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Review Article

MOUTH DISSOLVING TABLET : A NOVEL APPROACH FOR DRUG DELIEVERY

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ABSTRACT

Mouth dissolving tablets is one of the most generally recognized dosage forms and also the most popular dosage form, especially for pediatric patients due to incomplete development of the muscular and nervous system and a case of geriatric patients suffering from Parkinson's disease or hand tremors. Some solid dosage forms such as tablets and capsules nowadays face problems such as difficulty swallowing (dysphagia), leading to many cases of non-compliance and non-compliance and making the therapy ineffective Oral dosage form and oral route are the most preferred route of administration for various drugs have limitations like the first-pass metabolism. Fast dissolving tablets are one of them. It is more useful for the traveler and busy patients who don't have easy access to water. Mouth dissolving tablets are made by various technologies using super disintegrants. Tablets that dissolve in the mouth are more reliable than traditional dosage forms such as tablets, capsules, because they are better absorbed by patients. The advancement in this field allows the development of an economic and better way of disease management with avoidance of several problems related to the other delivery systems. Others contain agents to speed up tablet disintegration in the oral cavity and are more appropriately referred to as rapidly disintegrating tablets as they can take up to a minute to completely disintegrate.

INTRODUCTION

The oral passage of medicament administration for illness is measured as the most conventional route. Tablet is a commonly prescribed dosage form as of its accessibility in terms of self-administration, solidity and simplicity in development. Patients particularly pediatric and geriatric, often experience trouble in swallowing conventional tablets and this problem may prove worst during the traveling conditions due to the non-availability or restricted availability of water. These problems of conventional dosage forms can be encountered by the development of mouth dissolving tablets. These tablets disintegrate in the mouth within a very short span i.e 20-30 sec and comes in contact with saliva resulting in the therapeutic action of active agent. Mouth dissolving tablets show better patient compliance and acceptance with improved bioavailability, efficacy and biopharmaceutical properties, in contrast to conventional tablets.[1]

The phenomenon of mouth dissolution is a very supportive way for patients with life-threatening diseases such as nervous diseases, radioactivity therapy, Parkinson's disease, AIDS faced with dysphasia condition.

Administration of new dosage formulations like effervescent tablets, dry syrups to these patients involves distress due to the necessary intake of water. But mouth dissolving tablets do not require water ingestion for dosage administration and hence enhance patient compliance. There are various synonyms for mouth dissolving tablets like orally disintegrating tablets, fast dissolving tablets, fast melting tablets etc. The European pharmacopeia states that Oro disperse is the tablet that can dissolve very quickly in the mouth without water. The administration of FDTs differs from traditional tablets and the FDTs should have several unique properties to accommodate the fast disintegration time. They should dissolve or disintegrate in the mouth without water or with a very small amount of water, since the disintegrating fluid is the patient's saliva. The disintegrated tablet should become a smooth paste or liquid suspension that provides good mouthfeel and smooth swallowing. Rapid dissolution or disintegration typically requires

dissolution or disintegration of a tablet within one minute.

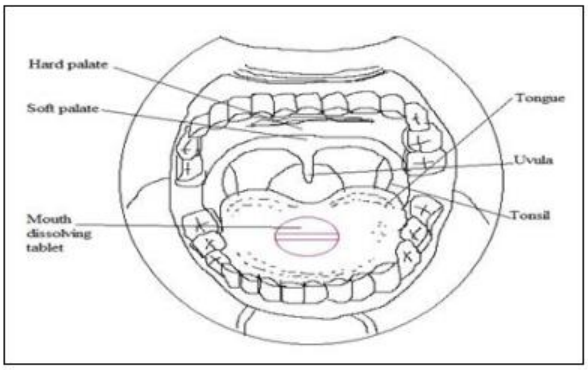

Figure 1: Administration of mouth dissolving Tablets

Significance of ODTs

MDT offer dual advantages of solid dosage forms and liquid dosage forms along with special Features which include:

