TABLETS

Definition:-

"Tablets are solid unit dosage form containing API & excipients used for oral dosage form with greatest dose precision."

Advantages:-

-Oral dosage form so avoid pain, infection & inflammation compared to I.V.

- They have specific release profile like enteric, delay release or immediate release profile.

- Accuracy of dosage is maintained.

-Physically & chemically stable.

- No chances of microbial growth.

-So, sterilization is not required.

-Suitable for larger scale production.

-Easiest & cheapest packaging.

-Low cost.

Disadvantages:-

-Hygroscopic substance can't be used.

- First pass metabolism occurs.

-Less bioavailability compared to I.V.

-Amorphous compounds & low density compounds are difficult to compress.

-Drugs having bitter taste require special treatment like coating or encapsulation, which increase production cost.

-High dose drugs are difficult to formulate as tablet dosage form.

-Drugs that are liquid in nature are difficult to formulate as a tablet.

-Swallowing of tablets especially by children and critically ill patients is very difficult.

• Formulation of Tablets

(Design/ Excipients used in tablets)

1) API
2) Diluent
3) Binder
4) Disintegrant
5) Lubricant
6) Glident
7) Anti-adherent
8) Colour
9) Flavour
10) Sweetner

1) Diluents/ Bulking agents/ Fillers

"Diluents are fillers to make up the required bulk of tablet when drug dosage is inadequate to produce the bulk."

Ideal Properties:-

- Chemically inert.
- Non-toxic.
- Cheap.
- Easily available.
- Should be compatible with other excipients.
- Resistant to microbial growth.
- Biocompatible.
- Colour-compatible.
- should have good bulk increasing property.

-do not alter bioavailability.

(i) Lactose

-Lactose is a first diluent, still it is most widely used.

-No reaction with API.

-2 types → (i) **Hydrous Lactose** & (ii) **Anhydrous Lactose**

-Hydrous lactose is used in wet granulation & undergoes **Millard reaction.**

- 2 grades of Lactose-
  - i) 60-80 # → Coarse
  - ii) 80-100 # → Regular

-Substitute- **Spray dried lactose.**

(ii) Starch

-Derived from potato, corn or wheat.
-Occasionally used as tablet diluent.
-Moisture content of USP grade starch is 11-14.
-Substitute- **Sta Rx-1500**
-used as directly compressible starch.
-used as self-lubricating agent.
-Composition → 5% of Amylose + 15% of Amylopectin + 80% unmodified starch.
-Two hydrolysed forms of starch:-

(i) Emdex
(ii) Celutab

(iii) Dextrose

-Trade name → **"CERELOSE®"**
-Hydrous & Anhydrous Dextrose available.
-Dextrose is now replaced to spray dried lactose.

(iv) Mannitol

-It is most expensive sugar used as tablet diluent.
-Pleasant feeling in mouth, widely used in chewable tablets.
-Sweet.
-Non-hygroscopic.

(v) Sorbitol

-It isomer of mannitol.
-combined with mannitol preparation to reduce cost.
-hygroscopic
-Both sugars are non-carcinogenic.

(vi) Sucrose

-Trade name → **"Sugar tab®"** (90-93% Sucrose + 7-10% invert sugar)
→ **"Dipac®"** (97% Sucrose + 3% Dextrin)
→ **"Nutab®"** (95% Sucrose + 4% invert sugar + 1% corn starch)

(vii) MCC (Micro-crystalline cellulose)

-Trade name → **"AVICEL®"**
-2 Grades → (i) **pH-101 (powder)** & (ii) **pH-102 (granules)**
-Expensive diluent compared to all.

2) Binders

"Binders are used either in dry or in liquid form during wet granulation to form granules or compact formation in directly compressible tablets."

Classification-

(i) Natural-

Ex- Acacia
-Tragacanth
-Gelatin

-2 types- (i) Dry form- Direct compression
(ii) Solution form- Wet granulaton

Disadvantages-
-Microbial growth possible.
-In wet granulation, this material quickly dry in temp. above 37°C.

(ii) Synthetic-

Ex- Starch paste- dispensing 10-20% starch in water by heating.
- Hydrolysis of starch = Dextrin + Glucose

-Liquid glucose- 50% of solution of glucose in water used as wet granulating agent.
-Sucrose- 50-74% sucrose solution also capable of producing wet granulation.
-Alginate & Cellulose derivatives= MC, HPMC
-PVP (in alcoholic solution)
-Excessive use of binder increases disintegration time.

3) Disintegrants

"Disintegrants are added in tablet formulation for disintegration of tablet, when it comes in contact with water in GIT, it draws water in tablet, causes swelling & bursting."

Ex- Starch
- starch derivatives
-Conc.= 5-20% of total weight of tablet.
- Modified starch → **Primogel & Explotab**
- Bentonite → 10%
- Disintegrants are added →
(i) Intragranular → during formation of granules.
(ii) Extragranular → during compaction of granules in machine.

-**Superdisintegrants-**
-Recently developed superdisintegrant reduces DT time.
Ex- Cross Carmellose Sodium → Trade name- **"Ac-Di-Sol®"**
- SSG
- Cross povidone

4) Lubricants

"These are agents which reduces the friction during tablet ejection between wall of tablet & wall of die."

-Lubricants should be added at final mixing step just before tablet compression.
Ex- Talc
- Mg. stearate
- Na. acetate
- Na. benzoate
- NaCl
- Ca. stearate
- Stearic acid

-Talc contains Iron, so used carefully in which drug breakdown is catalyzed by presence of Iron.
- Oil & mineral oil used in form of spray or directly or in solution form and then dried.

5) Glidents

"These are agents which promote the flow of tablet granules or powder material by reducing friction between particles."

Ex- Talc (5%)
- Corn starch (5-10%)
- Colloid silica (Aerosil)
- Ca. silicate
- $MgCO_3$
- MgO

6) Anti-adherents

"These are the agents which reduce sticking or adhesion of tablet to the faces of punches or wall of die."

7) Colours

Ex- D & C colours
- FD & C colours

8) Flavours

Used in -chewable
- Mouth dissolving (MDT)
-Buccal
- Oro-dispersible

9) Sweetners

Used in Lozenges.
Ex- Sachharine
- Aspartame

• Types of Tablets

[1] Oral tablets for ingestion-

Ex- Compression tablet
- Multiple tablet
- Delayed Action tablet
- Sugar coated tablet
- Film coated tablet
- Chewable Tablet

[2] Tablets used in oral cavity-

Ex- Buccal tablet
- Sub-lingual tablet
- Lozenges
- Dental cones

[3] Tablets administered by other routes-

Ex- Implantation tablet
- Vaginal tablet

[4] Tablets used to prepare solutions-

Ex-Effervescent tablet
-Dispensing tablet
- Hypodermic tablet
- Tablet triturate

➢ Chewable tablet:-

"Chewable tablets are to be chewed in the mouth in between the teeth after ingestion."
-Not require swallowing.
-Mannitol is widely used as diluent in this type of tablet.
-Generally it not require any disintegrant.
-Can be taken at any place, if water is not available.
-Ex- Antacid
- Multi-vitamin
- Chewable Aspirin tablet for children.

- **Layer Tablet:-**

"These are the compressed tablet in which granules of incompatible substances are compressed into two or more layer in tablet by using specific machine."

- **Buccal Tablet:-**

"These tablets are usually small & flat & held between cheek."

- **Sublingual Tablet:-**

-Placed under tongue.
-Ex- Nitroglycerine

- **Lozenges:-**

"These tablet forms are commonly used to treat throat infection in common cold."
-These tablets not disintegrate in mouth but slowly dissolve in 30 min or less.

- **Dental cones:-**

"These are small tablet placed in dental socket after tooth extraction, it prevents multiplication of bacteria in socket & reduce bleeding & dissolve within 20-40 min."

- **Implantation tablets:-**

"Implants are small tablets meant for insertion under the skin by giving small cut in the skin which is stitched after insertion of tablet."
-Implantation or Depot tablets are used for sub-cutaneous implantation in animal or human.
- They provide prolong drug release from month to 1 year.

- **Dispensing Tablets:-**

"These are given with suitable volume of water by pharmacist to patient, prepare solution from tablet at the time of administration."
Ex- Silver compounds
- Quaternary ammonium compounds
- Merbromine

- **Hypodermic tablets:-**

"Administered by parenteral route."
-Tablet → in vial → dissolved in sterile water → injected

• Granulation Techniques

"Granulation may be defined as a size enlargement process which converts small particles into physically stronger and larger agglomerates."

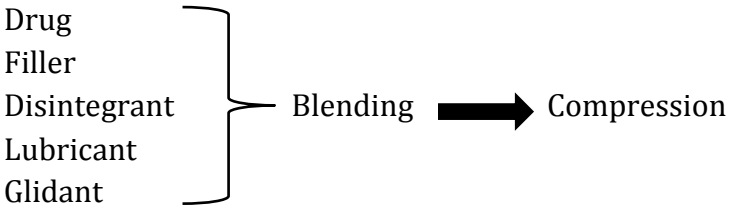
❖ Types of granulation methods:-

1) Direct compression
2) Wet granulation
3) Dry granulation

1) Direct Compression-

-Crystalline substances like NaCl, NaBr, KBr etc.. may be compressed directly.
-Direct compression materials should possess good flow property and compressibility & must be inert, tasteless, able to disintegrate and inexpensive.

Direct compression method



Advantages-

-Cost effectiveness.
-Suitable for moisture and heat sensitive components.
-Faster Dissolution.
-Less wear and tear of Punches.
-Simplified Validation.

Disadvantages-

-More prone to segregation (Non-uniformity of API & Excipients)
-Material cost is high because of low availability of directly compressible excipients.
-Weight variation is high

2) Wet Granulation-

-Most widely used process of agglomeration in pharmaceutical industry is wet granulation.
-It involves wet massing of the powder blend with a granulating liquid, wet sizing & drying.

➢ Steps involved in wet granulation-

1) Mixing of drug and excipients.
2) Preparation of Binder solution.
3) Mixing of binder solution with powder mixture to form wet mass.
4) Coarse screening of wet mass using a suitable sieve.
5) Drying of moist granules.
6) Screening of dry granules.
7) Mixing of screened granules with glident and lubricant.
8) Compression

➢ Special wet granulation techniques-

1) High Shear Mixture Granulation:-

-In this technique, blending & wet massing is accompanied by high mechanical agitation by an impeller and a chopper.
-Mixing, densification & agglomeration are achieved through shear and compaction force exerted by the impeller.

2) Fluid bed Granulation:-

-Fluidization is the operation by which fine solids are transformed into a fluid like state through contact with a gas.
-Fluid bed granulation is a process by which granules are produced in single equipment by spraying a binder solution onto a fluidized powder bed.

3) Extrusion and Spheronization:-

-It is a multiple step process capable of making uniform sized spherical particles.
-It is used to produce controlled release granules.

4) Spray Drying Granulation:-

-Unique technique that directly converts liquids into dry granules in a single step.

➢ Equipment for wet granulation-

1) High shear granulation-

-Little ford Lodgie granulator
-Little ford MGT granulator
-Diosna granulator

2) Granulator with drying facility-
-Fluidized bed granulator
-Day-nauta mixer processor
-Double cone or twin shell processor
-Topo granulator

3) Special granulator-
-Roto granulation
-Marumerizer

Advantages of Wet granulation-

-Useful for poor flow powders
-Useful for poorly compressible (fluffy) powders
-Colors and flavors can be added in granules for masking effect
-Possess good hardness and friability.

Disadvantages-

-High cost of fabrication.
-Loss of material during granulation & Screening.
-Not suitable for water sensitive & thermolabile compounds.
-Validation control is difficult.

