

TABLETS

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INTRODUCTION

Tablet is defined as a compressed solid dosage form containing medicaments with or without excipients. According to the Indian Pharmacopoeia Pharmaceutical tablets are solid, flat or biconvex dishes, unit dosage form, prepared by compressing a drug or a mixture of drugs, with or without diluents

The advantages of the Tablet dosage form are:

- They are unit dosage form and offer the greatest capabilities of all oral dosage form for the greatest dose precision and the least content variability.
- Cost is lowest of all oral dosage form.
- Lighter and compact.
- Easiest and cheapest to package and strip.
- Easy to swallowing with least tendency for hang-up.
- Sustained release product is possible by enteric coating.

- Objectionable odour and bitter taste can be masked by coating technique.
- Suitable for large scale production.
- Greatest **chemical and microbial stability over all oral dosage form.**
- Product identification is easy and rapid requiring no additional steps when employing an **embossed and/or monogrammed punch face.**

Disadvantages of Tablet dosage form are:

- Difficult to swallow in case of children and unconscious patients.
- Some drugs resist compression into dense compacts, owing to **amorphous nature, low density character**.
- Drugs with poor wetting, slow dissolution properties, optimum absorption high in GIT may be difficult to formulate or manufacture as a tablet that will still provide adequate or full drug bioavailability.
- Bitter tasting drugs, drugs with an objectionable odor or drugs that are sensitive to oxygen may require encapsulation or coating. In such cases, capsule may offer the best and lowest cost.

Different types of Tablets

(A) Tablets ingested orally:

1. Compressed tablet, e.g. Paracetamol tablet
2. Multiple compressed tablet
3. Repeat action tablet
4. Delayed release tablet, e.g. Enteric coated Bisacodyl tablet
5. Sugar coated tablet, e.g. Multivitamin tablet
6. Film coated tablet, e.g. Metronidazole tablet
7. Chewable tablet, e.g. Antacid tablet

(B) Tablets used in oral cavity:

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

(c) Tablets administered by other route:

1. Implantation tablet
2. Vaginal tablet, e.g. Clotrimazole tablet

(D) Tablets used to prepare solution:

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

Tablet Ingredients

In addition to active ingredients, tablet contains a number of inert materials known as additives or excipients. Different excipients are:

1. Diluent
2. Binder and adhesive
3. Disintegrants
4. Lubricants and glidants
5. Colouring agents
6. Flavoring agents
7. Sweetening agents

EXCIEPIENTS- *functions*

- Impart weight, accuracy, & volume(its allow acccuracy of dose)
- Improve solubility
- Increase stability
- Enhance bioavailability
- Modifying drug release
- Assist pdt identification
- Increase patient acceptability
- Facilitate dosage form design

- **1. Diluent:** Diluents are fillers used to make required bulk of the tablet when the drug dosage itself is inadequate to produce the bulk. Secondary reason is to provide better tablet properties such as improve cohesion, to permit use of direct compression manufacturing or to promote flow. A diluent should have following properties:
 1. They must be non toxic
 2. They must be commercially available in acceptable grade
 3. Their cost must be low
 4. They must be physiologically inert
 5. They must be physically & chemically stable by themselves & in combination with the drugs.
 6. They must be free from all microbial contamination.
 7. They do not alter the **bioavailability of drug**.
 8. They must be color compatible.

Commonly used tablet diluents

1. Lactose-anhydrous and spray dried lactose
2. Directly compressed starch-Sta Rx 1500
3. Hydrolyzed starch-Emdex and Celutab
4. Microcrystalline cellulose-Avicel (PH 101 and PH 102)
5. Dibasic calcium phosphate dehydrate
6. Calcium sulphate dihydrate
7. Mannitol
8. Sorbitol
9. Sucrose- Sugartab, DiPac, Nutab
10. Dextrose

2. Binders and Adhesives: These materials are added either dry or in wet- form to form granules or to form cohesive compacts for directly compressed tablet.

- Example: Acacia, tragacanth- Solution for 10-25% Conc.
- Cellulose derivatives- Methyl cellulose, Hydroxy propyl methyl cellulose, Hydroxy propyl cellulose
- Gelatin- 10-20% solution
- Glucose- 50% solution
- Polyvinylpyrrolidone (PVP)- 2% conc.
- Starch paste-10-20% solution
- Sodium alginate
- Sorbitol

3. Disintegrants: Added to a tablet formulation to facilitate its breaking or disintegration when it contact in water in the GIT.

