AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: http://www.ajptr.com/

Rapidly Disintegrating Tablet: A Potential Concept of Modern Formulation Technology

Ranu Biswas*, Avik Dutta

1. Gupta College of Technological Sciences, G.T.Road, Ashram More, Asansol-713301, Burdwan, West Bengal, India.

ABSTRACT

Development of fancy oral drug delivery systems has always attracted scientists because of improved patient compliance. Among them, mouth dissolving drug delivery systems (MDDDS) have acquired an important position in the market by overcoming previously encountered administration problems. A fast-dissolving drug delivery system, in most cases, is a tablet which is designed to allow administration in the mouth in the absence of water and readily dissolves or disintegrates in the saliva generally within <60 seconds with rapid dissolution of drug and absorption of which may produce rapid onset of action and ease of administration to patients who refuse to swallow a tablet, such as pediatric and geriatric patients and psychiatric patients. In some cases such as motion sickness, sudden episodes of allergic attack or coughing, and an unavailability of water, swallowing conventional tablets may be difficult. The risk of chocking or suffocation during oral administration is avoided, thus providing improved safety. 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. Apart from the conventional methods of fabrication, this review also provides the detailed concept of some unique patented technologies like Zydis, Lyoc, Quicksolv, Orasolv, Durasolv, Flashtab, Oraquick, Wowtab and Ziplet along with their advantages and limitations.

Key words: Rapidly Disintegrating Tablet, Mouth Dissolving Tablet, Fast Disintegrating Tablet, Fast Dissolving Tablet, Orally Disintegrating Tablet, Orodispersible Tablet.

* Corresponding Author Email: ranu_biswas@rediffmail.com

Received 7 May 2012, Accepted 18 May 2012

Please cite this article in press as: Biswas R *et al.*, Rapidly Disintegrating Tablet: A Potential Concept of Modern Formulation Technology American Journal of PharmTech Research 2012.

INTRODUCTION

Fast Dissolving Tablets are disintegrating or dissolve rapidly in the saliva without the need for water. Some tablets are designed to dissolve in saliva remarkably fast, within a few seconds, and are true fast-dissolving tablets. Others contain agents to enhance the rate of tablet disintegration in the oral cavity, and are more appropriately termed fast-disintegrating tablets, as they may take up to a minute to completely disintegrate. Oral delivery is currently the gold standard in the pharmaceutical industry where it is regarded as the safest, most convenient and most economical method of drug delivery having the highest patient compliance. This tablet format is designed to allow administration of an oral solid dose form in the absence of water or fluid intake. Such tablets readily dissolve or disintegrate in the saliva generally within <60 seconds. Fast or mouth dissolving tablets have been formulated for pediatric, geriatric, and bedridden patients. Such formulations provide an opportunity for product line extension in the many elderly persons will have difficulties in taking conventional oral dosage forms (viz., solutions, suspensions, tablets, and capsules) because of hand tremors and dysphagia. Swallowing problems also are common in young individuals because of their underdeveloped muscular and nervous systems. Other groups that may experience problems using conventional oral dosage forms include the mentally ill, the developmentally disabled, and patients who are uncooperative, on reduced liquid-intake plans, or are nauseated. In some cases such as motion sickness, sudden episodes of allergic attack or coughing, and an unavailability of water, swallowing conventional tablets may be difficult [1].

In the recent past, several new advanced technologies have been introduced for the formulation of mouth dissolving tablets (MDTs) with very interesting features, like extremely low disintegration time, exceptional taste masking ability, pleasant mouth feel and sugar free tablets for diabetic patients. The technologies utilized for fabrication of MDDDS include lyophilization[2], moulding[3], direct compression[4], cotton candy process [5], spray drying [6], sublimation[7], mass extrusion[8], nanonization [9] and quick dissolve film formation[10]. These techniques are based on the principles of increasing porosity and/or addition of superdisintegrants and water soluble excipients in the tablets. The formulations prepared from these techniques differ from each other on the basis of the factors like mechanical strength of final product, drug and dosage form stability, mouth feel, taste, rate of dissolution of the formulation in saliva, rate of absorption from saliva and overall drug bioavailability. Although, numerous technologies had been developed for the fabrication of these unique dosage forms in last two decades, but so far, no standardized technique has been designed or mentioned in

pharmacopoeias for their evaluation except in European Pharmacopoeia (EP), which defines orodispersible tablets as "uncoated tablets intended to be placed in the mouth where they disperse rapidly before being swallowed". EP also specifies that the orodispersible tablets should disintegrate within 3 minutes when subjected to conventional disintegration test used for tablets and capsules. This article presents a detailed review regarding the evaluation measures available in literature to characterize the MDTs, which have been designed keeping in view the special features of these novel drug delivery systems.

