A Comprehensive Review on Tablet Processing and Evaluation

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ABSTRACT
Tablets are the pharmaceutical oral solid dosage forms, widely used to produce systemic effect from many years, because of it's convenient administration to patients. Tablet is defined as unit solid dosage form meant for internal use, containing active ingredients with suitable excipients. It offers enormous advantages like economical, easy to prepare or manufacture, inertness with other ingredients and convenience during packaging, transportation and dispensing. Based on the formulation design, several techniques are involved to produce the product such as direct compression, granulation etc. which makes the desired preparation as per criteria. To ensure the quality of the product, evaluation parameter must be followed to give the required limits for the batch, which protects the effectiveness of the product, follows right release pattern of drug at right place at right time. In this review, the study involves the suitable techniques with its unit operation steps for the manufacturing of tablets followed by its pre-compression study and post-compression study with its limits or criteria specified as per Indian Pharmacopoeia (IP).

Keyword: Tablet, Tablet processing, Tablet evaluation

INTRODUCTION
About 90% of the drugs/medicines are administered through oral route to produce pharmacological effects as it is one of the easiest techniques of drug administration to obtain systemic effects [1, 2]. According to the IP, tablets are solid, flat or biconvex unit dosage containing medicament alone or medicament along with excipients prepared by compressing technique. Depending on the active pharmaceutical ingredients and excipients, weight of the tablet may get varied with its shape and size. Nevertheless, 70% of the medicaments are dispensed in tablet forms due to its variety of advantages like its simplicity, economy of manufacture, relative stability, easy in packaging, shipping, storage etc. through which they are considered as widely used conventional dosage forms.
There are some limitations like medicaments with low density, hygroscopicity, flow properties etc., due to which the medicaments are not able to manufactured [3]. In spite of that, there are some evaluation parameters which plays a major role for any dosage form to make its market [4-7].

**Advantages**

- They are the unit dosage forms containing medicament.
- Dose precision
- Less content variability
- Easy to administration to patients.
- Economical as compared with other dosages form.
- Easy to transport.
- Modified release of a drug can be achieved.
- Medicaments with bitter taste can be negotiated by coating.
- High stability with other dosage forms [8].

**Disadvantages**

- In case of paediatrics, administration of drugs is difficult.
- Drugs with low dissolution profile is not appropriate to give good bioavailability.
- Medicaments with low density, poor flow properties and amorphous in nature are difficult to compress.
- Hygroscopicity leads to degradation of tablet [8].

Tablet manufacturing involves various unit operation steps as in figure 1: [9, 10]

![Figure 1: Pharmaceutical tablets](image)

![Figure1: Various unit operation steps in tablet manufacturing.](image)
Types of tablet processing technologies: Direct Compression, Dry Granulation and Wet Granulation [11, 12].

1. **Directly compressed tablets:** It involves compressing of powdered materials directly without changing the physical nature into tablet forms. The method applicable for powdered material having crystalline structure, good compressibility and flow properties etc. Directly compressed tablets are manufactured by compression technique using tablet punching machine. Direct compression method is an innovative choice for tablet punching because it provides the efficient way to produce tablets in a shortest time period and has less complexity shown in figure 2 [11, 12].

**Advantages**
- No need to form granules.
- Easy to process.
- Less processing steps are required as compared to other techniques.
- Ingredients which are liable to degrade in presence of water and heat can be processed by this method.
- Low labour cost [6, 11]

**Disadvantages**
- Poor content uniformity might lead to difference in particle size and bulk density which may cause capping and lamination.
- A large dose drug may cause difficulty to process.
- Interaction may occur between the API and ingredients like diluents.
- Variation in unit dose and have low mechanical strength.
- Adhesion/sticking of powder may occur due to presence of moisture between material and punch surface.
- High friction and compression are required during tablet ejection and punching respectively [6, 10].

