



MOUTH DISSOLVING TABLETS: A NOVEL APPROACH TO DRUG DELIVERY

TEJVIR KAUR¹, BHAWANDEEP GILL², SANDEEP KUMAR³, G.D. GUPTA³

¹Lecturer, Department of Pharmacy, Government Medical College, Patiala, Rayat & Bahara College of Pharmacy, Kharar, HOD Pharmaceutics, Department of Pharmaceutics, ASBASJSM College of Pharmacy, Bela, Ropar Punjab 140111 India Email: tejvirronnet@gmail.com, gillbhawan84@gmail.com, Mr.sandeep1970@rediffmail.com, drgdg@rediffmail.com

Received: 17 July 2010, Revised and Accepted: 22 Aug 2010

ABSTRACT

Recent advances in Novel Drug Delivery Systems (NDDS) aim for designing dosage forms, convenient to be manufactured and administered, free of side effects, offering immediate release and enhanced bioavailability, so as to achieve better patient compliance. Though oral drug delivery systems, preferably, tablets are the most widely accepted dosage forms, for being compact, offering uniform dose and painless delivery. Yet, dysphagia is the most common disadvantage of conventional tablets. This is seen to afflict nearly 35% of the general population and associated with a number of conditions, like parkinsonism, mental disability, motion sickness, unconsciousness, unavailability of water etc. To overcome such problems, certain innovative drug delivery systems, like 'Mouth Dissolving Tablets' (MDT) have been developed. These are novel dosage forms which dissolve in saliva within a few seconds, when put on tongue. Such MDTs can be administered anywhere and anytime, without the need of water and are thus quite suitable for children, elderly and mentally disabled patients.

Keywords: Mouth dissolving tablets, MDT.

INTRODUCTION

Drug Delivery Systems (DDS) are a strategic tool for expanding markets/indications, extending product life cycles and generating opportunities. DDS make a significant contribution to global pharmaceutical sales through market segmentation, and are moving rapidly. Drug delivery systems are becoming increasingly sophisticated as pharmaceutical scientists acquire a better understanding of the physicochemical and biochemical parameters pertinent to their performance.

Despite of tremendous advancements in drug delivery, the oral route remains the perfect route for the administration of therapeutic agents because of low cost of therapy, ease of administration, accurate dosage, self-medication, pain avoidance, versatility, leading to high levels of patient compliance. Tablets and capsules are the most popular dosage forms.¹ But one important drawback of such dosage forms is 'Dysphagia' or difficulty in swallowing. This is seen to afflict nearly 35% of the general population. This disorder is also associated with a number of conditions like:

1. Parkinsonism
2. Motion sickness
3. Unconsciousness
4. Elderly patients
5. Children
6. Mentally disabled persons
7. Unavailability of water.²

Improved patient compliance has achieved enormous demand. Consequently demand for their technologies is also increasing many folds. To develop a chemical entity, a lot of money, hard work and time are required. So focus is rather being laid on the development of new drug delivery systems for already existing drugs, with enhanced efficacy and bioavailability, thus reducing the dose and dosing frequency to minimize the side effects.³

It is always the aim of a scientist or a dosage form designer to enhance the safety of a drug molecule while maintaining its therapeutic efficacy. Recent advances in Novel Drug Delivery Systems (NDDS) aim for the same by formulating a dosage form, convenient to be administered so as to achieve better patient compliance. Pharmaceutical technologists have put in their best efforts to develop a Fast Dissolving Drug Delivery System⁴, i.e Mouth Dissolving Tablet.

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 3 min. Most of the MDTs include certain super disintegrants and taste masking agents.

Ideal properties of MDT

A Mouth Dissolving Tablet should

- a. Not require water or other liquid⁵ to swallow.
- b. Easily dissolve or disintegrate in saliva within a few seconds.
- c. Have a pleasing taste.
- d. Leave negligible or no residue in the mouth when administered.⁶
- e. Be portable and easy to transport.
- f. Be able to be manufactured in a simple conventional manner within low cost.
- g. Be less sensitive to environmental conditions like temperature, humidity etc.^{6,7}

Advantages of MDT

- a. No need of water to swallow the tablet.⁸
- b. Can be easily administered to pediatric, elderly and mentally disabled patients.
- c. Accurate dosing⁹ as compared to liquids.
- d. Dissolution and absorption of drug is fast, offering rapid onset of action.
- e. Bioavailability of drugs is increased¹⁰ as some drugs are absorbed from mouth, pharynx and esophagus through saliva passing down into the stomach¹¹
- f. Advantageous over liquid medication in terms of administration as well as
- g. transportation
- h. First pass metabolism is reduced, thus offering improved bioavailability and thus reduced dose and side effects.
- i. Free of risk of suffocation due to physical obstruction when swallowed, thus
- j. offering improved safety.
- a. Suitable for sustained/controlled release actives.¹²
- b. Allows high drug loading.¹³

