

## **RESENT ASPECT OF MOUTH DISSOLVING TABLET- AN OVERVIEW**

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### **Abstract**

Recently pharmaceutical preparations used for elderly patients have been investigated to improve the treatment compliances and quality of life of patients. Recent advances in Novel Drug Delivery System (NDDS) aims to enhance safety and efficacy of drug molecule by formulating a convenient dosage form for administration and to achieve better patient compliance. One such approach is “Mouth Dissolving Tablet” The concept of Mouth Dissolving Drug Delivery System emerged from the desire to provide patient with conventional mean of taking their medication. Difficulty in swallowing (Dysphagia) is a common problem of all age groups, especially elderly and pediatrics, because of physiological changes associated with these groups of patients. Other categories that experience problems using conventional oral dosage forms includes are the mentally ill, uncooperative and nauseated patients, those with conditions of motion sickness, sudden episodes of allergic attack or coughing. Some times it may be difficult to swallow conventional products due to unavailability of water. These problems led to the development of novel type of solid oral dosage form called “Mouth Dissolving Tablets”. This tablet disintegrates instantaneously when placed on tongue, releasing the drug that dissolves or disperses in the saliva. On placing mouth-dissolving tablet in the mouth, saliva serves to rapidly dissolve the dosage form. The saliva containing the dissolved or dispersed medicament is then swallowed and the drug is absorbed in the normal way. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach & it may produce rapid onset of action. In such a cases Bioavailability of drug is significantly greater than those observed from conventional tablet dosage form.<sup>19</sup> The dispersible tablets allows dissolution or dispersion in water prior to administration but the Mouth Dissolving Tablet instead of dissolving or disintegrating in water is expected to

dissolve or disintegrate in oral cavity without drinking water. The disintegrated mass then slides down smoothly along the esophagus along with saliva.

## **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<sup>1</sup>. 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<sup>2</sup>. 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<sup>3</sup>. 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<sup>4</sup>. Fast dissolving tablets are also called as mouth-dissolving tablets, melt-in mouth tablets, Orodispersible tablets, rapimelts, porous tablets, quick dissolving etc. Fast dissolving tablets are those when put on tongue disintegrate instantaneously releasing the drug which dissolve or disperses in the saliva<sup>5</sup>. The faster the drug into solution, quicker the absorption and onset of clinical effect. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach<sup>6</sup>. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablets dosage form. The advantage of mouth dissolving dosage forms are increasingly being recognized in both, industry and academics<sup>7</sup>. Their growing importance was underlined recently when European pharmacopoeia adopted the term “ Orodispersible tablet” as a tablet that to be placed in the mouth where it disperses rapidly before swallowing. According to European pharmacopoeia, the ODT should disperse/disintegrate in less than three minutes. The basic approach in development of FDT is the use of superdisintegrants like cross linked carboxymethyl cellulose

(croscarmellose), sodium starch glycolate (primogel, explotab), polyvinylpyrrolidone (polyplasdone) etc, which provide instantaneous disintegration of tablet after putting on tongue, they release the drug in saliva. The bioavailability of some drugs may be increased due to absorption of drug in oral cavity and also due to pregastric absorption of saliva containing dispersed drugs that pass down into the stomach. Moreover, the amount of drug that is subjected to first pass metabolism is reduced as compared to standard tablet.

### **Criteria for Mouth Dissolving Tablets**

The tablets should

- ❖ Not require water to swallow, but it should dissolve or disintegrate in the mouth in matter of seconds.
- ❖ Be compatible with taste masking.
- ❖ Be portable without fragility concern.
- ❖ Have a pleasant mouth feel.
- ❖ Leave minimum or no residue in the mouth after oral administration.
- ❖ Exhibit low sensitive to environmental condition as temperature and humidity.
- ❖ Allow the manufacture of the tablet using conventional processing and packaging equipments at low cost.

