Mouth Dissolving Tablets: A Short Review

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Abstract—Despite a number of drawbacks, oral drug delivery systems continue to be the preferred method of medication delivery due to their extremely simple administration and increased patient compliance. By creating "mouth dissolving tablets" (MDTs), which dissolve swiftly without water in the mouth within a few seconds as a result of the act of super disintegrant or Optimising pore structure in the formulation, one issue with this unique drug delivery system can be resolved. These mouth-dispersing tablets are particularly useful for children, the elderly, and individuals with mental illness who have difficulty swallowing regular tablets and capsules. The numerous formulation features, super disintegrants used, and technologies created for MDTs, along with various excipients, assessment tests, are all described in this review.

Index Terms—Fast-disintegrating tablet, Sublimation, Mouth Dissolving Tablets, MDT.

INTRODUCTION

Despite amazing advancements in drug delivery systems, the oral route is still the preferred approach for administering therapeutic agents since it is simple to use, accurate in dosage, inexpensive1, self-medication, non-invasive2, and results in higher patient compliance. Due to their underdeveloped neurological and motor control, pediatric patients may experience issues with ingesting. Additionally, the efficacy of typical tablets or capsules used for oral administration is limited in patients who are travelling without access to water3.

Due to its ease of self-administration, compactness, and ease of production, the tablet is one of the most popular dosage forms in use today4. On the other hand, elderly, young, and mentally ill patients have trouble swallowing regular pills, which results in poor patient compliance. Mouth-dissolving or disintegrating tablets5 are an innovative medicine delivery technique that scientists have created to solve these issues (MDTs). These innovative tablet varieties dissolve, disperse, or disintegrate in saliva in a matter of seconds without the need for water. These MDTs should dissolve or disintegrate in less than three minutes, under the European Pharmacopoeia6.

People with swallowing disorders and bedridden patients will benefit more from this formulation. The advantages of MDTs include increased patient compliance, quick action, enhanced absorption, and good stability, which make these tablets a popular dosage form on the market today7.

Oro-dispersible pills, fast disintegrating tablets, orally disintegrating tablets, fast dissolving tablets, rapid dissolving tablets, porous tablets, quick melt tablets8, and rapid melt tablets are other names for mouth-dissolving tablets. Despite the fact that all of the above phrases are ODTs, the USP has accepted these dosage forms. "A solid dosage form that contains medicinal drugs or active chemicals that disintegrates very swiftly within a few seconds when placed up on tongue," is how the United States Food and Drug Administration (FDA) defines ODTs9.

The preparation of the mouth-dissolving tablets primarily involves two methods, the first of which involves the use of super disintegrants like croscarmellose sodium, sodium starch glycolate, and crosspovidone[10]. However, in a different procedure, freeze drying and vacuum drying are used to maximise the pore structure of the tablets. The oral cavity and pre-gastric absorption[11] of saliva containing dispersed pharmaceuticals that pass into the stomach can both boost the bioavailability of a number of medications. In addition, less medication than in conventional tablets is submitted to the first pass metabolism[12].

STANDARD CHARACTERISTICS OF FDTs

One sort of tablet called a "quick-breakdown" or "rapid dissolving" tablet is designed to break down in the

mouth when in contact with saliva in less than a minute, preferably under 45 seconds, and to form an easily swallowable suspension. It is most commonly referred to as "orodispersible tablets[13]." An estimated 50% of the population has trouble swallowing pills or tablets. Due to this issue, the prescribed medication is not taken, which has a negative impact on the treatment's efficacy.[14]

Therefore, orodispersible pills are simple to administer for patients who struggle with deglutition or for those who choose to take their medication without drinking anything at the same time. [15]

Modern innovations in innovative drug delivery (NDDS) aim to increase the safety and effectiveness of therapeutic molecules by creating an appropriate dose form that is simple to administer and increases patient compliance. Using oral dissolving pills is one such strategy (ODTs). ODTs are solid unit dose forms that dissolve or disintegrate quickly in the mouth without the usual need for chewing, swallowing, or drinking. The needs of the patient are met without compromising the ODTs' efficacy thanks to recent developments in dosage form design. The ODTs meet the needs of the patient, who has trouble swallowing traditional pills or capsules.[16]