3) Dry Granulation-

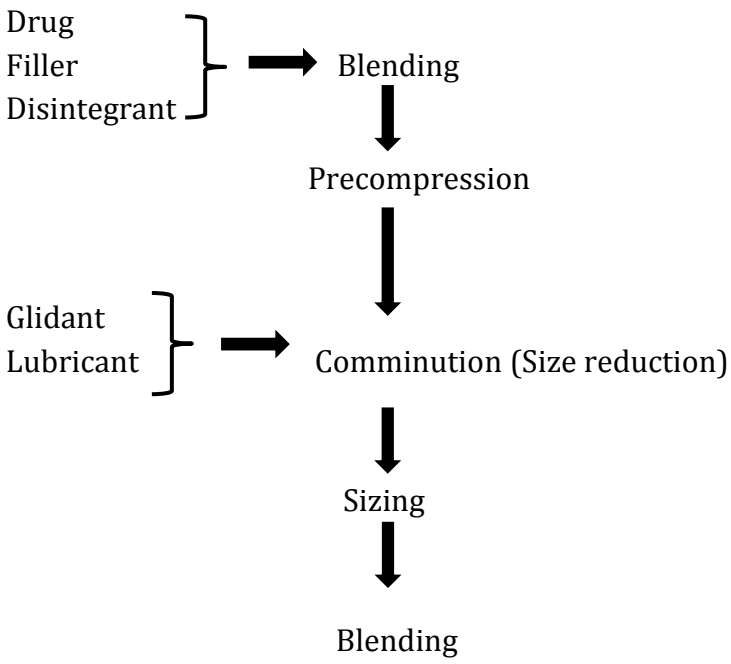
-In dry granulation process, the powder mixture is compressed without the use of heat and solvent.
-Not widely used.
-The two basic procedures are to form a compact of material by compressed and then to mill the compact to obtain granules.

➢ Steps involved in wet granulation-

1) Mixing of drug and excipients.
2) Mixing of milled powders
3) Compression into large, hard tablets to make slug.
4) Screening of slugs.
5) Mixing with lubricant and disintegrating agent
6) Tablet Compression

➢ Dry granulation techniques-

1) Slugging Process:-



2) Roller compaction:-

-The compaction of powder by means of pressure roll can also be done by a machine called **"Chilsonator".**

-The powder is fed between rollers which is mixed and screened through sieves.

Advantages of Dry granulation-

-For moisture sensitive material.
-For het sensitive material.
-Foe improved disintegration.

Disadvantages –

-It requires a specialized heavy duty tablet press to form slug.
-It does not permit uniform colour distribution.
-More product loss during processing.

• Physics of Tablet Compression
(Compression & Compaction)

Compressibility- It is the **ability of a powder to decrease in volume** under pressure.

Compression- Compression of a powder means **reduction in the bulk volume** of a material as a result of displacement of the gaseous phase under pressure.

Compaction- Compaction of a powder is a general term used to describe a situation in which **powdered material is subjected to some level of mechanical force**.

Consolidation- Consolidation is a process of making something stronger or more solid.

Decompression- During tablet manufacturing the compressional process is followed by a decompression stage, as the applied force is removed.
-This leads to a new set of stress within the tablets as a result of elastic recovery.

Deformation- It is referred to as change of geometry of a solid when it is subjected to opposing forces. The amount of deformation is called strain.

➢ Process of compression-

-In P'ceutical tablet manufacturing an appropriate volume of granules in a die cavity is compressed between upper and lower punch to consolidate the material into a single solid matrix which is subsequently ejected from the die cavity as an intact tablet.

-The events that occur in the process of compression:-

1) Transitional Repacking:-

-The particle size distribution of the granules and the shape of the granules determine the initial packing as the granulation movement occurs at lower pressure.
-The granules flow with respect to each other with the finer particles entering the void between the larger particles and the bulk density of the granules is increased.

2) Deformation at the point of contact:-

-When the particles of the granulation are so closely packed that no further filling of the void can occur, then a more further increase of compression force causes deformation at the point of contact.
-It is of two types:-

(i) Elastic Deformation- If the deformation is **disappear completely (return to original shape) upon release of stress**, it is an elastic deformation.

(ii) Plastic deformation- A deformation that **doesn't completely recover after release of the stress** is known as a plastic deformation.

3) Fragmentation and Deformation:-

-At higher pressure, fracture occurs when the stress within the particle become great enough to propagate cracks.
-Fragmentation causes further densification with the infiltration of the smaller fragments into void space.

4) Bonding:-

-Several mechanism of bonding in the compression process has been conceived but they have not been proved practically.
-Three theories of bonding are-
(i) The mechanical theory
(ii) The intermolecular theory
(iii) The liquid surface film theory

5) Deformation of the solid body:-

-As the applied force is further increased the bonded solid is consolidated toward a limiting density by plastic/ elastic deformation of tablet within the die.

6) Ejection:-

-As the lower punch rises and pushes the tablet upward, there is continued residual die wall friction.
-As the tablet is removed from the die the lateral pressure is relived and the tablet undergoes elastic recovery with an increase in the volume of that portion of the tablet removed from the die.

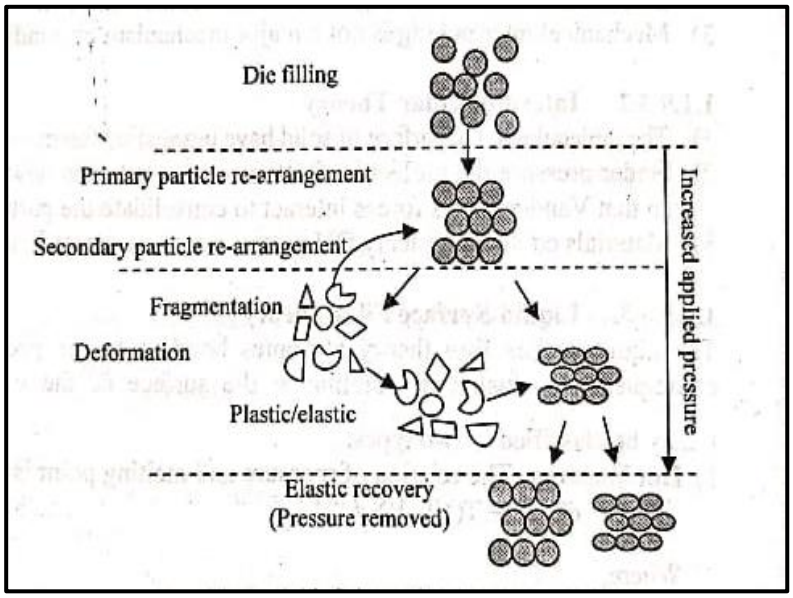


Figure:- **Powder compression cycle**

➢ Process of compaction-

-For compaction of dry powders, the bonding mechanisms may roughly be divided into three main types--- Solid bridges; Attraction forces and Mechanical interlocking.

-Particle fragmentation increases the number of surfaces available for bonding.

-While particle plastic deformation contributes mainly to bonding force.

-Thus, these two particles deformation mechanisms are bond producing and have a positive effect on tablet strength.

-Particle elastic deformation can lead to breakage of bonds after removal of the applied pressure as the tablet recovers in height.

-Thus, particle elastic deformation has a negative effect on tablet strength.

• Tablet Compression Machine
(Tablet Press)

-There are two types of press in common use during tablet production—the single punch (station) press and the rotary (multistation) press.
-In addition, hydraulic presses are used in research and development work forr the initial evaluation of the tableting properties of powders.

❖ Stages in Tablet Manufacturing

1) Die Filling-

-This is normally done 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 Formataion (Compression)-

-The upper punch comes downwards 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. (Decompression phase).

3) Ejection-

-During this phase, the lower punch rises until its tip reaches the level of the top of the die.
-Tablet is subsequently removed from the die and is pushed from die table by a pushing device (Scrap).

➢ Types of Tablet Punching Machines

1) Single Station Tablet Press

-Single punch tablet press is also called as an **"Eccentric press"** or single station press.
-It is most simplest machine for tablet manufacturing.
-Single station tablet press employs a single tooling station that is a die and a pair of punches.
-This tablet press is available as both manually operated and power driven.
-In this single punch tablet press, the compaction force on the fill material is exerted by only the upper punch while the lower punch is immovable such as action equivalent to hammering motion.
-TPM (Tablet per Minute) is approximately 60 to 200.

-The powder is held in a hopper which is connected to a hopper shoe (feed shoe) located at the die table.
-The hopper shoe (feed shoe) moves to and fro over the die.
-When the hopper shoe is located over the die, the powder is fed into the die by gravitational force.
-The amount of powder filled into the die is controlled by position of lower punch.
-When the hopper shoe is located beside the die, the upper punch comes down and the powder is compressed.
-After ejection, the tablet is pushed away by the hopper shoe as it moves back to the die for the next tablet.

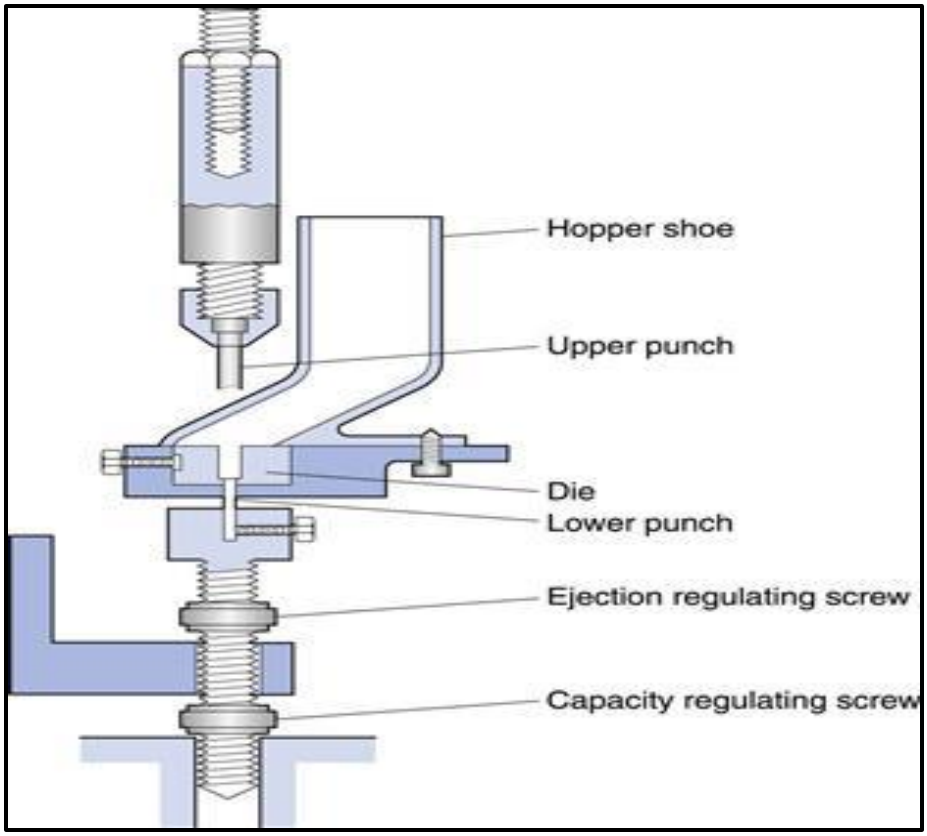


Figure:- **Single-Punch Tablet Press**

2) Multi-station Tablet Station Press/ Rotary Press

-The rotary press was developed to increase the output of tablets.
-The primary use of this machine is thus during scale-up in the latter part of the formulation work and during large scale production.
-Outputs of over 10,000 TPM can be achieved by rotary presses.
-A rotary press operates with a number of dies and sets of punches, which can vary considerably from three- for small rotary presses up to 60 or more- for large presses.
-The dies are mounted in a circle in the die table and both die table and the punches rotates together during operation of the machine, so that one die is always associated with one pair of punches.

-The vertical movement of the punches is controlled by tracks that pass over cams and rolls used to control the volume of powder fed into the die and the pressure applied during compression.
-The powder is held in a hopper whose lower opening is located just above the die table.
-The powder flows by gravity on to the die and is fed into the die by a feed frame.
-During powder compression, both punches operate by vertical movement.
-After tablet ejection, the tablet is knocked away as the die passes the feed frame.