### **Salient Feature of Mouth Dissolving Tablets**

- ❖ Ease of Administration to the patient who can not swallow, such as the elderly, stroke victims, bedridden patients, patient affected by renal failure and patient who refuse to swallow such as pediatric, geriatric & psychiatric patients.
- ❖ No need of water to swallow the dosage form, which is highly convenient feature for patients who are traveling and do not have immediate access to water.
- ❖ Rapid dissolution and absorption of the drug, which will produce quick onset of action.

- ❖ Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases bioavailability of drug is increased.
- ❖ Pre-gastric absorption can result in improved bioavailability and as a result of reduced dosage; improve clinical performance through a reduction of unwanted effects.
- ❖ Good mouth feel property helps to change the perception of medication as bitter pill particularly in pediatric patient.
- ❖ The risk of choking or suffocation during oral administration of conventional formulation due to physical obstruction is avoided, thus providing improved safety.
- ❖ New business opportunity like product differentiation, product promotion, patent extensions and life cycle management.
- ❖ Beneficial in cases such as motion sickness, sudden episodes of allergic attack or coughing, where an ultra rapid onset of action required.
- ❖ An increased bioavailability, particularly in cases of insoluble and hydrophobic drugs, due to rapid disintegration and dissolution of these tablets.
- ❖ Stability for longer duration of time, since the drug remains in solid dosage form till it is consumed. So, it combines advantage of solid dosage form in terms of stability and liquid dosage form in terms of bioavailability.

## **FUNDAMENTALS OF MOUTH DISSOLVING TABLET**

For rapid dissolution or disintegration of dosage form, water must rapidly penetrate into the tablet matrix to cause quick disintegration & instantaneous dissolution of the tablet. Several techniques are used to achieve these fundamentals, to formulate mouth-dissolving tablet. Some of the techniques are described below.

## **Techniques for preparing Mouth Dissolving Tablets**

Many techniques have been reported for the formulation of mouth dissolve tablets or Mouth dissolving tablets.

- ❖ Freeze drying / lyophilization
- ❖ Tablet Moulding
- ❖ Spray drying
- ❖ Sublimation
- ❖ Direct compression
- ❖ Mass extrusion

### **Freeze-Drying or Lyophilization<sup>12</sup>**

Freeze drying is the process in which water is sublimed from the product after it is frozen. This technique creates an amorphous porous structure that can dissolve rapidly. A typical procedure involved in the manufacturing of ODT using this technique is mentioned here. The active drug is dissolved or dispersed in an aqueous solution of a carrier/polymer. The mixture is done by weight and poured in the walls of the preformed blister packs. The trays holding the blister packs are passed through liquid nitrogen freezing tunnel to freeze the drug solution or dispersion. Then the frozen blister packs are placed in refrigerated cabinets to continue the freeze-drying. After freeze-drying the aluminum foil backing is applied on a blister-sealing machine. Finally the blisters are packaged and shipped. The freeze-drying technique has demonstrated improved absorption and increase in bioavailability. The major disadvantages of lyophilization technique are that it is expensive and time consuming; fragility makes conventional packaging unsuitable for these products and poor stability under stressed conditions.

## **Tablet Molding**

Molding process is of two types i.e. solvent method and heat method. Solvent method involves moistening the powder blend with a hydro alcoholic solvent followed by compression at low pressures in molded plates to form a wetted mass (compression molding). The solvent is then removed by air-drying. The tablets manufactured in this manner are less compact than compressed tablets and possess a porous structure that hastens dissolution. The heat molding process involves preparation of a suspension that contains a drug, agar and sugar (e.g. mannitol or lactose) and pouring the suspension in the blister packaging wells, solidifying the agar at the room temperature to form a jelly and drying at 30°C under vacuum. The mechanical strength of molded tablets is a matter of great concern. Binding agents, which increase the mechanical strength of the tablets, need to be incorporated. Taste masking is an added problem to this technology.

