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Review on "Mouth Dissolving Tablet as Fast Dissolving Drug Delivery System"

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ABSTRACT

Numerous formulations with enhanced performance and acceptability have been developed in response to the need for greater palatability in oral given medications. Over the past several decades, demand for mouth dissolving tablets (MDTs) has grown steadily, and the pharmaceutical sector has seen a tremendous expansion in this field. One of the special qualities of mouth dissolving tablets is that they dissolve quickly and release the medication as soon as they come into contact with saliva. This eliminates the need for water when administering the medication. The applications and techniques of taste masking in the past are reviewed in this article, which also focuses on the most current advancements in bitterness reduction for drugs taken orally. In addition to the conventional methods of manufacturing, this review offers a thorough understanding of a few distinct patents; these technologies created and commercialised formulations of mouth dissolving tablets (MDTs).

***KEYWORDS**: Fast dissolving drug delivery system, mouth dissolving tablet, taste masking, patented technologies, evaluation.*

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INTRODUCTION

Tablets are solid dosage forms that contain single dose of one or more drugs. They are designed for oral administration. A tablet is made up of the active drugs and excipients, which are powdered ingredients that are compressed or pressed into a solid dosage form. Due to its self-administration ease, compactness, and ease of production, tablets are the most commonly used dosage form. However, elderly and young patients have trouble taking regular tablets, which results in low patient compliance. "Melt in mouth" or "mouth dissolve (MD)" tablets are the novel drug delivery methods created by scientists to address this shortcoming. These unique tablet designs dissolve, dissolve, and spread in saliva. Their unique benefits, such as the ability to be administered anywhere and at any time without the need for water, make them suitable for both elderly and paediatric patients. They are also appropriate for patients who are bedridden, suffer from mental illness, or lack simple access to water. These tablets are a common dosage form on the market today because of their advantages in terms of patient compliance, quick onset of action, increased bioavailability, and excellent stability. [(1)] Candidates for this dosage form include a wide variety of medications, including antibiotics, analgesics, narcotics, cardiovascular, and

antihistamines. Techniques like tablet molding, spray drying, lyophilization, sublimation, and the inclusion of disintegrants are used to create fast-dissolving tablets. Zydis, OraSolv, DuraSolv, Flash Dose, wow tab (Without Water), and Flashtab are a few of the proprietary methods for creating fast-dissolving tablets. These novel tablet varieties dissolve, disintegrate, or disperse in saliva in a matter of seconds without the need for water. These MDTs should dissolve or disintegrate in less than three minutes, as per the European Pharmacopoeia. The formulation is more beneficial for people who are bedridden and who have swallowing issues. [2]

The advantages of MDTs include quick action, increased bioavailability, increased patient compliance, and excellent stability, which make these tablets a popular dosage form on the market today. Another name for mouth-dissolving tablets is Oro dispersible tablets, also known as fast disintegrating tablets, orally disintegrating tablets, quick disintegrating tablets, fast dissolving tablets, rapid dissolving tablets, porous tablets, quick melt tablets, and rapid melt tablets. [3, 4]

➢ VARIOUS TYPES OF TABLETS: [5]

- Oral Tablets for Ingestion:

Compressed tablets
Multiple compressed tablets
Layered tablets
Compression-coated tablets
Repeat-action tablets
Delayed-action and enteric-coated tablets
Sugar coated tablets
Film coated tablets

- Tablets Used in the Oral Cavity:

Mouth Dissolving Tablets
Sublingual tablets
Troches and lozenges
Dental cones
Buccal tablets
Chewable tablets

- Tablets Administered by Other Routes:

Implantation tablets
Vaginal tablets

- Tablets Used to Prepare Solutions:

Effervescent tablets
Dispensing tablets
Hypodermic tablets
Tablet triturates

➢ **ADVANTAGES OF MOUTH DISSOLVING TABLETS: [6, 7]**

- **Accurate dosing -** Being unit solid dosage forms, they offer the benefits of precise dosing, simple manufacturing, excellent physical and chemical stability, and are an ideal alternative for paediatric and geriatric patients.
- **Enhanced bioavailability -**The absorption of drugs through the mouth, pharynx, and oesophagus increases their bioavailability.
- **Rapid action –**Rapid tablet disintegration, along with rapid dissolution and absorption in the oral cavity, results in a rapid onset of therapeutic action.
- **Patient compliance -**No need of water to swallow the tablet. It is convenient for patients who are travelling and do not have easy access to water.
- **Ease of administration -**Convenient to administer, particularly for elderly, paediatric, mentally ill, and bedridden patients with swallowing difficulties.
- **Obstruction free -**There is less chance of suffocation in the airways from physical obstruction when swallowed, improving safety and compliance.
- **Enhanced palatability -**Excellent mouthfeel, particularly for paediatric patients as taste masking techniques are used to prevent the drug's bitter taste.
- **Simple packaging -**No specific packaging required. Offer fresh business possibilities through life cycle management, line extension, and product differentiation.
- **Cost effective -** Conventional processing and packaging equipment's allow the manufacturing of tablets at low cost.

➢ **DISADVANTAGES OF MDTS: [8]**

- MDT must be stored in a dry environment due to its hygroscopic character.
- Some time it possesses mouth feeling.
- Drugs with larger doses are difficult to formulate.
- It also exhibits the fragile, effervescence granules property.
- MDT needs special packaging in order to stabilise and protect stable products properly.

