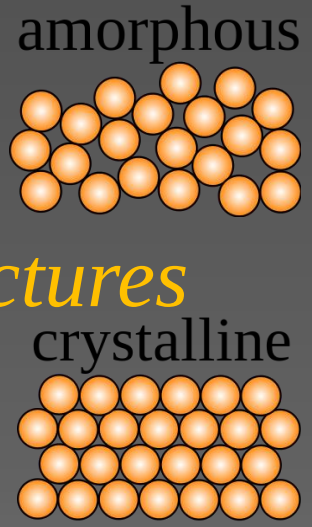
TIU
FACULTY OF PHARMACY
PHARMACEUTICAL TECHNOLOGY III
2020-2021

Solid Dosage Forms

Lec. Dr. Muath Sheet Mohammed Ameen

Lec. 1

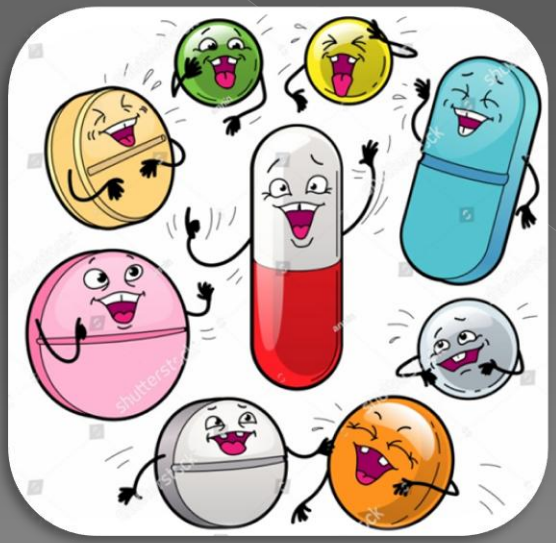
- Most active and inactive pharmaceutical ingredients occur in the solid state as



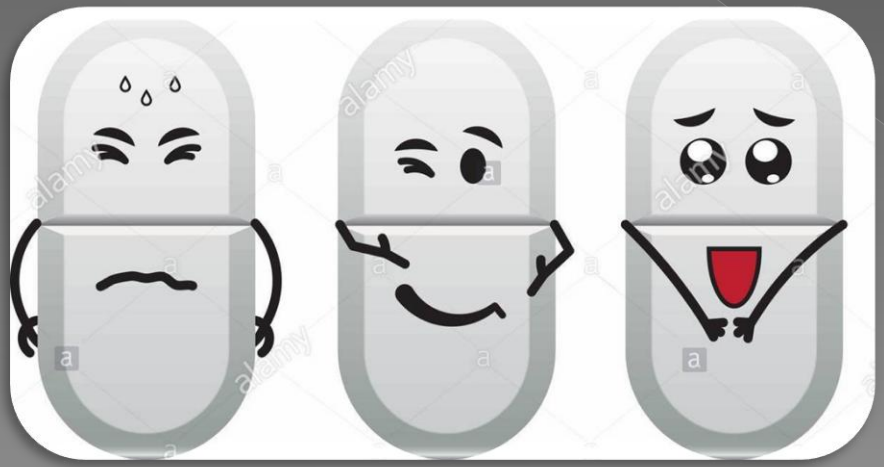
1. *Amorphous powders*
2. *Crystals of various morphologic structures*

- Powders are intimate mixtures of dry finely divided drugs and/or chemicals that may be intended for internal or external use.

- Powdered drugs may be blended with powdered fillers and other pharmaceutical ingredients to fabricate solid dosage forms as *tablets and capsules*



TABLETS



- Tablets are defined as the solid unit dosage form of medicaments with or without suitable diluents and prepared either by molding or by compression.

- They are vary greatly in shape, size and weight which depends on the amount of medicament and the mode of administration.

- Most commonly the tablets are disk shaped with convex surfaces they are also available in special shapes like round, oval, oblong, cylindrical, square, triangular etc.

- The tablets for oral administration may weigh from 0.2 to 0.8 gm

- They offer a number of advantages to the patient, prescriber, manufacturer and the manufacturing pharmacist.

Advantages

- Easiest and cheapest to package and ship
- Easy to carry
- Easy to swallow
- Attractive in appearance
- More accurate and uniform in weight
- Some of the tablets are divided into halves and quarters whenever the fractional dose is required

Advantages

- Unpleasant taste can be masked by sugar coating
- Special release profile products such as enteric or delayed-release products
- Better suited to large-scale production
- Best combined properties of chemical, mechanical and microbiologic stability
- Ease dispensing and possible control by pharmacists

Disadvantages

- Some drugs resist compression into dense compacts
- Drugs with poor wetting and slow dissolution properties may be difficult to formulate
- Bitter-tasting drugs or drugs that are sensitive to oxygen or atmospheric moisture may required encapsulation prior to compression.

Properties

The objective of the design and manufacture of the compressed tablet is to deliver orally the correct amount of drug in the proper form at the proper time and in the desired location.

Must be

- elegant
- free of defects such as chips, cracks, discoloration, contamination
- chemically and physically stable
- released the medicinal agents in the body in a predictable and reproducible manner

Types of Tablets

- Compressed tablets
- Enteric coated tablets
- Sugar coated tablets
- Film coated tablets
- Chewable tablets
- Effervescent tablets
- Buccal and sublingual tablets
- Matrix tablets

Compressed Tablets

- In the preparation of tablets by direct compression, both the **particle size** and particle size distribution of the therapeutic agent and the **excipients** are important determinants of the compression properties of the powder mix.

- Examples of excipients that are employed **for the formulation and manufacture of tablets by direct compression include: (1) diluent; (2) compression aid; (3) distintegrant; and (4) lubricants and glidants.**

Preparation of Tablets

There are three methods by which compressed tablet can be prepared

1. ***Direct Compression***
2. ***Dry Granulation***
3. ***Wet Granulation***

Direct Compression

The materials are compressed directly if they have

1. Crystalline property
2. Free flowing property
3. Binding characteristics

- Some materials have not compressed easily therefore they are required excipients like spray dried lactose, anhydrous lactose, mannitol, microcrystalline cellulose and calcium phosphate etc.

Formulations

For the formulation of tablets takes in consideration the following factors:

- Amount of drug dose present in tablet
- Types of excipients present in tablet
- Surface, appearance, disintegration, friability and dissolution of tablets.
- Compression pressure or punch dwell time or using precompression.

Formulations

- Compressed tablets usually consist of active medicaments mixed with a number of inert substances known as excipients.
- These excipients have a great influence on stability, bioavailability and the process by which dosage forms are prepared

- Excipients are chosen in tablet formulation to perform a variety of functions like

i) For providing essential manufacturing technology functions (binders, glidants, lubricants may be added)
ii) For enhancing patient acceptance (flavors, colorants may be added),
iii) For providing aid in product identification (colorants may be added),
iv) For Optimizing or modifying drug release (disintegrants, hydrophilic polymers, wetting agents, biodegradable polymers may be added),
v) For enhancing stability (antioxidant, UV absorbers may be added)

Formulations

Formulation of tablets requires following additives

Major Excipients	MISCELLANEOUS
Diluents or Fillers	Wetting agents
Binders or Adhesives	Dissolution retardants
Disintegrants	Dissolution enhancers
Glidants	Adsorbents
Lubricants	Buffers
Antiadhesives or Antisticking agent	Antioxidants
Coloring agent	Chelating agents
Flavoring agent	Preservatives
Sweeteners	

Diluents or Fillers

- Diluents make the required bulk of the tablet when the drug dosage itself is inadequate to produce tablets of adequate weight and size.
- Selection of diluent should be done after considering properties of diluent such as: Compactibility, flowability, solubility, disintegration qualities, hygroscopicity, lubricity and stability.
- Tablet diluent or filler may also be classified on the basis of their solubility in water as soluble and insoluble.

INSOLUBLE TABLET FILLERS OR DILUENTS	SOLUBLE TABLET FILLERS OR DILUENTS
Starch Powdered cellulose Microcrystalline cellulose Calcium phosphates Calcium carbonate Calcium sulphate	Lactose Sucrose Dextrose Mannitol Sorbitol

Diluents or Fillers

- Tablet diluents or fillers can be divided into following categories:

1. **Organic materials** - Carbohydrate and modified carbohydrates.

- Carbohydrate substa nces such as sugars, starches and celluloses may also function as binders during wet granulation process; but in direct compression system, they serve as the diluent.

2. **Inorganic materials** – Calcium phosphates and others.

- The inorganic diluents, do not exhibit binding properties when used in wet granulation and direct compression.

3. **Co-processed Diluents**

- Co-processing means combining two or more materials by an appropriate process.
- co-processed excipients are introduced in order to provide better tableting properties than a single substance or the physical mixture.

