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# IMMEDIATE RELEASE TABLETS: AN OVERVIEW

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## ABSTRACT

The aim behind any drug delivery system is to achieve a safe and effective therapy. Solid oral dosage form is the most popular and most preferred dosage form when compared to all other dosage forms in which tablets are one of the most frequently used oral dosage form. Immediate release tablets are also conventional type of drug delivery system which are designed to disintegrate and release their medicaments immediately after administration. Immediate release is achieved by the use of superdisintegrants like sodium starch glycolate, croscarmellose sodium, Poly Vinyl Pyrrolidone (PVP), etc. This article provides a deep knowledge about formulation of immediate release tablets, toolings, evaluation parameters, and stability studies.

**KEYWORDS:** Immediate release tablets, superdisintegrants, disintegration test.

## INTRODUCTION

Dosage forms are pharmaceutical drug products in the form in which they are marketed for use, with a specific mixture of active ingredients and inactive components in a particular configuration.

Licensed drugs are available in a wide variety of formulations including liquids for oral administration, injectable solutions, ointments or gels, transdermal patches, tablets, capsules, suppositories, and inhaled aerosols. The selection of a particular dosage form and route of administration depends on both the clinical circumstances, and the characteristics of the drug. The basic aim behind development of any drug delivery system (DDS) is to achieve a safe and effective therapy for the human beings. For decades together, oral drug delivery system plays a major role in the global pharmaceutical market. It is growing day by day because of being a convenient route for drug administration.[1]

Tablets are one of the most frequently used dosage forms, and they are typically made by a commercial process involving compression of a drug-containing mixture of materials in a high-throughput tableting machine.[2]

A large number of developments in the field of pharmaceutical technology have made manufacturing of tablet a science. In recent days tablets have become the most acceptable dosage forms as compared to other available dosage forms. The popularity of this dosage form is because of advantages such as ease of manufacturing, convenience in administration, high accuracy in dose, stability and safety. [3] Many patients require quick onset of action in a particular therapeutic conditions like headache, fever, anorexia, cardiovascular diseases, etc. and hence immediate release is required. A high incidence of ineffective therapy is estimated in 50% of the population due to delayed release. Tablets are solid dosage forms usually prepared with the aid of suitable pharmaceutical excipients. Tablets may vary in size, shape, weight, hardness, thickness, disintegration, and dissolution characteristics and in other aspects, depending on their intended use and method of manufacture. Tablets are mostly used in the oral administration of drugs. Many of these tablets are prepared with colorants and coatings of various types. Other tablets, such as those administered through sublingual, buccal, or vaginal route, are prepared to have features most applicable to their particular route of administration.

Tablets are prepared primarily by compression, with a limited number prepared by molding. Compressed tablets are manufactured with tablet machines capable of exerting great pressure in compacting the powdered or granulated material. Their shape and dimensions are determined by the use of various shaped punches and dies. Molded tablets are prepared on a large scale by tablet machinery or on a small scale by manually forcing dampened powder material into a mold, from which the formed tablet is then ejected and allowed to dry.

**Types of tablets (General Classification)**[4]

1. Compressed Tablets
2. Multiply Compressed Tablets
3. Sugarcoated tablets
4. Film-coated tablets
5. Gelatin-coated tablets
6. Enteric-coated tablets
7. Buccal and sublingual tablets
8. Chewable tablets
9. Effervescent tablets
10. Molded tablets
11. Tablet triturates
12. Hypodermic tablets
13. Dispensing tablets
14. **Immediate-release tablets**
15. Instantly disintegrating or dissolving tablets
16. Extended-release tablets
17. Vaginal tablets

**Types of tablets (Based on route of administration)**[5]

**1. Oral Tablets for Ingestion**

a) Compressed tablets
b) Multiple compressed tablets
- Layered tablets
- Compression-coated tablets

c) Repeat-action tablets
d) Delayed-action and enteric coated tablets
e) Sugar- and chocolate-coated tablets
f) Film-coated tablets
g) Chewable tablets

**2. Tablets used in the Oral Cavity**

a) Buccal tablets
b) Sublingual tablets
c) Troches and lozenges
d) Dental cones

**3. Tablets administered by other routes**

a) Implantation tablets
b) Vaginal tablets

**4. Tablets used to prepare Solutions**

a) Effervescent tablets
b) Dispensing tablets
c) Hypodermic tablets
d) Tablet triturates