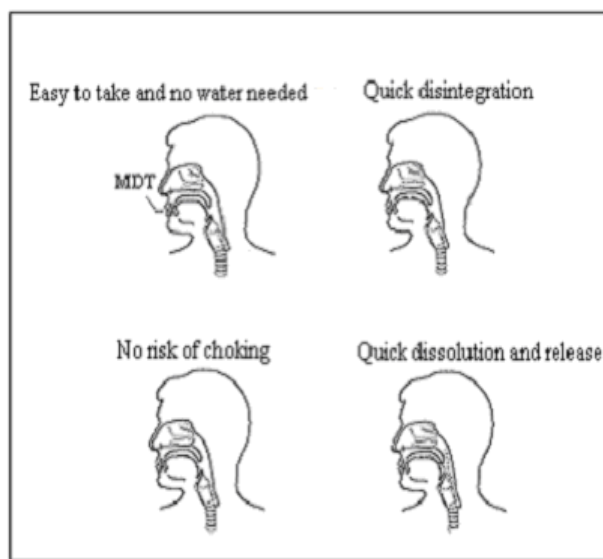


Fig. 1.1: Advantages of MDT

Main ingredients used in preparation of MDT

Important ingredients that are used in the formulation of MDTs should allow quick release of the drug, resulting in faster dissolution. This includes both the actives and the excipients. Disintegration and solubilization of a directly compressed tablet depend on single or combined effects of disintegrants, water-soluble excipients and effervescent agents.

Excipients balance the properties of the actives in FDDTs. This demands a thorough understanding of the chemistry of these excipients to prevent interaction with the actives. Determining the cost of these ingredients is another issue that needs to be addressed by formulators. The role of excipients is important in the formulation of fast-melting tablets. These inactive food-grade ingredients, when incorporated in the formulation, impart the desired organoleptic properties and product efficacy. Excipients are general and can be used for a broad range of actives, except some

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

The most important ingredients of a mouth dissolving tablets are:

Super disintegrants: Use of disintegrants is the basic approach in development of MDTs. Disintegrants play a major role in the disintegration and dissolution of MDT. It is essential to choose a suitable disintegrant, in an optimum concentration so as to ensure quick disintegration and high dissolution rates.¹⁴

Super disintegrants provide quick disintegration due to combined effect of swelling and water absorption by the formulation. Due to swelling of superdisintegrants, the wetted surface of the carrier increases, which promotes the wettability and dispersibility of the system, thus enhancing the disintegration and dissolution.¹⁵⁻¹⁷ The optimum concentration of the superdisintegrant can be selected according to critical concentration of disintegrant.

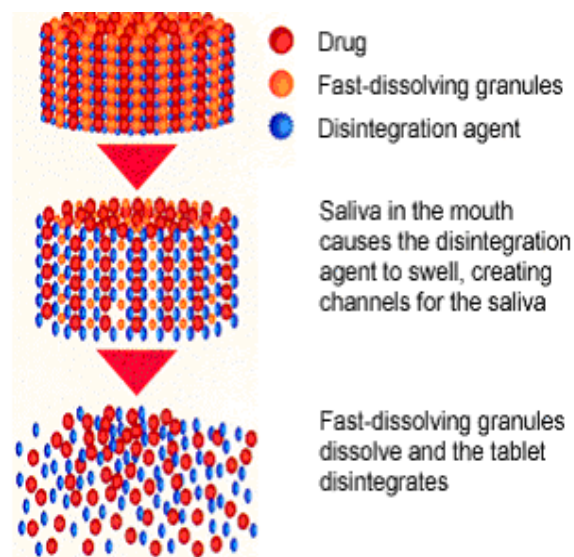


Fig. 1.2: Mechanism of Action of Superdisintegrants

Below this concentration, the tablet disintegration time is inversely proportional to the concentration of the superdisintegrant, whereas if concentration of superdisintegrant is above critical concentration, the disintegration time remains almost constant or even increases.¹⁸

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

Mechanism of action of disintegrants

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

- By capillary action
- By swelling
- Because of heat of wetting
- Due to release of gases
- By enzymatic action
- Due to disintegrating particle/particle repulsive forces
- Due to deformation

a. By capillary action

Disintegration by capillary action is always the first step. When we put the tablet into suitable aqueous medium, the medium penetrates into the tablet and replaces the air adsorbed on the particles, which weakens the intermolecular bond and breaks the tablet into fine particles. Water uptake by tablet depends upon hydrophilicity of the drug /excipient and on tableting conditions. For these types of disintegrants, maintenance of porous structure and low interfacial tension towards aqueous fluid is necessary which helps in disintegration by creating a hydrophilic network around the drug particles.