Diluents or Fillers

Organic Diluents	Inorganic Diluents
Lactose (α –Lactose monohydrate)	Dicalcium Phosphate Dihydrate (DCPD) (Emcompress ® or DiTab)
Lactose spray dried	Spherically Granulated Dicalcium Phosphate anhydrous (SGDCPA) (Fujicalin®)
Lactose anhydrous	**Co-processed Diluents**
Sucrose	Emdex® (Dextrose 93-99% and maltose 1-7%)
Mannitol	Calcium 90® (Calcium carbonate 90% and Starch, NF 9%)
Starch (Pregelatinized)	Microcellac® (75% lactose and 25% MCC)
Sorbitol	Sugartab® (Sucrose 90-93% and invert sugar 7-10%)
α-cellulose particles	Ludipress® (93% α-lactose monohydrate, 3.5% polyvinylpyrrolidone, and 3.5% crospovidone)
Microcrystalline cellulose (MCC)	

Binders or Adhesives

- Binders are added to tablet formulations to add cohesiveness to powders.
- These are used in dry or liquid form to reduce the amorphous nature of substance and convert into compressible form. Binder when used in liquid form gives better binding action as compared to when used in dry form.
- Direct Compression (DC) binders should be selected on the basis of compression behavior, volume reduction under applied pressure and flow behavior in order to have optimum binding performance.
- Most commonly used DC binders like
  - Avicel (PH 101) (MCC),
  - SMCC (Silicified Microcrystalline Cellulose),
  - Partially PGS, Low density starch,
  - DC lactose anhydrous and DC- DCPD

Types of Binders

Sugars	Natural Binders	Synthetic/ Semisynthetic Polymer
Sucrose	Acacia	MethylCellulose (MC)
Liquid glucose	Tragacanth	EthylCellulose (EC)
	Gelatin	Hydroxy Propyl Methyl Cellulose (HPMC)
	Starch Paste	Hydroxy Propyl Cellulose (HPC)
	Pregelatinized Starch (PGS)	Sodium Carboxy Methyl Cellulose
	Alginic Acid	Polyvinyl Pyrrolidone (PVP)
	Cellulose	Polyethylene Glycol (PEG)
	Guar gum	Polyvinyl Alcohols (PVA)
		Polymethacrylates

TIU
FACULTY OF PHARMACY
PHARMACEUTICAL TECHNOLOGY III
2020-2021

Solid Dosage Forms

Lec. Dr. Muath Sheet Mohammed Ameen

Lec. 2

Mechanism of Tablet Disintegrants

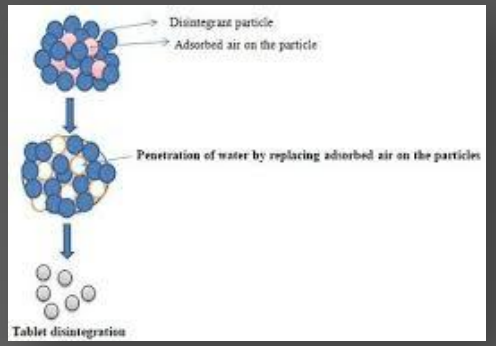
The tablet breaks to primary particles by one or more of the mechanisms

1. **Capillary action**
2. **Swelling**
3. **Heat of wetting**
4. **Disintegrating particle/particle repulsive forces**
5. **Deformation**
6. **Release of gases**
7. **Enzymatic action**

Mechanism of Tablet Disintegrants

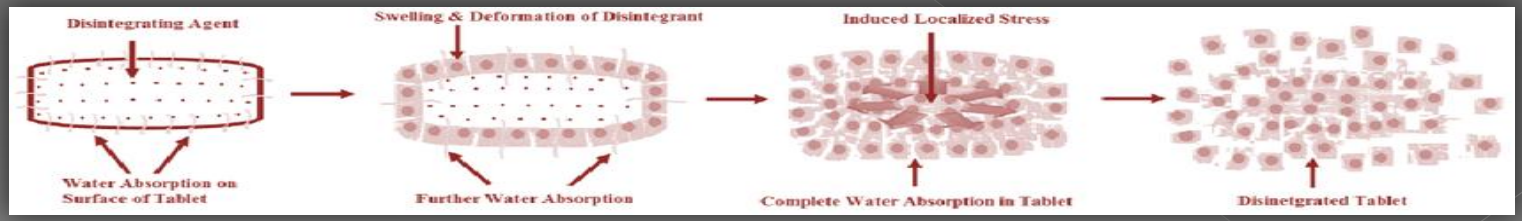
1. **By capillary action**

When we put the tablet into suitable aqueous medium, the medium penetrates into the tablet and replaces the air adsorbed on the particles, which weakens the intermolecular bond and breaks the tablet into fine particles.



2. **By swelling**

Sufficient swelling force is exerted in the tablet with low porosity



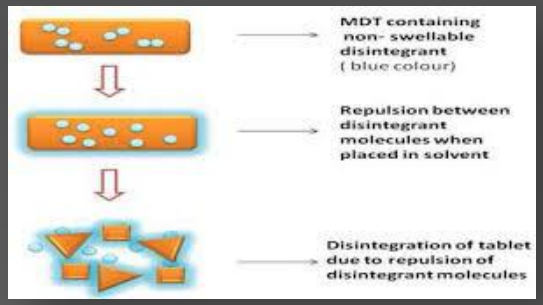
3. **Because of heat of wetting**

When disintegrants with exothermic properties gets wetted, localized stress is generated due to capillary air expansion, which helps in disintegration of tablet.

Mechanism of Tablet Disintegrants

4. **Due to disintegrating particle/particle repulsive forces**

The electric repulsive forces between particles are the mechanism of disintegration and water is required for it



5. **Due to deformation**

During tablet compression, disintegranted particles get deformed and these deformed particles get into their normal structure when they come in contact with aqueous media or water

6. **Due to release of gases**

The effervescent mixture is used when pharmacist needs to formulate very rapidly dissolving tablets or fast disintegrating tablet. Carbon dioxide released within tablets on wetting due to interaction between bicarbonate and carbonate with citric acid or tartaric acid

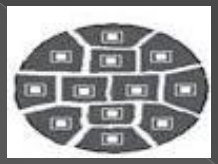
Mechanism of Tablet Disintegrants

7. **By enzymatic action**

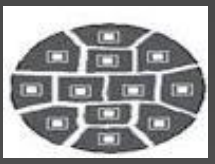
Disintegrating enzymes destroy the binding action of binder and helps in disintegration

Ex. Disintegrating Enzymes

ENZYMES	BINDER
Amylase	Starch
Protease	Gelatin
Cellulase	Cellulose and it's derivatives
Invertase	Sucrose



List of Disintegrants



DISINTEGRANTS	CONCENTRATION IN GRANULES (%W/W)	SPECIAL COMMENTS
Starch USP	5-20	Higher amount is required, poorly compressible
Starch 1500	5-15	-
Avicel®(PH 101, PH 102)	10-20	Lubricant properties and directly compressible
Solka floc®	5-15	Purified wood cellulose
Alginic acid	1-5	Acts by swelling
Na alginate	2.5-10	Acts by swelling
Explotab®	2-8	Sodium starch glycolate, superdisintegrant.
Polyplasdone®(XL)	0.5-5	Crosslinked PVP
Amberlite® (IPR 88)	0.5-5	Ion exchange resin
Methyl cellulose, Na CMC, HPMC	5-10	-
AC-Di-Sol®	1-3	Direct compression
	2-4	Wet granulation
Carbon dioxide	_	Created in situ in effervescent tablet

Glidants

- Glidants are intended to promote the flow of tablet granulation or powder mixture from hopper to the die cavity by reducing friction between the particles.

- It is not deformed by pressure of the tablet machine.

Glidants
Talc (superior) 1-10 %
Starch 2-10 %
Powdered cellulose 1-2 %
Colloidal silicon dioxide 0.1-1 % Excellent
Hydrophobic Colloidal Silica 0.1-1 %
Calcium stearate (poor glidant)

Lubricants

- Lubricants reduce inter-particular friction. It improve ejection of tablets from die wall and reduces the sticking problems and produce smooth tablets.
- Lubricants are classified according to their water solubility i.e. water insoluble and water soluble.
- Selection of lubricant is depends partly on mode of administration, type of tablet, desired disintegration and dissolution properties, physicochemical properties of granules or powder and cost.
- Water insoluble lubricants are most effective and used at reduced concentration than water soluble lubricants.

List of Lubricants

Insoluble	Concentration (% W/W)	Water Soluble	Concentration (% W/W)
Stearates (Magnesium Stearate, Calcium Stearate, Sodium stearate)	0.25 -1	Boric acid	1
Talc	1 -2	Sodium benzoate	5
Sterotex	0.25 – 1	Sodium oleate	5
Waxes	1 - 5	Sodium acetate	5
Stearowet (calcium stearate & SLS)	1 - 5	Sodium Lauryl sulfate (SLS)	1 – 5
Glyceryl behapate (Compritol®888) (Both lubricant and binder effects)	1 - 5	Magnesium lauryl sulfate (MLS)	1 - 2
Liquid paraffin	Up to 5	PEG 4000, 6000	2-5

Antiadhesives or Antisticking agents

- These materials are added to reduce sticking or adhesion of any of the tablet granulation or powder to the faces of the punches or to the die wall.
- The pressure of the machine deforms these materials.
- It reduces sticking, picking and chipping problems.

