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A review on mouth dissolving tablets

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Abstract
Mouth dissolving tablets (MDTs) are novel dosage forms containing drugs that disintegrate in the oral cavity within less than one minute leaving an easy-to-swallow residue. In the current trend the development of mouth dissolving tablets formulation is originate and gaining popularity because these tablets dissolve in the mouth within a few seconds without the help or need of any drinking agent like water. These tablets achieves the higher concentration in the body to provide the immediate action. Recently, the oral delivery is the gold standard in the pharmaceutical industry because it is the easiest, safest, economical and convenient method for the drug delivery and having highest patient compliance. Mouth dissolving tablets are suitable for the pediatric, geriatric, bedridden, mentally disabled patients and for active patients who are busy and traveling and may not have access to water and these will show the effective action in few minutes**.** Here in this article, we mainly highlights on, advantages, disadvantages, main ingredients, mechanism of action of disintegrants, approaches for preparation, patented technologies, evaluation parameters of mouth dissolving tablets.

Keywords: mouth dissolving tablets, patient compliance, disintegrants, patented technologies

Introduction

Patient compliance is one of the most important aspects in the pharmacy practice. Now days, pharmacy companies are coming up with development of new drug delivery systems to ensure the delivery of the drugs to the patients efficiently and with fewer side effects. This objective led to the emergence of the concept of Mouth Dissolving Tablets. A fast-dissolving drug delivery system, in most cases, is a tablet that dissolves or disintegrants in the oral cavity without the need of water or chewing. Most fast dissolving delivery system films must include substances to mask the taste of the active ingredient. This masked active ingredient is then swallowed by the patient's saliva along with the soluble and insoluble excipients. This attribute makes these dosage forms highly attractive product for the pediatric, geriatric and dysphagic patients [1, 2].

The MDT is also known as fast melting, fast dispersing, rapid dissolve, rapid melt, and or quick disintegrating tablet. All MDTs approved by the Food and Drug Administration (FDA) are classified as orally disintegrating tablets. Recently, the European Pharmacopeia adopted the term orodispersible tablet for a tablet that disperses or disintegrates in less than 3 minutes in the mouth before swallowing. Such a tablet disintegrates into smaller granules or melts in the mouth from a hard solid to a gel-like structure, allowing easy swallowing by patients. The disintegration time for good MDTs varies from several seconds to about a minute [3, 4, 5]. Orally disintegrating tablets provide an advantage particularly for pediatric and geriatric populations who have difficulty in swallowing conventional tablets and capsules. Additionally, pediatric patients may suffer from ingestion problems as a result of underdeveloped muscular and nervous control. Moreover, patients traveling with little or no access to water, limit utility of orally administered conventional tablets or capsules. Mouth dissolving of tablet results in quick dissolution and rapid absorption which provide rapid onset of action. Moreover, drug candidates that undergo pre-gastric absorption when formulated as MDTs may show increased oral bioavailability. It provides good stability, accurate dosing, easy manufacturing [6, 7]

MDT's are mainly used in some serious conditions like:

- Motion sickness [8, 9]
- Parkinsonism
- Pediatric and geriatric patients
- Unconsciousness
- Mentally disabled patients
- Absence of water

MDT**:** These are the tablets which dissolve or disintegrate quickly in the saliva to show their action within few seconds without the help if water. A mouth dissolving tablet mainly dissolves in the mouth within 15sec-3mins. Mostly the MDT's superdisintegrants and taste masking agents [10].

Ideal properties of Mouth Dissolving Tablets

1. Require no water for oral administration,yet dissolve/disperse/disintegrate in mouth in a matter of seconds.
2. It should have pleasant mouth feel.
3. It should have an acceptable taste masking property.
4. It should have sufficient hardness to withstand rigors during manufacturing processes and post manufacturing handling.
5. It should allow high drug loading.
6. Should leave minimal or no residue in mouth after disintegration.
7. Should exhibit low sensitivity to environmental conditions (temperature and humidity).
8. It Should allow the manufacture of tablet using conventional processing and packaging equipments.

9. It should be cost effective.

Advantages of MDT

- No need of water to swallow the tablet [11].
- Can be easily administered to pediatric, elderly and mentally disabled patients.
- Accurate dosing [12] as compared to liquids.
- Dissolution and absorption of drug is fast, offering rapid onsetof action.
- Bioavailability of drugs is increased [2] as some drugs are absorbed from mouth, pharynx and esophagus through saliva passing down into the stomach [13].
- Advantageous over liquid 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 [14].
- Allows high drug loading [15].