b. By swelling

Perhaps the most widely accepted general mechanism of action for tablet disintegration is swelling. Tablets with high porosity show poor disintegration due to lack of adequate swelling force. On the other hand, sufficient swelling force is exerted in the tablet with low porosity. It is worthwhile to note that if the packing fraction is very high, fluid is unable to penetrate in the tablet and disintegration is again slows down.

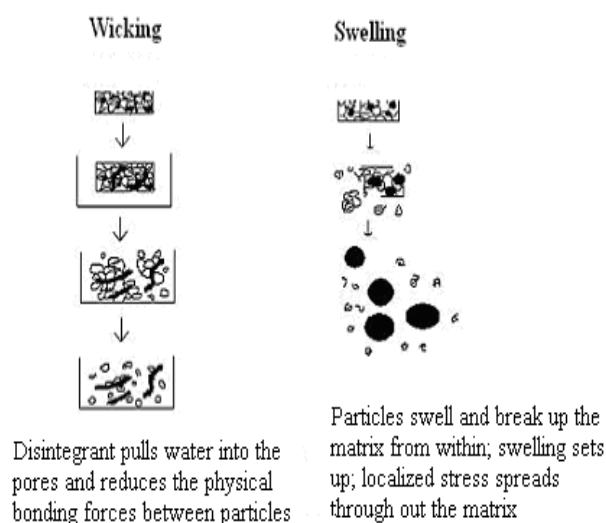


Fig.1.3: Disintegration of Tablet by Wicking and Swelling

c. Because of heat of wetting (air expansion)

When disintegrants with exothermic properties gets wetted, localized stress is generated due to capillary air expansion, which helps in disintegration of tablet. This explanation, however, is limited to only a few types of disintegrants and can not describe the action of most modern disintegrating agents.

d. Due to release of gases

Carbon dioxide released within tablets on wetting due to interaction between bicarbonate and carbonate with citric acid or tartaric acid. The tablet disintegrates due to generation of pressure within the tablet. This effervescent mixture is used when pharmacist needs to formulate very rapidly dissolving tablets or fast disintegrating tablet. As these disintegrants are highly sensitive to small changes in humidity level and temperature, strict control of environment is required during manufacturing of the tablets. The effervescent blend is either added immediately prior to compression or can be added in to two separate fraction of formulation.

e. By enzymatic reaction

Here, enzymes present in the body act as disintegrants. These enzymes destroy the binding action of binder and helps in disintegration.

Actually due to swelling, pressure exerted in the outer direction or radial direction, it causes tablet to burst or the accelerated absorption of water leading to an enormous increase in the volume of granules to promote disintegration.

f. Due to disintegrating particle/particle repulsive forces

Another mechanism of disintegration attempts to explain the swelling of tablet made with 'non-swelling' disintegrants. Guyot-Hermann has proposed a particle repulsion theory based on the observation that nonswelling particle also cause disintegration of tablets. The electric repulsive forces between particles are the mechanism of disintegration and water is required for it. Researchers found that repulsion is secondary to wicking.

g. Due to deformation

Hess had proved that during tablet compression, disintegrated particles get deformed and these deformed particles get into their normal structure when they come in contact with aqueous media or water. Occasionally, the swelling capacity of starch was improved when granules were extensively deformed during compression.

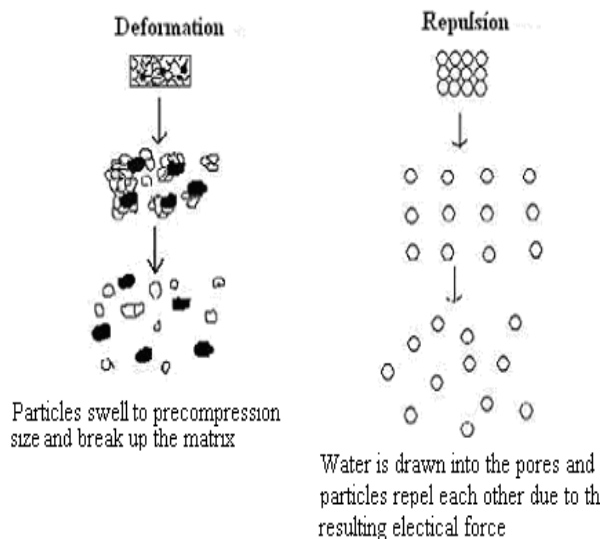


Fig. 1.4: Disintegration by Deformation and Repulsion

This increase in size of the deformed particles produces a break up of the tablet. This may be a mechanism of starch and has only recently begun to be studied.

