A REVIEW ON FORMULATION AND EVALUATION FOR MOUTH DISSOLVING TABLET

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ABSTRACT

Mouth dissolving tablets are gaining more prominence as a novel drug delivery system & emerges as one of the popular & widely accepted dosage forms, especially for pediatric patients because of incomplete development of muscular & nervous system & in case of geriatric patients suffering from Parkinson’s disorder or hand tremors, forms like tablets and capsules are now days facing the problems like dysphagia, resulting in the highincidence of non compliance and making the therapy ineffective. from both pharmaceutical industries as well as patients because they are convenient to be manufactured & administered, free of side effects, offering immediate release & enhance bioavailability , so as to achieve better patient compliance. One such problem can be solved in the novel drug delivery system by formulating “mouth dissolving tablets” (MDTs) which disintegrates or dissolves rapidly without water with in few seconds in the mouth due to the action of superdisintegrant or maximizing pore structure in the formulation. To obviate the problems associated with conventional dosage forms, mouth dissolving tablets have been developed having good hardness, dose uniformity, easy administration and serves as the first choice of dosage form for paediatrics, geriatrics and travelling patients. The MDTs were developed with an aim of having sufficient hardness, integrity and faster disintegration without water. Fast dissolving Tablets are disintegrating and/or dissolve rapidly in the saliva without the need for water. Some tablets are designed to dissolve in saliva remarkably fast, within a few seconds, and are true fast-dissolving tablets. Others contain agents to enhance the rate of tablet disintegration in the oral cavity, and are more appropriately termed fast-disintegrating tablets, as they may take up to a minute to completely disintegrate.
KEY WORDS: Mouth dissolving tablet, Patented technologies, Fast Dissolving, Rapid Disintegration.

INTRODUCTION

A solid dosage form is drug delivery system that includes tablets, capsules, sachets and pills as well as a bulk or unit-dose powders and granules. Oral dosage form is the most popular route for drug therapy. Over 80% of the drugs formulated to produce systemic effects in the United States are produced as oral dosage forms. The oral route remains the preferred route for administration of therapeutic agents because of accurate dosage, low cost therapy, self medication, non invasive method and ease of administration leading to high level of patient compliance. However, traditional tablets and capsules administered with a glass of water may be inconvenient or impractical for some geriatric patients because of changes in various physiological and neurological conditions associated with aging including difficulty in swallowing/dysphagia, hand tremors, deterioration in their eyesight, hearing, memory, risk of choking in addition to change in taste and smell. Solid dosage forms also present significant administration challenges in other patient groups, such as children, mentally challenged, bed ridden and uncooperative patients.

These are novel types of tablets that disintegrate/dissolve/disperse in saliva. Their characteristic advantages such as administration without water, anywhere, anytime lead to their suitability to geriatric and pediatric patients. They are also suitable for the mentally ill, the bedridden, and patients who do not have easy access to water. The benefits, in terms of patient compliance, rapid onset of action, increased bioavailability, and good stability make these tablets popular as a dosage form of choice in the current market. Recent market studies indicate that more than half of the patient population prefers ODTs to other dosage forms and most consumers would ask their doctors for ODTs (70%), purchase ODTs (70%), or prefer ODTs to regular tablets or liquids (>80%). Moreover, patients travelling with little or no access to water, limit utility of orally administered conventional tablets or capsules. Therefore, to cater the needs of such patients, recent advancements in technology have resulted in development of viable dosage alternatives popularly known as orally disintegrating tablets (ODTs).[1,2] During the past decade, the FDT (fast dissolving tablet) technology, which makes tablets dissolve or disintegrate in the mouth without additional water intake, has drawn a great deal of attention. The technology is also referred to as fast disintegrating tablet, fast dispersing tablet, rapid dissolve tablet, rapid melt tablet, quick
disintegrating tablet, and orally disintegrating tablet. The FDT formulation is defined by the Food and Drug Administration (FDA) as “a solid dosage form containing medicinal substances which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue”. The US Food and Drug Administration Center for Drug Evaluation and Research (CDER) defines, in the ‘Orange Book’, an ODT as “a solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue”. The significance of these dosage forms is highlighted by the adoption of the term, “Orodispersible Tablet”, by the European Pharmacopoeia which describes it as a tablet that can be placed in oral cavity where it disperses rapidly before swallowing.

![Diagram of the dissolution of mouth dissolving formulation](image)

**Significance of ODTs**

ODTs offer dual advantages of solid dosage forms and liquid dosage forms along with special Features which include:

1. An eight-year old with allergies who desires a more convenient dosage form than antihistamine syrup
2. A middle-aged woman undergoing radiation therapy for breast cancer may be too nauseous to swallow her H2-blocker
3. A schizophrenic patient in an institutional setting who may try to hide a conventional tablet under his or her tongue to avoid their daily dose of an atypical antipsychotic
4. A patient with persistent nausea, who may be journey, or has little or no access to water
5. Being unit solid dosage forms, provide luxury of accurate dosing, easy portability and manufacturing, good physical and chemical stability and an ideal alternative for pediatric and geriatric patients.
6. Bioavailability of drugs is enhanced due to absorption from mouth, pharynx and esophagus.
7. Fast onset of therapeutic action as tablet gets disintegrated rapidly along with quick dissolution and absorption in oral cavity.
8. No need of water to swallow the dosage form. Hence, it is convenient for patients who are traveling and do not have immediate access to water.
9. Convenient to administer specially for geriatric, pediatric, mentally disabled and bed ridden patients who have difficulty in swallowing.
10. No risk of suffocation in airways due to physical obstruction when swallowed, thus providing improved safety and compliance.
11. Good mouth feels, especially for pediatric patients as taste masking technique is used to avoid the bitter taste of drug.
12. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach, which enhances bioavailability of drugs.
13. Ability to provide advantage of liquid medication in the form of solid preparation.

Ideal Properties of MDTs \[^{4,6}\]

They should:
1. Not require water to swallow, but it should dissolve or disintegrate in the mouth in matter of seconds.
2. Be compatible with taste masking.
3. Be portable without fragility concern.
4. Have a pleasant mouth feel.
5. Leave minimum or no residue in the mouth after oral administration.
6. Exhibit low sensitive to environmental condition as temperature and humidity.
7. Allow the manufacture of the tablet using conventional processing and packaging equipments at low cost.
8. Has sufficient strength to withstand the rigors of the manufacturing process and post-manufacturing handling.
9. Is insensitive to environmental conditions such as humidity and temperature.
10. Is adaptable and amenable to existing processing and packaging machineries.
11. Is cost-effective

**Salient feature of fast dissolving drug delivery system.**[5]

Orally disintegrating tablets have many advantages over other dosage form such as effervescent tablets, dry syrups, chewing gums, or chewable tablets, which are commonly used to enhance patient compliance. Administration of effervescent tablets, granules or dry syrups require intake of water. Chewing large pieces of gum or tablet is difficult for elderly patient and sometime experience the bitter or unpleasant taste of drug if the taste masking coating rupture during mastication. An ideal fast dissolving tablet formulation should possess following characteristics

