A DETAIL REVIEW ON ORODISPERSIBLE TABLETS

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ABSTRACT

Orodispersible tablets are a novel dosage form that dissolves quickly in the mouth. This method of drug delivery is commonly used to increase patient adherence and bioavailability. Oral drug delivery and rapid tablet disintegration in the mouth without the use of water have made the orodispersible tablet the greatest alternative to traditional tablets, syrups, capsules, and other forms of medication. In the pharmaceutical business, the oral route is currently the gold standard, as it is considered the safest, most cost-effective, and most convenient way of drug delivery, resulting in the highest patient compliance. There is a range of benefits that they provide to the patient in terms of significant income from product line extensions. Oral disperisible tablets have been developed for bed rest patients, geriatric, and pediatric, as well as adults and patients who may not have access to water. Many elderly persons find it difficult to take traditional dosage forms due to hand tremors and dysphasia, so an orodispersible tablet offers an alternative. Swallowing issues can also occur in young people due to their underdeveloped muscular and nervous systems. Oral drug delivery and rapid tablet disintegration in the mouth without the use of water have made the orodispersible tablet the greatest alternative to traditional tablets, syrups, capsules, and other forms of medication. The ideal qualities, advantages, and disadvantages, as well as various manufacturing procedures and evaluation factors for orodispersible tablets, are discussed in this review paper.

KEYWORDS: Orodispersible tablets, Freeze-Drying, Tablet Molding, Sublimation.
INTRODUCTION
The most widely used and effective route for drug delivery is through the mouth. Oral medicine delivery methods that dissolve orodispersible tablet quickly in the mouth, without the use of water can help to overcome the difficulty of swallowing tablets. Dispersible systems are those that disintegrate or disappear in seconds to minutes of being placed. Tablets and thick gelatin capsules are difficult to swallow for many people. As a result, they do not follow the prescription, resulting in a high rate of non-compliance and unsuccessful treatment. Swallowing traditional tablets might be problematic in particular situations, such as motion sickness, nausea, abrupt episodes of allergy responses or coughing, and a lack of water. Patients with special needs, such as children and the elderly, have particular challenges. Fast Dissolving Tablets can help with such problems. This tablet dissolves quickly when placed on the tongue, releasing the medication, which dissolved in the saliva. Orally disintegrating tablets, mouth-dissolving tablets, quick-dissolving tablets, fast-disintegrating tablets, and fast-dissolving tablets are all terms for orodispersible tablets. The word orodispersible tablets were recently discovered by the European Pharmacopoeia. Orodispensible tablets are those that are placed into the mouth and disperse fast within 3 minutes before being ingested.

Ideal properties of orodispersible tablet
These dosage formulations have several useful qualities as follow
1. It should melt or dissolve in a matter of seconds in the mouth.
2. Excessive drug loading should be allowed.
3. Taste masking and other excipients should be suitable with them.
4. It should feel good in your mouth.
5. After oral delivery, they should leave nearly minimal residue with in mouth.
6. They must be strong enough to withstand the rigours of both the manufacturing and post-production processes.
7. They should be more resistant to changes in humidity and temperature in the environment.

The number of tablets produced should be at minimum cost.

Advantage of orodispersible tablet
1. Stability has been improved.
2. Suitable for controlled/long-term use Patients and prescribers benefit from increased compliance and convenience.

3. It promotes patient adherence and, in the case of antimicrobials, lowers the development of resistance.

4. It also simplifies the logistics of procurement and distribution.

5. ODTs are regarded as the preferred dosage form for rapid medication delivery.

6. Increased bioavailability can be attained since the medicine is rapidly released from this dose form and dissolves in the GIT tract without entering the stomach.

7. ODTs are highly practical for administering to a wide range of patients, including the disabled, travellers and those who are frequently on the go and don't always have access to water.

8. As saliva flows down into the stomach, some medications are taken in from the pharynx and oesophagus; in these circumstances, drug bioavailability is increased.

9. There is no need for water.

10. There is no need to chew.

11. Release actives for a better taste.

Allow for a lot of medication loading.\cite{5}

**Disadvantage of orodispersible tablets**

1. Pharmacological therapy cannot be used to intervene rapidly.

2. It may be necessary to provide the medication more often at times.

3. It's possible to dump doses.

4. Reduced ability to make precise dosage adjustments

5. ODT requires particular packaging for the effective stability and safety of the stable product.

6. Mechanical strength is usually lacking.

Generate a sour aftertaste and/or grittiness on the tongue.\cite{5,6}

**Various technologies are used in production of orodispersible tablet**

The following technologies used to prepare Orodispersible tablet:

a) Freeze-Drying or Lyophilization

b) Tablet Molding

c) Sublimation
d) Direct Compression  
e) Cotton Candy Process  
f) Mass-Extrusion  
g) Melt granulation  
h) Spray Drying  
i) Phase transition  
j) Nanonization\[7\]