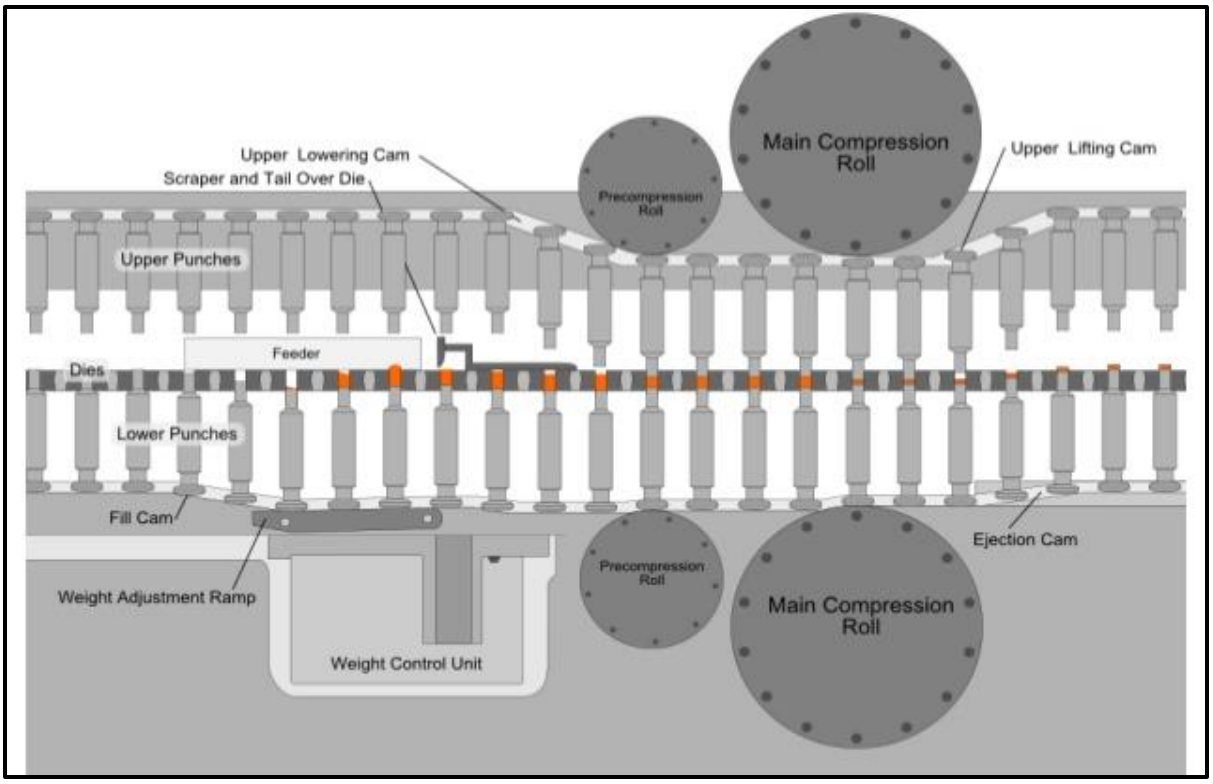


Figure:- **Rotary (Multi-Station) Tablet Press**

3) Computerised Hydraulic Press

-For computerized hydraulic presses, the movement of the punches can be controlled and varied considerably.
-Thus, tablets can be prepared under controlled conditions with respect to the loading pattern and loading rate.
-Possible applications are the investigation of the sensitivity of a drug to such variation, or to mimic the loading pattern of production presses to predict scale-up problems.
-Because of this application, this type of press is also referred to as a **"Compaction simulator".**

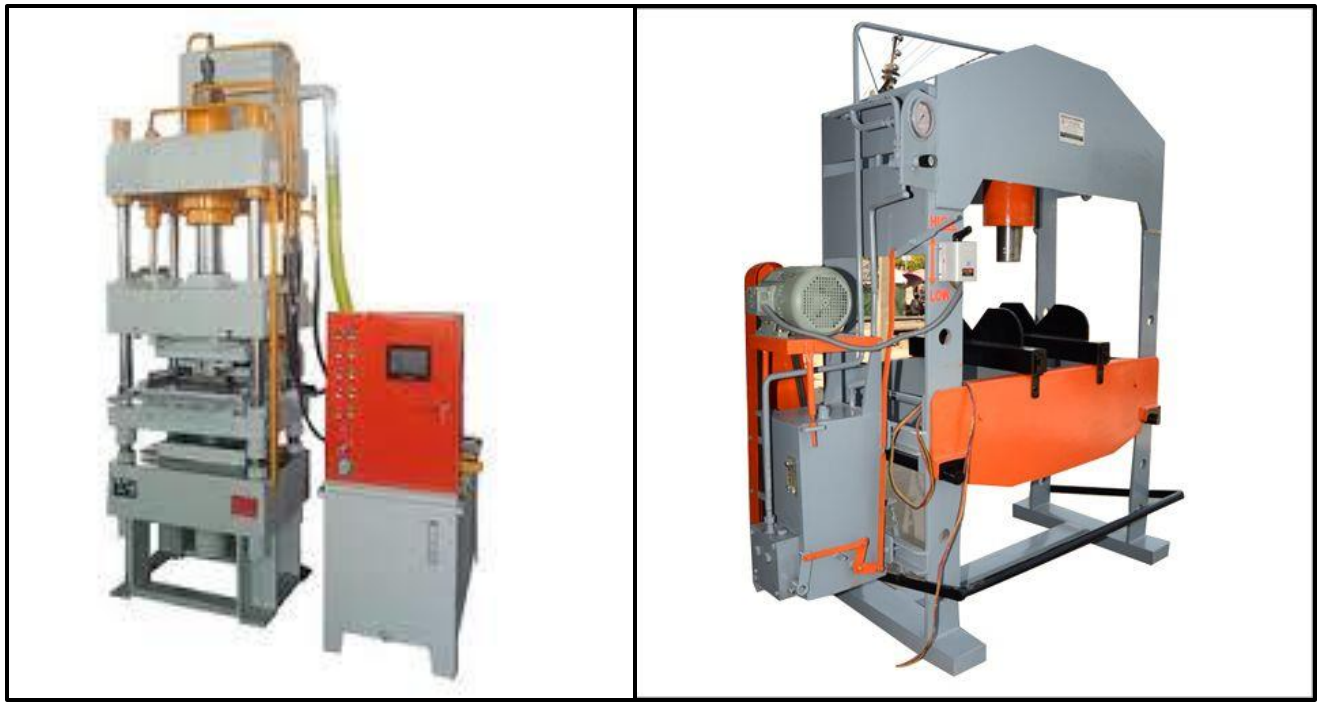


Figure:- **Computerised Hydraulic Press**

• Tablet Compression Tooling

"Tablet compression machines are made in keeping in view the type of dies and punches will be used on them. The dies and punches and their setup on compression machine is called tooling."

-Tooling is classified as **'B' and 'D'** mainly.
-The 'B' tooling dies and punch can be further have specifications as 'BB' and 'D' tooling can be utilized on 'B' tooling machine which is called as 'DB'.

Type of Tooling	Punch Length (mm)	Punch Diameter (mm)	Die Diameter (mm)	Height of dies (mm)	Max. Tab size (mm) Round/ Capsule
B	133.6	19	30.15	22.22	16/19
D	133.6	25.4	38.1	23.82	25/25
BB	133.6	19	24.0	22.22	13/14
DB	133.6	25.4	30.15	23.22	19/19

➢ Punches-

1) **Head:** The end of the punch that guides it through the cam track of tablet machine during Rotation.
2) **Head flat (Dwell Flat):** The flat area of the head that receives the compression force from Rollers (in upper punches) and determines the weight and ejection height (in lower punches).
3) **Outside head Angle**: The area gets in touch with the roller prior to head flat , while Compression.
4) **Inside Head Angle**: This is the area, which pulls down the lower punches after ejection and lifts the upper punches after compression.
5) **Neck:** The relived area between the head and barrel, which provides clearance for the cams.
6) **Barrel**: This area guides the punch (while going up and down) with reference to turret guides.
7) **Stem:** The area of the punch opposite the head, beginning at the tip and extending to the point where the full diameter of the barrel begins.
8) **Tip:** This determines size, shape & profile
9) **Tip face**: This area of punch is where the tablet is formed. Good surface finish is required here to get quality tablets.

10) **Working length**: This distance between bottom of the cup and the head flat is called as working length which determines weight and thickness of the tablet.
11) **Overall length**: Distance between top of the cup and the head flat.
12) **Key Angle**: The relationship of the punch key to the tablet shape. The keys position is influenced by the tablet shape, take-off angle, and turret rotation.
13) **Dwell time –** The time punches spends below the pressure roller while rotating in the machine.
14) **Clearance**: **Die bore dia – punch tip dia = Clearance.**

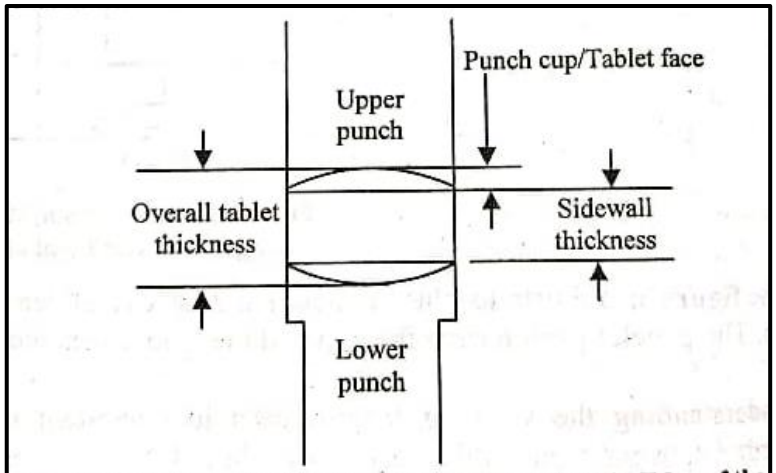


Figure 1.44: Cup Depth is the Distance from the Tip Edge of the Punch to the Lowest Point of the Cup. The cup determines the configuration and appearance of the tablet faces. The area between the two tablet faces is called the tablet sidewall

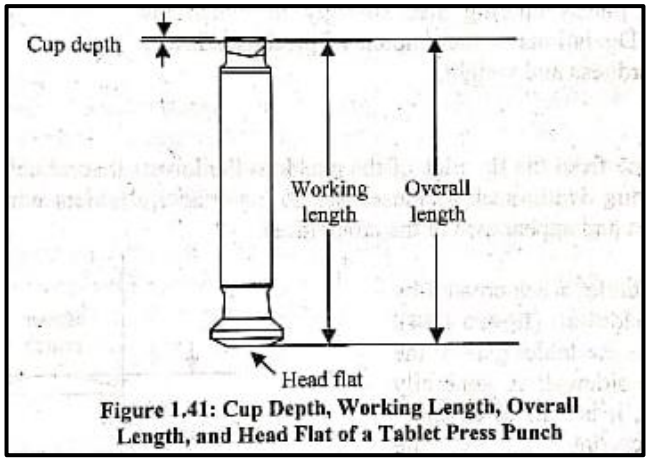


Figure 1.41: Cup Depth, Working Length, Overall Length, and Head Flat of a Tablet Press Punch

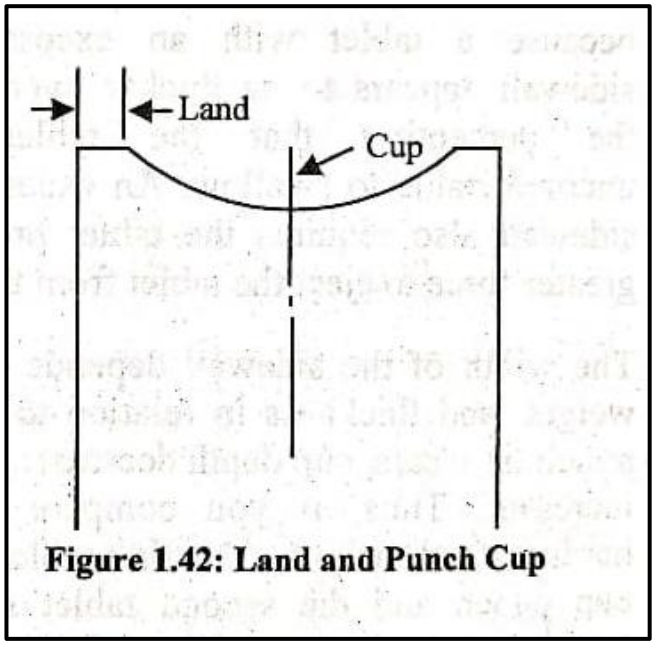


Figure 1.42: Land and Punch Cup

- **Type of Punches:-**

1) Flat-faced bevel-edged
2) Shallow concave
3) Standard concave
4) Deep concave
5) Extra deep
6) Modified ball

