ORODISPERSIBLE MINI-TABLETS: A REVIEW

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ABSTRACT

Recent advance in Novel drug delivery system aim for designing dosage forms, convenient to manufactured and administered free of side effects, offering various advantages such as better mouth feel, dose accuracy, improved stability, convenient dosing and offering immediate release and enhanced bioavailability. So, as to achieve better patient compliance. Mini tablets are tablets with a diameter equal to or smaller than 2–6 mm. Mini tablets are multiple unit dosage forms and are advantageous than pellets or any other oral dosage forms as they are easy to manufacture and stability problems are less. Many types of mini tablets are there. In the oral drug delivery system preferably tablets are the most widely accepted dosage forms, offering uniform dose and painless delivery. Yet, dysphagia is the most common disadvantage of conventional tablet. Patients with number of conditions like parkinsonism, mental disability, motion sickness, unconscious have difficulty in swallowing tablet. To overcome such problems orodispersible mini-tablets(ODMTs) have been developed. These are novel dosage forms which dissolve in saliva within a few seconds, when put on tongue. Such ODMTs can be administered anywhere and anytime without need of water and are thus quite suitable for children, elderly and mentally disabled patients.

KEYWORDS: Orodispersible Minitablets, Superdisintegrats, Methods.

INTRODUCTION

Tablets remain the most conventional and cost effective way to administer pharmaceuticals, however, traditional tablets present challenges for paediatric patients such as risk of aspiration and difficulty swallowing. The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site in the body to achieve promptly and then maintain the desired drug concentration. The most convenient and commonly employed route of drug delivery has historically been by oral ingestion. Solid dosage forms are popular because of low cost, ease of administration, accurate dosage self-medication, pain avoidance, and the most importantly the patient compliance. The most popular solid dosage forms are being tablets and capsules. One important drawback of such dosage forms is Dysphagia, or difficulty in swallowing is common among all age groups. Common complaints about the difficulty in swallowing tablets are size, surface, and taste of tablets. Geriatric and pediatric patients and traveling patients, who may not have ready access to water, are most in need of easy swallowing dosage forms. To fulfill these
medical needs, pharmaceutical technologists have developed a novel oral dosage form such as Orally disintegrating minitablets, Orally disintegrating films, Lyophilisates etc.

A single unit dose e.g. Matrix or tablet enclosed in diffusion membrane, is a depot which release drug during the passage of entire GI tract without disintegrating. The empty core or shell is discharged. To retain a depot effect the dose unit to be administered should be intact as dividing dosage form before administration would result in unintended rapid release. A multiple unit’s dose consists of many mini-units, e.g. Pellets or mini tablets contained in a capsule or a tablet. These mini-depots are dispersed and distributed throughout the gastro intestinal tract when the capsule or tablet disintegrates.

A multiple units tablet may thus be divided before ingestion without loss of depot effect, as the subunits act as self-contained depots. The dose in multiple unit dosage forms is divided into number of subunits, each one containing the drug. The dose is then the sum of the quantity of the drug in each subunit and the functionality of the entire dose is directly correlated to the functionality of the individual subunits. [1,2]

MINITABLETS:

Mini-tablets are small, flat or slightly curved tablet with a diameter ranging from 2.0-6.0 mm[4]. These mini-tablets can be filled into hard gelatin capsules or can be compressed as normal tablets or can be administered as individually. Mini-tablets also offer an alternative for pellets because of their relative ease of manufacturing and because dosage forms of equal dimensions and weight with smooth regular surface are produced in a reproducible and continuous way.

Mini-tablets are very suitable for coating in order to sustain the drug release but the coating process is expensive, time consuming and sometimes associated with reproducibility problems of release during storage.