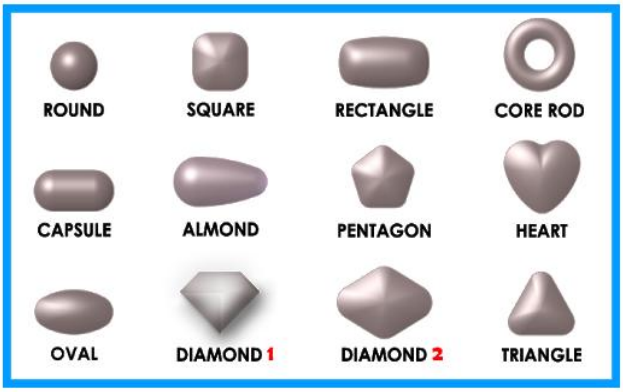


**Fig.1: Different Shapes of Tablets.**[6]

**Fig. 2:Compressed tablets**

**Fig. 3: Sugar coated tablets**

**Fig. 4: Multiple compressed tablet**

**Fig. 5: Film coated tablets**

**Fig. 6: Vaginal tablets**

**Fig. 7: Chewable tablets**

**Immediate Release Drug Delivery System.**[4]

Immediate release drug delivery system is also one of the conventional type of drug delivery systems. Immediate release tablets are designed to disintegrate and release their medicaments with no special rate controlling features such as special coatings and other techniques.

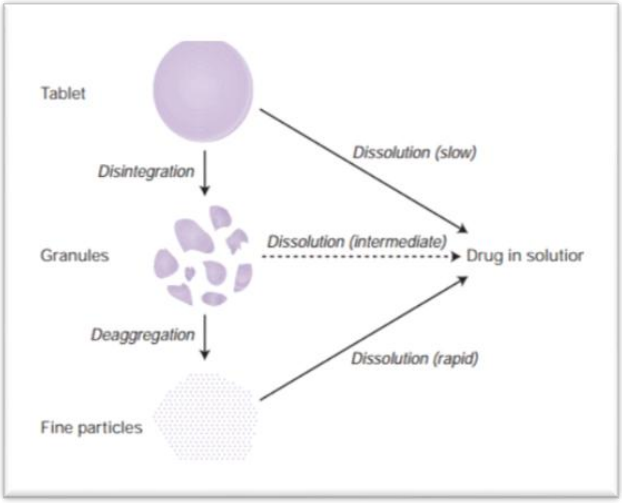


**Fig. 8: Processes involved in dissolution of a drug from a Tablet**[7]

**Ideal property of an immediate release dosage form:**
It should undergo fast disintegration, dissolution, absorption in the stomach and produce a rapid onset of action.

**Advantages**[5]
1. Enables an accurate dose of medicament.
2. Easy to transport in bulk.
3. Low manufacturing cost when compared to all other solid oral dosage forms.
4. More stable.

**Disadvantages**[5]
1. Some drugs resist compression into dense compacts, owing to their amorphous nature or flocculent, low-density character.
2. Drugs having poor wettability, slow dissolution properties may be difficult or impossible to manufacture as tablet.
3. Drugs with objectionable odor, bitter taste and sensitive to oxygen may require encapsulation prior to compression.

**Excipients used in the formulation of immediate release tablets**[5]
Excipients are inert substances used in the formulation of a drug. In the pharmaceutical industry, it is a catch-all term which includes various sub-groups comprising diluents or fillers, binders or adhesives, disintegrants, lubricants, glidants, flavours, colourants and sweeteners.

**Ideal properties of Excipients**
- Physiologically inert and chemically stable.
- Acceptable to regulatory agencies.
- Free from microbial contamination.
- Should be compatible with the API and other excipients.
- Must be commercially available in the pure form according to current Pharmacopoeial standards and economical.

