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Course Name	**: D. Pharm**
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Subject Name	**: Pharmaceutics**
Topic Name	**: Tablets**

Ch – 10

Tablets

. Tablets are solid unit dosage form containing medicament or medicaments usually circular flat or biconvex.

Advantages of tablet dosage form:

1. They are easy to carry.
2. They are easy to swallow.
3. They are attractive in appearance.
4. Unpleasant taste can be masked by sugar coating.
5. They do not require any measurement of dose. It provides a sealed covering which protects the tablets from atmospheric conditions like air, moisture and light etc.
6. Tablets provide prolonged stability to medicament. They have the best combined properties of chemical, mechanical and microbiological stability of all the oral dosage forms.
7. The incompatibilities of medicaments and their deterioration due to environmental factors are less in tablet forms.
8. Since they are generally produced on a large scale, therefore, their cost of production is relatively low, hence economical.

Disadvantages of tablet dosage forms:

- Some drugs resist compression into dense compacts, owing to their amorphous nature or flocculent, low-density character.
- Drugs with poor wetting, slow dissolution properties, intermediate to large dose, or any combination of these features may be difficult or impossible to formulate and manufacture as a tablet that will still provide adequate bioavailability.

Classification of tablets:

A. Tablets ingested orally:

a. Compressed tablet: **e.g.** Paracetamol tablet
b. Multiple compressed tablets:
c. Multi-layered tablets:
d. Sustained release tablets: **e.g.** Diclofenac (Voveran SR)
e. Enteric coated tablets: **e.g.** Aspirin Tablet
f. Sugar coated tablets: **e.g.** Multivitamin tablet
g. Film coated tablets: **e.g.** Metronidazole tablet
h. Chewable tablets: **e.g.** Antacid tablet

B. Tablet used in oral cavity:

a. Buccal tablets: **e.g.** Vitamin- C tablet
b. Sublingual tablets: **e.g.** Vicks Menthol tablet
c. Lozenge tablets and traches: **e.g.** Strepsils Orange with Vit C
d. Dental cones

C. Tablets administered by other routes:

1. Implantation tablets: **e.g.** Disulfiram Tablet
2. Vaginal tablets: **e.g.** Clotrimazole vaginal tablets

D. Tablets used to prepare solutions

1. Effervescence tablets: **e.g.** Dispirin tablet (Aspirin)
2. Dispensing tablets: **e.g.** Enzyme tablet
3. Hypodermic tablets: **e.g.** Morphine tablet
4. Tablet triturates: **e.g.** Enzyme tablet

Formulation of Tablet with API & Common Excipients:

1. **Diluents:** essential excipients for tablets to increase the weight or volume.
   E.g.: Dextrose, Lactose and Sucrose etc**.**
2. **Binders:** vital excipients for tablets to facilitate the agglomeration of powder into granules.
   E.g.: Starch Paste, Gelatin Solution etc.
3. **Disintegrants:** essential excipients for tablets to assist dosage form's breakup or disintegration into small units/fragments.
   E.g.: Starch, clays, celluloses, alginates, gums and cross-linked polymers.
4. **Lubricants:** vital excipients for tablets to reduce the frictional forces between particle-particle as well as particles and metal-contact surfaces.
   E.g.: Talc, magnesium stearate, calcium stearate, stearic acid, hydrogenated vegetable oils and polyethylene glycols (PEG).
5. **Glidant:** to promote the flow properties of tablet granules or power materials.
   E.g.: Corn Starch, Talc etc.
6. **Coloring agent:** to give a color or identification of the tablets as either pigment or coating materials.
   E.g.: FD&C (food, Drug & Cosmetic Dyes)
7. **Flavoring agent:** used only in some types of tablets such as chewable tablets or dispersible tablets or in coating suspension for bad smelled tablets. **E.g.:** Amlodipine + Olmesartan Medoxomil tablet.

8. **Sweetener or Sweetening agent:** especially used in the chewable, dispersible, sublingual tablet. E Sugar, Mannitol (72% as sweet as sugar, cooling & mouth filling effect), Saccharin, Cyclamate and Aspartame.
9. **Surfactant:** used for low solubility tablets to improve wetting and deaggregation of drug particles to get a rapid and improved dissolution.
10. **Release - Modifying Agents:** especially used to control drug release in modified-release formulations (prolonged-release or controlled-release tablet).
11. **Coating materials:**
    - Film former which may be enteric or non-enteric
    - Solvent
    - Plasticizer
    - Colorant
    - Opaquant-Extender
    - Miscellaneous coating solution components.

Techniques / Methods Used in Tablet Formulation

Tablets are commonly manufactured by

1. **Direct compression**
2. **Dry granulation**
3. **Wet granulation**

1. Direct Compression

1. Wet granulation and dry granulation methods having series of unit operations, both time consuming and potentially costly.
2. Potentially more attractive option for the manufacture of tablets involves powder mixing and subsequent compression of the powder mix, thereby obviating the need for granulation. This process is called direct compression.
3. The mechanism of particle-particle interactions in tablets produced by direct compression are similar to those operative in tablets produced by dry granulation and roller compaction.

