
Shweta Bhakare¹, Ajay G. Pise²

¹Department of Pharmaceutics, Dadasheb Balpande College of Pharmacy, Nagpur 440037, Maharashtra, India; ²Department of Quality Assurance, Dadasheb Balpande College of Pharmacy, Nagpur 440037, Maharashtra, India.

ABSTRACT

When it comes to the design of dosage forms, the ease of medication administration and patient compliance are given significant consideration. Recently developed and emerging technologies may be used to make durable, multifunctional tablets that have exceptional flavour masking properties and controlled release. It is possible to consume orally disintegrating tablets (ODTs) without drinking water since they breakdown in the mouth in less than 60 seconds and dissolve completely in the mouth. Rapid disintegration of the tablet results in rapid dissolving and, as a result, rapid beginning of action. ODTs are a suitable dosage form for special populations such as paediatrics, geriatrics, psychotic patients, patients who are unable to swallow properly, bedridden patients, unconscious patients, young patients with a poorly developed muscular and nervous system, patients who have hand tremors, and patients who travel frequently. Good stability, correct dosage, simplicity of manufacture, and reduced packing size are all advantages; self-administration is allowed throughout the trip since water is not necessary. It is also environmentally friendly. ODTs are a cost-effective technique of delivering medications. When a medicine is absorbed via the buccal cavity, oral drug delivery systems (ODTs) are very significant. For the production of ODTs, a variety of scientific procedures have been used, including spray drying, sublimation, freeze drying, moulding, and direct compression. Today, ODTs are more readily accessible as over-the-counter medications for the treatment of a broad range of disorders than they were before. The purpose of this article is to discuss the benefits, limits, formulation issues, manufacturing procedures, patented technologies, and commercially available formulations of ODTs in general.

Key Words: Oral Disintegrating Tablet, Techniques, Technology, Patent, Formulation, Challenges

INTRODUCTION

Orally disintegrating tablets are defined as follows by the United States Food and Drug Administration (USFDA) “A solid dosage form which contain a medicinal substance or active ingredient which disintegrates rapidly within a matter of seconds when placed upon a tongue”. ¹

USFDA responded to this challenge with the publication of Guidance for Industry: Orally Disintegrating Tablets are stand out a final guidance:

- ODTs should have an in vitro disintegration time of approximately 30 s or less.
- The orally disintegrating tablet weight should not exceed 500 mg. ²

First-generation Oral Disintegrating Tablet

However, while first-generation ODT technologies produce tablets that dissolve quickly in the mouth, provide convenience and ease of swallowing, and have enjoyed considerable success in the market, some of them fall short in terms of taste masking and the ability to accommodate high doses. Additionally, because most first-generation technologies can only handle small amounts of APIs, their therapeutic applications are limited and they are only used in immediate-release formulations. Most first-generation ODTs have high porosity and low density while also having poor hardness. As a result, they are fragile and difficult to handle. The upshot is that blister packaging, which is less convenient for patients than bottles and incurs more manufacturing costs, is often used instead. ³

Corresponding Author:
Dr. Ajay G. Pise, Professor, Department of Quality Assurance, Dadasheb Balpande College of Pharmacy, Nagpur 440037, Maharashtra, India ajaygpise@gmail.com.

ISSN: 2231-2188 (Print) ISSN: 2231-685X (Online)
Received: 18.03.2022 Revised: 27.03.2022 Accepted: 22.04.2022 Published: 20.05.2022
New generation of Oral Disintegrating Tablets
It is possible to combine a new generation of ODTs with a patented technique to improve taste masking, allow for a customised release profile, and increase bioavailability. This allows formulators to disguise even the most unpleasant tastes in medications by using large dosages of active pharmaceutical ingredients (API), hence expanding the spectrum of therapeutic uses. These ODTs are made up of fast dispersion micro grains, a direct compression mix, and an external tablet lubricating mechanism, among other things. As a consequence, an ODT with exceptional physical strength, mouthfeel, and disintegration qualities has been created. According to the intensity of the dose, the tablets dissolve in 15 to 30 seconds (depending on the dosage strength), resulting in an easy-to-swallow combination of API granules and carrier that is smooth and pleasant smelling. The tablets are manufactured on ordinary presses and may be printed on both sides. They have a friability of less than 0.5 percent and can be packed in bottles or blister packs, depending on the application.  