Disadvantages [16]

- Fast dissolving tablet is hygroscopic in nature so must be keep in dry place.
- Some time it possesses mouth feeling.
- MDT requires special packaging for properly stabilization & safety of stable product [17].

Main ingredients used in Preparatio of MDT

Important ingredients that are used in the formulation of MDTs should allow quick release of the drug, resulting in faster dissolution. This includes both the actives and the excipients. Disintegration and solubilzation of a directly compressed tablet depend on single or combined effects of disintegrants, water-soluble excipients and and effervescent agents. Excipients balance the properties of the actives in FDDTs. This demands a thorough understanding of the chemistry of these excipients to prevent interaction with the actives. Determining the cost of these ingredients is another issue that needs to be addressed by formulators. The role of excipients is important in the formulation of fast-melting tablets. These inactive food-grade ingredients, when incorporated in the formulation, impart the desired organoleptic properties and product efficacy. Excipients are general and can be used for a broad range of actives, except some actives that require masking agents. Binders keep the composition of these fast-melting tablets together during the compression stage.

The right selection of a binder or combination of binders is essential to maintain the integrity and stability of the tablet. The temperature of the excipient should be preferably around 30–35C for faster melting properties. Further, its incorporation imparts smooth texture and disintegration characteristics to the system. Binders can either be liquid, semi-solid, solid or mixtures of varying molecular weights such as polyethylene glycol. The choice of a binder is critical in a fast- dissolving formulation for achieving the desired sensory and melting characteristics, and for the faster release of active ingredients. Commonly available fats such as cocoa butter and hydrogenated vegetable oils can also be used.

Table 1: Material used in preparation of mouth dissolving tablet

Drug and Excipients	Supplied by
Telmisartan	A gift sample from Glenmark Pvt Ltd, Nashik.
Tulsion 671	A gift sample from Glenmark Pvt Ltd, Nashik
Crossprovidone	Molychem, Mumbai
Camphor	Vishal Chem, Mumbai
Mannitol	Merck
Sodium Saccrine	Merck
Talc	Molychem, Mumbai
Peppermint	Molychem, Mumbai

The most important ingredients of a mouth dissolving tablets are

Super disintegrants: Use of disintegrants is the basic approach in development of MDTs. Disintegrants play a major role in the disintegration and dissolution of MDT. It is essential to choose a suitable disintegrant, in an optimum concentration so as to ensure quick disintegration and high dissolution rates [18]. Super disintegrants provide quick disintegration due to combined effect of swelling and water absorption by the formulation. Due to swelling of superdisintegrants, the wetted surface of the carrier increases, which promotes the wettability and dispersibility of the system, thus enhancing the disintegration and dissolution [19, 20]. The optimum concentration of the superdisintegrant can be selected according to critical concentration of disintegrant. Below this concentration, the tablet disintegration time is inversely proportional to the concentration of the superdisintegrant, whereas if concentration of superdisintegrant is above critical concentration, the disintegration time remains almost constant or even increases [21].

Sodium starch glycolate, Ac-di-sol (crosscarmellose sodium), Crospovidone, Microcrystalline cellulose, Pregelatinised starch are some of examples of disintegrants.

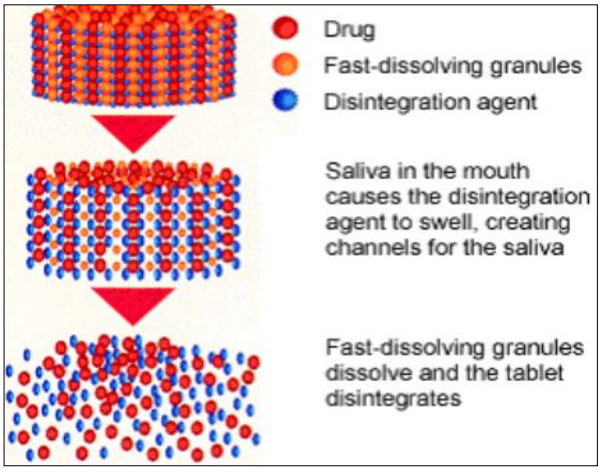

Fig 1: Mechanism of Action of Superdisintegrants

Mechanism of action of Disintegrants

The tablet breaks to primary particles by one or more of the mechanisms listed below:-

