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MOUTH DISSOLVING TABLETS: AN OVERVIEW

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ABSTRACT

The convenience of administration and improved patient compliance are important in the design of oral drug delivery system which remains the preferred route of drug delivery inspite of various disadvantages. One such problem can be solved in the novel drug delivery system by formulating “mouth dissolving tablets” (MDTs) which disintegrates or dissolves rapidly without water with in few seconds in the mouth due to the action of superdisintegrant or maximizing pore structure in the formulation. Mouth dissolving tablets are advantageous particularly for pediatric, geriatric and mentally ill patients who have difficulty in swallowing conventional tablets and capsules. The review describes the various formulation aspects, superdisintegrants employed and technologies developed for MDTs, along with various excipients, evaluation tests, marketed formulation and drugs used in this research area.

INTRODUCTION: The tablet is the most widely used dosage form existing today because of its convenience in terms of self administration, compactness and ease in manufacturing. However, geriatric, pediatric and mentally ill patients experiences difficulty in swallowing conventional tablets, which leads to poor patient compliance. To overcome these problems, scientists have developed innovative drug delivery system know as mouth dissolving/disintegrating tablets (MDTs). These are novel types of tablets that dissolve/ disintegrate/ disperse in saliva with in few seconds without water. According to European pharmacopoeia, these MDTs should dissolve/disintegrate in less than three minutes. The formulation is more useful for the bed-ridden and patients who have the swallowing problem. The benefits of MDTs is to improve patients compliance, rapid onset of action, increased bioavailability and good stability which make these tablets popular as a dosage form of choice in the current market [1, 2, 3.]

Mouth dissolving tablets are also called as orodispersible tablets, fast disintegrating tablets, orally disintegrating tablets, quick disintegrating tablets, fast dissolving tablets, rapid dissolving tablets, porous tablets, quick melt tablets and rapid melt tablets.However, of all the above terms United States Pharmacopoeia (USP) approved these dosage forms as ODTs. United States Food and Drug Administration (FDA) defined ODTs as “A solid dosage form containing medicinal substances or active ingredients which disintegrates rapidly with in a few seconds when placed up on tongue” [4, 5.]

Mouth dissolving tablets are formulated mainly by two techniques first use of super disintegrants like crosscarmellose sodium, sodium starch glycolate and crosspovidone. Another method is maximizing pore structure of the tablets by freeze drying and vacuum-drying. The bioavailability of some drugs may be increased due to absorption of drugs in oral cavity and also due to pregastric absorption of saliva containing dispersed drugs that pass down in to the stomach. Moreover the amount of drug that is subjected to first pass metabolism is reduced as compared to standard tablets [6, 7].

Requirements of Mouth Dissolving Tablets:

Ideal MDTs should [8]:

- Require no water for oral administration, yet dissolve / disperse/ disintegrate in mouth within seconds.
- Give good mouth feel.
- Have a satisfactory taste masking property.
- Be harder and less friable
- Leave minimal or no residue in mouth after administration

Advantages of MDTs [9, 10]:

Easy administration to the patients who can not swallow, such as the elderly, bedridden patients and patients who refuse to swallow like pediatric, geriatric and mentally retarded patients.

- Bioavailability of drug that is absorbed through pregastric absorption of drugs from mouth, pharynx and esophagus is increased
- Rapid drug therapy intervention
- Bitter taste can be masked by use of flavor and sweetener to produce good mouth feel particularly for pediatric patients
- The risk of chocking or suffocation during oral administration of conventional formulation due to physical obstruction is avoided, thus providing improved safety
- This is beneficial for traveling patients and busy people, who do not have easy access to water.
- Improved patient compliances

Challenges to develop MDTs:

- Rapid disintegration and sufficient mechanical strength of the tablet
- Avoid increase in tablet size
- Effective taste masking of bitter drugs
- Minimum or no residue in mouth
- Good package design and protect from moisture
- Has a pleasant mouth feel
- Sensitivity to environmental condition
- Formulate with low cost

Salient Features of MDTs:

- 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
- 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
- Good mouth feels property of MDTs helps to change the basic view of medication as bitter pill, particularly for pediatric patients
- Rapid dissolution of drug and absorption which may produce rapid, 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 drugs is increased

Limitations for MDTs:

- Drugs with relatively larger doses are difficult to formulate in to MDTs example like antibiotics ciprofloxacin with adult dose tablet containing about 500mg of the tablet.
- Patients who concurrently take anticholinergic medication may not be the best candidates for MDTs and patients like sjogren's syndrome or dryness of the mouth due to decrease saliva production may not be good candidates for these tablet formulation.