Sugar based excipients: Sugar based excipients are used for taste masking and as bulking agents. Most of the drugs are having unpleasant or bitter taste. And the basic requirement for designing MDTs is that the drug should not have disagreeable taste. So taste masking is necessary in most of the cases. Sorbitol, mannitol, xylitol, dextrose, fructose, etc. are mainly used. Aqueous solubility and sweetness impart a pleasing mouth feel and good taste masking.¹⁹ But not all sugar-based materials have fast dissolution rate and good compressibility or compactability. However technologies have been developed to make use of the sugar based excipients in the design of fast dissolving tablets.

Other ingredients commonly used are water soluble diluents, lubricants, antistatic agents, plasticizers, binders, colors and flavors.

Approaches for preparation of MDT²⁰

Various technologies used in the manufacture of Mouth Dissolving Tablets include:

1. Freeze-drying or lyophilization
2. Sublimation
3. Spray drying
4. Moulding
5. Mass extrusion
6. Direct compression

Freeze-drying²¹: The tablets prepared by freeze-drying or lyophilization are very porous in nature and disintegrate or dissolve rapidly when come in contact with saliva. In this process, water is sublimated from the product after freezing. First of all, the material is frozen to bring it below its eutectic point. Then primary drying is carried out to reduce the moisture to around 4% w/w of dry product. Finally, secondary drying is done to reduce the bound moisture to the required volume. Due to lyophilization, bulking agent and sometimes drug acquire glossy amorphous structure and thus dissolution is enhanced. A tablet that rapidly disintegrates in aqueous solution includes a partially collapsed matrix network that has been vacuum dried above the collapsed temperature of the matrix. The matrix is partially dried below the equilibrium freezing point of the matrix. Vacuum drying the tablet above its collapse temperature, instead of freeze drying below its collapse temperature provides a process for producing tablets with enhanced structural

integrity, while rapidly disintegrating in normal amounts of saliva. However the use of freeze-drying is limited due to high cost of equipment and processing. Other major disadvantages of the final dosage forms include lack of physical resistance in standard blister packs.

Sublimation: This process involves addition of some inert volatile substances like urea, urethane, naphthalene, camphor, etc to other excipients and the compression of blend into tablet. Removal of volatile material²² by sublimation creates pores in tablet structure, due to which tablet dissolves when comes in contact with saliva. Additionally several solvents like cyclohexane, benzene etc can also be used as pore forming agents. Mouth dissolving tablets with highly porous structure and good mechanical strength have been developed by this method.^{23, 24}

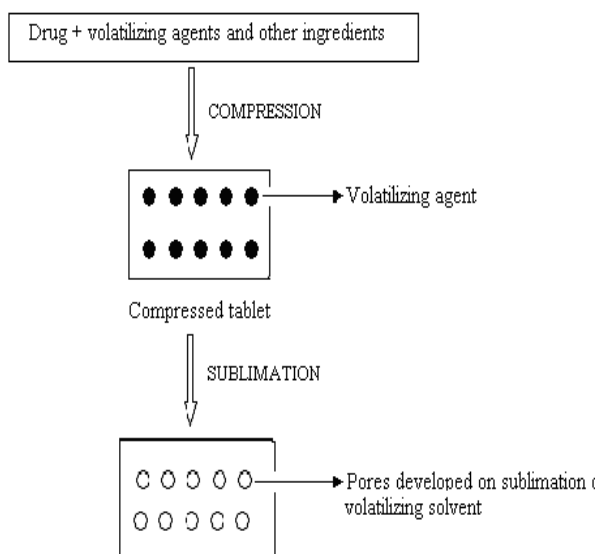


Fig. 1.5: Schematic Diagram of Sublimation Technique for Preparation of MDT

Spray drying: A highly porous and fine powder is prepared by spray drying an aqueous composition containing support matrix and other components. This is then mixed with active ingredient and compressed into tablet. Allen and Wang²⁵ used this technique to prepare mouth-dissolving tablets, which disintegrated within 20 s.