1. **By capillary action**
   Disintegration by capillary action is always the first step. When we put the tablet into suitable aqueous medium, the medium penetrates into the tablet and replaces the air adsorbed on the particles, which weakens the intermolecular bond and breaks the tablet into fine particles. Water uptake by tablet depends upon hydrophilicity of the drug /excipient and on tableting conditions. For these types of disintegrants, maintenance of porous structure and low interfacial tension towards aqueous fluid is necessary which helps in disintegration by creating a hydrophilic network around the drug particles.
2. **By swelling**
   Perhaps the most widely accepted general mechanism of action for tablet disintegration is swelling Tablets with high porosity show poor disintegration due to lack of adequate swelling force. On the other hand, sufficient swelling force is exerted in the tablet with low porosity. It is worthwhile to note that if the packing fraction is very high, fluid is unable to penetrate in the tablet and disintegration is again slows down.

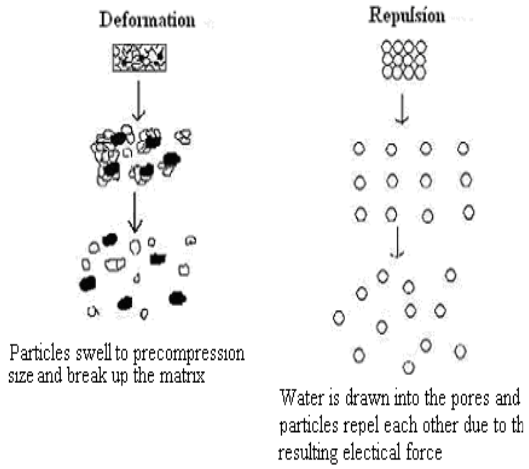

Fig 2: Disintegration of Tablet by Wicking and Swelling

3. **Because of heat of wetting (air expansion)**
   When disintegrants with exothermic properties gets wetted, localized stress is generated due to capillary air expansion, which helps in disintegration of tablet. This explanation, however, is limited to only a few types of disintegrants and cannot describe the action of most modern disintegrating agents.
4. **Due to release of gases**
   Carbon dioxide released within tablets on wetting due to interaction between bicarbonate and carbonate with citric acid or tartaric acid. The tablet disintegrates due to generation of pressure within the tablet. This effervescent mixture is used when pharmacist needs to formulate very rapidly dissolving tablets or fast disintegrating tablet. As these disintegrants are highly sensitive to small changes in humidity level and temperature, strict control of environment is required during manufacturing of the tablets. The effervescent blend is either added immediately prior to compression or can be added into two separate fraction of formulation.
5. **By enzymatic reaction**
   Here, enzymes present in the body act as disintegrants. These enzymes destroy the binding action of binder and helps in disintegration. Actually due to swelling, pressure exerted in the outer direction or radial direction, it causes tablet to burst or the accelerated absorption of water leading to an enormous increase in the volume of granules to promote disintegration.
6. **Due to disintegrating particle/particle repulsive forces**
   Another mechanism of disintegration attempts to explain the swelling of tablet made with 'non-swellable' disintegrants. Guyot- Hermann has proposed a particle repulsion theory based on the observation that nonswelling particle also cause disintegration of tablets. The electric repulsive forces between particles are the mechanism of disintegration and water is required for it. Researchers found that repulsion is secondary to wicking.
7. **Due to deformation**
   Hess had proved that during tablet compression, disintegranted particles get deformed and these deformed particles get into their normal structure when they come in contact with aqueous media or water. Occasionally, the swelling capacity of starch was improved when granules were extensively deformed during compression. This increase in size of the deformed particles produces a break up of the tablet. This may be a mechanism of starch and has only recently begun to be studied. Sugar based excipients: Sugar based excipients are used for taste masking and as bulking agents. Most of the dugs are having unpleasant or bitter taste. And the basic requirement for designing. MDTs is that the drug should not have disagreeable taste. So taste masking is necessary in most of the cases. Sorbitol, mannitol, xylitol, dextrose, fructose, etc. are mainly used. Aqueous solubility and sweetness impart a pleasing mouth feel and good taste masking [22].19 But not all sugar-based materials have fast dissolution rate and good compressibility or compactability. However technologies have been developed to make use of the sugar based excipients in the design of fast dissolving tablets. Other ingredients commonly used are water soluble diluents, lubricants, antistatic agents, plasticizers, binders, colors and flavors.