- Example: Starch- 5-20% of tablet weight.
- Starch derivative – Primogel and Explotab (1-8%)
- Clays- Veegum HV, bentonite 10% level in colored tablet only
- Cellulose
- Cellulose derivatives- Ac- Di-Sol (sodium carboxy methyl cellulose)
- Alginate
- PVP (Polyvinylpyrrolidone), cross-linked

- **Superdisintegrants: Swells up to ten fold within 30 seconds when contact water.**
- Example: Crosscarmellose- cross-linked cellulose, Crosspovidone- cross-linked povidone (polymer), Sodium starch glycolate- cross-linked starch. These cross-linked products swells with in 30 seconds when in contact with water.
- A portion of disintegrant is added before granulation and a portion before compression, which serve as **glidants or lubricant**.

- **4. Lubricant and Glidants:** Lubricants are intended to prevent adhesion of the tablet materials to the surface of dies and punches, reduce inter particle friction and may improve the rate of flow of the tablet granulation.

Glidants are intended to promote flow of granules or powder material by reducing the friction between the particles.

- Example: Lubricants- Stearic acid, Stearic acid salt - Stearic acid, Magnesium stearate, Talc, PEG (Polyethylene glycols), Surfactants
- Glidants- Corn Starch – 5-10% conc., Talc-5% conc., Silica derivative - Colloidal silicas such as Cab-O-Sil, Syloid, Aerosil in 0.25-3% conc.

- **5. Coloring agent: The use of colors and dyes in a tablet has three purposes:**

- (1) Masking of off color drugs

- (2) Product Identification

- (3) Production of more elegant product

- All coloring agents must be approved and certified by FDA. Two forms of colors are used in tablet preparation – FD &C and D & C dyes. These dyes are applied as solution in the granulating agent or Lake form of these dyes. Lakes are dyes absorbed on hydrous oxide and employed as dry powder coloring.
- Example: FD & C yellow 6-sunset yellow,FD & C yellow 5-Tartrazine ,FD & C green 3- Fast Green,FD & C blue 1-Brilliant Blue ,FD & C blue 2 - Indigo carmine

6. Flavoring agents: For chewable tablet-flavor oil are used

7. Sweetening agents: For chewable tablets: Sugar, mannitol.

- Saccharine (artificial): 500 time's sweeter than sucrose
- Disadvantage: Bitter aftertaste and carcinogenic
- Aspartame (artificial)
- Disadvantage: Lack of stability in presence of moisture.

Lactose

- Non-reactive in anhydrous or hydrous form
- Hydrous form undergoes maillard reaction leading to browning and discoloration of certain drugs, hence anhydrous form is preferred
- But anhydrous form picks up moisture when exposed to humidity.
- In wet granulation, hydrous lactose of two varieties are used 60-80 mesh (coarse) and 80-100 mesh (regular) grade.
- Lactose formulation show good release.
- Low cost diluent
- But may discolor in presence of amine drug bases or salts of alkaline compounds

Spray dried lactose

- Lactose is placed in aqueous solution, removed impurities and spray dried
- Mixture of large alpha monohydrate crystals and spherical aggregates of smaller crystals
- Good flowability but less compressibility
- Poor dilution potential
- Less compressibility upon initial compaction
- Problem of browning due to contamination of 5-hydroxyfurfural which was accelerated in the presence of basic amine drugs and catalyzed by tartarate, citrate and acetate ions

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- Fast-Flow lactose (early 1970s)
 - Spherical aggregates of microcrystals lactose monohydrate
 - Held together by a higher concentration of glass (amorphous lactose)
 - Much more compressible
 - Highly fluid
 - Non hygroscopic
 - Tablets are three to four times harder than regular spray dried

- Tabletose: agglomerate form of lactose
 - More compressible than spray dried but less compressible than Fast Flo lactose

Starch

- Can be corn, wheat or potato source
- USP grade of starch has poor flow & compression characteristics
- Also has high moisture content between 11 & 14 %.
- Specially dried starches also have standard moisture level of 2-4%
- Therefore used in wet granulation

Dextrose

- 90-92% dextrose, 3-5% maltose and the remainder higher glucose polysaccharides
- Available both anhydrous and a hydrate product
- Excellent compressibility and good flow
- Contain 8-10% moisture and may increase hardness after compression
- Largest particle size, therefore blending problem may occur
- Cerelese is also available