Technologies used for manufacturing of MDTs: In the recent past, several new advanced technologies have been introduced for the manufacturing of MDTs with ideal properties like less disintegration time, pleasant mouth feel, exceptional taste masking and sugar free tablets for diabetic patients. The technologies used for manufacturing of MDTs broadly classified in two category one is patented another one is non-patented technologies as shown in **Table 1** and **2** enlists various drugs explored for developing MDTs.

TABLE 1: TECHNOLOGY USED FOR MOUTH DISSOLVING TABLETS

Non-patented	Patented
Freeze drying Tablet molding Spray drying Mass extrusion Sublimation Cotton candy process Direct compression Melt granulation Phase transition process	Zydus technology Orasol technology Durasolv technology Wowtab technology Dispersible tablet technology Fashtab technology Oraquick technology Lyoc technology Quick technology Nanocrystal technology Frosta technology Pharmabrust technology

TABLE 2: DRUGS EXPLORED FOR MOUTH DISSOLVING TABLETS [4, 11-22]

CATEGORY	DRUG	CATEGORY	DRUG
NSAIDS	Ketoprofen Piroxicam Paracetomol Rofecoxib Nimesulide Ibuprofen Tepoxaline (Canine NSAID)	Anti depressants	Mitraxepine Fluoxetine
		Antiparkinsonism	Selegiline
		Antimigrane	Sumatriptan Rizatriptan benzoate Zolmitriptan
Anti ulcer	Famotidine Lansoprazole		

Anti-histaminic	Loratadine Diphenhydramine Meclizine	Antiemetics	Ramosetoron Hcl Ondansetron Baclofen
Hypnotics and sedatives	Zolpidem Clonazepam Atenolol	Miscellaneous	Hydrochlorthiazide Ethenzamide Tramodol Hcl Propyphenazone Spiranolactone Phloroglucinol Sildenafil
Antipsychotics	Olanzepine Risperidone Pirenzepine		

Non-Patented technologies:

Lyophilization or Freeze-drying: Formation of porous product in freeze-drying process is exploited in formulating MDTs. Lyophilization is a process, which includes the removal of solvent from a frozen suspension or solution of drug with structure-forming additives. Freeze-drying of drug along with additives imparts glossy amorphous structure resulting in highly porous and lightweight product. The resulting tablet has Rapid disintegration and dissolution when placed on the tongue and the freeze-dried unit dissolves instantly to release the drug.

However, the MDTs formed by lyophilization have low mechanical strength, poor stability at higher temperature, and humidity [23].

Molding: In this method, molded tablets are prepared by using water-soluble ingredients so that the tablets dissolve completely and rapidly. The powder blend is moistened with a hydro-alcoholic solvent and is molded into tablets under pressure lower than that used in conventional tablet compression. The solvent is then removed by air-drying .Molded tablets are very less compact than compressed tablets. These posses porous structure that increase dissolution [25].

Cotton candy process: This process is so named as it utilizes a unique spinning mechanism to produce floss-like crystalline structure, which mimic cotton candy. Cotton candy process [26] involves formation of matrix of polysaccharides or saccharides by simultaneous action of flash melting and spinning. The matrix formed is partially recrystallized to have improved flow properties and compressibility. This candy floss matrix is then milled and blended with active ingredients and excipients and subsequently compressed to MDTs.