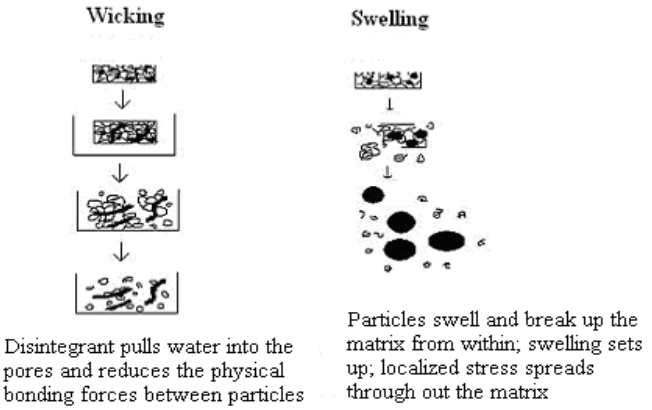

Fig 3: Disintegration by Deformation and Repulsion

Approaches for Preparation of MDT [23]

Mainly two types of technologies are used in the manufacture of Mouth Dissolving

Tablets include:

1. Conventional
2. Patented

I. Conventional

1. **Freeze drying** [24]

   The tablets prepared by freeze-drying or lyophilization are very porous in nature and disintegrate or dissolve rapidly when come in contact with saliva. In this process, water is sublimeated from the product after freezing. First of all, the material is frozen to bring it below its eutectic point. Then primary drying is carried out to reduce the moisture to around 4% w/w of dry product. Finally, secondary drying is done to reduce the bound moisture to the required volume. Due to lyophilization, bulking agent and sometimes drug acquire glossy amorphous structure and thus dissolution is enhanced. A tablet that rapidly disintegrates in aqueous solution includes a partially collapsed matrix network that has been vacuum dried above the collapsed temperature of the matrix. The matrix is partially dried below the equilibrium freezing point of the matrix. Vacuum drying the tablet above its collapse temperature, instead of freeze drying below its collapse temperature provides a process for producing tablets with enhanced structural integrity, while rapidly disintegrating in normal amounts of saliva. 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.

2. **Sublimation**

   This process involves addition of some inert volatile substances like urea, urethane, naphthalene, camphor, etc to other excipients and the compression of blend into tablet. Removal of volatile material [25] by sublimation creates pores in tablet structure, due to which tablet dissolves when comes in contact with saliva. Additionally several solvents like cyclohexane, benzene etc can also be used as pore forming agents. Mouth dissolving tablets with highly porous structure and good mechanical strength have been developed by this method [26, 27].

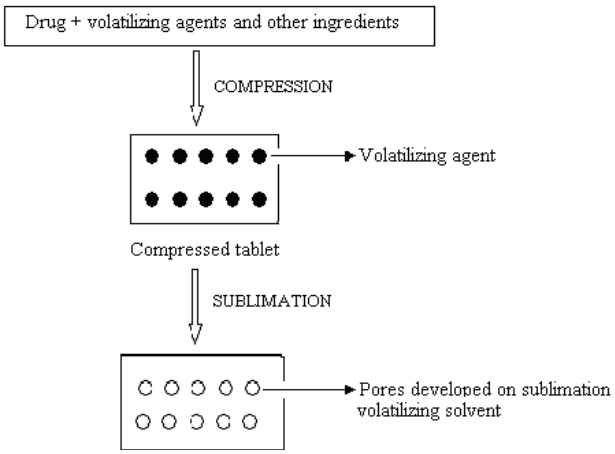

Fig 4: Schematic Diagram of Sublimation Technique for Preparation of MDT

3. **Spray drying**

   A highly porous and fine powder is prepared by spray drying an aqueous composition containing support matrix and other components. This is then mixed with active ingredient and compressed into tablet. Allen and Wang [28] used this technique to prepare mouth-dissolving tablets, which disintegrated within 20 s.

4. **Moulding**

   Tablets prepared by this method are solid dispersions. Physical form of drug in the tablets depends on whether and to what extent it dissolves in the wetted mass [29]. The drug can exist as discrete particles or micro particles in the matrix. It can dissolve totally to form a solid solution or dissolve partially in the molten carrier and remaining, if any, stays undissolved and dispersed in the matrix [30].27 Disintegration time, drug dissolution rate and mouth feel will depend on the type of dispersion. Different moulding techniques can be used to prepare mouth-dissolving tablets:

i. **Compression moulding:** The powder mixture previously wetted with a solvent like ethanol/water is compressed into mould plates to form a wetted mass.

ii. **Heat moulding:** A molten matrix in which drug is dissolved or dispersed can be directly moulded into Mouth dissolving tablets [31].

iii. **No vacuum lyophilization**: This process involves evaporation of solvent from a drug solution or suspension at a standard pressure [32]. Moulded tablets posess porous structure, which facilitates rapid disintegration and easy dissolution. Moulded tablets offer improved taste due to water-soluble sugars present in dispersion matrix. But moulded tablets lack good mechanical strength and can undergo breakage or erosion during handling and opening of blister packs [33]. However, adding sucrose, acacia or polyvinyl pyrrolidone can increase mechanical strength.