IDEAL PROPERTIES FDT

- Suitable for Conventional tablet processing and packaging
- Fragility Concern
- Good Mouth Feel
- Patient Compliance
- Economic
- Compatible with Taste Masking

ADVANTAGES OF FDTs [18]

1. Improved compliance/more practical, new business opportunities, product differentiation, line extension and lifecycle management, exclusive product promotion, and patent life extension.
2. No water required.
3. No chewing required.
4. Improved taste.
5. Enhanced stability.
6. Appropriate for controlled/sustained release actives.
7. Allows high drug load.
8. Ability to give advantages of liquid medication in the form of solid preparation.
9. Cost- effective.
10. Rapid drug therapy interference.
11. High drug loading is possible.
12. Have satisfactory taste and pleasant mouth feeling

DRUGs FORMULATED AS FDTs

Low dose, good aqueous media stability, acceptable mechanical strength, and compatibility with excipients are the requirements for pharmaceuticals that can be packaged as Fast Dissolving Tablets.[19]

COMMON EXCIPIENTS USED FOR FDTs PREPARATION

The following excipients are typically found in FDT, along with at least one of each of the following: sweeteners, flavors, diluents, swelling agents, and lubricants.[20]

Name of the excipients	Percentage Used
Disintegrants	1 to15%
Diluents/fillers	0 to 85%
Binder	5 to 10%
Antistatic Agent	0 to 10%

FORMULATION CHALLENGES OF FDTS

Challenges	Brief Description
Mechanical strength & disintegration time	MDTs are designed to achieve disintegration times that are typically under a minute. Maintaining adequate mechanical strength while doing so is a major difficulty. Many MDTs are readily damaged, and there are many chances that a patient will handle a fragile tablet that has been packed or transported and cause it to break. It makes perfect sense that increased mechanical strength will postpone the disintegration process.[21]
Masking of Taste	Many medications have a harsh taste. To prevent the bitter taste of the medicine from being detected in the oral cavity, appropriate taste masking must be used.[21]
The Mouth feel	Tablet should not disintegrate into bigger particles in the oral cavity. The particles generated after disintegration of the Tablet should be as small as possible. Tablet should leave minimal or

	no residue in mouth after oral administration. [21]
Environmental Sensitivity	Tablet usually should show low sensitivity to environment conditions such as humidity and temperature as most of the materials used in a Tablet are meant to dissolve in minimum quantity of water .(21)
Palatability	As the majority of drugs are unpalatable, tablets should contain the medicament in a taste-masked form. [21]
Mechanical strength to withstand sock	In order to allow ODTs to disintegrate in the oral void, they are made of either very porous and soft-molded matrices or compressed into tablets with very little compression force, which makes the tablets friable and/or brittle, difficult to handle, and often requiring specialized peel-off blister packing that may add to the cost. [21]
Hygroscopical property	Numerous orally disintegrating dosage forms are hygroscopic and cannot maintain physical integrity under normal conditions of temperature and humidity. Therefore they require protection from humidity which calls for specialized product packaging. [21]
Aqueous solubility	Due to the creation of eutectic mixtures, which lower the freezing point and lead to the formation of a glassy solid that may collapse upon drying due to the loss of supporting structure during the sublimation process, water-soluble pharmaceuticals present a variety of formulation issues. [21]
Tablet Size	It has been reported that the most easiest size of tablet to swallow is 7-9 mm even as the easiest size to handle was one larger than 8 mm.[21]
Fast Disintegration	FDTs be supposed to disintegrate in the mouth with no additional water or with a very small amount (e.g., 1–2 Ml) of water. [21]

FAST DISSOLVING DRUG DELIVERY SYSTEM CRITERIA: [22,23]

The tablets must

- Not need water to swallow, but it should dissolve or disintegrate in the mouth in matter of seconds.
- Be well-matched with taste masking.
- Be moveable without fragility concern.
- Have a pleasing mouth feel.
- Leave smallest amount or no residue in the mouth after oral administration.
- Exhibit low sensitive to environmental condition as temperature and humidity.

