A COMPREHENSIVE REVIEW OF MOUTH DISSOLVING FORMULATION

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Abstract

Mouth dissolving tablets are solid dosage forms containing drugs that disintegrate in the oral cavity within less than one minute leaving. 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 within few seconds in the mouth due to the action of superdisintegrant or maximizing pore structure in the formulation ODTs are a cost-effective way to distribute drugs. When a medicine is absorbed through the buccal cavity, ODTs constitute a critical drug delivery method. Spray drying, sublimation, and other scientific procedures like freeze drying, moulding, and direct compression.

Key words: Mouth dissolving tablets (MDTs), fast dissolving, mouth disintegration, Superdisintegrants.

Introduction

Numerous cases, especially senior find it delicate in swallowing tablets, capsules, fluids and thus don't comply with prescription , which results in high incidence of non-compliance acquainted exploration has redounded in bringing out numerous safer and new medicine delivery system. Rapidly disintegrating dissolving tablet is one of similar illustration, for the reason of rapid-fire disintegration or indeed with saliva . Considering quality of life, most of these sweats have been concentrated on ease of drug. Among the various doses forms developed to ameliorate the ease of administration, the mouth dissolving tablet (MDT) is the most extensively preferred marketable products (1).

Mouth dissolving tablets (MDTs) are a good dissolving miracle and probative route for life-hanging conditions similar as nervous illness, radioactivity remedy, Parkinson's complaint, and AIDS that face the dysphasia condition. MDT is also respectable for the mentally ill, bedridden, developmentally impaired cases, and in cases with underlying conditions that disrupt swallowing capability, similar as migraine, throat cancer, mouth ulcers, and throat infections. It's particularly applicable for individualities who are travelling, have difficulty penetrating water, and have habitual nausea and vomiting. Tablets that dissolve in the mouth have good stability, are simple to manufacture, and are simple for cases to handle (3,4).

Ideal Properties of MDT (6,7)

MDT should have following several ideal characteristics properties.

1. Not bear water to swallow.
2. fluently dissolve or disperse or disintegrate in the mouth within a many second
3. Have an respectable taste masking and other excipient property .
4. Have a pleasing mouthfeel.
5. It should bring-effective.

6. Be there harder and less friable
7. Leave minimum or no residue in mouth after administration.
8. Show signs of lower perceptivity to environmental conditions like temperature, moisture etc.
9. Be there adaptable and amenable for being processing and packaging technology.
10. Allow the yield of tablets with conventional division and packaging outfit.

Significance of Mouth Dissolving Tablet

Ease of administration to cases who cannot swallow, similar as the senior, strok victims and bedridden cases; cases who shouldn't swallow, similar as renal failure cases; and who refuse to swallow, similar as in some cases. Case's compliance for impaired bedridden cases andfor travelling and busy people, who don't have ready access to water. Good mouth feel property of Mouth Dissolving Drug Delivery helps to change the introductory view of drug as" bitter pill ", particularly for paediatric cases due to bettered taste of bitter medicines. Convenience of administration and accurate dosing as compared to liquid formulations. Benefit of liquid drug in the form of solid preparation. More rapid-fire medicine immersion from the pregastric area i.e. mouth, pharynx and oesophagus. Pregastric immersion can affect in bettered bioavailability, reduced dose and bettered clinical perform ance by reducing side goods (21-23).

As shown in Fig.1.

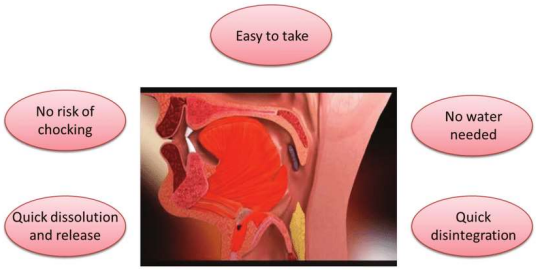

Fig1: significance of mouth dissolving tablet

Advantages of MDT:

Simple distribution for cases who are unfit to swallow, similar as the senior, those who are bedridden, those who have renal illness, and people with internal conditions
• Rapid intervention in medicine treatment
• By enabling medicines to be absorbed from the mouth, throat, and esophagus before they enter the stomach, it's possible to achieve increased bioavailability/ rapid-absortion
• Accessible for busy persons on the go as well as bedridden and hindered cases in terms of administration and case compliance
• A nice tongue feel quality, in especially for small children, helps to change the perception of drug as a bitter lozenge
• The Danger of choking or suffocating is dropped, adding safety, when physical obstacles are avoided during oral administration of standard formulations (8).