- Accurate dosing: Being unit solid dosage forms, provide luxury of accurate dosing, easy portability and manufacturing, good physical and chemical stability and an ideal alternative for pediatric and geriatric patients.
- Enhanced bioavailability: Bioavailability of drugs is enhanced due to absorption from mouth, pharynx and esophagus.
- Rapid action: Fast onset of therapeutic action as tablet gets disintegrated rapidly along with quick dissolution and absorption in oral cavity.
- Patient compliance: No need of water to swallow the dosage form. Hence, it is convenient for patients who are traveling and do not have immediate access to water.
- Ease of administration: Convenient to administer specially for geriatric, pediatric, mentally disabled and bed ridden patients who have difficulty in swallowing.
- Obstruction free: No risk of suffocation in airways due to physical obstruction when swallowed, thus providing improved safety and compliance.
- Enhanced palatability: Good mouth feels, especially for pediatric patients as taste masking technique is used to avoid the bitter taste of drug.
- Simple packaging: No specific packaging required. It can be packaged in push through blisters.
- Business Avenue: Provide new business opportunities in the form of product differentiation, line extension, uniqueness and life cycle management.
- Cost effective: Conventional processing and packaging equipment's allow the manufacturing of tablets at low cost.

Ideal Properties of MDTs

1. They should:
2. Not require water to swallow, but it should dissolve or disintegrate in the mouth in matter of seconds.
3. Be compatible with taste masking.
4. Be portable without fragility concern.
5. Have a pleasant mouth feel.
6. Leave minimum or no residue in the mouth after oral administration.
7. Exhibit low sensitive to environmental condition as temperature and humidity.
8. Allow the manufacture of the tablet using conventional processing and packaging equipment's at low cost

Challenges in formulating Fast dissolving tablets:

Palatability

Because most drugs are inedible, FDTs usually contain the drug in a taste-masked form. When administered, it breaks down or dissolves in the patient's oral cavity, releasing the active ingredients that come into contact with the taste buds. Therefore, drug taste masking becomes critical for patient compliance.

Mechanical strength

In order for FDTs to disintegrate in the oral cavity, they are either made from very porous and soft-moulded matrices or compressed into tablets with very low compression force, making the tablets friable and/or brittle, difficult to handle and often requiring a special peel-off blister pack which can increase costs. Only wow tab and dorsal technologies can produce tablets hard and durable enough to pack into multi-dose bottles.

Hygroscopicity

Several orally disintegrating dosage forms are hygroscopic and cannot maintain their physical integrity under normal temperature and humidity conditions. Therefore, they must be protected from moisture, which requires special product packaging.

Amount of drug

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

Aqueous solubility

Water-soluble drugs pose various formulation challenges as they form eutectic mixtures that result in freezing point depression and the formation of a glassy solid that can collapse upon drying due to loss of support structure during the sublimation process. Such collapse can sometimes be prevented by using various matrix-forming excipients, such as mannitol, which can induce crystallinity and thus impart rigidity to the amorphous composite.

Size of tablet

The ease of administering a tablet depends on its size. It has been reported that the easiest tablet size to swallow is 7-8mm, while the easiest to handle size was one over 8mm. Therefore, it is difficult to achieve a tablet size that is both easy to take and easy to use.

Requirements of fast dissolving tablets

- **Patient factors**
- Fast dissolving dosage forms are suitable for those patients are not able to swallow tablets and capsules like pediatric and geriatric patients.
- Patients who have difficulty in swallowing or chewing solid dosage forms.
- Patients in compliance due to fear of choking.
- Very old patients of depression who may not be able to swallow the solid dosage forms.
- An eight-year-old patient with allergies desires a more convenient dosage form than antihistamine syrup.
- A middle-aged patient undergoing radiation therapy for breast cancer may be too nauseous to swallow her H2-blocker.
- A schizophrenic patient who may try to hide a conventional tablet under his or her tongue to avoid their daily dose of an atypical antipsychotic.
- A patient with persistent nausea, who may be a journey, or has little or no access to water.