Criteria for Rapidly Disintegrating Drug Delivery System: [11]

The tablets should

- Not require water to swallow, but it should dissolve or disintegrate in the mouth in matter of seconds.
- Be compatible with taste masking.
- Be portable without fragility concern.
- Have a pleasant mouth feel. Leave minimum or no residue in the mouth after oral administration.
- Exhibit low sensitive to environmental condition as temperature and humidity.
- Allow the manufacture of the tablet using conventional processing and packaging equipments at low cost.

Salient Feature of Rapidly Disintegrating Drug Delivery System:[11]

- Ease of Administration to the patient who cannot swallow, such as the elderly, stroke victims, bedridden patients, patient affected by renal failure and patient who refuse to swallow such as pediatric, geriatric & psychiatric patients.
- No need of water to swallow the dosage form, which is highly convenient feature for patients who are traveling and do not have immediate access to water.
- Rapid dissolution and absorption of the drug, which will produce quick onset of action.
- Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases bioavailability of drug is increased.
- Pre-gastric absorption can result in improved bioavailability and as a result of reduced dosage; improve clinical performance through a reduction of unwanted effects.
- Good mouth feel property helps to change the perception of medication as bitter pill particularly in pediatric patient.

- The risk of chocking or suffocation during oral administration of conventional formulation due to physical obstruction is avoided, thus providing improved safety.
- New business opportunity like product differentiation, product promotion, patent extensions and life cycle management.
- Beneficial in cases such as motion sickness, sudden 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.

Benefits of Rapidly Disintegrating Tablet: [11]

- 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 un-cooperative, or are on reduced liquid intake plans or are nauseated.
- 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 Rapidly Disintegrating Tablet: [11]

- □ The tablets usually have insufficient mechanical strength. Hence, careful handling is required.
- □ The tablets may leave unpleasant taste and/or grittiness in mouth if not formulated properly.

Mechanism of Superdisintegrants: [11]

There are four major mechanisms for tablets disintegration as follows:

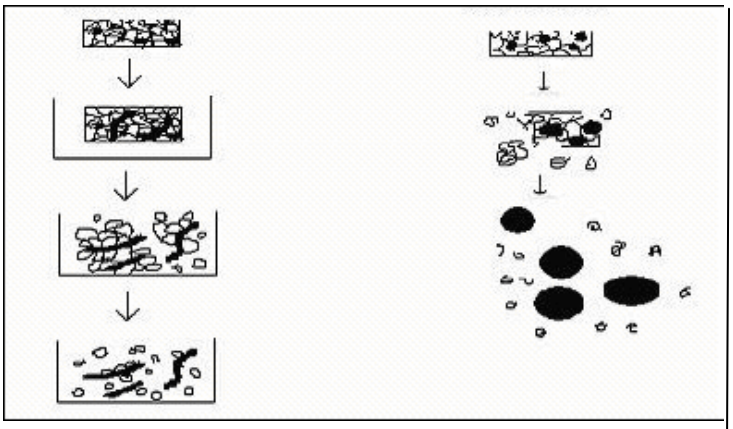
1. Swelling:

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.

2. Porosity and capillary action (Wicking):

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.

WICKING **SWELLING**



Water is pulled by disintegrant and Reduced the physical Bonding force between particles