2. Dry Granulation

- When tablet ingredients are sensitive to moisture and unable to withstand elevated temperature during drying and when the tablet ingredient have insufficient cohesive properties, slugging may be used to form granules.
- This technique is used in preparation of aspirin, aspirin combination, and acetophenetidin.

Excipients used in this method:

- **Diluents/ filler:** anhydrous lactose/ lactose monohydrate, starch, dibasic calcium phosphate, and MCC
- **Disintegrants:** Starch, MCC, Sodium starch glycolate, Croscarmellose sodium, Crospovidone.
- **Lubricants:** Stearates (Mg. stearate, steric acid), Glyceryl fatty acid esters, poly oxy ethylene stearates, SLS.
- **Glidants:** Talc, Colloidal silicon dioxide.
- **Miscellaneous Excipients:** Colours, sweetening agents, etc.

3. Wet Granulation:

- It is most commonly used method for the manufacturing of tablets.
- Water is frequently used as the granulation fluid (and heat is employed to dry the formed granules), it is important to ensure that the therapeutic agent is chemically stable during the granulation process.
- The wet granulation exhibit sufficient mechanical properties to be subsequently exposed to other unit operations, Eg: film coating.
- Tablet quality is directly affected by the choice and concentration of binder and the type and volume of granulation fluid. Due to the number of unit operations to the required, the manufacture of tablets by wet granulation is not as efficient as other methods. Eg: direct compression.

Tablets defects/ special problem in compressing tablet process

- Weight variation (granule size and size distribution)
- Capping and lamination
- Picking of tablets
- Chipping and splitting
- Sticking
- Embossing/print defect
- Layered tablet splitting
- Low hardness/ low mechanical strength
- Variable hardness
- Mottling
- Double impression
- Black spot/stain

Quality control of tablets

Tablets should be subjected to a number of tests before they are deemed fit for marketing and consumption. These tests can be divided into two broad categories namely

1. **Pharmacopoeial or official tests**
    1. Content of active ingredient/ absolute drug content test/ assay of active ingredient.
    2. Weight uniformity test/ weight variation test
    3. Content uniformity test
    4. Disintegration time test
    5. Dissolution test
2. **Non-pharmacopoeial or non-official tests**
    1. Crushing strength test/ hardness test
    2. Friability test.
    3. Tensile strength determination.

1. **Shape of tablets:** Circular with flat or convex faces.
2. **Appearance:** Uncoated tablet under lens either a relatively uniform texture or a stratified structure. No signs of coating.
3. **Content of active ingredient:** The amount of active ingredient in tablet is determined

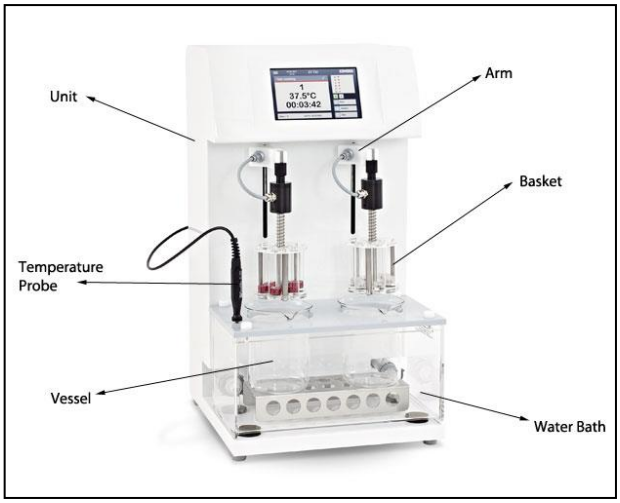
by doing the assay. Generally 20 tablets or such other number as may be indicated in the monograph are used in the assay. The result lies within the range for the content of active ingredient in the monograph. The stated limits are between 90 and 110%.

Weight of medicament in each tablet	Subtract from the lower limit for the sample of			Add to the upper limit for sample of		
	15	10	5	15	10	5
0.12 g or less	0.2	0.7	1.6	0.3	0.8	1.8
More than 0.12 g and less than 0.3 g	0.2	0.5	1.2	0.3	0.6	1.5
0.3 g or more	0.1	0.2	0.8	0.2	0.4	1.0

4. **Uniformity of weight:** Weigh 20 tablets selected at random and determine their average weight. Not more than 2 of the individual weights may deviate from the average weight by more than the percentage deviation given in the table and none should deviate by more than twice that percentage.

Sr. No	Average weight of a tablet deviation	Percentage
1	80 mg or less	10
2	More than 80 mg and less than 250 mg	7.5
3	250 mg or more	5

5. **Uniformity of content:** Percentage of medicament is calculated by doing assay for a particular drug. 20 tablets are taken, powdered and assayed. The average weight of medicament present in each tablet is calculated which is then compared with the desired weight. The pharmacopoeia has prescribed the limit in percentage of medicament per tablet in the monograph.
6. **Disintegration test:** Disintegration of a tablet means to break a tablet into smaller particles after swallowing. The time required to disintegrate the tablet is called disintegration time.



