IJIRR

International Journal of Information Research and Review
Vol. 05, Issue, 05, pp.5451-5459, May, 2018

REVIEW ARTICLE

MOUTH DISSOLVING TABLETS: AN OVERVIEW OF FORMULATION TECHNOLOGY

***Bhavana Tambe**

SMBT Institute of D. Pharmacy, Dhamangaon, Nashik, India

ARTICLE INFO

Article History:

Received 05th February, 2018
Received in revised form
19th March, 2018
Accepted 17th April, 2018
Published online 30th May, 2018

Keywords:

Mouth dissolving Tablets,
Fast disintegrating,
Orally Disintegrating
Tablets, Conventional techniques,
Rapid Disintegration

ABSTRACT

Mouth dissolving tablets are well established dosage forms available in the market. The numerous advantages that they offer to the patients in terms of compliance as well as to the manufacturers in terms of huge revenues by line extension of products are well known. In spite of such popularity, there seems to be lack of a standardized system to characterize these dosage forms. Enormous work has been done in this field, wherein some of the researchers have developed their own methods of evaluation. Methods to improve patient's compliance have always attracted scientists towards the development of fancy oral drug delivery systems. Among them, mouth dissolving drug delivery systems (MDDDS) have acquired an important position in the market by overcoming previously encountered administration problems and contributing to extension of patent life. MDDDS have the unique property of rapidly disintegrating and/or dissolving and releasing the drug as soon as they come in contact with saliva, thus obviating the requirement of water during administration. Therefore, these dosage forms have lured the market for a certain section of the patient population which include dysphasic, bed ridden, psychic, geriatric and pediatrics patients. Several techniques have been developed in the recent past, to improve the disintegration quality of these delicate dosage forms without affecting their integrity. This article focuses on the technologies available and the advances made so far in the field of fabrication of mouth dissolving tablets.

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 (Nayak *et al.,* 2009). The oral cavity is an attractive site for the administration of drugs because of ease of administration. Various dosage forms like Tablets, Capsules, Liquid preparations are administered by oral route **(**Sharma, 2008**)**. During the last decade, mouth dissolving tablet (MDT) technologies that make tablets disintegrate in the mouth without chewing and additional water intake have drawn a great deal of attention. The MDT is also known as fast melting, fast dispersing, rapid dissolve, rapid melt, and or quick disintegrating tablet. All MDTs approved by the Food and Drug Administration (FDA) are classified as orally disintegrating tablets. Recently, the European Pharmacopeia adopted the term oral dispersible tablet for a tablet that disperses or disintegrates in less than 3 minutes in the mouth before swallowing. Such a tablet disintegrates into smaller granules or melts in the mouth from a hard solid to a gel-like structure, allowing easy swallowing by patients. The disintegration time for good MDTs varies from several seconds to about a minute **(**Fu Yourong *et al.,* 2004; Chaudhari *et al.,* 2007; Nayak *et al.,* 2008**)**. Orally disintegrating tablets provide an advantage particularly for pediatric and geriatric populations who have difficulty in swallowing conventional tablets and capsules. Additionally, pediatric patients may suffer from ingestion problems as a result of underdeveloped muscular and nervous control. Moreover, patients traveling with little or no access to water, limit utility of orally administered conventional tablets or capsules. Mouth dissolving of tablet results in quick dissolution and rapid absorption which provide rapid onset of action. Moreover, drug candidates that undergo pre-gastric absorption when formulated as MDTs may show increased oral bioavailability. It provides good stability, accurate dosing, easy manufacturing **(**Prajapati and Patel, 2010; Mohan and Ghosh, 2010**)**. Fast dissolving tablets are also known as mouth-dissolving tablets, melt-in mouth tablets, Oral dispersible tablets, rapid melts, porous tablets, quick dissolving tablet. Fast dissolving tablets dissolve or disintegrate in the oral cavity without the need of water. Most fast dissolving tablets must include substances to mask the bitter taste of the active ingredient. This masked active ingredient is then swallowed by the patient's saliva along with the soluble and insoluble excipients **(**Kuchekar *et al.,* 2003; Allen and Wang, 1997**)**.

Corresponding author:* **Bhavana Tambe,
SMBT Institute of D. Pharmacy, Dhamangaon, Nashik, India.