Particles swell and break up the matrix form within

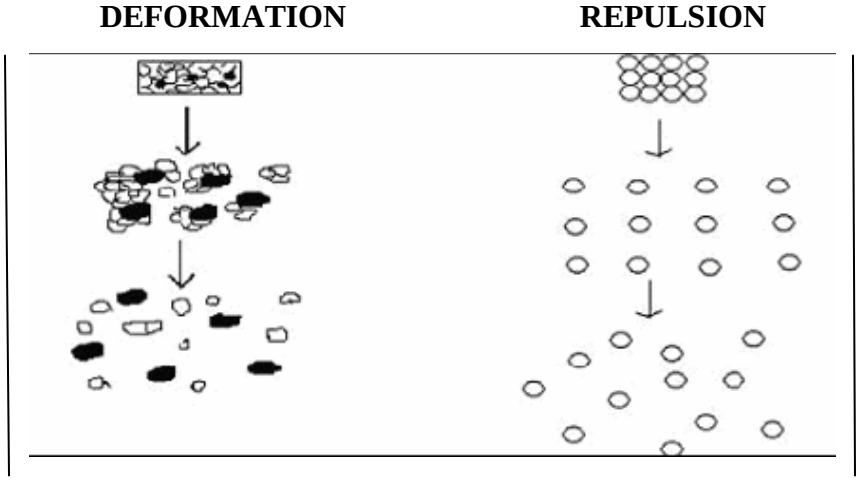
3. Due to disintegrating particle/particle repulsive forces

Another mechanism of disintegrant attempts to explain the swelling of tablet made with 'nonswellable' disintegrants. Guyot-Hermann has proposed a particle repulsion theory based on the observation that no swelling particle also causes 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.

4. Due to deformation

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



Particles swell to precompression Size and break up matrix other

Water is drawn into pores and particles repel each because of Resulting electric force.

Manufacturing technologies used now a day for RDT's: [12]

Some of the new advanced technologies which are commonly being used in last few decades are summarized as:-

1. Freeze drying/Lyophilization
2. Molding
3. Direct Compression
4. Cotton Candy Process
5. Spray drying
6. Sublimation
7. Mass Extrusion
8. Nanonization
9. Fast Dissolving Films

1. **Freeze drying or lyoplilization:**

   It is one of the first generation techniques for preparing MDT, in which sublimation of water takes place from the product after freezing. The formulations show enhanced dissolution characteristics due to the appearance of glossy amorphous structure to bulking agents and sometimes to drug. The ideal drug characteristics for this process are relative water insolubility with fine particle size and good aqueous stability in suspensions. Primary problems associated with water-soluble drugs are formation of eutectic mixture,

because of freezing point depression and formation of glassy solid on freezing, which might collapse on sublimation. The addition of mannitol or crystal forming materials induces crystalline and imparts rigidity to amorphous material. The advantage of using freeze-drying process is that pharmaceutical substances can be processed at non elevated temperature, thereby eliminating adverse thermal effects. High cost of equipment and processing limits the use of this process. Other disadvantages include lack of resistance necessary for standard blister packs of the final dosage forms.

2. Tablet Molding:

There are two types of molding process 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). Air-drying is done to remove the solvent. The tablets manufactured so formed are less compact than compressed tablets and posses a porous structure that hastens dissolution. In the heat molding process a suspension is prepared that contains a drug, agar and sugar (e.g. mannitol or lactose). This suspension is poured in the blister packaging wells, and then agar is solidified at the room temperature to form a jelly and dried at 30°C under vacuum. The main concern about these molded tablets is their mechanical strength, which can be achieved by using binding agents. The spray congealing of a molten mixture of hydrogenated cottonseed oil, sodium carbonate, lecithin, polyethylene glycol and an active ingredient into a lactose based tablet triturate form was used to prepare the taste masked drug particles. As compared to the lyophillization technique, tablets produced by the molding technique are easier to scale up for industrial scale manufacturing.

3. Direct Compression:

Direct compression represents the simplest and most cost effective tablet manufacturing technique. MDT can be prepared by using this technique because of the availability of improved excipients especially super-disintegrate and sugar based excipients.

(a) Super-disintegrants:

The rate of disintegration gets affected by the addition of superdisintegrants and hence the dissolution. Other ingredients like water-soluble excipients and effervescent agents also increase the disintegration.

(b) Sugar based excipients:

The sugar based excipients which are commonly used are especially bulking agents (like dextrose, fructose, lactilol, maltilol, maltose, mannitol, sorbitol, starch hydrolysate,

polydextrose and xylitol) which display high aqueous solubility and sweetness, and hence impart taste masking property and provide pleasing mouth feel. Mizumito et al 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 but low dissolution rate.