Disadvantages:

1. The tablets frequently do n't have enough mechanical strength.
2. Careful running is needed as a result still, they may have a poor taste and feel gritty in the mouth if the capsules aren't prepared rightly.
3. Cases using anticholinergic specifics simultaneously as well as those with Sjogren's pattern or dry mouth brought on by reduced saliva product may not be the stylish campaigners for these tablet formulation.
4. Because they're hygroscopic, MDTs must be kept in a dry terrain.
5. To maintain maximum stability and product security, mouthwash capsules bear special packaging (9).

Technologies for Mouth Dissolving Tablets:

1.Conventional Technologies:

- Freeze Drying
- Tablet Molding
- Direct Compression
- Spray Drying
- Sublimation

2. Patented Technologies:

- Zydis Technology
- Durasolv Technology
- Wowtab Technology

Conventional Technologies:

Freeze Drying

A process in which water is sublimated from the product after frezzing. Lyophilization is a pharmaceutical technology which allows drying of heat sensitive medicines and natural at low temperature under conditions that allow junking of water by sublimation. Lyophilization results in medications, which are largely pervious, with a veritably high specific face area, which dissolve fleetly and show bettered immersion and bioavailability. The process involved in the snap- drying technology as shown in Fig. 2 (10).

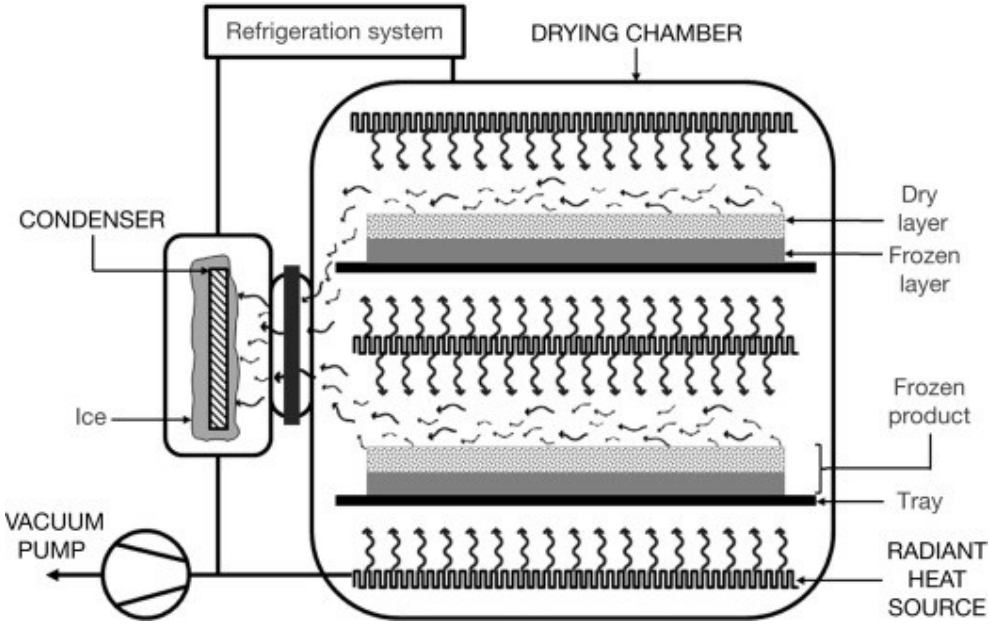

Fig. 2. Freeze Drying

Tablet molding technology

Molded tablets are made with water-soluble constituents to ameliorate rapid-fire drug immersion through the mucosal filling of the mouth. This technology has the advantage of having a pervious structure, which improves solubility and increases bioavailability while reducing first- pass metabolism of some drugs. generally, answerable complements like saccharides are used in the molding process to ameliorate the mouth feel and tablet breakdown. still, the low mechanical strength of moldered tablets causes handling corrosion and breakage (11).