The taste masked drug particles were prepared by spray congealing a molten mixture of hydrogenated cottonseed oil, sodium carbonate, lecithin, polyethylene glycol and an active ingredient into a lactose based tablet triturate form. Compared to the lyophilization technique, tablets produced by the molding technique are easier to scale up for industrial manufacture.

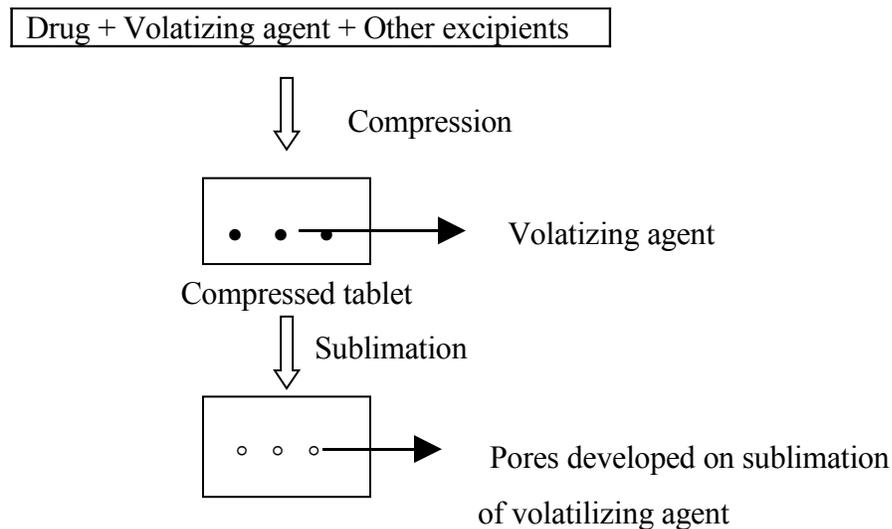
## **Spray Drying<sup>17</sup>**

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 superdisintegrants. Tablets manufactured from the spray-dried powder have been reported to disintegrate in less than 20 seconds in aqueous medium. The formulation contained bulking agent like mannitol and lactose, a superdisintegrant like sodium starch glycolate & croscarmellose sodium and acidic ingredient (citric acid) and/or alkaline ingredients (e.g. sodium bicarbonate). This spray-dried powder, which compressed into tablets showed rapid disintegration and enhanced dissolution.

## Sublimation

To generate a porous matrix, volatile ingredients are incorporated in the formulation that is later subjected to a process of sublimation. Highly volatile ingredients like ammonium bicarbonate, ammonium carbonate, benzoic acid, camphor, naphthalene, urea, urethane and phthalic anhydride may be compressed along with other excipients into a tablet. This volatile material is then removed by sublimation leaving behind a highly porous matrix. Tablets manufactured by this technique have reported to usually disintegrate in 10-20 sec. Even solvents like cyclohexane; benzene can be used as pore forming agents.

**Fig. No 1:**Steps involved in sublimation



## Direct Compression

Direct compression represents the simplest and most cost effective tablet manufacturing technique. This technique can now be applied to preparation of ODT because of the availability of improved excipients especially superdisintegrants and sugar based excipients.

➤ **Superdisintegrants:**

In many orally disintegrating tablet technologies based on direct compression, the addition of superdisintegrants principally affects the rate of disintegration and hence the dissolution. The presence of other formulation ingredients such as water-soluble excipients and effervescent agents further hastens the process of disintegration.

**(b) Sugar Based Excipients:**

This is another approach to manufacture ODT by direct compression. The use of sugar based excipients especially bulking agents like dextrose, fructose, isomalt, lactilol, maltitol, maltose, mannitol, sorbitol, starch hydrolysate, polydextrose and xylitol, which display high aqueous solubility and sweetness, and hence impart taste masking property and a pleasing mouthfeel. Mizumoto et al have classified sugar-based excipients into two types on the basis of molding and dissolution rate.