4. Cotton Candy Process:

The FLASHDOSE® is a MDDDS manufactured using Shearform™ technology in association with Ceform TI™ technology to eliminate the bitter taste of the medicament. A matrix known as 'floss', with a combination of excipients, either alone or with drugs is prepared by using shear form technology. Like cotton-candy fibers floss is fibrous material made of saccharides such as sucrose, dextrose, lactose and fructose at temperatures ranging between 180–266 °F. However, other polysaccharides such as polymaltodextrins and poly-dextrose can be transformed into fibers at 30–40% lower temperature than sucrose. Due to this modification thermo labile drugs can be safely incorporated into the formulation. This process results in a highly porous product and offer very pleasant mouth feel due to fast solubilization of sugars in presence of saliva. The manufacturing process can be divided into four steps as detailed below:

(a) Floss blend: -

The floss mix is prepared by blending the 80% sucrose in combination with mannitol/dextrose and 1% surfactant. The surfactant maintains the structural integrity of the floss fibers by acting as crystallization enhancer. This process helps in retaining the dispersed drug in the matrix, thereby minimizes the migration out of the mixture.

(b) Floss processing:

The floss formation machine uses flash heat and flash flow processes to produce matrix from the carrier material. The machine is similar to that used in 'cotton-candy' formation which consists of a spinning head and heating elements. In the flash heat process, the heat induces an internal flow condition of the carrier material. This is followed by its exit through the spinning head (2000–3600 rpm) that flings the floss under centrifugal force and draws into long and thin floss fibers, which are usually amorphous in nature.

(c) Floss chopping and conditioning:

In this step fibers are converted into smaller particles in a high shear mixer granulator. The partial crystallization is done by spraying ethanol (1%) onto the floss and subsequently evaporated it to impart improved flow and cohesive properties to the floss. This is called Conditioning.

(d) Blending and compression:

Finally, the chopped and conditioned floss fibers are blended with the drug and other excipients and compressed into tablets. Exposure of the dosage forms to elevated temperature and humidity conditions (40 °C and 85% RH for 15min) improves the mechanical strength of tablets due to expected crystallization of floss material that result in binding and bridging, to improve the structural strength of the dosage form.

5. Sprays-Drying:

Allen et al., have used spray-drying for the production of MDTs. The formulations contained hydrolyzed and non hydrolyzed gelatin as a supporting agent for the matrix, mannitol as a bulking agent and sodium starch glycolate or croscarmellose as a disintegrant. By adding an acid (e.g., citric acid) or an alkali (e.g., sodium bicarbonate) disintegration and dissolution were further enhanced. The porous powder was obtained by spray drying the above suspension which was compressed into tablets. Tablets manufactured by this method shows disintegration time < 20 sec in an aqueous medium.

6. Sublimation:

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

7. Mass-Extrusion:

This technology involves softening of the active blend using the solvent mixture of water soluble polyethylene glycol and methanol. This softened mass is extruded through the extruder or syringe and a cylindrical shaped extrude is obtained which are finally cut into even segments using heated blade to form tablets. Granules of bitter drugs can be coated using this method to mask their taste.

8. **Nanonization:**

   A recently developed Nanomelt technology involves reduction in the particle size of drug to nano size by wet-milling technique. Surface adsorption of the nano crystals of the drug is done on selected stabilizers for stabilizing them against agglomeration, which are then incorporated into MDTs. This technique is mainly advantageous for poor water soluble drugs and also for a wide range of doses (up to 200 mg of drug per unit).

9. **Fast Dissolving Films:**

   It is a newer developing front in MDDDS that provides a very convenient means of taking medications and supplements. In this technique, water soluble film forming polymer (pullulan, CMC, HPMC, HEC, HPC, PVP, PVA etc.), drug and other taste masking ingredients are dissolved in non-aqueous solvent to prepare non-aqueous solution, which on evaporation of solvent forms a film. Resin adsorbate or coated micro particles of the drug can be incorporated into the film if the drug is bitter. This film when placed in mouth melts or dissolves rapidly and releases the drug in solution or suspension form. This system forms the thin films of size less than 2x2 inches which dissolves within 5 sec with instant drug delivery and flavored taste.