FAST DISSOLVING DRUG DELIVERY SYSTEM'S SALIENT FEATURE [24]

- Simplicity of administration to patients who cannot swallow, including the elderly, stroke victims, bedridden patients, patients with renal failure, and patients who refuse to swallow, including pediatric, geriatric, and psychiatric patients.
- • The dose form does not need to be swallowed with water, which is a very useful feature for patients who are on the go and do not always have access to water.
- • Rapid drug solubility and absorption, resulting in a rapid commencement of action.
- • As saliva descends into the stomach, several medications are absorbed from the mouth, pharynx, and esophagus. In such circumstances, the drug's bioavailability is boosted.
- • Pre-gastric absorption may lead to increased bioavailability and reduced dosage, which will improve clinical performance by lowering side effects.
- • A better tongue feel contributes to changing patients' perceptions of medication as a bitter tablet, especially in younger patients.
- • By avoiding physical obstructions during oral administration of the standard formulation, the risk of choking or suffocation is reduced, improving safety.
- • New business opportunities including life cycle management, product differentiation, and product promotion.
- • Useful in situations where a lightning-fast response is required, such as motion sickness, rapid allergy attacks, or coughing

- • A higher bioavailability, especially in the case of hydrophobic and insoluble medicines, as a result of the tablets' rapid dissolving and disintegration.
- Constancy for longer period of time, since the drug remains in solid dosage form till it is consumed. So, it combines advantage of solid dosage form in terms of stability and liquid dosage form in terms of bioavailability.

FAST DISSOLVING TABLETS'S BENEFITS: [24]

- Aadministered anytime, anywhere, and without water.
- Suitability for geriatric and paediatric patients who have trouble swallowing, as well as for other populations who might have trouble taking conventional oral medication because they are mentally ill, developmentally disabled, or uncooperative, or because they are nauseated. • Useful in situations like motion sickness, severe allergic attacks, or coughing where an ultra rapid onset of action is necessary.
- • Due to the tablets' rapid dissolution and disintegration, there is a better bioavailability, particularly for drugs that are insoluble or hydrophobic.
- • Longer-lasting stability due to the medication's continued use in solid dosage form. As a result, it combines the benefits of liquid dosage form in terms of bioavailability and solid dosage form in terms of stability.

MOUTH DISSOLVING TABLETS'S LIMITATIONS [25]

- The tablets typically have inadequate mechanical strength. Therefore careful handling is required.
- The tablets may leave unpleasant taste and/or grittiness in mouth if not formulated properly.

DIFFERENT TECHNOLOGIES USED FOR MANUFACTURING OF MDTS:[25]

Recent years have seen the introduction of a number of innovative cutting-edge technologies for the production of MDTs with excellent characteristics like a shorter time to disintegrate, a nice mouthfeel, exceptional flavour masking, and sugar-free tablets for diabetic patients. The technologies employed in the production of MDTs can be divided into two categories: those that are patented and those that are not.

LYOPHILIZATION OR FREEZE-DRYING:

In the creation of MDTs, the production of porous products during the freeze-drying process is utilised. In the process of lyophilization, the solvent is taken out of a medication suspension or solution that has been frozen and contains additives that help give the drug its structure. The addition of chemicals and freeze-drying of the medication creates a glossy, amorphous structure that results in a very porous and light product. When the finished tablet is placed on the tongue, it dissolves quickly and promptly releases the medication from the freeze-dried unit. However, the MDTs produced by lyophilization have poor stability at higher temperatures and limited mechanical strength. [25]

MOLDING:

The moulded tablets are made using this approach utilising water-soluble components, allowing for quick and full dissolution. The powder mixture is wet with a hydroalcoholic solvent before being compressed into tablets at a lower pressure than usual. After that, air drying is used to remove the solvent. Compressed tablets are much more compact than moulded tablets. These are porous, which speeds up dissolution. [26]

COTTON CANDY PROCESS:

This method is so named because it uses a single spinning gear to create crystal structures that resemble floss and cotton candy. By simultaneously spinning and flash melting polysaccharides or saccharides, a matrix of cotton candy is created. For better flow and compressibility, the matrix created is partially recrystallized. The subsequent milling, blending, and compression of this candy floss matrix into MDTs includes the addition of active components and excipients. [27]

SPRAY DRYING:

Due to the process's solvent evaporation, this technology creates powders that are incredibly porous and fine.