➢ **CHARACTERISTICS OF MOUTH DISSOLVING DELIVERY SYSTEM: [9, 10]**

- Easy to administered: Fast Dissolving Delivery Systems are simple to use and manage, which improves patient compliance. Typically, elderly individuals have trouble swallowing the dosage forms like tablets and capsules.
- Taste of the drug: MDDD system typically contain the medication in taste-masked form

because most medications are unpleasant to consume. Taste masking of drug essential to patient compliance because delivery system dissolve or disintegrate in the patient's mouth.

- Hygroscopicity: Several fast-dissolving dosage forms are hygroscopic and unable to keep their physical integrity when exposed to humidity, requiring special packaging.
- Friability: Mouth dissolving tablets are typically packaged in specialised peel-off blister packaging because they prepared with less force during compression. These properties make the tablets brittle and/or friable, making handling them difficult.
- Mouth feel: Patients should be given a product that feels good in their mouths because mouth feel is important. Large tablet fragments that are slowly dissolve in saliva would cause a disagreeable gritty sensation. By reducing the particle size, this problem can be solved.

➢ CRITERIA FOR EXCIPIENTS USED IN THE PREPARATION OF MDTs: (11)

- It must be capable of disintegrate rapidly.
- It should not have any interaction with the drug and other ingredients or excipients such as agents used for taste masking of bitter drug.
- It should not interfere in the efficacy and organoleptic properties of the product.
- The concentration of the binder must be in adequate range and the binder should not affect the final integrity means disintegration and stability of the product.
- The properties of all the ingredients should not affect the MDTs.

The excipients used to formulate MDTs should have a melting temperature between 30-35^{0}C.

➢ CHALLENGES IN FORMULATION OF MDTs: (12)

- **Taste masking of drugs:**

Taste masking being an essential requirement for MDTs for commercial success. Drugs with bitter taste are difficult to formulate into mouth dissolving tablet. When a medication is administered orally, it is necessary to mask its bitter flavour. The choice of technology depends on the medication's bitterness and if it is compatible with taste-masking substances that do not reduce the bioavailability of the drug.

- **Quick disintegration of tablets: (13)**

In case of MDTs, the tablet disintegrates and dissolve within 3 min in salivary fluid present in mouth, an essential stage for the effectiveness of MDTs is their rapid disintegration, which can be accomplished through a variety of mechanisms, including

- **Swelling and Deformation:**

When a disintegrant (superdisintegrant) is added to the tablet formulation, it is believed to impart disintegration by a mechanism known as swelling and deformation. This mechanism is based on how the disintegrant swells when it absorbs water and rupturing the tablet matrix. due to induced localized stress within the tablet and thereby increasing the available space area and also promoting a more rapid release of the drug substance.

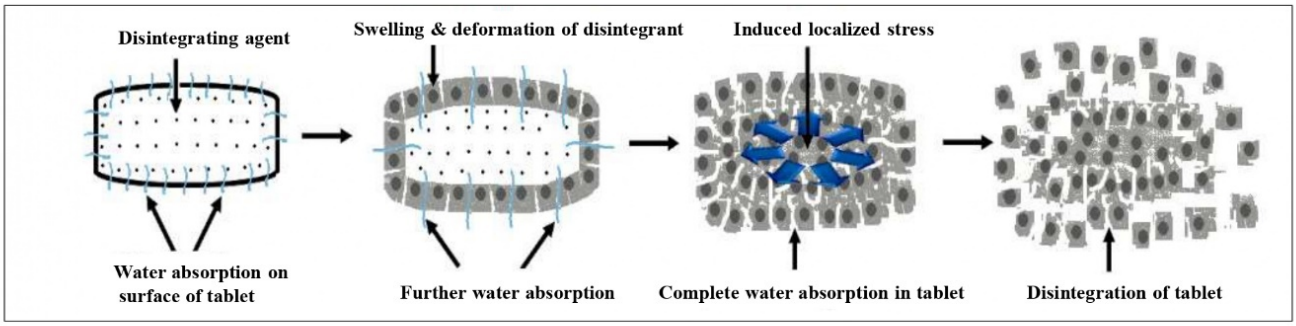

Fig 1. Swelling and Deformation

- **Porosity and Capillary Action (Wicking)**

This mechanism imparts its action by makes the tablet porous and provides the pathway for penetration of fluid into the tablet. Less cohesiveness and compressibility allow fluid to be sucked or wicked into these porous capillaries, and when these linkages rupture, the tablet disintegrates.