List of Antiadhesives	
Antiadhesive	**Concentration (%W/W)**
Talc	1 – 5 Excellent
Corn starch	3 – 10 Excellent
Colloidal silica	0.1 – 0.5
DL-Leucine	3 – 10 Excellent
Sodium lauryl sulfate	<1
Stearates	<1

Coloring Agent

- Colors are added to tablet formulation for following purposes: to disguise off color drugs, product identification and for production of more elegant product.
- Most widely used colorants are dyes and lakes which are FD & C and D & C approved

Some commonly used pharmaceutical colorants (synthetic)
FD & C COLOR
Red 3
Red 40
Yellow 5
Yellow 6
Blue 1
Blue 2
Green 3

Flavoring agent

- Flavors are added to tablet formulation in order to make them palatable enough in case of chewable tablet and lozenges by improving the taste.
- Flavors are incorporated either as solids (spray dried flavors) or oils (cinnamon, coriandar, caraway etc.) or aqueous (water soluble) flavors.
- Solids that is dry flavors are easier to handle and generally more stable than oils.
- Oil is usually added at the lubrication step because of its sensitivity to moisture and their tendency to volatilize when heated during drying. It may also be adsorbed onto an excipient and added during the lubrication process.
- The maximum amount of oil that can be added to granulation without affecting tableting characteristics is 0.5 to 0.75 %w/w.
- Aqueous flavors are less used because of its instability on aging.

Sweeteners

- Sweeteners are added to tablet formulation to improve the taste of chewable tablets.

Some of the sweeteners used in tablet formulation	
Natural Sweeteners	Artificial Sweeteners
Mannitol	Saccharin
Lactose	Cyclamate
Sucrose	Aspartame
Dextrose	-

Wetting Agents

- Wetting agents are added to tablet formulation to aid water uptake during disintegration and assist drug dissolution. e.g sodium lauryl sulfate (SLS) and Sodium diisobutyl sulfosuccinate.

Dissolution Retardants

- Dissolution retardants as the name suggest, retards the dissolution of active pharmaceutical ingredient(s).
- Waxy materials like stearic acid and their esters can be used as dissolution retardants

Dissolution Enhancers

- Dissolution enhancers as the name suggest, enhance the dissolution rate of active pharmaceutical ingredient(s).
- Fructose, Povidone, Surfactants are used as dissolution enhancer.

Adsorbents

- Adsorbents are capable of retaining large quantities of liquids without becoming wet; this property of absorbent allows many oils, fluid extracts and eutectic melts to be incorporated into tablets.
- Most commonly used adsorbents in pharmaceuticals are anhydrous calcium phosphate, starch, magnesium carbonate, bentonite, kaolin, magnesium silicate, magnesium oxide and silicon dioxide.

Buffers

- Buffers are added to provide suitable microenvironmental pH to get improved stability and / or bioavailability.
- Most commonly used buffering agent in tablet formulation includes sodium bicarbonate, calcium carbonate, and sodium citrate.

Antioxidants

- Antioxidants are added to maintain product stability, they act by being preferentially oxidized and gradually consumed over shelf life of the product.

- Most commonly used antioxidants include ascorbic acid and their esters , alpha-tocopherol , ethylene diamine tetra acetic acid , sodium metabisulfite , sodium bisulfite , Butylated Hydroxy Toluene (BHT) , Butylated Hydroxy Anisole (BHA) , citric acid , and tartaric acid

Chelating Agents

- Chelating agents are added to protect against autoxidation; they act by forming complexes with the heavy metal ions which are often required to initiate oxidative reactions.

- Ethylenediamine tetracetic acid and its salts, Dihydroxy Ethyl Glycine, Citric Acid and Tartaric Acid are most commonly used chelators

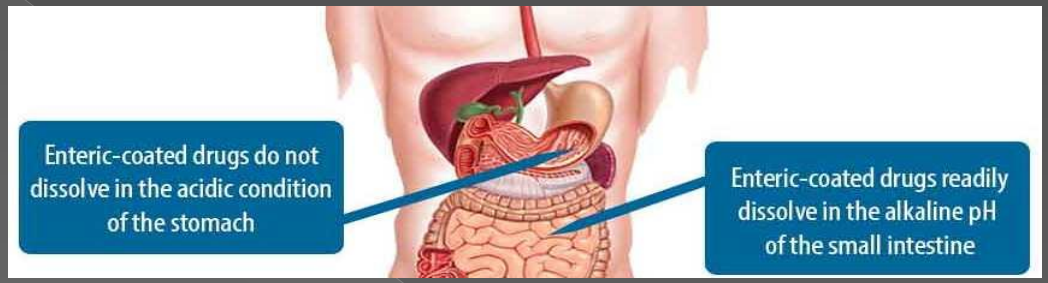
Preservatives

- Preservatives are added to tablet formulation in order to prevent the growth of micro-organisms.

- Parabens like methyl, propyl, benzyl, butyl p-hydroxy benzoate are used as preservatives.

Enteric Coated Tablets

- All enteric coated tablets (which remain intact in the stomach but quickly release in the upper intestine) are a type of delayed-action tablet.



Polymers used for enteric coated tablets	
Polymers	**pH**
Cellulose acetate phthalate (CAP)	rapid dissolution at a pH > 6
Polyvenyl acetate phthalate (PVAP)	5.0
HPMC phthalate (HPMCP)	5.0-5.5
HPMC acetate succinate (HPMCAS) (3 Grade)	Low pH 5 Medium pH 5.5 high pH 6.5
Cellulose acetate trimellitate (CAT)	4.7–5.0
These polymers, being acid esters, are insoluble in gastric media	

Sugar-Coated Tablets

- These are conventional tablets that have been coated with a concentrated sugar solution to improve the appearance of the formulation and/or to mask the bitter taste of the therapeutic agent.

- The use of sugar coatings has dramatically decreased due to the advent of film-coated tablets (as a result of the improved mechanical properties of the latter coating).

Film-Coated Tablets

- These are conventional tablets that have been coated with a polymer or a mixture of polymers (and, when required, a plasticizer to render the coating flexible).
- Polymers have been used to mask the unpleasant taste and odor.
- Film coatings show improved mechanical properties when compared to sugar coatings.
- Film coatings are generally less elegant than sugar coatings.
- In film coating process, coating time and cost of production are decreased and got better strength of tablets compared to sugar coating process.

Film-Coated Tablets

- Examples of polymers that are used to film-coat tablets (and which dissolve in the stomach to enable tablet disintegration and drug dissolution) include:
  - **Hydroxypropylmethylcelluose (HPMC)**
  - **Hydroxypropylcellulose (HPC)**
  - **Eudragit E100**
- In addition to improving the appearance of conventional tablets, film coatings are employed to control the rate and duration of drug release or to target drug release to certain regions of the gastrointestinal tract, e.g. the colon.
- Drug release occurs by diffusion through the insoluble coating and subsequent partitioning into the gastrointestinal fluids.

Examples of polymers that may be used for this purpose include:

1) **Ethylcellulose (EC)**
2) **Eudragit RS and RL.**

TIU
FACULTY OF PHARMACY
PHARMACEUTICAL TECHNOLOGY III
2020-2021

Solid Dosage Forms

Lec. Dr. Muath Sheet Mohammed Ameen

Lec. 3

Chewable Tablets

- These tablets are chewed within the buccal cavity prior to swallowing. The main applications for this dosage form are:
- for administration to children and adults who have difficulty in swallowing conventional tablets.
- Antacid formulations in which the size of the tablet is normally large and the neutralisation efficacy of the tablet is related to particle size within the stomach.
- Conversely, chewable tablets are not conventionally used if the drug has issues regarding taste acceptability.

Excipients used in the formulation of chewable tablets

a)Diluents:

These are added to chewable tablet formulations to increase the bulk volume of the tablet.

i. **Mannitol**

It is inert and nonhygroscopic that is suitable base in chewable tablet formulations and also acts as sweetening agent (about 70% as sweet as sucrose)

ii. **Sorbitol**

Sorbitol is particularly useful in chewable tablets owing to its pleasant, slightly sweet taste and cooling sensation. It is hygroscopic

iii. **Dextrose**

It is used as diluent and binder in direct-compression chewable tablets. Its sweetness level is approximately 70% that of sucrose.

iv. **Lactose**

It is most widely used pharmaceutical excipient. its extremely low sweetness level (20 % of sucrose).

v. **Sucrose**

For directly compress, **sucrose crystals include Di-Pac® (97% sucrose plus 3% modified dextrins), Sugartab (90 to 93% sucrose plus 7 to 10% invert sugar) and NuTab (95% sucrose, 4% invert sugar, and 0.1 to 0.2% each of corn starch and magnesium stearate)**.

Excipients used in the formulation of chewable tablets

b) Flavoring agents

Flavorants are commonly used to impart pleasant flavor and often odor to chewable tablets.

Flavour	Groups for Taste Types
Sweet	Vanilla, grape, maple, honey, stone fruits, berries
Sour (Acidic)	Citrus, raspberry, anise, cherry, strawberry, root beer
Salty	Mixed fruit, mixed citrus, butterscotch, maple, nutty, buttery, spice
Bitter	Liquorice, coffee, mint, cherry, grapefruit, wine, fennel, peach,
Metallic	Grape, lemon-lime, burgundy
Alkaline	Mint, chocolate, cream, vanilla

Excipients used in the formulation of chewable tablets

c) Sweetening agents

Sweeteners are added primarily to chewable tablets when the commonly used carriers such as mannitol, lactose, sucrose, and dextrose do not sufficiently mask the taste of the active substance or components.