1. Ease of Administration to the patient who cannot swallow, such as the elderly, stroke victims, bedridden patients, patient affected by renal failure and patient who refuse to swallow such as pediatric, geriatric & psychiatric patients.
2. No need of water to swallow the dosage form, which is highly convenient feature for patients who are traveling and do not have immediate access to water.
3. Rapid dissolution and absorption of the drug, which will produce quick onset of action.
4. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases bioavailability of drug is increased.
5. Pregastric absorption can result in improved bioavailability.
6. Dosage; improve clinical performance through a reduction of unwanted effects.
7. Good mouth feel property helps to change the perception of medication as bitter pill particularly in pediatric patient.
8. The risk of choking or suffocation during oral administration of conventional formulation due to physical obstruction is avoided, thus providing improved safety.
10. Beneficial in cases such as motion sickness, sudden episodes of allergic attack or coughing, where an ultra-rapid onset of action required.
11. An increased bioavailability, particularly in cases of insoluble and hydrophobic drugs, due to rapid disintegration and dissolution of these tablets.
12. Stability for longer duration of time, since the drug remains in solid dosage form.
Advantages of mouth dissolving tablet\(^7\)

1. Administered without water, anywhere, anytime.
2. Administration to the patients who cannot swallow such as the elderly, stroke victims, bedridden patients, patients affected by renal failure & patients who refuse to swallow such as pediatric, geriatric & psychiatric patients.
3. Beneficial in cases such as motion sickness, sudden episodes of allergic attack or coughing, where an ultra-rapid onset of action required.
4. Achieve increased bioavailability/rapid absorption through pregastric absorption particularly in cases of insoluble and hydrophobic drugs, due to rapid disintegration and dissolution starts from mouth, pharynx & esophagus as saliva passes down.
5. Convenient for administration and patient compliant for disabled, bedridden patients, and the patients who are un-cooperative, or are on reduced liquid intake plans or are nauseated and for travelers and busy people.
6. Good mouth feel property helps to change the perception of medication as bitter pill particularly in pediatric patients.
7. The risk of choking or suffocation during oral administration of conventional formulations due to physical obstruction is avoided, thus providing improved safety.
8. New business opportunity like product differentiation, product promotion, patent extension and life cycle management.
9. Stability for longer duration 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.
11. Convenient for administration and patient compliant for disabled, bedridden patients and for travelers and busy people, who do not always have access to water.
12. The risk of choking or suffocation during oral administration of conventional formulations due to physical obstruction is avoided, thus providing improved safety.
13. Beneficial in cases such as motion sickness, sudden episodes of allergic attack or coughing, where an ultra rapid onset of action required

Limitations of mouth dissolving tablets\(^8,9\)

The tablets usually have insufficient mechanical strength. Hence, careful handling is required.

1. The tablets may leave unpleasant taste and/or grittiness in mouth if not formulated properly.
2. Drugs with relatively larger doses are difficult to formulate into FDT e.g. antibiotics like ciprofloxacin with adult dose tablet containing about 500 mg of the drug.

3. Patients who concurrently take anticholinergic medications may not be the best candidates for FDT. Similarly patients with dryness of the mouth due to decreased saliva production may not be good candidates for these tablet formulations.

**Drug candidates suitable for Mouth dissolving tablets**[9]

Selection of drug candidate for MDT is a very crucial step while developing such dosage forms because of the following factors:

1. Drugs which require controlled or sustained release are unsuitable candidates of fast dissolving oral dosage forms.

2. Drugs which are very bitter or otherwise unacceptable taste because taste masking cannot be achieved.

3. Patients with Sjogren’s syndrome or dryness of the mouth due to decreased saliva production may not be good candidates for FDT formulations.

4. Patients who concurrently take anticholinergic medications may not be the best candidates for these drugs.

5. The drugs which have significantly different pharmacokinetic profiles compared with the same dose administered in a conventional dosage form. E.g. selegiline, apomorphine, buspirone etc.

6. The drugs that produce a significant amount of toxic metabolites mediated by first pass liver metabolism and gastric metabolism and for drugs that have a substantial fraction of absorption in the oral cavity and segments of the pre-gastric GIT.

7. Drugs having ability to diffuse and partition into the epithelium of the upper GIT (log P > 1, or preferable > 2); and those able to permeate oral mucosal tissue are considered ideal for FDT formulations.

8. Drugs with a short half-life and frequent dosing

**Challenges in formulating Mouth dissolving tablets:**[10]

**Palatability**

As most drugs are unpalatable, MDTs usually contain the medicament in a taste-masked form. It disintegrate or dissolve in patient’s oral cavity, thus releasing the active ingredients.
Mechanical strength
In order to allow MDTs to disintegrate in the oral cavity, they are made of either very porous and soft-molded matrices or compressed into tablets with very low 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.

Hygroscopicity
Many orally disintegrating dosage forms are hygroscopic and cannot maintain physical integrity under normal conditions of temperature and humidity.

Amount of drug
The application of technologies used for MDTs is limited by the amount of drug that can be incorporated into each unit dose. For lyophilized dosage forms, the drug dose must be less than 400 mg for insoluble drugs and 60 mg for soluble drugs.

Size of tablet
It has been reported that the easiest size of tablet to swallow is 7-8 mm while the easiest size to handle was one larger than 8 mm. Therefore, the tablet size that is both easy to take and easy to handle is difficult to achieve.

Aqueous Solubility
Water-soluble drugs pose various formulation challenges because they form eutectic mixtures, which result in freezing-point depression and the formation of a glassy solid that may collapse upon drying because of loss of supporting structure during the sublimation process.

Amount of drug
According to USP generally, the ODT tablet weight should not exceed 500 mg. For lyophilized dosage forms, the drug dose should be lower than 400 mg for insoluble drug and less than 60 mg for soluble drug.

Excipients used for preparation of MDT
Superdisintegrants
The proper choice of disintegrant or superdisintegrant and its consistency of performance are of critical importance to the formulation development of mouth dissolving tablets. Superdisintegrant have been developed to improve the disintegration processes.
Superdisintegrants are generally used at a low level in the solid dosage form, typically 1–10% by weight relative to the total weight of the dosage unit. The disintegrants have the major function to oppose the efficiency of the tablet binder and the physical forces that act under compression to form the tablets.