**Freeze-Drying or lyophilization**

It's a method for making Orodispersible Tablets. The main idea is to remove the solvent from a prepared solution that has been kept frozen to create an amorphous porous structure that dissolves quickly.\[8\] The medication is encapsulated in a water-soluble matrix and freeze-dried to form a porous shape. When lyophilized tablets are inserted in the oral cavity, saliva quickly penetrates pores and disintegrates the tablets in a fraction of a second. Heat-sensitive medications, also known as thermo-labile compounds, benefit from lyophilization. In most cases, the freeze-drying process has the following steps: To bring the material below the eutectic point, it is frozen. The moisture level of the dried product is reduced to around 4% w/w by primary drying. Secondary drying is used to decrease moisture to the final volume required.\[9\] Advantage is Faster dissolution than comparable solid products in the market and Disadvantages is Equipment costs are high, and blister packs lack physical resistance.\[8,9\]

**Tablet molding**

Due to the fact that the dispersion matrix is commonly formed of water-soluble carbohydrates, molded tablets disintegrate faster and have a better taste. In most situations, the active ingredient is taken in through the mouth's mucosal lining. To make tablets, wet the powder mixture using a hydroalcoholic solvent before pressing it between plates in mold to generate a moistened mass (compressing molding). After that, the solvent is evaporated by air drying. In the end, the procedure is similar to that employed in the production of tablet triturates. The porous nature of these tablets’ aids in the dissolving process and tablets that have been compressed are less compact.\[10\]

Advantages: In comparison to the lyophilization procedure, the molding approach produces tablets that are less difficult to adapt to adapt to an industrial scale.
Disadvantages: Because of their low mechanical strength, molded tablets are prone to erosion and shattering during handling. The strength of the tablets can be increased by hardening them, but this takes place at the cost of their disintegration time.\textsuperscript{[11]}

**Sublimation**
This method involves adding volatile substances (such as urea, naphthalene, ammonium bicarbonate, camphor, urethane, and others) Other tablet excipients are added, and the combination is compressed into tablets. Sublimation is used to eliminate entrapped volatile material, resulting in the emergence of a porous structure. These compressed tablets, which have a high porosity (about 30%), dissolved in saliva in 15 seconds. As pore generating agents, a variety of solvents such as cyclohexane, benzene, and others can be utilized. This approach was used to synthesize an orodispersible tablet with a porous structure and excellent mechanical strength.\textsuperscript{[12]}

**Direct compression**
It is the simplest method of producing tablets. Direct compression uses standard equipment, widely available excipients, and a small number of processing stages. High doses can also be accommodated, and the final tablet weight can easily beat other manufacturing methods. Because of the presence of better tablet excipients, such as sugar-based and disintegrants excipients, this technology also uses for fast dissolving tablets. It has advantages over other tablet manufacturing processes, such as wet granulation, and it is extremely efficient.\textsuperscript{[13]} The compressed mixture must have satisfactory flow characteristics and cohere under pressure, obviating the necessity for pre-processing like wet granulation. Super disintegrants play an important part in the disintegration and dissolution of orodispersible tablets formed via direct compression in many circumstances. For a high disintegration rate, selecting the appropriate type and number of disintegrates is critical. Other formulation strategies, effervescent excipients or water-soluble excipients compounds, can improve dissolution or disintegration qualities even further.\textsuperscript{[14]}

**Cotton candy process**
This method creates a floss-like crystalline structure using a unique spinning mechanism. The formation of a polysaccharide or saccharide matrix is involved in the cotton candy process.\textsuperscript{[15]} To make a matrix, this approach includes melting and spinning polysaccharides or saccharides at the same time. To improve flow properties and compressibility, the matrix
form is partially recrystallized. It's then milled, blended, and mixed with the active ingredients. After that, it's compressed to make an Orodispersible tablet.\textsuperscript{[16]}

**Mass-Extrusion**

Softening the active substance with a solvent mixture of water-soluble polyethylene glycol and Methanol, then extruding or syringing the softened bulk to form a cylinder-shaped extrusion, which is then sliced into even segments to make tablets with a hot blade. This approach can also be used to disguise the flavour of bitter pharmaceutical granules. This procedure is used to make flavour-masked Granules. Different Super disintegrate were used to make the tablet. For example, sodium starch glycolate, sodium croscarmellose, and cross povidone.\textsuperscript{[17]}