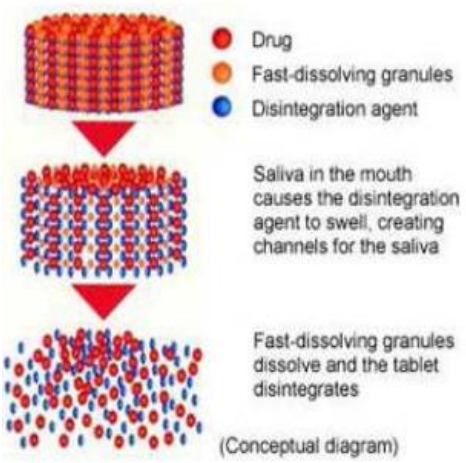

Figure 2: Conceptual diagram of FDTs

Effectiveness factor

Increased bioavailability and rapid onset of action are a key claim of these formulations. Distribution in the saliva in the oral cavity leads to pregastric absorption of some ions of the formulation in cases where the drug dissolves quickly. Buccal, pharyngeal, and gastric regions are all areas of absorption for many drugs. Any pregastric absorption avoids first-pass metabolism and can be of great benefit for drugs subject to hepatic metabolism. In addition, safety profiles can be improved for drugs that produce significant amounts of toxic metabolites mediated through first-pass hepatic and gastric metabolism and for drugs that exhibit GIT segments.

Manufacturing and marketing factors

As a drug nears the end of its patent term, it is common for pharmaceutical manufacturers to develop a new and improved dosage form of a given drug. A new dosage form allows a manufacturer to expand market exclusivity, patent protection and unique product differentiation. For example, Eisai Inc. launched Aricept FDT, a line extension of donepezil for Alzheimer's disease, in Japan in 2004 and in the US in 2005 in response to a generic lawsuit filed by Ranbaxy in the US.

Excipients used for the preparation of MDT

MDT contain one superdisintegrants, a diluent, a lubricant. Contain optionally a swelling agent, a permeabilizing agent, sweeteners and flavoring agents.

Super disintegrants

As the days go by, the demand for the more rapidly disintegrating formulation increases. Because this pharmacist has to formulate explosives, i.H. Super disintegrants that are effective at lower concentrations and

have greater disintegration efficiency. The super disintegrant must quickly wick saliva into this tablet to create the hydrostatic pressure and volumetric expansion necessary to provide rapid disintegration in the mouth.

Bulking materials

Fillers are very important in the development of fast dissolving tablets. They perform the functions of a diluent, filler and cost reducer. Fillers improve the texture of the tablets, which consequently promotes disintegration in the mouth, in addition to increasing the volume and reducing the concentration of the active ingredient in the formulation. The bulking agents for this formulation should be sugar-based such as mannitol, polydextrose, lactose derivatives such as directly compressible lactose (DCL) and starch hydrolysate for higher water solubility and good sensory perception. In particular, mannitol has high water solubility and good sensory perception, as it provides a cooling effect due to its negative heat of solution. Fillers are added in the range of 10% to about 90% by weight of the final composition. Sugar-based excipients are of two types, classifying them based on the rate of formation and dissolution:

Type 1 saccharides: (lactose and mannitol) which exhibit low moldability but high dissolution rate.

Type 2 saccharides: (maltose and maltitol) which exhibit high moldability but low dissolution rate.

Emulsifying agents

Emulsifiers are more important in formulating fast-dissolving tablets. They aid in rapid disintegration and drug release without the need for chewing, swallowing, or drinking water. In addition, emulsifiers stabilize the immiscible mixtures and increase bioavailability. A variety of emulsifiers for fast-dissolving tablet formulations include alkyl sulfates, propylene glycol esters, lecithin, sucrose esters, and others. These can be added in the range of 0.05 to about 15% by weight of the final formulation.

Lubricants

Though not essential excipients, these can aid in making the tablets more palatable after they disintegrate in the mouth. Lubricants reduce grittiness and help in the drug transit process from the oral to the stomach.