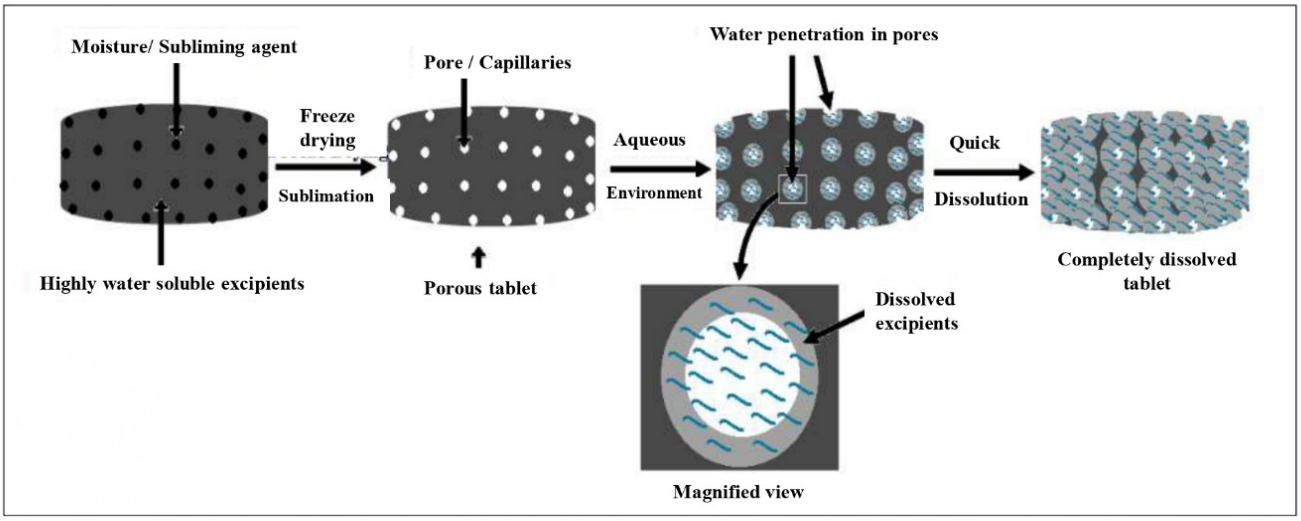

Fig 2. Quick Dissolution mechanism using porosity

- **Enzymatic Reaction**

Enzymes present in the body breaks the bond between particle and helps in disintegration by faster absorption of water leading to increase in the volume of particles to promote disintegration.

- **Release of Gases**

Interaction between Sodium bicarbonate and citric acid produces carbon dioxide which generates pressure within the tablet and causes the disintegration of the tablet and must be added to the formulation either immediately prior to compression or can be added in two separate fractions of formulation.

- **Industrial Adaptability**

MDTSs must be mechanically strong enough and robust to survive the rigours of manufacture in order to be adaptive in industrial manufacturing, handling and low sensitivity to environmental conditions (temperature and humidity) as well as cost effectiveness with adaptable and amenable to existing process and instruments.

- **Patient compliance**

MDTs reduce swallowing problems and prevent convert refusal in uncooperative patients, potentially reducing conformation with medical staff and must be compatible in term of taste, appearance, absence of undissolved particles, no requirement of water along with less time of stay in mouth.

- **Palatability**

The particles that are produced after the MDTs break apart should be as small as possible. Moreover, the addition of flavours and cooling agents like menthol improve the mouthfeel.

- **Hygroscopicity**

Many orally disintegrating dosage forms are hygroscopic and unable to maintain their physical integrity at normal temperatures and humidity conditions. They must therefore be protected from humidity, which necessitates the use of specialised product packing.

- **Amount of drug**

The quantity of drugs that can be included in each unit dose limits the application of technologies used for fast-dissolving tablets.

- **Size of tablet**

The size of a tablet affects how easily it can be administered. It has been said that tablets between 7-8 mm in size are the easiest to swallow, while those larger than 8 mm are the simplest to manage. Consequently, it is challenging to create tablets that are both simple to handle and easy to swallow.

- **Aqueous solubility**

Water-soluble pharmaceuticals provide a number of formulation issues due to the development of eutectic mixtures, which induce freezing-point depression and the formation of a glassy solid, which may collapse upon drying due to the loss of supporting structure during the sublimation process. The use of matrix-forming excipients like mannitol, which can induce crystallinity and hence contribute stiffness to the amorphous composite, might occasionally avoid such collapse.

➢ TASTE MASKING TECHNOLOGIES: [14]

Various physical and chemical techniques that prevent the interaction of the taste bud with drugs are frequently used for taste masking.

- **Flavour Modification and Sweeteners**

Being the easiest method for taste masking, using flavours from synthetic or natural sources allows for the modification of drugs unpleasant tastes. By occupying the taste buds and squelching the flavour of the drug, flavours and sweeteners drown out the unpleasant flavour. Citrus fruits have historically been used to disguise the mildly bitter and sour tastes of drugs, but this technique does not work for extremely bitter medications. It is also used to increase the palatability of formulations. Choosing flavours and sugars depends on how they taste and release energy. e.g., While sweeteners like saccharin sodium and acesulfame potassium (aspartame) provide immediate sweetness, monoammonium glycyrrhizate provides lingering sweetness and can be used alone or in conjunction with other sweeteners.

- **Viscosity Modification**

By creating a covering layer on the tongue and serving as a barrier between drug particles and taste buds, thickening agents like natural gums or carbohydrates can increase the viscosity of liquid formulations, thereby reducing the diffusion of drug from saliva into the taste buds and masking the unpleasant taste of the drug. Polyethylene glycols and carboxy methylcellulose are introduced to increase viscosity in liquid formulations, which unexpectedly also masks the taste of medicines with a bad taste while also increasing the stability of the liquid formulation.

- **Host Guest Locking Method**

In the host guest locking technique, the guest drug occupies a cavity in the host molecule, and two approaches are used to mask the taste of the guest drug.

1. By reducing its oral solubility and
2. By reducing the number of drug particles come in contact with taste buds.

Bitterness elimination is depended upon the complexation of Drug: Cyclodextrin, amount of complex association constant, host / guest ratio and temperature. For bitter drug forming a 1:1(Drug: CDs) complex with cyclodextrins, more than 99% of the bitter drug is complexed with cyclodextrins and as complexed molecule cannot react with the taste bud in the buccal cavity.