Direct Compression:

These are the simple and most provident styles to prepare Mouth Dissolving Tablet. The mixture of the medicine and other factors are compressed without any primary treatment. Only a many medicines can be formulated by using this system. Generally a super disintegrate is used in the expression which enhances the rate of disintegration and hence the rate of dissolution greatly. Tablet disintegrated time can be optimized by concentrating the disintegrant. Below critical concentration tablet disintegration time is equally commensurable to the attention of the disintegrating agent. Above the critical concentration the disintegraton time remains constant with the high attention of disintegrant. The major drawback of effervescent excipients is their hygroscopicity. Another approach to be used sugar-grounded excipients which demonstrate high waterless solubility and give pleasing mouth feeling. Generally used excipients are dextrose, fructose. Lactilol , maltilol , maltose, mannitol, sorbitol, starch-hydrosysate , polydextrose and xylitol. The process involved in the drying contraction technology is shown in Fig. 3 (12).

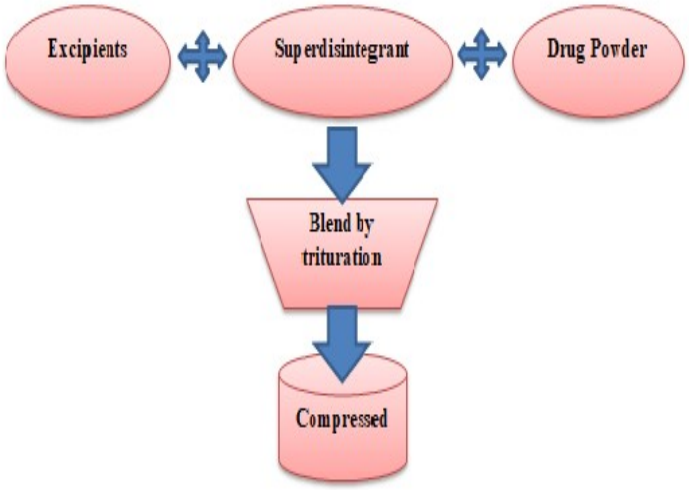

Fig .3. Direct compression

Spray Drying:

The spray- drying is used to produce Mouth dissolving tablets. These formulation contained hydrolyzed or non hydrolyzed gelatin as the supporting agent for the matrix, mannitol as a bulking agent and sodium bounce glycolate or croscarmellose as a disintegrant. By adding an acid(e.g., citric acid) and alkali(e.g., sodium bicarbonate) disintegration and dissolution were further enhanced. The pervious greasepaint was attained by the spray drying the below suspense which was compressed into tablets. Tablets manufactured by this system shows decomposition time< 20 sec in an aqueous medium. The process involved in the spray drying technology is shown in Fig. 4 (13).

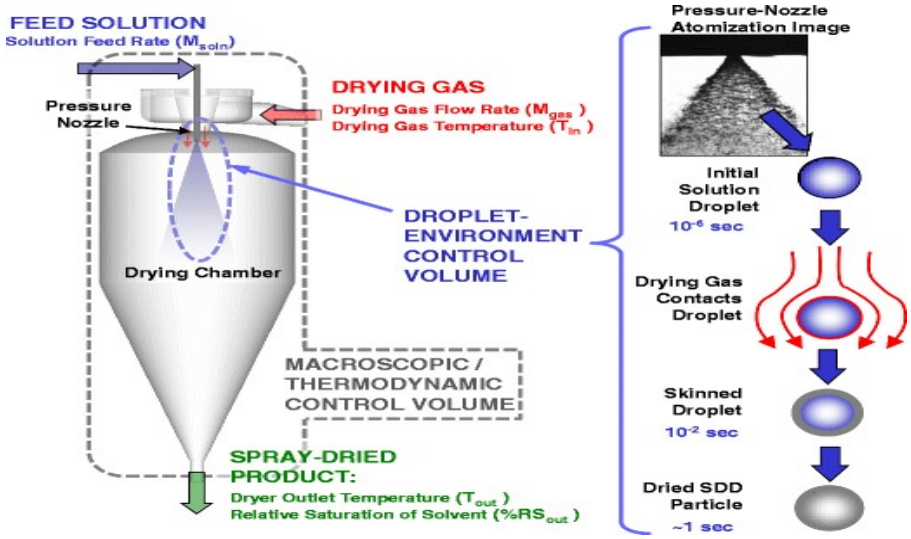

Fig 4 . Spray drying

Sublimation:

