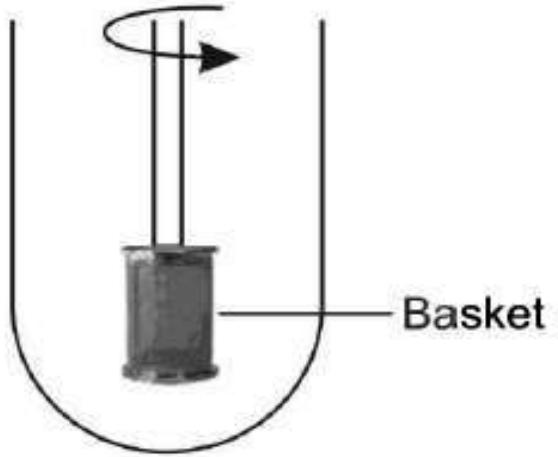
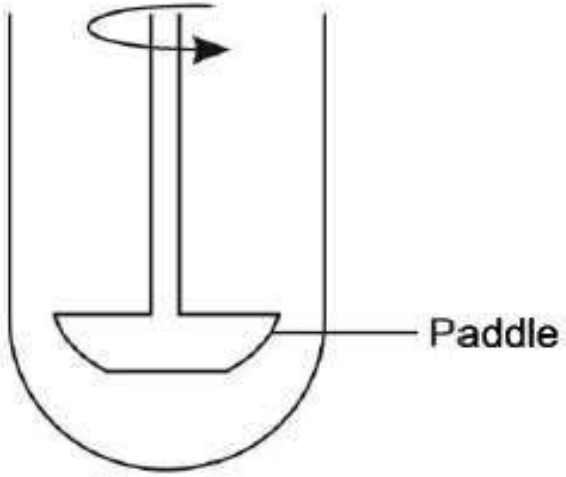
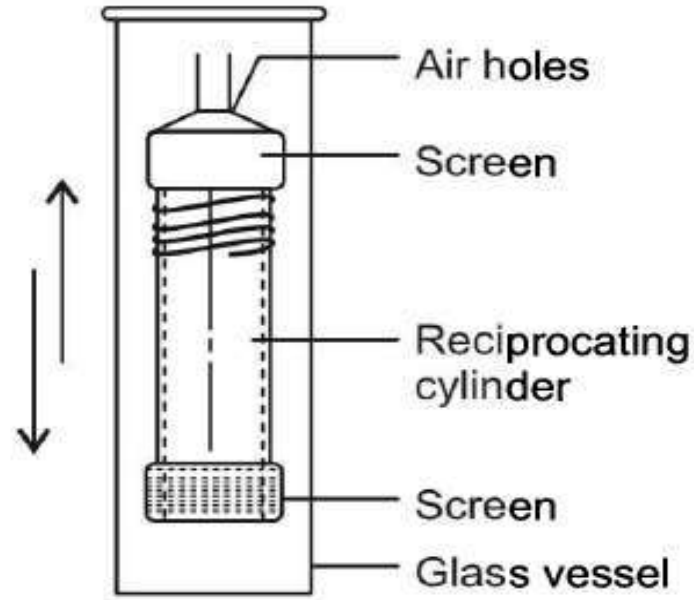
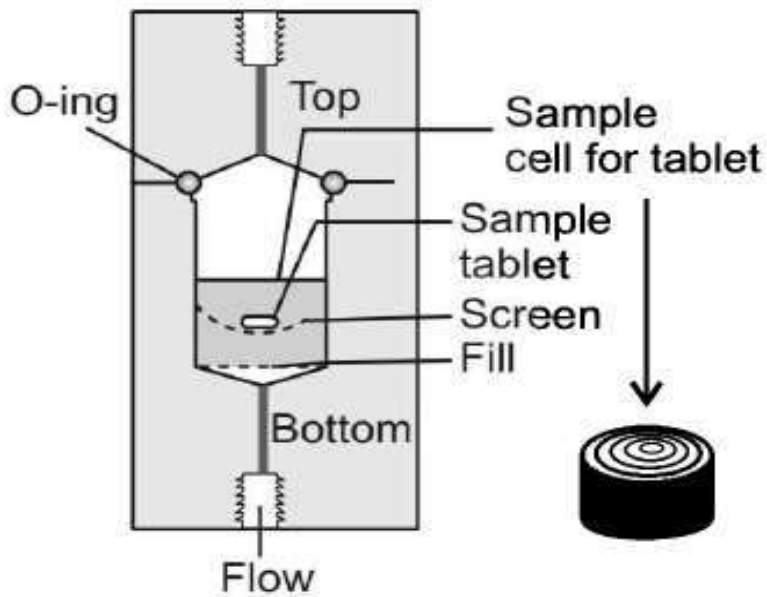