- **Drug Particle coating**

Involves covering the entire surface of the particle with enough coating to hide the bitter flavour of the drug from patients. To coat the bitter medicines, any nontoxic polymer that is insoluble at pH 6.2 and soluble at acidic pH is okay, as long as it is inert in nature.

- **Taste Masking by Ion Exchange Resins**: Ion exchange resins are cross-linked, high-molecular-weight polyelectrolytes that are water insoluble and contain repeating salt-forming groups that swap their mobile ions of equal charge with drug molecules. Because complexed drugs resonate do not release drug in oral cavity due to absence of exchangeable ions (at pH 6.7) in saliva, bitter drugs are perceived as tasting bitter in the oral cavity at the taste buds.
- **Solid Dispersion:** It is used to disperse one or more active pharmaceutical ingredients in an inert matrix or carrier in solid form to conceal bitter medicines. Methods used include melting method, solvent method, and melting solvent method. According to the definition of solid dispersion, it is "a dispersion involving the formation of eutectic mixtures of drugs with water soluble carriers by melting their physical mixture." In melting method, drug and solid carrier melted together, cooled and solidified whereas in solvent method, taste masking done by dissolving the drug and carrier in common solvent followed by evaporation.
- **Multiple Emulsions:** Multiple emulsions are complex poly dispersed systems having oil in water and water in oil emulsion simultaneously existence, stabilized by lipophilic and hydrophilic surfactants respectively, prepared by dissolution of drug in inner aqueous phase of w/o/w emulsion under good shelf stability condition. This technique successfully utilizes in masking the bitter taste of chloroquine (broad-spectrum antimalarial drug).
- **Chemical Modification**

1. Formation of salt or derivatives: Drugs that lose their flavour as a result of salt formation lose their ability to dissolve in saliva and become less permeable to taste buds. For example, Penicillin modified as N, N- di benzyl ethylenediamine diacetate salts is tasteless.

2. Prodrug formation: Prodrug, a chemically modified inert drug precursors, which upon biotransformation converts into pharmacologically active parent compound shows its activity.

- **Desensitizing agents**: By interfering with taste transduction, the process by which flavour signals from mouth to brain are transmitted, desensitising agents like phenols and sodium phenolates desensitise taste buds and thereby mask the bitter taste of drugs.
- **By using lipoproteins**: The bitter taste of drugs is most efficiently reduced by a lipoprotein made of lipids (phosphatidic acid) and protein (β lactoglobulin). Quinine, papaverine, caffeine, L-leucine, and propranolol are examples of basic and hydrophobic drugs with a very bitter taste. Phosphatidic acid-lactoglobulin effectively mask bitter taste of these drugs by binding to the hydrophobic region of receptor membranes and inhibiting the responses to the bitter substances.
- **By using amino acids**: When combined with bitter medications, amino acids and their salts (alanine, taurine, glutamic acid, and glycine) lessen the bitter taste of the drugs. For instance, glycine was utilized to prepare the granules of ampicillin, which were then combined with extra glycine, sweeteners, and flavours before being compressed into tablets.

➢ **MANUFACTURING TECHNILOGY FOR MDTs:** [15]

- **Freeze Drying/ Lyophilization**

Freeze-drying is process of removing water from an object after it has been frozen. Compared to other solid products on the market, freeze-dried forms give faster dissolution. The bulking agent and, in some cases, the medication receive a glossy, amorphous structure during the lyophilization process, which improves the formulation's dissolution properties. The high expense of the processing and equipment, however, limits the use of freeze-drying.

- **Tablet Moulding**

Solid dispersions are created when tablets are moulded. The substance may be present in the matrix as separate particles or as tiny particles. It can either completely dissolve in the molten carrier to create a solid solution or partially dissolve with the remaining particles remaining undissolved and distributed throughout the matrix.

Moulding process is of two types:

- **Solvent method-**

The powder mixture is moistened with hydroalcoholic fluid and formed into tablets at low compression pressure in moulded plates to create a wetted mass. (Compression moulding). After that, air drying is used to eliminate the solvent. These tablets' porous construction speeds up the dissolution.

- **Heat method-**

The powder mixture is moistened with hydroalcoholic fluid and formed into tablets at low compression pressure in moulded plates to create a wetted mass. (Compression moulding). After that, air drying is used to eliminate the solvent. These tablets' porous construction speeds up the dissolution. Typically, moulded tablets don't have a lot of mechanical power. When handling and opening blister packets, the moulded tablet frequently erodes and breaks.

- **Sublimation**

Compressed tablets with low porosity and highly water-soluble excipients as the tablet matrix material frequently take longer to dissolve in water. Heinnemann & Rose have created porous tablets that are strong mechanically and dissolve rapidly. The mixture of other tablet excipients and inert solid components, such as urea, urethane, ammonium carbonate, camphor, and naphthalene, was compressed into tablets. A porous structure was produced as a result of the sublimation of volatile substance. Makino has described a technique for making tablets that dissolve quickly by using water to create the pore structure. By using the sublimation method, compressed tablets containing D-Mannitol and camphor have been created. The tablets have good mechanical strength and break down in 10–20 seconds.

- **Spray-Drying**

Spray drying can create highly porous and fine powders because the processing liquid quickly evaporates during the drying process. Allen and Wang used the spray drying method to create tablets that dissolve quickly. They created a formulation using sodium starch glycolate as disintegrant, mannitol as a bulking agent, hydrolyzed and non-hydrolyzed gelatin as a support matrix, citric acid and/or sodium hydroxide as an alkali to improve dissolution. The tablets made from spray-dried powder dissolved in 20 seconds when come in contact with water.