Mini tablets reduce intra and inter subject variability and also reproducible release profiles can be obtained. Majority of the drugs absorption is more in upper part of small intestine (duodenum), for a drug to reach the small intestine it had to pass through stomach. So, drug absorption depends on gastric emptying time. If the gastric emptying is too fast drug may not absorb to required level or if it too slow it may get mix-up with gastric contents and may adsorb to food which gives unintended effects. These effects are more in case of single unit dosage forms because of their size but in case of mini tablets will not depend on gastric emptying and easily get passed through pylorus. So mini tablets are beneficial over the normal size tablets to reduce intra and inter subject variability.
Mini tablets will give reproducible plasma drug concentrations. Plasma drug concentration is directly proportional to the absorption. Absorption is more and even with mini tablets as they are distributed all over the surface which is not in case of tablets/ capsules. So by formulating mini tablets better plasma drug profiles can be obtained.

Mini tablets can be easily divided and administered without loss of activity. Elderly and paediatric patients who sometimes chew the tablets which releases drug all at once and may cause toxicity in case of normal tablet but in case of Mini tablets, they can be chewed as here each mini depot in the formulation act individually dose dumping may not occur. For local irritating drugs, mini tablet formulation decreases the irritation effect than that of single unit formulations. \[3,4\]

![Mini tablets](image)

**Fig. 1 Minitablets**

**Advantages of mini-tablets :**

- Mini-tablets have less inter subject and intra subject variability.
- They have less risk of dose dumping.
- Mini-tablets are easy to manufacture compared to pellets as they have equal dimensions, weight with smooth regular surface. They can be produced in a reproducible and continuous manner.
- Mini-tablets are good coating substrates as they have excellent size uniformity, regular shape and a smooth surface.
- They offer high drug loading, a wide range of release rate patterns, and also fine tuning of these release rate.
- They offer high degree of dispersion in the GI tract, thus minimizing the risk of high local drug concentrations.
- Unlike pellets, mini-tablets does not require any solvent for its production, as a result problems with stability can be avoided.
- Complex manufacturing steps can be minimized in case of mini-tablets when compared to pellets which may require fluid bed granulator for granulation or coating as mini-tablets can be manufactured easily by simple tableting techniques. [5]

**Comparison of Minitablets with other dosage form**

**Table 1 comparison of Minitablets with single unit dosage form**

<table>
<thead>
<tr>
<th>Minitablets</th>
<th>Single unit dosage form</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-dependent on gastric emptying, easily get pass through pylorus.</td>
<td>Dependent on gastric emptying</td>
</tr>
<tr>
<td>Distributed all over the surface, which result absorption is more.</td>
<td>Not distributed all over surface.</td>
</tr>
<tr>
<td>In this, “Each mini-depot in formulation act individually” So less chance of toxicity. Dose dumping may not occurs.</td>
<td>In this, “Drug all at once” So may cause toxicity Dose dumping may occur.</td>
</tr>
</tbody>
</table>

**Table 2 Comparison of Minitablets with granules**

<table>
<thead>
<tr>
<th>Minitablets</th>
<th>Granules</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compare to granules require less coating materials.</td>
<td>Require more coating material.</td>
</tr>
<tr>
<td>Regular shaped, smooth surface, constant surface, high mechanism strength</td>
<td>Irregular shape</td>
</tr>
<tr>
<td>Dosage form of Minitablets is smaller than granules.</td>
<td>Dosage form of granules are larger.</td>
</tr>
</tbody>
</table>

**Types of Mini-Tablets**:[4]

Minitablets can be classified on the basis of target site, manufacturing method and patient needs as follow:

1. **Paediatric Mini-Tablets**
2. **Orally Disintegrating Mini-Tablets**
3. **Gastro retentive Mini-Tablets**
4. **Bio-adhesive Mini-Tablets**
5. **pH responsive Mini-Tablets**
6. **Biphasic Mini-Tablets**

**Paediatric Mini-Tablets:**

For children, syrups, tablets and capsules are commonly used dosage forms. Syrups are liquid dosage forms which are simple to administer and dose can be easily altered to patient needs on the other side drawbacks with these liquids dosage forms are chemical, physical, and microbial...
instability, taste issues, lack of controlled release and formulation problems. In case of tablets as they are big in size, so difficulty in swallowing and dose adjustment is difficult. Some time we have to break the tablets and administer which causes loss of activity of the tablets. Patient compliance is another issue with the conventional dosage forms. To overcome all the above issues formulating mini tablets can result in good patient acceptance. Mini-tablets are easily accepted by children than other dosage forms like tablets, syrups, and capsules etc.

