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REVIEW ON MOUTH DISSOLVING TABLET

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ABSTRACT

Now day's formulation research is breaking barriers of conventional methods. Recently, MDTs have take over an important position in the market by overcoming previously administration problems and contributing to extension of patient life, which have difficulty in swallowing tablets and capsules. Upon introduction into the mouth, these tablets dissolve/ disintegrate in the mouth without additional water for easy administration of pharmaceutical ingredients. Oral fast-dissolving tablets, are an examples of a few existing technologies with the potential to accommodate various physicochemical, pharmacokinetic and pharmacodynamics characteristic of drugs. Fast dissolving tablets (FDTs) have received ever-increasing demand during the last decade, and the field has become a rapidly growing area in the pharmaceutical industry. This article reviews the Need, advantages, limitations, various formulation technologies [conventional], marketed product of Fast dissolving tablets.

KEYWORDS: Mouth dissolving tablets, fast Dissolving Tablets, MDT's, Direct compression, Superdisintegrants.

INTRODUCTION

In recent decades, a variety of pharmaceutical research has been conducted to develop new dosage forms. Considering quality of life, most of these efforts have been focused on ease of medication. Among the various dosage forms developed to improve the ease of administration, the mouth dissolving tablet (MDT) is the most widely preferred commercial products. Solid dosage forms are popular because of low cost, ease of administration, accurate dosage self medication, pain avoidance and the most importantly the patient compliance. The most popular solid dosage forms are being tablets and capsules.[1,3] However

in case of dyspepsia of geriatric patients, the underdeveloped muscular and nervous system in young individuals and incase of uncooperative patient, many problems is occur but swallowing is common phenomenon which leads to poor patient compliance. To improve these drawbacks fast dissolving tablets or orally disintegrating tablets has immersed as alternative oral dosage forms.[2] As a result of increased life expectancy, the elderly constitute a large portion of the worldwide population today.[4-5] A fast dissolving drug delivery system, in most cases, is a tablet that dissolves or disintrigrants 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.[6-7] The fast dissolving tablets display a fast and spontaneous deaggregation in the mouth, soon after the contact with saliva, though they can be handled or extracted from the package without alteration. The active agent can thus rapidly dissolve in the saliva and be absorbed through whatever membrane it encounters, during deglutition, unless it is protected from pregastric absorption. To full-fil these requirements, tablets must be highly porous, incorporating hydrophilic excipients, able to rapidly absorb water for a rapid deaggregation of the matrix.[8-9]

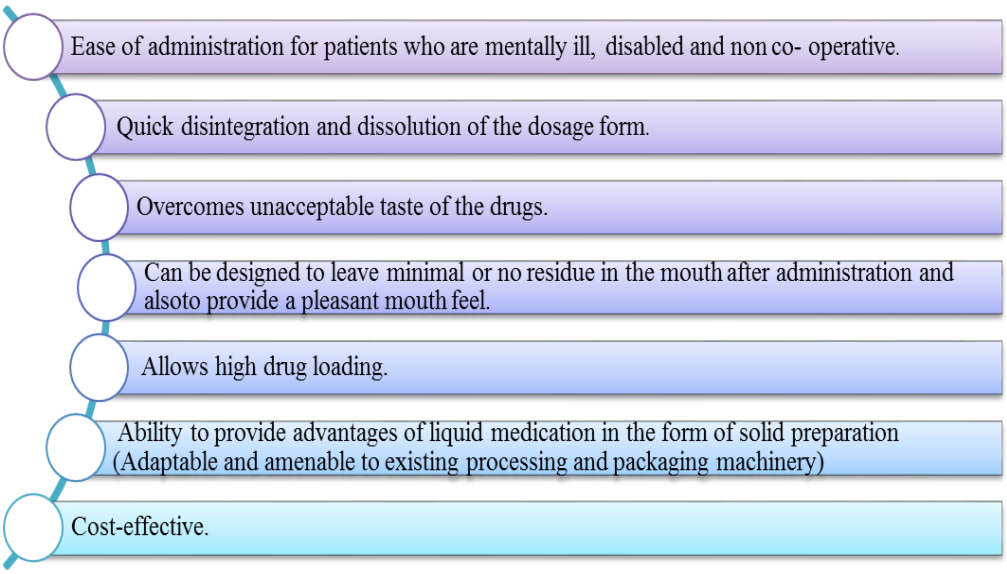
Mouth dissolving tablet (MDT)