Spray drying: This technology produces highly porous and fine powders as the processing solvent is evaporated during the process [27]. In this method to prepare MDTs hydrolyzed and non- hydrolyzed gelatin were used as supporting matrix, mannitol as bulking agent and sodium starch glycolate or crosscarmellose sodium as superdisintegrant. Disintegration and dissolution were further increased by adding acidic substances like citric acid or alkali substance like sodium bicarbonate. This formulation technique gives porous powder and disintegration time < 20 sec [28, 29].

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 tablets [30].

Melt granulation: In this process, MDTs can be prepared by incorporating a hydrophilic waxy binder (super polystate) PEG-6-stearate. Super polystate is a waxy material with an m. pt. of 33-37°C and a hydrophilic- lipophilic balance of 9. It not only acts as a binder and increases the physical resistance of tablets, but also helps in the disintegration of tablets as it melts in the mouth and solubilizes rapidly leaving no residue. Super polystate was incorporated in the formulation of MDTs by melt granulation method where granules are formed by the molten form of this material [31].

Phase transition process: Kuno *et. al*.,[32] investigated processes for the disintegration of MDTs by phase transition of sugar alcohols using erythritol (m. pt. 122°C), xylitol (m. pt. 93-95°C), trehalose (97°C), and mannitol (166°C). Tablets were produced by compressing a powder containing two sugar alcohols with high and low melting points and subsequent heating at a temperature between their melting points. Before heating process, the tablets do not have sufficient hardness because of low compatibility. The tablet hardness was increased after heating process, due to the increase of inter particle bonds or the bonding surface area in tablets induced by phase transition of lower melting point sugar alcohol.

Sublimation: The presence of a highly porous structure in the tablet matrix is the key factor for rapid disintegration of MDTs. Even though the conventional tablets contain highly water-soluble ingredients, they often fail to disintegrate rapidly because of low porosity. To improve the porosity, volatile substances such as camphor can be used in tabletting process, which sublimated from the formed tablet [33]. Developed MDTs utilizing camphor, a subliming material that is removed from compressed tablets prepared using a mixture of mannitol and camphor. Camphor was sublimated in vacuum at 80°C for 30 min after preparation of tablets.

Direct compression methods: This technique is easy way to formulate MDTs since limited number of processing steps, low manufacturing cost and also accommodate high dose the final weight of tablet can easily exceed that of other production method [34]. The disintegration and dissolution of directly compressed tablets depends on single or combined effect of disintegrant, water soluble excipients and effervescing agents. Disintegrant efficacy is strongly affected by tablet size and hardness. Disintegration properties can be optimized by medium or low tablet size, low hardness and low physical resistance .It is essential to choose a suitable and an optimum concentration of disintegrant to ensure fast disintegration and high dissolution rates.[6,34,35,52] The addition of water soluble excipients or effervescent agent can further increase dissolution or disintegration properties. Super disintegrants provide fast disintegration due to combine effect of swelling and water absorption by the formulation [1].

As an effect of swelling of super disintegrant the wetted surface of the carrier increase, which promotes wettability and dispersibility of the system and there by increase the disintegration and dissolution [36, 37, 38]. The optimum concentration of superdisintegrant can be selected according to critical concentration of disintegrant. Below this concentration the tablet disintegration time is inversely proportional to the concentration of superdisintegrant, where as if concentration of superdisintegrants incorporated in tablet is above the critical concentration, the disintegration time remains approximately constant or even increases [34]**.** Some of the super disintegrants employed are discussed in **Table 3**.

TABLE 3: SUPER DISINTEGRANTS USED IN MOUTH DISSOLVING TABLETS [43, 44]

SUPER DISINTEGRANT	NATURE	PROPERTIES	MECHANISM
Crosspovidone	Crosslinked homo polymer of *N*-vinyl-2-pyrrolidone	Particle size - 100 µm, Insoluble in water, gives smoother mouth feel	Both swelling and wicking
Cross carmellose sodium	Cross-linked form of sodium CMC	Particle size 200 mesh, insoluble in water	Swelling
Sodium starch glycolate	Crosslinked low substituted carboxymethyl ether of poly-glucopyranose	Particle size 140 mesh, insoluble in organic solvents, disperses in cold water and settles in the form of a highly saturated layer	Water uptake followed by rapid and enormous swelling

Acrylic acid derivatives [43] (Yang *et al*. 2004)	Poly(acrylic acid) super porous hydrogel	Particle size 106 µm, DT- 15 + 2 S	Wicking action
Effervescent mixture	Citric acid, tartaric acid, sodium bicarbonate	Crystalline nature	Effervescence
Sodium alginate	Sodium salt of alginic acid	Slowly soluble in water, hygroscopic in nature	Swelling
NS-300 [43] (Ozeki *et al.* 2003)	Carboxy methyl cellulose	Particle size 106 µm, DT - 20 S	Wicking type
ECG-505 [43] (Ozeki *et al*. 2003)	Calcium salt of CMC	Particle size 106 µm, DT - 80 S	Swelling type
L-HPC [43] (Ozeki *et al.* 2003)	Low hydroxy propyl cellulose	Particle size 106 µm, DT-90S	Both swelling and wicking

Patented Technologies:

Zydus technology [39]: This technology includes physical trapping of the drug in a matrix composed of a saccharide and a polymer. **[40, 41]** Polymers generally employed are partially hydrolyzed gelatin, hydrolyzed dextran, dextrin, alginates, polyvinyl alcohol, polyvinyl pyrrolidine, acacia, and these mixtures. The methodology involves solution or dispersion of components prepared and filled in to blister cavities, which are frozen in a liquid nitrogen environment. The frozen solvent is removed or sublimed to produce porous wafers.

Desired characteristics of Zydus technology

- Drug should be chemically stable
- Water insoluble
- Particle size should be smaller than 50 µm.
- Dose for water-soluble drugs is limited (60 mg)

Lyoc [42]**:** Lyoc technology is patented by PHARMALYOC. Oil in water emulsion is prepared and placed directly into blister cavities followed by freeze-drying. Non-homogeneity during freeze-drying is avoided by incorporating inert filler to increase the viscosity finally the sedimentation. High proportion of filler reduces porosity of tablets due to which disintegration is lowered.

Quick solv [45]: This technology is patented by Janssen Pharmaceuticals. It utilizes two solvents in formulating a matrix, which disintegrates instantly. Methodology includes dissolving matrix components in water and the solution or dispersion is frozen. Then dry the matrix by removing water using an excess of alcohol (solvent extraction). Thus the product formed has uniform porosity and adequate strength for handling.

Nanocrystal technology [46]: This is patented by Elan, King of Prussia. Nanocrystal technology includes lyophilization of colloidal dispersions of drug substance and water-soluble ingredients filled in to blister pockets. This method avoids manufacturing process such as granulation, blending, and tabletting, which is more advantageous for highly potent and hazardous drugs. As manufacturing losses are negligible, this process is useful for small quantities of drug.

Flashtab technology [47]: This is patented by Ethypharm France. This technology includes granulation of excipients by wet or dry granulation method and followed by compressing into tablets. Excipients used in this technology are of two types. Disintegrating agents include reticulated polyvinylpyrrolidine or carboxy methylcellulose. Swelling agents include carboxy methylcellulose, starch, modified starch, microcrystalline cellulose, carboxy methylated starch, etc. These tablets have satisfactory

physical resistance. Disintegration time is within 1 min.

Orasolv technology [48, 49:] This technology is patented by CIMA Labs. This includes use of effervescent disintegrating agents compressed with low pressure to produce the MDTs. The evolution of carbon dioxide from the tablet produces fizzing sensation, which is a positive organoleptic property. Concentration of effervescent mixture usually employed is 20-25% of tablet weight.

As tablets are prepared at low compression force, they are soft and fragile in nature. This initiated to develop Paksolv,[50] a special packaging to protect tablets from breaking during storage and transport. Paksolv is a dome-shaped blister package, which prevents vertical movement of tablet with in the depression. Paksolv offers moisture, light, and child resistance packing.

Durasolv technology [51:] This technology is patented by CIMA Labs. The tablets produced by this technology utilize the conventional tableting equipment. Tablets in this are formulated by using drug, nondirect compression fillers, and lubricants. Nondirect compressible fillers are dextrose, mannitol, sorbitol, lactose, and sucrose, which have advantage of quick dissolution and avoid gritty texture, which is generally present in direct compressible sugar. The tablets obtained are strong and can be packed in conventional packing in to bottles and blisters.

Wow tab technology [52, 53]: Yamanouchi patented this technology. WOW means with out water. This technology utilizes conventional granulation and tableting methods to produce MDTs employing low- and high-moldability saccharides. Low moldability saccharides are lactose, mannitol, glucose, sucrose, and xylitol. High-moldability saccharides are maltose, maltitol, sorbitol, and oligosaccharides. When these low- and high-moldable saccharides are used alone tablets obtained do not have desired properties of rapid disintegration and hardness, so combinations are used. This technology involves granulation of low-moldable saccharides with high-moldable saccharides as a binder and compressing into tablets followed by moisture treatment. Thus tablets obtained showed adequate hardness and rapid disintegration.

Dispersible tablet technology [54]: Lek, Yugoslavia patents this technology. It offers development of MDTs with improved dissolution rate by incorporating 8-10% of organic acids and disintegrating agents. Disintegrating agent facilitates rapid swelling and good wetting capabilities to the tablets that results in quick disintegration. Disintegrants include starch, modified starches, microcrystalline cellulose, alginic acid, cross-linked sodium carboxy methyl cellulose and cyclodextrins. Combination of disintegrants improves disintegration of tablets usually less than 1 min.

Pharmaburst technology [4]: SPI Pharma, New Castle, patents this technology. It utilizes the coprocessed excipients to develop MDTs, which dissolves within 30-40 s. This technology involves dry blending of drug, flavour, and lubricant followed by compression into tablets. Tablets obtained have sufficient strength so they can be packed in blister packs and bottles.

Frosta technology [4]: This technology patents by Akina. It utilizes the concept of formulating plastic granules and compressing at low pressure to produce strong tablets with high porosity. Plastic granules composed of:

- Porous and plastic material,
- Water penetration enhancer, and
- Binder

The process involves usually mixing the porous plastic material with water penetration enhancer and followed by granulating with binder. The tablets obtained have excellent hardness and rapid disintegration time ranging from 15 to 30 s depending on size of tablet.

Oraquick: This technology is patented by K.V.S. Pharmaceuticals [55]. It utilizes taste masking microsphere technology called as micromask, which provides superior mouth feel, significant mechanical strength, and quick disintegration/dissolution of product. This process involves preparation of microparticles in the form of matrix that protects drug, which can be compressed with sufficient mechanical strength. Low heat of production in this process makes it appropriate for heat sensitive drugs. Oraquick product dissolves within few seconds.

TABLE 4: MOUTH DISSOLVING TABLET AVAILABLE IN INDIAN MARKET

Brand name	Active ingredient	Company
Domray MD	Domperidone	Ray Remedies
Veirid MD	Domperidone	Shreyam Health Care
Vornidon MD	Domperidone	Olcare Lab
Zotacet MD	Cetirizine Hcl	Zota Pharma
Olanex Instab	Olanzepine	Ranbaxy
Manza RDT	Olanzepine	Mano Pharma (Orchid)
Romilast	Montelukast	Ranbaxy
Torrox MT	Rofecoxib	Torrent
Ziflam	Rofecoxib	Kopran
Doloroff	Rofecoxib	Mdccc
Rofaday MT	Rofecoxib	Lupin
Dolib MD	Rofecoxib	Panacea
Orthoref MD	Rofecoxib	Biochem
Rbcox-25 MD	Rofecoxib	Shalman Pharma
Roffec MD	Rofecoxib	Excare Lab
Roftab MD	Rofecoxib	Olcare Lab
Zofex-25 MD	Rofecoxib	Zota Pharma
Valus	Valdecoxib	Glenmark
Nency MD	Nimesulide	Zenon Health Care
Nexus MD	Nimesulide	Lexus
Nimex MD	Nimesulide	Mexon Health Care
Nimez-MD	Nimesulide	Zota Pharma
Nisure-MD	Nimesulide	Suzen Pharma
Nimulid-MD	Nimesulide	Panacea
Olnim-MD	Nimesulide	Olcare Lab
Sulbid-Md	Nimesulide	Alpic remedies
Topmide	Nimesulide	Antigen Health Care
Nimpain MD	Nimesulide	Prompt Cure Pharma
Mosid MT	Mosapride	Torrent