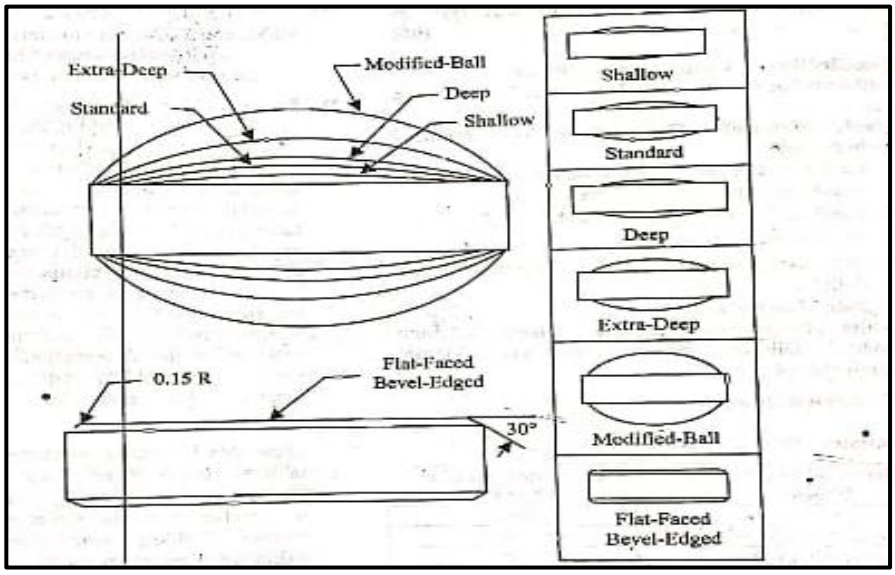


Figure:- **Types of Punches**

➢ Dies-

1) **Die.O.D.:** The outside diameter of the die, which is compatible with the die pockets in the press.
2) **Die Height**: The overall height of the die.
3) **Die Bore**: The cavity where the tablet is made. The Cavity's shape and size determine the same form of tablet.
4) **Taper dies**: dies with tapered bore on one or both sides. They are used for easy ejection of tablets (mainly for double layered tablets).
5) **Die Groove:** The groove around the periphery of the die, which allows the die to be fixed in the press.
6) **Lined (Insert) Dies**: Dies fitted with a linear insert made from a much harder, more wear resistant material such as tungsten carbide and ceramic.

- # Use and Care of Tablet Compression Tooling:-

-Appropriate Cleaning, maintenance, storage and use of compression tooling may reduce compression problems such as Capping, Weight variation as well as thickness variation.
-It will also help in ensuring a longer life for punches and dies.

-SOPs and records should be in place for the cleansing, issuing, maintenance and associated activities relating to tooling.

1) Cleaning- It is done to ensure removal of residues to avoid contamination or cross-contamination.
-When cleaning is done manually, appropriate materials should be used which are not toxic, which will not damage the tooling, and which will not become a source of contamination.

2) Inspection and Assessment- Visual assessment/ inspection should be done to ensure appropriate general condition of tooling.

3) Repairing- Check any damage such as punches, dies or corrosion in head angles.
-Repair should not further damage tools.
-Care should be taken as repairs may alter tool dimensions.

4) Measuring- Measure all tools after repairs and polishing.
-Use micrometers, height gauges or digital equipments.
-Should include head form, barrel diameter, tip diameter, overall length, critical working length, die outer diameter, die bore diameter.
-This ensure compliance in maintaining tablet weight.

5) Polishing- Automated polishing is now preferred over manual polishing.
-Polishing results in mirror finish and smooth surfaces.

6) Lubricating- Preservatives and rust inhibitors prevents corrosion when not in use.
-Tools should be dry before lubricant is applied.

7) Storage- Suitable storage methods and place and environment should be assisted.

8) Issuing, Use and returns-
-Responsible person would normally issue a set and ensure that the set is returned after use.
-It is often advised that punches be rotated in a set when issued for use.
-The use should be monitored in terms of number of tablets compressed.
-Records should be maintained (including destruction of tooling).

• Coating of Tablets

"Coating of tablets are defined as Tablet covered with one or more layer of mixture of various substances."

Objectives:-

-To mask the taste, colour or odour of the drug.

- To provide physical & chemical protection of drug.

-To protect the drug from gastric environment of stomach with gastro-resistant enteric coating.

-To control the release of drug.

-To incorporate another drug to avoid chemical incompatibility.

-To improve p'ceutical elegance by use of special colour & printing.

-To improve drug stability.

➢ Formulation of coating solution

1) Film former
2) Solvent
3) Colour
4) Plasticizer
5) Opaquent extender
6) Flavour / Sweetner
7) Surfactant
8) Preservatives

- **Solvent-**

  -Function of solvent system is to dissolve or disperse polymers & other additives.
  -Water is widely used as solvents but ingredients hydrolysed in water, uses organic solvents like Ethanol, Methanol, Acetone.

- **Colour-**

-Colourants are soluble in solvent system.
- For light shade use 0.01% conc.
-For dark shade use 2.0% conc.

'Opalux' – Opaquent colour for sugar coating
'Opaspray' – Opaquent colour for film coating
'Opadry' – Contain plasticizer, pigment in dry form & dispersed in aqueous or organic soluntion.
- Provide attractive coating.

- **Opaquent extenders-**

-They provide white coating or mask the colour of tablet coat.
-Expensive compared to inorganic material but less colorant is used.
Ex- TiO_2, Talc, $CaSO_4$, MgO, $Al(OH)_3$

- **Plasticizer-**

-Film can be modified by external or internal plasticizers.
-Internal plasticizers modify physical& chemical properties of polymers.
-External plasticizers can be Non-volatile liquid or another polymers incorporated with primary polymeric film former.
-Provides → Plasticity
- Flexibility
- Tensile strength

-Conc. = 1-50%
-Ex-
- Castor oil
- PEG
- TWEEN
- SPAN
- Glycerine
- PPG

➢ Types of Coating

1) Sugar coating
2) Enteric coating
3) Film coating
4) Specialized coating

[1] Sugar coating

"Compressed tablet may be coated with coloured or uncoloured sugar layer."
-Coating is water soluble & dissolve faster after ingestion.

Objectives-

-To mask the bitter taste.
-To increase appearance.
-Smoothing of tablet.
-Obtain modified release profile.

Steps of sugar coating-

1) Sealing
2) Sub-coating
3) Glossing & Smoothing
4) Colouring
5) Polishing

1) Sealing-

-It provide moisture barrier & harden the tablet surface.
-Without seal coat, tablet absorb excess of moisture, leading to tablet softening and faster disintegration which affect physical & chemical instability of finished product.

Ex- **Shellac**
- **Zein**

-It is an effective sealant, not increase dissolution time & DT time.

Ex- CAP (Cellulose acetate phthalate)
- HPMC
- HPC
- Polyvinyl acetate phthalate

2) Sub-coating-

-It is applied for round the edges & build up the tablet size.
-It increase 50-100% tablet wt.
-This step involve applying of binder solution & followed by dusting with powder then dry it.

Ex. Of binder→ -Gelatin
-Sucrose
-Acacia gum
-PEG

Ex. Of Dusting powder →-Talc
-$CaCO_3$
-TiO_2

3) Glossing/ Smoothing/ Syruping -

-To cover & fill imperfection in Tablet surface caused by sub-coating.
-Syrup also contains Pigments, starch, gelatin, acacia & Opacifier.

4) Colour coating-

-In this step, multiple application of syrup solution with colouring matter.
-Soluble dyes are used to achieve desired colour.

5) Polishing-

-Tablet can be polished in **standard coating pan** by applying powder wax or warm solution wax in volatile oil.
Ex- Bees wax
- Paraffin wax
- Carnauba wax

- **Defects of sugar coating:-**

-Brittle in nature, so chipping & cracking problem arise.
- Not proper drying then → Sticking & Picking occurs.
- Mottling.

[2] Film coating

"Film coating means deposition of thin film of polymer surrounding the tablet core."

- **Film forming material:-**

Ideal Properties-

- should be inert with medicament/API.
- Non-hygroscopic.
- Easily available.
- should give lustrous shiny effect.
- easily remove the coating after administration.

- **Types of film forming material-**

(i) Enteric material
(ii) Non-Enteric material

(i) Enteric material-

→ **CAP (Cellulose Acetate Phthalate)**

-Widely used in industry.
-FMC (American chemical Manufacturing company) developed patented Aqueous enteric coating, known as **"Aquatric®"**
-It is composed of Cellulose acetate phthalate with particle size 0.05-3 µm.

Disadvantages-

-It dissolve only above pH=6 & delay the absorption of drugs.
-Brittle in nature.
-Unstable due to presence of acetyl grp.
-Hygroscopic.

→ **HPMCP (Hydroxy propyl methyl cellulose phthalate)**

-It is soluble at pH= 5-5.5
-3 grades → HP-50
→ HP-55
→ HP-55-S

-Due to absence of acetyl group, stable in nature.

→PVAP (Polyvinyl acetate phthalate)

-It is having pH independent solubility.

-Supplied as ready to use in enteric system.

→ Acrylate polymer

- **"Eudragit®"**

-Grades of Eudragit → E_E [pH=5]
→ E_L [pH=6]
→ E_S [pH=7]
→ E_{RL} [pH independent]
→ E_{RS} [pH independent]

→ CAT (Cellulose Acetate Trimallitate)

(ii) Non-Enteric material-

→ EC (Ethyl Cellulose)

-Also known as **"Aquacoat®"**

→ HPMC (Hydroxy Propyl Methyl Cellulose)

→ MHEC (Methyl Hydroxy Ethyl Cellulose)

-Water insoluble & soluble in few organic solvent.

→ HPC (Hydroxy Propyl Cellulose)

-It is soluble in water below 40°C.

-used for sub-coating.

→ Povidone

-4 viscosity grades available by their 'K' value-

(i) K_{15} (Mol. Wt. = 10,000)
(ii) K_{30} (Mol. Wt. = 40,000) → widely used as binder.
(iii) K_{60} (Mol. Wt. = 1,60,000)
(iv) K_{90} (Mol. Wt. = 3,60,000)

[3] Enteric coating-

"This type of coating is used to protect core from disintegration in the acid environment of the stomach, to deliver the drug in small intestine."

Objectives-

-To prevent the degradation of acid sensitive API.
-To prevent irritation of stomach by certain drugs like sodium salicylate.
-Delivery of API into intestine.
-To provide a modified release of drug.

Kinds of enteric layer system-

1) One-Layer System- Coating is applied in one homogenous layer.
2) Two-Layer System- To prepare Enteric tablets of high quality and pleasing appearance.
-The enteric formulation is applied first, followed by coloured film.
-Both layers can be of enteric polymer or only the basic layer contains enteric polymer while top layer is fast disintegrating & water-soluble polymer..

Properties of Enteric coating material-

- Resistant to gastric fluids
-Susceptible/permeable to intestinal fluid
-Compatibility with most coating solution components and the drug substrate
-Formation of continuous film
-Nontoxic, cheap and ease of application
-Ability to be readily printed

Enteric materials-

→ **CAP (Cellulose Acetate Phthalate)**
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-Unstable due to presence of acetyl grp.
-Hygroscopic.

→ **HPMCP (Hydroxy propyl methyl cellulose phthalate)**
→**PVAP (Polyvinyl acetate phthalate)**
→ **Acrylate polymer**

→ **CAT (Cellulose Acetate Trimallitate)**

Note- Description to be written from film-forming material discussed above.

[4] Specialized coating

-Types→
(i) Compression coating
(ii) Dip coating
(iii) Electrostatic coating
(iv) Vacuum coating

(i) Compression coating:-

"It require specialized tablet compression machine, finished pdt. is tablet within a tablet."
-When tablet core can not tolerate organic solvent or water, at that time compression coating is used for taste masking & delay release of pdt.
-Incompatibile ingredient can be separated by this process.

Disadvantage- Expensive
- Not widely used

(ii) Dip coating:-

-Coating by dipping tablet into coating liquid.
-Wet tablet are dried in conventional coating pan.
-Alternate dipping & drying steps are repeated to achieve desired coating.

Disadvantage- Slow
-Small scale process

(iii) Electrostatic coating:-

"This method is effective by applying coating solution to conductive substance."
-Strong electrostatic charge is applied to the coating material containing conducting ionic species of opposite charge in core material.

Advantages- Complete & uniform coating

Disadvantages- Coating used only for conducting substances.