Moulding: Tablets prepared by this method are solid dispersions. Physical form of drug in the tablets depends on whether and to what extent it dissolves in the wetted mass.²⁶ The drug can exist as discrete particles or micro particles in the matrix. It can dissolve totally to form a solid solution or dissolve partially in the molten carrier and remaining, if any, stays undissolved and dispersed in the matrix.²⁷ Disintegration time, drug dissolution rate and mouth feel will depend on the type of dispersion. Different moulding techniques can be used to prepare mouth-dissolving tablets:

- Compression moulding:** The powder mixture previously wetted with a solvent like ethanol/water is compressed into mould plates to form a wetted mass.
- Heat moulding:** A molten matrix in which drug is dissolved or dispersed can be directly moulded into Mouth dissolving tablets.²⁸
- No vacuum lyophilization:** This process involves evaporation of solvent from a drug solution or suspension at a standard pressure.²⁹

Moulded tablets possess porous structure, which facilitates rapid disintegration and easy dissolution. Moulded tablets offer improved taste due to water-soluble sugars present in dispersion matrix. But moulded tablets lack good mechanical strength and can undergo

breakage or erosion during handling and opening of blister packs.³⁰ However, adding sucrose, acacia or polyvinyl pyrrolidone can increase mechanical strength.

Mass extrusion^{31,32}: In this technique, a blend of active drug and other ingredients is softened using solvent mixture of water soluble polyethylene glycol, using methanol and then the softened mass is extruded through the extruder or syringe to get a cylinder of product, which is finally cut into even segments with the help of heated blades to get tablets. The dried cylinder can be used to coat the granules of bitter tasting drugs and thereby masking their bitter taste.

Direct compression: The disintegrant addition technology^{33,34} (direct compression) is the most preferred technique to manufacture the tablets due to certain advantages:

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

Tablet size and hardness strongly affect the disintegrant efficacy. Hard and large tablets have more disintegration time than normally required. Very soft and small tablets have low mechanical strength. So, an optimum kind and concentration of disintegrant should be chosen to achieve quick disintegration and high dissolution rates. Above the critical concentration level, however, disintegration time remains approximately constant or even increases.³⁵

Patented Technologies for preparation of MDT:

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

Zydis technology: 'Zydis' is the first mouth dissolving dosage form in the market. It is a unique freeze-dried tablet in which the active drug is incorporated in a water-soluble matrix, which is then transformed into blister pockets and freeze dried to remove water by sublimation. Zydis matrix is made up of a number of ingredients in order to obtain different objectives. Polymers such as gelatin, dextran or alginates are added to impart strength during handling. These form a glossy and amorphous structure. Mannitol or sorbitol is added to impart crystallinity, elegance and hardness. Various gums may be added to prevent sedimentation of dispersed drug particles. Water is used as a medium to ensure the formation of a porous dosage form. Collapse protectants like glycine may be used to prevent shrinkage of dosage form during freeze drying and long-term storage.³⁶ If necessary, suspending agents and pH adjusting agents may be used. Preservatives may also be added to prevent microbial growth. Zydis products are packed in blister packs to protect the formulation from environmental moisture. A secondary moisture proof foil punch is often required as this dosage form is very moisture sensitive. When put into the mouth, Zydis unit quickly disintegrates and dissolves in saliva.

Drawbacks:

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

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

Durasolv technology: This too has been developed by CIMA labs. This is one of the suitable technologies to prepare products

requiring low amounts of active drug. This technology uses drug, fillers and a lubricant to prepare the tablet. Conventional tableting equipment is used to prepare the tablet. Due to higher force of compaction used, tablets prepared are rigid. Dosage form can be packaged into conventional packaging system like blisters.

Wowtab technology: Yamauchi pharmaceutical company patented this technology. 'wow' means 'without water'. The active ingredients may constitute upto 50% w/w of the tablet. In this technique, saccharides of both low and high mouldability are used to prepare the granules. Mouldability is the capacity of a compound to be compressed.

Highly mouldable substance has high compressibility and thus shows slow dissolution. The combination of high and low mouldability is used to produce tablets of adequate hardness. Active ingredients are mixed with low mouldability saccharides and then granulated with high mouldability saccharides and then compressed into tablet. The Wowtab product dissolves quickly in 15 s or less. Wowtab product can be packed in both into conventional bottle and blister packs.³⁷

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

Drawbacks:

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

Flashtab technology³⁸: Prographarm labs. have a patent over this technology. In this technology, microgranules of the taste-masked active drug are used. These may be prepared by using conventional techniques like coacervation, microencapsulation, and extrusion-spheronisation. All these processes utilize conventional tableting technology. These taste-masked micro crystals of active drug, disintegrating agent, a swelling agent and other excipients like soluble diluents etc are compressed to form a multiparticulate tablet that disintegrates rapidly.