ADVANTAGES OF AN ORALLY DISINTEGRATING TABLET
Following are the advantages of orally disintegrating tablet:
1. Compliance on the part of the patient.
2. It has a rapid beginning of effect and may have a higher bioavailability than other medications.
3. Beneficial for individuals with pediatric, geriatric, and mental conditions.
4. It is appropriate for use when travelling in areas where water may not be readily accessible.
5. No special packaging is needed; push through blisters may be used to package the product.
6. A smooth mouth feel and a pleasant taste are provided.
7. Manufacturing equipment that is conventional in nature.
8. It is cost-effective.
9. The oral solid dose form is chemically stable.

CHARACTERISTICS OF AN IDEAL ORALLY DISINTEGRATING TABLET
Orally disintegrating drug delivery system should possess following characteristics:
1. A technique of manufacturing that is both efficient and cost-effective.
2. Do not need the use of water for oral administration.
3. Within seconds, the tablet will dissolve, spread, and decompose inside of the mouth.
4. Provide a pleasant tongue feel while also hiding the flavour.
5. They are less friable and have a reasonable amount of toughness.
6. After administration, there should be little or no residual in the mouth.
7. Production is carried out utilising traditional manufacturing methods.

CHOICE OF DRUG CANDIDATE
Suitable drug candidate for orally disintegrating tablet should posses:
1. There is no bitter flavour.
2. Excellent stability in both water and saliva.
3. The dosage should be kept as low as possible.

Unsuitable drug candidate for orally disintegrating tablet should include:
1. A short half-life and the need for repeated dosing
2. The drug has a very bitter taste.
3. The need for regulated or sustained release is required.

TECHNIQUES OF ORALLY DISINTEGRATING TABLET

Freeze Drying
When you dry something at a low temperature under conditions that entail the elimination of water through sublimation, you are lyophilizing it. The drug is suspended in a water-soluble matrix, which is subsequently freeze dried to create a porous structure with high porosity. When put in the oral cavity, the lyophilized tablets disintegrate fast in less than 5 seconds as a result of the rapid penetration of saliva into the pores of the tablet when it is frozen. Heat-sensitive medications, also known as thermo-labile compounds, may benefit from lyophilization. Using the freeze drying approach, investigators created a lyophilized tablet. It is possible to manufacture a lyophilized tablet by distributing the medication ketoprofen in an aqueous solution of highly water soluble carrier consisting of gelatin, glycine, and sorbitol in blister packs and then subjecting the tablet to lyophilization in blister packs. It was discovered that the rise in solubility of ketoprofen from lyophilized tablet matrix was roughly three times more than the increase in solubility of the plain drug, and that this was attributable to the supersaturation caused by the amorphous form of the medication.

Spray Drying
Spray drying has the potential to generate extremely porous and fine powders that dissolve quickly in water. Using a particulate support matrix, which is created by spray drying an aqueous composition containing the support matrix and other components to form a highly porous and fine powder, this technique can be applied to a variety of applications. This is then combined with the active components and crushed...
into tablets for administration. Varieties of supporting agents such as gelatin (hydrolyzed and non-hydrolyzed), mannitol (a bulking agent), sodium starch glycocyte or crosscarmellose sodium (a disintegrating agent), as well as acids (such as citric acid) and/or alkalis (such as sodium bicarbonate) have been reported to be used in formulations to improve disintegration and dissolution characteristics. When a tablet compacted from spray dried powder was submerged in an aqueous media, it decomposed within 20 seconds of contact. Explorers employed a spray drying process to create pills that dissolve quickly. The tablets created using this technology, according to the manufacturer, will dissolve in 20 seconds. 9