With this technique, MDTs were made using sodium starch glycolate or crosscarmellose sodium as the superdisintegrant, sodium starch glycolate or nonhydrolyzed gelatin as the supporting matrix, and both hydrolyzed and nonhydrolyzed gelatin as the bulking agent. By adding alkali or acidic substances like sodium bicarbonate, dissolution and disintegration were accelerated even further. With this method of formulation, porous powder is produced, with a 20-second disintegration time.[27]

Mass extrusion:

In this method, the active blend is softened using a solvent solution of water-soluble polyethylene glycol and methanol, and the softened mass is then ejected through an extruder or syringe to divide the product's cylinder into even segments using a heated blade to produce tablets.

MELT GRANULATION

By using this method, MDTs can be created by adding PEG-6-stearate, a hydrophilic waxy binder (super polystate). The waxy substance super polystate has a melting point between 33 and 37 degrees Celsius with a hydrophilic-lipophilic balance of 9. It helps tablets dissolve because it melts in the mouth and solubilizes quickly, leaving little trace, in addition to acting as a binder and increasing the physical resistance of tablets. Super polystate was added to MDT formulations using the melt granulation technique, in which the molten form of the material forms the granules.[27]

PHASE TRANSITION PROCESS

Erythritol (m. pt. 122°C), xylitol (m. pt. 93-95°C), trehalose (97°C), and mannitol (166°C) are used in this technique for the breakdown of MDTs via phase transition of sugar alcohols. In order to make tablets, a powder containing two sugar alcohols with contrasting melting points was compressed, and then heated to a temperature between the two alcohols' melting points. The tablets lack sufficient hardness prior to heating due of their poor compatibility. Due to the phase transition of lower melting point sugar alcohol, which enhanced the interparticle linkages or bonding surface area in tablets, the hardness of the tablet increased after heating.[28]

SUBLIMATION

The key to fast disintegration of MDTs is the presence of a very porous structure in the tablet matrix. Even while typical tablets contain chemicals that are extremely water soluble, they frequently fail to dissolve quickly due to limited porosity. Utilizing volatile compounds during the tableting process, such as camphor, which sublimated from the produced tablet, can increase porosity. developed MDTs employing camphor, a subliming component that is taken out of compressed tablets made using a mannitol and camphor combination. After making the tablets, camphor was sublimated in a vacuum for 30 minutes at 80 degrees.[28]

DIRECT COMPRESSION METHODS

Due to its low production costs, ability to handle high doses, and reduced number of processing steps, this method is a straightforward way to synthesise MDTs because the final tablet weight can easily surpass that of other production methods. Directly compressed tablets can disintegrate and dissolve either individually or in combination with effervescing agents, water-soluble excipients, and disintegrants. Tablet size and hardness have a significant impact on disintegrant efficacy. [29]

Low hardness, medium or low pill size, and low physical resistance all help to improve the disintegration qualities. To guarantee quick disintegration and high dissolution rates, it is crucial to select a disintegrant concentration that is appropriate and optimal.

Excipients that are soluble in water or effervescent agents can be combined to further enhance dissolution or disintegration qualities. Due to the combined effects of swelling and water absorption, super disintegrants promote rapid disintegration. The wetted surface of the carrier increases as a result of the super disintegrant's swelling, which improves the system's wettability and dispersibility and, as a result, speeds up disintegration and dissolution.

According to the critical concentration of the disintegrant, the best super disintegrant

concentration can be chosen. When super disintegrants are incorporated into tablets, the disintegration time is inversely proportional to their concentration under this concentration; however, if their concentration is higher than the critical concentration, the disintegration time is either constant or even increases.[30]

PATENTED TECHNOLOGIES FOR FAST DISSOLVING TABLETS

Zydis Technology:

