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Mouth melting tablets an overview

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ABSTRACT

Mouth Melting tablets/ fast disintegrating tablets (FDTs) are receiving increased demand from last few decades and the field has become a very fast growing area in the pharmaceutical industry. After administration into the mouth, these tablets dissolve or disintegrate in the mouth without any additional water for easy administration of active pharmaceutical ingredients. These tablets readily dissolve or disintegrate in the saliva generally within seconds. Fast dissolving tablets/ mouth melting tablets have been formulated for pediatric, geriatric, bedridden patients and for active patients who are busy and traveling and may not have access to water. These tablet formulations provide a very good 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 dysphasia.

Keywords: Mouth Melting Tablets, Fast disintegrating tablets, Super disintegrates, Direct compression, Wetting time.

INTRODUCTION

Tablets are the most widely used dosage forms because of their very convenience in terms of self-administration, compactness and easiness in manufacturing. However, many patients like children and elderly have difficulty in swallowing tablets and capsules and consequently unable to take medicine as prescribed. About 50% of the population is affected by such problems, resulting in the high incidence of non-compliance and failure in effective therapy. To overcome such problems, mouth melting tablets or orally disintegrating tablets have emerged as an alternative dosage forms. These tablets are also well known as quick dissolve, fast dissolving, rapid disintegrating, and mouth dissolving; melt in mouth, Orodispersible or orally disintegrating tablets [5, 10, 13].

Drug delivery systems (DDS) are the strategic tools for expanding markets/indications, extending product life cycles and generating opportunities. Oral route is the most popular route for systemic effects due to its ease of administration/ ingestion, pain, avoidance, versatility and most importantly, patient compliance. Solid oral delivery systems do not require sterile conditions and are therefore, less expensive to manufacture. It's also having high patient compliance, high-precision dosing, and manufacturing efficiency make tablets the solid dosage form of choice.

Excipients and equipment choices will be significantly affected should solid dosage form

technologies change in response to the unprecedented shifts in the drug discovery such as genomics. Should next generation drugs are predominantly protein or peptide based, tablets may no longer may be the dominant format give the difficulty of dosing such moiety. Injections are generally not favored for use by patients unless facilitated by sophisticated auto injectors. Inhalation is also one good alternative system to deliver these drugs, but the increased research into biopharmaceuticals so far has generate predominantly chemical entities with low molecular weights. The development of increased oral protein delivery technology by Fast dissolving Tablets which may release these drugs in the mouth are very much promising for the delivery of high molecular weight protein and peptide . The oral route remains the most perfect route for the administration of therapeutic agents because of the low cost of therapy, manufacturing and easiness of administration lead to high patient compliance [3, 9, 15, 16, 19, 21, 25, 28].

DESIRED CRITERIA FOR MOUTH DISSOLVING DRUG DELIVERY SYSTEM

- It should require no water for oral administration, yet dissolve/disperse/disintegrate in mouth in a matter of seconds.
- Have a pleasing mouth feel.
- Have an acceptable taste masking property.
- Should be harder and friable.
- Leave minimal or no residue in the mouth after oral administration.
- Exhibit low sensitivity to environmental conditions such as humidity and temperature.
- Have manufactured using conventional processing and packaging equipment at low cost.
- 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 [4, 8].

IDEAL CHARACTERISTICS OF FAST DISSOLVING DELIVERY SYSTEM [24]

Mouth-feel

Mouth-feel is critical, and patients should receive a product that feels pleasant. Any large particles from the disintegrating tablet that are insoluble or slowly soluble in saliva would lead to an unpleasant gritty feeling. This can be overcome by keeping the majority of the particles below the detectable size limit. In some cases, certain flavors can an improved mouth-feel perception, resulting in a product that is perceived as being less gritty, even if the only change is the flavor. Effervescence can be added to aid disintegration and improve mouth-feel by reducing the “dryness” of a product.

Hygroscopicity

Several fast dissolving dosage forms are hygroscopic and cannot maintain physical integrity under normal conditions of temperature and humidity. Hence they need protection from humidity, which calls for specialized product packaging.