**Orally Disintegrating Mini-Tablets:**

Oral dispersible tablets (ODTs) are the novel dosage form which rapidly disintegrates in the mouth (1-3 min) within matter of seconds to minute without the need of water upon oral administration, unlike other conventional oral solid dosage form. Oral Dispersible Tablets (ODTs) are also known as “fast dissolve”, “rapidly disintegrating”, “quick-dissolve”, “crunch-melt”, “bite-dispersible”, “mouth-dissolve”, and “orodispersible” tablets. Oral dispersible mini tablets (ODMTs) are more suitable for paediatric patients because of their small size, pleasant mouth feel and fast disintegration in mouth.

**Gastro retentive Mini-Tablets or Floating Mini-tablets:**

Gastro retentive mini-tablets are intended to release drug in stomach for prolonged time. Generally for tablets to float on GI fluids content, tablet can be formulated by using gas generating agents. These tablets whom comes in contact with food it generate CO2 and generated gas is trapped with swellable hydrocolloid which makes tablet to float on GI fluid and retain it into stomach.

**Bio-adhesive vaginal Mini-Tablets:**

The dosage forms which are aimed for vaginal delivery should be easy to administer without irritation or discomfort and should have even distribution and long retention time there by increasing patient compliance and adhere to therapy. Bio adhesive mini-tablets can be used for vaginal drug delivery to deliver drug accurately and for long period of time. In mini-tablets, dose is divided into multiple units which will spread evenly in vaginal cavity with improved coverage in vaginal epithelium. Bio adhesive mini-tablets act by swelling and forming micro gels and releasing drug in controlled manner and there by maximum bioavailability can be achieved.

**pH responsive Mini-Tablets:**

The pH of human Gastro Intestinal Tract varies greatly {Stomach 1.5-3.0, upper part of small intestine (Duodenum) 4.0-5.0, lower parts of small intestine (jejunum) and (ileum) 6.5-7.5, and colon 5.6-6.9}. pH responsive drug release is required when absorption of drug is more at a particular site this can be achieved by coating with pH responsive release polymers. Generally
coating is done to granules and then they are filled into capsules to achieve the required release at required pH. In case of pellets control of size and size distribution is important before coating. To get reproducible results, desirable pellet size and a narrow particle size distribution are required in pellets which are difficult to achieve.

To overcome this problem in place of pellets Mini tablets can be used. Mini tablets are easy to manufacture and coating them is easy when compared to pellets as they have smooth surfaces. Uniform size can be obtained so less variation with in unit to unit. Reproducible results can be achieved by uniform coating. So, mini tablets can be used as an alternative to pellets.

![Fig. 2 Pellets and Mini tablets size and Distribution](image)

**Biphasic Mini-Tablets:**

Biphasic mini-tablets contains two layers, one is fast releasing layer and second is slow releasing layer. First layer releases drug immediately after oral administration and second layer releases drug slowly in a controlled manner. This type can be beneficial for drugs used for hypertension where repetitive dosing can be reduced. Different drugs can be compressed into mini-tablets and can be filled in same capsule to treat different disease.