5. **Mass extrusion** [34, 35]

   In this technique, a blend of active drug and other ingredients is softened using solvent mixture of water soluble polyethylene glycol, using methanol and then the softened mass is extruded through the extruder or syringe to get a cylinder of product, which is finally cut into even segments with the help of heated blades to get

tablets. The dried cylinder can be used to coat the granules of bitter tasting drugs and thereby masking their bitter taste.

6. **Direct compression**

The disintegrant addition technology [36, 37] (direct compression) is the most preferred technique to manufacture the tablets due to certain advantages:

- High doses can be accommodated and final weight of the tablet can exceed that of other methods.
- Easiest way to manufacture the tablets.
- Conventional equipment and commonly available excipients are use
- A limited no. of processing steps are involved.
- Cost-effectiveness.

Tablet size and hardness strongly affect the disintegrant efficacy. Hard and large tablets have more disintegration time than normally required. Very soft and small tablets have low mechanical strength. So, an optimum kind and concentration of disintegrant should be chosen to achieve quick disintegration and high dissolution rates. Above the critical concentration level, however, disintegration time remains approximately constant or even increases [38].

II. Patented Technologies for Mouth Dissolving Tablets

Several technologies are available for preparing Mouth dissolving tablets. But some commercially useful technologies are:

Zydis technology

'Zydis' is the first mouth dissolving dosage form in the market. It is a unique freeze-dried tablet in which the active drug is incorporated in a water-soluble matrix, which is then transformed into blister pockets and freeze dried to remove water by sublimation. Zydis matrix is made up of a number of ingredients in order to obtain different objectives. Polymers such as gelatin, dextran or alginates are added to impart strength during handling.

These form a glossy and amorphous structure. Mannitol or sorbitol is added to impart crystallinity, elegance and hardness. Various gums may be added to prevent sedimentation of dispersed drug particles. Water is used as a medium to ensure the formation of a porous dosage form. Collapse protectants like glycine may be used to prevent shrinkage of dosage form during freeze drying and longterm storage [39]. If necessary, suspending agents and pH adjusting agents may be used. Preservatives may also be added to prevent microbial growth. Zydis products are packed in blister packs to protect the formulation from environmental moisture. A secondary moisture proof foil punch is often required as this dosage form is very moisture sensitive. When put into the mouth, Zydis unit quickly disintegrates and dissolves in saliva.

Drawbacks

- A water insoluble drug can be incorporated only upto 400 mg per tablet or less. On the other hand water soluble drug can be incorporated only upto 60 mg
- Fragility and poor stability of dosage form during storage under stressful conditions.

Orasolv technology

It is CIMA lab's first mouth dissolving formulation. This technology involves taste masking of active drug. Effervescent disintegrating agent is also used. Conventional blenders and tablet equipments are used for preparation of tablets. Less force of compaction is used for manufacturing so as to obtain soft and quickly disintegrating tablets. There is a limitation of this technology that soft and fragile tablets are formed, therefore needed to be packed in specially designed pick and place package system.

Durasolv technology

This too has been developed by CIMA labs. This is one of the suitable technologies to prepare products requiring low amounts of active drug. This technology uses drug, fillers and a lubricant to prepare the tablet. Conventional tabletting equipment is used to prepare the tablet. Due to higher force of compaction used, tablets prepared are rigid. Dosage form can be packaged into conventional packaging system like blisters.

Wowtab technology

Yamanauchi pharmaceutical company patented this technology. 'wow' means 'without water'. The active ingredients may constitute upto 50% w/w of the tablet. In this technique, saccharides of both low and high mouldability are used to prepare the granules. Mouldability is the capacity of a compound to be compressed. Highly mouldable substance has high compressibility and thus shows slow dissolution. The combination of high and low mouldability is used to produce tablets of adequate hardness. Active ingredients are mixed with low mouldability saccharides and then granulated with high mouldabiity saccharides and then compressed into tablet. The Wowtab product dissolves quickly in 15 s or less. Wowtab product can be packed in both into conventional bottle and blister packs [40].