It has been concluded the faster the dissolution, faster the absorption (only the unionized form of drug) and onset of action. Some drugs are absorbed from the oral cavity, pharynx and esophagus as the saliva passes down into the stomach. Thus the bioavailability of drug is significantly more than those observed from conventional tablets dosage form **(**Pebley *et al.,* 1994**)**. The time for disintegration of fast disintegrating tablets is generally considered to be less than one minute[11-14]. The fast dissolving solid dosage form turns into a soft paste or liquid form for easy swallowing, and thus it is free of risk of choking (Fu *et al.,* 2004; Bogner and Wilkosz, 2002). In recent years, a variety of improved methods for delivering drugs have been developed with the aim of improving bioavailability, convenience and patient compliance. Some tablets are designed to dissolve in saliva within a few seconds, and so called true fast-dissolving tablets. Fast dissolving technology offers following advantages **(**Reddy *et al.,* 2002; Kuchekar and Arumugam, 2001; Bhaskaran and Narmada, 2002; Indurwade *et al.,* 2002; Devrajan and Gore, 2000**)**.

- Improved compliance/added convenience
- No water needed
- No chewing needed
- Better taste
- Improved stability
- Suitable for controlled as well as fast release actives
- Allows high drug loading.
- Ability to provide advantages of liquid medication in the form of solid preparation.
- Adaptable and amenable to existing processing and packaging machinery
- Cost- effective.

Ideal Properties (Sharma, 2008; Kumari *et al.,* 2010)

An ideal MDT should:

- Require no water for oral administration.
- Have a pleasing mouth feel.
- Have an acceptable taste masking property.
- Be harder and less friable.
- Leave minimal or no residue in mouth after administration.
- Exhibit low sensitivity to environmental conditions (temperature and humidity).
- Allow the manufacture of tablet using conventional processing and packaging equipments.

Advantages (Sharma, 2008; Kumari *et al.,* 2010)

- Administration to the patients who cannot swallow, such as the elderly, bedridden patients, patients affected by renal failure & patients who refuse to swallow such as pediatric, geriatric & psychiatric patients.
- Rapid drug therapy intervention.
- Achieve increased bioavailability/rapid absorption through pre-gastric absorption of drugs from mouth, pharynx & esophagus as saliva passes down.
- Convenient for administration and patient compliant for disabled, bedridden patients and for travelers and busy people, who do not always have access to water.
- Good mouth feel property helps to change the perception of medication as bitter pill particularly in pediatric patients.
- The risk of chocking or suffocation during oral administration of conventional formulations due to physical obstruction is avoided, thus providing improved safety.
- New business opportunity like product differentiation.

Salient Features (Sharma, 2008)

- Ease of administration to patients who refuse to swallow a tablet, such as pediatric and geriatric patients and, psychiatric patients.
- Convenience of administration and accurate dosing as compared to liquids.
- Rapid dissolution of drug and absorption which may produce rapid, onset of action.
- Some drugs are absorbed from the pharynx and esophagus as the saliva passes down into the stomach, in such cases bioavailability of drugs is increased.
- Ability to provide advantages of liquid medication in the form of solid preparation.
- Pre-gastric absorption can result in improved bioavailability and as a result of reduced dosage, improved clinical performance through a reduction of unwanted effects.

Disadvantage (Kumari *et al.,* 2010):

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

The need for development of fast disintegrating tablets (Hirani et al., 2009)

Patient factors: Fast disintegrating dosage forms are particularly suitable for patients, who for one reason or the other; find it inconvenient to swallow traditional tablets and capsules with an 8-oz glass of water. These include the following: Geriatric patients mainly suffering from conditions like hand tremors and dysphasia. Pediatric patients who are unable to swallow easily because their central nervous system and internal muscles are not developed completely. Traveling patients suffering from mot ion sickness and diarrhea that do not have easy access to water.

Effectiveness factor: Increased bioavailability and faster onset of action are a major claim of these formulations. Dispersion in saliva in oral cavity causes pre-gastric absorption from some formulate ions in those cases where drug dissolves quickly. Buccal, pharyngeal and gastric regions are all areas of absorption for many drugs. Any pre-gastric absorption avoids first pass metabolism and can be a great advantage in drugs that undergo hepatic metabolism. Furthermore, safety profiles may be improves for drugs that produce significant amounts of toxic metabolites mediated by first-pass liver metabolism and gastric metabolism, and for drugs that have a substantial fract ion of absorption in the oral cavity and pre-gastric segments of GIT.

Formulation challenges in formulation of fast dissolving tablets (fdts)

Mechanical strength and disintegration time: It is obvious that increasing the mechanical strength will delay the disintegration time.

So a good compromise between these two parameters is always essential. FDTs are formulated to obtain disintegration time usually less than a minute. While doing so, maintaining a good mechanical strength is a prime challenge (Bhandari *et al.,* 2008).