- **Mass-Extrusion**

This method involves softening the blend using a solvent mixture of methanol and water-soluble polyethylene glycol, then ejecting the softened mass through an extruder to make tablets by cutting cylinder of product into uniform segments using a hot blade. The dried cylinder can also be used to coat drug granules with a bitter flavour, concealing their flavour.

- **Direct Compression**

It is the simplest method for making tablets. Direct compression uses standard machinery, readily accessible excipients, and a minimal number of processing stages. Additionally, large doses can be accommodated, and the final tablet weight can easily be greater than that of other production processes. Disintegrants, water-soluble excipients, and an effervescent agent may work separately or in combination to cause the disintegration of directly compressed tablets. Size and toughness of tablets have a significant impact on disintegrant effectiveness. Large and tough pills have a longer disintegration time than is typically needed. Insufficient physical resistance is the cause of tablet border breakage during handling and tablet rupture during blister alveolus opening. Disintegrants play a significant part in the direct compression-produced mouth-dissolving tablets' disintegration and dissolution processes. Choosing the right kind and quantity of disintegrant is crucial for achieving a high breakdown rate. Based on the force equivalent concept, which combines the measurement of swelling force development and quantity of water absorption, disintegration efficiency is calculated. Force equal describes the disintegrant's capacity to convert absorbed water into swelling force.

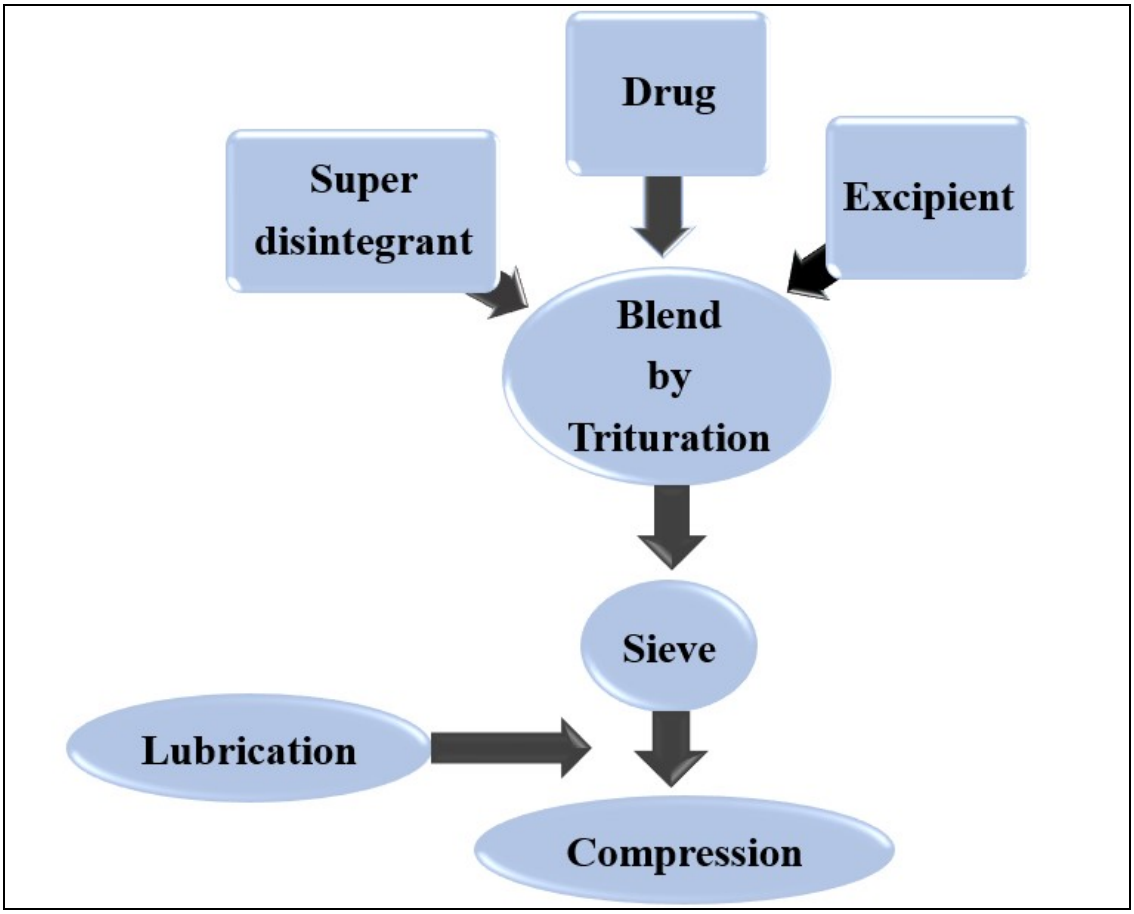

Fig 3. Direct Compression method

➢ PATENTED TECHNOLOGIES FOR MOUTH DISSOLVING TABLETS: [16, 17]

- **Zydis Technology**

In the Zydis technology, within a matrix of a rapidly dissolving carrier material drug is physically trapped or dissolved. This results in a unique freeze-dried tablet. Zydis units don't need water to help with digestion because the freeze-dried structure instantly disintegrates when placed in the mouth. The Zydis matrix is made up of a variety of components with various goals in mind. Polymers such as gelatin, dextran, or alginates are included to give strength and resilience during handling. These take the shape of a glossy, amorphous structure that gives off strength. Saccharides like sorbitol or mannitol are added to create crystallinity, beauty, and hardness. To produce porous pieces that break down quickly, water is used in the manufacturing process. Various gums are employed

during the production process to avoid the sedimentation of dispersed drug fragments. Glycine and other collapse protectors stop Zydis units from contracting during the freeze-drying process or during long-term preservation. Blister packs are used to package Zydis goods in order to shield the formulation from environmental moisture.