**Table 1: List of excipients and functions.**[5,8]

| Excipients | Functions | Examples |
|---|---|---|
| Diluents | Diluents are used to create desired bulk, flow properties, and compression characteristics of tablets. | Dibasic calcium phosphate, Lactose, Microcrystalline cellulose, Starch, Precipitated calcium carbonate, Sorbitol, etc. |
| Binders | Binders are used either in dry or in wet form to produce adhesion of powder particles in tablet granulation. | Acacia, Alginic acid, Sodium carboxy methyl cellulose, Ethylcellulose, Povidone, Pregelatinized starch. |
| Disintegrants | They are added to facilitate a breakup or disintegration of the tablet when it comes in contact with fluids in gastrointestinal tract. | Starch, Starch derivatives, Clays, Cellulose, Cellulose derivatives, Alginates, PVP, Cross-linked PVP, etc. |
| Flavours | These are added to improve the flavour of the product. | Peppermint, Vanilla, Orange, Banana, Cinnamon and Mango. |
| Colourants | The colors and dyes are added to disguise of off-color drugs, and production of a more elegant product identification. | FD & C and D & C dyes<br>**Natural Colorants:**<br>Amaranth - Reddish brown<br>β-carotene – Pale yellow to dark orange<br>Caramel – Dark brown<br>Ponceau – Red<br><br>**Synthetic colorants:** |

| | | |
|---|---|---|
| | | Indigocarmine (FD&C blue #2) – Dark blue<br>Sunset Yellow FCF (FD & C yellow #6) – Reddish yellow<br>Tartrazine (FD&C yellow #5 - Light orange)<br>Quinoline Yellow SS(FD&C Yellow #11) – Bright yellow with green shade<br>Quinizarine Green SS (D&C Green #6) - Green |
| Sweeteners | They are added to impart a palatable taste to the product. | Sucrose, Dextrose, Mannitol, Sucralose, Saccharin sodium, Aspartame, etc. |
| Lubricants | They are intended to reduce the friction during tablet ejection between the walls of the tablet and the wall of the die cavity in which the tablet is formed. | Stearic acid, its salts and its derivatives, Talc, Polyethylene glycols, Surfactants and Waxes. |
| Glidants | They are intended to promote flow of the granules or powder materials by reducing friction between the particles. | Colloidal Silicon dioxide (Aerosil), Corn starch, Talc, etc. |
| Antiadherents | It prevents tablet ingredients from sticking to punches and dies during production. | Magnesium stearate, Talc |

## Manufacturing methods[4]

Immediate release tablets can be made by three methods.

1. Wet granulation
2. Dry Granulation and
3. Direct Compression

### Wet granulation

In wet granulation**,** granules are formed by binding the powders together by an adhesion, instead of compaction using a solution, suspension, slurry containing a binder**.** Binder is incorporated in dry or wet form into the powder mixture using Sigma blade and planetary mixers**.**

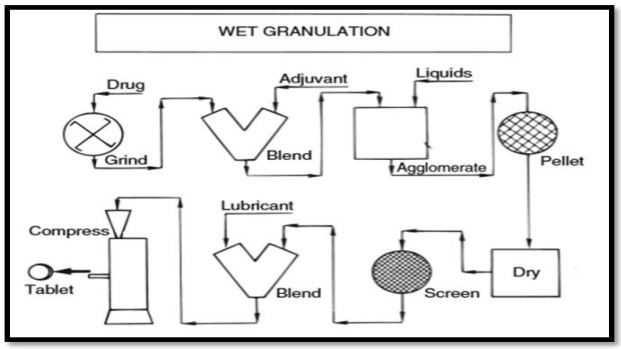


**Fig. 9: Process involved in Manufacturing of tablet by Wet granulation.**

### Dry granulation

This is a valuable technique in situations where the effective dose of a drug is sensitive to heat, moisture, or both, which precludes wet granulation. Drugs like aspirin and vitamins are prepared by dry granulation. It involves the compaction of the components of a tablet using a tablet press or specially designed machinery called roller compactor**.**