The medicine is physically confined or dissolved inside the matrix of the fast-dissolving carrier material in the Zydis formulation, a unique freeze-dried tablet. The freeze-dried structure instantly disintegrates when zydis units are placed in the mouth; water is not required to facilitate swallowing. The zydis matrix is made up of a variety of materials that are all intended to accomplish different goals. Polymers such as gelatin, dextran, or alginates are included to add strength and resilience during handling. These take the form of a strong, glossy amorphous structure. Saccharides like sorbitol or mannitol are added to materials to increase crystallinity, elegance, and toughness. In the manufacturing process, water is employed to ensure the formation of porous units for fast disintegration, and different gums are used to stop the sedimentation of dispersed drug particles. During the freeze-drying process or during long-term storage, collapse protectants like glycine stop zydis units from shrinking. To shield the formulation from environmental moisture, Zydis products are packaged in blister packs. [30]

Durasolv Technology:

Durasolv is the one of the patented technology of CIMA labs. The tablets made by this technology consist of drug, filler and a lubricant. Tablets are prepared by using conventional tabletting equipment and have good rigidity. These be able to be packaged into conventional packaging system like blisters. Durasolv is an suitable technology for product requiring low amounts of active ingredients. (30)

Orasolv Technology:

Orasolv Technology was created in CIMA labs. This technique masks the taste of the active medication. Additionally, it contains an effervescent disintegrant. To reduce the amount of time needed for oral dissolving, tablets are manufactured using the direct compression technique at low compression force. The tablets are made using standard blenders and tablet machines. The manufactured tablets are pliable and squishy.[31]

Flash Dose Technology:

Fuisz was the first to patent flash dosage technology. The first commercial product introduced by Biovail Corporation is the "Nurofen Meltlet," an unique formulation of ibuprofen in the form of melt-in-mouth tablets created using flash dosage technology. Flash dosage tablets are made of "floss," a self-binding shear form matrix. Flash heat processing is used to create shear form matrices.[31]

Wow tab Technology:

Yamanouchi Pharmaceutical Co. has patented the technology behind Wow tabs. WOW is short for "Without Water." In this research, a combination of low and high mouldability saccharides is used to create a robust tablet that melts quickly. The active component is combined with a low moldability saccharide, such as lactose, glucose, and mannitol, then granulated with a high mouldability saccharide, such as maltose or oligosaccharides, and then compacted into tablets.[32]

Flash tab Technology:

Prographarm laboratories have obtained a patent for its Flash tab technology. The active ingredient in the tablet created using this technology is in the form of tiny crystals. The traditional methods of coacervation, micro encapsulation, and extrusion spheronization can be used to create drug micro granules. All processing was done using standard tabletting technology. [33]

EVALUATION OF THE MOUTH DISSOLVING TABLET

MDTs formulations have to be evaluated for the following evaluation test parameters,

Organoleptic properties:
Dimensionally describeable, trackable, and controllable tablet size and shape. Tablet Tablet thickness is a crucial element in both replicating appearance and counting with filling machinery. The uniform thickness of the tablets is used as a counting mechanism by some filling equipment.[34]

Tablet thickness:
In addition to being included when utilising filling equipment, tablet thickness is a crucial property to reproduce. The constant tablet thickness can be used as a counting mechanism by some filling equipment. We took ten tablets, and we used a micrometre to measure their thickness.[35]

Uniformity of weight:
Twenty tablets were ingested, and their weights were calculated individually and collectively on a digital weighing balance in accordance with the I.P. protocol for homogeny of weight. The group weight was used to calculate the average weight of one pill. The weight variation test would provide a reliable way to assess the uniformity of the medication content.[36]

Average weight of Tablet (mg)	Permissible difference (%)
130 or less	10
130-324	7.5
More than 324	5

Tablet hardness:
Due to the unique procedures and materials employed in the manufacturing, achieving one of ODT's key strengths is challenging. To encourage early dissolution in the mouth, the ODT's hardness threshold is typically kept at a lower range. Conventional hardness testers can be used to determine the tablet's hardness. The force needed to break a tablet across its diameter is referred to as the tablet's hardness. The hardness of the tablet determines how resistant it is to breaking, chipping, or abrasion when handled before use and during storage transformation. Using a Monsanto Hardness tester, the hardness of each formulation's tablet was assessed.[37]