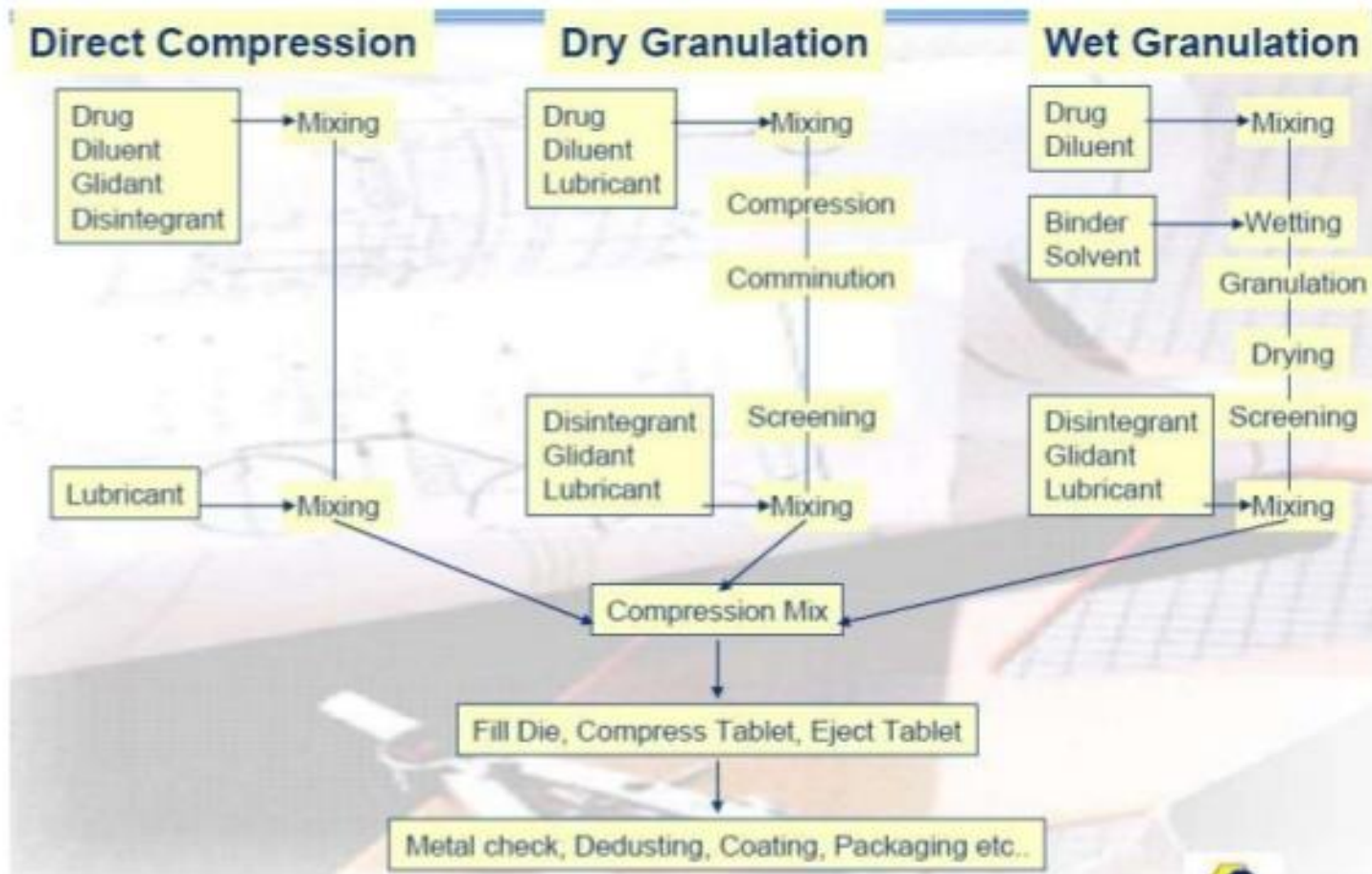
Cellulose

– Microcrystalline cellulose (Avicel)

Derived from a special grade of purified alpha wood cellulose by severe acid hydrolysis to remove the amorphous cellulose portions, yielding particles consisting of bundles of needlelike microcrystals

- PH101 powder and PH102 are the two grades available.
- most compressible with Highest dilution potential
- A strong compact formed due to strong hydrogen bonds ,and ruptured due to passage of water
- Extremely low coefficient of friction, no lubricant
- Not used as only filler because of its cost and density,
- used in the conc of 10-25% as a filler-binder-disintegrant,

Tableting methods



Powders intended for compression into tablets must possess two essential properties

❖ Powder fluidity or flowability

- The material can be transported through the hopper into the die
- To produce tablets of a consistent weight
- Powder flow can be improved mechanically by the use of vibrators, incorporate the glidant

❖ Powder compressibility

- The property of forming a stable, intact compact mass when pressure is applied is called powder compressibility

❖ Easily mixed with other particles

❖ Homogenous colouring etc

❖ Friction and adhesion properties

Dry compaction/Roller compaction

- On a large scale compression granulation can also be performed on a roller compactor.
- Granulation by dry compaction can also be achieved by passing powders between two rollers that compact the material at pressure of up to 10 tons per linear inch.
- Materials of very low density require roller compaction to achieve a bulk density sufficient to allow encapsulation or compression.
- One of the best examples of this process is the densification of aluminum hydroxide.
- Roller compactor is capable of producing as much as 500 kg/hr of compacted ribbon like materials which can be then screened and milled in to granules for compression.