Selection Of Superdisintegrants:[13]

Although superdisintegrants primarily affect the rate of disintegration, but when used at high levels they can also affect mouth feel, tablet hardness and friability. Hence, various ideal factors to be considered while selecting an appropriate superdisintegrants for a particular formulationshould:

1. Produce rapid disintegration, when tablet comes in contact with saliva in the mouth/oral cavity.
2. Be compactable enough to produce less friable tablets.
3. Produce good mouth feel to the patients. Thus, small particle size is preferred to achieve patient compliance.
4. Have good flow, since it improves the flow characteristics of total blend

Various Superdisintegrants and Their Properties

<table>
<thead>
<tr>
<th>Superdisintegrants</th>
<th>Commercially available grades</th>
<th>Mechanism of action</th>
<th>Special comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crosslinked cellulose</td>
<td>Croscarmellose®, Ac-Di-Sol®, NymceZSX®, Primellose®</td>
<td>Swells 4-8 folds in &lt;10seconds Swelling and wicking both.</td>
<td>Swells in two dimensions Direct compression or Granulation Starch free.</td>
</tr>
<tr>
<td>Crosslinked PVP</td>
<td>CrosspovidonM®, Kollidon®, Polyplasdone</td>
<td>Swells very little and returns to original size after compression but act by capillary action.</td>
<td>Water insoluble and spongy in nature so get porous tablet.</td>
</tr>
<tr>
<td>Crosslinked starch</td>
<td>Explotab®, Primogel®</td>
<td>Swells 7-12 folds in &lt; 30 seconds.</td>
<td>Swells in three dimensions and high Level serves as sustain release matrix.</td>
</tr>
<tr>
<td>Crosslinked alginicacid</td>
<td>Alginic acid NF</td>
<td>Rapid swelling in aqueous medium or wicking action.</td>
<td>Promote disintegration in both dry or wet granulation</td>
</tr>
<tr>
<td>Soy polysaccharides</td>
<td>Emcosoy®</td>
<td>Rapid Dissolving</td>
<td>Used in nutritional products.</td>
</tr>
<tr>
<td>Crosslinked polymer of Polycarboxylic acids</td>
<td>Kyron T-314</td>
<td>High swelling tendency of Hydration. Swelling Index 12</td>
<td>Elimination of lump formation. It is suitable for the both wet granulation as well as</td>
</tr>
</tbody>
</table>
The requirement placed on the tablet disintegrants should be clearly defined. The ideal disintegrant has:

1. Poor solubility
2. Poor gel formation
3. Good hydration capacity
4. Good molding and flow properties
5. No tendency to form complexes with the drugs

There are three methods of incorporating disintegrating agents into the tablets:

1. Internal Addition (Intragranular)
2. External Addition (Extragranular)
3. Partly Internal and External

In external addition method, the disintegrant is added to the sized granulation with mixing prior to compression.

### Disintegrants used in MDT’s

<table>
<thead>
<tr>
<th>Disintegrants</th>
<th>Mechanism</th>
<th>Conc. %w/w</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starch</td>
<td>It enables water to draw into the structure by capillary action, thus leading to disruption of tablet.</td>
<td>5-20</td>
</tr>
<tr>
<td>Pregelatinized starch</td>
<td>It increases dissolution rate by rapid disintegration due to superior swelling capacity.</td>
<td>5-15</td>
</tr>
<tr>
<td>Sodium Starch Glycolate</td>
<td>It absorbs water readily leading to an increase in volume of granules result in rapid and uniform disintegration.</td>
<td>1-3</td>
</tr>
<tr>
<td>Cross-linked polyvinyl Pyrrolidone</td>
<td>It acts by capillary action water is responsible for its tablet disintegration property.</td>
<td>0.5-5</td>
</tr>
<tr>
<td>(CrossPovidone, Crosspovidon M®, Kollidon®, Polyplasdone®)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cellulose (Ac-Di-Sol, Nymce ZSX®, Primellose®, Solutab®)</td>
<td>They have ability to swell on contact with water results in rapid tablet disintegration.</td>
<td>1-3</td>
</tr>
<tr>
<td>Microcrystalline Cellulose (Avicel)</td>
<td>Allowing water to enter the tablet matrix by means of capillary pores, which break the hydrogen bonding between adjacent bundles of cellulose microcrystals</td>
<td>10-20</td>
</tr>
<tr>
<td>Alginates (Alginic Acid, Satialgine®)</td>
<td>It has High affinity for water absorption and high sorption.</td>
<td>1-5</td>
</tr>
<tr>
<td>Soy polysaccharides</td>
<td>Rapid swelling in aqueous medium orwicking action, it</td>
<td>5-15</td>
</tr>
</tbody>
</table>
**Bulking materials:** \[^{[15]}\]

Bulking materials are significant in the formulation of fastmelting tablets. The materia contributes functions of a diluent, filler and cost reducer. Bulking agents improve the textural characteristics that in turn enhance the disintegration in the mouth, besides; adding bulk also reduces the concentration of the active in the composition. The recommended bulking agents for this delivery system should be more sugar-based such as mannitol, polydextrose, lactitol, DCL (direct compressible lactose) and starch hydrolystate for higher aqueous solubility and good sensory perception. Bulking agents are added in the range of 10 percent to about 90 percent by weight of the final composition.

**Emulsifying agents**

Emulsifying agents are important excipients for formulating fast-melting tablets they aid in rapid disintegration and drug release without chewing, swallowing or drinking water. In addition, incorporating emulsifying agents is useful in stabilizing the immiscible blends and enhancing bioavailability. A wide range of emulsifiers is recommended for fast-tablet formulation, including alkyl sulfates, propylene glycol esters, lecithin, sucrose esters and others. These agents can be incorporated in the range of 0.05 percent to about 15 percent by weight of the final composition.

**Lubricants**

Lubricants, though not essential excipients, can further assist in making these tablets more palatable after they disintegrate in the mouth. Lubricants remove grittiness and assist in the drug transport mechanism from the mouth down into the stomach.
Flavours and sweeteners. [16]
Flavours and taste-masking agents make the products more palatable and pleasing for patients. The addition of these ingredients assists in overcoming bitterness and undesirable tastes of some active ingredients.

Various manufacturing techniques for MDDDS[17]
include:
1. Lyophilization
2. Moulding
3. Direct Compression
4. Cotton Candy Process
5. Spray Drying
6. Sublimation
7. Mass Extrusion
8. Nanonization
9. Fast Dissolving Films

Freeze-Drying or Lyophilization

Freeze Drying
Freeze drying is the process in which water is sublimed from the product after it is frozen. It creates an amorphous porous structure that can dissolve rapidly. In this process active drug is dissolved or dispersed in an aqueous solution of a carrier/polymer. The mixture is poured in the walls of the preformed blister packs. The trays holding the blister packs are passed through liquid nitrogen freezing tunnel to freeze the drug solution or dispersion. Then the frozen blister packs are placed in refrigerated cabinets to continue the freeze-drying. After freeze-drying the aluminum foil backing is applied on a blister-sealing machine. The freeze-drying technique has demonstrated improved absorption and increase in bioavailability. The major disadvantages of lyophilization technique are that it is expensive and time consuming; fragility makes conventional packaging unsuitable for these products and poor stability under stressed conditions. Zydis technology (ZT) is a patented technique, which had been used for drugs like famotidine, loperamide, piroxicam, oxazepam, lorazepam, domeperidone, brompheniramine, olanzepine, ondansetron and rizatriptan. Thirteen products are currently available in the market, which had been manufactured using this technology. In U.S., the MDT products available are: Claritin RediTab, Dimetapp Quick Dissolve, Feldene Melt,
Maxalt- MLT, Pepcid RPD, Zofran ODT and Zyprexa Zydis. In the worldwide market, Zydis formulations are also available for oxazepam, lorazepam, loperamide, and enalapril. ZT utilizes a unique freeze-drying process to manufacture finished dosage units which significantly differ from conventional oral systems. The process involves the following steps:

**Stage 1**
bulk preparation of an aqueous drug solution or suspension and its subsequent precise dosing into preformed blisters. It is the blister that actually forms the tablet shape and is, therefore, an integral component of the total product package.