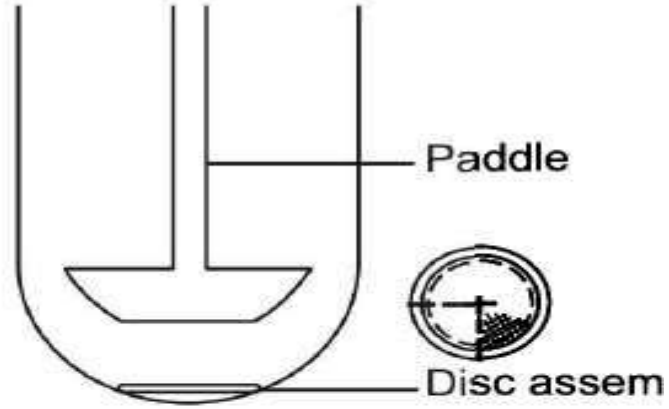
Fig-7: Basket type apparatus

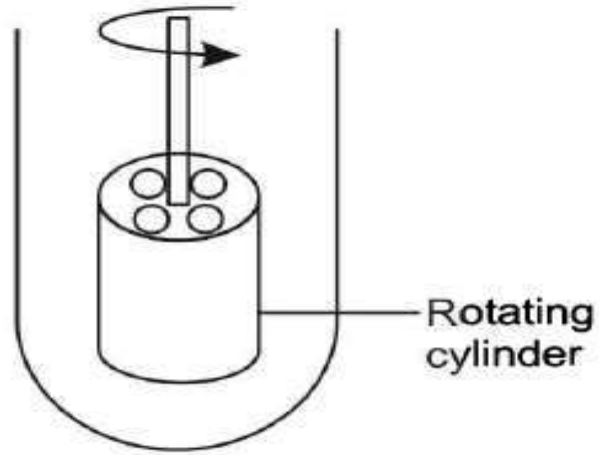
USP-approved dissolution apparatus

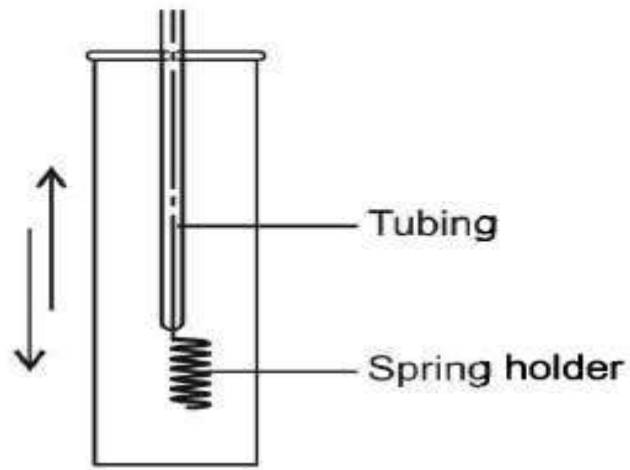
USP Dissolution apparatus	Important characteristic	Dosage form evaluated	Diagram
Apparatus 1 Basket apparatus	A rotating mesh (40 mesh standard) stainless steel basket in a hemispherical vessel	Immediate-release product Extended-release product Floating dosage forms Nutritional supplements	
Apparatus 2 Paddle apparatus	A rotating stainless steel metallic blade attached to shaft in a hemispherical vessel	Immediate-release product Extended-release product Chewable, sublingual tablet Powder, granules Suppositories Nutritional supplements	

USP Dissolution apparatus	Important characteristic	Dosage form evaluated	Diagram
Apparatus 3 Reciprocating cylinder (Bio-Dissolution apparatus)	A set of glass reciprocating cylinders in cylindrical flat-bottomed glass vessels and screens to fit the tops and bottoms of the reciprocating cylinders	Extended-release product	
Apparatus 4 Flow-through cell	A low-volume (often <30 ml) dissolution cell and a reservoir to continually provide fresh solvent to maintain sink conditions.	Extended-release product Implants Suppositories Soft gelatine capsules	

Apparatus 5 Paddle-over-disk	A rotating paddle over a disk in a hemispherical vessel	Transdermal patch
Apparatus 6 Cylinder apparatus	A rotating stainless steel cylinder in a hemispherical vessel. Presence of 4 holes improves circulation of dissolution media	Transdermal patch
Apparatus 7 Reciprocating holder	A holder (disk, cylinder, spring, or pointed rod) that oscillates up and down in a cylindrical vessel	Transdermal patch Osmotic pump devices Extended release tablets Coated delivery systems







➢ Content uniformity:

• This test is done to ensure that every tablet contains the amount of drug substance intended with little variation within a batch.

Procedure:

- Randomly select 30 tablets. 10 of these assayed individually.
- The Tablet pass the test if 9 of the10 tablets must contain not less than 85% and not more than 115% of the labeled drug content and the 10^{th} tablet may not contain less than 75% and more than 125% of the labeled content.
- If these conditions are not met, remaining 20 tablets assayed individually and none may fall outside of the 85 to 115% range

➢Weight variation:

- Tablet weight is mainly affected by factors such as tooling of the compression machine, head pressure, machine speed and flow properties of the powder. Inconsistent powder or granulate density and particle size distribution are common sources of weight variation during compression.
- Uniformity of weight is an in process test parameter which ensures consistency of dosage units during compression.

Procedure :

- Take 20 tablets and weighed individually.
- Calculate average weight and compare the individual tablet weight to the average.
- The tablet pass the U.S.P. test if no more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit

limits for weight variation of tablets

IP/BP	Limit	USP
80 mg or less	10%	130mg or less
More than 80mg or Less than 250mg	7.5%	130mg to 324mg
250mg or more	5%	More than 324mg