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Mouth Dissolving Tablets-Pediatric and Geriatric Patient Compliance Dosage Forms

R. Santosh Kumar and U. Sruthi

GITAM Institute of Pharmacy, GITAM (Deemed To Be University) Rushikonda, Visakhapatnam-530045, Andhra Pradesh, India.

ABSTRACT

The oral route of administration remains the most convenient route of administration but the major disadvantage is dysphagia (difficulty in swallowing) to overcome these problems novel drug delivery systems have developed mouth dissolving tablets with improved patient compliance. Mouth dissolving tablets are solid dosage forms which dissolve rapidly when kept in mouth. The first choice of drugs for pediatric, geriatric, mentally disable patients and also for patients who are traveling can administer the tablet any time without the need for water. Conventional technologies and patented technologies are the two different technologies used in the manufacturing of MDTs. This review describes the various aspects of MDT formulation, super disintegrants, and technologies used for developing MDT, along with evaluation

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***Address for Correspondence:**

R. Santosh Kumar, GITAM Institute of Pharmacy, GITAM (Deemed to be University), Gandhinagar, Visakhapatnam-530045, Andhra Pradesh, INDIA.

INTRODUCTION [1,2,3]:

The oral route of administration is the better-adapted route of administration of different therapeutic agents. It is generally preferred route due to its advantages such as convenience in case of self-administration, compactness and easy manufacturing. Infact of having so many advantages, the most common drawback of in oral dosage forms like tablets and capsules is difficulty in swallowing, particularly in the case of pediatric and geriatric patients, and mentally disabled patients. To overcome these problems, Pharmaceutical scientists have developed mouth dissolving/disintegrating tablets (MDTs). These Mouth Dissolving Tablets take less than three minutes to dissolve in the oral cavity. Mouth dissolving tablets have good taste and flavour and mask the bitter taste of the drugs. MDTs are most useful for the bed-ridden and patients who have the swallowing problems. Mouth dissolving tablets are also known as oral dispersible tablets, fast disintegrating tablets, orally disintegrating tablets, quick disintegrating tablets, fast-dissolving tablets, rapid dissolving tablets. Mouth dissolving tablets are formulated by two different methods one be patented technology and another one is non patented technology. The advantages of MDTs are a considerable dosage form, onset of action, self-administration, no risk, no pain increased bioavailability of the drug.

Requirement of Mouth Dissolving Tablets:

Ideal Properties of Mouth Dissolving Tablets [5]:

1. No need for water while swallowing the tablet.
2. It should have a pleasant mouthfeel.
3. It should mask the bitter taste.
4. It should be harder and less friable.
5. No residue should be left in the mouth after administration.
6. Low-cost therapy.

Advantages of Mouth Dissolving Tablets [6,7]:

1. Mouth dissolving tablets are more convenient to pediatric, geriatric, mentally retarded and psychiatric patients.
2. Bioavailability of the drug increased due to its absorption of from mouth, pharynx, and oesophagus as saliva passes down to the stomach and also avoids hepatic metabolism.
3. It is suitable for patients who are traveling where there is no access to water.
4. It masks the bitter taste and gives a pleasant mouthfeel.
5. The fast disintegration of tablets and also shows the rapid onset of action.

6. Mouth dissolving tablets offer all the advantages of solid dosage forms and it is convenient to administration compared to liquids dosage form due to its accurate dosage form.

Salient Features of Mouth Dissolving Tablets :

1. Easy to administration for the patients who refuse to swallow a tablet, such as pediatric and geriatric patients and, psychiatric patients.

2. Accurate dose is consumed .

3. No need to drink water while swallowing the dosage form, it is highly convenient for the patients who are traveling and do not have water.

4. It masks the bitter taste of the drug so it is convenient for pediatric to swallow the tablet.

5. The drug is dissolved within 15 seconds and rapid, onset of action.

6. Bioavailability of drugs is increased.

Limitations of Mouth Dissolving Tablets:

1. Antibiotics like ciprofloxacin have large doses are difficult to formulate in mouth dissolving tablets.

2. Patients who take anticholinergic medication and who suffer from dryness of the mouth may not be allowed to take MDTs because it decreases saliva production while taking this tablet formulation.