**ORODISPERSIBLE DOSAGE FORM**

Orodispersible Tablets(ODTs) are defined as “A solid dosage form that contain medicinal substances and which disintegrates quickly within matter of seconds, when put on tongue. Oral route of administration is the most popular route for systemic effects due to its ease of ingestion of accurate dosage with pain avoidance, self-medication, and most important patient compliance. Orodispersible tablets also known as “Fast dissolving tablets”, “melt-in-mouth”, “Fast Disintegrating tablets”, “Mouth-Dissolving”, “Orally Disintegrating”, “rapid dissolve”, “Quick-disintegration”, “Fast-melt”, “Mouth Dissolving” and Effervescent drug absorption system.
Fast dissolving tablet can be administered to the patients who cannot swallow tablet/capsule such as paediatric, elderly, stroke victim, bedridden patients etc. ODTs can be administered without need of water, anywhere and anytime. ODTs are very beneficial in case of motion sickness, coughing, suede episodes of allergic attack where rapid onset of action required.

Most orodispersible tablets must include substances to mask the bitter taste of the active ingredients then swallowed by patient’s saliva along with the soluble and insoluble excipients. It has been concluded that rapid dissolution, rapid the absorption (only the unionized form of the drug) and onset of action.

Some drugs absorbed from oral cavity, pharynx and esophagus as the saliva passes down into stomach. Thus bioavailability of drug is more than those observed from conventional dosage form.

The disintegration time of orodispersible tablets is generally considered to be less than one minute. [7]

The orodispersible solid dosage form turns into soft paste or liquid form for easy swallowing, and thus it is free of risk of choking. Orodispersible dosage form offers various advantages as following:

**Advantages of Orodispersible Dosage Form:**[8]

- Ease of administration to patients who can’t swallow a tablet, such as geriatric patients, mentally ill, disabled and uncooperative patients.
- No need of water to swallow the tablet.
- Can be easily administered to paediatric, elderly and mentally disabled patients.
- Accurate dosing as compared to liquids.
- Dissolution and absorption is fast, offering rapid onset of action.
- Bioavailability of drug is increased as some drugs are absorbed from mouth, pharynx and esophagus through saliva passing down into stomach.
- Advantageous over liquid in medication in terms of administration as well as transportation.
- First pass metabolism is reduced, thus offering improved bioavailability and thus reduced dose and side effects.
- Free of risk of suffocation due to physical obstruction when swallowed, thus offering improved safety.
- Suitable for sustained/ controlled release actives.
Allow high drug loading.

**Fig. 3 Advantages of Orodispersible Tablet**

**Disadvantages of Orodispersible dosage form**

- Orodispersible tablets are hygroscopic in nature so must be kept at controlled temperature, i.e., humidity and temperature.
- For proper stabilization and safety of a stable product, ODTs require special packaging.
- Usually have insufficient mechanical strength. Hence, careful handling is required.
- Leave an unpleasant taste and/or grittiness in mouth if not formulated properly.

**Ideal characteristic of ODTs**

- ODTs should disintegrate in the mouth without additional water.
- The disintegrated tablets should become a soft paste or liquid suspension, which can provide good mouth feel and smooth swallowing.
- The “fast disintegration” usually means disintegration of tablets in less than 1 minute, but it is preferred to have disintegration as soon as possible.
- Because ODTs dissolve or disintegrate in the patient’s mouth, the drug will be partially dissolved in close proximity to the taste buds.
- A pleasant taste inside the mouth becomes critical for patient acceptance. Unless the drug is tasteless or does not have an undesirable taste, taste-masking techniques should be used.
- The taste-masking technology should also be compatible with ODT formulation. For example, if drug particles are coated to minimize unpleasant taste, coating should not be broken during compression or dissolved during wet granulation.
- Taste masking of bitter tasting drug is critical to the success of ODT formulations.
- For the ideal ODT technology, properties of drug should not significantly affect the tablet property.
- Because ODTs are designed to have a quick dissolution/disintegration time, tablet porosity is usually maximized to ensure rapid absorption of water into tablet.
- In addition, low compression pressure causes fast dissolving dosage forms to be soft, friable and unsuitable for packaging in conventional blisters or bottles. A strategy to increase mechanical strength without sacrificing tablet porosity or requiring a special packaging to handle fragile tablets should be provided.
- A good package design or other strategy should be created to protect ODTs from various environmental conditions especially from moisture. [10]