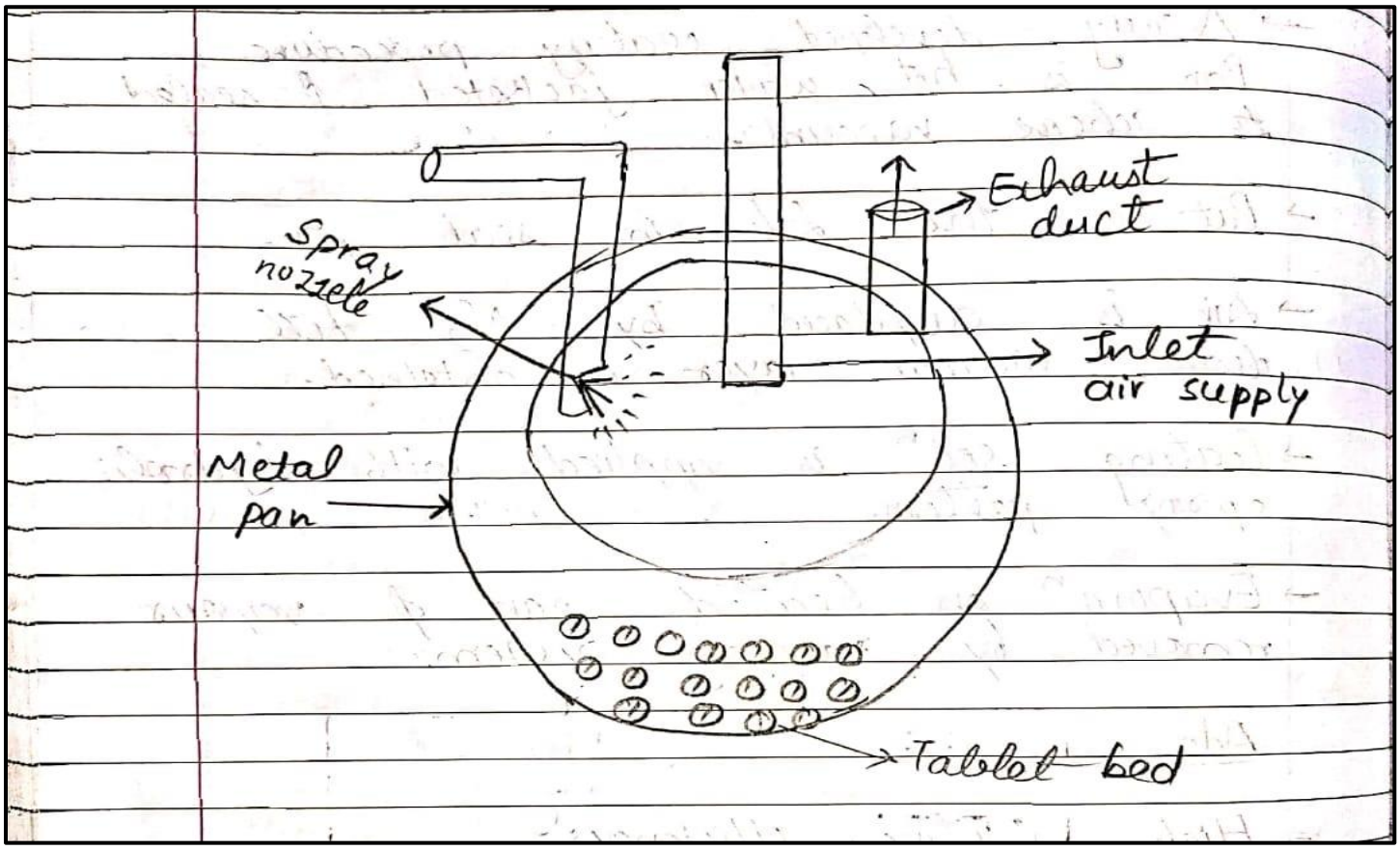
(iv) Vacuum coating:-

-Newly developed coating procedure.
-Pan is hot water jacketed & sealed to achieve vacuum.
-Put the tablet in seal pan.
-Air is displaced by N_2 till desire vacuum layer is obtained.
-Coating solution is applied with hydrolic spray pattern.
-Evaporation on heated pan & vapour removed by vacuum system.

➢ Coating Equipments-

1) Standard coating pan
2) Perforated coating pan
3) Fluidized bed coater

[1] Standard Coating Pan

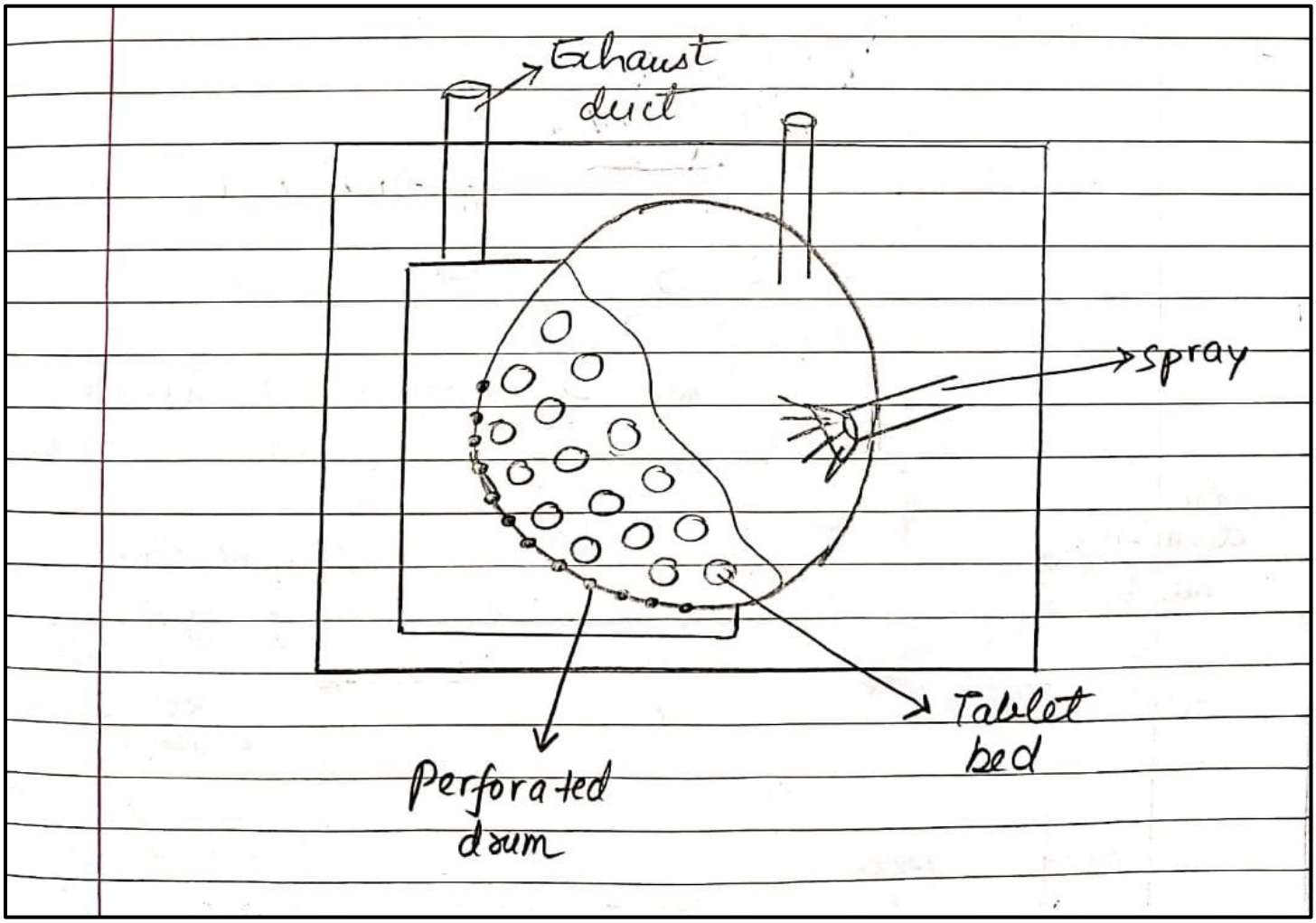


-Circular metal pan is mounted on a stand & rotated on its horizontal axis by motor.
-Diameter of pan is 8-60 inches.
-Coating solution are applied to the spray pattern on rotating tablet bed.
-Heated air is directed into the pan on tablet surface.
-Extra air is removed by exhaust duct.
-For special drying, use **"Pellegrini Pan."**

[2] Perforated Coating Pan

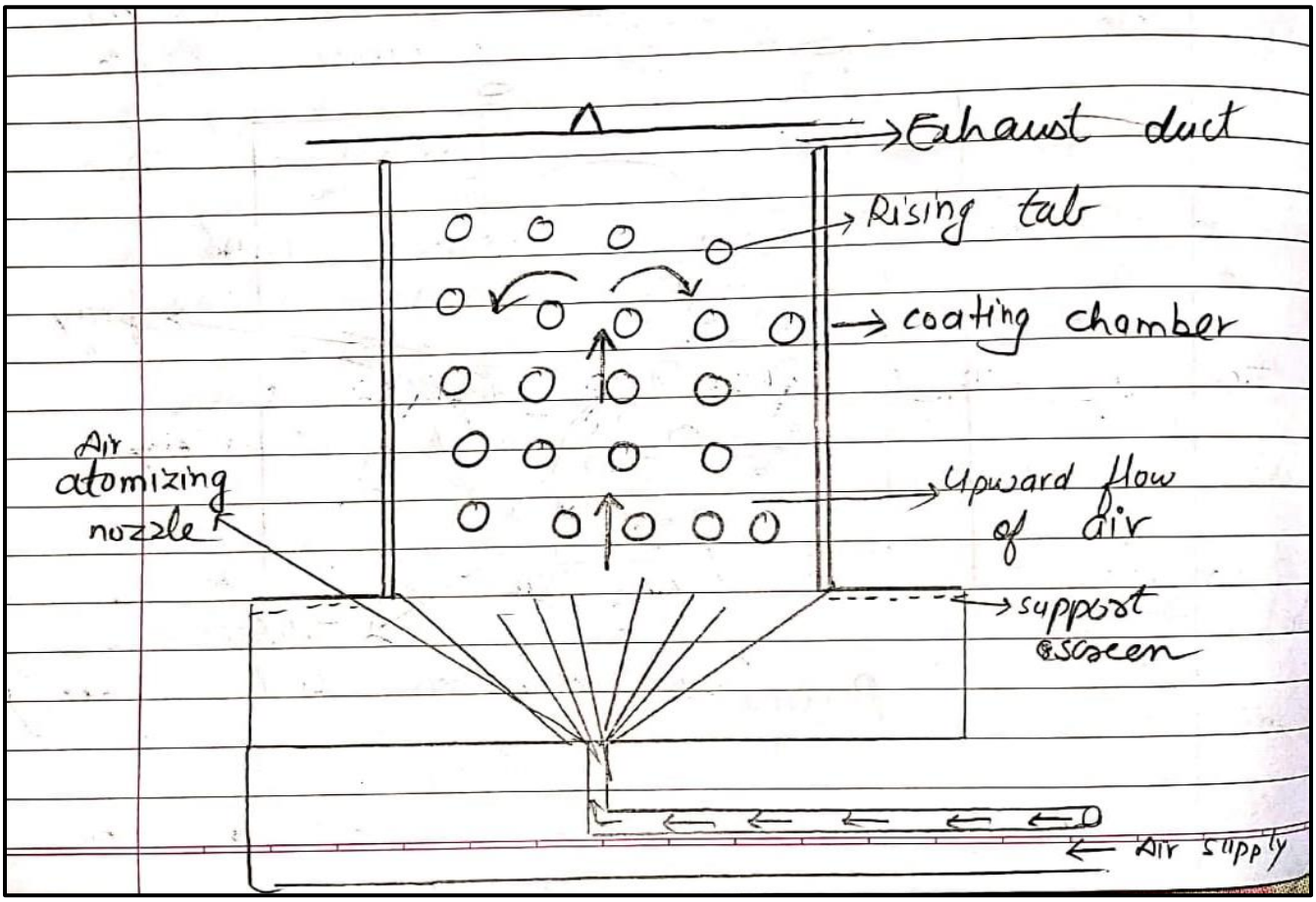
Types-

(i) Accelacota
(ii) Hi-coater
(iii) Glat-coater
(iv) Dri-coater



-This equipment consists of perforated or partially perforated drum rotated on horizontal axis.
-Dry air is passed into the drum on tablet bed & exhaust through perforation of drum.
-Efficient drying system with high coating capacity, used for sugar & film coating.