Molding
The solid dispersions produced by this process are used to make the tablets. Molded tablets have a better flavour than unmolded tablets because of the water-soluble carbohydrates included in the dispersion matrix. Different molding techniques can be used to prepare mouth-dissolving tablets:

a. Compression molding: This procedure comprises moistening the powder mix with a hydro-alcoholic solvent, compressing it onto mould plates, and then drying it in the open air to eliminate any remaining solvent. Such tablets are less compact than compressed tablets and have a porous structure that aids in the speedy disintegration of the tablet contents.

b. Heat molding: The moulding of orodispersible tablets may be accomplished directly from a molten matrix in which the medication is dissolved or distributed. The heat moulding method includes the settling of a molten material containing a dispersed or dissolved medication, which results in the formation of tablets. It is necessary to produce a suspension or solution of the medicine, agar, and sugar, which will be put into the blister packing during this procedure. It is then dried under pressure at 30°C while the agar solution solidifies at ambient temperature to make a jelly. Because of the presence of water-soluble carbohydrates in the newly developed orally disintegrating tablets, it was discovered that they improved the mouth feel. 10

Phase Transition Process
To make orally disintegrating tablets without the need of specialised equipment, it is necessary to use a mix of low and high melting point sugar alcohols, as well as a phase transition during the production process. Tablet made by compressing a powder containing two sugar alcohols with differing melting points and then heating it at a temperature between their two melting points is used in this instance. To make orally disintegrating pills, erythritol and xylitol powders were compressed and then heated at around 93°C for 15 minutes, according to the manufacturer. The median pore size of the tablets was raised after heating, and the hardness of the tablets was also enhanced after heating. The crystal state of the lower melting point sugar alcohol was not a factor in the increase in tablet hardness that occurred after heating and ageing. The influence of the production process on the qualities of orally disintegrating tablets produced employing phase transition of sugar alcohol has been examined. After heating, a rise in interparticular bonding or binding surface area occurs, which results in an increase in tablet hardness. Prior to heating, a tablet’s hardness was insufficient due to a poor compatibility. 11

Melt Granulation
PEG 6-stearate (Superpolystate®) was used as a hydrophilic waxy binder in the formulation developed to produce an orally disintegrating tablet. It has a melting point between 33 and 37 degrees Celsius and an HLB value of 9. It has a binding effect on the tablet and boosts the physical resistance of the tablet. The pill disintegrates more quickly when placed in the mouth, and no residue is left in the oral cavity as a result. Researchers used the melt granulation technique to create the first orally disintegrating tablets of Carbamazepine. The granules were made without the use of solvents or water by melting polyethylene glycol (PEG-4000) as a melting binder and lactose monohydrate as hydrophilic filler and then drying them. Researchers discovered that the dissolution patterns of granules containing crosspovidone as an intragranulating agent were almost identical to those of granules made without it. Additionally, the extragranular addition of a minor quantity of crosspovidone resulted in a further improvement in the disintegration rate and dissolving performance of the compound. 12

Sublimation
In this process, volatile chemicals (such as camphor, ammonium bicarbonate, naphthalene, urea, urethane and other similar substances) are added to other tablet excipients before the combination is compacted into tablets. The sublimation of entrapped volatile material results in the creation of a porous structure, which is subsequently eliminated from the system. Despite the fact that these compressed tablets have a high porosity (about 30%), they dissolve swiftly in saliva, dissolving within 15 seconds. A variety of solvents, including as cyclohexane, benzene, and others, may also be employed as pore generating agents to create pores in the membrane. Through the use of this technology, it has been possible to create orodispersible tablets with a highly porous structure and great mechanical strength. Scientists created very porous compressed tablets using a compression technique. They employed mannitol as a tablet matrix material and camphor as a subliming agent in the production of their tablets. Camphor was removed from the tablets by sublimating them in a vacuum at 800 degrees Celsius for 30 minutes, causing pores to form in the tablets. To produce a fast-dissolving tablet, researchers presented
a technique that used water as a porous substance to build pores in the tablet. When they made the tablets, they soaked them with water (1-3 percent weight-for-weight) before compressing them into tablets containing active component and carbohydrates (glucose, mannitol, xylitol, etc). After that, the water was evaporated, resulting in an extremely porous tablet.  