**Stage 2**
passing the filled blisters through a specially designed cryogenic freezing process to control the ultimate size of the ice crystals which ensures that the tablets possess a porous matrix to facilitate the rapid disintegration property. These frozen units are then transferred to large-scale freeze dryers for the sublimation process, where the majority of the remaining moisture is removed from the tablets.

**Stage 3**
Sealing the open blisters using a heat-seal process to ensure stability and protection of the product from varying environmental conditions.

**Advantages**
The major advantage of using this technique is that the tablets produced by this technology have very low disintegration time and have great mouthfeel due to fast melting effect

**Tablet Moulding**
In this method, molded tablets are prepared by using water-soluble ingredients so that the tablets dissolve completely and rapidly. The powder blend is moistened with a hydro-alcoholic solvent and is molded into tablets under pressure lower than that used in conventional tablet compression. The solvent is then removed by air-drying. Molded tablets are very less compact than compressed tablets. These possess porous structure that increase dissolution Moulded tablets invariably contain water-soluble ingredients due to which the tablets dissolve completely and rapidly.
Solvent Molding
In this technique, the powder blend is moistened with hydro alcoholic solvent and molded into tablets at low compression pressure in molded plates to form wetted mass (compression molding). The solvent is then removed by air-drying. These tablets possess a porous structure that hastens the dissolution.

Heat Molding
In this technique, a suspension is prepared that contains drug, agar and sugar (e.g. mannitol or lactose) and pouring the suspension in the blister packaging wells, solidifying the agar at the room temperature to form a jelly and drying at 30 °C under vaccum. This technique is associated with the problem of poor taste-masking. To overcome this problem, taste masked active drug particle can be used into a lactose based tablet triturate form. These taste masked particles of drug are prepared by spray congealing of a molten mixture of hydrogenated cottonseed oil, sodium bicarbonate, lecithin, polyethylene glycol and drug into lactose based tablet triturate form. Compared to the freeze drying or lyophilization technique, tablets produced by the molding technique are easier to scale up for industrial manufacture.

Moulding by Vacuum Evaporation without Lyophilization
This process involves pouring of the drug excipient mixture (in the form of a slurry or paste) into a mould of desired dimension, freezing the mixture to form a solidified matrix and finally subjecting it to vacuum drying at a temperature within the range of its collapse temperature and equilibrium freezing temperature. This results in the formation of a partially collapsed matrix. This method differs from the lyophilization technique, as in the former the evaporation of free unbound solvent occurs from a solid through the liquid phase to a gas, under controlled conditions, instead of the sublimation which takes place in the latter process.

Direct Compression
It is the easiest way to manufacture tablets. Conventional equipment, commonly available excipients and a limited number of processing steps are involved in direct compression. Also high doses can be accommodated and final weight of tablet can easily exceed that of other production methods.

Disintegrants
Addition of disintegrants in MDT, leads to quick disintegration of tablets and hence improves dissolution. In many fast dissolving tablet technologies based on direct compression, the
disintegrants principally affect the rate of disintegration and hence the dissolution. Microcrystalline cellulose, cross linked carboxymethyl cellulose sodium, cross linked polyvinyl pyrrolidone and partially substituted hydroxypropyl cellulose, though water insoluble, absorb water and swell due to capillary action and are considered as effective disintegrants in the preparation of fast dissolving tablets. In many MDT products based on DC process, the disintegrants mainly affect the rate of disintegration and hence dissolution which is further enhanced in the presence of water soluble excipients and effervescent agents. The introduction of superdisintegrants has increased the popularity of this technology. Tablet disintegration time can be optimized by focusing on the disintegrant concentration. Below a critical disintegrant concentration, tablet disintegration time becomes inversely proportional to disintegrant concentration.

**Effervescent Agents**

The evolution of CO2 as a disintegrating mechanism forms the basis of the patented Orasolv technology (OT) and is frequently used to develop over-the-counter formulations. The product contains microparticles and is slightly effervescent in nature. Saliva activates the effervescent agent which causes the tablet to disintegrate. The OT had been utilized in fabrication of six marketed products: four Triaminic Softchew formulations, Tempra FirsTabs and Remeron SolTab.

**Sugar-Based Excipients**

This is another approach to manufacture FDT by direct compression. The use of sugar based excipients especially bulking agents like dextrose, fructose, isomalt, lactitol, maltitol, maltose, mannitol, sorbitol, starch hydrolysate, polydextrose and xylitol, which display high aqueous solubility and sweetness, and hence impart taste masking property and a pleasing mouth feel. Sugar-based excipient is classified into two types on the basis of molding and dissolution rate.

**Type I** saccharides (e.g., lactose and mannitol) exhibit low mouldability but high dissolution rate.

**Type II** saccharides (e.g., maltose and maltitol) exhibit high mouldability but low dissolution rate.

Mouldability is defined as the capacity of the compound to be compressed/ moulded and to dissolve. It does not refer to the formation of a true mould by melting or solvent wetting process. The mouldability of Type I saccharide can be improved by granulating it with a
Type II saccharide solution. The above technology forms the basis of WOWTAB which involves the use of fluidized bed granulation for the surface treatment of Type I saccharide with Type II saccharide. This technique has been used in the production of Benadryl Fast melt tablets. Here, two different types of saccharides are combined to obtain a tablet formulation with adequate hardness and fast dissolution rate.

**Cotton Candy Process**\(^{[19]}\)

This process is so named as it utilizes a unique spinning mechanism to produce floss-like crystalline structure, which mimic cotton candy. Cotton candy process involves formation of matrix of polysaccharides or saccharides by simultaneous action of flash melting and spinning. The matrix formed is partially recrystallized to have improved flow properties and compressibility. This candy floss matrix is then milled and blended with active ingredients and excipients and subsequently compressed to MDTs. However, other polysaccharides such as polymaltodextrins and polydextrose can be transformed into fibers at 30–40% lower temperature than sucrose. This modification permits the safe incorporation of thermolabile drugs into the formulation. The tablets manufactured by this process are highly porous in nature and offer very pleasant mouthfeel due to fast solubilization of sugars in presence of saliva.

**Spray-Drying**\(^{[20]}\)

This technology produces highly porous and fine powders as the processing solvent is evaporated during the process. In this method to prepare MDTs hydrolyzed and non-hydrolyzed gelatin were used as supporting matrix, mannitol as bulking agent and sodium starch glycolate or crosscarmellose sodium as superdisintegrant. Disintegration and dissolution were further increased by adding acidic substances like citric acid or alkali substance like sodium bicarbonate. This formulation technique gives porous powder and disintegration time < 20 sec, have used spray-drying for the production of MDTs. Disintegration and dissolution were further enhanced by adding an acid (e.g., citric acid) or an alkali (e.g., sodium bicarbonate). The suspension of above excipients was spray-dried to yield a porous powder which was compressed into tablets.