Materials	Relative sweetness [b]
Aspartame [a]	200
Cyclamate [a]	30 – 50
Glycyrrhizin [a]	50
Saccharins [a]	500
Dextrose (glucose)	0.7
Fructose (laevulose)	1.7
Lactose	0.2
Maltose	0.3
Mannitol	0.5 – 0.7
Sorbitol	0.5 – 0.6
Sucrose	1

[a] Regulatory status must be checked before use
[b] Sucrose is taken as a standard of 1 for comparison

Excipients used in the formulation of chewable tablets

d) Colorants

- Colorants are used in the manufacture of chewable tablets for the following reasons:

1. To increase aesthetic appeal to the consumer
2. To aid in product identification and differentiation
3. To mask unappealing or non-uniform color of raw materials
4. To complement and match the flavor used in the formulation

- **Only FD & C colors and D & C colors** are used in the manufacture of chewable tablets.

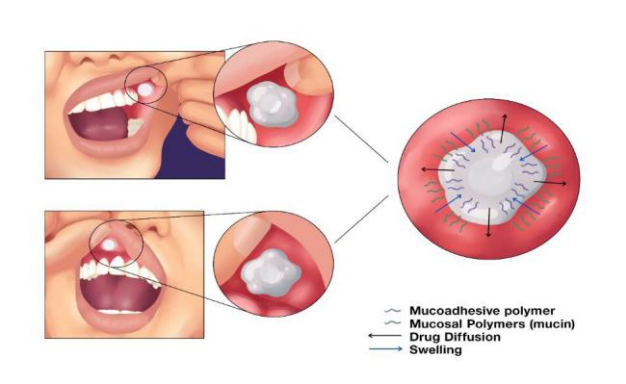
- **Lakes** are used in chewable tablets made **by direct compression** in a concentration range of **0.1 to 0.3%.**

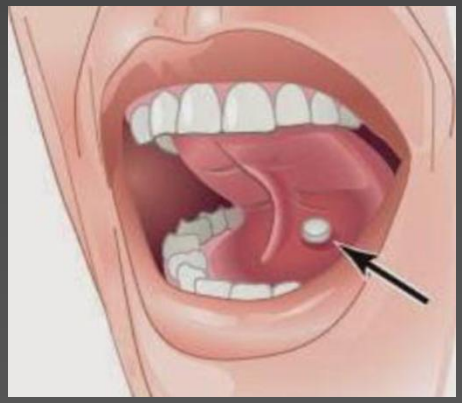
Effervescent Tablets

- Effervescent tablets are added to aqueous solutions where they will rapidly disintegrate and produce either a drug suspension or an aqueous solution.
- The disintegration of the tablet is due to a chemical interaction that occurs between two components: **(1) an organic acid (e.g. citric acid); and (2) sodium bicarbonate in the presence of water**. The evolution of carbon dioxide from this reaction results in tablet disintegration. The patient then consumes the solution/suspension.
- The main advantage of the use of effervescent tablets is the production of a dosage form from which the therapeutic agent is more rapidly absorbed than from alternative solid-dosage forms (e.g. conventional tablets).
- Conversely, the main disadvantages of this type of dosage form are the possible (un)availability of water and the need to package these tablets in moisture-impermeable packaging (typically aluminium foil), to inhibit the interaction between the acid and sodium bicarbonate due to the presence of environmental moisture.

Buccal and Sublingual Tablets

- Buccal and sublingual tablets are dosage forms that are held within the oral cavity and slowly dissolve; the drug is absorbed across the buccal mucosa to produce a systemic effect.
- The type of tablet dictates the location within the oral cavity. Accordingly buccal tablets are positioned between the cheek and the gingiva whereas sublingual tablets are positioned underneath the tongue.
- These tablets are employed to achieve either rapid absorption into the systemic circulation (e.g. glyceryl trinitrate sublingual tablets) or, alternatively, to enable systemic drug absorption in situations where oral drug delivery is inappropriate, e.g. nausea.
- Drug absorption across the buccal mucosa avoids first-pass metabolism.
- Typically buccal and sublingual tablets should be formulated to dissolve slowly in vivo over a 15-30 min period (and not disintegrate) and to be retained at the site of application and should not contain components that stimulate the production of saliva.



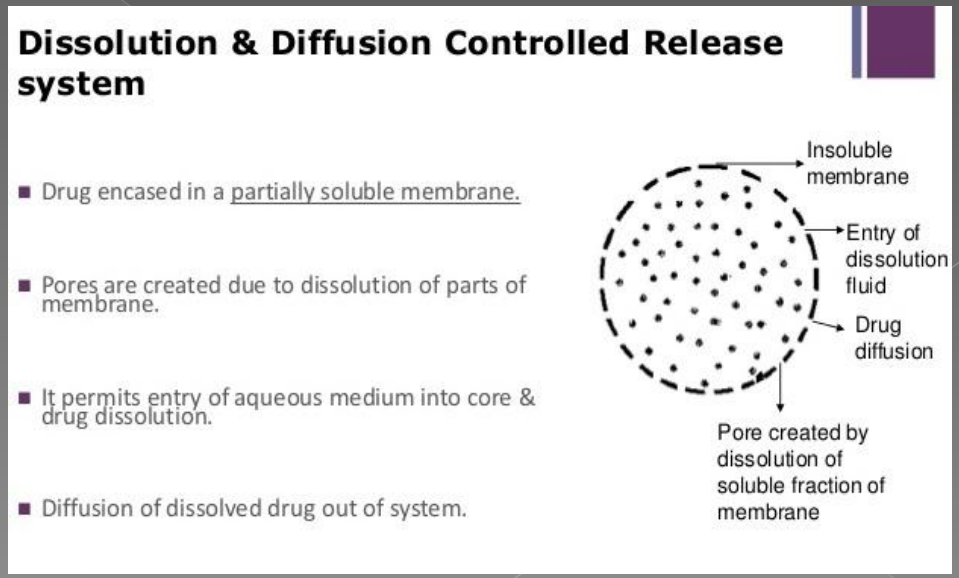


Most Used Polymers for Buccal Mucoadhesive Tablets
Ethylcellulose (EC)
Methylcellulose (MC)
Hypromellose Carboxymethylcellulose (CMC)
Hypromellose Carboxymethylcellulose (CMC)
Hydroxyethylcellulose (HEC)
Hydroxypropylmethylcellulose (HPMC)
Gums (Xanthan, Badam, Gellan, Guar and Alginate)
Acrylates-Carbomers (CBM)
Chitosan

Excipients Used In Sublingual Tablets
Excipients (Uses)
HPMC (Binder, Stabilizing agent)
Lactose Monohydrate (Diluent, Binder)
Crosspovidone (Superdisintegrant)
Cross carmellose sodium (Superdisintegrant)
Sodium starch glycolate (Superdisintegrant)

Matrix Tablets

- Matrix tablets are the type of controlled drug delivery systems, which release the drug in continuous manner.
- In a matrix system, the drug substance is homogenously mixed into the rate controlling material as crystalline, amorphous or in rare cases molecular dispersion.
- These release the drug by dissolution controlled and/or diffusion controlled mechanisms.



Classification of Matrix Tablet

- Classification based on the characteristics of rate controlling

1. Hydrophilic type matrix
2. Hydrophobic type matrix
3. Biodegradable type matrix
4. Mineral type matrix

Hydrophilic Type Matrix

- In this system, the rate controlling materials are water soluble and/or swellable.
- Matrix is a well mixed composite of one or more drugs with gelling agent.
- Commonly available hydrophilic polymers include:

1. HPMC, hydroxypropylcellulose (HPC), hydroxylethylcellulose (HEC) .
2. Water soluble natural gums of polysaccharides such as xanthum gum, alginate.
3. Water swellable, but insoluble, high molecular weight homopolymers (Carbopol 71G NF, 971P, 934P).
4. Polyvinyl acetate and povidone mixture (Kollidone SR).
5. Ionic methacrylate copolymers (Eudragit L30D).

Lipid Type Matrix

- These matrices are prepared by lipid waxes and related materials.
- Drug release from such matrices occurs through both pore diffusion and erosion.
- Release characteristics are, therefore, more sensitive to digestive fluid composition than to totally insoluble polymer matrix.
- Carnauba wax in combination with stearyl alcohol or stearic acid has been used as retardant base for many sustained release formulation.

Biodegradable Type Matrix

- These consist of the polymers which comprised of monomers linked to one another through functional groups and have unstable linkage in the backbone.
- They are biologically degraded or eroded by enzymes generated by surrounding living cells or by non-enzymatic process in to oligomers and monomers that can be excreted or metabolized.
- Examples are natural polymers such as proteins and polysaccharides; modified natural polymers; synthetic polymers such as aliphatic poly (esters) and polyanhydrides.

Mineral Type Matrix

- These consist of polymers which are obtained from various species of seaweeds.

- Example is alginic acid which is a hydrophilic carbohydrate obtained from the species of brown seaweeds (Phaephyceae) by the use of dilute alkali.