Flavors (taste masking agents) and sweeteners

Flavors and taste-masking agents are useful in the formulation, they make the products more palatable and comfortable for patients. Ingestion of these ingredients helps in overcoming bitterness and undesirable taste of some active ingredients. Natural as well as synthetic flavorings can be used to improve the organoleptic properties of fast dissolving tablets. A wide range of sweeteners are available including sugar, dextrose and fructose, as well as non-nutritive sweeteners such as aspartame, sodium saccharin, sugar alcohols and sucralose. The addition of sweeteners gives the formulation a pleasant taste and volume.

SELECTION OF SUPERDISINTEGRANTS:

Although super-disintegrants primarily affect the rate of disintegration, but when used at high levels they can also affect mouth feel, tablet hardness and friability. Hence, various ideal factors to be considered while selecting an appropriate super-disintegrants for a particular formulation should:

- Produce rapid disintegration, when tablet comes in contact with saliva in the mouth/oral cavity.
- Be compactable enough to produce less friable tablets.
- Produce good mouth feel to the patients. Thus, small particle size is preferred to achieve patient compliance.
- Have good flow, since it improves the flow characteristics of total blend.

Table 1: Various manufacturing techniques for MDT include:

Sr. No	**Patented Technology**	**Basis of Technology**	**Technology developed by Company**	**Active Ingredient (Brand Names)**
1	**Zydus**	**Lyophilization**	**R.P.Scherer ,Inc.**	Loratidine (Claritin Reditab
2	Quicksolv	Lyophilization	Janssen pharmaceutics	Cisapride monohydrate (Propulsid
3	**Lyoc**	**Lyophilization**	**Farmalyoc**	Phlorogluci nol Hydrate
4	**Flashtab**	**Direct compression**	**Ethypharm**	Ibuprofen (Nurofen FlashTa
5	Orasolv	Direct	Direct	Paracetamo

		compressio n	compression	l (Tempra Quicklets)
6	Durasolv	Direct compressio n	Cima Labs, Inc.	NuLev) Zolmitripta n
7	Wowtab	Direct compressio n	Yamanouchi Pharma Tech. Inc	Famotidine (Gaster D)
8	Ziplets	Direct compressio n	Eurand International	Ibuprofen (Cibalgina DueFast)
9	Advatab	Microcaps and diffuscap CR Technology	Eurand International	AdvaTab cetrizine, AdvaTab Paracetamo l
10	Flashdos e	Cotton Candy Process	Fuisz Technology, Ltd	Tramadol HCl (Relivia Flash dose)
11	Oraquick	Micromask taste masking	KV Pharm.Co.,In c.	Hyoscyami ne SulfateOD T

- Lyophilization
- Moulding
- Direct Compression
- Cotton Candy Process
- Spray Drying
- Sublimation
- Mass Extrusion
- Nanonization
- Fast Dissolving Films

Freeze-Drying or Lyophilization

In the freeze drying process, the water is sublimated from the product after it is frozen. Zydis Technology (ZT) is a patented technique that has been used for drugs such as famotidine, loperamide, piroxicam, oxazepam, lorazepam, domeperidone, brompheniramine, olanzepine, ondansetron and rizatriptan. Thirteen products made using this technology are currently available on the market. The following MDT products are available in the US: Claritin Reditab, Dimetapp Quick Dissolve, Feldene Melt, Maxalt-MLT, Pepcid RPD, Zofran ODT and Zyprexa Zydis. In the global market, Zydis formulations are also available for oxazepam, lorazepam, loperamide and enalapril. ZT uses a unique freeze-drying process to produce finished dosage units that differ significantly from traditional oral systems. The process includes the following steps:

Stage 1 - bulk preparation of an aqueous drug solution or suspension and its subsequent precise dosing into preformed blisters. It is the blister that actually forms the tablet shape and is, therefore, an integral component of the total product package.

Stage 2 - passing the filled blisters through a specially designed cryogenic freezing process to control the ultimate size of the ice crystals which ensures that the tablets possess a porous matrix to facilitate the rapid disintegration property. These frozen units are then transferred to large-scale freeze dryers for the sublimation process, where the majority of the remaining moisture is removed from the tablets.

Stage 3 - Sealing the open blisters using a heat-seal process to ensure stability and protection of the product from varying environmental conditions.