Taste masking: As most drugs are unpalatable, rapid disintegrating drug delivery systems usually contain the medicament in a taste masked form. Delivery systems disintegrate or dissolve in patient's oral cavity, thus releasing the active ingredients which come in contact with the taste buds; hence, taste-masking of the drugs becomes critical to patient compliance (Reddy and Ghosh, 2002).

Aqueous solubility: Water-soluble drugs pose various formulate ion challenges because theyform eutectic mixtures, which result in freezing-point depression and the format ion of a glassy solid that may collapse upon drying because of loss of supporting structure during the sublimate ion process. Such collapse sometimes can be prevented by using various matrix-forming excipients such as mannitol than can induce crystallinity and hence, impart rigidity to the amorphous composite (Seager, 1998; Liesa and Atherton, 1993)

Hygroscopicity: Hygroscopicity is, of course, an important characteristic of a powder. It can be shown, roughly, for a fairly soluble compound that the hygroscopicity is related to its solubility. FDTs should have low sensitivity to humidity. This problem can be especially challenging because many highly water-soluble excipients are used in formulation to enhance fast-dissolving properties as well as to create good mouth feel. Those highly water-soluble excipients are susceptible to moisture; some will even deliquesce at high humidity. A good package design or other strategy should be created to protect FDTs from various environmental conditions (Carstensen, 1977; Van Campen *et al.,* 1980; Chang *et al.,* 2000).

Amount of drug: The application of technologies used for FDTs is limited by the amount of drug that can be incorporated into each unit dose. For lyophilized dosage forms, the drug dose must be lower than 400 mg for insoluble drugs and less than 60 mg for soluble drugs. This parameter is particularly challenging when formulating a fast-dissolving oral films or wafers (Sharma, 2008).

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 larger than 8 mm. Therefore, the tablet size that is both easy to take and easy to handle is difficult to achieve (Kumari *et al.,* 2010).

Mouth feel: FDTs should not disintegrate into larger particles in the oral cavity. The particles generated after disintegration of the FDTs should be as small as possible. Moreover addition of flavours and cooling agents like menthol improve the mouth feel (Pebley and Jager, 1994).

Sensitivity to environmental conditions: FDTs should exhibit low sensitivity to environment conditions such as humidity and temperature as most of the materials used in FDTs are meant to dissolve in minimum quantity of water (Reddy and Ghosh, 2002).

Criteria for excipient used in formulation of fdts

- It must be able to disintegrate quickly.
- Their individual properties should not affect the ODTs.
- It should not have any interaction with drug and other excipients.
- It should not interfere in the efficacy and organoleptic properties of the product.
- When selecting binder (a single or combination of binders) care must be taken in the final integrity and stability of the product.
- The melting point of the excipients used should be in the range of 30-35oC.
- The binder may be in liquid, semi solid, solid or polymeric in nature (Hirani *et al.,* 2009; Sehgal *et al.,* 2012; Mohanachandran *et al.,* 2011).

Excipients used in fdt's preparation: Excipients used in FDTs contain at least one superdisintegrant, a diluent, a lubricant and optionally a swelling agent, a permeabilizing agent, sweeteners and flavourings. Table 1 Name and weight percentage of various excipients (Sharma, 2008)

Super Disintegrants: As day's passes, demand for faster disintegrating formulation is increased. So, pharmacist needs to formulate disintegrants i.e. Superdisintegrants which are effective at low concentration and have greater disintegrating efficiency and they are more effective intragranularly. This superdisintegrants act by swelling and 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 (Kumari *et al.,* 2010; Kumaresan, 2008; Deshmukh, 2012).

Factors to be considered for selection of Superdisintegrants

Disintegration: The disintegrant must quickly wick saliva into the tablet to generate the volume expansion and hydrostatic pressure necessary to provide rapid disintegration in the mouth.

Compactibility: It is desirable to have ODT with acceptable hardness and less friability at a given compression force to produce robust tablets that avoid the need to use specialized packaging while maximizing production speed.

Mouth feel: Large particles can result in a gritty feeling in mouth. Thus, small particles are preferred. If the tablet forms a gel-like consistency on contact with water, However, it produces a gummy texture that many consumer find objectionable.

Flow: In typical tablet formulation, super disintegrants are used at 2-5 wt % of the tablet formulation. With ODT formulation, disintegrant level can be significantly higher (Kumari *et al.,* 2010).

Bulking Materials

Bulking materials are significant in the formulation of fast-dissolving tablets. The material contributes functions of a diluents, 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.

Mannitol in particular has high 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.

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.