Properties of a powder which must be in limits which are following -
- Homogeneity, Flowability and segregation tendency
- Compression properties.
- Friction, compatibility and adhesion properties [4].

2. **Granulation:** Granulation, a method of unit operation, to enlarge the particles by agglomeration phenomenon, which is one of the convenience method to produce a pharmaceutical dosage forms such as tablets [6, 13].

Granulation process involves formation of large particles from the small fine or coarse particles called as granules. Generally, granulation is done after drying of powder mass with the active ingredient (API), through which a smooth homogenization of each ingredient can be easily achieved [6, 13].

Granulation narrow down the segregation problems leads to ensures superior compressibility in the compacting process, allows to use high amount of API in the tablet [6, 13].

However, granulation process take lot of time as compared with direct compression including risk of product loss and contamination during the different unit operation steps such as drying, sieving, mixing etc. leads to increase cost of dosage form as compared with direct compression [4, 6, 13, 14].

**TYPES OF GRANULATION TECHNIQUE**

(a) **Dry granulation:** It is defined as the process of granules formation by slugging means preparation of granules without using any liquid solution [1]. This method adopted when a product is heat & moisture sensitive [15, 16]. The processing steps involved in dry granulation are shown in figure 2.
(b) **Wet granulation**: In wet granulation, ingredients such as API, diluents, disintegrants etc. are blended well together in a V-Blender, at high speed for mixing of solid substances. In this method, the powder mixer is adhered by suitable binder which leads to “adhesion”. The binder is added slowly by diluting it with suitable solvent before the addition to form wet granules to the mixed mass of powder which can be turn in dried granules by expelling the solvent in the presence of heat. After drying, the particle size of granules is reduced by passing through the small mesh screen. Then, to promote flow behaviour of granules, lubricant and glidant are added as fine powder and then processed for the compression to obtain tablets as in figure 2 [16, 17].

![Diagram of tablet manufacturing process]

Figure 2: The processing steps involved in tablet manufacturing.

**EVALUATION PARAMETERS OF TABLETS**

1. **Pre-Compression Study**

   a) **Angle of Repose (AR)**: AR is the maximum possible angle in-between the surface of a pile of powder/granules and the horizontal plane. AR can be used to compute the interparticle force/friction force in a bulk powder/granules by:

   \[
   \tan \theta = \frac{h}{r} \quad \text{or} \quad \theta = \tan^{-1}\left(\frac{h}{r}\right)
   \]

   Where, \( \theta \) is the angle of repose, \( h \) is the height, and \( r \) is the radius.

   **Method** - Fixed funnel method - In this method pouring of powder through funnel is stopped when the pile reaches a predetermined height and width, then the flow ability of the powder or granules was calculated by above formula [6, 18].

   ![Diagram of angle of repose determination]

   Figure 3: Determination of melting point.
b) **Bulk Density**: Defined as the mass of a powder to the bulk volume. It can measure by bulk density apparatus as shown in Figure 4. The bulk density of a powder or granules can be depending on particle size distribution, shape of the particles and the adhesion between the particles of powder and granules.

**Method** - A quantity of accurately weighed powder (M) was introduced into a 100ml measuring cylinder and the volume occupied by the bulk (Vt) can be marked. Then, the bulk density is calculated using below formula [6, 18, 19]:

\[
\text{Bulk Density (BD)} = \frac{\text{Weight of the Powder (M)}}{\text{Volume of Powder or granules occupied (Vt)}}
\]

![Digital bulk density apparatus](image)

Figure 4: Digital bulk density apparatus

c) **Tapped density**: It is a measure used to describe void space of powder obtained after tapping the bulk quantity of powder in a measuring cylinder.