Lyoc

Lyoc technology lyophilizes or freeze-dries an aqueous solution, suspension or emulsion of an active ingredient and excipients. Lyoc's high porosity results in faster disintegration times than compressed tablets. The Lyoc manufacturing process creates a stable product without the use of additives, preservatives or gelatin. This process is environmentally friendly and inexpensive because it does not require any organic solvents. Lyoc technology is compatible with CIMA taste masking techniques, custom release, high dose and fixed dose combination products.

Quicksolv

is a porous solid form obtained by freezing an aqueous dispersion/solution of the drug-containing matrix and then drying it by removing the water using excess alcohol (solvent extraction). The final form decomposes very quickly, but is limited to a low potency and can only be used for those drugs that are insoluble in the extraction solvent. The ideal drug properties required for this technology are relatively low water solubility, fine particle size <50 µm and good aqueous stability in suspension.

Advantages

The major advantage of using this technique is that the tablets produced by this technology have very low disintegration time and have great mouthfeel due to fast melting effect.

Disadvantages

Although being a fairly routine process, lyophilization has some

disadvantages like it is a relatively expensive and time consuming process. Furthermore, the product obtained is poorly stable and fragile, rendering conventional packaging unsuitable.

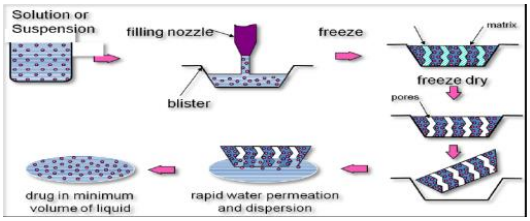

Figure 3: Lyophilization Technology. Patented technology based on this process is Zydis technology

Tablet Moulding

Moulded tablets invariably contain water-soluble ingredients due to which the tablets dissolve completely

and rapidly. Following are the different tablet moulding techniques.

Compression Moulding Process

In this manufacturing process, the powder mixture is moistened with a hydroalcoholic solvent and then pressed into mold plates to form a wetted mass (compression molding). The solvent is then removed by air drying, a process similar to the preparation of tablet trituration's. Such tablets are less compact than compressed tablets and have a porous structure that accelerates dissolution.

Heat-Moulding Process

Heat-moulding process involves setting the molten mass containing a dispersed drug. This process uses agar solution as a binder and a blister packaging well as a mould to manufacture the tablet. A suspension containing drug, agar and sugar is prepared followed by pouring the suspension into the blister packaging well, solidifying the agar solution at room temperature to form a jelly and finally drying at approximately 30 °C under vacuum.

Moulding by Vacuum Evaporation without Lyophilization

This process involves pouring of the drug excipient mixture (in the form of a slurry or paste) into a mould of desired dimension, freezing the mixture to form a solidified matrix and finally subjecting it to vacuum drying at a temperature within the range of its collapse temperature and equilibrium freezing temperature. This results in the formation of a partially collapsed matrix. This method differs from the lyophilization technique, as in the former the evaporation of free unbound solvent occurs from a solid through the liquid phase to a gas, under controlled conditions, instead of the sublimation which takes place in the latter process.

Direct Compression

DC is the simplest and least expensive tableting technique for MDTs because it can be manufactured using conventional tableting and packaging machinery and also due to the availability of tabletting excipients with improved flow, compressibility and disintegration properties, particularly disintegrants, effervescents and sugar-based excipients.

Disintegrants

In many MDT products based on the TLC process, the disintegrants mainly influence the rate of disintegration and thus the dissolution, which is further improved in the presence of water-soluble excipients and effervescents. The introduction of super explosives increased the popularity of this technology. Tablet disintegration time can be optimized by focusing on disintegrant concentration. Below a critical disintegrant concentration, the tablet disintegration time becomes inversely proportional to the disintegrant concentration. However, above the critical concentration level of the explosive, the disintegration time remains approximately constant or the decrease is significant.