Taste Masking

The materials for taste-masking purpose have often been classified depending upon the basic taste. Flavoring and perfuming agents can be obtained from either natural or synthetic sources. Natural products include fruit juices, aromatic oils such as peppermint and lemon oils, herbs, spices, and distilled fractions of these. They are available as concentrated extracts, alcoholic or aqueous solutions, syrups, or spirit. Apart from these conventional materials, many compositions have been found to show effective taste-masking abilities with improved flavor such as alkaline earth oxide, alkaline earth hydroxide, or an alkaline hydroxide. Another composition includes phosphorylated amino acid such as phosphotyrosine, phosphoserine, and phosphothreonine and mixtures thereof. Anethole effectively masked bitter taste as well as the aftertaste of zinc, which is used in treating the common cold. Clove oil and calcium carbonate, which has been found to be particularly useful to mask the unpalatable active in formulations which are intended to be chewed or dissolve in mouth prior to ingestion in solution (Johnson et al., 1991; Billany and Aulton, 1996; Catania and Johnson, 1997; Nelson, 1988; Eby and Georage, 1991; Pandya and Callan, 1998).

Emulsifying Agent

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 dissolving 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 (Pandya and Callan, 1998).

Techniques for Preparing Fast disolving Tablets (Seager, 1998; Renon and Corveleyn, 2000)

Many techniques have been reported for the formulation of Fast dissolving tablets or Oral dispersible tablets.

- Freeze drying / lyophilization
- Tablet Moulding
- Spray drying
- Sublimation
- Direct compression
- Mass extrusion

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. A typical procedure involved in the manufacturing of ODT using this technique is mentioned here. The active drug is dissolved or dispersed in an aqueous solution of a carrier/polymer. The mixture is done by weight and 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. Finally the blisters are packaged and shipped. 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 types i.e. solvent method and heat method. Solvent method involves moistening the powder blend with a hydro alcoholic solvent followed by compression at low pressures in molded plates to form a wetted mass (compression molding). The solvent is then removed by air-drying. The tablets manufactured in this manner are less compact than compressed tablets and posses a porous structure that hastens dissolution. The heat molding process involves preparation of a suspension that contains a 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 vacuum. The mechanical strength of molded tablets is a matter of great concern. Binding agents, which increase the mechanical strength of the tablets, need to be incorporated. Taste masking is an added problem to this technology. The taste masked drug particles were prepared by spray congealing a molten mixture of hydrogenated cottonseed oil, sodium carbonate, lecithin, polyethylene glycol and an active ingredient into a lactose based tablet triturate form. 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 bulkingagent and sodium starch glycolate or crosscarmellose or crospovidone are used assuperdisintegrants. Tablets manufactured from the spray-dried powder have been reported to disintegrate in less than 20 seconds in aqueous medium. The formulation contained bulking agent like mannitol and lactose, a superdisintegrant like sodium starch glycolate and croscarmellose sodium and acidic ingredient (citric acid) and/or alkaline ingredients (e.g. sodium bicarbonate). This spray-dried powder, which compressed into tablets showed rapid disintegration and enhanced dissolution.

Sublimation

To 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.