**Sublimation**\(^{[21]}\)

Sublimation has been used to produce MDTs with high porosity. A porous matrix is formed by compressing the volatile ingredients along with other excipients into tablets, which are finally subjected to a process of sublimation. Inert solid ingredients with high volatility (e.g.,
ammonium bicarbonate, ammonium carbonate, benzoic acid, camphor, hexamethylene tetramine, naphthalene, phthalic anhydride, urea and urethane) have been used for this purpose. Solvents such as cyclohexane and benzene were also suggested for generating the porosity in the matrix. Makino et al., reported a method using water as a pore-forming material.

Steps involved in Sublimation technology

**Mass-Extrusion**\(^{[22]}\)

In this technology involves softening the active blend using the solvent mixture of water-soluble polyethylene glycol and methanol and subsequent expulsion of softened mass through the extruder or syringe to get a cylinder of the product into even segments using heated blade to form tablets This process can also be used to coat granules of bitter drugs to mask their taste.

**Nanization**\(^{[23]}\)

This technique is especially advantageous for poorly water soluble drugs. Other advantages of this technology include fast disintegration/dissolution of nanoparticles leading to increased absorption and hence higher bioavailability and reduction in dose, cost effective manufacturing process, conventional packaging due to exceptional durability and wide range of doses (up to 200 mg of drug per unit).
Fast Dissolving Films\cite{24}

This technique, a non-aqueous solution is prepared containing water soluble film forming polymer (pullulan, carboxy methylcellulose, hydroxypropyl methylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, polyvinyl pyrrolidone, polyvinyl alcohol or sodium alginate, etc.), drug and other taste masking ingredients, which is allowed to form a film after evaporation of solvent. In case of a bitter drug, resin adsorbate or coated microparticles of the drug can be incorporated into the film. This film, when placed in mouth, melts or dissolves rapidly, releasing the drug in solution or suspension form. The features of this system include paper thin films of size less than 2X2 inches, dissolution in 5 sec, instant drug delivery and flavoured after taste.

Patented Technologies Used For Manufacturing Mout Dissolving Tablets\cite{25,26}

Orasolv®.

This technology is patented by CIMA Labs. This includes use of effervescent disintegrating agents compressed with low pressure to produce the FDTs. The evolution of carbon dioxide from the tablet produces fizzing sensation, which is a positive organoleptic property. Concentration of effervescent mixture usually employed is 20-25% of tablet weight. As tablets are prepared at low compression force, they are soft and fragile in nature. This initiated to develop Paksolv, a special packaging to protect tablets from breaking during storage and transport. Paksolv is a dome-shaped blister package, which prevents vertical movement of tablet within the depression. Paksolv offers moisture, light, and child resistance packing.

Durasolv®.

This technology is patented by CIMA Labs. The tablets produced by this technology utilize the conventional tableting equipment. Tablets in this are formulated by using drug, nondirect compression fillers, and lubricants. Nondirect compressible fillers are dextrose, mannitol, sorbitol, lactose, and sucrose, which have advantage of quick dissolution and avoid gritty texture, which is generally present in direct compressible sugar. The tablets obtained are strong and can be packed in conventional packing in to bottles and blisters.

Wowtab®.

Yamanouchi patented this technology. WOW means with out water. This technology utilizes conventional granulation and tableting methods to produce FDTs employing low- and high-moldability saccharides. Low moldability saccharides are lactose, mannitol, glucose, sucrose,
and xylitol. High-moldability saccharides are maltose, maltitol, sorbitol, and oligosaccharides. When these low- and high-moldable saccharides are used alone tablets obtained do not have desired properties of rapid disintegration and hardness, so combinations are used. This technology involves granulation of low-moldable saccharides with high-moldable saccharides as a binder and compressing into tablets followed by moisture treatment. Thus tablets obtained showed adequate hardness and rapid disintegration.

**Flashtab®.**

Flashtab® tablets were developed by Prographarm, France. In this technique, most of the excipients are used as for conventional compressed tablets. A disintegrating agent and a swelling agent are used in combination with coated drug particles to produce a tablet that disintegrates in the mouth in one minute. Flashtab® matrix tablet contains a swelling agent such as modified starch or microcrystalline cellulose and a superdisintegrant such as crospovidone or croscarmellose. The system may also contain a highly water soluble polyol such as mannitol, sorbitol, maltitol or xylitol with binding properties if no swelling agent is used. The direct coating procedure is used for taste masking of the active ingredient. In the Flashtab® technique, the excipients are first granulated using wet or dry granulation. Then they are mixed with coated drug particles and compressed into tablets using conventional processing equipment.

**Zydis®.**

Zydis® technique is owned by R P Scherer, a subsidiary of Cardinal Health. A Zydis® tablet is produced by lyophilizing or freeze-drying the drug in a water soluble matrix material, usually consisting of gelatin. Freeze-drying is done in blisters, where sublimation removes water, which are then sealed and further packed. The resultant product is very porous, light and fragile and disintegrates immediately on contact with saliva. The Zydis® formulation is also self-preserving since the final water concentration in the freeze-dried product is very low and prevents microbial growth. The ideal drug candidates for Zydis® are the ones showing relatively low water solubility, with fine particles and good aqueous stability in the suspension. For water soluble drugs, the upper limit for drug loading is very low (approx. 60 mg). The basic problem of water soluble drugs is the formation of a eutectic mixture, which results in freezing point depression and formation of glossy solids on freezing, leading to supporting structure collapse during sublimation. This problem can be solved by adding a crystal forming agent such as mannitol.
Flashdose® technology was invented by Fuisz Technologies, USA, now owned by Biovail (Canada). Fuisz Technologies has developed three oral drug delivery systems that involve fast dissolution. The first two generations are quick-dissolving Soft Chew and EZ Chew tablets which require some chewing. Most recently Fuisz also developed Flashdose® technology, which uses a unique spinning mechanism to produce a flash-like crystalline structure, much like cotton candy. These crystalline sugars can then incorporate APIs and be compressed into tablets. Flashdose® dosage form utilizes the shearform technique in association with CeformTM to mask the bitter taste of the medicament. CeformTM technique which produces uniform microspheres with very narrow particle size distribution has been patented by Fuisz. The shearform technology used in the preparation of the matrix is known as floss, which is made from a combination of excipients. The floss cotton candy-like fibers are made up of saccharides such as sucrose, dextrose, lactose and fructose. Sucrose required a temperature of 82–130 °C to be transformed into fibers while other polysaccharides such as polymaltodextrins and polydextrose require 30–40% lower temperature than sucrose.

The Flashdose® manufacturing process can be divided into four steps

1. Floss blend
Approximately 80% of sucrose in combination with mannitol or dextrose and 1% of surfactant (approx.) are blended to form the floss mixture, in which the surfactant acts as a crystallization enhancer for maintaining the structure and integrity of floss fibers. Also, the enhancer helps conversion of amorphous sugars into crystalline sugar. In this process, dispersed API is retained in the matrix by minimizing its migration out of the mixture.