It is a tablet that disintegrates and dissolves rapidly in the saliva, within a few seconds without the need of drinking water or chewing. A mouth dissolving tablet usually dissolves in the oral cavity within 15 s to 3min. Most of the MDTs include certain super disintegrates and taste masking agents.

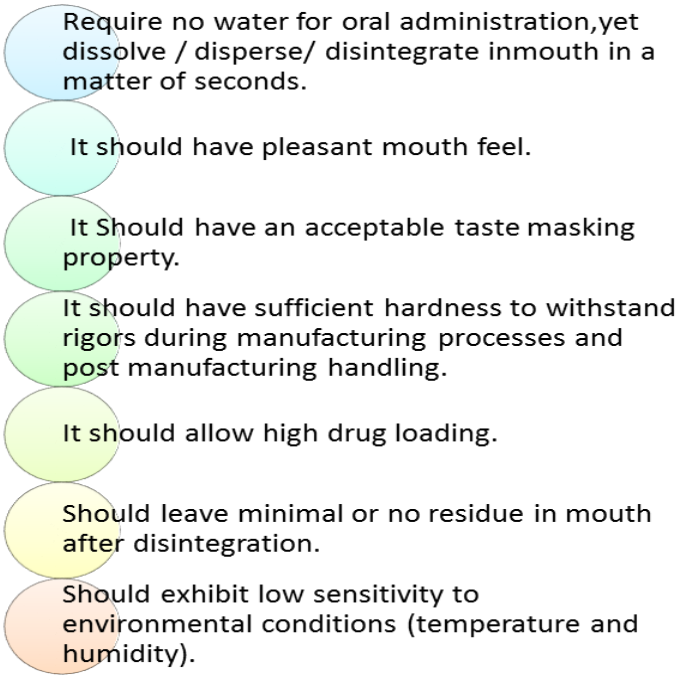
Mechanism[10]**:** Bioavailability of a drug depends in absorption of the drug, which is affected by solubility of the drug in gastrointestinal fluid and permeability of the drug across gastrointestinal membrane. The solubility of a drug mainly depends on physiochemical properties of the drug. The rate of drug dissolution is greatly influenced by disintegration of the tablet.

Disintegrants are important excipient of the tablet formulation, they are always added to tablet to induce breakup of tablet when they are comes in contact with aqueous fluid and this process of desegregation of constituent particles before the drug dissolution occurs, is known as disintegration process and excipients which induce this process are known as disintegrants.

Salient Features of Fast Dissolving Drug Delivery System



Ideal properties of Mouth Dissolving Tablets



Major advantages of mouth dissolving tablets

- Administered without water, anywhere, any time.
- Suitability for geriatric and pediatric patients, who experience difficulties in swallowing and for the other groups that may experience problems using conventional oral dosage form, due to being mentally ill, the developmentally disable and the patients who are uncooperative.

- Beneficial in cases such as motion sickness, suede episodes of allergic attack or coughing, where an ultra rapid onset of action required.
- An increased bioavailability, particularly in cases of insoluble and hydrophobic drugs, due to rapid disintegration and dissolution of these tablets.
- 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.

Limitations of Mouth Dissolving Tablets

- Mechanical strength of final product.
- Drug and dosage form stability.
- Mouth feel.
- Taste: the tablets may leave unpleasant taste and/or grittiness in mouth if not formulated
- properly.
- Rate of dissolution of drug formulation in saliva.
- Swallowability.
- Rate of absorption from the saliva solution and
- Overall bioavailability.
- Dryness of the mouth due to decreased saliva production may not be good candidates for these tablet formulations.