Another DC based technology; Flashtab contains coated drug crystals and microgranules along with disintegrants. Two types of disintegrants are used in this technology: a disintegrant (e.g. modified cellulose) which has a high swelling power and a swelling agent (e.g. starch) which has a low swelling power. bid al and Watanabe used microcrystalline cellulose (MCC) and low-substituted hydroxypropyl cellulose (HPC) to prepare MDTs, with the ratio of MCC to HPC varying from 8:2 to 9:1, and Sugihara studied the application of agar powder as a disintegrant based on its property , absorb water and swell greatly without forming a gel at physiological temperature.[49]

Effervescent Agents

The evolution of CO2 as a disintegrating mechanism forms the basis of the patented Orasolv technology (OT) and is frequently used to develop over-the-counter formulations. The product contains microparticles and is slightly effervescent in nature. Saliva activates the effervescent agent which causes the tablet to disintegrate. The OT had been utilized in fabrication of six marketed products: four Triaminic Softchew formulations, Tempra FirsTabs and Remeron SolTab.

Sugar-Based Excipients

Another approach to manufacture MDTs by DC is the use of sugar-based excipients (e.g., dextrose, fructose, isomalt, lactitol, maltitol, maltose, mannitol, sorbitol, starch hydrolysate,

polydextrose and xylitol) which display high aqueous solubility and sweetness and hence, imparts taste masking and a pleasing mouth feel. Mizumoto et al., have classified sugar-based excipients into two types based on their mouldability and dissolution rate.

Type I saccharides (e.g., lactose and mannitol) exhibit low mouldability but high dissolution rate.

Type II saccharides (e.g., maltose and maltitol) exhibit high mouldability but low dissolution rate

Mouldability is defined as the capacity of the compound to be compressed/ moulded and to dissolve. It does not refer to the formation of a true mould by melting or solvent wetting process. The mouldability of Type I saccharide can be improved by granulating it with a Type II saccharide solution. The above technology forms the basis of WOWTAB which involves the use of fluidized bed granulation for the surface treatment of Type I saccharide with Type II saccharide. This technique has been used in the production of Benadryl Fast melt tablets. Here, two different types of saccharides are combined to obtain a tablet formulation with adequate hardness and fast dissolution rate.

Cotton Candy Process

The FLASHDOSE is an MDDDS manufactured using Shearform technology in conjunction with Ceform TI technology to eliminate the drug's bitter taste. Shearforming technology is used to produce a matrix known as dental floss, which is made from a combination of excipients, either alone or with drugs. Dental floss is a fibrous material similar to cotton candy fibers, commonly made from saccharides such as sucrose, dextrose, lactose and fructose at temperatures between 180266 F. However, other polysaccharides such as polymaltodextrins and polydextrose can be converted to fibers at 30-40%. lower temperature than sucrose. This modification enables the safe incorporation of thermolabile drugs into the formulation. The tablets produced by this process are highly porous in nature and offer a very pleasant mouthfeel due to the rapid solubilization of sugars in the presence of saliva.

Spray-Drying

Have used spray drying to produce MDTs. The formulations contained hydrolyzed and non-hydrolyzed gelatin as matrix proppant, mannitol as bulking agent and sodium starch glycolate/croscarmellose as disintegrating agent. Disintegration and dissolution were further enhanced by the addition of an acid (e.g. citric acid) or an alkali (e.g. sodium bicarbonate). The suspension of the above excipients was spray dried to give a porous powder which was compressed into tablets. Tablets made by this method disintegrated in <20 seconds in an aqueous medium.

Sublimation

Sublimation has been used to produce high porosity MDTs. A porous matrix is formed by compressing the volatile ingredients along with other excipients into tablets that finally undergo a sublimation process. For this purpose, inert solid components with high volatility (e.g. ammonium bicarbonate, ammonium carbonate, benzoic acid, camphor, hexamethylenetetramine, naphthalene, phthalic anhydride, urea and urethane) have been used. Solvents such as cyclohexane and benzene have also been suggested to create porosity in the matrix. Makino et al. reported a method using water as the pore-forming material.

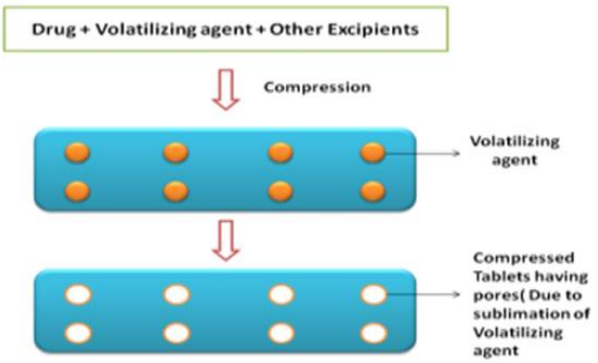

Figure 4: Sublimation technique. Evaporation of volatile agent results in formation of porous tablets thereby causing fast disintegration

Mass-Extrusion

This technology involves softening the drug mixture using the solvent mixture of water-soluble polyethylene glycol and methanol and ejecting the softened mass through the extruder or syringe to obtain a cylindrically shaped extrudate, which is finally cut into regular segments with a heated blade in order to to form tablets. This process can also be used to coat grains of bitter drugs to mask their taste.

Nanonization

A recently developed nano-melting technology involves reducing the particle size of the drug to nano-size by grinding the drug using a proprietary wet-milling technique. The drug nanocrystals are stabilized against agglomeration by surface adsorption to selected stabilizers, which are then incorporated into MDTs. This technique is particularly advantageous for poorly water-soluble drugs. Other advantages of this technology are the rapid disintegration/dissolution of nanoparticles, leading to increased absorption and thus higher bioavailability and dose reduction, a cost-effective manufacturing process, conventional

packaging due to exceptional shelf life, and a wide dose range (up to 200 mg drug per Unit).

Fast Dissolving Films

It is a new frontier in MDDDS that offers a very convenient means of taking medication and supplements. In this technique, a non-aqueous solution is prepared containing water-soluble film-forming polymer (pullulan, carboxymethyl cellulose, hydroxypropyl methyl cellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, polyvinylpyrrolidone, polyvinyl alcohol, or sodium alginate, etc.), drugs, and other taste-masking ingredients, which one forms a film after the solvent evaporates leaves. In the case of a bitter drug, resin adsorbates or coated microparticles of the drug can be incorporated into the film. This film quickly melts or dissolves when placed in the mouth, releasing the drug in solution or suspension form. Features of this system include paper-thin films less than 2\" x 2\", resolution in 5 seconds, instant drug delivery, and flavored aftertaste.

EVALUATION PARAMETERS:

The prepared blend was evaluated by following tests.

1.The angle of repose.

2.Bulk density.

3.Tapped density.

4.Carr's index.

5.Hauser's ratio.

Angle of repose

Funnel method for determining the angle of repose. The accurately weighed mixture was placed in a funnel. The height of the funnel was adjusted so that the top of the funnel touched the top of the heap of mixture. The excipient mixture (as a solid dispersion) was allowed to flow freely through the funnel onto the surface. The diameter of the powder cone was measured. The angle of repose was calculated using the following equation

$$\tan\theta = \frac{h}{r} \qquad (1)$$

Where h and r are the height and radius of the powder cone

Bulk density

Bulk density was determined by pouring a weighed quantity of blend into a graduated cylinder and measuring the volume and weight.

BD =Weight of the powder/Volume of the packing.

Tapped density

It was determined by setting up a graduated cylinder containing a known mass of drug-excipient mixture. The cylinder was dropped onto a hard surface under its own weight from a height of 10 cm at 2 second intervals. Tapping continued until no further change in volume was noted.

$$\text{TBD} = \frac{\text{Weight of the powder}}{\text{volume of the tapped packing}} \qquad (2)$$

Compressibility index

The Compressibility Index of the blends was determined by Carr's compressibility index.