2. Floss processing
The floss formation machine consisting of a spinning head and heating element is similar to the cotton candy type. The matrix is produced by subjecting the carrier material to flash heat and flash flow processing. In the flash heat process, the carrier material is heated sufficiently to create the internal flow condition and then exit through the spinning head, which throws the floss by centrifugal force. Sufficient centrifugal force is generated by spinning head rotation at approximately 2000–3600 rpm. The heating blocks are positioned around the circumference of the crown and are outlined outside on the rim of the heaters. Narrowing the width of the aperture and increase in the path length of the existing material result in the production of fibers. The fibers produced are usually amorphous.
3. Floss chopping and conditioning
The fibers are conditioned to smaller particle size in a high shear mixer granulator by chopping and rotation. The conditioning is performed by partial crystallization, which is carried out by spraying ethanol (< 1 %) on the floss. The resultant evaporated floss fibers possess the cohesive properties and improved flow properties.

4. Tablet blend and compression
The resultant floss fibers are then blended with API along with other required tablet excipients and compressed into tablets. A modification of this process is a curing step. The curing step is added to improve the mechanical strength of the barely molded flash dose dosage form in plastic blister pack dispersion. The curing step involves exposure of the dosage form to elevated temperature and humidity conditions such as 40 °C and 85 % RH for 15 min. The curing step is carried out for crystallization of the floss material.

Oraquick®.
Oraquick® formulation was developed by utilizing patented taste masking technologies such as FlavourTech and MicroMask. In MicroMask technology, the taste masking process is done by incorporating the drug into the matrix microsphere and KV Pharmaceutical claims that MicroMask has good taste masking compared to Flavour Tech. In Oraquick® technique, tablets are prepared by dissolving the sugar (sucrose, mannitol, sorbitol, xylose, dextrose, fructose or mannose) and protein (albumin or gelatin) in a suitable solvent such as water, ethanol, isopropyl alcohol and ethanol-water mixture. The matrix solution is then spray-dried to give highly porous granules. Porosity of the resultant granules depends upon the quantity of solvent used in the process.

Lyoc®.
Lyoc® technique is owned by Cephalon Corporation. CIMA is a subsidiary of Cephalon and it currently manages the Lyoc R&D efforts. This was the first freeze drying technique used for the manufacturing of ODTs. The liquid solution or suspension preparation involves fillers, thickening agents, surfactants, non-volatile flavouring agents and sweeteners along with APIs. The resultant homogeneous liquid is placed in blister cavities and subjected to freeze-drying. Lyoc® tablets do not contain preservatives. To prevent inhomogeneity due to sedimentation during this process, the formulation requires a large proportion of undissolved inert filler (mannitol) in order to increase the viscosity of the in process suspension. The high proportion of filler reduces the potential porosity of the dried dosage form and results in...
denser tablets, with disintegration rates comparable to the loosely compressed oral melt formulations.

**Advatab®.**

Advatab® tablets disintegrate rapidly in the mouth, typically in less than 30 s to allow for convenient oral drug administration without water. These tablets are especially suited to patients that experience difficulty in swallowing capsules and tablets. Advatab® is different from other ODT technologies in that it can be combined with Eurand’s complimentary particle technologies like Microcaps® (world leading taste masking technology) and Diffucaps® (controlled release technology). A combination of Advatab® and Microcaps® creates products that offer the dual advantage of a patient’s preference together with superior taste and smooth mouth feel. This is critical advantage as the unpleasant taste of drugs restricts application of other ODT technologies.

**Frosta® (Akina).**

The Frosta® approach utilizes conventional wet granulation processing and tablet machines for extremely cost effective production of fast-melting tablets. In this technique, plastic granules are formulated and compressed at low pressure to produce strong tablets with high porosity. Plastic granules are composed of three components porous and plastic material, water penetration enhancer and binder. The process involves mixing of the porous plastic material with water penetration enhancer followed by granulation with binder. The tablets obtained have excellent hardness and rapid disintegration time, ranging from 15 to 30 s depending on the size of the tablet.

**Quick-Dis Technology®.**

The novel intraoral drug delivery system, trademarked Quick-Dis™, is Lavipharm’s proprietary patented technology and is a thin, flexible and quick-dissolving film (81). The film is produced by the solvent casting method. In this technique, water-soluble hydrocolloids like gelatin, pectin, gum acacia, gum arabic, hydroxypropylmethylcellulose or starch were completely dissolved in water to form a homogenous viscous solution. Other ingredients such as emulsifying agents, solubilizing agents, wetting agents, taste-modifying agents, plasticizers, water-soluble inert fillers, preservatives, buffering agents, coloring agents, and stabilizers along with APIs were dissolved in a small portion of aqueous solvent using a high-shear processor. The active mixture was then added to the viscous hydrocolloid solution to form a homogeneous viscous solution. The Quick-Dis™ drug delivery system can be
dispensed in various packaging configurations, ranging from unit-dose pouches to multiple-dose blister packages.

**Nanocrystal Technology/nanomelt®.**

For mouth dissolving tablets, Elan’s proprietary Nanocrystal® technology improves compound activity and final product characteristics. Decreasing the particle size increases the surface area, which in turn leads to an increase in the dissolution rate and this is the main principle behind the Nanocrystal™ technology. This technique is especially used for poorly water-soluble drugs. Nanocrystal™ particles are nano-sized drug substances, typically less than 1000 nm in diameter, which are produced by milling using a proprietary wet milling technique and are stabilized against agglomeration to create a suspension that behaves like a solution. Nanocrystal™ orally dissolving technology provides for:

1. Pharmacokinetic benefits, which mainly include bioavailability of orally administered nanoparticles (< 2 mm) in the form of a rapidly disintegrating tablet matrix;
2. Product differentiation based upon a combination of proprietary and patent-protected technology elements;
3. Exceptional durability, enabling use of conventional packaging equipment and formats (i.e., bottles and/or blisters);
4. Wide range of doses (up to 200 mg of API per unit);
5. Use of conventional, compendial inactive components;

Nanocrystal colloidal dispersions of drug substance are combined with water-soluble, generally regarded as safe (GRAS) ingredients, filled into blisters and lyophilized. The resultant wafers dissolve in very small quantities of water in seconds. This approach is mainly used when working with highly potent or hazardous materials because it avoids a number of manufacturing steps such as granulation, blending and tableting, which generate large quantities of aerosolized powder and constitute a much higher risk of toxicity.

**Evaluation Parameters:**[27]

**Weight variation test**

The weight variation test is carried out in order to ensure uniformity in the weight of tablets in a batch. First the total weight of 20 tablets from each formulation is determined and the average is calculated. The individual weight of the each tablet is also determined to find out the weight variation.
The % weight variation of each individual tablet from the average weight is calculated by the given formula:

\[ \% \ Weight \ Variation = \frac{\text{Individual weight of each tablet} - \text{Average weight of 20 tablets}}{\text{Average weight of 20 tablets}} \times 100 \]

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Average weight of Tablets (mg)</th>
<th>Maximum % difference allowed</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>130 or less</td>
<td>10</td>
</tr>
<tr>
<td>2</td>
<td>130-324</td>
<td>7.5</td>
</tr>
<tr>
<td>3</td>
<td>More than 324</td>
<td>5</td>
</tr>
</tbody>
</table>

**Hardness test**

The hardness of tablet is an indication of its strength. Measuring the force required to break the tablet across tests it. The force is measured in kg and the hardness of about 3-5 kg/cm² is considered to be satisfactory for uncoated tablets. Hardness of 10 tablets from each formulation is determined by Monsanto hardness tester, Pfizer hardness tester, Dr. Schleuniger Pharmatron-5Y etc.