[3] Fluidized bed coater



-Fluidization of tablet is achieved in coating chamber by upward flow of air.
-Air flow is control, so that more air enter in center of chamber.
-Tablet rise in chamber & tablet fall toward chamber wall & move downward & re-enter at the air system at the bottom of chamber.

-Processing parameter-
-Temp.
-Pressure
-Viscosity of solution
-Spray pattern
-Droplet size
-Drying time

➢ Problems/ Defects of Coating-

1) Picking & Sticking

Sticking→ Over wetting & over film tackiness (sticky) cause **tablet to stick on each other or coating pan.**

Picking → Part of film may remain stick to the pan or another tablet giving picked appearance of tablet surface.

Problems-

-under dried tablet
-tablet quality is poor
-over wetting
-larger amount of liquid application

Remedies-

-proper drying of tablet
-increase drying time
-reduce liquid application rate & improve quality of tablet

2) Roughness

-Rough surface is a defect when coating is applied by spray.
-Some droplets of the spray before reach at surface & dried produce roughness,
-Roughness also increases with pigment conc. & polymer conc. in coating solution.

3) Orange peel effect

-Coating texture is similar to the surface of orange.
-Improper spreading of coating solution before drying cause bumpy or orange peel effect.

Problems-

-High viscosity of coating solution
-Improper spray

Remedies-

-Thinning of coating solution

4) Bridging & Filling-

Bridging→ During drying, **film may shrink & pull away from sharp corners** resulting bridging of surface.

Filling→ This defect occur when **coating material fills over lattering or logo** of tablet.

Problems-
-High viscosity of coating solution
-Poor design of embossing
-Improper application of solution
-Effect of Plasticizer

Remedies-
-Reduce viscosity
-Proper Plasticizer
-Proper spray pattern

5) Blistering

-Coated tablet require drying, but **too rapid evaporation of solvent** from the core & effect of high temp. on strength, elasticity of film results in blistering.

6) Hazing/ Dull/ Bloom

-It occurs due to **high processing temp**. for particular formulation.
-It occurs when cellulosic polymer apply for coating.
-It can also occurs when coated tablet is exposed to high humidity condition.

7) Twinning

-This defect is found in capsule shaped tablet.
-When two capsule shaped tablets stick with each other twinning defect occurs.

8) Mottling

-When solution containing **colour is not prepared properly or improper spray of colour** or coating solution is there, Mottling is observed.

Remedies-
-Use soluble or colour dyes.

9) Flacking/ Peeling

-**Removal of coated material** from tablet, is called peeling or flacking.
-It is due to inadequate adhesion b/w film coat & tablet surface.

10) Erosion → Occurs in soft tablet

➢ Evaluation of Coated Tablets -

-Tensile strength
-Crushing strength
-Hardness – Tester have been used to measure force required to peel, break the film from tablet surface.
-Disintegration test
-Dissolution test
-Stability study – In stability chamber
-- Constant Temperature
-- Constant Humidity (%RH)
-Film surface
-Smoothness
-Roughness
-Colour uniformity (Visual inspection)
-Mechanical properties
-Determination of qualitative, quantitative effect of additives (Plasticizer & Opaquent)

IPQC tests of Tablets

(In-Process Quality control tests)

-In-Process Quality Control (IPQC) are the checks that are carried-out before the manufacturing process is completed.
-The function of in-process controls is monitoring and –If necessary – adaptation of the manufacturing process in order to comply with desired specifications.
-In-process materials should be tested for identity, strength, quality and purity as appropriate and approved or rejected by **Quality Control Unit.**
-Rejected in-process materials should be identified and controlled under a quarantine system designed to prevent their use in manufacturing.

→ **Tests specified:-**
(i) Tablet or capsule weight variation
(ii) Disintegration time
(iii) Content uniformity & homogeneity
(iv) Dissolution time & rate
(v) Clarity or pH of solution

- **Quality Control:-**

-This includes—
1) Measured value obtained from process equipment. Ex- Temperature
2) Measured value obtained by persons. Ex- Time
3) Product attributes. Ex- Weight, hardness, friability
4) Measured value obtained from the room environment. Ex- Particle counts
5) Tests following completion of intermediate products.

- **Process Control:-**

-During manufacturing and packaging a lot of data are recorded which represents control factors of the manufacturing process.
-These data may be process parameters or product attributes.
-The results of the measurement may indicate that a corrective action is required to maintain the process and the product within the specified ranges.
-The limits within which modifications may be carried-out to match measured values must be determined in advance.

- **Scope and kind of tests:-**

-The scope of the tests depends on the extent of process control, i.e., the more reliable the process, the smaller the scope of the tests.
-The types of tests carried-out depend on the dosage forms being produced.

Physical Parameters	Temperature, Time, Pressure, Weight, Hardness, DT time, Particle size, LOD, Viscosity, Osmolarity, pH
Attributive Features	Visible impurities, Colour, Integrity, Fractional part

-Physical parameters are checked using only suitable measuring instruments.
-These instruments are calibrated by in-process control personnel.

-The testing of attributive features is an important in-process control task.
-This is particularly of importance in relation with filling of solutions and solid dosage forms as well as packaging.
-AQL (Acceptable Quality Limit) are normally used as the basis for the test procedures.

➢ Sampling:-

Contents of Sampling Procedure-

1) State type of sample container to be used.
2) Describe collection technique-
   (i) Prevent contamination of product being sampled.
   (ii) Prevent contamination of sample taken.
   (iii) Aseptic technique if required
3) Specify sampling utensils—Define type & requirements (clean, sterile, pyrogen free)
4) Describe method for obtaining representative samples.
5) Describe scheme for identifying samples-

-Name of item, Batch no., Date taken, Sampler's name etc…

➢ Testing:-

-Samples are tested to verify following-

1) Identity
2) Component conformity
3) Container/Closure conformity
4) Examination of Contamination

• Evaluation of Tablets

(Quality control tests of Tablets)

1) General Appearance
2) Hardness
3) Friability
4) Weight Variation
5) Content Uniformity
6) Disintegration test
7) Dissolution test

[1] General Appearance

(i) Size & Shape-

-Crown thickness → Measured by Micrometer

-Size of tablet → Measured by Vernier calipers.

(ii) Colour-

-Colour quantification is determined by- Reflectance spectrophotometry
- Tristimulus colorimetry
- Micro-reflectance photometry

[2] Hardness

-It is the force required to break the tablet in diametric compression test.

-Hardness is also called as **"Crushing strength."**

Devices used:-

-Monsento's Hardness tester
-Strong-cobb tester
-Pfizer tester
-Erweka tester
-Scheluniger tester

Standard hardness → **4 to 5 Kg/cm²**

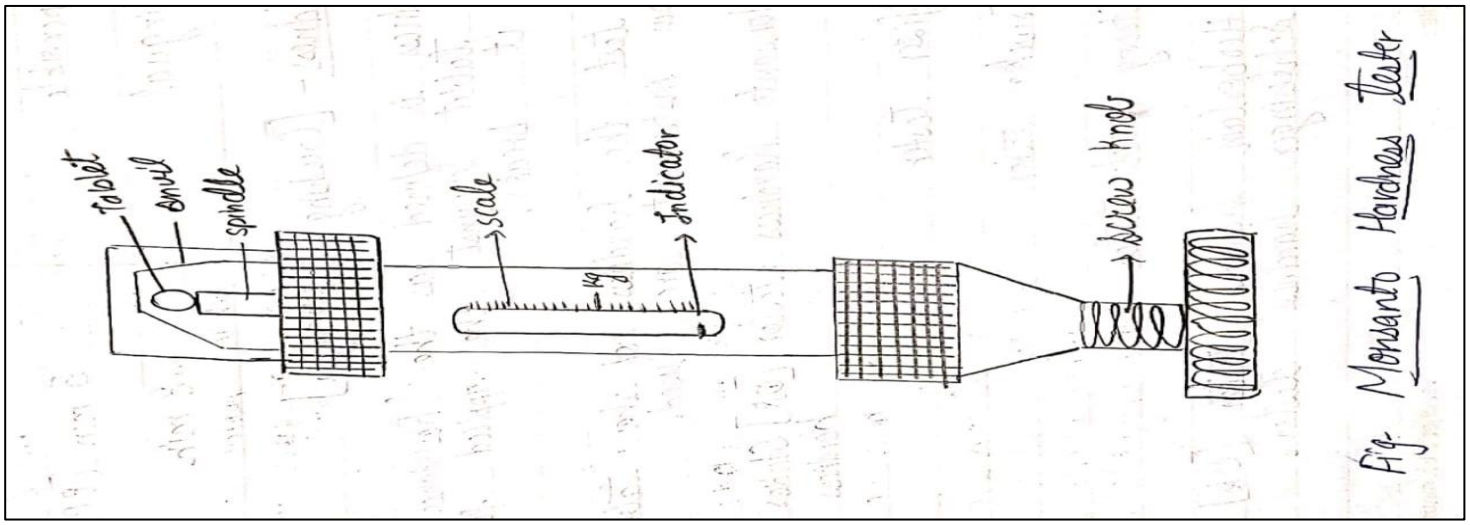


Fig- Monsanto Hardness Tester

[3] Friability

-Used for determination of drug loss during transportation & is determined by **"Roche Friabilator."**
-Speed- 25rpm
-Time- 4 min.
-Total revolution- 100
-% Acceptance → NMT 1%

$$\% \text{ Friability} = \frac{\text{Initial wt} - \text{Final wt}}{\text{Initial wt}} \text{X } 100$$

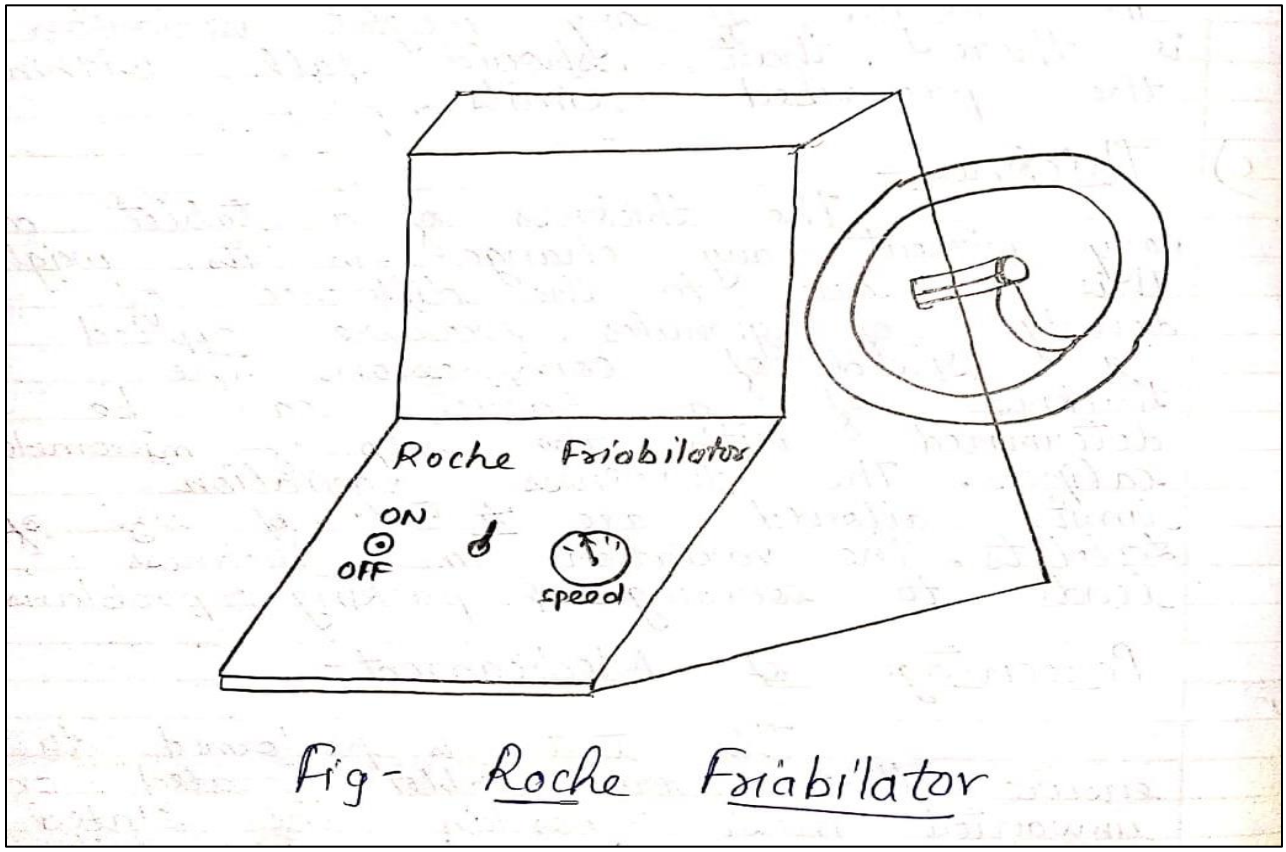


Fig- Roche Friabilator

[4] Weight Variation

-Total tablets used= 20
-Weigh 20 tablets & Calculate average weight
-**Not more than two of the individual tablet weight deviates from the avg. wt. by more than percentage shown in the table.**

Average weight of tablet		Maximum % of difference allowed
IP	**USP**	
80 mg or less	130 mg or less	**± 10%**
80-250 mg	130-324 mg	**± 7.5%**
More than 250 mg	325 or more	**± 5%**

[5] Content Uniformity

-Total tablets taken for the test= 30
-9 out of 10 tablets should contain 85-115% content & 10^{th} tablet may contain 75-125% content.
-If above condition is not satisfied then other 20 tablets should be assayed & no one should fall outside range of 85-115%.