**Popular Disintegrants used in Tablets with mechanism and concentration**[11]

**Table 3 Disintegrants used in tablets**

<table>
<thead>
<tr>
<th>Sr.no.</th>
<th>Disintegrants</th>
<th>Mechanism</th>
<th>Concentration %w/w</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Starch</td>
<td>Disintegrate forms pathways throughout the tablet matrix that enable water to draw into the structure by capillary action, thus leading to disruption of tablet.</td>
<td>5-20%</td>
</tr>
<tr>
<td>2</td>
<td>Pregelatinized starch</td>
<td>Responsible for increased dissolution rate from this tablet is rapid disintegration due to superior swelling capacity.</td>
<td>5-15%</td>
</tr>
<tr>
<td>3</td>
<td>Sodium Starch Glycolate (Explotab and Primogel)</td>
<td>Involves rapid absorption of water leading to an enormous increase in volume of granules result in rapid and uniform disintegration.</td>
<td>1-3%</td>
</tr>
<tr>
<td>4</td>
<td>Cross-linked polyvinyl Pyrrolidone (CrossPovidone, CrosspovidonM, Kollidon, Polyplasdone)</td>
<td>The capillary activity of cross povidone for water is responsible for its tablet disintegration property.</td>
<td>0.5-5%</td>
</tr>
<tr>
<td>5</td>
<td>Cellulose (Ac-Di-Sol, Nymce ZSX, Primellose Solutab)</td>
<td>They show their ability to swell on contact with water results in rapid tablet disintegration.</td>
<td>1-3%</td>
</tr>
<tr>
<td></td>
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<tr>
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<td>------------------------------------------------------------------</td>
<td>----------</td>
</tr>
<tr>
<td>6</td>
<td>Microcrystalline Cellulose (Avicel)</td>
<td>Allowing water to enter the tablet matrix by means of capillary pores, which break the hydrogen bonding between adjacent bundles of cellulose microcrystals and exhibit very good disintegrant property.</td>
<td>10-20%</td>
</tr>
<tr>
<td>7</td>
<td>Alginates (Alginic Acid, Satialgine)</td>
<td>High affinity for water absorption and high sorption capacity make it an excellent disintegrant.</td>
<td>1-5%</td>
</tr>
<tr>
<td>8</td>
<td>Soy polysaccharides (Emcosoy)</td>
<td>Natural super disintegrant, Rapid swelling in aqueous medium or wicking action. Does not contain any starch or sugar. Used in nutritional products.</td>
<td>5-15%</td>
</tr>
<tr>
<td>9</td>
<td>Gums (Guar Gums, Gum Karaya, Agar, Gellan Gum)</td>
<td>As disintegrants because of their tendency to swell in water</td>
<td>3-8%</td>
</tr>
<tr>
<td>10</td>
<td>Chitin and Chitosan</td>
<td>Moisture sorption and water uptake was found the major mechanism of disintegration while dissolution related to swelling capacity</td>
<td>1-5%</td>
</tr>
<tr>
<td>11</td>
<td>Smecta</td>
<td>Their layered leaves like structure consist of aluminium and octahydradal layers sandwiched between two tetrahydral silica layers. It has a large specific area and high affinity for water makes it good disintegrant.</td>
<td>5-15%</td>
</tr>
<tr>
<td>12</td>
<td>Isapghula Husk</td>
<td>Plantago ovata seeds husk has high swellability and gives uniform and rapid disintegration.</td>
<td>5-15%</td>
</tr>
<tr>
<td>13</td>
<td>Polacrillin Potassium (Kyron)</td>
<td>It swells up at very fast rate upon contact with water or gastrointestinal fluid and act as an effective tablet disintegrant.</td>
<td>10-20%</td>
</tr>
<tr>
<td>14</td>
<td>Ion Exchange Resins Ambrelite IPR 88, Indion, Doshion</td>
<td>Resins have ability to swell in the presence of water, showed disintegration of tablet.</td>
<td>0.5-5%</td>
</tr>
<tr>
<td>15</td>
<td>Gas-Evolving disintegrants (Citric Acid, Tartaric Acid, Sodium Bi-Carbonate)</td>
<td>These react in contact with water to liberate carbon-dioxide that disrupts the tablet.</td>
<td>&gt;10%</td>
</tr>
</tbody>
</table>