Evaluation of fast dissolving tablets[61]

Weight variation

The weight variation test is performed to ensure the consistency of the weight of the tablets in each batch. First the total weight of 20 tablets of each formulation is determined and the average calculated. The individual weight of each tablet is also determined to find out the weight variation. The weight variation is given by the formula.

$$\%\ \text{Weight variation} = \frac{\text{Individual weight}}{\text{Average weight}} \times 100 \qquad (3)$$

Hardness

Hardness is also called as crushing strength (fc) of the tablet, the force required to break a tablet in a diametric compression was measured using Monsanto tablet hardness tester. It is expressed by in kg/cm2.

Friability

Tablet friability determined with Roche Friabilator. Friability is the weight loss of the tablet in the container due to the removal of the fine particles from the surface. A friability test is conducted to determine the tablet's ability to withstand abrasion during packaging, handling and shipping. Weigh the 20 tablets from each batch and place them in a Roche Friabilator rotating at 25 rpm for 4 minutes. Dust off all tablets and weigh again. The friability (F) is given by the formula

$$F = \frac{W(\text{initial})}{W(\text{final})} \qquad (4)$$

Wetting time

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

$$\frac{dl}{dt} = r\Upsilon\cos\theta/(4\eta l) \qquad (5)$$

where l is the penetration length, 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 evident that the pore size becomes smaller and the wetting time increases as the compressive force increases or the porosity decreases. There is a linear relationship between disintegration and wetting time. Thus, wetting is the important step for the decomposition process to take place. A double-folded piece of tissue paper was placed in a Petri dish (internal diameter 6.5 cm) containing 6 ml of water. The tablet was placed on the paper and then the time in seconds for the tablet to be completely wet was measured. The procedure was slightly modified by keeping water at 37 ± 0.5 c. The wetting time refers to the time it takes for the tablet to dissolve when held motionless on the tongue.

In vitro drug release

The release of the drug in vitro was determined by estimating the dissolution profile, a USP 2 paddle device was used and the paddle was rotated at 50 rpm, phosphate buffer (pH 6.8) (900 ml) was used as the dissolution medium.

Mechanical Strength

Tablets should be of sufficient strength to withstand mechanical shock during handling during manufacture, packaging and shipping. Friability and fracture toughness are two important parameters in evaluating a tablet for mechanical strength.

Crushing strength

Breaking strength, in simple terms, is the force required to break a tablet by compressing it in a radial direction. It is an important parameter in the formulation of orally disintegrating tablets, since excessive crushing strength significantly reduces disintegration time. In the present study, tablet crush strength was measured using Pfizer hardness testers. An average of three observations are reported.

Friability testing

The crushing test may not be the best measure of potential behaviour during handling and packaging. The resistance to the surface abrasion may be a more relevant parameter. Friability of each batch was measure in "Electro lab-friabilator". 10preweighed tablets were rotated at 25 rpm for 4 min, the tablets were then reweighed and the percentage of weight loss was calculated.

Rapidly disintegrating property

To evaluate a tablet for their rapid disintegration properties, following tests were carried out.

Modified disintegration test

An accurate method for conducting dosage form disintegration tests has several limitations and they are not sufficient for measuring very short disintegration times. The disintegration time for fast dissolving tablets needs to be modified since disintegration without water is required, so the test should mimic disintegration in the salivary contents. For this parameter, a 10 cm diameter Petri dish was filled with 10 ml of water. The tablet was carefully placed in the center of the petri dish and then the time it took for the tablet to completely break up into fine particles was noted.

Disintegration in oral cavity

The time required for the tablets to completely disintegrate in the oral cavity was determined by 6 healthy subjects given tablets of the optimal formulation. Water Absorption Ratio A piece of tissue paper folded twice was placed in a small Petri dish containing 6 ml of water. The tablet was placed on the paper and the time required for complete wetting was measured. The wet tablet was then weighed. The water absorption ratio, denoted R, was determined using the following equation:

$$R = 10\frac{wa}{wb} \qquad (6)$$

Where wb= weight of tablet before water absorption and

wa =weight of the tablet after water absorption

CONCLUSION

The MDTs have potential advantages over conventional dosage forms, with their improved patient compliance, convenience, bioavailability and rapid onset of action. 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.

CONFLICTS OF INTEREST

The authors declare that there is no conflict of interests.

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