Flashdose Technology

This technology is patented by Fuisz. This system uses the combination of both Shearform and Ceform technologies in order to mask the bitter taste of the drug. A sugar based matrix, called 'Floss' is used, which is made up of a combination of excipients (crystalline sugars) alone or in combination with drugs. Nurofen meltlet, a new form of Ibuprofen, as a mouth-dissolving tablet is the first commercial product prepared by this technology and launched by Biovail Corporation.

Drawbacks

- The dosage form can accommodate only up to 600 mg of drug.
- Tablets produced are highly friable, soft and moisture sensitive. Therefore specialized packing is required.

Flashtab technology [41]

Prographarm labs. Have a patent over this technology. In this technology, microgranules of the taste-masked active drug are used. These may be prepared by using conventional techniques like coacervation, microencapsulation, and extrusion spheronisation. All these processes utilize conventional tabletting technology. These taste-masked micro crystals of active drug, disintegrating agent, a swelling agent and other excipients like soluble diluents etc are compressed to form a multiparticulate tablet that disintegrates rapidly.

Shearform Technology
In this technology, a shear form matrix, 'Floss' is prepared. Feedstock prepared with a sugar carrier is subjected to flash heat processing. In this process, sugar is simultaneously subjected to centrifugal force and to a temperature gradient, which causes the temperature of the mass to rise and hence an internal flow condition is created, permitting part of it to move with respect of the mass. The flowing mass comes out through the spinning head that flings the floss. The produced floss is amorphous in nature. So by various techniques, it is further chopped and recrystallised to provide a uniform flow, thus facilitate blending. Then the recrystallised matrix, active drug and other excipients are blended together and finally compressed into tablets. Active drug and other excipients may be blended with the floss before recrystallising it.

Ceform technology
This technology involves preparation of microspheres of the active drug. Drug material alone or in combination with other pharmaceutical substances, and excipients is placed into a precision engineered rapidly spinning machine. The centrifugal force comes into action, which throws the dry drug blend at high speed through small heated openings. Due to the heat provided by carefully controlled temperature, drug blend liquefies to form a sphere, without affecting the drug stability. The microspheres thus formed are compressed into tablets. As the drug and excipients both can be processed simultaneously, it creates a unique microenvironment in which the materials can be incorporated into the microspheres that can alter the characteristics of the drug, such as enhancing solubility and stability.

Nanocrystal technology [42]
For MDT, Elan's proprietary NanoCrystal technology can enable formulation and improve compound activity and final product characteristics. Decreasing particle size increases the surface area, which leads to an increase in dissolution rate. This can be accomplished predictably and efficiently using NanoCrystal technology. NanoCrystal particles are small particles of drug substance, typically less than 1000 nanometers (nm) in diameter, which are produced by milling the d For fast dissolving tablets, Elan's proprietary NanoCrystal technology can enable formulation and improve compound activity and final product characteristics. Decreasing particle size increases the surface area, which leads to an increase in dissolution rate. This can be accomplished predictably and efficiently using NanoCrystal technology.

NanoCrystal™ Fast dissolving technology provides for
a. Pharmacokinetic benefits of orally administered nanoparticles (<2 microns) in the form of a rapidly disintegrating tablet matrix
b. Exceptional durability, enabling use of conventional packaging equipment and formats (i.e., bottles and/or blisters).
c. Wide range of doses (up to 200mg of API per unit).
d. Employment of non moisture sensitive substances

Nano Crystal colloidal dispersions of drug substance are combined with water-soluble GRAS (Generally Regarded As Safe) ingredients, filled into blisters, and lyophilized. The resultant wafers are remarkably robust, yet dissolve in very small quantities of water in seconds.

Evaluation of mouth dissolving tablets
General Appearance
The general appearance of a tablet, its visual identity and over all "elegance" is essential for consumer acceptance. Include in are tablet's size, shape, colour, presence or absence of an odour, taste, surface texture, physical flaws and consistency and legibility of any identifying marking.

Size and Shape
The size and shape of the tablet can be dimensionally described, monitored and controlled.

Weight variation
20 tablets were selected randomly from the lot and weighted individually to check for weight variation. Weight variation specification as per I.P. is shown in table [43, 44].