[6] Disintegration test

-Tablets- 6 selected randomly
-Glass tubes= 6
-Upper & lower end closed with #10 mesh screen.
-Beaker contains= 900 mL of SGF or SIF
-Temp. =37 ± 2°C
-Speed = 28-32 rpm (reciprocation per min) up & down

Tablet	Disintegration time
Dispersible & Effervescent Tablets	3 min
Uncoated Tablets	15 min
Film coated	30 min
Sugar coated	60 min
Enteric coated	2 hrs in gastric fluid media & 1 hr in intestinal fluid

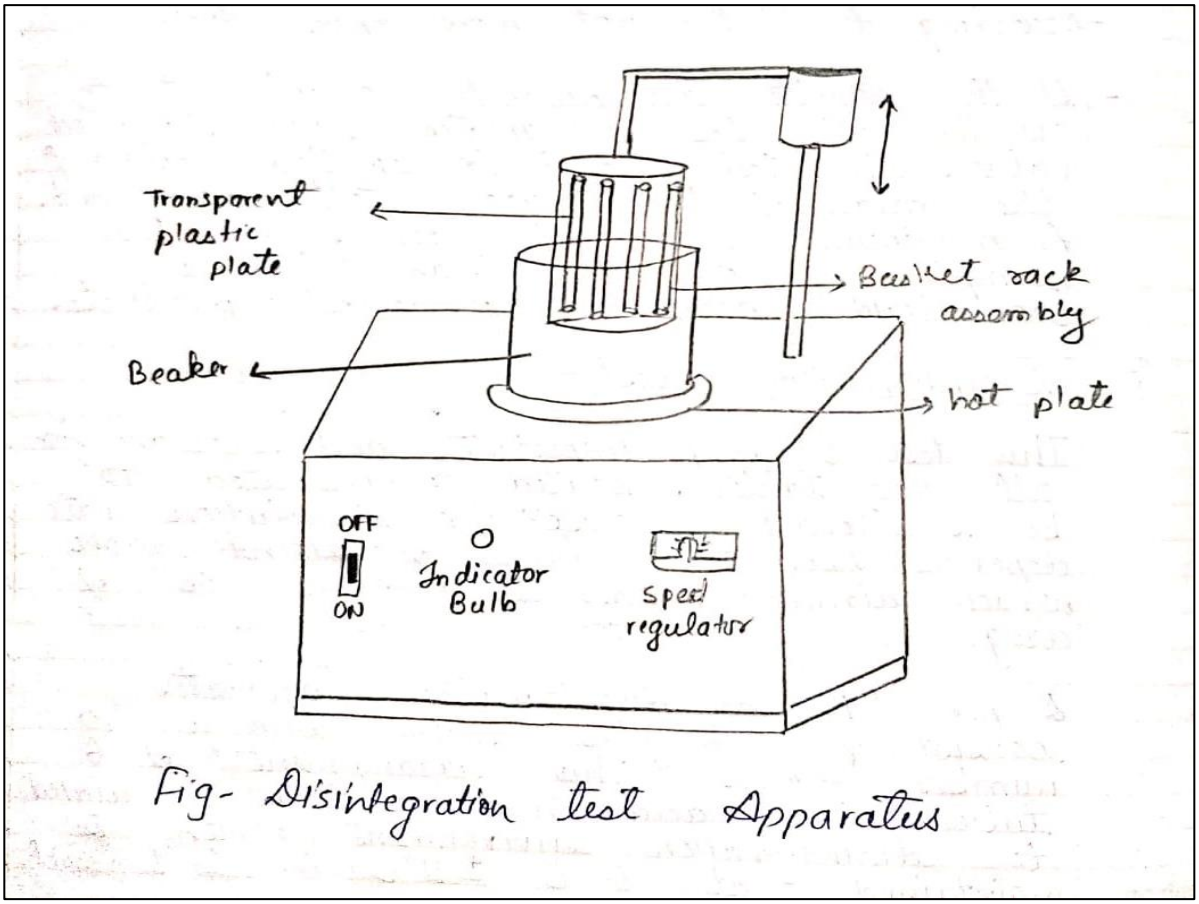


Fig- Disintegration test Apparatus

[7] Dissolution test

-Dissolution test is an index for comparing bioavailability.
-Dissolution rate is directly related to efficacy of the drug.

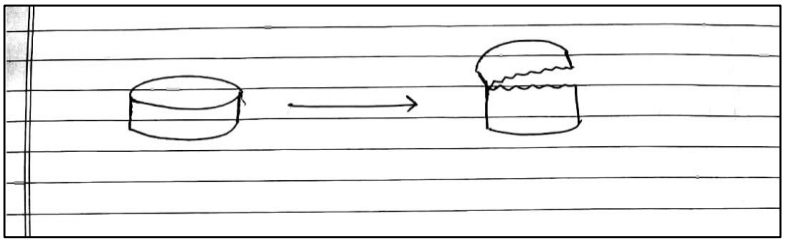
Types of dissolution apparatus as per USP		
USP apparatus	**Type**	**Use**
Apparatus I	Rotating Basket	Capsule, Modified release
Apparatus II	Paddle	Tablets, Modified release
Apparatus III	Reciprocating cylinder	Modified release
Apparatus IV	Flow through cell	Rapid degrading drug
Apparatus V	Paddle over disc	Transdermal patch, Ointment
Apparatus VI	Rotating cylinder	Transdermal patch
Apparatus VII	Reciprocating disc	Transdermal patch

-Limits (USP)-
-Samples are withdrawn in the interval of every 15 min & filter through 1µm size membrane.
-Not less than 75% should be dissolved in 45 min.
-90% of the drug should be dissolved in 30 min. (industrial limit).

• Problems/ Defects of Tablets
(Processing/ Manufacturing Defects)

[1] Capping

-Capping is the term used, when **upper or lower segments of the tablet separates horizontally**, either partially or completely from the main body of the tablet.
-It comes off as a cap, during ejection from tablet punching machine.



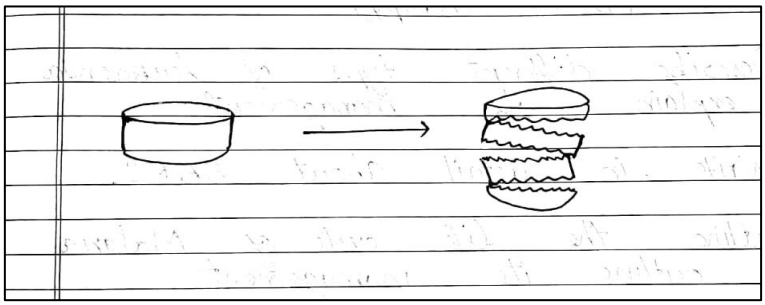
-Due to air entrapment in compression & subsequent expansion during ejection (Stress relaxation) of a tablet from die.
-As air is released from granules; it can push very fine dry granules & fines outward.
-Particles do not stick together & prevents the granules from being compressed successfully leading to capping.

Problems-
-Large amount of fines in granules.
-Too dry or improper dried granules.
-Insufficient amount of binder.
-Insufficient lubricant.
-chilled or cold granules.
-Poorly finished dies.
-Deep concave punches.
-Incorrect adjustment of swipe-off blades.
-High turret speed.

Remedies-
-Remove all fines.
-Dry granules properly.
-Increase amount of binder.
-Increase lubricant.
-Compress at room temp.
-Polish dies properly.
-Use flat punches.
-Reduce turret speed.

[2] Lamination (Layering)

-Lamination is the **separation of a tablet in two or more distinct horizontal layers**.



-More compression force, granules elastic deformation & Fracture prevents 'locking' of tablet layers resulting in lamination.

Problems-

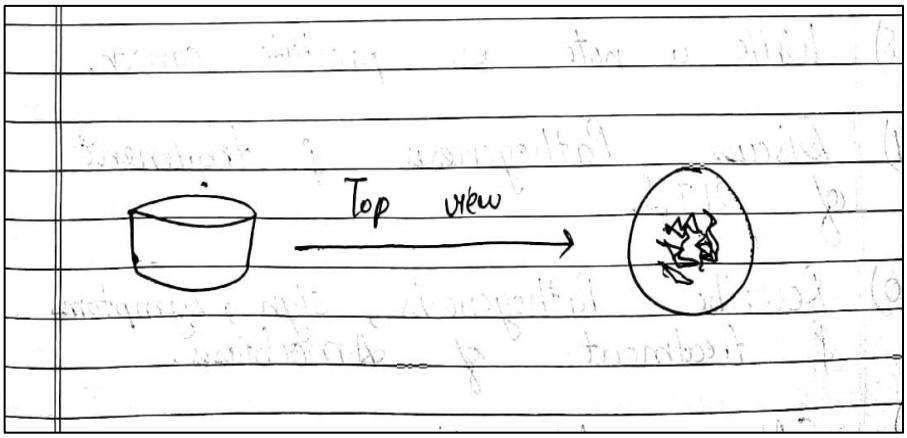
-Oily or wax material in granules.
-Too much lubricant.
-Rapid relaxation & Decompression.

Remedies-

-Modify mixing process.
-Decrease lubricant.
-Use tapered die.

[3] Cracking

-Fine, small **cracks observed on the upper & lower central surface** of the tablet are referred as cracks.



Problems-
-Large size of granules.
-Too dry granules.
-Cold compression.
-Deep concave punches

Remedies-
-Reduce granule size.
-Add fines.
-Compress at room temp.
-Use tapered die.

[4] Chipping

-Chipping is defined as **the breaking of the tablet edges**, while tablet leaves the press.
-It may be due to incorrect equipment.
-Due to misaligned ejection.

[5] Sticking

-Sticking refers to the **tablet material adhering to the die wall**.
-Sticking also causes production of tablet with rough edges.
-It also damage punch heads.

Problems-
-Granules not dried properly.
-Too little or improper lubrication.
-Hygroscopic granular material.
-Deep concave punches.
-High turret speed.

Remedies-
-Dry granules properly.
-Increase lubricant.
-Reduce turret speed.
-Compress under controlled humidity.
-Optimize the amount of binder.

[6] Picking

-Picking happen when a **small amount of material from a tablet is sticking to & being removed off the tablet surface** by a punch face.
-Minimized by use of the tapered die.

[7] Binding

-**"Binding in the die"**, is the term used when the **tablet adhere, seize or tear in the die**.
-A film is formed in the die & ejection of tablet is hindered.
-It occurs due to excessive moisture in granules & lack of lubrication.

[8] Mottling

-Mottling is the term used to describe an **unequal distribution of colour on surface** of tablet, with light or dark spots.

Problems-
-A colored drug used along with colourless excipients.
-A dye migrates to the surface of granules while drying.
-Improperly mixed dye.

Remedies-
-Use appropriate colorants.
-Change solvent system.
-Mix properly & Reduce the size of powder.

[9] Double Impression

-Double impression is seen in only those punches, which have a **monogram or logo** on them.