Evaluation of Rapidly Disintegrating Tablet: [11, 13, 14]

1. Wetting time: [11]

Wetting time is closely related to the inner structure of the tablets and to the hydrophilicity of the excipient. According to the following equation proposed by Washburn E.W (1921), the water penetration rate into the powder bed is proportional to the pore radius and is affected by the hydrophilicity of the powders.

dl/dt = r¡cosq**/(4**h**l)**

Where l is the length of penetration, r is the capillary radius, ¡ is the surface tension, h is the liquid viscosity, t is the time, and q is the contact angle. It is obvious that pores size becomes smaller and wetting time increases with an increase in compression force or a decrease in porosity. A linear relationship exists between wetting time and disintegration time. Thus wetting is the important step for disintegration process to take place. A piece of tissue paper folded double was placed in a Petri plate (internal diameter is 6.5 cm) containing 6ml of water. The tablet was placed on the paper and the time for complete wetting of the tablet was measured in seconds. The method was slightly modified by maintaining water at 37^0c. Wetting time corresponds to the time taken for the tablet to disintegrate when kept motionless on the tongue.

2. Mechanical Strength:

Tablets should possess adequate strength to withstand mechanical shocks of handling in manufacturing, packaging and shipping. Crushing strength and friability are two important parameter to evaluate a tablet for its mechanical strength.

A).Crushing Strength:

It is the force required to break a tablet by compression in the radial direction, it is an important parameter in formulation of mouth dissolve tablets because excessive crushing strength significantly reduces the disintegration time. In the present study the crushing strength of the tablet was measured using Pfizer hardness testers. An average of three observations is reported.

B) Friability testing:

The crushing test may not be the best measure of potential behavior during handling and packaging. The resistance to surface abrasion may be a more relevant parameter. Friability of each batch was measure in "Electro lab friabilator". Ten preweighed tablets were rotated at 25 rpm for 4 min, the tablets were then re weighed and the percentage of weight loss was calculated.

3. Rapidly Disintegrating Property:

To evaluate the tablets for their rapid disintegration properties, following tests were carried out.

A) Modified disintegration test:

The standard procedure of performing disintegration test for these dosage forms has several limitations and they do not suffice the measurement of very short disintegration times. The disintegration time for ODT needs to be modified as disintegration is required without water, thus the test should mimic disintegration in salivary contents. For this purpose, a petridish (10 cm diameter) was filled with 10 ml of water. The tablet was carefully put in the center of petridish and the time for the tablet to completely disintegrate into fine particles was noted.

B) Disintegration Time

The methods for evaluation of in-vivo disintegration time had been explained in literature. However, the results from this type of test typically reveal unsatisfactory reproducibility and are not reliable as the difference in disintegration time is few seconds in most cases. In addition, the in-vivo disintegration test has its own limitation of issues related to ethics and the safety of the volunteers. At present, the disintegration time of MDTs is measured using the disintegration test for conventional tablets that is described in the Pharmacopoeias. EP has set the limit of 3 mins for disintegration time of MDTs using conventional disintegration apparatus. However, no special apparatus is mentioned in the pharmacopoeias for disintegration test of MDTs and the conventional method available seems to be inappropriate for MDTs. This is because of the

extreme operating conditions in the disintegration apparatus which fails to provide a significant discrimination among the rapidly disintegrating tablets. Furthermore, the conventional test employs a relatively huge volume of test solution (900 ml) compared to the volume of saliva in human buccal cavity which is less than 6 ml. Therefore, the results obtained from the conventional disintegration test do not reflect the actual disintegration rate in the human mouth which usually ranges from 5–30 secs [9, 21, 22]. To overcome these issues, several new methods have been proposed, which are reviewed here.

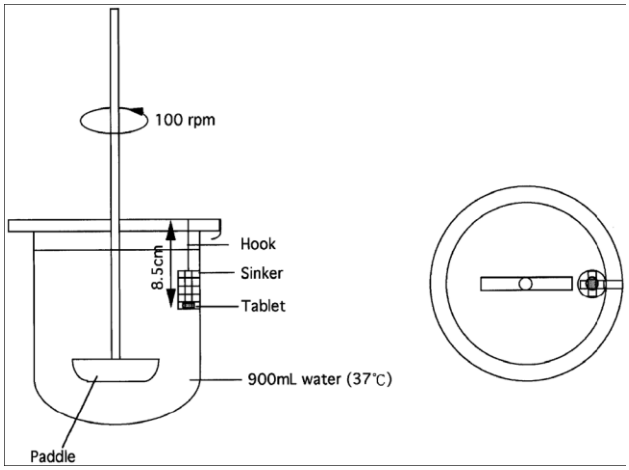


Figure: 1 Schematic view of modified dissolution apparatus for disintegration test.