Table 2: Weight variation specification as per IP

Average Weight of Tablet	% Deviation
80 mg or less	±10
More than 80 mg but less than 250 mg	±7.5
250 mg or more	±5

Assay
Twenty tablets from each batch were weighed accurately and powdered powder equivalent to 100 drug was shaken with 100 ml of 0.1N Hydrochloric acid in 100 ml amber colored volumetric flask and from this 10 ml was pipette out and then dilute up to 100 ml. From standard solution again 10 ml pipette out and diluted up to 100 ml in ml [45, 46].

Tablet hardness
The strength of tablet is expressed as tensile strength (Kg/cm2). The tablet crushing load, which is the force required to break a tablet into halves by compression. It was measured using a tablet hardness tester (Pfizer Hardness Tester) [47].

Content uniformity
Five tablets were powdered and the blend equivalent to 4 mg of Tizanidine Hcl was weight and dissolved in suitable quantity of pH 1.2 solutions. Solution was filtered and diluted and drug content analyzed spectro-photometrically at 228 nm [48].

Measurment of tablet tensile strength
The tablet tensile strength is the force required to break a tablet by compressing it in the radial direction and is measured using a tablet hardness tester. For measuring the hardness of the tablets, the plunger of the hardness tester is driven down at a speed of 20 mm/min. Tensile strength for crushing (T) is calculated using equation:

$$T = 2F / \pi dt$$

Where F is the crushing load, and d and t denote the diameter and thickness of the tablet, respectively [48]. Though, this is a widely used and accepted method for hardness testing, it is not applicable to very delicate tablets prepared by Lyophilization technique wherein the liquid suspension of drug and excipients is freeze dried in the

blister pocket and the dried tablets are finally sealed in the blister. Special aluminum blisters with peel off blister covers are used as packaging material for these tablets. Flash dose tablets prepared by cotton candy process are also poor candidates for this test [45. 46]. This test is best suited for tablets prepared by direct compression and moulding methods. However, the tensile strength of these tablets is always kept low which needs to be compromised to keep the disintegration time as minimum as possible.

Friability

The pharmacopoeial limit of friability test for a tablet is not more than 1% using tablet friability apparatus, carried out at 25 rpm for 4 min (100 rotations). However, it becomes a great challenge for a formulator to achieve friability within this limit for MDT product keeping hardness at its lowest possible level in order to achieve a minimum possible disintegration time. This test is again not applicable for lyophilized and flash dose tablets, but is always recommended for tablets prepared by direct compression and molding techniques to ensure that they have enough mechanical strength to withstand the abrasion during shipping and shelf life [27, 49].

Moisture uptake study

MDTs usually contain high concentration of hydrophilic excipients with the minimum possible hardness which together contributes to their increased susceptibility to moisture uptake. In order to maintain their physical integrity and surface texture, special attention is required during the storage and packaging of these dosage forms. Therefore, moisture Uptake studies are strongly recommended for MDTs. The test can be carried out by keeping ten tablets along with calcium chloride in a desiccators maintained at 37 °C for 24 hrs to ensure complete drying of the tablets. The tablets are then weighed and exposed to 75% RH, at room temperature for 2 weeks. The required humidity can be achieved by keeping saturated sodium chloride solution in the desiccators for 24 hrs. The tablets are reweighed and the percentage increase in weight is recorded. If the moisture uptake tendency of a product is high, it requires special dehumidified area for manufacturing and packing. The materials with high moisture resistant properties should be used for packaging for e.g. Alu strip pack, Alu- Alu blister or polyethylene sealing on blister. The use of appropriate quantity of desiccant in HDPE bottle packs with minimum head space is highly recommended to ensure stability of the product during its shelf life [49, 50, 51, 52].

Wetting time and water absorption ratio

A study 24 on wetting time and water absorption ratio reported the use of a piece of double folded tissue paper placed in a petridish containing 6 ml (Ph 6.8) of water. One tablet was placed on this paper and the time for complete wetting of tablet was noted as wetting time. The wetted tablet was then weighed and the water absorption ratio, R, was determined according to equation:

$$R = 100 (Wa.Wb)/Wb$$

Where Wb and Wa are the weights of tablet before and after water absorption, respectively

Disintegration time

The methods for evaluation of in-vivo disintegration time had been explained in literature [53-55].

However, the results from this type of test typically reveal unsatisfactory reproducibility and are not reliable as the difference in disintegration time is few seconds in most cases. In addition, the *in-vivo* disintegration test has its own limitation of issues related to ethics and the safety of the volunteers [56].