Friability

In order to allow fast dissolving tablets to dissolve in the mouth, they are made of either very porous or soft molded matrices or compressed into tablets with very low compression force, which makes the tablets friable and/or brittle which are difficult to handle, often requiring specialized peel off blister packing. To overcome this problem, some companies introduced more robust forms of fast dissolving tablets, such as Wow tab by Yamanouchi-Shadlee and Dura Solve by CIMA labs.

Salient features of mouth melting tablets

- This system provides rapid dissolution of drug and absorption which may produce rapid onset of action.
- Ease of administration to patients who refuse to swallow a tablet such as pediatric, geriatric patients and psychiatric patients.
- No need of water to swallow the dosage form, which is highly convenient especially for patients who are traveling and do not have immediate access to water.

- Convenience of administration and accurate dosing as compared to liquids.
- 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 [4].

Techniques of mouth melting tablet formulation

The fast-dissolving property of the mouth melting tablets is attributed to quick ingress of water into tablet matrix resulting in very fast disintegration. Hence, the basic approaches to develop mouth melting tablets include:

- Maximizing the porous structure of the tablet matrix.
- Incorporating the appropriate disintegrating agent/agents.
- Using highly water-soluble excipients in the formulation [22].

Various manufacturing techniques mouth melting tablets include

Lyophilization
Spray drying
Moulding
Direct Compression
Sublimation
Mass Extrusion
Nanonization
Fast Dissolving Films

Lyophilization

In freeze-drying process, the water is sublimed from the product after it is frozen. Jaccard and Leyder used lyophilization to develop an oral formulation that not only dissolved rapidly but also exhibited improved bioavailability of several drugs such as spironolactone and trolendomycin.

Step A

Bulk formulation of an aqueous drug solution or suspension and its subsequent precise dosing into pre-formed blisters. It is the blister that actually forms the tablet shape and is, therefore, an integral component of the total product package.

Step 2

Passing the filled blisters through a specially developed 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.

Step 3

Sealing the open blisters using a heat-seal process to ensure stability and protection of the product from varying environmental conditions [11, 14].

Tablet moulding

Moulded tablets invariably contain water-soluble ingredients due to which the tablets dissolve fully and rapidly. Following are the different tablet moulding techniques as given below:

Spray drying

In this technique, gelatin can be used as a supporting agent and as a matrix, mannitol as a bulking agent and sodium starch glycolate or croscarmellose or crospovidone are used as super disintegrants. Tablets manufactured from the spray-dried powder have been reported to disintegrate in less than 20 seconds in aqueous medium.

Compression moulding process

This process involves moistening the powder blend with a hydroalcoholic solvent followed by pressing into mould plates to form a wetted mass (compression moulding). The solvent is then

removed by air drying, a process similar to the manufacture of tablet triturates. Such tablets are less compact than compressed tablets and possess a porous structure that hastens dissolution [22].

Heat-moulding process

This 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 [19].

Moulding by vacuum evaporation without lyophilization

It 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 [23].

Direct Compression (DC)

DC is the simplest and most cost effective tablet manufacturing technique for MDTs as they can be fabricated using conventional tablet manufacturing and packaging machinery and also due to availability of tabletting excipients with improved flow, compressibility and disintegration properties, especially tablet disintegrants, effervescent agents and sugarbased excipients.

Disintegrants

In many MDT products based on DC process, the disintegrants mainly affect the rate of disintegration and hence dissolution which is further enhanced in the presence of water soluble excipients and effervescent agents. The introduction of superdisintegrants has increased the popularity of this technology [26].

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 [6, 29, 30]

Sugar-based excipients

Another approach to manufacture mouth melting tablets 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 [20].

Sublimation

Sublimation has been used to produce mouth melting tablets with high porosity. A porous matrix is formed by compressing the volatile ingredients along with other excipients in tablets, which are finally subjected to a process of sublimation. Inert solid ingredients with high volatility (e.g., ammonium bicarbonate, ammonium carbonate, benzoic acid, camphor, hexamethylene tetramine, naphthalene, phthalic anhydride, urea and urethene) have been used for this purpose. Solvents like cyclohexane and benzene were also suggested for generating the porosity in the matrix [12, 17].

Mass-extrusion

In this technology softening of the active blend done using the solvent mixture of water soluble polyethylene glycol and methanol and expulsion of softened mass through the extruder or syringe to get a cylindrical shaped extrude which are finally cut into even segments using heated blade to form tablets. This process can also be used to coat granules of bitter drugs to mask their taste [2].