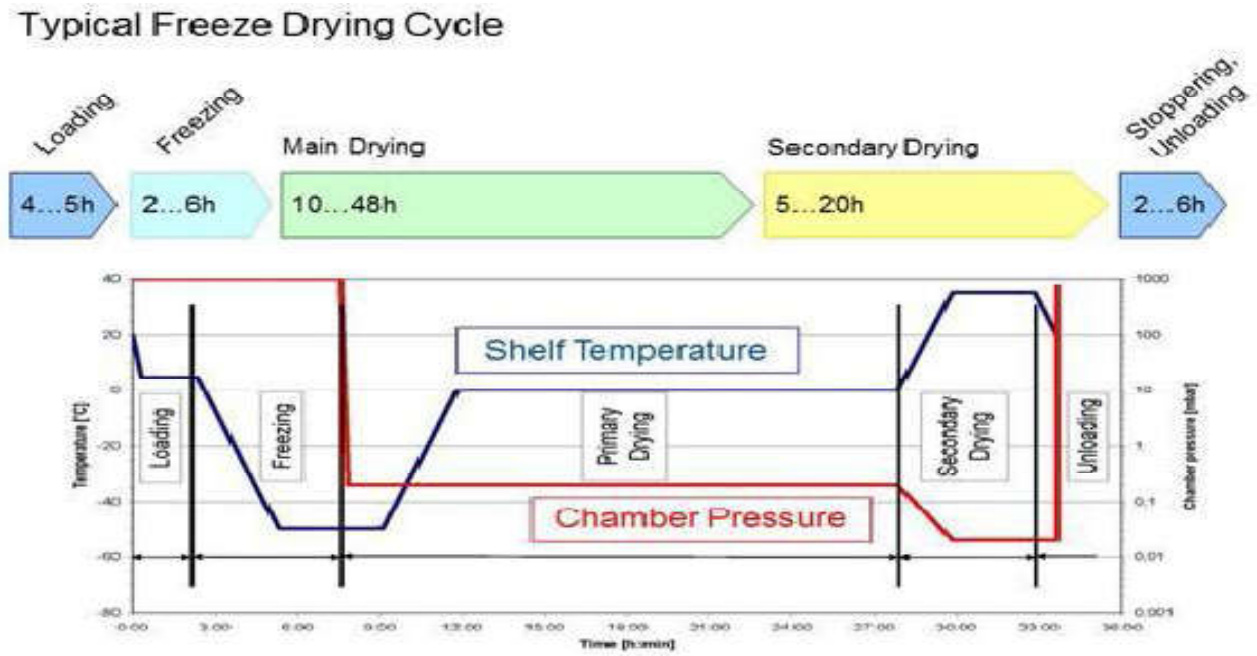

Fig. 1. Typical Freeze Drying Cycle

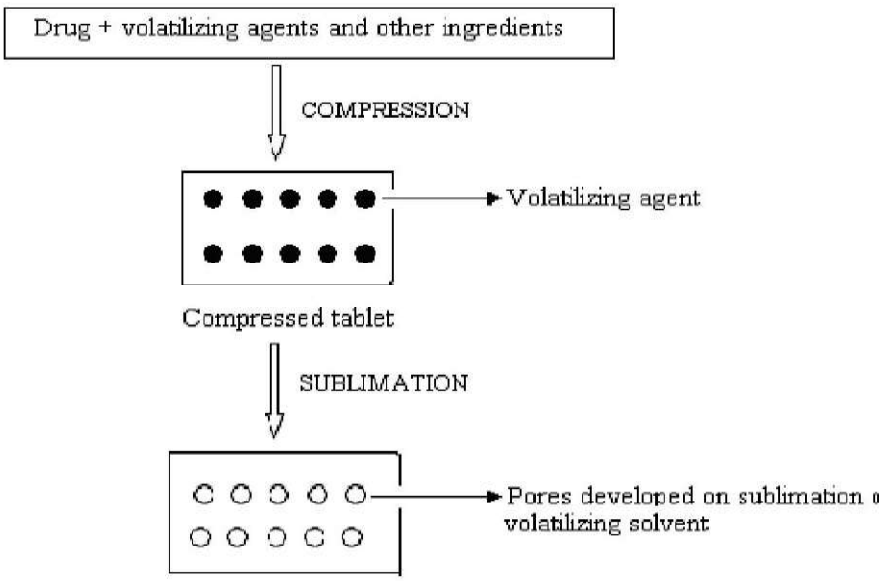

Fig. 2. Schematic Diagram of Sublimation Technique for

This volatile material is then removed by sublimation leaving behind a highly porous matrix. Tablets manufactured by this technique have reported to usually disintegrate in 10-20 sec. Even solvents like cyclohexane; benzene can be used as pore forming agents.

Preparation of MDT

Direct Compression

Direct compression represents the simplest and most cost effective tablet manufacturing technique. This technique can now be applied to preparation of ODT because of the availability of improved excipients especially superdisintegrants and sugar based excipients.

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.

Sugar Based Excipients

This is another approach to manufacture ODT 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. Mizumito et al have classified sugar-based excipients 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. The dried cylinder can also be used to coat granules for bitter drugs and thereby achieve taste masking.

Important Patented Technologies for Fast Dissolving Tablets

Zydis Technology

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.

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.

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 and have good rigidity. These can be packaged into conventional packaging system like blisters. Durasolv is an appropriate technology for product requiring low amounts of active ingredients.

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.

Table 1. 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
Zyrof Meltab	Rofecoxib	Zydus, 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,
Febrectol Paracetamol	France	Prographarm, Chateauneuf,
Maxalt MLT Rizatriptan Merck and Co.	NJ	U.S.A
Zelapar TM Selegiline Amarin Corp.	London	UK

Table 2. Some of Promising Drug Candidates for Mouth Dissolving Tablets [59]

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

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.

Flash Dose Technology

Flash dose technology has been patented by fuisz. Nurofen meltlet, a new form of ibuprofen as melt in mouth tablets prepared using flash dose technology is the first commercial product launched by biovail corporation. Flash dose tablets consist of self-binding shear form matrix termed as “floss”. Shear form matrices are prepared by flash heat processing.

Wow tab Technology

Wow tab 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 mouldability saccharide (eg. lactose, glucose, and mannitol) and granulated with a high mouldability saccharide (eg. Maltose, oligosaccharides) and compressed into tablet.