**Method** - The pre-weighed powder was filled in measuring cylinder. Then it was tapped in bulk density test apparatus. After 100 taps the volume was measured [6, 20].

\[
\text{Tapped Density} = \frac{\text{Weight of the Powder (M)}}{\text{Tapped Volume of Packing (Vt)}}
\]

d) **Hausner’s ratio**: It is the ratio of bulk volume to tapped volume or tapped density to bulk density. It is a measure of compressibility of powder. Tapped density and bulk density of powder material were used to measure Hausner’s Ratio. [6, 20]:

\[
\text{Hausner’s ratio} = \frac{\text{Tapped density (t)}}{\text{Bulk density (d)}}
\]

Where, t is the tapped density and d is bulk density.

e) **Carr’s Index or Percentage Compressibility**: Compressibility is indirectly related to the relative flow rate, cohesiveness and particle size distribution of the powder. Tapped density and bulk density of powder material was used to measure compressibility of a powder material [6, 20].

\[
\text{Carr’s Index (\%)} = \left(\frac{\text{Tapped Bulk Density (TBD) - Loose Bulk Density (LBD)}}{\text{Tapped Bulk Density (TBD)}}\right) \times 100
\]

Where, LBD = Loose Bulk Density

TBD = Tapped Bulk Density
Table 1: Flow Character of Angle of Repose, Carr’s Index (%) & Hausner’s Ratio [6, 18, 20]

<table>
<thead>
<tr>
<th>Flow character</th>
<th>Excellent</th>
<th>Good</th>
<th>Fair</th>
<th>Passable</th>
<th>Poor</th>
<th>Very poor</th>
<th>Poorest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compressibility Index (%)</td>
<td>1 to 10</td>
<td>11 to 15</td>
<td>16 to 20</td>
<td>21 to 25</td>
<td>26 to 31</td>
<td>32 to 37</td>
<td>&gt; 37</td>
</tr>
<tr>
<td>Hausner’s Ratio</td>
<td>1 to 1.11</td>
<td>1.12 to 1.18</td>
<td>1.19 to 1.25</td>
<td>1.26 to 1.34</td>
<td>1.35 to 1.45</td>
<td>1.46 to 1.59</td>
<td>&gt; 1.60</td>
</tr>
<tr>
<td>Angle of Repose (θ)</td>
<td>25 to 30</td>
<td>31 to 35</td>
<td>36 to 40</td>
<td>41 to 45</td>
<td>46 to 55</td>
<td>56 to 65</td>
<td>&gt; 66</td>
</tr>
</tbody>
</table>

2. Post compression study (Official and Non-Official test of tablets)

- Non-Official Test

(a) Appearance: Appearance is the one of the first quality parameter for the acceptance of tablet. General elegance and its identity play a major role for the consumer satisfaction. Acceptance of the appearance of batches of the tablet has been done based on the following factors such as size, colour, shape, odour, taste etc [1, 5, 21, 22].

(b) Size and shape: Determined by thickness. Size and shape of a tablets plays a unique role in patient compliance. Smallest the size of tablets, easy to administration. To determine the thickness of a tablet, device known as Micrometer can be used. Acceptable limit, if the batch falls within the range of ±5% of standard deviation [1, 5, 21, 22].

(c) Organoleptic properties: Colour should be uniformly distributed throughout the tablet without any sign of mottling. Colour of the tablet should be compared with the standard colour according to the IP [1, 5, 21].

(d) Uniformity of thickness: The uniformity of thickness is measured by selecting the random sample of for each and determined individually. If the thickness of tablet varies from each other than the batch considered as fail. It can be measured by using Vernier calliper [1, 5, 21, 22].

(e) Weight variation test: According to IP, 20 tablets from each batch should be selected randomly and the weight of the individual tablet are taken and any variation in the weight of individual tablets are noted. Below is the acceptable limit of percentage deviation in weight variation shown in Table 2 [5, 6, 22].

Table 2: Percentage deviation in weight variation.