Polymers Used In Matrix Tablets

Hydrogel	Soluble polymers	Biodegradable polymers	Non-biodegradable polymers	Mucoadhesive polymers	Natural gums
Polyhydroxyethyle methylacrylate (PHEMA)	Polyethylene glycol (PEG)	Polylactic acid (PLA)	Polyethylene vinyl acetate (PVA)	Polycarbophil	Xanthan gum
Cross-linked polyvinyl alcohol (PVA)	polyvinyl alcohol (PVA)	Polyglycolic acid (PGA)	Polydimethyl siloxane (PDS)	Sodium carboxy methyl cellulose	Guar gum
Cross-linked polyvinyl pyrrolidone (PVP)	Polyvinylpyrrolidone (PVP)	Polycaprolactone (PCL)	Polyether urethane (PEU)	Polyacrylic acid	Karaya gum
Polyethylene oxide (PEO)	Hydroxypropyl methylcellulose (HPMC)	Polyanhydrides	Polyvinyl chloride (PVC)	Tragacanth	Locust bean gum
Polyacrylamide (PA)		Polyorthoesters	Cellulose acetate (CA)	Methylcellulose	
			Ethyl cellulose (EC)	Pectin	

Tablet Compression Operation

- For the compression of granules in the form of tablets, various types of machines are used as follows:

1. Single punch machines
2. High-speed rotary tablet machines
3. Multilayer rotary tablet machines

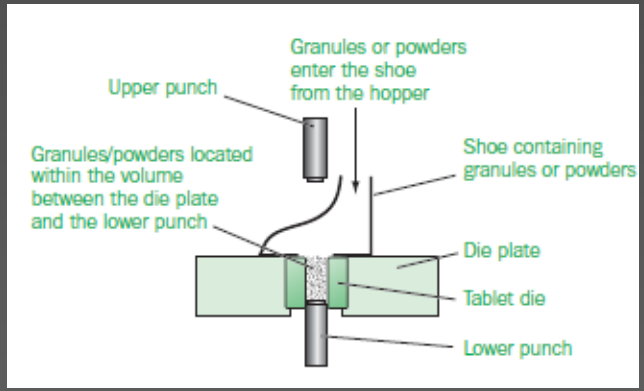
Single punch machines

- For small-scale production, a single punch tablet machine is used to prepare small quantity of tablets.

- The output of tablets from a single punch machine is about 200 tablets per minute.

The compression process in tableting

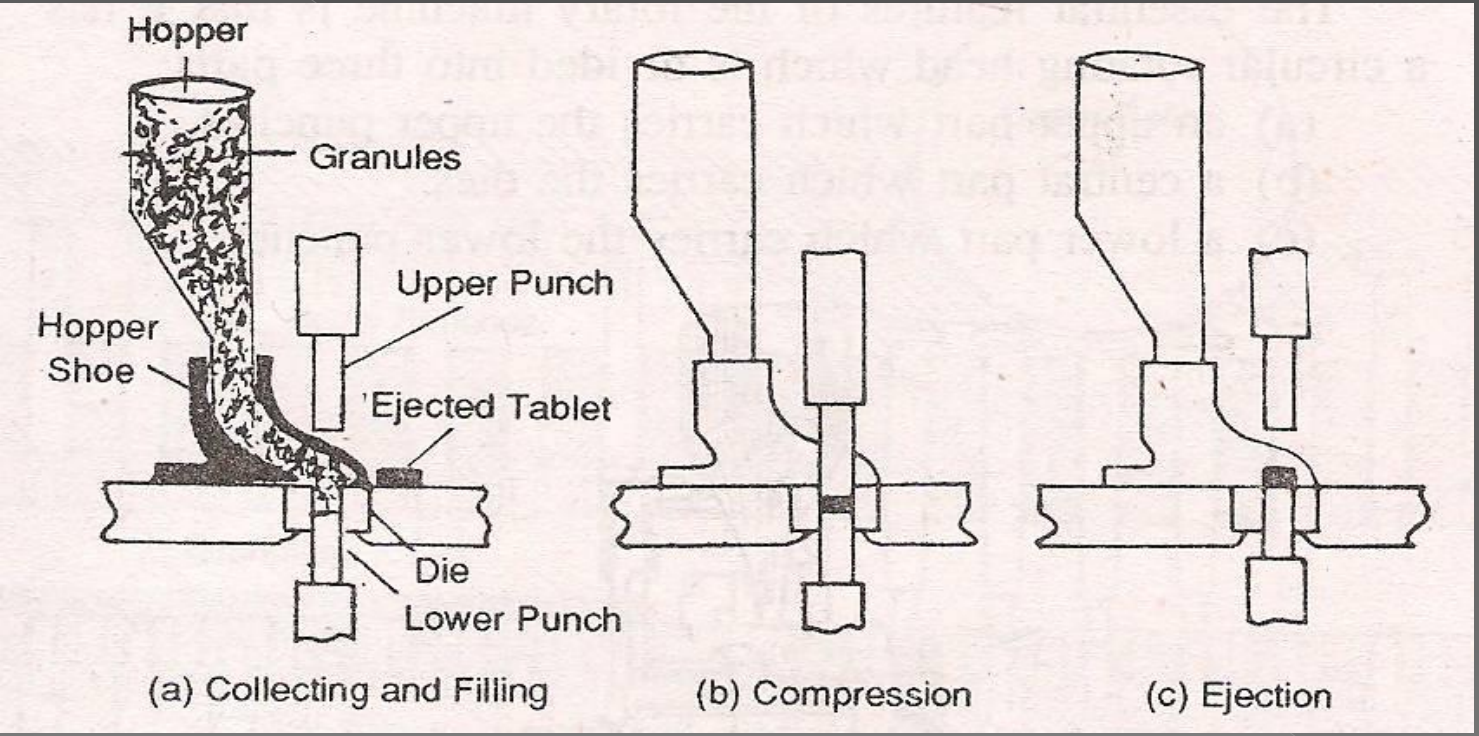
- The formulated powders or granules are fed (usually by gravitational flow) into the die section, i.e. in the space between the lower and upper punches, from the hopper on the tablet press.



- The volume of space occupied by the granules/powders is defined by the position of the lower punch and the die plate (also where the feed shoe of the hopper resides).

- Accordingly, the mass of solid material within this space (and hence the size of the tablet) is altered by increasing/decreasing the position of the lower punch.

Single Punch Machines



TIU
FACULTY OF PHARMACY
PHARMACEUTICAL TECHNOLOGY III
2020-2021

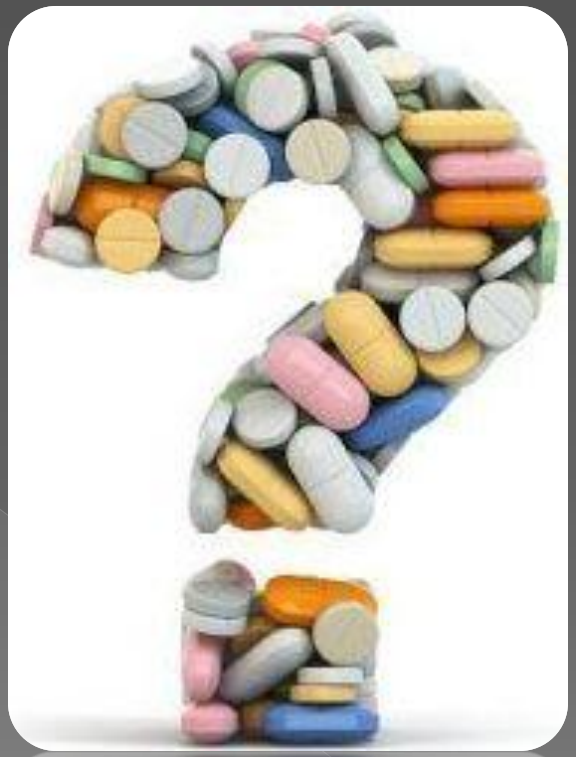
Solid Dosage Forms

Lec. Dr. Muath Sheet Mohammed Ameen

Lec 4

Evaluation of Tablets

- General appearance
- Organoleptic Properties
- Mechanical strength
- Content Uniformity Test
- Weight Variation
- Disintegration
- Dissolution



General Appearance

- Size
- Shape
- Color
- Odor
- Taste
- Surface texture
- Physical flaws
- Consistency

Size and Shape

Tablet thickness varies with changes in

- Die fill
- Particle size distribution through granulation
- Packing of particles mix being compressed
- Weight of tablet
- Compression process

The thickness and diameter of tablets are measured by different micrometer calipers

Micrometer Calipers

Technique employed in production control involves measuring

the thickness and diameter of 5 or 10 tablets by **different micrometer caliper**.

Tablet thickness should be controlled within ± 5% variation of a standard value.