TABLE 5: MOUTH DISSOLVING TABLET AVAILABLE IN INTERNATIONAL MARKET

Brand name	Active ingredient	Company
Zomig ZMT and Rpimelt	Zolmitriptan	Astra Zeneca
Alavert	Loratadine	Wyeth Consumer Healthcare
Cibalginadue FAST	Ibuprofen	Novartis Consumer Health
Hyoscyamine Sulfate ODT	Hyoscyamine sulfate	ETHEX Corporation
NuLev	Hyoscyamine sulfate	Schwarz Pharma
Nurofen FlashTab	Lbuprofen	Boots Healthcare
Kemstro	Baclofen	Schwarz Pharma
Fluoxetine ODT	Fluoxetine	Bioavail
Benadryl Fastmelt	Diphenhydramine	Pfizer
Zolpidem ODT	Zolpidem tartrate	Bioavail
Nasea OD	Ramosetoron	Yamanouchi
Ralivia FlashDose	Tramadol HCL	Bioavail
Gaster D	Famotidine	Yamanouchi
Excedrin Quick Tabs	Acetaminophen	Bristol-Myers Squibb
Claritin RediTabs	Loratadine	Sching Corporation
Remeron SolTab	Mirtazepine	Organon Inc.
Feldene Melt	Piroxicam	Pfizer
Tempra Quicklet- Tempra Firs Tabs	Acetaminophen	Bristol-Myers Squibb
Maxalt-MLT	Rizatriptan benzoate	Merck
Propulsid Quicksolv	Cisapride monohydrate	Janssen
Pepcid ODT	Famotidine	Merck
Imodium Instant melts	Loperamide HCL	Janssen
Zyprexa	Olanzapine	Eli Lilly
Childrens Dimetapp ND	Loratadine	Wyeth Consumer Healthcare
Zofran ODT	Ondansetron	Glaxo Smith Kline
Klonopin Wafers	Clonaxepam	Roche
Risperidal M-Tab	Ripseridone	Janssen
Zelapar	Selegiline	Elan/Amarin Corporation
Zubrin (pet drug)	Tepoxaline	Schering Corporation
Aricept ODT	Donepzil HCL	Eisai and Pfizer
Fazalco	Clonzapine	Alamo Pharmaceuticals
Permax	Pergolide	Amarin Corporation
Febrectol	Paracetamol	Prographarm
Benadryl Fast melt	Diphenhydramine and pseudoephedrine	Warner Lambert

Evaluation of Mouth dissolving Tablet [56, 57]: MDTs formulations have to be evaluated for the following evaluation test.

- **General Appearance:** The general appearance of a tablet, its visual identity and over all elegance is essential for consumer acceptance. It includes tablets size, shape, colour, presence or absence of an odour, taste, surface texture, physical flaws and consistency and legibility of any identifying marking.
- **Size and Shape:** The size and shape of the tablet can be dimensionally described, monitored and controlled.
- **Tablet thickness:** Tablet thickness is an important characteristic in reproducing appearance and also in counting by using filling equipment. Some filling equipment utilizes the uniform thickness of the tablets as a counting mechanism. Ten tablets were taken and their thickness was recorded using micrometer.

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

Average weight of Tablets (mg)	Maximum percentage difference allowed
130 or less	10
130-324	7.5
More than 324	5

- **Tablet hardness:** Hardness of tablet is defined as the force applied across the diameter of the tablet in the order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. Hardness of the tablet of each formulation was determined using Monsanto Hardness tester.