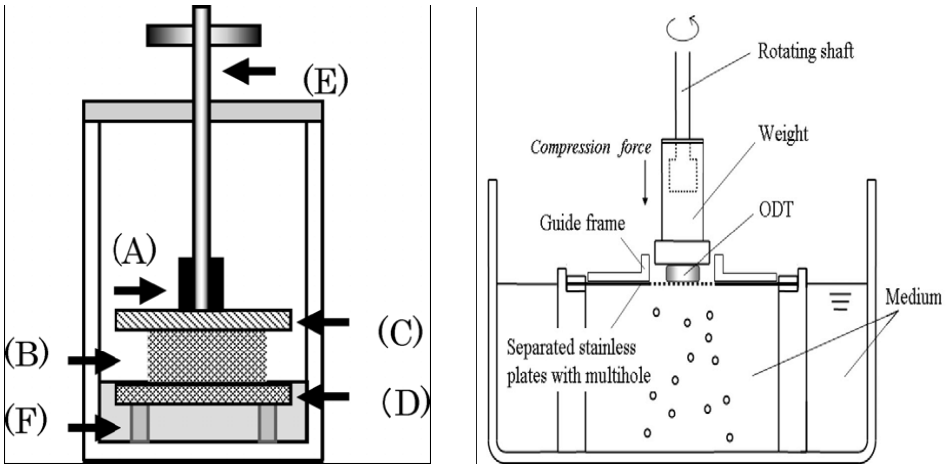


Figure 2 :(a) Apparatus of rotary shaft method for MDT (A) weight, (B) MDT, (C) wetting sponge, (D) wire gauze, (E) rotary shaft, (F) medium. (b) Improved rotary shaft apparatus

C) Disintegration Test with Rotary Shaft Method

In another study, Narazaki et al., [22] proposed a better disintegration method for MDTs as shown in Figure 2 (a). In the experimental method, the MDT was placed on the wire gauze (D), slightly immersed in the medium, and then compressed by a rotary shaft (E) which was employed to provide mechanical stress on the tablet by means of its rotation and weight. Purified water at

temperature 37 °C was used as the medium. The critical parameters of the proposed method were the rotation speed and the mechanical stress. Using this new method, it would be possible to predict a more realistic disintegration rate in human. The compression force can be easily adjusted using the weight (A). The rotary shaft crushes the MDT which disintegrates into the medium. The endpoint was measured visually using a stopwatch.

D) Disintegration in oral cavity

The time required for complete disintegration of tablets in oral cavity was obtained from six healthy volunteers, who were given tablets from the optimum formulation.

4. Water absorption Ratio-

A piece of tissue paper folded twice was placed in a small Petri dish containing 6 ml of water. A tablet was put on the paper & the time required for complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio, R, was determined using following equation,

$R=10(w_a/w_b)$ where,

W_b is weight of tablet before water absorption & w_a is weight of tablet after water Absorption.

5. In-vitro dispersion time-

Tablet was added to 10 ml of phosphate buffer solution, ph 6.8 at 37±0.5ºC, Time required for complete dispersion of a Tablet was measured.

TECHNOLOGY USED FOR THE PREPARATION OF RAPIDLY DISINTEGRATING TABLET:

Rapid-dissolving characteristic of FDTs is generally attributed to fast penetration of water into tablet matrix resulting in its fast disintegration. Several technologies have been developed on the basis of formulation aspects and different processes and patented by several pharmaceutical companies. Table 1 of patented technology is given below;

Table 1: Patented technology for preparation of Rapidly Disintegrating Tablets.[11-12, 15-19]

Sl no.	Technique	Basis of Technology	Developed by Company	Advantage	Disadvantage
01.	Zydis	Lyophilization	R.P.Scherer, Inc.	Quick dissolution, Self-preserving and increased bioavailability.	Expensive process, poor stability at higher temperature and humidity.
02.	Orasolv	Direct compression	Cima Labs, Inc.	Taste-masking is twofold, quick dissolution	Low mechanical strength.
03.	Durasolv	Direct compression	Cima Labs, Inc.	Higher mechanical strength than Orasolv, Good rigidity.	Inappropriate with larger dose.