Organoleptic Properties

- Color of a product must be uniform

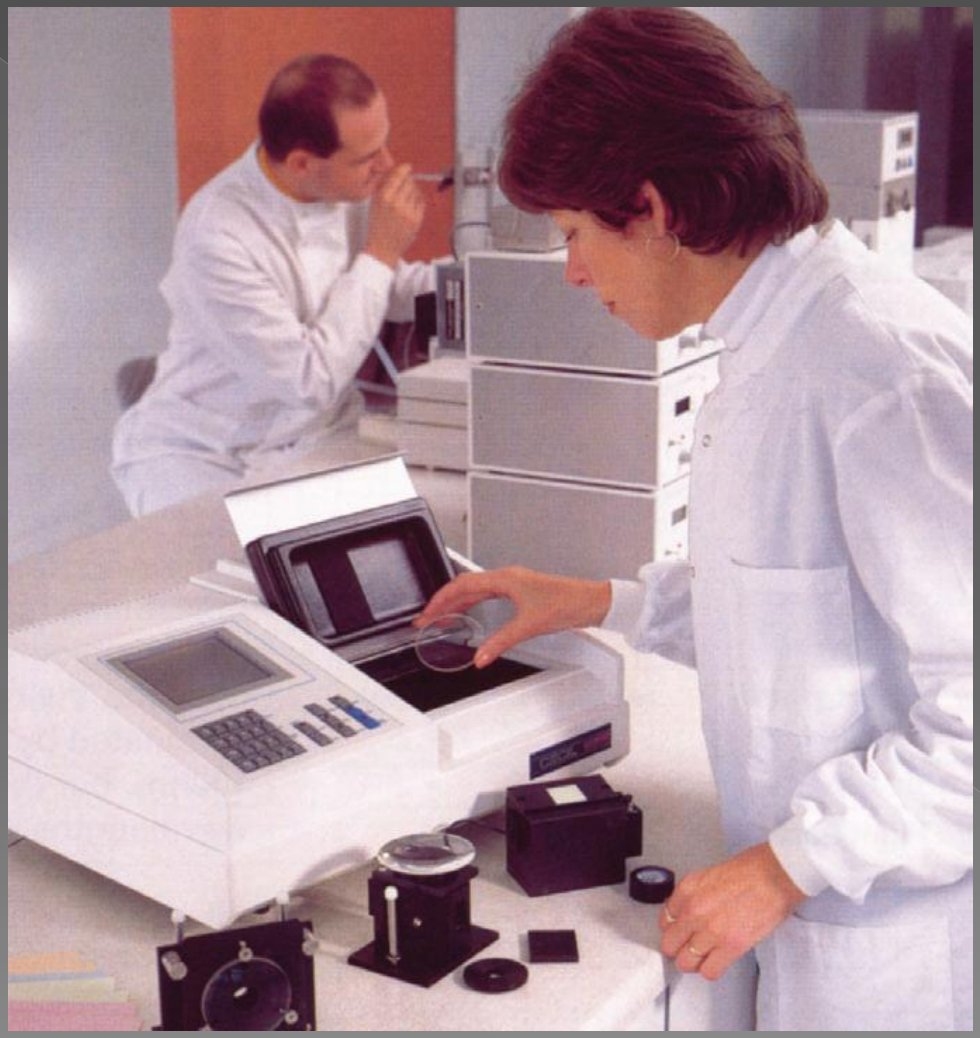
  Color uniformity measured by

1. Reflectance spectrophotometry
2. Tristimulus colorimetric measurements
3. Microreflectance photometer

- Odor (provide an indication of the quality of tablets) as the presence of an odor in a batch of tablets could indicate a stability problem, such as the characteristic odor of acetic acid in degrading aspirin tablets.

- Taste is also important for consumer acceptance of certain tablets (e.g. chewable tablets)

Reflectance Spectrophotometry



Mechanical Strength

The mechanical strength of a tablet provides a measure of the bonding potential of the material concerned that is useful in the selection of excipients.

The mechanical properties of pharmaceutical tablets are quantifiable by

- Friability
- Hardness or crushing strength
- Tensile strength

Friability Test

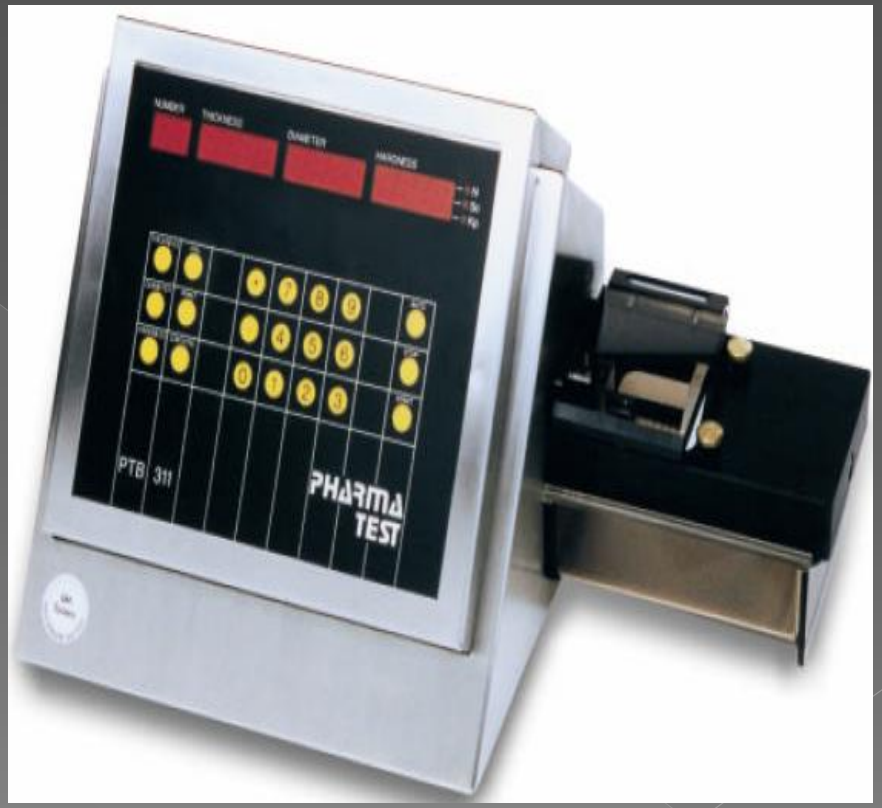
- It is designed to evaluate the ability of the tablet to withstand abrasion in packaging, handling and shipping
- 100 revolution or 4 minute rolling is required
- The standard test procedure is to take a sample of 10 tablets (a sample equivalent to 6.5 grams should be taken if the tablets weigh less than 650 mg)
- Loss weight of tablet due to abrasion is measure the friability of tablet
- Maximum weight loss less than 1% is acceptable
- Friability values are not calculated for capping problem

Friability Test

Hardness (crushing strength)

- Measures the force required to break the tablet when the force generated by a coil spring is applied diametrally to the tablet
- Measure resistance of tablets to capping, abrasion or breakage under conditions of storage, transportation and handling before usage

Tablet Hardness Tester



Manual (Monsanto)

Electronic

Hardness (crushing strength)

Force unit is measured in Kilogram

- Plain tablets = 4 -10
- Hypodermic and chewable tablet = 3
- Some sustained release tablets = 10 - 20

- Hardness of tablets depends on

1. Density and porosity
2. Shape
3. Chemical properties
4. Binding agent
5. Pressure applied during compression

Tensile Strength

- The measurement of tensile strength provide a more fundamental measure of the mechanical strength of the compacted material and takes into account the geometry of the tablet.

- Tensile strength is calculated from breaking strength to account for tablet dimensions.

- It is calculated based on diametral compression testing for round flat face tablets as follows:

$$\sigma_t = 2\ F / \pi DH$$

where σ_t is the tensile fracture strength of the tablet, F is the load needed to break the tablet, and D and H are the diameter and thickness respectively.

Content Uniformity Test

- By the USP method, 30 tablets are randomly selected, 10 of these tablets are assayed individually according to the method described in the individual monograph.

- Unless otherwise stated in the monograph, the requirements for content uniformity are met if the amount of active ingredient in nine (9) of the ten (10) tablets lies within the range of 85% to 115% of the label claim.

- The tenth tablet may not contain less than 75% or more than 125% of the labelled drug content.

Weight Variation

- The weight of tablet is routinely measured to help ensure that a tablet contains the proper amount of drug.
- The USP has provided limits for the average weight of uncoated compressed tablets.
- Weighing 20 tablets individually, calculating the average weight and compared with individual weight
- The prescribed limits for weight variation of tablets illustrated in table 1

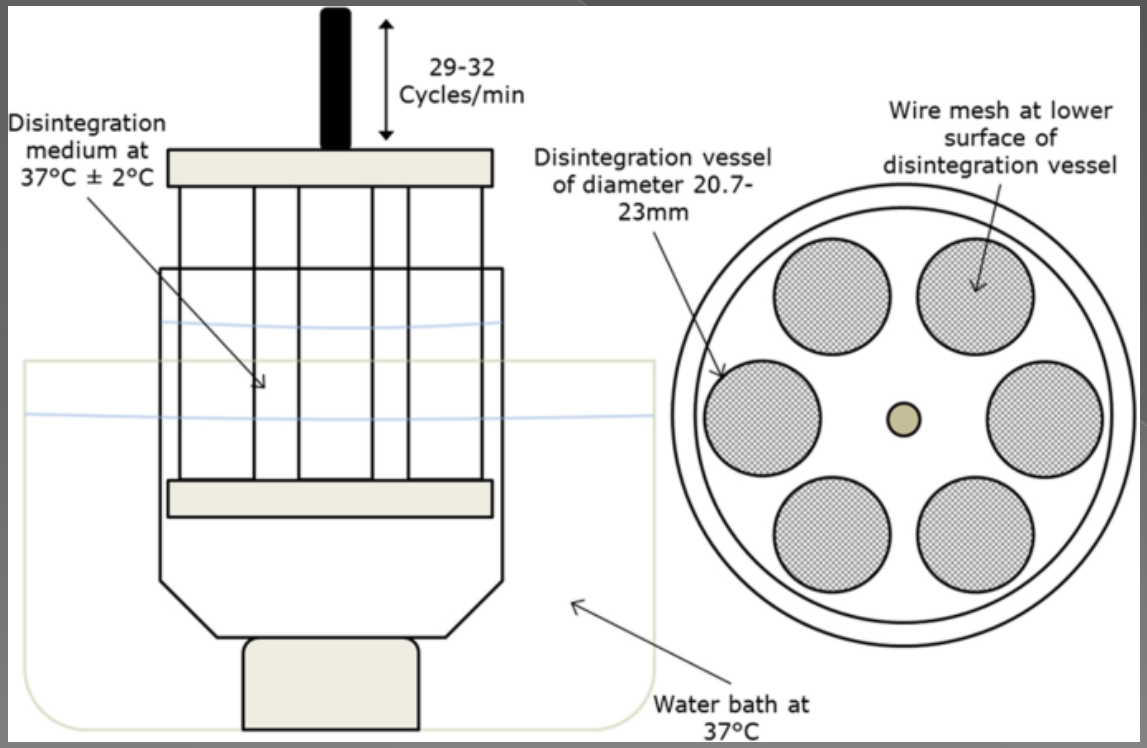
Table 1: Weight variation tolerance for uncoated tablets