**Friability**

Friability is the loss of weight of tablet in the container due to removal of fine particles from the surface. Friability test is carried out to assess the ability of the tablet to withstand abrasion in packaging, handling and transport. Roche friabilator is employed for finding the friability of the tablets. Weigh the tablets which have average weight more than 6.5gm from each batch and place in Roche friabilator that will rotate at 25 rpm for 4 minutes. Dedust the all tablets and weigh again. The percentage of friability can be calculated using the formula:

\[ \% \ Friability = \frac{W_1 - W_2}{W_1} \times 100 \]

Where, \( W_1 \) = Weight of tablet before test, \( W_2 \) = Weight of tablet after test.

**Wetting time**

Wetting time and water absorption ratio are the significant parameters for mouth dissolving tablets. The following method for calculating the wetting time of the tablet. A piece of filter paper (circularly cut) was placed in a small petri plate containing water soluble dye solution. Tablet was placed on the paper and the time required for complete wetting of the tablet was determined (Figure 7). Bi Y. et al. used a tissue paper folded twice and was placed in a small culture dish (i.d = 6.5 cm) containing 6 ml of water.
Water absorption ratio
A small piece of tissue paper folded twice is placed in a small petridish containing 6 ml of water. Put a tablet on the paper and the time required for complete wetting is measured. The wetted tablet is then reweighed. Water absorption ratio, R is determined by using following formula
\[ R = 100 \times \frac{W_a - W_b}{W_b} \]
Where, \( W_b \) is the weight of tablet before water absorption, \( W_a \) is the weight of tablet after water absorption.

Disintegration time:[28]
Disintegration time for randomly selected 6 tablets was measured using disintegration test apparatus. The average time required for disintegration was calculated and compared with standards.

**Disintegration Test with Rotary Shaft Method**
In another study, Narazaki et al., proposed a better disintegration method for MDTs. In the experimental method, the MDT was placed on the wire gauze(D), slightly immersed in the medium, and then compressed by a rotary shaft (E) which was employed to provide mechanical stress on the tablet by means of its rotation and weight. Purified water at temperature 37 °C was used as the medium. The critical parameters of the proposed method were the rotation speed and the mechanical stress. Using this new method, it would be possible to predict a more realistic disintegration rate in human. The compression force can be easily adjusted using the weight (A). The rotary shaft crushes the MDT which disintegrates into the medium. The endpoint was measured visually using a stopwatch.
(a) Apparatus of rotary shaft method for MDT (A) weight, (B) MDT, (C) wetting sponge, (D) wire gauze, (E) rotary shaft, (F) medium. (b) improved rotary shaft apparatus.

**In-vitro dispersion time**
Tablet was added to 10 ml of phosphate buffer solution, pH 6.8 at 37±0.5°C. Time required for complete dispersion of a tablet was measured.

**In-vitro dissolution studies**
In-vitro dissolution study is performed by using USP Type II Apparatus (Paddle type) at 50 rpm. The amount of drug dissolved is determined by suitable analytical technique. And selected 6 tablets were subjected to drug release studies using USP dissolution apparatus, in dissolution medium volume of 900 ml was used and a temperature of 37±0.5°C was maintained. 5 ml of the sample was collected for every 5 minutes interval till 30 minutes and replaced with 5 ml of fresh buffer solution.
Stability studies
The optimized formulation of MDTs is subjected to stability study as per ICH guidelines to assess their stability with respect to their physical appearance and release characteristics. Various stability studies like accelerated stability study, intermediate and long term stability studies were done during preformulation. The sample was subjected to higher temperature or humidity or both, to know their impact on the stability of mouth dissolving tablet.

Stability testing of drug\(^{29}\)
Temperature dependent stability studies: The fast dissolving tablets are packed in suitable packaging and stored under the following conditions for a period as prescribed by ICH guidelines for accelerated studies;
1. 40 ± 1°C
2. 50 ± 1°C
3. 37 ±1oC
4. RH 75% ± 5%

The tablets were withdrawn after a period of 15 days and analyzed for physical characterization (Visual defects, Hardness, Friability, Disintegration, Dissolution etc.) and drug content. The data obtained is fitted into first order equations to determine the kinetics of degradation. Accelerated stability data are plotting according Arrhenius equation to determine the shelf life at 25oC

Packaging of MDTs: \(^{30}\)
Packing is one of the important aspects in manufacturing MDTs. The products obtained by various technologies vary in some of the parameters especially in mechanical strength to a great extent. The products obtained by lyophilization process including various technologies such as Zydis, Lyoc, Quicksolv, and Nanocrystal are porous in nature, have less physical resistance, sensitive to moisture, and may degrade at higher humidity conditions. For the above reasons products obtained require special packing. Zydis units are generally packed with peelable backing foil. Paksolv is a special packaging unit, which has a dome shaped blister, which prevents vertical movement of tablet within the depression and protect tablets from breaking during storage and transport, which is used for Orasolv tablet. Some of the products obtained from Durasolv. WOW Tab, Pharmaburst oraquick, Ziplets, etc.
technologies have sufficient mechanical strength to withstand transport and handling shock so they are generally packed in push through blisters or in bottles.

**Drugs To Be Promising In Corporated In Mouth Dissolving Tablets**[^1][^2]

**Analgesics and Anti-inflammatory Agents**
Aloxiprin, Auranofin, Azapropazone, Benorylate, Diflunisal, Etodolac, Fenbufen, FenoprofenCalcim, Flurbiprofen, Ibuprofen, Indomethacin, Ketoprofen, Meclofenamic Acid, Mefenamic Acid, Nabumetone, Naproxen, Oxyprozin, Oxyphenbutazone, Phenylbutazone, Piroxicam, Sulindac.

**Anti-bacterial Agents**
Benethamine Penicillin, Cinoxacin, Ciprofloxacin, Clarithromycin, Clofazimine, Cloxacillin, Demeclocycline, Doxycycline, Erythromycin, Ethionamide, Imipenem, Nalidixic Acid, Nitrofurantoin, Rifampicin, Spiramycin, Sulphabenzamide.

**Anti-coagulants**
Dicoumarol, Dipyridamole, Nicoumalone, Phenindione.

**Anti-Depressants**
Amoxapine, Cilazindol, Maprotiline, Mianserin, Nortriptyline, Trazodone, Trimipramine Maleate., Acetohexamide, Chlorpropamide, Glibenclamide, Gliclazide, Glipizide, Tolazamide, Tolbutamide.