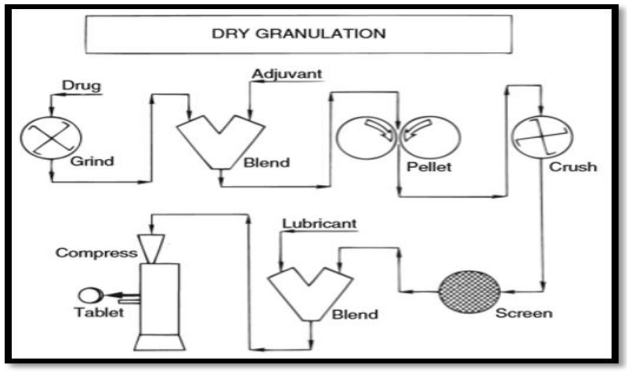


**Fig.10: Process involved in manufacturing of tablet by dry granulation.**

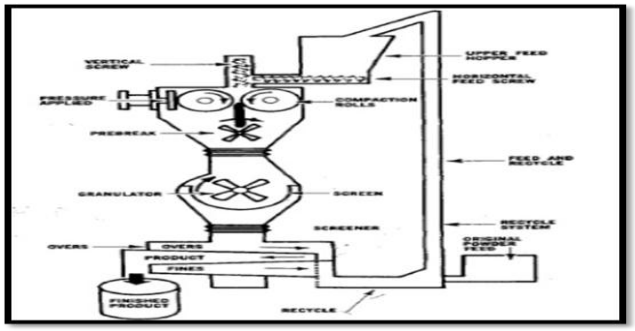

**Fig. 11: Chilsonator roller compactor.**

### Direct Compression

In direct compression, crystalline materials, in addition to possessing good flow and compressibility, must be pharmaceutically inert, tasteless, reworkable, able to disintegrate, and inexpensive. The procedures used in direct compression are basically screening or milling and mixing followed by compaction. Some examples of drugs that may be compressed directly are Aspirin, Allopurinol, Diazepam, Diclofenac sodium, etc.

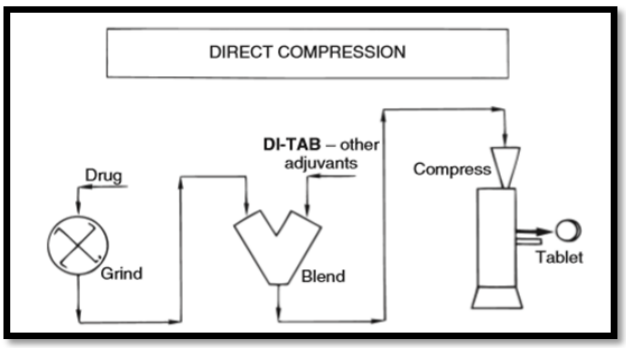


**Fig. 12: Process involved in manufacturing of tablet by direct compression.**

**Compression**[5]

Tablets are made by compressing a formulation containing a drug or drugs with excipients on stamping machines called presses. All rotary presses are engineered for fast and economical production of all kinds of tablets. Larger machines can readily produce several millions of tablets per day. Precompression stations are also available to help amorphous, flocculent, and low-density drugs to make the compression easy.

**Tablet tooling**[9]

The following types of Tooling are used in tablet compression.

'B' -Tooling
'D' - Tooling
'BB'-Tooling
'DB' – Tooling

**Tablet Tooling Parts** (Punches and dies)

**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**: 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**: The area guides the punch (while going up and down) with reference to turret guides.

**7. Stem:** The area of the punch opposite to the head, beginning at the tip and extending to the point where the full diameter of the barrel begins. If the chamfer is present, the barrel usually reaches its full diameter just above the chamfer.

**8. Tip:** Determines size, shape & profile of the tablet.

**9. Tip face**: The area of punch where the tablet is formed. Good surface finish is required to get quality tablets.

**10. Overall length**: Distance between top of the cup and the head flat.

**11. Working length**: The distance between bottom of the cup and the head flat.

**12. Key Angle**: The relationship between the punch key and the tablet shape. The keys position is influenced by the tablet shape, take-off angle, and turret rotation.

**13**. **Domed Heads:** Increases the dwell time and hence help to achieve the better tablet hardness.

**14. Dwell time:** The time punches spends below the pressure roller while rotating in the machine.

**Types of Punches**

- Flat- faced bevel- edged.
- Shallow concave (Round/ Capsule shaped)
- Standard concave (Round/ Capsule shaped)
- Deep concave (Round/ Capsule shaped)
- Extra deep.
- Modified ball