**Techniques for preparing Orodispersible Tablets**

Various techniques for ODTs preparation are as follow:

- Direct compression
- Freeze drying/ Lyophilization
- Moulding
- Sublimation
Direct compression (DC)

Direct Compression is the simplest and most cost-effective tablet manufacturing technique for MDTs as they can be fabricated using conventional tablet manufacturing and packaging machinery and also due to availability of tabulating excipients with improved flow, compressibility and disintegration properties, especially tablet disintegrates, effervescent agents and sugar-based excipients. Another DC-based technology; Flash tab contains coated crystals of drug and micro granules along with disintegrates.

In this technology, two types of disintegrates are used:

- a disintegrating agent (e.g., modified cellulose), which has a high swelling force
- a swelling agent (e.g., starch) which has a low swelling force.

Freeze drying/ Lyophilization

A process in which water is sublimated from the product after freezing is called freeze drying. Freeze dried forms offer more rapid dissolution than other available solid products. The lyophilisation process imparts glossy amorphous structure to bulking agent and sometimes to the drug, thereby enhancing the dissolution characteristic of the formulation. However, the use of freeze drying is limited due to high cost of equipment and processing. Other major disadvantages of the final dosage forms include lack of physical resistance in standard blister packs. R. P. Scherer patented Zydis technology by employing freeze drying process for the preparation of mouth-dissolving tablets.

![Fig. 4 Vacuum Evaporation with lyophilization](image)
Moulding

Tablets produced by moulding are solid dispersions. Physical form of the drug in the tablets depends whether and to what extent it dissolves in the molten carrier. The drug can exist as discrete particles or micro particles dispersed in the matrix. It can dissolve totally in the molten carrier to form solid solution or dissolve partially in the molten carrier and the remaining particles stay undissolved and dispersed in the matrix. Disintegration time, drug dissolution rate and mouth feel will depend on the type of dispersion or dissolution. Moulded tablets disintegrate more rapidly and offer improved taste because the dispersion matrix is, in general made from water soluble sugars. Typically, moulded tablets do not possess great mechanical strength. Erosion and breakage of moulded tablet often occur during handling and opening of blister packs.\textsuperscript{[12-16]}

Sublimation

Because of low porosity, compressed tablets composed of highly water-soluble excipients as tablet matrix material often do not dissolve rapidly in the water. Porous tablets that exhibit good mechanical strength and dissolve quickly have been developed. Inert solid ingredient (ex. Urea, urethane, ammonium carbonate, camphor, naphthalene) were added to other tablet excipients and the blend was compressed into tablet. Removal of volatile material by sublimation. Sublimation generated a porous structure. Compressed tablets containing mannitol and camphor have been prepared by sublimation technique. The tablets dissolve within 10-20 seconds and exhibit sufficient mechanical strength for practical use.\textsuperscript{[17]}

\begin{figure}
\centering
\includegraphics[width=0.5\textwidth]{sublimation.png}
\caption{Sublimation}
\end{figure}
Spray drying

Spray drying can be used to prepare rapidly dissolving tablets. This technique is based upon a particulate support matrix that is prepared by spray drying an aqueous composition containing support matrix and other components to form a highly porous and fine powder. This is then mixed with active ingredient and compressed into tablet. [18]