Technologies used for manufacturing of Mouth Dissolving Tablets:

Depending upon its ideal properties of mouth dissolving tablets two different manufacturing techniques are employed .

1. Convectional technologies.
2. Patented technologies.

1. Conventional Technologies:

Lyophilization or Freeze-drying [8]:

In this process water is refined from the product after freezing, this process is called freeze-drying. It shows rapid dissolution than compared to other solid dosage forms. The lyophilized drugs along with excipients impart glossy crystalline forms resulting in high porosity. The major drawback of this technique is that it is expensive and time taking the MDTs formed by this process have low mechanical strength, it shows low stability during high temperatures.

Molding [9]:

By using water-soluble ingredients molded tablets are prepared which disintegrate completely and fastly. Firstly the blender is moistened with hydroalcoholic solvent and molded into tablets under low pressure and by using the air-drying method the solvent is removed. compared to compressed tablets molded tablets do not possess great mechanical strength. the porous structures increase the dissolution. breakage of the molded tablets often seen during tablet handling. If hardness agents are added to the process the rate of tablet solubility decreases.

Spray drying [10,11]:

This process produces highly porosity drugs and fine powders. the solvent is evaporated in the manufacturing. The hydrolyzed and non- hydrolyzed gelatin was used as a supporting matrix for the production of mouth dissolving tablets. Mannitol is used as a bulking agent and super disintegrants such as sodium starch glycolate. By adding acidic substances like citric acid the disintegration and dissolution increase. This disintegration time < 20 sec .

Mass extrusion [12]:

This process involves demulcent of the active mixture using the solvent like water-soluble polyethylene glycol and methanol by which subsequent expulsion of softened mass through the syringe to get a cylinder of the product and then cut into pieces using heated blade to form a tablet. These processes also used to coat the bitter taste of the drug.

Phase transition process [13]:

Kuno et al proposed this method to prepare mouth dissolving tablets. In this process, MDT is formed by compressing ingredients along with erythritol and xylitol and then heated to 93 °C for 15 min. Before heating, the tablets don't have sufficient hardness due to its slow compatibility. But after heating tablet hardness is increased due to an increase in inter particular bond.

Sublimation [14]:

The compressed tablets show slow dissolution due to its low porosity even though they contain high water-soluble ingredients. To overcome these problems inert volatile substances like camphor, ammonium bicarbonate, ammonium carbonate, benzoic acid, camphor, urea, and urethane are added along with other ingredients and mixed together and compressed and subjected to sublimation to improve its porosity. The tablets obtained have high porosity and exhibit good mechanical strength so it gets fastly dissolved in the saliva within 15 seconds.

Direct compression methods [15,16]:

It is the easiest technique used for manufacturing of mouth dissolving tablets . In this method traditional equipment and generally available excipients are used and low manufacturing cost. High doses can receive end weight of the tablet which can overtake the other production methods. It is important to choose a correct concentration of disintegrant to get fast disintegration. Superdisintegrants provides quick disintegration as they are more effective at lower concentrations with high disintegrating efficiency and mechanical strength. according to the critical concentration of disintegrant the optimum concentration of super disintegrate is selected, if the concentration of the tablet disintegration is below then critical concentration then disintegration time is inversely proportional to the concentration of super disintegrant or if the concentration of the tablet disintegration is above the critical disintegration than the disintegration time remains the same or even increases.

2. Patented Technologies:

Zydus technology [17,18]:

R.P. Scherer, Inc patented this technology. it is the first mouth dissolving/disintegrating tablet in the market. It is a unique type of freeze-dried process in which the drug is physically trapped into a matrix which is composed of saccharides and polymers . It does not require water while taking the tablet due to its unique freeze-dried structure it disintegrates instantaneously in the mouth. Partially hydrolyzed gelatin, hydrolyzed dextran, dextrin, alginates, polyvinyl alcohol, polyvinyl pyrrolidine, acacia are the generally used polymers which impart strength during handling and also gives crystallinity, elegance, and hardness

to the tablets. .The product dispensed in a special blister pack as the tablets are lightweight and fragile.

Nanocrystal technology [19]:

Elan, King of Prussia patented this technology. In this technology, colloidal dispersions of drug substance and water-soluble ingredients are freeze-dried and filled into blister pockets. This process is commonly useful for small quantities of a drug because granulation, blending, and tableting which are highly potent methods are not used in this tablet manufacturing.