Average weight of tablets (mg)	Maximum percentage difference allowed
130 or less	10
130 – 324	7.5
More than 324	5

Disintegration

- For a drug to be absorbed from a solid dosage form after oral administration, it must first be in solution and break up of tablets
- Generally, the test is useful as a quality assurance tool for conventional dosage forms.
- Procedures are stated for running disintegration times for uncoated tablets, plain-coated tablets, enteric coated tablets, buccal tablets and sublingual tablets.
- BP requires that the uncoated tablets disintegrate in 15 minutes and coated tablets, up to 2 hours may be required

Disintegration Apparatus



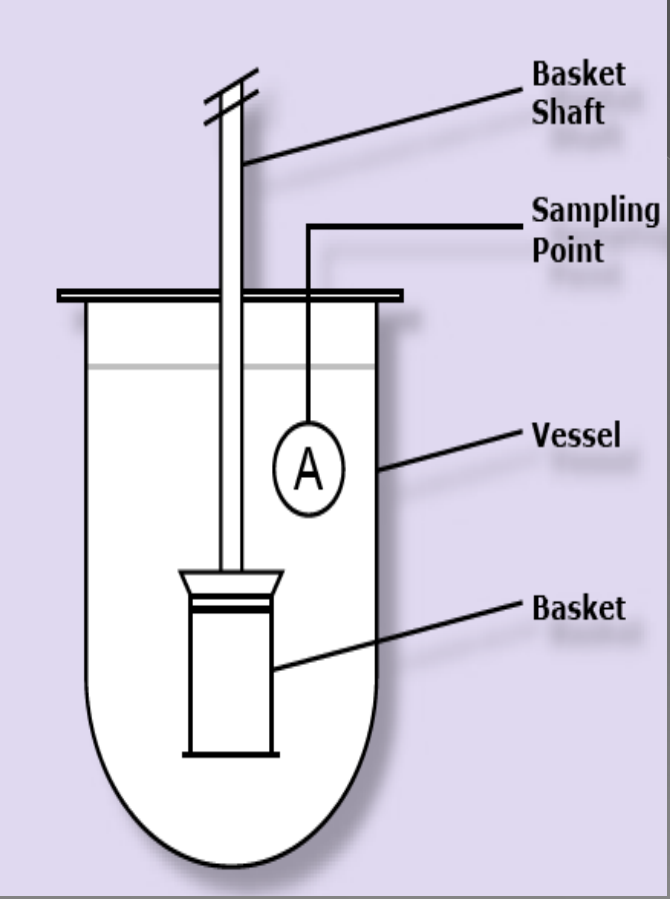
Dissolution

- The rate of dissolution of a solid drug plays an important role in the absorption and physiological availability of the drug in the blood stream.
- Two apparatuses are used for determining dissolution rates:

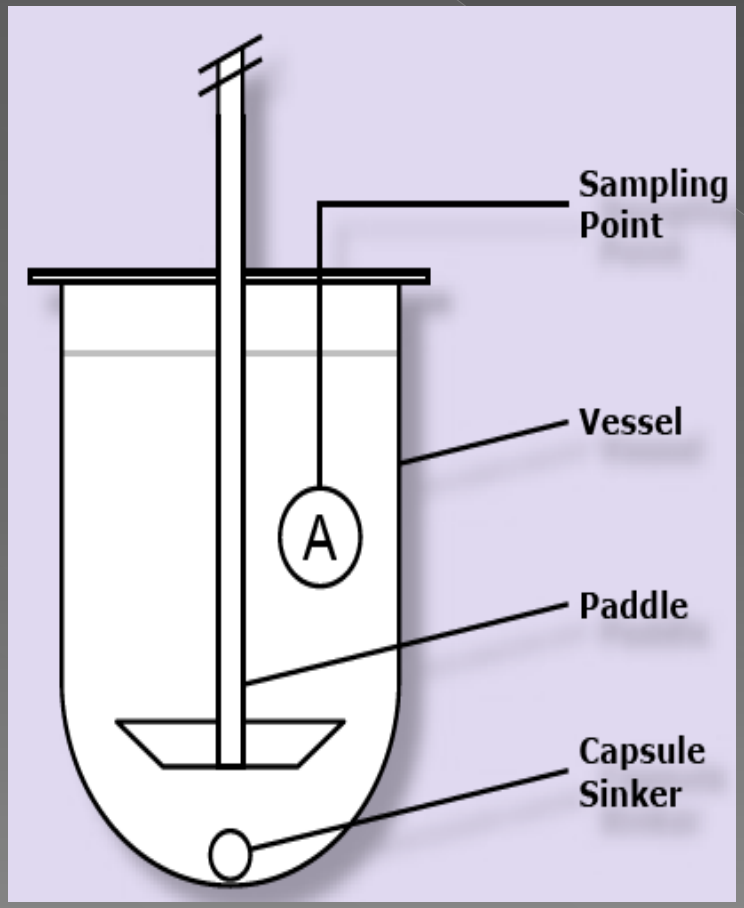
1. **Apparatus 1 (Basket type):** a single tablet is placed in a small wire mesh (10 or 20 or 40 meshes) basket that connected to bottom of the shaft and rotated by a variable speed motor.
2. **Apparatus 2 (Paddle type)**: the same equipment as in apparatus 1 is used, except that the basket is replaced by a paddle, formed from blade a shaft as the stirring element.

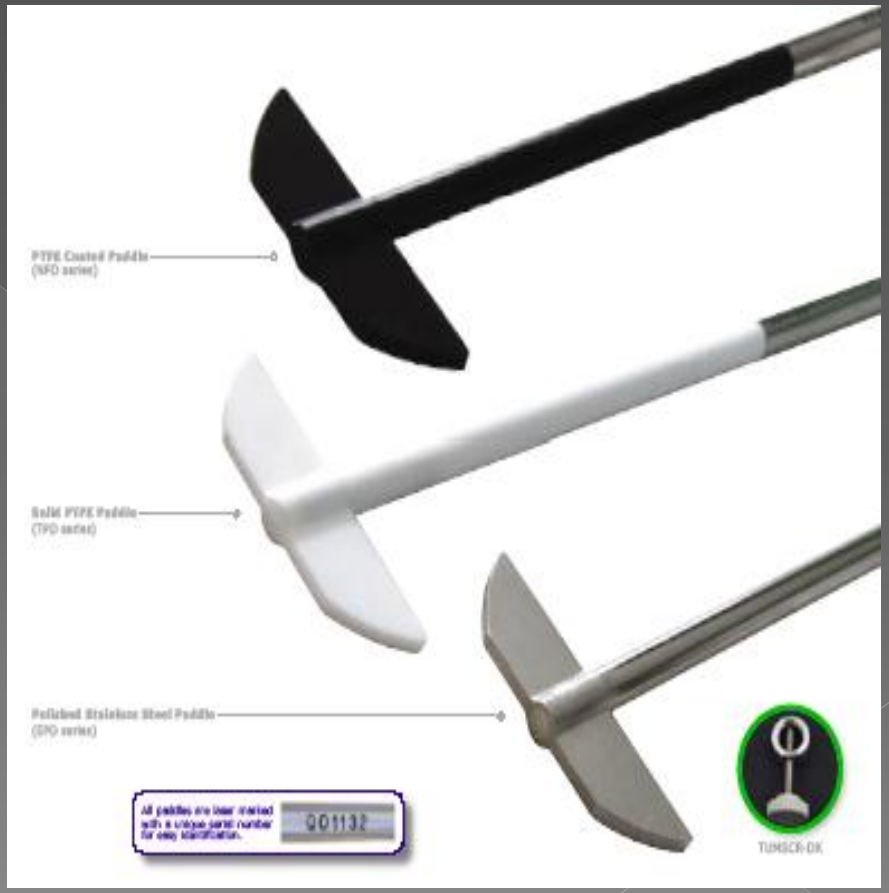
Dissolution Apparatus

Apparatus 1 (Basket)