04.	Flashdose	Cotton Candy Process	Fuisz Technology, Ltd.	High surface area for dissolution.	High temperature required to melt the matrix can limit the use of heat-sensitive drugs, sensitive to moisture and humidity.
05.	Flashtab	Direct compression	Ethypharm	Only conventional tabletting technology	------
06.	Wow tab	Direct compression	Yamanouchi Pharma Tech. Inc.	Adequate dissolution rate and hardness.	No significant change in bioavailability.
07.	Oraquick		KV Pharm.Co., Inc.	Faster and efficient production, appropriate for heat-sensitive drugs.	------
08.	Ziplet	Direct compression	Eurand International	Good mechanical strength, satisfactory properties can be obtained at high dose (450 mg) and high weight (850 mg).	As soluble component dissolves, rate of water diffusion in to tablet is decreased because formation of viscous concentrated solution.

Drugs to be promising incorporated in Rapidly Disintegrating Tablets:[20-22] There are no particular limitations as long as it is a substance which is used as a pharmaceutical active ingredient.

- **Analgesics and Anti-inflammatory Agents:**

  Naproxen, Oxaprozin, Oxyphenbutazone,Ibuprofen Phenylbutazone, Piroxicam,Sulindac.

- **Anthelmintics :**

Albendazole, Dichlorophen, Iverrnectin, Mebendazole OxfendazoleThiabendazole.

- **Anti-Arrhythmic Agents:**

  Amiodarone, Disopyramide, Flecainide Acetate, Quinidine Sulphate,

- **Anti-bacterial Agents:**

  Ciprofloxacin, Clarithromycin, Clofazimine, Cloxacillin, Doxycycline, Erythromycin, Ethionamide,Rifampicin, Sulphacetamide, Sulphadiazine, Sulphafurazole,Sulphamethoxazole,

- **Anti-coagulants:**

Dicoumarol, Dipyridamole, Nicoumalone, Phenindione. Anti-Depressants: Amoxapine,Ciclazindol, Maprotiline, Mianserin, Nortriptyline, Trazodone, Trimipramine Maleate., Chlorpropamide, Glibenclamide, Glipizide, Tolazamide, Tolbutamide.

- **Anti-Epileptics:**

  Carbamazepine, Clonazepam, Ethotoin, Methoin, Methsuximide, , Valproic Acid.

- **Anti-Fungal Agents:**

  Amphotericin, Clotrimazole Fluconazole, Fiucytosine, Griseofulvin,

- **Anti-Gout Agents:**

  Allopurinol,Probenecid.

- **Anti-Hypertensive Agents:**

  Amlodipine, , Benidipine, Darodipine, Dilitazem, Minoxidil.

- **Anti-Malarials:**

  Chloroquine,Mefloquine, Proguanil, Pyrimethamine, Quinine Sulphate

  Carbimazole, Propylthiouracil.

- **Diuretics:**

  Acetazolarnide, Amiloride,.

- **Gastro-Intestinal Agents:**

  Cimetidine, Diphenoxylate, Domperidone, Famotidine, Loperamide Nizatidine, Omeprazole, Ondansetron, Ranitidine,

FUTURE PERSPECTIVE:

With continued innovations in pharmaceutical excipients, one can expect the emergence of more novel technologies for MDTs in the days to come. These innovations may involve modifying formulation composition and processing to achieve new performance end-points or the merger of new technological advances with traditional pharmaceutical processing techniques for the production of novel mouth dissolving dosage forms. It is reasonable to expect that future trends in innovations of drug delivery systems will continue to bring together different technological disciplines to create novel technologies.

CONCLUSION:

Extensive works had been carried out till date in order to evaluate the MDTs and among them many are proved to have significant discriminatory power. However, the final selection of an appropriate evaluation method depends on the consideration of the manufacturing technology, taste masking approach employed and the excipients used in the product development process.

Despite the fact that a lot of these dosage forms are available in the market, still a lot of work needs to be done to standardize the evaluation techniques and streamline the regulatory issues. Apart from all, application of electronic sensor array – "E-tongue" and Electro Force® Disintegration tester seem to have a bright future ahead in the area of MDTs evaluation.