Type 1 saccharides (lactose and mannitol) exhibit low mouldability but high dissolution rate.

Type 2 saccharides (maltose and maltitol) exhibit high mouldability and low dissolution rate.

**Mass-Extrusion<sup>23, 24</sup>:**

This technology involves softening the active blend using the solvent mixture of water-soluble polyethylene glycol and methanol and subsequent expulsion of softened mass through the extruder or syringe to get a cylinder of the product into even segments using heated blade to form tablet. The dried cylinder can also be used to coat granules for bitter drugs and thereby achieve taste masking.

## **Important Patented Technologies for Mouth Dissolving Tablets**

**1. Zydis Technology<sup>25</sup>:**

Zydis formulation is a unique freeze dried tablet in which drug is physically entrapped or dissolved within the matrix of fast dissolving carrier material. When zydis units are put into the mouth, the freeze-dried structure disintegrates instantaneously and does not require

water to aid swallowing. The zydis matrix is composed of many material designed to achieve a number of objectives. To impart strength and resilience during handling, polymers such as gelatin, dextran or alginates are incorporated. These form a glossy amorphous structure, which imparts strength.

To obtain crystallinity, elegance and hardness, saccharides such as mannitol or sorbitol are incorporated. Water is used in the manufacturing process to ensure production of porous units to achieve rapid disintegration while various gums are used to prevent sedimentation of dispersed drug particles in the manufacturing process. Collapse protectants such as glycine prevent the shrinkage of zydis units during freeze-drying process or long-term storage. Zydis products are packed in blister packs to protect the formulation from moisture in the environment.

## **2. Durasolv Technology<sup>26, 27</sup>:**

Durasolv is the patented technology of CIMA labs. The tablets made by this technology consist of drug, filler and a lubricant. Tablets are prepared by using conventional tableting equipment and have good rigidity.

These can be packaged into conventional packaging system like blisters. Durasolv is an appropriate technology for product requiring low amounts of active ingredients.

## **3. Orasolv Technology<sup>28</sup>:**

CIMA labs have developed Orasolv Technology. In this system active medicament is taste masked. It also contains effervescent disintegrating agent. Tablets are made by direct compression technique at low compression force in order to minimize oral dissolution time. Conventional blenders and tablet machine is used to produce the tablets. The tablets produced are soft and friable.

## **4. Flash Dose Technology<sup>29, 30</sup>:**

Flash dose technology has been patented by fuisz. Nurofen meltlet, a new form of ibuprofen as melt in mouth tablets prepared using flash dose technology is the first commercial product launched by biovail corporation. Flash dose tablets consist of self-binding shear form matrix termed as “floss”. Shear form matrices are prepared by flash heat processing.

### **5. Wow tab Technology <sup>30</sup>:**

Wow tab technology is patented by Yamanouchi Pharmaceutical Co. WOW means “Without Water”. In this process, combination of low mouldability saccharides and high mouldability saccharides is used to obtain a rapidly melting strong tablet. The active ingredient is mixed with a low mouldability saccharide (eg. lactose, glucose, and mannitol) and granulated with a high mouldability saccharide (eg. Maltose, oligosaccharides) and compressed into tablet.

### **6. Flash tab Technology <sup>29,30</sup> :**

Prographarm laboratories have patented the Flash tab technology. Tablet prepared by this system consists of an active ingredient in the form of micro crystals. Drug micro granules may be prepared by using the conventional techniques like coacervation, micro encapsulation and extrusion spheronisation. All the processing, utilized conventional tableting technology.