FORMULATION OF MDTs[11,12,13,14]

Drug

The ultimate characteristics of a drug for dissolution in the mouth and pre gastric absorption from MDTs include:

- Free from bitter taste
- Dose lower than 20 mg
- Small to Moderate molecular weight
- Good solubility in saliva
- Ability to permeate through oral mucosal tissue

Bulking materials

Bulking materials are significant in the formulation of fast-melting tablets. The material 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.

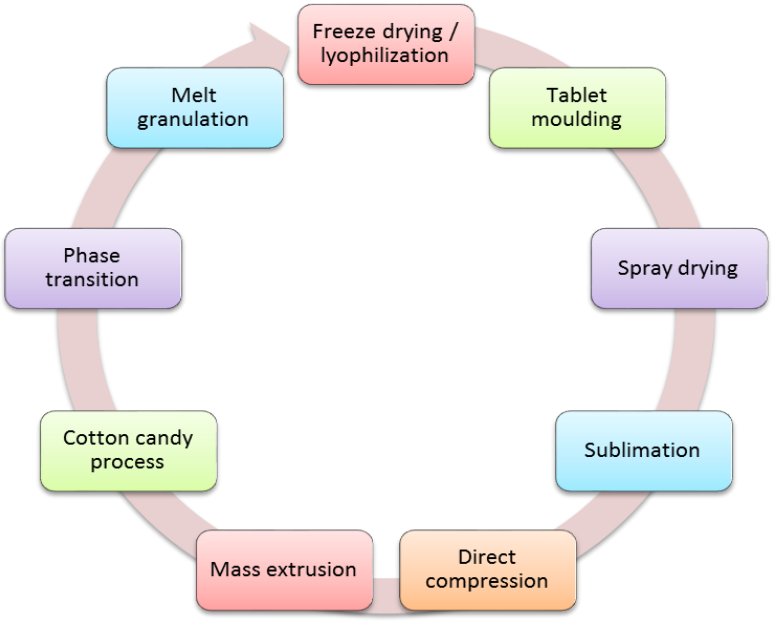
Flavours and sweeteners

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.

Superdisintegrants

A disintegrant is an excipient, which is added to a tablet or capsule blend to aid in the breakup of the compacted mass when it is put into a fluid environment.

Many techniques have been used for the formulation of Fast dissolving tablets



Freeze-drying or lyophilization

Freeze drying is the process in which water is sublimed from the product after it is frozen. This technique creates an amorphous porous structure that can dissolve rapidly. The freeze-drying technique has demonstrated improved absorption and increase in bioavailability. The major disadvantages of lyophillization technique are that it is expensive and time consuming; fragility makes conventional packaging unsuitable for these products and poor stability under stressed conditions

Tablet molding

Molding process is of two type i.e. solvent method and heat method. Solvent method involves moistening the powder blend with a hydroalcoholic solvent followed by compression at low pressures in molded plates to form a wetted mass (compression molding). The solvent is then removed by airdrying. The tablets manufactured in this manner are less compact than compressed tablets and posses a porous structure that hastens dissolution. Compared to the lyophillization technique, tablets produced by the molding technique are easier to scale up for industrial manufacture.

Spray drying

In this technique, Gelatin can be used as a supporting agent and as a matrix, Mannitol as a bulking agent and Sodium starch glycolate or Croscarmellose or Crospovidone are used as

superdisintegrants. Tablets manufactured from the spraydried powder have been reported to disintegrate in less than 20 seconds in aqueous medium.

Sublimation

Generate a porous matrix, volatile ingredients are incorporated in the formulation that is later subjected to a process of sublimation. Highly volatile ingredients like Ammonium bicarbonate, Ammonium carbonate, Benzoic acid, Camphor, Naphthalene, Urea, Urethane and Phthalic anhydride may be compressed along with other excipients into a tablet. Tablets manufactured by this technique have reported to usually disintegrate in 10-20 sec.

Direct compression

Direct compression represents the simplest and most cost effective tablet manufacturing technique.