**Melt granulation**

A melt granulation system is a method of efficiently agglomerating pharmaceutical powders using a meltable binder. This approach has the benefit of not requiring the use of water or an organic solvent when compared to traditional granulation. In this drying process is not carry out, so that procedure require less energy and time than wet granulation. It's a fantastic technique to speed up the dissolution of drugs like griseofulvin, which aren't particularly water-soluble. A hydrophilic waxy binder is used in this process to formulate MDT with appropriate mechanical integrity (superpolystate, PEG-6Stearate). Waxy substance like Superpolystate have melting point 33-37°C and have HLB value near 9. As a result, increase the strength and resistance of tablets by act as binder and it will also aid in their breakdown because it liquefy in the mouth and dissolves fast, leaving no behind.\textsuperscript{[16],[17]}

**Spray drying**

This approach employs a particulate support matrix, which is created by spray drying an aqueous composition containing the support matrix and other materials into a fine powder. Following that, the active ingredients were added, and the mixture was crushed into tablets. Supporting agents include hydrolysed and non-hydrolysed gelatines, mannitol as a bulking agent, sodium starch glycolate or croscarmellose sodium as a disintegrating agent, and an acidic and/or alkaline material to aid disintegration and dissolution. When submerged in an aqueous media, a tablet compacted from spray-dried powder disintegrated in 20 seconds.\textsuperscript{[18]}
Phase transition
A mixture of high and low melting point sugar alcohols, and a phase transition during the manufacturing process, was necessary to make an Orodispersible tablet, without the use of any specific equipment. Tablets are made by pressing a powder made up of two sugar alcohols of different melting points and then heating them at a temperature halfway between them.

Orodispersible tablets were made by compressing xylitol sugar alcohol (MP: 93-95°C) and erythritol sugar alcohol (MP: 122 °C) powder and heating at 93°C for 15 minutes. the tablet hardness increased after heating with increase in pore size. The low melting point of sugar alcohol's crystal state did not affect the gain in tablet hardness during heating and storage.\[19\]

Nanization
This process involves milling the medicine using a unique wet milling technique to reduce the size of particle of drug to nano size. Surface absorption on chosen Stabilizers prevents agglomeration of the drug's nanocrystals, which are subsequently combined into mouth-dissolving Tablets. This technique is ideal for medications that aren't very water-soluble.\[18,19\]

Evaluations
Pre-compression parameters
The following are different evaluation parameters before the powder combination was formed.

1. The angle of repose
The angle of repose is calculated by using funnel method. A funnel is used to collect the precisely weighed blend. The height of the funnel is set so that the tip of the funnel just brushes against the blend heap's apex. The drug-excipient mixture is allowed to run freely through the funnel and onto the surface. The powder cone's diameter is measured, and by using the equation below we can measure angle of repose

\[\tan \Theta = \frac{h}{r}\]

h for the cone height and r for cone's radius, respectively. The material is free-flowing if angle of repose is less than 30 degrees.\[20\]
Table no. 1: Angle of repose table as per IP.

<table>
<thead>
<tr>
<th>Flow property</th>
<th>Angle of repose (in degree)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excellent</td>
<td>25-30</td>
</tr>
<tr>
<td>Good</td>
<td>31-35</td>
</tr>
<tr>
<td>Fair</td>
<td>36-40</td>
</tr>
<tr>
<td>Passable</td>
<td>41-45</td>
</tr>
<tr>
<td>Poor</td>
<td>46-55</td>
</tr>
<tr>
<td>Very poor</td>
<td>56-65</td>
</tr>
<tr>
<td>Very, very poor</td>
<td>&gt;66</td>
</tr>
</tbody>
</table>

2. Bulk density

Bulk Density was estimated by measuring the volume and weight of a precisely weighed quantity of mixture by using graduated cylinder.[21]

Bulk density = Mass of powder/volume of packing

3. Tapped density

A graduated cylinder with a given mass of drug-excipients mixture is used to determine the tapped density. Under its own weight, the cylinder is permitted to drop from a height of 10 cm upon a hard surface at 2-second intervals. The tapping will continue when there's no more variance in volume.[22]

Tapped Density = (Mass of the powder/volume of the tapped packing)

4. Carr’s Index (Compressibility)

The compressibility index also known as Hausner ratio both of them measures of the property of the powder to be compressed. The drug's packing ability was assessed based on changes in volume caused by packing rearrangement during tapping. The following is how Carr's compressibility index was derived.

Carr's index = [Tapped density - Bulk density/Tapped density] X 100

Table no. 2: Carr’s index table as per IP.

<table>
<thead>
<tr>
<th>Compressibility Index (%)</th>
<th>Flow Character</th>
<th>Hausner ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>Excellent</td>
<td>1.00-1.11</td>
</tr>
<tr>
<td>11-15</td>
<td>Good</td>
<td>1.12-1.18</td>
</tr>
<tr>
<td>16-20</td>
<td>Fair</td>
<td>1.19-1.25</td>
</tr>
<tr>
<td>21-25</td>
<td>Passable</td>
<td>1.26-1.34</td>
</tr>
<tr>
<td>26-31</td>
<td>Poor</td>
<td>1.35-1.45</td>
</tr>
<tr>
<td>32-37</td>
<td>Very poor</td>
<td>1.46-1.59</td>
</tr>
<tr>
<td>&gt;38</td>
<td>Very, very poor</td>
<td>&gt;1.60</td>
</tr>
</tbody>
</table>
5. **Hausner ratio**

The Hausner ratio is a measurement of the drug's frictional resistance. The optimal range is between 1.2 and 1.5.