Flashtab technology [20]:

Ethypharm France patented this technology. In this formulation the wet and dry granulation methods are used for granulation of excipients the two types of excipients are used in this techniques i.e disintegrating agents and selling agents The commonly used disintegrating agents are reticulated polyvinylpyrrolidone or carboxymethylcellulose and the commonly used swelling agents are carboxymethylcellulose, starch, modified starch, microcrystalline cellulose The disintegrating time of this tablets is within 1 min

Orasolv technology [21,22]:

CIMA Labs patented this technology to produce the MDTs The effervescent disintegrating agents compressed with low pressure. 20-25% of the tablet concentration contains effervescent agent soft and fragile tablets are produced due to its low compression force. These tablets are developed in a controlled environment at a very low relative humidity. moisture impermeable blisters are used for packaging

Durasolv technology [23]:

CIMA Labs patented this technology. To prepare products with a low amount of active drug this is the best suitable technology. Drug, nondirect compression fillers, and lubricants are used in the manufacturing of these tablets. dextrose, mannitol, sorbitol, lactose, and sucrose are the nondirect compressible fillers used for fast dissolution and to avoid grainy structure which is commonly present indirectly compressible sugar. Bottles and blisters are used in the packing of this dosage form.

Wow tab technology [24,25] :

This technology is patented by Yamanouchi. The WOW in the WOWTAB signifies the tablet is to be given without water. sugar and sugar like excipients promote this technology. Low and high – moldability saccharides are prepared by granulation and tableting methods. lactose, mannitol, glucose, sucrose are low moldability saccharides whereas maltose, maltitol, sorbitol, and oligosaccharides are high moldability tablets. These two moldability saccharides are combined to obtain a tablet formulation with adequate hardness and fast dissolution rate. The tablets produced by this unit have adequate hardness and fast disintegration time.

Dispersible tablet technology [26]:

This technology is patented by Lek, Yugoslavia. In this technology, 8-10% of organic acids and disintegrating agents are added to improve the dissolution rate of MDTs. Disintegrating agent promotes fast swelling and increases the wetting capacity of the tablets which results in quick disintegration. Starch, modified starches, microcrystalline cellulose are some of the disintegrating agents. Mixing of disintegrants improves the disintegration time of tablets which is commonly less than 1 min.

Pharmaburst technology [4]:

This technology is patented by SPI pharma. Pharma burst technology utilizes the shelf co-processed excipients to develop MDTs. It depends on the type of active ingredients and the tablets dissolve within 30- 40 seconds. In this process, the drug, flavouring agents, and lubricant are blended and are compressed into a standard tablet by the press with stock tooling. This process is carried under normal temperature and moisture conditions. Blister packs or bottles are used in the packing of these units.

Frosta technology [4]:

This technology patented by Akina. It applies the concept of compressing plastic granules at a low pressure to form strong tablets with high porosity. These granules contain three classes of components:

1. A Porous and plastic material,
2. A Water penetration enhancer, and
3. A Binder

The process involves commonly blending of the porous plastic material with a water penetration enhancer and it is followed by granulating with a binder. The tablets obtained by this unit have admirable hardness and quick disintegration time ranging from 15 to 30 s depending on the size of a tablet.

Oraquick technology [27]:

The Oraquick disintegrating tablets composition applies a patented taste-masking technology. These tablets are manufactured by low-heat technique so it is suitable for heat-sensitive drugs. This technology is patented by K.V.S. Pharmaceuticals and These tablets dissolve within a few seconds and give superior mouthfeel.

Evaluation of Mouth dissolving Tablet [28,29]:

Evaluation of mouth dissolving tablets include the following evaluation tests

· **General Appearance**:

General appearance of tablets includes visual testing such as size, shape, colour, presence or absence of an odour, taste, surface texture, physical flaws, and consistency in identifying marking.

· **Size and Shape:**

The size and shape of the tablet can be described and monitored.

· **Tablet thickness**:

Tablet thickness is an important characteristic in the evaluation of tablets. Micrometres are used for recording tablet thickness.

· **Uniformity of weight:**

In this method, twenty tablets were taken and their weight was determined individually. The maximum weight of one tablet was determined from the collective weight. The weight variation test would be the most accepted method of determining the drug content.