Flash tab Technology

Prographarm laboratories have patented the Flash tab technology. Tablet prepared by this system consists of an active ingredient in the form of micro crystals. Drug micro granules may be prepared by using the conventional techniques like coacervation, micro encapsulation and extrusion spheronisation. All the processing utilized conventional tableting technology.

Preparation of mouth dissolving tablets

All the materials were passed through 60 # screens prior to mixing. Drug, Croscarmellose sodium, Sodium Starch Glycolate, and Mannitol were mixed using a glass mortar and pestle. All the materials were directly compressible so this uniformly mixed blend was compressed into tablets using concave face round tooling on a 16-station rotary tablet machine.

Evaluation of mouth dissolving tablets

Weight variation test (Kuchekar *et al.,* 2003) : Weight variation test was done by weighing 20 tablets individually, by using Sartorious balance (Model CP- 224 S). Calculating the average weight and comparing the individual tablet weight to the average weight.

Tablet thickness (Kuchekar *et al.,* 2003): The thickness was measured by placing tablet between two arms of the Varnier calipers. 5 tablets were taken and their thickness was measured.

Tablet hardness (Kuchekar *et al.,* 2003): The tablet hardness, which is the force required to break a tablet in a diametric compression force. The hardness tester used in the study was Monsanto hardness tester, which applies force to the tablet diametrically with the help of an inbuilt spring.

Tablet friability (Banker *et al.,* 2006): The friability of the tablets was measured in a Roche friabilator (Camp-bell Electronics, Mumbai). Tablets of a known weight (Wo) or a sample of 20 tablets are dedusted in a drum for a fixed time (100 revolutions) and weighed (W) again. Percentage friability was calculated from the loss in weight as given in equation as below. The weight loss should not be more than 1 %. Determination was made in triplicate.

% Friability = 100 (Wo -W) / Wo

Wetting time (Kundu and Sahoo, 2008); The wetting time of the tablets can be measured using a simple procedure. Five circular tissue papers of 10 cm diameter are placed in a petridish with a 10 cm diameter. Ten millimeters of water- containing Eosin, a water-soluble dye, is added to petridish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as a wetting time.

Water absorption ratio (%) (Kundu and Sahoo, 2008; Chakraborthy *et al.,* 2008**):** A piece of tissue paper folded twice was placed in a small petridish (Internal Diameter = 6.5 cm) containing 6 ml of water. A tablet was placed on the paper and the time required for complete wetting was then measured. The water absorption ratio (R) was determined using the following equation. R = 100 (Wa -Wb) / Wb Where, Wb is the weight of the tablet before water absorption and Wa is the weight of the tablet after water absorption.

In-vitro disintegration test (Banker *et al.,* 2006) : The test was carried out on 6 tablets using Tablet disintegration tester ED-20 (Electrolab, Mumbai, India) distilled water at 37ºC ± 2ºC was used as a disintegration media and the time in second taken for complete disintegration of the tablet with no palable mass remaining in the apparatus was measured in seconds.

In-vitro dissolution study (United State Phamacopeia Convention, 2004) : The release rate of Drug from mouth dissolving tablets was determined using United State Pharmacopoeia (USP) XXIV dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of phosphate buffer pH 6.8 as a dissolution medium, at 37±0.50C and 50 rpm. A sample (10 ml) of the solution was withdrawn from the dissolution apparatus at 2.5, 5, 7.5, 10, 15, 20, 25, 30, 35 and 40min. The samples were filtered through a 0.45 membrane filter. Absorbance of these solutions was measured at 254 nm using a Shimadzu UV-1700 UV/VIS spectrophotometer. Cumulative percentage of drug release was calculated using an equation obtained from a standard curve.

Future prospects of MDT

The technologies depicted in this article demonstrate how recent advances in formulation development and processing technologies meet the efforts to achieve more sophisticated drug delivery system (Oral Disintegrating/Mouth Dissolving Tablets). MDT needs to be formulated for pediatric, geriatric, bedridden, psychotic patients, for those patients who are busy in traveling, has difficulty in swallowing and may not have access to water. 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 pre-gastric 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.

REFERENCES

Allen, LV. and Wang, B. 1997. Particulate support matrix for making a rapidly dissolving tablet, US Patent 5595761.

Banker, GS. and Anderson, NR. 2006. In: Lachman L, Lieberman, HA., Kanig, JL. The Theory and Practice of Industrial Pharmacy. 3rd ed. Mumbai: Varghese Publishing House; 1987; 293- 399. 55.Sreenivas SA, Gadad AP, Patil MB. *Indian Drugs*, 43: 35-37.