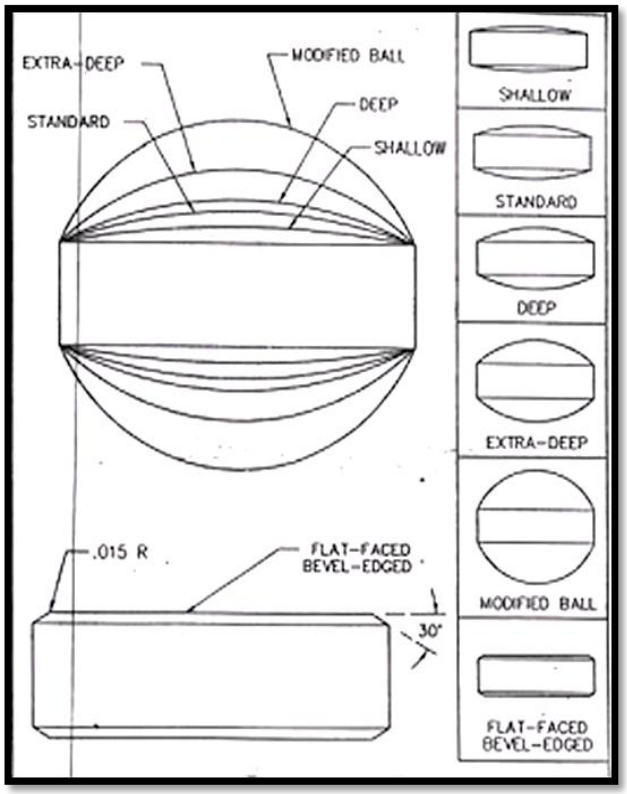


**Fig. 13: Types of punches.**

**Table 2: List of immediate release tablets.[4]**

| Name of the drug | Trade name | Strength | Category |
|---|---|---|---|
| Acetaminophen | Tylenol | 325, 500 mg | Analgesics and antipyretic agent. |
| Acyclovir | Zovirax | 400, 800 mg | Antiviral agent |
| Allopurinol | Zyloprim | 100, 300 mg | Antigout and antiurolithic agent |
| Amitriptyline HCl | Elavil HCl | 10, 25, 50, 75, 100, 150 mg | Antidepressant agent |
| Carbamazepine | Tegretol | 200 mg | Anticonvulsant agent |
| Chlorambucil | Leukeran | 2 mg | Antineoplastic agent |
| Cimetidine | Tagamet | 200,300,400,800 mg | $H_2$ receptor antagonist |
| Ciprofloxacin | Cipro | 100, 250, 500, 750 mg | Antibacterial agent |
| Diazepam | Valium | 2, 5, 10 mg | Sedative, skeletal muscle relaxant |
| Digoxin | Lanoxin | 0.125, 0.25 mg | Cardiotonic agent |
| Enalapril | Vasotec | 2.5, 5, 10, 20 mg | Antihypertensive agent |
| Furosemide | Lasix | 20, 40, 80 mg | Diuretics and antihypertensive agent |
| Griseofulvin | Fulvicin | 250, 500 mg | Antifungal agent |
| Haloperidol | Haldol | 0.5, 1, 2, 5, 10, 20 mg | Tranquilizing agent |
| Ibuprofen | Motrin | 400, 600, 800 mg | Analgesics and antipyretic agent |
| Levothyroxine sodium | Synthroid | 0.025, 0.05, 0.075, 0.1, 0.125, 0.15, 0.2, 0.3 mg | Thyroid hormone |
| Loratadine | Claritin | 10 mg | Antihistamines |
| Nitroglycerine | Nitrostat | 0.3, 0.4, 0.6 mg | Antianginal agent |
| Penicillin V | Pen Vee K | 250, 500 mg | Anti-infective agent |
| Warfarin sodium | Coumadin | 1, 2, 2.5, 4, 5, 6, 7.5, 10 mg | Anticoagulating agent |

**Evaluation of tablets**

To design tablets and monitor tablet quality, quantitative evaluations like precompression and post compression parameters must be assessed.

**Pre compression parameters**[10,11,12]

1. Bulk density
2. Tapped density
3. Compressibility Index
4. Hausner's ratio
5. Angle of repose

**Bulk Density**

Accurately weighed 50 gm of blend, previously passed through #20 sieve is transferred into 100 ml graduated cylinder. Carefully the powder is levelled without compacting, and the unsettled apparent volume is measured.

**Bulk density (g/ml) = Weight of the powder (g)/Bulk volume of powder (ml)**

**Tapped Density (TD)**

Accurately weighed 50 gm of the blend is transferred into 100 ml graduated cylinder and initial volume is observed. The cylinder is tapped initially 500 times from a distance of 14±2 mm and the tapped volume is measured to the nearest graduated units using tap density apparatus. The tapping is repeated for additional 750 times and the tap volume is measured to the nearest graduated unit. The tapped bulk density in gm/ml is calculated by using the following formula.