The apparatus consists of a rigid basket-rack assembly supporting 6 cylindrical glass tubes held vertically by two superimposed transparent plastic plates with six holes having the same diameter as the tubes. Woven wire gauze made from stainless steel is attached to the underside of the lower plate. The assembly should be raised and lowered between 28 and 32 times per minute in the liquid at 37^0C.

The tablets are kept immersed in the liquid within the tubes by means of cylindrical Guided discs. The assembly is suspended in the liquid medium in a 1000 ml beaker. The apparatus is operated generally for 15 minutes and observed for disintegration of tablets. The tablets pass the test if all the tablets disintegrate. In case one or two tablets fail to disintegrate, repeat the test on 12 additional tablets. The tablets pass the test if not less than 16 of the total 18 tablets tested have disintegrated.

7. Dissolution test: The test is done for measuring the amount of time required for a given percentage of drug substance in a tablet to go into solution under specified condition in vitro.

The apparatus consists a cylindrical covered vessel made of glass or other transparent material having 1000 ml capacity. The vessel is fitted with a lid having 4 holes, one for shaft of stirrer, second for placing thermometer and remaining two for removing the sample.

An electric motor which is capable of rotating the basket (woven wire cloth having aperture size 425 micrometer) in the vessel at varied speed between 25 and 150 revolutions per minute.

1000 ml of water at 37^0 C + 0.5 ^{o} C in placed and specified number of tablets are placed in the dry basket. The motor is started and the rotation speed is adjusted to 1000 rpm or as directed in the monograph. Withdraw the stated volume of solution from the vessel after 45 minutes or after the time specified in the monograph. Filter and determine the amount of active ingredient present in it. The tablets pass the test if for each of the five replicates; the amount of active ingredient in solution is not less than 70% of the stated amount

Diagram:

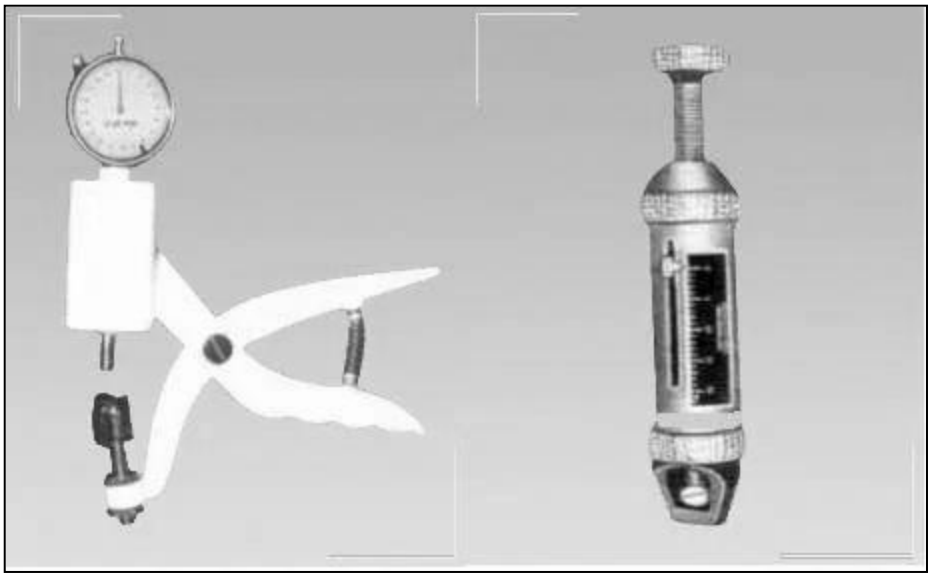
Dissolution Test Apparatus

8. Hardness test: Manufacturers have set their own limit for the hardness. Monsanto hardness tester or Pfizer tablet hardness tester are the devices used for finding the mechanical strength of tablets.

Monsanto hardness tester has a graduated scale which gives the reading in kg/sq. cm. The tablet to be tested is placed between the spindle and anvil. The pressure is applied till the tablet breaks.

Pfizer tablet hardness tester is based on the principle of an ordinary plier. The tablet is placed between the jaw of the plier and the pressure is applied by pressing the handles with hand until the tablet breaks.

Diagram:



9. Friability test: This test is performed to evaluate ability of the tablet to with stand wear and tear in packing, handling, and transporting. The apparatus used to perform this test is known as "Friabilator".

The apparatus consists of a plastic chamber, which is divided into two parts and it revolves at a speed of 25 rpm. Twenty tablets are weighed and placed in a plastic chamber. The chamber is rotated for 4 minutes or 100 revolutions. During each revolution the tablet falls from a distance of 6 inch. The tablets are removed from the chamber after 100 revolutions and weighed. Loss in weight indicates the friability. The tablets are considered to be of good quality if the loss in weight is less than1%.

Diagram: