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Review Article

MOUTH DISSOLVING TABLET: APPROACHES TECHNOLOGY

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ABSTRACT
Mouth dissolving tablets are disintegrating and 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. Fast- or mouth dissolving tablets have been formulated for paediatric, geriatric, and bedridden patients and for active patients who are busy and travelling and may not have access to water.
KEYWORDS: Mouth dissolving tablets, superdisintegrants, evaluation of mouth dissolving tablet.

INTRODUCTION

Oral routes of drug administration have wide acceptance up to 50-60% of total dosage forms. Solid dosage forms are popular because of ease of administration, accurate dosage, self medication, pain avoidance and most importantly the patient compliance. The most popular solid dosage forms are being tablets and capsules; one important drawback of this dosage forms for some patients, is the difficulty to swallow[1]. Drinking water plays an important role in the swallowing of oral dosage forms. Often times people experience inconvenience in swallowing conventional dosage forms such as tablet when water is not available, in the case of the motion sickness (kinetosis) and sudden episodes of coughing during the common cold, allergic condition and bronchitis. For these reason, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention. Orodispersible tablets are not only indicated for people who have swallowing difficulties, but also are ideal for active people[2].

This is an innovative tablet technology where the dosage form containing active pharmaceutical ingredients disintegrates rapidly, usually in a matter of seconds, without the need for water, providing optimal convenience to the patient. The European Pharmacopoeia defines Orodisperse as a tablet that can be placed in the mouth where it disperses rapidly before swallowing. Researchers have formulated ODT for various categories of drugs, which are used for therapy in which rapid peak plasma concentration is required to achieve desired pharmacological response. These include neuroleptics, cardiovascular agents, analgesics, anti-allergic and drugs for erectile dysfunction.

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Advantages of mouth dissolving tablets

- Ease of administration to patients who cannot swallow, such as the elderly, stroke victims and bedridden patients; patients who should not swallow, such as renal failure patients; and who refuse to swallow, such as paediatrics, geriatric and psychiatric patients.
- Patient's compliance for disabled bedridden patients and for travelling and busy people who do not have ready access to water.
- Convenience of administration and accurate dosing as compared to liquid formulations.
- Benefit of liquid medication in the form of solid preparation.
- More rapid drug absorption from the pre-gastric area i.e. mouth, pharynx and oesophagus which may produce rapid onset of action.

Pregastric absorption can result in improved bioavailability, reduced dose and improved clinical performance by reducing side effects[3,4].

New business opportunities: product differentiation, line extension and life-cycle management, exclusivity of product promotion convenience of administration and accurate dosing as compared to liquid formulations.

Ideal properties of mouth dissolving tablets

- Not require water to swallow and should dissolve or disintegrate in the mouth within few seconds.
- Allow high drug loading.
- Be compatible with taste masking and other excipients.
- Have a pleasing mouth feel.
- Leave minimal or no residue in the mouth after oral administration.
- Have sufficient strength to withstand the rigors of the manufacturing process and post manufacturing handling.
- Exhibit low sensitivity to environmental conditions such as humidity and temperature.
- Be adaptable and amenable to existing processing and packaging machinery.
- Allow the manufacture of tablets using conventional processing and packaging equipments at low cost.
- Exhibit low sensitivity to environmental condition[5, 6].

Superdisintegrants

Disintegrating agents are substances routinely included in the tablet formulations to aid in the breakup of the compacted

mass when it is put into a fluid environment. They promote moisture penetration and dispersion of the tablet matrix. In recent years, several newer agents have been developed known as "Superdisintegrants". These newer substances are more effective at lower concentrations with greater disintegrating efficiency and mechanical strength. On contact with water the superdisintegrants swell, hydrate, change volume or form and produce a disruptive change in the tablet. Effective superdisintegrants provide improved compressibility, compatibility and have no negative impact on the mechanical strength of formulations containing high-dose drugs.