(a) Superdisintegrants In many orally disintegrating tablet technologies based on direct compression, the addition of superdisintegrants principally affects the rate of disintegration and hence the dissolution. The presence of other formulation ingredients such as water-soluble excipients and effervescent agents further hastens the process of disintegration.

(b) 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, Lactilol, Maltilol, Maltose, Mannitol, Sorbitol, Starch hydrolysate, Polydextrose and Xylitol, which display high aqueous solubility and sweetness and hence impart taste masking property and a pleasing mouthfeel. Sugar-based excipients are classified into two types on the basis of molding and dissolution rate.

Type 1: Saccharides (Lactose and Mannitol) exhibit low mouldability but high dissolution rate.

Type 2: Saccharides (Maltose and Maltilol) exhibit high mouldability and low dissolution rate.

Mass-extrusion

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 tablet.

Cotton candy process

This process is so named as it utilizes an inimitable spinning mechanism to produce floss like crystalline structure, which mimics cotton candy. This technique involves formation of matrix of polysaccharides or saccharides by simultaneous action of flash melting and spinning. The matrix formed is partially recrystallized to have better flow properties and compressibility. This matrix is milled and blended with active ingredients as well as excipients and subsequently compressed to FDTs.

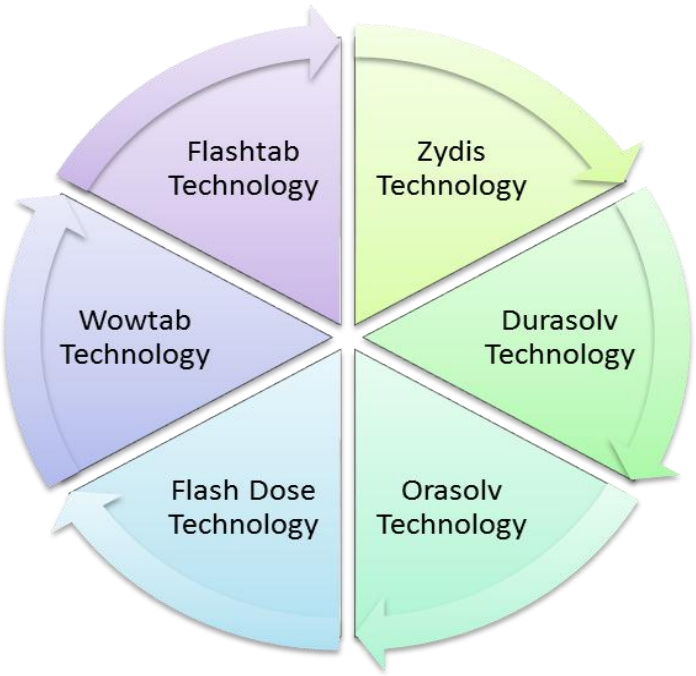
Phase transition

Kuno et al proposed a novel method to prepare FDTs with sufficient hardness by involving the phase transition of sugar alcohol. In this technique, FDTs are produced by compressing and subsequently heating tablets that contain two sugar alcohols, one with high and other with a low melting point.

Melt granulation

Melt granulation is a process in which Pharmaceutical powders are efficiently agglomerated by the use of binder which can be a molten liquid, a solid or a solid that melts during the process. For accomplishing this process, high shear mixers are utilized, where the product temperature is raised above the melting point of binder by a heating jacket or by the heat of friction generated by impeller blades.

Patented Technologies for Fast Dissolving Tablets[1,2,15,16,17]



1. Zydis Technology[18]

Zydis formulation is a unique freeze dried tablet in which drug is physically entrapped or dissolved within the matrix of fast dissolving carrier material. When zydis units are put into the mouth, the freeze-dried structure disintegrates instantaneously and does not require water to aid swallowing. The zydis matrix is composed of many material designed to achieve a number of objectives. To impart strength and resilience during handling, polymers such as gelatin, dextran or alginates are incorporated. These form a glossy amorphous structure, which imparts strength. To obtain crystallinity, elegance and hardness, saccharides such as mannitol or sorbitol are incorporated. Water is used in the manufacturing process to ensure production of porous units to achieve rapid disintegration while various gums are used to prevent sedimentation of dispersed drug particles in the manufacturing process. Collapse protectants such as glycine prevent the shrinkage of zydis units during freeze drying process or long-term storage. Zydis products are packed in blister packs to protect the formulation from moisture in the environment.