Hausner Ratio = Tapped density/Bulk density

**Evaluation of orodispersible tablet**

Orodispersible tablets were investigated for thickness, hardness, friability, weight variation test, drug content, and in-vitro release rate.

1. **Appearance:** A tablet's overall appearance, visual identity, and overall "elegance" are all important for consumer acceptance, as are the tablet's size, shape, color, fragrance, physical faults, surface texture, taste, consistency and also legibility of almost any identifiable marks.[23]

2. **Shape and size:** The tablet's size and shape can be dimensionally characterized, monitored, and controlled.

3. **Tablet thickness:** The thickness of five tablets is measured with a vernier calliper is simple method to measure thickness of tablet.

4. **Weight variation:** To calculate weight variation, 20 pills were chosen at random from the same batch and weighted individually. The table shows the weight variation specifications according to I.P.[24]

   **Table no. 3: As per I.P weight variation.**

<table>
<thead>
<tr>
<th>IP/BP</th>
<th>Limit</th>
<th>USP</th>
</tr>
</thead>
<tbody>
<tr>
<td>80mg or less</td>
<td>10%</td>
<td>130mg or less</td>
</tr>
<tr>
<td>80mg to 250mg</td>
<td>7.5%</td>
<td>130mg to 324mg</td>
</tr>
<tr>
<td>250mg or more</td>
<td>5%</td>
<td>More than 324mg</td>
</tr>
</tbody>
</table>

5. **Tablet hardness:** Tablet hardness is determined how much force is required to break the tablet. The force is calculated in kilograms, and uncoated tablets with a hardness of roughly 3-5 kg/cm² are regarded as satisfactory. Monsanto, Pfizer, and other hardness testers are used to measure the hardness of 10 tablets from each formulation.

6. **Friability:** The friability of a sample of six tablets is measure by using a Roche Friabilator. The tablets were undergone shock and damage in a friabilator that rotated at speed of 25 rpm and dropped the tablets from a height of 6 inches with every rotation.[25] The tablets are rotating in the friabilitor for minimum 4 minutes. At the end of the test,
the tablets are dusted and weighed accurately. Loss in weight of the tablet is a requirement for friability and is represented in percentage as

\[
\% \text{ Friability} = \frac{\text{Loss in weight}}{\text{Initial weight}} \times 100 \text{ Limit - less than 1%}
\]

7. **Wetting time:** The contact angle affects the wetting time of the dosage form.

   It must be assessed to learn more about the tablet's disintegration properties. A shorter wetting time indicates that the tablet will disintegrate faster. The time it takes for a tablet to totally wet is measured by placing it on a double-folded piece of tissue paper and storing it in a little Petri dish (ID = 6.5 cm) containing 6 ml of water.

8. **Disintegration time:** Six tablets are used to measure disintegration time by using the apparatus as per I.P.-1996. The disintegration media was distilled water at 37°C ± 2°C, and the time it took for the tablet to totally dissolve with no appetising substance visible in the instrument was determined in seconds. Modified Disintegration Test: For these dose forms, the standard disintegration test approach has considerable limitations, and it is insufficient for determining very low disintegration times. Because disintegration is necessary without water, the disintegration duration for a fast-disintegrating tablet must be adjusted. As a result, the test should replicate salivary disintegration. For this study, a Petri dish (10 cm in diameter) was loaded with 10 ml of water.\(^{[24],[25]}\)

9. **Dissolution test:** Oral disintegrating tablets are dissolvable in the way as conventional tablets are. The USP 2 paddle device, with 50 rpm speed of paddle, is the most ideal and popular option for dissolution testing of oral disintegrating tablets. The USP 1 apparatus may have some utility for such tablets, but due to the physical features of tablets, it is employed less commonly.

10. **Stability study:** The rapid disintegrating tablets are packaged and stored according to ICH recommendations for the duration of the accelerated study. This depends on temperature.

   a) 40 ± 1 °C
   b) 50 ± 1°C
   c) 37 ±1 °C and RH 75% ± 5%

   After 15 days, the tablets were removed and examined for physical flaws (Visual faults, Friability, hardness and Dissolution, Disintegration among other things) as well as drug
content. At 25° C, accelerated stability data is plotted by help of the Arrhenius equation to determine the shelf life.\[^{25}\]

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