- **DuraSolv Technology**

The patented technology of CIMA labs is called DuraSolv. This technology creates tablets with a medication, fillers, and lubricant. Typical tableting equipment is used to create tablets, which have a high degree of rigidity. These can be put into a standard packaging method, such as blisters. A technology like DuraSolv is suitable for goods that only need small quantities of active ingredients.

- **OraSolv Technology**

OraSolv Technology developed at CIMA labs. This system masks the flavour of the active medication. Effervescent disintegrating substance is also present. To reduce the amount of time needed for oral dissolution, tablets are produced using the direct compression method at low compression force. The pills are produced using standard blenders and tablet presses. The manufactured tablets are packaged in specialised select and place systems and are soft and friable.

- **Flash Dose Technology**

Fuisz has patented flash dose technology. The first commercial product released by Biovail Corporation is an innovative form of ibuprofen called a "Nurofen Meltlet," which is made using flash dose technology. The self-binding shear form matrix used in flash dose pills is referred to as "floss." Through the use of flash thermal processing, shear form matrices are created.

- **Wowtab Technology**

Yamanouchi Pharmaceutical Co. has a trademark on Wowtab Technology. WOW means "Without Water." To create a rapidly melting, robust tablet, a combination of low mouldability and high mouldability saccharides is used in this procedure. The active component is combined with a saccharide that is low in moldability, granulated with a saccharide that is high in moldability, and compressed into a tablet.

- **Flashtab Technology**

Prographarm laboratories have patented the Flashtab technology. This system produces tablets with an active ingredient in the shape of microcrystals. All processing was done using standard tableting equipment.

- **Frosta® Technology for Making Fast-Melting Tablets**

The "Frosta®" fast-melting tablet device was developed by Akina. The Frosta® method makes use of traditional wet granulation processing and tablet machinery to produce fast-melting tablets at a low cost. Frosta tablets are stable in an open-air atmosphere and strong with less than 1% friability. No other specialised equipment is required for the manufacture of Frosta tablets, which are produced using standard tablet machines.

- **Pharmaburst**

The novel, simple-to-use "quick dissolve" tablet delivery technology from SPI Pharma is called Pharmaburst. Pharmaburst is an "off the shelf" excipient that makes it much easier and more affordable to create quick dissolve formulations internally.

- **Dispersible technology**

This technology has a patent owned by Lek in Yugoslavia. Water does not readily dissolve dihydroergotoxine in its free base state. Dispersible tablets containing 0.810%, ideally about 4% by weight, of an organic acid led to an improved dissolution rate of dihydroergotoxine methanesulphonate. A disintegrating substance was one of the crucial excipients used in the cimetidine formulation. Starch or modified polysaccharides, microcrystalline cellulose, alginic acid, cross-linked sodium carboxymethyl cellulose, and cyclodextrin polymers are some of the disintegrating agents. Dihydroergotoxine and cimetidine were advertised as having a one-minute disintegration time in water at ambient temperature.

- **Ora Quick technology**

K. V. S. Pharmaceuticals have a patent over this technology. It makes use of a taste-masking microsphere technology known as a micro mask, which offers a better mouth feel than taste-masking substitutes, considerable mechanical strength, and quick product disintegration /dissolution. The method of taste masking doesn't use any sort of solvents. As a result, it produces goods better and more quickly.

➢ **Evaluation test for mouth dissolving tablets:**

- **Pre-compression Evaluation of Powder Blend:** [18, 19, 20]

The powder blend was evaluated for the flow properties viz. Bulk density, Tapped density, Carr's index, Hausner's ratio and Angle of repose.

1. Bulk density-

The bulk density indicates the pore volume within the powder blend. Accurately weighed quantity of powder (*M in gm*) was transferred to measuring cylinder, and bulk volumes (*Vb in ml*) were measured. Bulk density was calculated by using formula,

$$Bulk\ density = \frac{Mass\ of\ powder(M)}{Bulk\ volume\ of\ the\ powder\ (Vb)}$$

2. Tapped density-

The tapped density of a powder blend is calculated to exclude the volume occupied by the voids and pores within the powder blend. Accurately weighted quantity of powder (*M in gm*) was transferred to measuring cylinder. The measuring cylinder was mounted on bulk density apparatus, and run for 100 tapings. The tapped volume of powders was measured (*Vt in ml*), and tapped density was calculated using formula,

$$Tapped\ density = \frac{Mass\ of\ powder(M)}{Tapped\ volume\ of\ the\ powder\ (Vt)}$$

3. Carr's Index-

It is a quick and straightforward indirect method to measure the relative strength of interparticle and frictional forces of bulk powders. It is expressed in % and given by formula,

$$Carr's\ index\ (\%) = \frac{Tapped\ Density(TD) - Bulk\ Density(BD)}{Tapped\ Density(TD)} \times 100$$

4. Hausner's ratio-

The powder's flowability and packing properties are determined by Hausner's ratio. It is ratio of Tapped density to Bulk density. A low Hausner's ratio indicates that powder particles are closely packed, with less voids and good flowability. This ratio indicates the ability of the bulk powder to rearrange in the particulate space presenting themselves during external forces like taping or vibration. Hausner's ratio is calculated using formula-:

$$Hausner's\ ratio = \frac{Tapped\ density(TD)}{Bulk\ density(BD)}$$

Standard Values of Carr's index and Hausner's Ratio as per Pharmacopoeia are as shown in Table 1.