The introductory principle involved in preparing fast dissolving tablets by the sublimation technquie is addition of the volatile salt tableting factors, mixing the factors to the gain a mainly homogeneous mixture & volatizing a volatile salt. The removal for volatile salt creates pores in the tablet, which help in achieving rapid disintegration when the tablet comes in contact with saliva Camphor, Naphthalene, Urea, ammonium bicarbonate, etc, can be used to prepare porous tablets of good mechanical strength. used mannitol as the diluent and camphor as a volatile material to prepare porous compressed tablets. These tablets were subordinated to the vacuum at 80 °C for 30 min to eliminate the camphor and therefore form the pores into the tablet. employed water as a severance forming material in order to prepare pervious tablets with excellent mechanical strength and dissolution character. These way involved in the sublimation technology in Fig. 5**(14 -_17)**

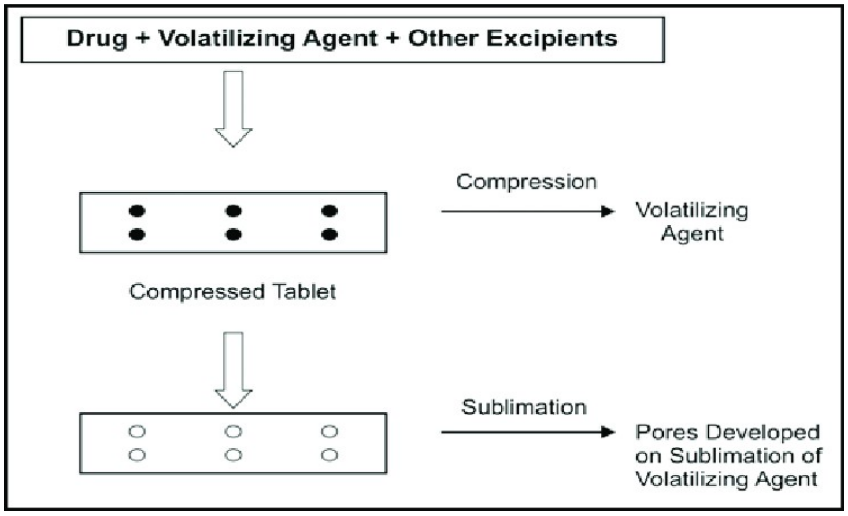

Fig. 5. Sublimation

Patented Technologies

Zydis technology:

Zydis is a unique snap dried oral solid lozenge form that can be administered without water and it dissolves incontinently on tongue in lower than 3 sec. The medicine is physically trapped in a water soluble matrix, and also indurate dried to produce a product that fleetly dissolves. The matrix consists of water answerable saccharides and polymer(gelatin, dextran, alginates) to give rapid-fire dissolution and to allow sufficient physical strength to repel running. Water is used during the process to produce pervious units for rapid-fire disintegration . various gums are used to exclude sedimentation problem of dispersed medicine. Glycine is used to help the loss of zydis unit during the process and long term storehouse. As the zydis doses form is weak in physical strength, unit is contained in peelable fester pack, which allows junking of product without damaging it. An ideal medicine seeker for zydis would be chemically stable and water insoluble and should have small particle size(lower than 50 microns). Water solouble drugs might form eutectic fusions and not indurate adequately, hence the dose is limited to 60 mg. larger medicine patches might present sedimentation problem during processing**(18)**

Durasolv technology:

It's also a patented technology by CIMA lab, producing alternate generation MDT's. The tablets prepared by this technology contain medicine, paddings, lubricant and tablets prepared by conventional

accoutrements . Durasolv formulations have advanced mechanical strength than its predesessors due to operation of advanced contraction pressure. Durasolv product is so durable that it can be packed in either traditional fester pack or vials. It's one of the applicable technologies for product taking low quantities of active constituents(19).