-At the moment of compression, tablet receive imprint of punches

↓

But in some machines

↓

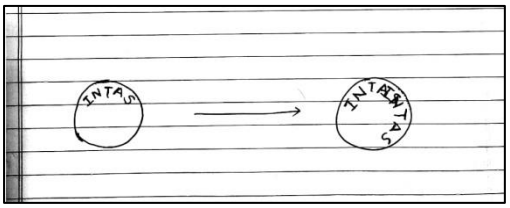
Lower punch **freely drops & travels uncontrolled short Distances** before riding up the ejection

↓

During this free travel, punch rotates & make a new impression

↓

Resulting in Double impression



• Mouth Dissolving Tablets (MDT)

"MDT is a single unit dosage form that disintegrates in the oral cavity, containing medicaments which disintegrate rapidly in few seconds"

-Also called as – Fast melting
-Fast dissolving
-Oral disintegrating
-Oro-dispersible

Advantages-

-Enhance compliance.
-Overcome difficulty in swallowing by pediatric & geriatric patients.

-First generation MDT → **"Orasolv technology"**
-it is soft tablet.
-dissolve in mouth
-contains- Fillers
-Sweetners
-Lubricants
-Glidents
-Flavours
-Coloring agents
-Manufacturing method = Direct compression method.

-Second generation MDT → **"Durasolv technology"**
-it is fast & rapid than Orasolv.
-it contains readily water soluble excipients.
-Manufactured by Direct compression.

-MDTs are packed in Blisters or Pouches.

➢ Evaluation of MDTs-

-Weight variation
-Hardness
-Friability
-Wetting time
-Water Absorption ratio
-Mechanical strength
-Dispersion time
-Disintegration test

-Dissolution test (in simulated salivary fluid)
-*in-vivo* Testing

Advantages-

-Ease of administration to patients who cannot swallow, such as elderly, stroke victims, paediatrics & psychiatric patients.
-Good Patient compliance for travelling and busy people.
-Can be administered without water.
-Convenience of administration and accurate dosing.
-More rapid drug absorption from the pre-gastric area, to produce rapid onset of action.

Disadvantages-

-Have insufficient mechanical strength.
-Careful handling is required.
-Tablets have unpleasant taste if not formulated properly.

• Floating Tablets

-It is one of the successful way to achieve a gastric retentive system.

"Floating tablets are designed on the principle approach of low density dosage forms that float on gastric fluids & thereby retained for extended periods."

-Examples of drugs utilized in this system include **Propantheline & Benactyzine HCl**, which is low dose drugs, intended to produce local effects in the stomach.

-This may contain a gas-generating chemical such as $NaHCO_3$.

-One such system that was extensively investigated in the 1990s was the **Hydrodynamically Balanced System (HB).**

Floating Tablets

↓

Effervescent System

Contains- Methocel
-Chitosan
-$NaHCO_3$
-Citric acid
-Tartaric acid

↓

Contact with GI Fluid

↓

CO_2 generated

Non-Effervescent System

Contains- Polysaccharide
- Polystyrene
-Hydrocolloid
-Polycarbonate

↓

Swells in contact with GI Fluid

-Floating tablets- two types-

(I) Single layer => CO_2 generating component in one matrix.

(II) Bilayer => CO_2 generating component in one layer + Hydrocolloid in another layer.

-Preparation- By direct compression or Dry or wet granulation.

➢ Evaluation of Floating tablets-

-Size & shape
-Total floating time
-Floating lag time
-Buoyancy capabilities
-Content uniformity

-Drug release
-Dissolution test
-Friability
-Weight variation
-*In-vivo* methods
-X-ray methods
-Gamma-Scintigraphy
-Gastroscopy
-Ultrasonography

Advantages-

-prolong action.
-used for drug meant for local application to stomach. Ex- Antacid, Ulcer healing drugs.
-used to keep drug floating in case of severe diarrhoea where normal tablet is removed.
-used for drugs having short half life.
-Improves Patient Compliance.

Disadvantages-

-Not used for Acid-labile drugs.
-it requires sufficient high amount of fluid in stomach to float.
-Food can delay the action.
-Gastric emptying time varies from patient to patient.
-Chances of nausea & vomiting.

• Buccal Tablets

-Within the oral mucosal cavity, the buccal region offers an attractive route of administration for controlled systemic drug delivery.
-**Buccal delivery is the administration of drugs through the mucosal membrane lining the cheeks.**
-Although the sublingual mucosa is known to be permeable than the buccal mucosa , the latter is the preferred route for systemic transmucosal drug delivery.
-This is because the buccal mucosa has an expanse of smooth muscle and relatively immobile mucosa, which makes it a more desirable region for retentive systems.
-Thus, the buccal mucosa is more appropriate for sustained delivery applications and the delivery of less permeable molecules and peptide drugs.

➢ Manufacturing of buccal tablets

1) Compression Moulding-

-Tablets manufactured by the compression moulding process exhibit rapid disintegration & dissolution, which is usually within 5-10 seconds.
-These tablets face special challenges during handling and shipping, because of the poor mechanical strength, and may require special packaging.
-Alternatively, the mechanical strength of the tablets may be enhanced by employing a suitable binder.
-The compression moulding process involves moistening of the formulation blend with a solvent, followed by moulding into tablets under low pressure.
-The moist tablets are finally dried.
-The lower compression pressure employed for moulding and drying of the moist tablet produces a highly porous tablet structure with enhanced dissolution.

2) Direct Compression-

-The direct compression method is commonly used for commercial manufacture of buccal tablets.
-It is simple and cost-effective process.
-Buccal tablets manufactured by the direct compression method exhibit good mechanical strength and acceptably fast disintegration.
-The directly compressible buccal tablet formulation contains directly compressible soluble excipients, a superdisintegrant and a lubricant.
-The choice of suitable disintegrant and its amount are critical for achieving a fast disintegration and dissolution rate.
-Sometimes effervescent agents are used to increase disintegration and dissolution of buccal tablets.

3) Freeze Drying-

-The process of freeze drying is expensive, time-consuming and produces tablets of poor mechanical strength.
-For these reasons, it is not commonly used to manufacture buccal tablets.
-However, it does have advantage over other process, as the tablets made by this process have high porosity, and disintegrate and dissolve instantly.
-It is a process of choice for the products that are unstable or are heat sensitive.
-The process involves lowering the temperature of the product in an aqueous medium to below freezing point, following by applying a high-pressure vacuum.
-To extract the water in the form of vapour, which is collected as the ice on a condenser, a gradual temperature rise is applied during the drying process.
-The resulting tablets are usually light and have highly porous structures that allow rapid dissolution or disintegration.

➢ Evaluation of Buccal tablets-

-Size & shape
-Content uniformity
-Drug release
-DT time
-Hardness
-Dissolution test
-Friability
-Weight variation
-*In-vivo* methods
-Permeation Experiments
-Mucoadhesive tests

Advantages-

-direct entry of the drug in systemic circulation.
-Avoids first pass metabolism.
-Easy administration.
-Can be removed from site of application. (Retrieval is possible)

Disadvantages-

-Need for the tablet to maintain its position for many hours against buccal motion & salivary flow.
-Smaller area of tissue available for drug absorption, compared to stomach, intestine & Lungs.
-Low tissue permeability and the small area limit the dose of the drug that can be delivered

• Colon Targeted Tablets

-Drug delivery to the colon is beneficial not only for the oral delivery of proteins and peptides drugs, but also for the delivery of low mol. Wt. compounds.
-It is used to treat diseases associated with the colon or large intestine such as ulcerative colitis, diarrhoea and colon cancer.
-Also, colon has the longer retention time and appears highly responsive to agents that enhance the absorption of poorly absorbed drugs.

-The colon is a site where both local and systemic delivery of drugs can take place.
-Local delivery allows topical treatment of IBD.
-Specific targeting of drugs to the colon is recognized to have several therapeutic advantages.
-Drugs, which are destroyed by the stomach acid or metabolized by pancreatic enzymes, are slightly affected in the colon & sustained colonic release of drugs can be useful in the treatment of nocturnal asthma, angina and arthritis.
-Treatment of colonic diseases such as ulcerative colitis, colorectal cancer and Crohn's disease is more effective.

-Preparation- By direct compression or wet granulation.

➢ Evaluation of Colon targeted tablets-

(1) *In-vitro* Evaluation-

(i) *In-vitro* Dissolution test-

-By Basket apparatus.
-The different media that are used for the dissolution testing of colon targeted drug delivery are pH 1.2 to simulated gastric fluid, pH 6.8 to simulated intestinal fluid, pH 7.4 to simulated large intestinal fluid.
-The colon targeted drug delivery systems are tested for 2hr in 0.1N HCl, 3hr in pH 6.8 phosphate buffer & finally at pH 7.4 phosphate buffer.

(ii) *In-vitro* Enzymatic test-

-Drug release study is performed in buffer medium containing enzymes pectinase, dextranase or rat or guinea pig or rabbit cecal contents.

(2) *In-vivo* Evaluation-

-The *in-vivo* evaluation of the CDDS is done in dogs, guinea pigs, rats and pigs as they resemble the anatomical & physiological conditions, micro flora of human GIT.

Other tests-

- Size & shape
-Content uniformity
-Drug release
-Dissolution test
-Friability
-Weight variation
-Hardness
-DT time

Advantages-

-Used for effective treatment of IBD, Ulcerative colitis, crohn's disease.
-Low systemic side-effects.
-Prevents gastric irritation.
-Lower first pass metabolism.
-Provides suitable environment for proteins that are sensitive to GI fluids & enzymes.
-Increased patient compliance.
-Decreased frequency of administration, hence economical to patient.
-High retention time, so good bioavailability.

Disadvantages-

-Evaluation techniques like Dissolution in both *in-vitro* & *in-vivo* is difficult & tedious.
-Results are Non-reproducible in animals.
-pH, transit time, gastric emptying, food intake varies from patient to patient. Hence, Not so effective.
-Effect of colonic microflora to dosage form.
-Dosage form have to pass through many tight junctions like ileo-cecal junction, where chances of breakdown.
-Dose dumping (pre-mature drug release) in SR & CR forms, leading to therapeutic failure.

• Matrix Tablets

"Matrix tablets refers to dosage forms where the drug is uniformly dissolved or dispersed in a release-retarding material."
-Such devices can be formulated as conventional matrix, or bi- or tri-layered matrix systems.

➢ Manufacturing of Matrix tablets

1) Hydrophilic Matrix-

-The matrix is one where the release-retarding material is water-swellable or swellable-cum-erodible hydrocolloid such as high mol. Wt. HPMCs, HPC, HEC, xanthan gum, sodium alginate, guar gum & cross-linked polymers of acrylic acid.

-2 types-
(i) Free-Swelling Matrix- In this matrix, polymer swelling is unhindered.
(ii) Restricted-Swelling Matrix- In this matrix, the surface of the device is partially coated with an impermeable polymer film that restricts the hydration of swellable matrix material.

2) Hydrophobic Matrix-

-In this matrix, the release-retarding material is either-
i) Slowly soluble, erodible, or digestible, ex- Waxes such as glyceryl monostearate, cetyl alcohol, vegetable oil, beeswax, carnauba wax, etc…
ii) Insoluble or non-digestible, ex- Ethylcellulose, polymethacrylates, etc…

-2 types of hydrophobic matrix-
(i) Porous (Heterogeneous) Matrix- This matrix is the one where the drug & release-retarding matrix microparticles are simply mixed with eachother and compressed into a tablet.
(ii) Non-porous (Homogenous) Matrix- This matrix is the one in which the release-retarding matrix material is first melted and the drug is then incorporated in it by thorough mixing.

It may be of 2 types-
a) Dissolved Drug Non-porous system
b) Dispersed Drug Non-porous system

➢ Evaluation of Matrix tablets-

- Size & shape
-Content uniformity
-Drug release
-Dissolution test
-Friability
-Weight variation
-Hardness
-DT time
-Swelling studies
-*In-vitro* studies
-Stability study
-Model independent approaches
-Dissolution Efficiency
-Mean Dissolution Time
-Similarity Factor (f_2)
-Difference Factor (f_1)

Advantages-

-Easy to manufacture.
-Versatile.
-Used for high mol. Wt. compounds.
-Improves Bioavailability.
-Increased stability.
-Reduce the toxicity by slowing drug absorption.

Disadvantages-

-The remaining matrix must be removed after the drug has been released.
-High cost of preparation.