**Tapped density (g/ml) = Weight of the powder taken(g)/Tapped Volume(ml)**

**Fig. 14: Tap Density Apparatus.**

**Compressibility Index**

The propensity of the powder to be compressed is measured by compressibility index and it also helps in measurement of settling property and inter particulate interactions.

$$\text{Compressibility Index (\%)} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

**Hausner's Ratio**

The Hausner's ratio is a number that is correlated to the flow property of a powder or granular material.

**Hausner's ratio = Tapped density/Bulk density**

**Angle of repose**

The angle of repose is determined by cylinder/funnel method. Accurately weighed powder blend is allowed to flow freely through cylinder/funnel onto the plain surface to form a cone from a certain height. The diameter of the cone is measured and angle of repose is calculated using the following equation.

**Angle of repose (θ) = $\tan^{-1}$ (h/r)**
Where, h = height of the cone
r = radius of the cone

**Fig. 15: Flowability tester.**

**Table 3: Flowability according to Angle of repose, Hausner's ratio and Compressibility Index.**

| Flow character | Angle of repose ( °) | Hausner's ratio | Compressibility Index(%) |
|---|---|---|---|
| Excellent | 25-30 | 1.00 – 1.11 | ≤10 |
| Good | 31-35 | 1.12 – 1.18 | 11 – 15 |
| Fair | 36-40 | 1.19 – 1.25 | 16 – 20 |
| Passable | 41-45 | 1.26 – 1.34 | 21 – 25 |
| Poor | 46-55 | 1.35 – 1.45 | 26 – 31 |
| Very poor | 56-65 | 1.46 – 1.59 | 32 – 37 |
| Very, very poor | >66 | >1.60 | ≥38 |

**Evaluation of immediate release tablets[5]**

**a) Physical appearance**

The tablets are visually inspected for smoothness, absence of cracks, chips, and other undesirable characteristics. If they are coloured, it includes examination for mottling and other evidence of non-uniform colour distribution.

**b) Weight variation test**

Weight variation test is carried out in order to ensure uniformity in the weight of tablets in a batch. Individual weights of 20 tablets are taken randomly from whole batch. Individual weight is then compared with the average weight for the weight variations.

**Table 4: Limits for weight variation test.**

| Average weight of tablet (mg) | | % Difference |
|---|---|---|
| IP/BP | USP | |
| 80 mg or less | 130 mg or less | ± 10% |
| More than 80 mg or less than 250 mg | 130 mg to 324 mg | ± 7.5% |
| 250 mg or more | More than 324 mg | ± 5% |

**c) Tablet Thickness**

The thickness of a tablet is decided by the diameter of the die, the amount of fill permitted to enter the die, the compaction characteristics of the fill material, and the force or pressure applied during compression. Tablet thickness is measured by Digital Vernier Caliper.


**Fig. 16: Vernier caliper.**

**d) Tablet Hardness**

Hardness is the measurement of the force required to break the tablet across its diameter using a hardness tester. 10 tablets are randomly selected from a complete batch and hardness is determined by using different hardness testers likeMonsanto, Pfizer, Schleuniger and Erweka hardness tester. A force of about 4 kg/cm$^2$ is considered as the minimum requirement for a satisfactory tablet. It is expressed in N or kg/cm$^2$.

**Fig. 17: Digital hardness tester.**

**e) Friability**

Friablity is tested using Roche Friabilator in which the tablets are subjected to the combined effect of abrasion and shock. The tablets are carefully de-dusted and weighed prior to testing. The tablet are placed in the drum revolving at 25 rpm and dropping the tablets at a height of 6 inches in each revolution. The test is done for 4 minutes that is for 100 revolutions. The tablets are dusted and weighed accurately. The tablets that loose less than 0.5 to 1.0 % of weight are considered to be compliant.

$$\% \text{ Friability} = \frac{\text{Initial weight - Final weight}}{\text{Initial weight}} \times 100$$

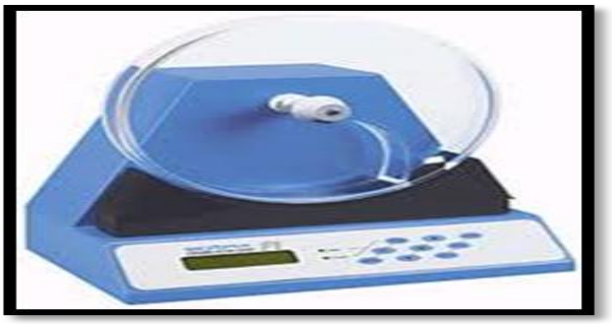

**Fig. 18: Roche friabilator.**

**f) Disintegration test**

Disintegration test is performed by using USP disintegration apparatus. The apparatus consists of a basket-rack assembly, a 1000-mL beaker, a thermostatic arrangement for heating the fluid to 35–39° C, and a device for raising and lowering the basket in the immersion fluid at a constant frequency rate of 28 –32 cycles/min. The basket-rack assembly consists of 6 open-ended transparent tubes, attached with 10 mesh screen at the bottom.