<table>
<thead>
<tr>
<th>Average weight of the tablets</th>
<th>Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>80 mg or &lt; 80 mg</td>
<td>±10%</td>
</tr>
<tr>
<td>&gt;80 mg and &lt; 250 mg</td>
<td>±7.5%</td>
</tr>
<tr>
<td>250 mg or &gt;250 mg</td>
<td>±5%</td>
</tr>
</tbody>
</table>

(f) Water absorption ratio: Tablet are placed on the twice folded piece of tissue paper which is kept in a petridish having an internal diameter of 6.5 cm filled with 6 ml of water. Note the wetting time of the tablet and then wetted tablets are weighed. This procedure should be followed three times for each batch and standard deviation is also calculated from the obtained results. The water absorption ratio R, is calculated using the formula [23]:

\[ R = 100 \times \frac{W_a - W_b}{W_b} \]

Wb is the weight of the tablet before absorption,
Wa is the weight of the tablet after absorption.

- OFFICIAL TEST

(a) Hardness: The strength of a tablet to stand against applied load/pressure is known as hardness. It is also known as crushing strength. Randomly take 5-10 tablets from prepared batch and hardness should be determined by
crushing the tablet by hardness tester and then find-out the average and standard deviation. Hardness is determined by using hardness tester (Monsanto) shown in Figure 5. The value of hardness was calculated in kg/cm² [1, 5, 6, 21-23].

![Figure 5: Monsanto hardness tester](image)

(b) **Friability**: Friability test applied to evaluate physical strength of tablets when they subjected to mechanical shock or attrition. Friability apparatus consists of a transparent synthetic polymer drum which have polished internal surface (diameter of 283-291 mm and a depth of 36-40 mm). The drum has two sides out of which one is removable. A curved projection with inner radius (75.5-85.5 mm) which extending towards outer wall of the drum facilitating movement of tablets inside the drum. The central ring has an outer diameter of 24.5-25.5 mm. The drum is rotating at 25 ± 1 rpm for 4 minutes (Figure 6) [1, 5, 6, 21-25].

\[
\text{Percentage of friability} = \left(\frac{W_{\text{initial}} - W_{\text{final}}}{W_{\text{initial}}}\right) \times 100.
\]

![Figure 6: Tablet friability apparatus](image)

(c) **Content of active ingredients**: Determined by the method of assay for the same take 20 tablets and crushed it into powder form. Then, weigh suitable amount of powdered drug into a volumetric flask and dilute it up to 200ml followed by filtration. Now take the sample for analysis by analytical method. If a smaller number of tablets are available than which should be not be less than 5, may be observed. The content of active ingredient must be applying as per limits i.e. in-between 90% to 110% [1, 5, 6, 21-26].

\[
\text{Drug content} = \text{Concentration of the drug in (mcg/ml)} \times \text{volume of medium} \times \text{dilution factor} \times \frac{1}{1000}
\]
Table 3: The limits of content of active ingredient

<table>
<thead>
<tr>
<th>Weight of API in each tablet</th>
<th>Subtract from lower limit for samples of</th>
<th>Add to the upper limit for samples of</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>0.12 g or less</td>
<td>0.2</td>
<td>0.7</td>
</tr>
<tr>
<td>More than 0.12 g but less than 0.3 g</td>
<td>0.2</td>
<td>0.5</td>
</tr>
<tr>
<td>0.3 g or more</td>
<td>0.1</td>
<td>0.2</td>
</tr>
</tbody>
</table>

(d) **In vitro disintegration test:** Disintegration is defined as the phenomenon of conversion of large particles of tablet into small particles. Disintegration time of a tablet is determined by using disintegration testing apparatus specified as in IP. It can be determined by disintegration apparatus as in Figure 7 [1, 5, 6, 21-26].