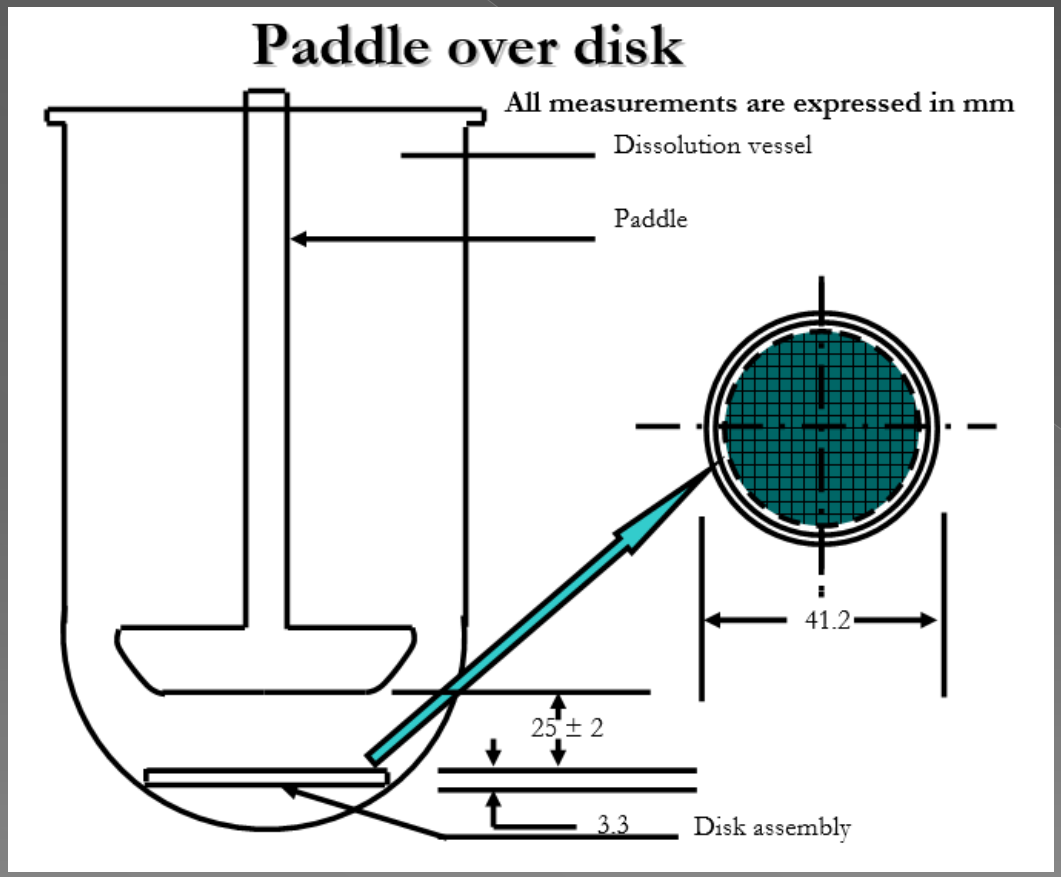


Apparatus 2 (Paddle)





Apparatus 5 (Paddle over Disk) (Modified Apparatus 2)



Defects of Tabletting

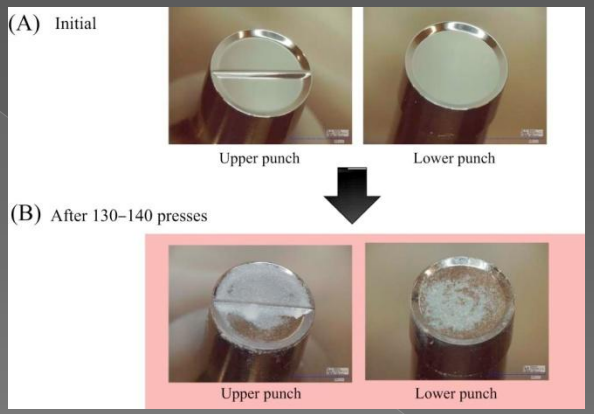
- Some faults in the formulation or in the tabletting equipment.

- These defects are

1. Picking and sticking
2. Capping and Lamination of tablets
3. Mottling
4. Chipping
5. Poor flow
6. Double Impression

Picking and Sticking

- In picking, a small surface of the tablet material is removed by the punches and adheres to the surface of punches and tablets show a pitted surface due to presence scratches on the punches and wetting granules



- In sticking, the granules adhere to the die wall and thereby lower punch can not move freely. Due to worn out dies and punches.

Picking and Sticking

Remedies:

- Re-drying of granules
- The worn-out dies and punches must be replaced
- Changing the type of binder and using a less adhesive type binder
- Addition of lubricant in the granules

Capping and Lamination

- In capping, the upper and lower surface of the tablet partially or completely separates out from the main body of the table.
- In lamination, the tablet separates in two or more layers
- Correction by regranulating the material, altering the pressure adjustments or reducing the speed of machine

Capping

Causes:

- Overdrying of the granules
- The presence of either excess of fine powder in granule or less amount of fine powder in granules.
- The wear and tear of punches is responsible for capping
- The wrong setting of dies and punches
- The use of too soft granules also lead to capping

Remedies:

- Water should be added in the form of spray in the granules
- Proper granules and required amount of powder must be used.
- The wear and tear punch must be replaced.
- The proper setting of dies and punches.

Lamination

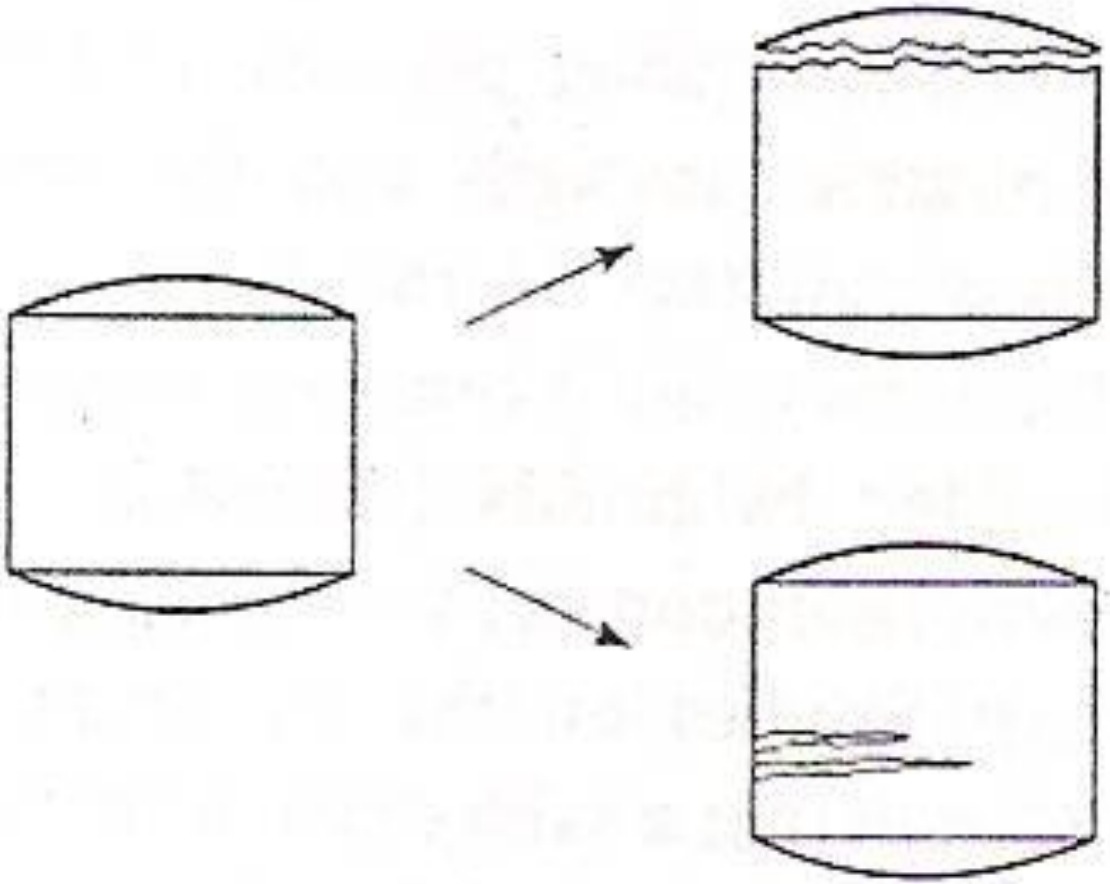
Causes:

- Entrapped air in the granules
- Excess powder on the granules
- Insufficient binder in the formulation.

Remedies:

- Altering the Pressure adjustment
- Required amount of powders must be maintained
- Increasing the percentage of the binders
- Changing the types of binders in the formulation.

Capping and Lamination Figure

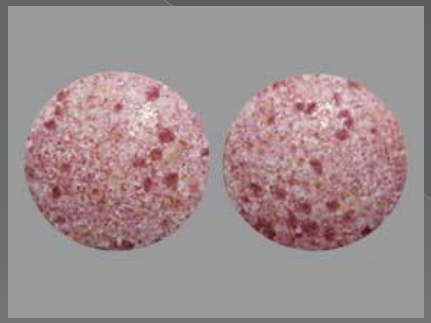


Capping

Lamination

Mottling

- This defect occurs in the colored tablets and this defect may be caused either due to the difference of colors in the drugs and excipients or due to the migration of dyes during drying of granules.



- Defect is solved by changing the solvent system or by drying the granules at a low temperature.

Chipping

Chipping is the breaking of tablet edges.

Causes:

- Due to the improper setting of feed frame. Feed frame is the device where granules come from the hopper and also helps to fill the die cavity with the granules.

Remedies:

- Proper setting of the feed frame.

Poor Flow

- Incomplete filling of dies by the powder material due to poor flow of material from hopper to die wall.

Causes:

- Speed of tablet machine
- Different density of powder material as well as additives.

Remedies:

- Addition of glidant e.g talcum, colloidal silica

Double Impression

- One dark and one lighter impression on tablet surface is called double impression.
- It is the problem due to mechanical hazards specially with punches.

Cause:

- Uncontrolled free rotation of the lower punch during ejection of the compressed tablets.

Remedy:

- Fitted anti turning device with lower punch, which prevents the rotation of the lower punch.