Table 1. Standard Values of Carr's index and Hausner's Ratio

Carr's Index	Hausner's ratio	Property
≤10	1.00-1.11	Excellent
11-15	1.12-1.18	Good
16-20	1.19-1.25	Fair
21-25	1.26-1.34	Passable
26-31	1.35-1.45	Poor
32-37	1.46-1.59	Very poor
>38	>1.60	Very very poor

5. Angle of Repose-

Maximum angle that can be formed between a pile of powder's surface and a horizontal plane is known as the angle of repose. The angle of repose is correlated with the interparticle friction and the flowability of cohesion less material. It is the aggregate angle of an unconstrained heap of solutes with the horizontal. The angle of repose is a useful tool for calculating the frictional force in loose powder or granules. To calculate the powder blend's angle of repose, fixed funnel and standing cone method was used. The funnel's height was modified such that its tip just touches the highest point of the powder heap. Accurately measured quantity of powder blend was allowed to pass freely through a fixed funnel over a horizontal surface.

Then, powder cone's diameter was measured, angle of repose was calculated using following equation,

$$\tan\theta = \frac{h}{r}$$

$$\theta = tan^{-1}\frac{h}{r}$$

Where,
θ is the angle of repose, measured in degrees (^{0})
h is height of pile, measured in cms
r is radius of the base of pile, measured in cms.

Standard Values of Angle of Repose as per Pharmacopoeia are as shown in Table 2.

Table 2. Standard values of Angle of Repose

Angle of Repose	Flow property
25-30	Excellent
31-35	Good
36-40	Fair
41-45	Passable
46-55	Poor
56-65	Very poor
>66	Very, very poor

➢ **Post-compression Evaluation of MDT:** [21, 22, 23]

1. Tablet Appearance-
The general appearance of tablet includes shape, colour, surface texture.

2. Thickness-
Tablet thickness is measured for determination of uniformity in tablet size. Tablet thickness from each batch was measured using Vernier Caliper.

3. Weight Variation Test-
As per IP, weight variation test was carried out by random selection of 20 tablets. Initially individual weights of each tablet were measured followed by calculating average weight of 20 tablets. The value of weight variation tests was expressed in percentage (%) and calculated by using formula,

$$Average\ weight\ of\ Tablet = \frac{Total\ weight\ of\ 20\ Tablets}{20}$$

$$Weight\ Variation\ (\%) = \frac{IW\ of\ Tablet - AW\ of\ Tablets}{AW\ of\ Tablets} \times 100$$

IW= Individual Weight

AW= Average Weight

As per USP, the tablet complies the test if NMT 2 of the individual tablets deviate from the average weight by more than the percentage deviation as shown in Table 7.9 and none deviates by more than twice that percentage.

The results were compared with limits for weight variation test as per IP, BP, USP as given in Table 3.

Table 3. Limits for weight variation test as per IP, BP, USP

Average Weight (mg)		Percent Deviation (%)
IP/BP	USP	
80 mg or less	130 mg or less	± 10 %
More than 80 mg or less than 250 mg	130 mg to 324 mg	± 7.5 %
250 mg or more	More than 324 mg or more	± 5 %

4. Hardness-
The force needed to break a tablet across its diameter is referred to as the tablet's hardness. It helps to determine resistance of tablet for chipping, abrasion, or breaking during storage, transportation and handling. The hardness

of the tablet of from each formulation batch was determined using the Monsanto hardness tester. It consists of a barrel containing compressible spring held between spindle and anvil. Initially the screw knob was unturned, tablet was placed between anvil and spindle and zero reading was taken. Then screw knob was turned until tablet completely breaks and force of fracture was recorded in kilogram. The procedure was repeated for randomly selected tablets from each batch. The hardness can be expressed in kg/cm^2.

5. Friability test-

Friability test is carried out to determine physical strength of the tablets. Friability test was carried out using Friability tester (FT 1020 Labindia). It contains a plastic chamber that rotates at 25 revolutions per minute while dropping the tablets from a height of 6 inches with each revolution. The device enables the tablets for combined effect of abrasions and stress. Initially randomly selected 10 tablets were dedusted and weighed (Initial weight). The friabilator was loaded with pre-weighed tablets and operated for 25 RPM for 4 minutes. Then tablets unloaded from chamber, dedusted and reweighed (Final weight). The Friability (expressed as %) was calculated using formula,

$$Friability\ (\%) = \frac{Initial\ weight - Final\ weight}{Initial\ weight} \times 100$$

6. Wetting time-

Wetting time is closely related to the inner structure of the tablet and to the hydrophilicity of the excipients. As per equation proposed by Washburn E.W. IN 1921, the water penetration rate into the powder bed is proportional to the pore radius and is affected by hydrophilicity of the powders.