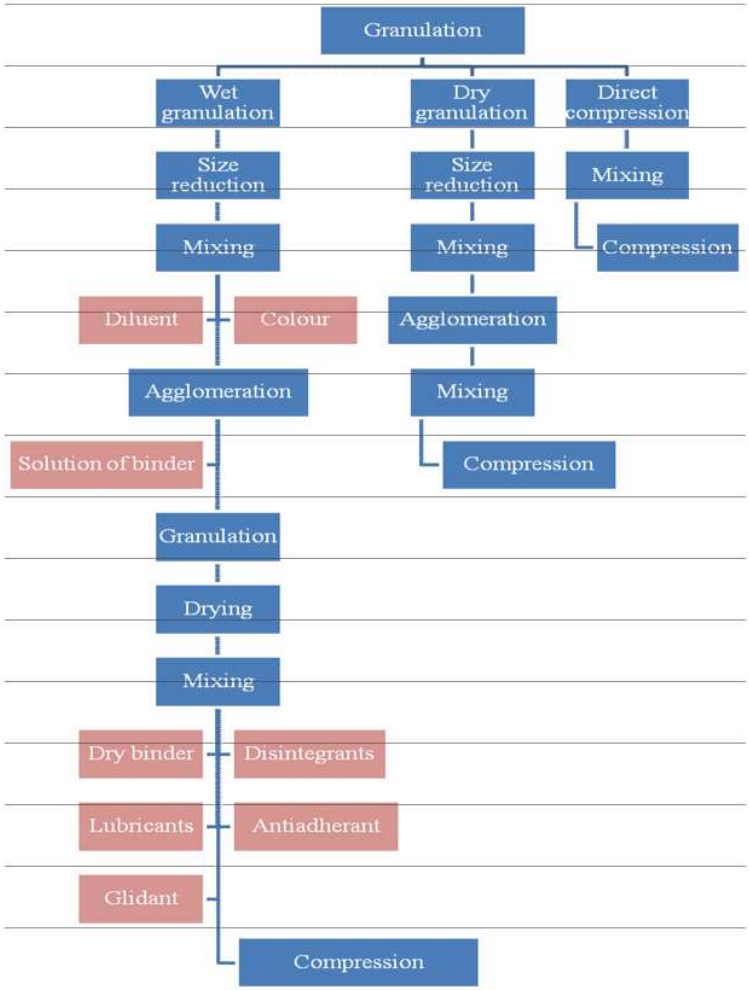
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Table 1: Superdisintegrants employed in MDT

Super Disintegrants	Nature	Mechanism of Action	Brand Name
Cross Carmellose	Modified Cellulose	Wicking due to fibrous structure swelling with minimal gelling	AC-Di-Sol Nymce 25x
Cross Povidone	Cross linked PVP	Water wicking swelling and possibly some deformation Recovery	Kollidon polyplasdone
Aliginic Acid N F	Cross linked Aliginic Acid	Wicking Action	Satialgine
Soy Polysaccharide	Natural disintegrants	-	EMCOSOY
Sodium Starch glycolate	Modifide starch	Rapid and Extensive	Explotab Primogel
C-HPC	Low Hydroxy Propyl Cellulose	Both swelling and wicking	-
Acrylic Acid Derivative	Poly(Acrylic Acid)	Wicking action	-
Ion Exchange Resins	Resins		Amberlite (IPR 88)

Tablet Forming Processing



Evaluation of mouth dissolving tablets

General Appearance

The general appearance of a tablet, its visual identity and over all "elegance" is essential for consumer acceptance. Include in are 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

The size and shape of the tablet can be dimensionally described, monitored and controlled.

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 in table 2.

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Table 2: Weight variation specification as per IP[8]

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

Assay

Twenty tablets from each batch were weighed accurately and powdered powder equivalent to 100 mg drug was shaken with 100 ml of 0.1N Hydrochloric acid in 100 ml amber coloured volumetric flask and from this 10 ml was pipette out and then dilute up to 100 ml. From standard solution again 10 ml pipette out and diluted up to 100 ml in ml[9, 10].

Tablet hardness

The strength of tablet is expressed as tensile strength (Kg/cm2). The tablet crushing load, which is the force required to break a tablet into halves by compression .It was measured using a tablet hardness tester (Pfizer Hardness Tester) [11].

Content uniformity

Five tablets were powdered and the blend equivalent to 4 mg of Tizanidine Hcl was weight and dissolved in suitable quantity of pH 1.2 solutions. Solution was filtered and diluted and drug content analyzed spectrophotometrically at 228 nm[12].

Measurement of tablet tensile strength

The tablet tensile strength is the force required to break a tablet by compressing it in the radial direction and is measured using a tablet hardness tester. For measuring the hardness of the tablets, the plunger of the hardness tester is driven down at a speed of 20 mm/min. Tensile strength for crushing (T) is calculated using equation:

$$\text{Eq. } T = 2F / \pi dt$$

Where F is the crushing load, and d and t denote the diameter and thickness of the tablet, respectively23. Though, this is a widely used and accepted method for hardness testing, it is not applicable to very delicate tablets prepared by Lyophilisation technique wherein the liquid suspension of drug and excipients is freeze dried in the blister pocket and the dried tablets are finally sealed in the blister. Special aluminium blisters with peel off blister covers are used as packaging material for these tablets. Flash dose tablets prepared by cotton candy process are also poor candidates for this test[8, 13]. This test is best suited for tablets prepared by direct compression and moulding methods. However, the tensile strength of these tablets is always kept low which needs to be compromised to keep the disintegration time as minimum as possible.

Friability

The pharmacopoeial limit of friability test for a tablet is not more than 1% using table friability apparatus, carried out at 25 rpm for 4 min (100 rotations. However, it becomes a great challenge for a formulator to achieve friability within this limit for MDT product keeping hardness at its lowest possible level in order to achieve a minimum possible disintegration time. This test is again not applicable for lyophilized and flash dose tablets, but is always recommended for tablet speared by direct compression and molding techniques to ensure that they have enough mechanical strength to withstand the abrasion during shipping and shelf life[11, 14].