**Anti-Fungal Agents**

**Anti-Hypertensive Agents:**
Amlodipine, Carvedilol, Benidipine, Darodipine, Dilitazem, Diazoxide, Felodipine, Guanabenz Acetate, Indoramin, Isradipine, Minoxidil, Nicardipine, Nifedipine, Nimodipine, Phenoxybenzamine, Prazosin, Reserpine, Terazosin.

**Anti-Malarials**
Amodiaquine, Chloroquine, Chlorproguanil, Halofantrine, Mefloquine, Proguanil, Pyrimethamine, Quinine Sulphate. **Anti-Migraine Agents:** DihydroergotamineMesyiate, Ergotamine Tartrate, Methysergide Maleate, Pizotifen Maleate, Sumatriptan Succinate.
Anti-Muscarinic Agents
Atropine, Benzhexol, Biperiden, Ethopropazine, Hyoscine Butyl Bromide, Hyoscyamine, Mepenzolate Bromide, Orphenadrine, Oxyphenylcimine.

Anti-Neoplastic Agents and Immunosuppressants
Aminoglutethimide, Amsacrine, Azathioprine, Busulphan, Chlorambucil, Cyclosporin, Dacarbazine, Estramustine, Etoposide, Lomustine, Melphalan, Mercaptopurine, Methotrexate, Mitomycin, Mitotane, Mitozantrone, Procarbazine, Tamoxifen Citrate, Testolactone.

Anti-Thyroid Agents
Carbimazole, Propylthiouracil.

Anxiolytic, Sedatives, Hypnotics and Neuroleptics

Cardiac Inotropic Agents
Amrinone, Digoxin, Digoxin, Exonimone, Lanatoside C, Medigoxin.

Corticosteroids
Beclomethasone, Betamethasone, Budesonide, Cortisone Acetate, Desoxymethasone, Dexamethasone, Fludrocortisone Acetate, Flunisolide, Flucortolone, Fluticasone Propionate, Hydrocortisone, Methylprednisolone, Prednisolone, Prednisone.

Diuretics
Acetazolamide, Amiloride, Bendrofluazide, Bumetanide, Chlorothiazide, Chlorthalidone, Ethacrynic Acid, Frusemide, Metolazone, Spironolactone, Triamterene.

Gastro-Intestinal Agents
Bisacodyl, Cimetidine, Cisapride, Diphenoxylate, Domperidone, Famotidine, Loperamide, Mesalazine, Nizatidine, Omeprazole, Ondansetron, Ranitidine, Sulphasalazine.
Histamine-Receptor Antagonists
Acrivastine, Astemizole, Cinnarizine, Cyclizine, Cyproheptadine, Dimenhydrinate, Flunarizine, Loratadine, Meclozine, Oxatomide, Terfenadine, Triprolidine.

Oral Vaccines
Vaccines designed to prevent or reduce the symptoms of diseases of which the following is a representative: Influenza, Tuberculosis, Meningitis, Hepatitis, Whooping Cough, Polio, Tetanus, Diphtheria, Malaria, Cholera, Herpes, Typhoid, HIV, Aids, Measles, Lyme Disease, Travellers Diarrhea, Hepatitis A, B, C, Otitis Media, Dengue Fever, Rabies, Parainfluenza, Rubella, Yellow Fever, Dysentry, Legionnaires Disease, Toxoplasmosis, Q-Fever, Haemorrhagic Fever, Argentina Haemorrhagic Fever, Caries, Chagas Disease, Urinary Tract Infection caused by E.Coli, Pneumococcal Disease, Mumps and Chikungunya.

Proteins, Peptides and Recombinant Drugs
Insulin (Hexameric/Dimeric/Monomeric Forms), Glucagon, Growth Hormone (Somatotropin), Polypeptides Or Their Derivatives, (Preferably With A Molecular Weight From 1000 To 300,000), Calcitonins And Synthetic Modifications Thereof, Enkephalins, Interferons (Especially Alpha-2 Inter Feron For Treatment Of Common Colds).

Sex Hormones
Clomiphene Citrate, Danazol, Ethinyloestradiol, Medroxyprogesterone Acetate, Mestranol, Methyltestosterone, Norethisterone, Norgestrel, Oestriadiol, Conjugated Oestrogens, Progesterone, Stanozolol, Stibestrol, Testosterone, Tibolone.

<table>
<thead>
<tr>
<th>S.No</th>
<th>Trade Name</th>
<th>Active Drug</th>
<th>Manufacturer</th>
</tr>
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<tbody>
<tr>
<td>1.</td>
<td>Felden fast melt</td>
<td>Piroxicam</td>
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<tr>
<td>2.</td>
<td>Claritin redi Tab</td>
<td>Loratidine</td>
<td>Schering Plough Corp., USA</td>
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<td>3.</td>
<td>Maxalt MLT</td>
<td>Rizatriptan</td>
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<td>4.</td>
<td>Zyprexia</td>
<td>Olanzapine</td>
<td>Eli Lilly, Indianapolis, USA</td>
</tr>
<tr>
<td>5.</td>
<td>Zofran ODT(4or8mg)</td>
<td>Ondansetron</td>
<td>GlaxoWellcome, Middlesex, UK</td>
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<tr>
<td>6.</td>
<td>Zoming-ZMT</td>
<td>Zolmitriptan</td>
<td>AstraZeneca, Wilmington, USA</td>
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<tr>
<td>8.</td>
<td>TempraQuiclets</td>
<td>Acetaminophen</td>
<td>Bristol Myers Squibb, NY, USA</td>
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<td>9.</td>
<td>Febrectol</td>
<td>Paracetamol</td>
<td>Prographarm, Chateauneuf, France</td>
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<td>Nimulid MDT</td>
<td>Nimesulide</td>
<td>Panacea Biotech, New delhi , India</td>
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<td>11.</td>
<td>Torrox MT</td>
<td>Rofecoxib</td>
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<td>Risperidone</td>
<td>Janssen Pharmaceutics</td>
</tr>
</tbody>
</table>
CONCLUSION
Mouth dissolving tablets have better patient acceptance and compliance and may improved biopharmaceutical properties, patient compliance, convenience, bioavailability improved efficacy, and better safety compared with conventional oral dosage forms. MDTs are more widely available as OTC products for the treatment of allergies, cold, and flu symptoms. MDTs formulations obtained by some of these technologies have sufficient mechanical strength, quick disintegration/dissolution in the mouth without water. These tablets are designed to dissolve or disintegrate rapidly in the saliva generally within <60 seconds (range of 5-50 seconds). The development of a Mouthdissolving tablet also provides an opportunity for a line extension in the market place. A wide range of drugs (e.g., neuroleptics, cardiovascular drugs, analgesics, antihistamines, and drugs for erectile dysfunction) can be considered candidates for this dosage form. As a drug entity nears the end of its patent life, it is common for pharmaceutical manufacturers to develop a given drug entity in a new and improved dosage form. A new dosage form allows a manufacturer to extend market exclusivity, while offering its patient population a more convenient dosage form or dosing regimen.

REFERENCES
24. Debjit Bhowmik et al., Fast dissolving tablet: A review on revolution of novel drug delivery system and new market opportunities, Der Pharmacia Lettre, 2009; 1 (2) 262-276