2. Durasolv Technology

Durasolv is the patented technology of CIMA labs. The tablets made by this technology consist of drug, filler and a lubricant. Tablets are prepared by using conventional tabletting equipment at high mouldability and low These can be packaged into conventional packaging system like blisters. Durasolv is an appropriate technology for product requiring low amounts of active ingredients.

3. Orasolv Technology

CIMA labs have developed Orasolv Technology. In this system active medicament is taste masked. It also contains effervescent disintegrating agent Tablets are made by direct compression technique at low compression force in order to minimize oral dissolution time. Conventional blenders and tablet machine is used to produce the tablets. The tablets produced are soft and friable.

4. Flash Dose Technology:- By this technology sugar based matrix known as floss which made from combination of excipients either alone or in combination of drugs. Nurofen meltelt, a new form of ibuporfen is based on same technology.

5. Wowtab Technology:- Wowtab Technology is patented by Yamanouchi Pharmaceutical Co. WOW means “Without Water “. In this process, combination of low mouldability

saccharides and high mouldability saccharides is used to obtain a rapidly melting strong tablet. The active ingredient is mixed with a low moldability saccharide and granulated with a high moldability saccharide and compressed into tablet.

6. Flashtab technology:- Prographarm patented this technology in which tablet consists of active ingredients in form of microcrystals. Rest of all procedure is followed in conventional technology.

Evaluation of Mouth Dissolving Tablet

MDTs formulations have to be evaluated for the following evaluation test[19,20]

General Appearance

The general appearance of a tablet, its visual identification and over all 'elegance' is essential for consumer acceptance. These include tablet's size, shape, colour, presence or absence of an odour, taste, surface texture, physical flaws.

Tablet Thickness

Tablet thickness is an important characteristic in reproducing appearance and also in counting by suing filling equipment. Some filling equipment utilizes the uniform thickness of the tablets as a counting mechanism. Ten tablets were taken and their thickness was recorded using micrometer.

Uniformity of Weight

I.P procedure for uniformity of weight was followed, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be satisfactory method of determining the drug content uniformity.

Hardness

Hardness of tablet is defined as the force applied across the diameter of the tablet in order to break the tablet, them resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. Hardness of the tablet of each formulation was determined using Pfizer Hardness Tester.

Friability

Friability of the tablets was determined using Roche friabilator. This device subjects the tablets to the combined effect of abrasions and shock in a plastic chamber revolving at 25 rpm and dropping the tablets at a height of 6 inch in each revolution. Pre-weighed sample of tablets was placed in the friabilator and were subjected to 100 revolutions. Tablets were de dusted using a soft muslin cloth and reweighed. The friability (F%) is given by the formula,

$$\textbf{Friability} = (I.W - F.W)/I.W \times 100$$

In vitro Disintegration Test

Disintegration of fast disintegrating tablets is achieved by saliva in the mouth, however amount of saliva in the mouth is limited and no tablet disintegration test was found in USP and IP to simulate in vivo conditions. A modified version of the simple but novel method developed was used to determine disintegration time of the tablets.