Wowtab technology:

Yamanauchi pharmaceutical company patented this technology. ‘ wow’ means ‘ without water’. The active constituents may constitute upto 50 w/ w of the tablet. In this technique , saccharides of both low and high mouldability are used to prepare the grains. Mouldability is the capacity of a emulsion to be compressed. largely mouldable substance has high compressibility and therefore shows slow dissolution. The combination of high and low mouldability is used to produce tablets of acceptable hardness. Active constituents are mixed with low mouldability saccharides and also granulated with high mouldabiity saccharides and also compressed into tablet. The Wowtab product dissolves quickly in 15 s or lower. Wowtab product can be packed in both into conventional bottle and blister packs [20].

preformulation studies mouth dissolving tablet

[21,22]

Preformulation study relates to medicinal and logical disquisition carried out pacing and supporting expression development sweats of the lozenge form of the medicine substance. Preformulation yields introductory knowledge necessary to develop suitable expression for the toxicological use. It gives information demanded to define the nature of the medicine substance and give frame work for the medicine combination with pharmaceutical excipients in the doses form. Hence, the following preformulation studies were performed on the attained sample of medicine.

1. Bulk Density (Db*):*

It is the ratio of total mass of powder to the bulk volume of powder. It is expressed in g/ml and is given by

Db = M/ Vb

Where, M is the mass of powder ,Vb is the bulk volume of the powder.

2. Tapped Density (Dt*):*

It is the ratio of total mass of the powder to the tapped volume of the powder. It is expressed in g/ml and is given by

Dt = M / Vt

Where, M is the mass of powder , Vt is the tapped volume of the powder.

3. Angle of Repose *(*q*):*

The friction forces in a loose powder can be measured by the angle of repose (q). It is an indicative of the flow properties of the powder. It is defined as maximum angle possible between the surface of the pile of powder and the horizontal plane

tan (q **) = h / r**

q = **tan-1 (h / r)**

Where, **q** is the angle of repose, **h** is the height in cms, **r** is the radius in cms.

Table 1: Angle of Repose as an Indication of Powder Flow Properties

Sr. No.	Angle of Repose	Type of Flow
1	<20	Excellent
2	20-30	Good
3	30-34	Passable
4	>34	Very poor

4. Carr's index (or) % compressibility*:*

It indicates powder flow properties. It is expressed in percentage and is give

I = Dt – Db × 100/Dt

Where, Dt is the tapped density of the powder and Db is the bulk density of the powder.

Evaluation of mouth dissolving tablets

1) Weight variation*:*[23]

Weight variation specification as per I.P. is shown in Table 2

Table 2: Weight Variation Specification as per IP

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

2) Hardness:

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

3) Friability (F): [24]

Friability of the tablet determined using Roche friabilator or Electro lab 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 I height of 6 inches in each revolution. Pre-weighted sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. Tablets were dusted using a soft muslin cloth and reweighed. The friability (F) is given by the formula.

F = W initial – W final x 100 / W initial

4) Mechanical Strength:

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

5) Crushing Strength:

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

6) Wetting time: [24]

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

dl/dt = r¡cosq**/(4**h**l)**

Where l is the length of penetration, r is the capillary radius, ¡ is the surface tension, h is the liquid viscosity, t is the time, and q is the contact angle. It is obvious that pores size becomes smaller and wetting time increases with an increase in compression force or a decrease in porosity. A linear relationship exists between wetting time and disintegration time. Thus wetting is the important step for disintegration process to take place. Wetting time corresponds to the time taken for the tablet to disintegrate when kept motionless on the tongue.

7) In vitro dispersion time[25]

Tablet was placed in 10 ml phosphate buffer solution, pH 6.8±0.5°C. Time required for complete dispersion of a tablet was measured.

8) In-vitro disintegration time[26]

The process of breakdown of a tablet into smaller particles is called as disintegration. The in-vitro disintegration time of a tablet was determined using disintegration test apparatus as per I.P. specifications. One tablet was placed in each of the 6 tubes of the basket. Add a disc to each tube and run the apparatus using pH 6.8 (simulated saliva fluid) maintained at 37±20C as the immersion liquid. The assembly should be raised and lowered between 30 cycles per minute in the pH 6.8 maintained at 37±20C. The time in seconds taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured and recorded.

9) Thickness Variation: [27]

Ten tablets from each formulation were taken randomly and their thickness was measured with a digital screw gauge micrometer. The mean SD values were calculated.

Conclusion

Mouth dissolving tablets can offer several biopharmaceutical advantages similar as bettered effectiveness over conventional doses forms. For illustration, they bear lower quantities of active component to be effective and offer better medicine bioavailability than regular tablets and capsules.

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