- **Friability:** It is measured of mechanical strength of tablets. Roche friabilator was used to determine the friability by following procedure. A pre weighed tablet was placed in the friabilator. Friabilator consist of a plastic-chamber that revolves at 25 rpm, dropping those tablets at a distance of 6 inches with each revolution. The tablets were rotated in the friabilator for at least 4 minutes. At the end of test tablets were dusted and reweighed, the loss in the weight of tablet is the measure of friability and is expressed in percentage as;

  %Friability = loss in weight / Initial weight x 100

- ***In Vivo* Disintegration test:** The test was carried out on 6 tablets using the apparatus specified in I.P.-1996 distilled water at 37°C ± 2°C was used as a disintegration media and the time in second is taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured in seconds.

- **Wetting time:** The method reported by Yunixia *et al*., was followed to measure tablet wetting time. A piece of tissue paper (12 cm X 10.75 cm) folded twice was placed in a small petridish (ID = 6.5 cm) containing 6 ml of Sorenson's buffer pH 6.8. A tablet was put on the paper, and the time for complete wetting was measured. Three trials for each batch and the standard deviation were also determined.

- ***In vitro* dispersion time:** *In vitro* dispersion time was measured by dropping a tablet in a beaker containing 50 ml of Sorenson's buffer pH 6.8. Three tablets from each formulation were randomly selected and in vitro dispersion time was performed.

- **Stability testing of drug (temperature dependent stability studies):** The fast dissolving tablets are packed in suitable packaging and stored under the following conditions for a period as prescribed by ICH guidelines for accelerated studies;

  - 40 ± 1°C
  - 50 ± 1°c
  - 37 ±1^{o}C
  - RH 75% ± 5%

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

Packaging of MDTs: Packing is one of the important aspects in manufacturing MDTs. The products obtained by various technologies vary in some of the parameters especially in mechanical strength to a great extent. The products obtained by lyophilization process including various technologies such as Zydis, Lyoc, Quicksolv, and Nanocrystal are porous in nature, have less physical resistance, sensitive to moisture, and may degrade at higher humidity conditions. For the above reasons products obtained require special packing. Zydis units are generally packed with peelable backing foil.

Paksolv is a special packaging unit, which has a dome shaped blister, which prevents vertical movement of tablet with in the depression and protect tablets from breaking during storage and transport, which is used for Orasolv tablet. Some of the products obtained from Durasolv. WOW Tab, Pharmaburst oraquick, Ziplets, etc. technologies have sufficient mechanical strength to withstand transport and handling shock so they are generally packed in push through blisters or in bottles.

Patient counseling in effective use of MDTs: As pharmacists are ideal persons to know about the recent technologies, thus have opportunity to educate the patients for effective treatment.

Counseling of patients about this dosage form can avoid any confusion and misunderstanding in taking MDTs. Patient information that needs to be provided include:

- Storage of this dosage form as some of MDTs developed may not have sufficient mechanical strength, which needs to be handled carefully.
- Patients with Siogren's syndrome or dryness of mouth or who take anticholinergic drugs may not be suitable candidates for administering MDTs. Although no water is required to allow drug to disperse quickly and efficiently but decreased volume of saliva may slow the rate of disintegration/dissolution and may reduce the bioavailability of the product.
- Patients need to be clearly told about the difference between effervescent and MDTs. Some of technologies use effervescence, which experience a pleasing tingling
- Effect on the tongue.
- Although chewable tablets are available in market and patient need to be counseled about differences between chewable and MDTs tablets. These MDTs can be used easily in children who have lost their primary teeth and in geriatric patients who have lost their teeth permanently.

With the pharmacists counseling, intervention and assistance about MDTs, all patients receiving this novel dosage form could be more properly and effectively treated with greater convenience.

CONCLUSIONS: The MDTs have potential advantages over conventional dosage forms, with their improved patient compliance, convenience, bioavailability and rapid onset of action had drawn the attention of many manufactures over a decade. MDTs formulations obtained by some of these technologies have sufficient mechanical strength, quick disintegration/dissolution in the mouth without water.

These MDTs can be used easily in children who have lost their primary teeth and in geriatric patients who have lost their teeth permanently. They remain solid during storage, which aid in stability of dosage forms and transform into liquid form within few seconds after its administration. As they have significant advantages as both solid and liquid dosage forms, MDTs may be developed for most of the available drugs in near future.

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