Friability:
It can be difficult for a formulator to keep an ODT's% friability within acceptable bounds because all ODT manufacturing processes increase the% friability values. This parameter must therefore be examined, and the findings must fall within the acceptable range (0.1-0.9%). The mechanical strength of tablets is measured. The following approach was done to determine the friability using the Roche friabilator. The friabilator was loaded with a pre-weighed tablet. With each revolution, the plastic chamber of a friabilator, which rotates at 25 revolutions per minute, drops the tablets six inches away. For at least 4 minutes, the tablets were spun in the friabilator. The drop in tablet weight was measured after the test tablets had been dusted and reweighed. Friability is the measure of friability and is expressed in percentage as[38];
%Friability = loss in weight / Initial weight x 100

In-Vivo Disintegration test:
Six tablets were tested using the equipment described in I.P.-1996. Distilled water was used as the disintegration media at a temperature of 37°C 2°C, and the time in seconds required for full tablet breakdown with no appetising mass left in the apparatus was recorded.[39]

Wetting time:
To measure tablet wetting time, the procedure described by Yunixia et al. was used. In a tiny petridish (ID = 6.5 cm) filled with 6 ml of Sorenson's buffer pH 6.8, a piece of tissue paper (12 cm X 10.75 cm) was folded twice. On the paper, a tablet was placed, and the duration of complete wetting was timed. The standard deviation and three trials for each batch were also calculated.[40]
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In vitro dispersion time:
Six tablets were tested using the equipment described in I.P.-1996. Distilled water was used as the disintegration medium at a temperature of 37°C 2°C, and the time in seconds required for the tablet

to completely disintegrate with no appetising mass left in the device was recorded. By dropping a tablet into a beaker that was filled with 50 ml of Sorenson's buffer pH 6.8, the in vitro dispersion time was calculated. Three tablets were chosen at random from each formulation, and in vitro dispersion time was measured.[42]

Dissolution test:

Drugs that may dissolve under certain conditions are typically described in USP monographs. For the same purposes as their conventional tablet equivalents, ODT should be evaluated using additional media such as 0.1 N Hcl, pH 4.5, and pH 6.8 buffers. Experience has shown that the USP 2 paddle apparatus, with a typical paddle speed of 50 rpm, is the most suited and popular option for the dissolve test of ODT tablets. ODTs often dissolve quite quickly under the USP monograph conditions. Thus, a comparable profile can be obtained using slower paddle speeds. The formation of a mound in the dissolution vessel is possible with large tablets weighing close to or surpassing one gramme and having reasonably dense particles; this can be avoided by increasing the paddle speed.[43]

CONCLUSION

Due to its potential advantages over conventional dosage forms—better patient compliance, ease, bioavailability, and quick beginning of action—many manufacturers have been paying attention to MDTs for more than a decade. Some of these technologies have produced MDT formulations with enough mechanical strength and rapid disintegration/dissolution in the mouth without water. Both geriatric patients who have lost all of their teeth and children who have lost their main teeth can utilise these MDTs without any problems. They remain solid while in storage, helping to maintain the stability of dosage forms, and change into liquid form shortly after being administered. In the near future, MDTs might be created for the majority of the medications already on the market because they offer significant advantages as both solid and liquid dosage forms.

FDTs are dose forms designed to dissolve or disintegrate swiftly in the saliva, typically in a matter of seconds. FDTs have a number of benefits over traditional dose forms, including increased patient compliance, improved efficacy, and bioavailability. Children and elderly people are more comfortable thanks in particular to FDTs. Depending on the medicine and additives utilised, many procedures can be employed to manufacture FDTs. FDTs often have less mechanical strength. But it is possible to create FDTs with adequate mechanical strength by using some innovative technologies and additives.

An important principle used in the creation of the fast-dissolving tablet was to increase pore structure. Researchers have experimented with vacuum drying and freeze-drying methods to enhance the pore structure of tablet matrix. Freeze drying is cumbersome and results in a delicate and porous product. In order to increase the porosity of the tablets, a subliming agent was added before using a vacuum-drying process in the current study. By adding flavour masking chemicals, even bitter medications can be included to FDTs. FDT research is still under progress. FDTs also provide extensive marketing, which helps the dosage form succeed in the market. Future medication formulations will often be FDTs due to the market potential.

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