Shearform Technology: In this technology, a shearform matrix, 'Floss' is prepared. Feedstock prepared with a sugar carrier is subjected to flash heat processing. In this process, sugar is simultaneously subjected to centrifugal force and to a temperature gradient, which causes the temperature of the mass to rise and hence an internal flow condition is created, permitting part of it to move with respect of the mass. The flowing mass comes out through

the spinning head that flings the floss. The produced floss is amorphous in nature. So by various techniques, it is further chopped and recrystallised to provide a uniform flow, thus facilitate blending. Then the recrystallised matrix, active drug and other excipients are blended together and finally compressed into tablets. Active drug and other excipients may be blended with the floss before recrystallising it.

Ceform technology: This technology involves preparation of microspheres of the active drug. Drug material alone or in combination with other pharmaceutical substances,

and excipients is placed into a precision engineered rapidly spinning machine. The centrifugal force comes into action, which throws the dry drug blend at high speed through small heated openings. Due to the heat provided by carefully controlled temperature, drug blend liquefies to form a sphere, without affecting the drug stability.

The microspheres thus formed are compressed into tablets. As the drug and excipients both can be processed simultaneously, it creates a unique microenvironment in which the materials can be incorporated into the microspheres that can alter the characteristics of the drug, such as enhancing solubility and stability.

Nanocrystal technology³⁹: For MDT, Elan's proprietary NanoCrystal technology can enable formulation and improve compound activity and final product characteristics.

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

NanoCrystal™ Fast dissolving technology provides for:

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

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

Table 1.1: Comparison of fast dissolving techniques

ZYDIS (R.P. SCHERER, INC.)		
Novelty	Handling/Storage	Drug release/bioavailability
First to market Freeze Dried	Do not push tablet through foil Do not use dosage form from damaged package	Dissolves in 2 -10 s May allow for pre-gastric absorption leading to enhanced bioavailability
	Sensitive to degradation at humidities > 65%	
ORASOLV (CIMA LABS, INC.)		
Unique taste masking	Packaged in patented oil packs	Disintegrates in 5 - 45 s depending upon the size of the tablet No significant change in drug bioavailability
Lightly compressed		
DURASOLV (CIMA LABS, INC.)		
Similar to Orasolv, but with better mechanical strength	Packaged in foil or bottles Package in bottles	Disintegrates in 5 - 45 s depending upon the size of the tablet No significant change in drug bioavailability
WOWTAB (YAMAOUCHI PHARMA TECHNOLOGIES, INC.)		
Compressed dosage form	Avoid exposure to moisture or humidity.	Disintegrates in 5 - 45 s depending upon the size of the tablet

Proprietary taste masking	Avoid exposure to moisture or humidity. Require specialized packaging.	No significant change in drug bioavailability
FLASHDOSE (FUISZ TECHNOLOGIES, LTD.)		
Unique spinning mech ^m producing floss-like crystalline structure as cotton candy	Avoid exposure to moisture and humidity	Dissolves within 1 min. Enhanced bioavailability.
FLASHTAB (PROGRAPHARM GROUP)		
Compressed dosage form containing drug as microcrystals		Dissolves within 1 min

Table 1.2: Some of Promising Drug Candidates for Mouth Dissolving Tablets⁴⁰

S. No.	Category	Examples
1.	Antibacterial agents	Ciprofloxacin, tetracycline, erythromycin, rifampicin, penicillin, doxycycline, nalidixic acid, trimethoprim, sulphacetamide, sulphadiazine etc.
2.	Anthelmintics	Albendazole, mebendazole, thiabendazole, ivermectin, praziquantel, pyrantel embonate, dichlorophen etc.
3.	Antidepressants	Trimipramine maleate, nortriptyline HCl, trazodone HCl, amoxapine, mianserin HCl, etc.
4.	Antidiabetics	Glibenclamide, glipizide, tolbutamide, tolazamide, gliclazide, chlorpropamide etc.
5.	Analgesics/anti-inflammatory agents	Diclofenac sodium, ibuprofen, ketoprofen, mefenamic acid, naproxen, oxyphenbutazone, indomethacin, piroxicam, phenylbutazone, etc.
6.	Antihypertensives:	Amlodipine, carvedilol, diltiazem, felodipine, minoxidil, nifedipine, prazosin HCl, nimodipine, terazosin HCl etc.
7.	Antiarrhythmics	Disopyramide, quinidine sulphate, amiodarone HCl, etc.
8.	Antihistamines	Acrivastine, cetrizine, cinnarizine, loratadine, fexofenadine, triprolidine, etc.
9.	Anxiolytics, sedatives hypnotics and neuroleptics	Alprazolam, diazepam, clozapine, amylobarbitone, lorazepam, haloperidol, nitrazepam, midazolam phenobarbitone, thioridazine, oxazepam, etc.
10.	Diuretics	Acetazolamide, clorthiazide, amiloride, furosemide, spironolactone, bumetanide, ethacrynic acid, etc.
11.	Gastro-intestinal agents	Cimetidine, ranitidine HCl, famotidine, domperidone, omeprazole, ondansetron HCl, granisetron HCl, etc.
12.	Corticosteroids	Betamethasone, beclomethasone, hydrocortisone, prednisone, prednisolone, methyl prednisolone, etc.
13.	Antiprotozoal agents	metronidazole, tinidazole, omidazole, benznidazole, clioquinol, decoquinate etc.