Mass Extrusion
It is used in this technique to soften a mixture of active drug and other ingredients using a solvent mixture of water soluble polyethylene glycol and methanol, and then the softened mass is extruded through an extruder or a syringe to produce a cylinder of product, which is then cut into even segments with the help of heated blades to produce tablets. The dried cylinder may be used to coat the granules of bitter-tasting medications, masking their harsh flavour in the process.  

Cotton Candy Process
It is achieved by the use of a special spinning mechanism that produces a crystalline structure that looks like floss. The development of a matrix of polysaccharides or saccharides occurs as a result of the simultaneous action of flash melting and spinning in the cotton candy process. The matrix that has been created has been partly recrystallized in order to increase its flow properties and compressionibility. This candy floss matrix is then ground and combined with the active components and excipients before being crushed into an orally disintegrating tablet form for administration. This technique is capable of accommodating higher drug concentrations while also providing increased mechanical strength. The high process temperature, on the other hand, restricts the use of this technique.  

Direct Compression
This is the most often used approach due to the ease with which it may be implemented and the low cost involved. In order to do this, disintegrants, water-soluble excipients, and/or effervescent agents must be added to the mixture at various stages. Superdisintegrants are most often employed at the optimal concentration (about 2-5 percent) in order to ensure quick disintegration while maintaining a pleasant mouth feel. For an oral disintegrating tablet, Bi et al. investigated the disintegrant ability of a combination of microcrystalline cellulose and low substituted hydroxypropyl cellulose (MCC-L-HPC). They discovered that the lowest disintegration time was recorded in the range of the MCC:L-HPC ratio (8:2 to 9:1). Cousin and colleagues developed an orally disintegrating tablet that included carboxymethyl cellulose as a disintegrating agent and a swelling agent made of modified starch or microcrystalline cellulose as the swelling agent. The pills dissolve in less than 60 seconds after they are placed in the mouth. A rapid dissolving tablet of galanthamine hydrobromide was developed, and it is composed of a diluent that is a spray dried mixture of lactose monohydrate and microcrystalline cellulose in the ratio of 75:25, a cross linked polymeric disintegrant such as crosspovidone, and a direct compression process for the preparation of rapid dissolving tablets. It was discovered that tablets made from treated agar powder disintegrating at a rate comparable to other superdisintegrating agents when they prepared an ondansetron mouth dissolving tablet using treated agar as a superdisintegrating agent.  

PATENTED TECHNOLOGIES FOR ORALLY DISINTEGRATING DRUG DELIVERY SYSTEM
The various technologies are developed for the preparations of Orally Disintegrating Drug Delivery System are:  

1. Zydis
2. Wowtab
3. Durasolv
4. Frosta
5. Flashdose
6. Nanocystal Technology
7. EFVDAS
8. Multiflash
9. Lycos
10. Flashtab
11. OraSolv
12. AdvaTab
13. OraQuick
14. Quick-Dis Technology
15. FastMelt

The list of patented technology pertaining to orally disintegrating drug delivery systems, developed by various international companies and their products are enlisted in Table 1.