![In vitro disintegration test apparatus](image)

**Figure 7: In vitro disintegration test apparatus**

**Basket-rack assembly:** It consists of a basket-rack (1000ml beaker), thermostatic arrangements and a mechanical apparatus for upward and downward movement of the basket into the solution with a constant frequency of between 28-32 cycles per minute (Figure 8) [1, 5, 6, 21-28].
(e) *In vitro Dissolution Test (DT)*

As per IP, DT is designed to account the dissolution of oral solid dosage forms and other dosage forms. The test observations must be compliance with standards specified in official compendium for tablet. It can be determined by dissolution apparatus mentioned in Figure 9.
Different parts of the apparatus which come in contact with the dissolution medium must be chemically inert. An apparatus is made up of stainless steel type 316 coated with a suitable material to ensure the compliance with sample and provide suitable environment for significant motion, agitation or vibration [6, 11, 22].

**Paddle Apparatus I**

An assembly consisting of the following:

a) A transparent cylindrical vessel with hemispherical bottom have 1000ml capacity. Inside diameter is 98-106mm (Fig.10) fitted with upper rim and lid having a number of openings [22].

b) A speed regulated motor able to maintain the rotation of a driving shaft and a blade forming a paddle within 4% specified monograph (Fig.10). The shaft is positioned in such a manner that its axis should be in a limit
of 2mm of the axis of the vessel and the lower edge of the blade is 23-27 mm from the inner bottom of the vessel. The apparatus runs in such a manner so as its paddle rotates smoothly without any wobble [22].

c) Dissolution medium inside the water-bath should maintain the temperature at 36°C to 37°C. [22].

**Basket Apparatus 2**

![Diagram of Basket Apparatus 2](image)

Figure 11: Apparatus showing dimensions in mm of dissolution apparatus II

The assembly of Apparatus II is same as in Apparatus I except the paddle, there is a basket, D. The basket is mainly consisting of two parts: The top part, with a vent, which is attached to the shaft, C. It is plugged with three spring clips, that allow removal of the lower part for insertion of the sample under examination and that tightly hold the lower part of the basket mess with the vessel axis during rotation. The lower removable component of the basket is made of welded-steam cloth, consists of a wire with thickness of 0.254mm in diameter and 0.381mm square openings (Figure 11), construct into a cylinder of sheet metal with confined rim around the top and the bottom [22].

For acidic media, the basket should be plated with layer of gold about 2.5 mm. The distance of the basket and the inside bottom of the cylindrical vessel, is maintained at 23 to 27 mm during the examination [22].
Dissolution medium

As per IP, if the solution is buffer, the pH of solution is adjusted within 0.05 units or as specified. For a single time as specified the test may be operated for shorter period of time as mentioned in official compendium. If the multiple times are specified in official compendium, samples should be withdrawn with under a tolerance of ±2% at the stated times [6, 22, 29-31].

Table 4: Acceptance criteria of conventional tablet

<table>
<thead>
<tr>
<th>Level</th>
<th>Number tested</th>
<th>Acceptance criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>S₁</td>
<td>6</td>
<td>Each unit is not less than D* +5 percent**</td>
</tr>
<tr>
<td>S₂</td>
<td>6</td>
<td>Average of 12 units (S₁ + S₂) is equal to or greater than D, and no unit is less than D -15 percent**.</td>
</tr>
<tr>
<td>S₃</td>
<td>12</td>
<td>Average of 24 units (S₁ + S₂ +S₃) is equal to or greater than D, more than 2 units are less than D -15 percent** and no unit is less than D -25 percent**.</td>
</tr>
</tbody>
</table>

*D is the amount of dissolved active ingredient specified in the individual monograph, expressed as a percentage of the labelled content.

**Percentages of the labelled content.

CONCLUSION

Tablets are the conventional oral solid dosage forms which is most acceptable and convenient as compared to any other type of dosage forms. These tablets are prepared usually by direct compression or wet granulation. It is
necessary for pharmaceutical manufacturers to measure quality control parameters of given dosage form so as to produce every batch, of product complying with its pertinent attributes. Thus, every batch of the tablets manufactured should have to undergo various in-process as well as finished product testing.

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