Future prospects of MDT

Mouth dissolving tablets can offer several biopharmaceutical advantages such as improved efficiency over conventional dosage forms. For example, they require smaller amounts of active ingredient to be effective, improve absorption profiles, and offer better drug bioavailability than regular tablets and capsules. In addition, MDTs may be suitable for the oral delivery of drugs such as protein and peptide-based therapeutics that have limited bioavailability when administered by conventional tablets. These products usually degrade rapidly in the stomach. Because drugs delivered in MDTs may be absorbed in the pregastric sites of highly permeable buccal and mucosal tissues of the oral cavity, they may be suitable for delivering relatively low-molecular weight and highly permeable drugs. Future possibilities for improvements in MDTs and drug delivery are bright, but the technology is still relatively new. Several drug delivery technologies that can be leveraged on improving drug therapy from MDTs have yet to be fully realized.

Table 1.3: Marketed Products of MDT

Trade Name	Active Drug	Manufacturer
Nimulid-MD	Nimesulide	Panacea Biotech, New Delhi, India
Feldene Fast Melt	Piroxicam	Pfizer Inc., NY, U.S.A
Zyprof Meltab	Rofecoxib	Zyodus, Cadila, India
Pepcid RPD	Famotidine	Merck and Co., NJ, U.S.A
Romilast	Montelukast	Ranbaxy Labs Ltd., New Delhi, India
Torrox MT	Rofecoxib	Torrent Pharmaceuticals, Ahmedabad, India
Olanex Instab	Olanzapine	Ranbaxy Labs Ltd., New Delhi, India
Zofran ODT	Ondansetron	Glaxo Wellcome, Middlesex, UK
Mosid-MT	Mosapride citrate	Torrent Pharmaceuticals, Ahmedabad, India
Febrectol	Paracetamol	Prographarm, Chateaufeu, France
Maxalt MLT	Rizatriptan	Merck and Co., NJ, U.S.A
Zelapar TM	Selegiline	Amarin Corp., London, UK

REFERENCES

- Chein YW. Oral Drug Delivery and Delivery Systems. 2nd ed. New York: Marcel Dekker; 1992.
- Chang R, Guo X, Burnside BA and Couch RA. A Review of Fast Dissolving Tablets. PharmTech 2000; 24(6): 52-58.
- Kuchekar BS, Bhise SB and Arungam V. Design of Fast Dissolving Tablets. Indian J Pharm Edu 2005; 35:150.
- Slowson M and Slowson S. What to do when patients cannot swallow their medications. Pharma Times 1985; 51: 90-96.
- Indurwade NH, Rajyaguru TH and Nakhat PD. Novel approach: Fast dissolving tablets. Indian Drugs 2002; 39(8): 405-41.
- Seager HJ. Drug delivery products and zydys fast dissolving dosage forms. Pharm Pharmacol 1998; 50:375-382.
- Gohel M, Patel M, Amin A, Agrawal R, Dave R and Bariya N. Formulation design and optimization of mouth dissolve tablets of nimesulide using vacuum drying technique. AAPS Pharm Sci Tech 2004; 5:36.
- Reddy LH, Ghosh B and Rajneesh. Fast dissolving drug delivery system: A review of literature. Indian J Pharm Sci 2002; 64 (4): 331-336.
- Habib W, Khankari R and Hontz J. Fast-dissolving drug delivery systems: Critical review in therapeutics. Drug Carrier Systems 2002; 17(1): 61-72.
- Bradoo R, Shahani S, Poojary S, Deewan, B and Sudarshan S. Fast dissolving drug delivery systems. JAMA India 2001; 4(10):27-31.
- Biradar SS, Bhagavati ST and Kuppasad IJ. Fast dissolving drug delivery systems: A brief overview. The Int J Pharmacol 2006; 4(2).
- Bhaskaran S, Narmada GV. Rapid Dissolving tablet A Novel dosage form. Indian Pharmacist 2002; 1:9-12.
- Devrajan PV and Gore SP, Melt- in- mouth tablets: innovative oral drug delivery system. Express Pharma Pulse 2000; 7(1):16.
- Makino T, Yamada M, and Kikuta J. Fast dissolving tablet and its production.
- US Patent 1998; No. 5720974.
- Bolhuis GK, Zuurman K and Te-Wierik GH. Improvement of dissolution of poorly soluble drugs by solid deposition on a super disintegrant. Part 2. Choice of super disintegrants and effect of granulation. Eur J Pharm Sci 1997; 5(2): 63-69.