· **Tablet hardness:**

The limit of hardness for the MDTs is normally kept in a lower range to facilitate the fast disintegration of the tablet

in the mouth. The hardness of the tablet may be measured using a conventional hardness test.

· **Friability:**

It is the mechanical strength of tablets. Roche friabilator is the apparatus used to determine the friability of tablets. A pre-weighed tablet was placed in the friabilator. Friabilator consists of a plastic-chamber that revolves at 25 rpm, dropping those tablets in each revolution.

For 4minutes the tablets are rotated in fibillator at the end of the test the tablets were dusted and reweighted and the loss of the tablets is measured

· ***In Vivo*** **Disintegration test :**

In this test 6 tablets are placed in distilled water which is used as a disintegrating medium and time taken for complete disintegration of tablets without any palatable mass remaining in the apparatus is measured.

· **Wetting time:**

To measure the tablet wetting time ,a a piece of tissue paper folded twice and placed in a petri dish containing 6 ml of Sorenson's buffer pH 6.8 and the tablet is placed on the paper, and the time taken for complete wetting is recorded and measured. Three trials for each batch are recorded and the standard diversion is also determined.

· ***In vitro*** **dispersion time:**

By placing a tablet in a beaker containing 50 ml of Sorenson's buffer pH 6.8 the dispersion time is measured and three trails for each batch are recorded.

Stability testing of drug:

As recommended by ICH guidelines for accelerated studies the mouth dissolving tablets are packed and stored under favourable conditions

- 40 ± 1°C
- 50 ± 1°c
- 37 ±1oC
- RH 75% ± 5%

The tablets which remain reserved for 15 days is tested for its physical appearances such as visual defects, hardness, friability, disintegration, dissolution, and its drug content. The data is recorded and adapted to determine the kinetics of degradation by first-order reactions. Arrhenius equation is plotted to determine the shelf life at 25 ^{0}C for accelerated stability.

Packaging of MDTs:

The most important aspect of the manufacturing of MDTs is packing. The products which are obtained by different technologies differ in few specifications especially in mechanical strength to an extreme degree. Zydis, Lyon, Quicksolv, and Nanocrystal which are collected by the lyophilization process are porous in nature and have low physical resistance, and sensitive to moisture. Considering the above reasons the compounds require special packing. Peelable backing foils are used for packing zyids units. Dome-shaped blisters are special packaging units used in paksol and Orasolv which avoid the movement of tablets and prevent breaking of tablets during storage and transport. The products obtained from Durasolv i.e. WOW Tab, Pharmaburst OraQuick, Ziplets are generally packed in push-through blisters or in bottles as they have sufficient mechanical strength to withstand handling and transport.

Patient counselling in effective use of MDTs:

As pharmacists have the opportunity to educate the patients for effective treatment as they know recent technologies

- Confusion and misunderstanding about MDTs can be cleared by counselling the patients and the information provided to the patient include:
- Storage of some MDTs should be handled carefully considering they do not have tolerable mechanical strength.
- The patients who take anticholinergic drugs and suffering from dryness of mouth are not advisable to take MDTs. Despite the fact that no water is needed to allow the drug to diffuse fastly and accurately. However the low amount of saliva may decrease the rate of disintegration and can diminish the bioavailability of the product.
- The patients should definitely know the difference between effervescent and MDTs because Some of the technologies use effervescence.
- The patient needs to be counselled about differences between chewable and MDTs tablets. These MDTs can be used easily taken geriatric patients and pediatric.

By the pharmacist's advice, and assistance about MDTs, all patients have better knowledge about MDTs so they can effectively be treated with greater convenience.

CONCLUSION:

Mouth dissolving tablets are novel approach under a solid oral drug delivery system. Mouth dissolving tablets are a convenience to all age group patients (includes pediatrics, geriatrics) psychotic patients. They are the first patient's choice as waters are not required for administrating so it can be administrated while traveling. Mouth dissolving tablets are cheaper than other conventional tablets and they are enhancing the drug release for poorly soluble drugs. Mouth dissolving systems are future prospective as research are going on to develop mouth dissolving tablets for available drugs as they provide fast onset of action which is the first doctors requirement for treatment of diseases.

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