Bhandari, S., Mittapalli, RK., Gannu, R. and Rao, YM. 2008. Orodispersible tablet: An overview, *Asian Journal of Pharmaceutics*, 2:2-11.

Bhaskaran, S. and Narmada, GV. 2002. *Indian Pharmacist.,* 1(2), 9-12.

Billany, MR. and Aulton, ME. 1996. Pharmaceutics; The science of Dosage form Design, New York: Churchill Livingstone, *International Edition,* p 263.

Bogner, RH. and Wilkosz, MF. 2002. Fast-dissolving tablets: new dosage convenience for patients, U.S. *Pharm*., 27 34–43.

Brown, D. 2001. Orally disintegrating tablets: Taste over speed. *Drug Delivery Technology,* 3 (6): 58-61.

Carstensen, JT. 1977. Pharmaceutics of Solids and Solid Dosage Forms. *Wiley Interscience*, New York, p 5-11.

Catania, JS. And Johnson, AD. 1997. U. S. Patent 5633006.

Chakraborthy, S., Khandai, M. and Singh, SP. 2008.Patra N. *Int J Green Pharm.,* 22-25.

Chang, RK., Guo, X., Burnside, BA. and Couch, RA. 2000. Fast-dissolving tablets. *Pharmaceutical Technology North America*, 24:52–58.

Chaudhari P.D., Chaudhari S.P., Lanke S.D. and Patel N. 2007. Formulation and in vitro evaluation of teste masked orodispersible dosage form of Levocetirizine dihydrochloride; *Indian journal of pharmacuitical Education and research,* 41(4).,319-327.

Deshmukh, VN. 2012. Mouth Dissolving Drug Delivery System: A Review. *International Journal of Pharm Tech Research*,4(1) 412-421.

Devrajan, PV. and Gore, SP. 2000. Express Pharma Pulse, 7(1), Nov. 23,16.

Eby, III. and Georage, A. 1991. U.S. Patent 5002970.

Fu Yourong , Yang S., Jeong S. H., Kimura S.,and Park K., 2004. Therapeutic Drug Carrier Systems, Orally Fast Disintegrating Tablets:Developments, Technologies, Taste-Masking and Clinical Studies; *Critical Reviews*™, 21(6).,433–475.

Fu, Y., Yang, S., Jeong, SH., Kimura, S. and Park, K. 2004. Orally fast disintegrating tablets: development, technologies, taste-masking and clinical studies, Crit. Rev. Ther. *Drug Carr. Syst.,* 21 (6), 433–475.

Hirani, JJ., Rathod, DA. and Vadalia, KR. 2009. Orally Disintegrat ing Tablets: A Review*, Tropical Journal of Pharmaceutical Research*, 8 (2): 161-172.

Hirani, JJ., Rathod, DA. and Vadalia, KR. 2009. Orally Disintegrating Tablets: A Review. *Tropical Journal of Pharmaceutical Research,* 8 (2):161-172.

Indurwade, NH., Rajyaguru, T.H. and Nakhat, PD. 2002. *Indian Drugs,* 39(8), 405-09.

Johnson, JR., Wang, LH., Gordon, MS. and Chowhan, ZT. 1991. Effect of formulation solubility and hygroscopicity on disintegrating efficiency in tablets prepared by wet granulation. *Journal of Pharmaceutical Sciences,* 80:469–71.

Kuchekar, BS., Atul, Badhan, C. and Mahajan, H.S. 2003. Mouth dissolving tablets: A novel drug delivery system, *Pharma Times*, 35, 7-9.

Kuchekar, BS. and Arumugam, V. 2001. *Indian J. Pharm. Edu.,* 35, 150.

Kumaresan, C. 2008. Orally Disintegrating Tablet - Mouth dissolving, Sweet Taste and Target Release Profile. *Pharmaceutical review,* 6.

Kumari, S., Visht, S., Sharma, P.K. and Yadav, R.K. 2010. Fast dissolving Drug delivery system : Review Article; *Journal of Pharmacy Research,* 3(6).,1444-1449.

Kumari, S., Visht, S., Sharma, PK. and Yadav, RK. 2010. Fast dissolving Drug delivery system: Review Article. *Journal of Pharmacy Research,*3(6): 1444-1449.

Kumari, S., Visht, S., Sharma, PK. and Yadav, RK. 2010. Fast dissolving Drug delivery system: Review Article; *Journal of Pharmacy Research,*3(6):1444-1449.

Kumari, S., Vishtm, S., Sharma, PK. and Yadav, RK. 2010. Fast dissolving Drug delivery system: Review Article. *Journal of Pharmacy Research,* 3(6):1444-1449.