Mass extrusion

This technology involves softening the active blend using the solvent mixture of water soluble polyethylene glycol, using methanol and expulsion of softened mass through the extruder or syringe to get a cylinder of the product into even segments using heated blade to form tablets. The dried cylinder can also be used to coat granules of bitter tasting drugs and thereby making their bitter taste. [19]

Cotton candy process

The FLASHDOSE® is a MDDS manufactured using Shear form™ technology in association with Ceform TI™ technology to eliminate the bitter taste of the medicament. The Shear form technology is employed in the preparation of a matrix known as “floss”, made from a combination of excipients, either alone or with drugs. The floss is a fibrous material similar to cotton-candy fibers, commonly made of saccharides such as sucrose, dextrose, lactose and fructose at temperatures ranging between 180–266 °F. The manufacturing process can be divided into four steps as detailed below. [20]

- Floss Blend
- Floss Processing
- Floss Chopping and Conditioning
- Blending and Compression

Nanonization

A recently developed Nanomelt technology involves reduction in the particle size of drug to nanosize by milling the drug using a proprietary wet-milling technique. The nano crystals of the drug are stabilized against agglomeration by surface adsorption on selected stabilizers, which are then incorporated into MDTs. This technique is especially advantageous for poorly water soluble drugs. [21]
List of Minitablets available in market[^4]

Table 4 minitablets available in market

<table>
<thead>
<tr>
<th>Generic names</th>
<th>Brand names</th>
<th>Clinical Significance</th>
<th>Developer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancrelipase</td>
<td>Ultresa</td>
<td>Used in digestive disorder.</td>
<td>Aptalis Pharma</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>Olanex</td>
<td>Treatment of schizophrenia</td>
<td>Ranbaxy</td>
</tr>
<tr>
<td>Zafirlukast</td>
<td>Zuvair</td>
<td>Treatment of asthma</td>
<td>Dr.Reddy Laboratories Ltd.</td>
</tr>
<tr>
<td>Donepezil</td>
<td>Donaz</td>
<td>Treatment of Alzheimer’s disease.</td>
<td>Glenmark Pharmaceuticals</td>
</tr>
<tr>
<td>Prasugrel</td>
<td>Effient</td>
<td>Used in acute coronary syndrome</td>
<td>Eli Lilly and company Ltd.</td>
</tr>
<tr>
<td>Vorapaxar</td>
<td>Zontivity</td>
<td>Use to prevent heart attacks and strokes</td>
<td>Merck &amp; co. Inc</td>
</tr>
</tbody>
</table>

Evaluation of orodispersible Minitablets

Evaluation of the blend[^24,^25]

a) Bulk density
b) Tapped density
c) Compressibility index
d) Hausner’s ratio
**a. Bulk Density**

Bulk density is determined as per the standards of USP method-I. Weighed amount of the blend is taken and transferred to a measuring cylinder. Bulk volume of the blend is noted as per the reading on the measuring cylinder, and the bulk density is calculated using the following formula:

\[
\text{Bulk density} = \frac{\text{Mass of the blend}}{\text{Bulk Volume of the blend}}.
\]

**b. Tapped Density**

Tapped Density is determined using the tapped density tester. Weighed amount of the blend is poured into the graduated cylinder of the tester, which is then operated for 500 taps. Tapped density is calculated by the following formula:

\[
\text{Tapped density} = \frac{\text{Mass of blend}}{\text{Tapped Volume of the blend}}.
\]

**c. Compressibility Index (Carr Index)**

Compressibility index is an important measure and is calculated from the readings of bulk and tapped densities. It indicates the flow properties of the blend. Low percentage of Carr index indicates free flowing powder, whereas high Carr index represents poor flowing powder.

\[
\text{CI} = \frac{(\text{TD} - \text{BD}) \times 100}{\text{TD}}
\]

Where,

- \( \text{Cl} \) = Carr Index
- \( \text{TD} \) = Tapped density
- \( \text{BD} \) = Bulk density

**d. Hausner’s Ratio**

Even Hausner’s ratio indicates the flow properties of the powder blend and is measured by the ratio of tapped density to bulk density.