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

Where l is the length of penetration, r is the capillary radius, Υ is the surface tension, η is the liquid viscosity, t is the time, and θ is the contact angle. It is obvious that pore size becomes smaller and wetting time increases with an increase in compression force or a decrease in porosity. Thus, wetting is the important step for disintegration process to take place.

Procedure- A piece of tissue paper folded double was placed in a Petri plate containing 6ml of water. The tablet was placed on the paper and the time for complete wetting of the tablet was measured in seconds. The method was slightly modified by maintaining water at 37°C. Wetting time corresponds to the time taken for the tablet to disintegrate when kept motionless on the tongue.

7. Water absorption ratio-

In wetting time determination, weight of tablet (Wb) before wetting time test and weight of tablet after wetting time test (Wa) were measured. The water absorption ratio R was calculated using the formula,

$$R = \frac{Wa - Wb}{Wb} \times 100$$

Where,
Wa is weight of tablet after test,
Wb is weight of tablet before test.

8. *In-vitro* disintegration test-

The disintegration is a physical process related to mechanical breakdown of a tablet into smaller particles/granules representing the breakage of interparticle interactions generated during tablet compaction of granulated particles of API and excipients. Superdisintegrants play an important role in reducing tablet disintegration time by mechanisms viz. swelling, wicking and volume expansion. Superdisintegrants work by initial swelling of tablet followed by disintegration of tablet into smaller particles.

Procedure-: The USP disintegration test apparatus (DT 1000 Labindia) containing basket rack assembly was used. It consists of 6 glass tubes which are 3 inches long, open at the top and bottom and held against a 10-mesh screen at the bottom end. For disintegration test, one tablet was placed in each tube and the basket rack is placed in 900 ml phosphate buffer pH 6.8 (37 ± 0.5°C). A motor drives the basket up and down through distance 5 to 6 cm at a frequency of 28 to 32 cycles per minute. Perforated plastic discs were added to each tube which impart an abrasive action to the tablets and tablets remain floated. The time required for the tablet to completely disintegrate and leave no palpable mass in the tube was measured in seconds.

The test complies if the tablets disintegrate and all particles pass through 10-mesh screen in specified time.

9. Drug content-

It is an investigative or analytical procedure for assessing or measuring the presence, amount or functional activity of the drug. It mainly determines the concentration of a drug compared to labelled amount.

Ten tablets were randomly selected, crushed and powder blend equivalent to 10 mg of drug was dissolved in pH 6.8 phosphate buffer, and volume was made up upto 100 ml with pH 6.8 phosphate buffer. The solution was sonicated for 1 hour. From this solution, 1ml aliquot was withdrawn and diluted to 10 ml with pH 6.8 phosphate buffer. Solution was filtered and absorbance was measured spectrophotometrically (V-530, Jasco) at λmax 262 nm against by using pH 6.8 phosphate buffer as a blank. Total amount of drug present in each tablet was calculated using formula-:

$$Drug\ content(\%) = \frac{Absorbance\ of\ test}{Absorbance\ of\ standard\ at\ the\ same\ dilution} \times 100$$

10. In-vitro dissolution test-

In-vitro dissolution test is carried out to evaluate the variables that affect the rate and extent of drug release from finished dosage forms and in turn, *in-vivo* performance of the drug product. Also, it ensures that the product or batch being evaluated is having consistent quality and performance.

In-vitro dissolution test of was carried out by using USP dissolution test apparatus II (Paddle type, DS 8000 Labindia). The dissolution medium used was 900 ml of pH 6.8 Phosphate buffer, equilibrated at 37±0.5°C and paddle rotation speed maintained at 50 RPM. Aliquots of 5 ml were withdrawn at specified time and replaced with equal volume of fresh dissolution medium at 37±0.5°C. Aliquots withdrawn were filtered and analyzed at λmax 262 nm using UV visible spectrophotometer (V-530, Jasco).

11. Stability studies-

The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity, and light. Stability studies include testing of those attributes of the drug substance that are susceptible to change during storage and are likely to influence quality, safety, and/or efficacy. The testing should cover, as appropriate, the physical, chemical, biological, and microbiological attributes.

Randomly selected tablets were stored in amber colored rubber stoppered vials, at room temperature and elevated temperature i.e., 40 ± 2^0C / 75 ± 5% RH, in a Stability chamber (Bio-Technics India) for a period of 3 months.

Conclusion:

Due to their increased patient compliance, ease of administration, bioavailability, and quick start of action, MDTs have attracted the interest of several manufacturers for more than ten years. These advantages may outweigh those of traditional dosage forms. Using some of these technologies, FDT formulations are produced with enough mechanical strength and dissolve quickly in the mouth without the need for water. This particular market area has a definite possibility for the emergence of new and improved oral products. Roughly one-third of the population, mostly the younger and older populations, has swallowing issues. This implies that oral tablet drug therapy is not followed through on, which lowers the total efficacy of treatment. The tablets are made to dissolve or disintegrate quickly in saliva, usually in less than 60 seconds (with a range of 5 to 50 seconds). Additionally, the creation of a quick-dissolving tablet presents a chance for a product line expansion and Many medications (such as analgesics, antihistamines, cardiovascular medications, neuroleptics, and medications for erectile dysfunction) may be suitable candidates for this dose form. Pharmaceutical companies frequently develop a certain therapeutic entity in a new and better dosage form when the drug entity approaches the end of its patent life. A business can increase market exclusivity and provide a more convenient dosage form or dosing regimen to its patient by developing a new dosage form.

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