Kundu, S. and Sahoo, PK. 2008. *Pharma Times.,* 40(4): 11-15.

Liang, AC. and Chen, LH. 2001. Fast-dissolving intraoral drug delivery systems, Expert Opin. Ther. *Patents*, 11(6).

Lies, MC. and Atherton, AD.1993. Copping NM. US Patent 5,188,825.

Mohan A. and Ghosh S.K. 2010. Fast Dissolving Tablets: Past, Present and Future; *Indian drug.,* 47(6).,5-11.

Mohanachandran, PS., Sindhumol, PG. and Kiran, TS. 2011. Superdisintegrants: An overview, *International Journal of Pharmaceutical Sciences Review and Research*, 6:105-109.

Morita, Y., Tsusima, Y., Yasui, M., Termoz, R., Ajioka, J. and Takayama, K. 2002. Evaluation of Disintegration Time of Rapidly Disintegrating Tablets via a Novel Method Utilizing a CCD Camera, *Chem. Pharm. Bull.,* 50(9), 1181-1186.

Nayak, U.K., Patra S.K., Rout P.K., Patro B.K. and Nayak B.S., 2008. Development and optimization of promethazine theoclate Mouth dissolving tablets; *The Indian pharmacist.,* 65- 68.

Nelson, SL. 1998. U.S. Patent 5766622.

Pandya, HB, and Callan, TP. 1998. U.S. Patent 5, 837, 286.

Patel, S., Taher and Sengupta Mukul, 2013. Fast Dissolving Tablet Technology – A Review.*World Journal of Pharmacy and Pharmaceutical Sciences,* 2 (2): 485-508.

Pebley, WS. and Jager, NE. 1994. US Patent No.5, 298261,5-17.

Pebley, WS. and Jager, NE. 1994. Thompson SJ, Rapidly disintegrating tablets, US Patent No.5, 298,261.

Prajapati G.B. and Patel S.B., 2010. Formulation, Evaluation and Optimization of Orally Disintegrating Tablet of Piroxicam; *International Journal of PharmTech Research,* 1893-1899.

Reddy, LH. and Ghosh, BR. 2002. Fast dissolving drug delivery systems: A review of the literature, *Indian Journal of Pharmaceutical Sciences,* 64(4): 331-336.

Reddy, LH. and Ghosh, BR. 2002. Fast dissolving drug delivery systems: A review of the literature, *Indian Journal of Pharmaceutical Sciences,* 64(4):331-336.

Reddy, LH., Ghose, B. and Rajneesh, 2002. *Indian J. Pharm. Sci.,* 64(4), 331- 336.

Renon, J.P. and Corveleyn, S. 2000. Freeze-dried rapidly disintegrating tablets, US Patent No. 6,010,719.

S. J.R., Nayak S., Amlan S., Deep V.V., Khemariya P., Sumbhate S. and Nayak **S.** 2009. Taste masking of

Lornoxicam by polymer carrier system and formulation of oral disintegrating tablets; *International Journal of Drug Delivery,* 27-31.

Schiermeir, S. and Schmidt, PC. 2002. Fast dispersible ibuprofen tablets, *Eur. J. Pharm Sci.,* 15, 295- 305,

Seager, H. 1998. Drug delivery products and zydis fast dissolving dosage form, *J. Pharm. Phamacol.,* 50, 375-382.

Seager, H. 1998. Drug-delivery products and Zydis Fast-dissolving dosage form. *Journal of Pharmacy and Pharmacology,* 50: 375- 382.

Sehgal, P. et al. 2012. Fast dissolving tablets: a new venture in drug delivery. *American Journal of Pharm Tech Research.,* 2(4):252-279.

Sharma S. 2008, New generation of tablet: Fast dissolving tablet; *Latest review,* Vol VI .

Sharma, S. 2008. New Generation of Tablet: Fast Dissolving Tablet. Latest Reviews. *Pharmainfo.Net.,* 6(1).

Sharma, S. 2008. New generation of tablet: Fast dissolving tablet; *Latest review,* Vol VI .

Sharma, S. 2008. New Generation of Tablet: Fast Dissolving Tablet. Latest Reviews. *Pharmainfo.Net .,* 6(1).

Siewert, M., Dressman, J., Brown, C. and Shah, V. 2003. FIP/AAPS Guidelines for Dissolution/In Vitro Release Testing of Novel/Special Dosage Forms, *Dissolution Technologies,*

United State Phamacopeia Convention. NF Ashian edition; 2004; 74-75.

Van Campen, L., Zografi, G. and Carstensen, JT. 1980. An approach to the evaluation of hygroscopicity for pharmaceutical solids. *International Journal of Phar maceutics*,5:1–18.

****