Hausner’s ratio = Tapped density / Bulk density

**Evaluation Tests for orodispersible Mini-tablets**[^26-29]

- a. Hardness
- b. Thickness
- c. Diameter
- d. Weight variation test
- e. % friability
- f. Wetting time
- g. Dispersion time
- h. Disintegration time
- i. In-vitro dissolution study
j. Stability studies

**Hardness**
The hardness of the tablet is determined using Pfizer hardness tester and expressed in kg/cm².

**Thickness**
Thickness of the tablet is measured using a digital callipers and screw gauge. It is expressed in terms of mm.

**Weight Variation Test**
For this test, 20 tablets are selected randomly from the batch and the individual weight of each tablet is noted. From this, the average weight is calculated. According to USP, none of the individual tablet weight should be less than 90% and more than 110% of the average weight.

**Friability (F)**
Friability test is conducted using Roche friabilator. For this, usually 20 mini-tablets are selected randomly from each batch and their initial weight ($W_i$) is noted. These tablets are then transferred to the drum of friabilator and rotated at appropriate rpm for definite time period. After which the mini-tablets are collected and weighed again ($W_f$). The percentage friability is then calculated by the following formula:

$$F=(1- \frac{W_i}{W_f}) \times 100$$

Where,

- $W_i$ = initial weight
- $W_f$ = final weight

**Wetting time**
Tissue paper were cut circularly and placed in petridish. A tablet was kept over tissue paper carefully and 10 ml of water is added. The time required to reach at the top surface of tablet and completely wet them was noted.

**In vitro dispersion time**
Tablet was added to 10 ml of phosphate buffer solution pH 6.8 (pH of saliva) at $37 \pm 0.5^\circ$C. time required for complete dispersion of tablet was measured.

**Invitro Disintegration time**
*In vitro* disintegration time carry out by using 200ml distilled water in 250ml beaker at $37\pm0.5^\circ$C temperature.

**In vitro dissolution studies**
In vitro drug release studies are carried out in USP type II dissolution test apparatus at specific rpm and temperature for definite time period in suitable buffer solution. All these factors depend on that particular formulation. From this, 10 ml of sample is withdrawn and analyzed using UV spectrophotometer at appropriate wavelength. After this, drug release is tested for definite time period, at same temperature and same rotational speed. At all time points (0, 5, 10, 15 and 30 minutes), 10 ml of the sample is withdrawn, and analyzed using UV spectrophotometer.\footnote{30}

**Stability Studies**

Stability studies are an integral part of the drug development process and they play an important role during the registration of pharmaceutical products. They are conducted as per ICH guidelines. Stability studies helps to identify the changes in the quality of a drug substance with time under the influence of environmental factors like temperature, humidity and light. It gives an idea regarding the recommended storage conditions and re-test periods. Stability assessment of a substance helps in the determination of its degradation products. In this, the tablets are stored in suitable containers and analyzed at specific intervals for various parameters like appearance, assay of API, determination of degradation products, hardness, disintegration time, dissolution time etc., Stability studies are conducted at following conditions. \footnote{31}

**Storage conditions:** 40°C ± 2°C /75%RH ± 5%RH, 25°C ± 2°C /60% RH ± 5% RH

**CONCLUSION**

The popularity of ODTs has increased tremendously over the last decade. Based on the literature surveyed, it may be concluded that Orodispersible tablets are particularly beneficial to the pediatric, geriatric, bedridden, and psychotic patients affected by dysphagia. These tablets get converted into a suspension with the salivary fluid in the oral cavity thereby showing rapid onset of action with improved bioavailability, better patient acceptance and offer better safety as compared to conventional oral dosage forms.

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