Wetting Time

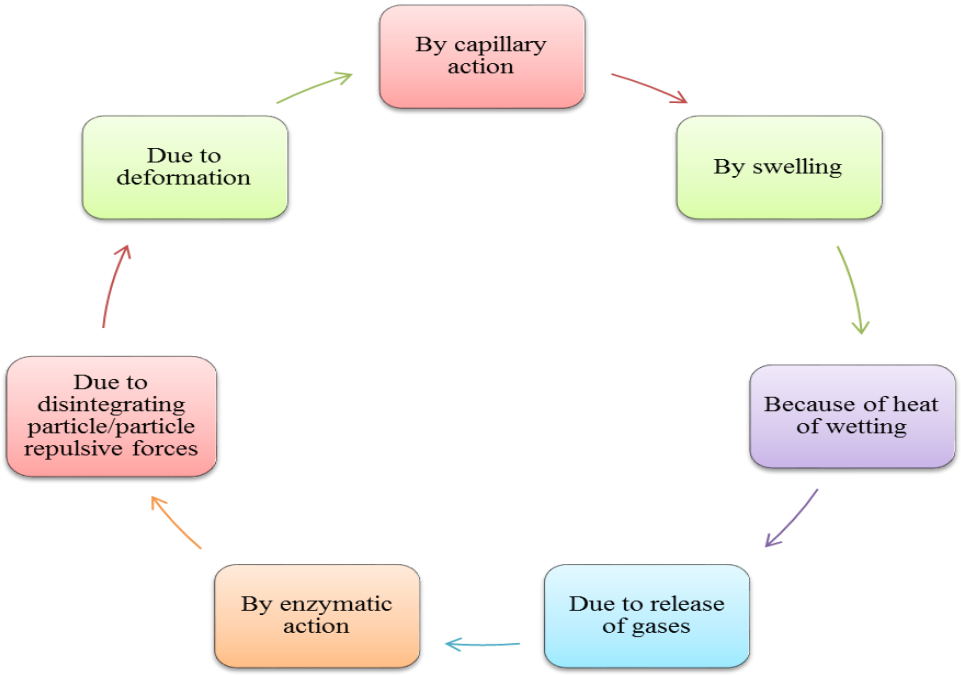
The method was followed to measure tablet wetting time. A piece of tissue paper (12 cm X 10.75 cm) folded twice was placed in a small Petri dish (ID = 65 cm) containing 6 ml of Sorenson's buffer (pH 6.8), A tablet was put on the paper, and the time for the complete wetting was measured. Three trials for each batch were performed and the standard deviation was also determined.

In vitro Dispersion Time

In vitro dispersion time was measured by dropping a tablet in a glass cylinder containing 6 ml of Sorenson's buffer (pH 6.8). Three tablets from each formulation were randomly selected and in vitro dispersion time was performed.

Mechanism of Action of Disintigrants[21-22]

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



Drug candidates for fast dissolving tablets[23]

- **Antibacterial agents:** Ciprofloxacin, Tetracycline, Erythromycin, Rifampicin, Penicillin, Doxycyclin, Nalidixic acid, Trimethoprim, Sulphacetamide, Sulphadiazine. Anthelmintics: Albendazole, Mebendazole, Thiabendazole,Livermectin, Praziquantel, Pyrantel Embonate, Dichlorophen.
- **Antidepressants:** Trimipramine Maleate, Nortriptyline HCl, Trazodone HCl, Amoxapine, Mianserin HCl.
- **Antidiabetics:** Glibenclamide, Glipizide, Tolbutamide, Tolazamide, Gliclazide, Chlorpropamide.
- **Analgesics/anti-inflammatory agents:** Diclofenac sodium, Ibuprofen, Ketoprofen, Mefenamic acid, Naproxen, Oxyphenbutazone, Indomethacin, Piroxicam, Phenylbutazone.
- **Antihypertensives:** Amlodipine, Carvedilol, Diltiazem, Felodipine, Minoxidil, Nifedipine, Prazosin HCl, Nimodipine,Terazosin.
- **Antiarrhythmics:** Disopyramide, Quinidine sulphate, Amiodarone HCl.
- **Antihistamines:** Acrivastine, Cetrizine, Cinnarizine, Loratadine, Fexofenadine, Triprolidine.

CONCLUSION

The MDTs have potential advantages over conventional dosage forms, with their improved patient compliance, convenience, bioavailability and rapid onset of action had drawn the attention of many manufactures over a decade. The development of a fast-dissolving tablet also provides an opportunity for a line extension in the marketplace; a wide range of drugs (For example, neuroleptics, cardiovascular drugs, analgesics, antihistamines, and drugs for erectile dysfunction) can be considered candidates for this dosage form. Pharmaceutical marketing is another reason for the increase in available fast dissolving/ disintegrating products.

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