REFERENCES:

1. Lindgren S, Janzon L. Prevalence of swallowing complaints and clinical findings among 50-79-year-old men and women in an urban population. Dysphagia 1991; 6: 187–192.
2. Hanawa T. New oral dosage form for elderly patients: preparation and characterization of silk fibroin gel. Chem Pharm Bull 1995; 43: 284–288.
3. Gisel EG. Oral motor skills following sensorimotor intervention the moderately eating impaired child with cerebralpalsy. Dysphagia 1994; 9: 180–192.
4. Virely P, Yarwood R. Zydis - a novel, fast dissolving dosage form. Manuf Chem 1990; 61: 36–37.
5. Pebley WS, Jager NE, Thompson SJ. Rapidly disintegrating tablet. US Patent No. 5, 298, 261. 1994 March 29.
6. Watanabe Y. New compressed tablet rapidly disintegrating in the mouth using crystalline cellulose and a Disintegrant. Biol Pharm Bull 1995; 18: 1308–1310.
7. Myers GL, Battist GE, Fuisz RC. Process and apparatus for making rapidly dissolving dosage units and product there from. PCT Patent WO 95/34293-A1.1995 Dec 21.
8. Allen LV, Wang B. Process for making a particulate support matrix for making a rapidly dissolving tablet. US Patent No. 5,587,180. 1996 Dec 24.
9. Koizumi KI, Watanabe Y, Morita K, Utoguchi N, Matsumoto M. New method for preparing high porosity rapidly saliva soluble compressed tablets using mannitol with Camphor, a subliming material. Int J Pharm. 1997; 152: 127–131.
10. Bhaskaran S, Narmada GV. Rapid dissolving tablets a novel dosage form. Indian Pharmacist. 2002; 1: 9–12.
11. Debjit Bhowmik, Chiranjib.B, Krishnakanth, Pankaj, R.Margret Chandira. Fast Dissolving Tablet: An Overview. J Chemical Pharma Res 2009; 1(1): 163-177.
12. Dali S, Subhashis C, Sanjay S, Brahmeshwar M. Mouth Dissolving Tablets I: An Overview of Formulation Technology. Sci Pharm. 2009; 77: 309–326.
13. Kuchekar BS, Mahajan S, and Bandhan AC. Mouth dissolve tablets of sumatriptan. Indian Drugs 2004; 41(10): 592-598.

14. Lalla JK, Mamania HM. Fast dissolving rofecoxib tablets. Indian J Pharm Sci 2004; 59(4): 23-26.
15. Modi A, Tayade P. Enhancement of dissolution profile by solid dispersion (kneading) technique. AAPS Pharm. Sci. Tech.2006; 7(3): 68.
16. Reig AR, Plazas F, Galvan CJ, Heras NJ, Artes FM, Gabarron HE. Acceptance survey of a fast dissolving tablet pharmaceutical formulation in allergic patients, Satisfaction and expectancies. Allergol Immunopathol. (Madr.) 2006; 34(3): 107-12.
17. Ahmed IS, Nafadi MM, Fatahalla FA. Formulation of a fast-dissolving ketoprofen tablet using freeze-drying in blisters technique. Drug Dev Ind Pharm 2006; 32(4): 437-42.
18. Cirri M, Valleri M, Mura P, Maestrelli F, Ballerini R. Development of fast-dissolving tablets of flurbiprofen-cyclodextrin complexes. Drug Dev Ind Pharm 2005; 31(7): 697-707.
19. Takagi H, Kajiyama A, Yanagisawa M. Rapidly disintegrable pharmaceutical composition. U.S.Patent No. 6,899,899. 2005.
20. Francesco Cilurzo.Fast-dissolving mucoadhesive microparticulate delivery system containing piroxicam. Eur J Pharm Sci 2005; 24: 355-361.
21. Rasetti-Escargueil C, Grange V. Pharmacokinetic profiles of two tablet formulations of piroxicam. Int J Pharm 2005; 13:129-34.
22. Abdelbary G, Eouani C, Prinderre P, Joachim J, Reynier J, Piccerelle P. Determination of the in vitro disintegration profile of rapidly disintegrating tablets and correlation with oral disintegration. Int J Pharm. 2005; 1(2): 29-41.