17. Knitsch KW, Hagen A, Munz E and Determann H. Production of porous tablets. US Patent 1979; No. 4134943.
18. Heinemann H and Rothe W. Preparation of porous tablets. US Patent 1976; No. 3885026.
19. Caramella C, Ferrari F, Bonferoni MC and Ronchi, M. Disintegrants in solid dosage forms. *Drug Dev Ind Pharm* 1990; 16:2561.
20. Bagul Udhav S, Bagul Nitish S, Kulkarni Minal S, Dr Sawant SD, Dr Gujjar KN and Bidkar AA. Manufacturing technologies for mouth dissolving tablets. www.pharmainfo.net.
21. Parakh SR and Gothoskar AV. A review of mouth dissolving tablet technologies. *Pharm Tech* 2003; 27(11):92-98.
22. Nail SL and Gatlin LA. Freeze Drying: Principles and Practice, Parenteral Medications, in *Pharmaceutical Dosage Forms*. 2nd ed. Vol. 2. Marcel Dekker, New York; 1993:163.
23. Kuchekar BS, Badhan CA and Mahajan HS. Mouth dissolving tablets: A novel drug delivery system. *Pharma Times* 2003; 35:7-10.
24. Yarwood RJ, Kearny P and Thomson AR. Process for preparing solid pharmaceutical dosage forms. US Patent 1998; No. 5738875.
25. Mizumoto T, Masuda Y and Fukui M. Intrabuccally dissolving compressed moldings and production process thereof. US Patent 1996; No. 5576014.
26. Kaushik D, Dureja H and Saini TR. Mouth dissolving tablets: A Review. *Indian Drugs* 2004; 41(4):187-192.
27. Gole DJ, Levinson RS and Carbone J. Preparation of pharmaceutical and other matrix systems by solid state dissolution. US Patent 1993; No. 5215756.
28. Shangraw R, Mitrejev A and Shah M. A new era of tablet disintegrants. *Pharm Technol* 1980; 4(10):49-57.
29. Dobet L. Fast disintegrating tablets. PCT Patent 1999; No. 44580-Ai.
30. Acosta C, Tabare R, and Quali A. Fast-melt tablet and method of making same. US Patent 1998; No. 5807.
31. Panigrahi D, Baghel S and Mishra B. Mouth dissolving tablets: An overview of preparation techniques, evaluation and patented technologies. *J Pharm Res* 2005; 4(3):35-38.
32. Dr. Amin FA, Shah T, Bhadani M and Patel M. Emerging trends in development of orally disintegrating tablet technology. pharmainfo.net.
33. Patel BP. Fast dissolving drug delivery systems: An update. pharmainfo.net.
34. Bi Y, Sunanda H, Yonezawa Y, Danjo K and Lido K. Preparation and evaluation of a compressed tablet rapidly disintegrating in oral cavity. *Chem Pharm Bull* 1996; 44(11):2121-2127.
35. Watanabe Y, Koizumi K, Zama Y, Kiriya M, Mastumoto Y and Mastumoto M. New compressed tablet rapidly disintegrating in saliva in the mouth using crystalline cellulose and a disintegrant. *Bio Pharm Bull* 1995; 18(9):1308.
36. Ringard J and Guyot-Hermann AM. Calculation of disintegrant critical concentration in order to optimize tablets disintegration. *Drug Dev Ind Pharm* 1998; 14 (15):2321-2339.
37. Sreenivas SA, Dandagi PM, Gadad AP, Godbole AM, Hiremath SP, Mastiholimath VSM and Bhagwati ST. Orodispersible tablets: New fangled drug delivery system: A review. *Indian J Pharm Educ* 2005; 39(4):177.
38. Allen LV, Wang B and Davis LD. Rapidly dissolving tablet. US Patent 1998; No. 5,807,576.
39. Liang AC and Chen HL. Fast-dissolving intraoral drug delivery systems. *Expert Opin Ther Patents* 2001; 11(6):981-986.
40. www.ElanNanoCrystal_Technology.html
41. Allen LV and Wang B. Particulate support matrix for making rapidly dissolving tablets. US Patent 1997; No. 5,595,761.