Nanonization

A very newly developed Nanomelt technology involves reduction in the particle size of drug to nanosize by milling the drug using a proprietary wet-milling technique. The nanocrystals of the drug are stabilized against agglomeration by adsorption on selected stabilizers, which are then incorporated into Mouth melting tablets. This technique is especially advantageous for poorly water soluble drugs. Other advantages of this technology include fast disintegration/dissolution of nanoparticles

leading to increased absorption and hence higher bioavailability and reduction in dose, cost effective manufacturing process, conventional packaging due to exceptional durability and wide range of doses (up to 200 mg of drug per unit) [7].

Fast dissolving films

It provides a very convenient means of taking medications and supplements. In this technique, a non-aqueous solution is prepared containing water soluble film forming polymer (pullulan, carboxy methylcellulose, hydroxypropyl methylcellulose, hydroxyl ethylcellulose, hydroxyl propylcellulose, polyvinyl pyrrolidone, polyvinyl alcohol or sodium alginate, etc.), drug and other taste masking ingredients, which is allowed to form a film after evaporation of solvent. In case of a bitter drug, resin adsorbate or coated microparticles of the drug can be incorporated into the film [1**]**

Evaluation of mouth melting tablets

Tablets from all the formulation were subjected to following quality control test.

General appearance

The general appearance of a tablet, its visual identity and over all "elegance" is essential for consumer acceptance and tablet's 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

Tablet 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.

Weight variation

20 tablets were selected randomly from the lot and weighted individually to check for weight variation. Weight variation specification as per I.P. is shown below.

Average Weight of Tablet	% Deviation
80 mg or less	±10
More than 80 mg but less than 250 mg	±7.5
250 mg or more	±5

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 (F)

Friability of the tablet determined using Roche friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at height of 6 inches in each revolution. Pre weighted sample of tablets was placed in the friabilator and were subjected to the 100 revolutions.

The friability (F) is given by the formula.

$$F = (W_{int.} - W_{fin}) / W_{int.} * 100$$

Where, Wint - Weight of tablets before friability. Wfin - Weight of tablets after friability.

Wetting time and water absorption ratio

Wetting time of dosage form is related to the contact angle. It needs to be assessed to give an insight into the disintegration properties of the tablets; a lower wetting time implies a quicker disintegration of the tablet. For this purpose, a tablet is placed on a piece of tissue paper folded twice and kept in a small Petri dish (ID = 6.5 cm) containing 6 ml of water, and the time for complete wetting is measured.

Water absorption ratio

A piece of tissue paper folded twice was placed in a small Petridish 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 (wa/wb)

Where, wa is weight of tablet before water absorption & wb is weight of tablet after water absorption.

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.

In vitro dissolution test

The development of dissolution methods for FDTs is comparable to the approach taken for conventional tablets and is practically identical. Dissolution conditions for drugs listed in a pharmacopoeia monograph, is a good place to start with scouting runs for a bioequivalent FDT. Other media such as 0.1 M HCl and buffer (pH 4.5 and 6.8) should be evaluated for FDT much in the same way as their ordinary tablet counterparts. It has been suggested that USP 2 paddle apparatus is the most suitable and common choice for orally disintegrating tablets, with a paddle speed of 50 rpm commonly used.

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.

1) 40 ± 1 °C
2) 50 ± 1°c
3) 37 ±1 ° C and RH 75% ± 5%

The tablets were withdrawn after a period of 15 days and analyzed for physical characterization (Visual defects, Hardness, Friability, Disintegrations and 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°C [27, 31].

CONCLUSION

Fast disintegrating/ Mouth melting tablets have a very good patient compliance and also it may offer improved biopharmaceutical properties, improved efficacy and better safety compared with conventional oral dosage forms. Nowadays, fast dissolving tablets are more widely available as over-the-counter products for the treatment of nausea, allergies, and cold and flu symptoms. The target population has also expanded to those who want convenient dosing anywhere, anytime, without water. This dosage form shows future potential for these products is promising because of the availability of new technologies combined with strong market acceptance and patient demand. There are a lot future possibilities for improvements in fast disintegrating and drug delivery are bright, but the technology is still relatively new. A number of drug delivery technologies that can be leveraged on improving drug therapy from these dosage forms.

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