Moisture uptake study

MDTs usually contain high concentration of hydrophilic excipients with the minimum possible hardness which together contributes to their increased susceptibility to moisture uptake. In order to maintain their physical integrity and surface texture, special attention is required during the storage and packaging of these dosage forms. Therefore, moisture Uptake studies are strongly recommended for MDTs. The test can be carried out by keeping ten tablets along with calcium chloride in a desiccators maintained at 37 °C for 24 hrs to ensure complete drying of the tablets. The tablets are then weighed and exposed to 75% RH, at room temperature for 2 weeks. The required humidity can be achieved by keeping saturated sodium chloride solution in the desiccators for 24 hrs. The tablets are reweighed and the percentage increase in weight is recorded. If the moisture uptake tendency of a product is high, it requires special dehumidified area for manufacturing and packing. The materials with high moisture resistant properties should be used for packaging for e.g. alu strip pack, alu-alu blister or polyethylene sealing on blister. The use of appropriate quantity of desiccant in HDPE bottle packs with minimum head space is highly recommended to ensure stability of the product during its shelf life[15, 16].

Wetting time and water absorption ratio

A study 24 on wetting time and water absorption ratio reported the use of a piece of double folded tissue paper placed in a Petridis containing 6 ml (Ph 6.8) of water. One tablet was placed on this paper and the time for complete wetting of tablet was noted as wetting time. The wetted tablet was then weighed and the water absorption ratio, R, was determined according to equation:

$$\text{Eq. } R = 100 (Wa.Wb)/Wb$$

Where Wb and Wa are the weights of tablet before and after water absorption, respectively.

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Disintegration time

The methods for evaluation of in-vivo disintegration time had been explained in literature 2830. 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 use in 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[17, 18].

Disintegration test with rotary shaft method

In another study, proposed a better disintegration method for MDTs. In the experimental method, the MDT was placed on the wire gauze (D), slightly immersed in another study, proposed a better disintegration method for MDTs .In the experimental method ,the MDT was placed on the wire gauze 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 inhuman. The compression force can be easily adjusted using the weight (A). The rotary shaft crushes the MDT which disintegrates in to the medium. The endpoint was measured visually using a stop watch .The below mentioned apparatus was modified by Harada et31 al by placing a sponge at the surface of shaft weight to increase friction with the MDT. Therefore, the weight transmits the torque of the rotating shaft to the ODT and grinds it on the stainless steel perforated plate which is used in place of wire gauge. The electrodes are attached on each side of the plate. The rotation speed and weight were optimized to set the mechanical pressure. When the weight makes contact with separated plates, the electric sensor conveys a signal that indicates the end point of the disintegration test of the ODT [19].

Disintegration test texture analyzer

In another study, a texture analysis apparatus was used to measure the start and end time points of tablet disintegration. A constant penetration force was applied to tablets via a cylindrical flat-ended probe. The tablet, under constant force, is immersed in a defined volume of distilled water and the time is plotted against the distance, which the probe travelled into the tablet. Typical time–distance profiles, generated by the texture-analysis software, enabled the calculation of the starting and ending time of disintegration[20, 21].

Disintegration test using electro force 3100

An instrument "Electro Force® 3100" has recently been designed by the Bose Corporation with an objective to simulate the disintegration condition of the MDTs in mouth. It is based on application of low force to measure small displacements and disintegration rate as a function of manufacturing process of a variety of MDTs. The instrument typically consists of a lower plate to hold the tablet on which a force of about 10 mN is applied followed by addition of approximately 5 ml of water maintained at 37 °C. It has the advantage of providing better resolution than those available instruments with moderate to high force test 31. This is the first equipment of its type which is available in the market for evaluation of ODT. This tabletop system can be used by the manufacturers and regulatory agencies to monitor and evaluate the different fabrication technologies of MDTs[22].

Dissolution testing of mouth dissolving tablets

The conventional method of dissolution could be extended to in-vitro evaluation of MDT The dissolution conditions for the reference listed drugs available in USP can be utilized for preliminary in-vitro studies to mimic better in-vivo conditions. Apart from the above, multimedia dissolution studies in various buffer solutions of different pH viz. 0.1 N HCl; pH 4.5 and 6.8buffers should be carried out for interpretation of their in-vivo performance and pharmaceutical equivalence. USP apparatus II (paddle) with a speed seems to be most suitable and common choice with appropriate dissolution media volume to maintain sink condition.

Evaluation of effectiveness of test masking

The formulation's organoleptic properties like taste, mouth-feel and appearance are of considerable importance in differentiating products in the market and can ultimately determine the success of a product.

CONCLUSION

Overviews of various types of superdisintegrants which are available have been discussed. Tablet disintegration has received considerable attention as an essential step in obtaining fast drug release. Disintegration remains a powerful influence and precursor for drug absorption. Disintegration of tablet or capsule is depending upon the type and quantity of disintegrants. The development of fast dissolving or disintegrating tablets provides an opportunity to take an account of tablet disintegrants. Therefore, there is a huge potential for the evaluation of new disintegrants or modification of an existing disintegrants into superdisintegrants, so as to formulate fast dissolving dosage form.

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