At present, the disintegration time of MDTs is measured using the disintegration test for conventional tablets that is described in the Pharmacopoeias. EP has set the limit of 3 mins for disintegration time of MDTs using conventional disintegration apparatus. However, no special apparatus is mentioned in the pharmacopoeias for disintegration test of MDTs and the conventional method available seems to be inappropriate for MDTs. This is because of the extreme operating conditions in the disintegration apparatus which fails to provide a significant discrimination among the rapidly disintegrating tablets. Furthermore, the conventional test employs a relatively huge volume of test solution (900 ml) compared to the volume of saliva in human buccal cavity, which is less than 6 ml [57].

Dissolution testing of mouth dissolving tablets

The conventional method of dissolution could be extended to in-vitro evaluation of MDT. The dissolution conditions for the reference listed drugs available in USP can be utilized for preliminary in-vitro studies to mimic better in-vivo conditions. Apart from the above, multimedia dissolution studies in various buffer solutions of different pH viz. 0.1 N HCl; pH 4.5 and 6.8 buffers should be carried out for interpretation of their in-vivo performance and pharmaceutical equivalence [58]. USP apparatus II (paddle) with a speed of 50 rpm seems to be most suitable and common choice with appropriate dissolution media volume to maintain sink condition.

Evaluation of effectiveness of test masking

The formulation's organoleptic properties like taste, mouth-feel and appearance are of considerable importance in differentiating products in the market and can ultimately determine the success of a product [59].

Table 3: Marketed brands of MDTs [60]

Brand name	Active ingredient	Application	Company
Claritin® RediTabs®	Loratadine	Antihistamine	Scherig corporation
Feldene Melt®	Piroxicam	NSAIDs	Pfizer
Maxalt® -MLT®	Rizatritpan benzoate	Migrane	Merck
Pepeid® ODT	Femotidene	Anti-ulcer	Merck
Zyperxa®	Olazepine	Psychotropic	Eli Lilly
Zofran® ODT	Olandansetron	Antiemetic	Galaxo Smith kline
Resperdal® M-TabTM	Resperidone	Schizophrenia	Janssen
ZubrinTM (Pet drug)	Tepoxelin	Canine NSAIDs	Scherig corporation

ZelaparTM	Selegiline	Parkinsons disease	Elanl Amarin corporation
Klonopin® wafer	Clonazepam	Sedation	Roche
Childrens Dimetapp® ND	Loratadine	Allergy	Wyeth consumer Healthcare
Imodium Istant Melts	Loperamide HCL	Antidiarrheal	Jannsen
Propulsid® Quicksolv ®	Cisapride Monohydrate	Gastrointestinal prokinetic Agent	Jannsen
Tempra Quicksolv®	Acetaminophen	Analgesic	Bristol-Mters squibb
Remeron® Soltab®	Mirtazapine	Anti-dipression	Organon Inc.
Triaminic® Softchews®	Various combination	Pediatric cold cough,Allergy	Novartis consumer Health
Zomig-ZMT® and Rapimelt®	Zolmitriptan	Anti-migraine AstraZeneca	AstraZeneca Alavert® Loratadine Allergy
DuraSolv® Alavert®	Loratadine	Allergy	Wyeth Consumer Healthcare
NuLev®	Hyoscyamine sulfate	Anti-ulcer	Schwarz Pharma
Kemstro™	Baclofen	Anti-spastic analgesic	Schwarz Pharma
Benadryl® Fastmelt®	Diphenhydramine citrate	sinus pressure relief	Pfizer
Nasea OD	Ramosetoron HCl	Anti-emetic	Yamanouchi
Gaster D	Famotidine	Anti-ulcer	Yamanouchi
Excedrin® QuickTabs	Acetaminophen	Pain reliever	Bristol-Myers

Conclusion

Over the last decade, the popularity of MDTs has increased enormously due to its better patient acceptance and compliance and having the better biopharmaceutical properties. Compared with conventional oral dosage forms, they require smaller amounts of active ingredient to provide the effective action and improve absorption profiles, and offer better drug bioavailability than regular tablets and capsules. There are about more than 40 drugs have been formulated into marketed as mouth dissolving tablets by using various technologies. These are novel dosage forms which dissolve in saliva within a few seconds, when put on tongue. Such MDTs can be administered anywhere and anytime, without the need of water and are thus quite suitable for children, elderly and mentally disabled patients.

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