**Table 1: Orally disintegrating tablets patent technologies and products.**

<table>
<thead>
<tr>
<th>Technology</th>
<th>Patent Technology</th>
<th>Company</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>LYOPHILIZED</td>
<td>Zydis</td>
<td>Catalent</td>
<td>Grazax, Claritin</td>
</tr>
<tr>
<td></td>
<td>Lyoc</td>
<td>Cephalon</td>
<td>Loperamide</td>
</tr>
<tr>
<td></td>
<td>Quickslv</td>
<td>Janssen</td>
<td>Risperdal</td>
</tr>
<tr>
<td>COMPRESSED</td>
<td>AdvaTab</td>
<td>Eurand</td>
<td>Cetirizine</td>
</tr>
<tr>
<td>TABLET</td>
<td>Orasolv/ Flashtab</td>
<td>Cima Labs</td>
<td>Niravam</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ethypharm</td>
<td>Ibuprofen</td>
</tr>
<tr>
<td>SUGAR FLOSS</td>
<td>Flashdose</td>
<td>Biovial</td>
<td>Ralivia</td>
</tr>
<tr>
<td>MOLDED</td>
<td>WOWtab</td>
<td>Yamanouchi</td>
<td>Benadryl</td>
</tr>
<tr>
<td>TABLET</td>
<td></td>
<td>Astellas</td>
<td>FastMelt</td>
</tr>
</tbody>
</table>
CHALLENGES IN FORMULATING ORALLY DISINTEGRATING TABLET

**Palatability**
Because the majority of medications are unpalatable, orally disintegrating drug delivery systems often include the medication in a flavor-masked form. The delivery mechanisms breakdown or dissolve in the oral cavity of the patient. Because the active chemicals are released when the medication comes into touch with the patient’s taste receptors, taste-masking of the medication becomes crucial to patient compliance. 18

**Mechanical strength**
Because they are composed of soft-molded matrices or compacted into tablets with very little compression force, FDTs are friable and brittle when they are placed in the oral cavity, allowing them to dissolve in the mouth. The use of certain technologies may result in tablets that are sufficiently hard and robust to enable them to be packed in multiple-dose containers. 19

**Hygroscopicity**
Under normal settings, certain orally disintegrating dosage forms are hygroscopic, and as a result, these dosage forms lose their physical integrity. The most significant factor is the temperature and humidity. As a result, protecting them against humidity is critical, necessitating the use of particular product packaging. 20

**Amount of drug**
Every unit dosage can only contain a certain quantity of medicine due to the limitations of the manufacturing process. It is necessary that the medication dose for lyophilized dosage forms is not more than 400 mg for insoluble pharmaceuticals and less than 60 mg for soluble drugs. It was observed that while making fast-dissolving oral films or wafers, this parameter is the most difficult to control. 21

**Aqueous solubility**
The majority of the medications are water-soluble. There are several formulation issues associated with these compounds because they create eutectic mixtures, which result in freezing-point depression and the creation of glassy solids that may collapse when dried as a consequence of the sublimation process. The use of mannitol, which imparts stiffness to the amorphous composite, may occasionally prevent collapse from occurring. 22

**Size of tablet**
The size of a pill has an impact on how easy it is to swallow while you are taking it. It has been claimed that the simplest size of tablet to swallow is 7-8 mm, with a tablet bigger than 8 mm being the most difficult to grasp and swallow. The difficulty arises from the need to create a tablet size that is both simple to transport and simple to hold. 23

**CONCLUSION**
All of the currently available ODT technologies are based on the same fundamental concept: to maximise the porous structure of the tablet matrix in order to achieve rapid tablet disintegration in the buccal cavity while also providing good taste masking properties and adequate mechanical strength to the patient. Among the future hurdles for many ODT producers are cost reduction via the use of ordinary equipment, packaging variety, increased mechanical strength and flavour masking potential, and improved mechanical strength and flavour masking potential. Patients’ desire, as well as the availability of different technologies, has improved the acceptability of oral disintegrating tablets, which has resulted in the extension of the patent life of a medicine in certain cases. This article describes the processes and technologies that have been developed recently to aid in the production of mouth dissolving tablets. The introduction of new unique technologies for ODTs in the future days should be taken into consideration. As a result, in the near future, ODTs will have enormous potential as a drug delivery mechanism for the majority of medications.

**CONFLICT OF INTEREST**
No conflict of interest is declared.

**FUNDING INFORMATION**
No agency provided any funding.

**ACKNOWLEDGEMENT**
The authors are highly thankful to the Principal and college management for their support.

**REFERENCES**