Limitations of dry granulation

- 1- Dry granulation often produces a higher percentage of fines or non compacted products, which could compromise the quality or create yield problems for the tablet.
- 2- It requires drugs or excipients with cohesive properties.

Wet granulation

The most popular method (over 70%)

Granulation is done

- To prevent segregation of the constituents of the powder blend.
- To improve flowability of the powder mixture.
- To improve the compaction characteristics of the powder mixture due to better distribution of the binder within the granules.
- To improve homogeneity and thus ensure content uniformity

Wet granulation is a process of using a solution binder to the powder mixture. The amount of liquid can be properly managed; overwetting = the granules to be too hard, underwetting = too soft and friable.

Aqueous solutions are safer than other solvents.

Procedure of Wet Granulation

Step 1: Weighing and Blending

Step 2: wet granulate prepared by adding the binder solution

Step 3: Screening the damp mass into pellets or granules (6-8 mesh)

Step 4: Drying the granulation in thermostatically controlled ovens

Step 5: Dry screening:

Step 6: Mixing with other ingredients: A dry lubricant, antiadherent and glidant is added to the granules either by dusting over the spread-out granules or by blending with the granules. Dry binder, colorant or disintegrant may be also added in this step.

Step 7: Tableting: Last step in which the tablet is fed into the die cavity and then compressed.

Limitations of wet granulation:

- 1- Multiple separate steps are involved.
- 2- Not suitable for heat and moisture sensitive drugs

Equipments

Traditionally, dry mixing in wet granulation process has been carried out using,

- ✓ Sigma blade mixer,
- ✓ Heavy-duty planetary mixer.

List of equipments used in granulation

High Shear granulation:

- i) Little ford Lodgie granulator
- ii) Little ford MGT granulator
- iii) Diosna granulator
- iv) Gral mixer

Granulator with drying facility:

- i) Fluidized bed granulator
- ii) Day nauta mixer processor
- iii) Double cone or twin shell processor
- iv) Topo granulator

Special granulator:

- i) Roto granulator
- ii) Marumerizer

Compression

Tableting procedure

- Filling
- Compression
- Ejection

Tablet compression machines

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

- **Single punch machine**
- **Multi-station rotary presses**
- The head of the tablet machine that holds the upper punches, dies and lower punches in place rotates
- As the head rotates, the punches are guided up and down by fixed cam tracks, which control the sequence of filling, compression and ejection.
- The portions of the head that hold the upper and lower punches are called the upper and lower turrets
- The portion holding the dies is called the die table

Compression cycle

- Granules from hopper empty in the **feed frame (A)** containing several interconnected compartments.
- These compartments spread the granulation over a wide area to provide time for the **dies (B)** to fill.
- The **pull down cam (C)** guides the lower punches to the bottom, allowing the dies to overfill
- The punches then pass over a **weight-control cam (E)**, which reduces the fill in the dies to the desired amount
- A **swipe off blade (D)** at the end of the feed frame removes the excess granulation and directs it around the turret and back into the front of the feed frame
- The lower punches travel over the **lower compression roll (F)** while simultaneously the upper punches ride beneath the **upper compression roll (G)**

- The upper punches enter a fixed distance into the dies, while the lower punches are raised to squeeze and compact the granulation within the dies
- After the moment of compression, the upper punches are withdrawn as they follow the **upper punch raising cam (H)**
- The lower punches ride up the **cam (I)** which brings the tablets flush with or slightly above the surface of the dies
- The tablets strike a sweep off blade affixed to the front of the **feed frame (A)** and slide down a chute into a receptacle
- At the same time, the lower punches re-enter the **pull down cam (C)** and the cycle is repeated

- The principle modification from earlier equipment has been an increase in production rate which is regulated by
 - Number of tooling sets
 - Number of compression stations
 - Rotational speed of the press



High speed
rotary machine



Multirotary
machine

Processing problems

- **Capping** is the partial or complete separation of the top or bottom crowns of a tablet from the main body of the tablet.
- **Lamination** is separation of a tablet into two or more distinct layers. Both of these problems usually result from air entrapment during processing.
- **Picking** is removal of a tablet's surface material by a punch.
- **Sticking** is adhesion of tablet material to a die wall. These two problems result from excessive moisture or substances with low melting temperatures in the formulation

- **Mottling** is an unequal color distribution on a tablet, with light or dark areas standing on otherwise uniform surface. This results from use of a drug with a color different from that of the tablet excipients or from a drug with colored degradation products.
- Weight variation-granule size distribution, poor flow,punch variation
- Hardness variation
- Double impression-monograms or engraving on punch