One tablet is placed in each tube (six) of the basket. Water/simulated gastric fluid is used as medium at 37±2ºC. The apparatus is operated until each of the tablet disintegrates and all particles pass through #10 mesh in the specified time (Not more than 15 mins for immediate release tablets). The tablet should disintegrate within 15 minutes or as specified in the individual monograph.

**Fig. 19: Disintegration test apparatus.**

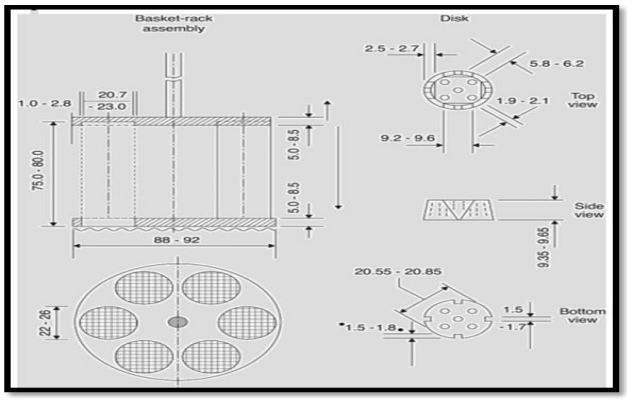


**Fig. 20: Disintegration test apparatus (all dimensions are mentioned in mm).**

**g) Dissolution test**

The dissolution test is carried out by using USP Type II apparatus (Paddle Type). In this test, 900/1000 ml volume of the dissolution medium is placed in the vessel and maintained at a temperature of 37± 0.5ºC, the paddle is rotated at 75 rpm and at regular intervals of time(as stated in the monograph) samples are withdrawn and analyzed for drug release.

**Fig. 21: Dissolution test Apparatus.**

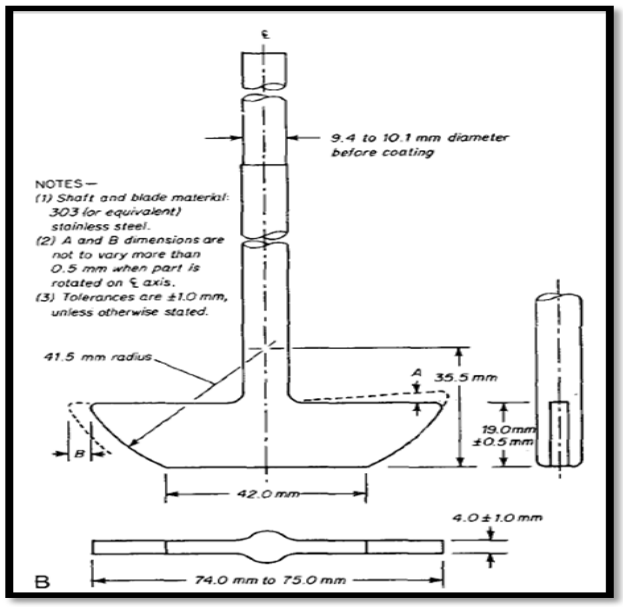


**Fig. 22: USP dissolution apparatus (Paddle type).**

**Stability studies**[13]

The purpose of stability testing is to provide evidence on which the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity, and light. Stability testing permits the establishment of recommended storage conditions, retest periods, and shelf lives.

**Table 5: Testing Conditions (ICH guidelines).**

| Study | Conditions | Minimum time period |
|---|---|---|
| Long-term testing | 25± 2°C/60±5% RH or 30± 2°C/65±5% RH or 30± 2°C/75±5% RH | 12 months or 6 months |
| Intermediate testing | 30± 2°C/65±5% RH | 6 months |
| Accelerated testing | 40± 2°C/75±5% RH | 6 Months |

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