## **Mechanism of Superdisintegrants**

There are four major mechanisms for tablets disintegration as follows

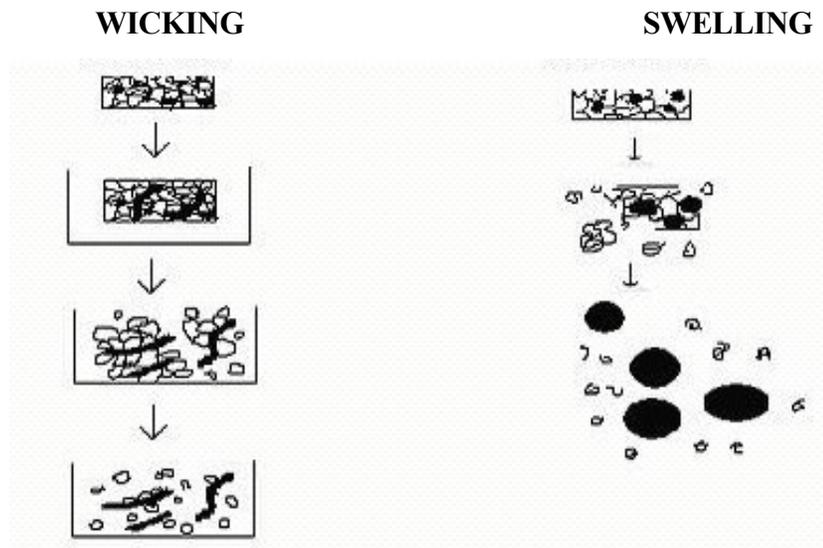
### **➤ Swelling:**

Perhaps the most widely accepted general mechanism of action for tablet disintegration is swelling. Tablets with high porosity show poor disintegration due to lack of adequate swelling force. On the other hand, sufficient swelling force is exerted in the tablet with low porosity. It is worthwhile to note that if the packing fraction is very high, fluid is unable to penetrate in the tablet and disintegration is again slows down.

### **➤ Porosity and capillary action (Wicking):**

Disintegration by capillary action is always the first step. When we put the tablet into suitable aqueous medium, the medium penetrates into the tablet and replaces the air adsorbed on the particles, which weakens the intermolecular bond and breaks the tablet into

fine particles. Water uptake by tablet depends upon hydrophilicity of the drug /excipient and on tableting conditions. For these types of disintegrants maintenance of porous structure and low interfacial tension towards aqueous fluid is necessary which helps in disintegration by creating a hydrophilic network around the drug particles.



Water is pulled by disintegrant  
And reduced the physical  
Bonding force between particles

Particles swell and break up  
the matrix form within

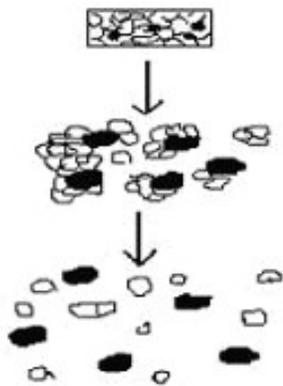
### 3. Due to disintegrating particle/particle repulsive forces

Another mechanism of disintegratn attempts to explain the swelling of tablet made with 'non-swellaable' disintegrants. Guyot-Hermann has proposed a particle repulsion theory based on the observation that nonswelling particle also cause disintegration of tablets. The electric repulsive forces between particles are the mechanism of disintegration and water is required for it. Researchers found that repulsion is secondary to wicking.

#### 4. Due to deformation

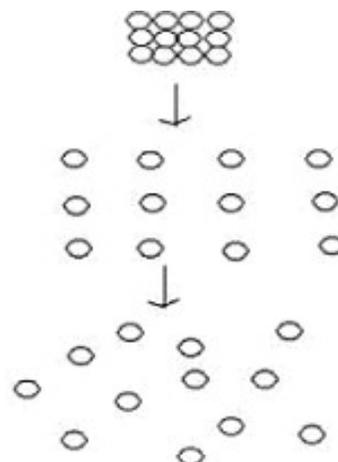
During tablet compression, disintegrated particles get deformed and these deformed particles get into their normal structure when they come in contact with aqueous media or water. Occasionally, the swelling capacity of starch was improved when granules were extensively deformed during compression. This increase in size of the deformed particles produces a break up of the tablet. This may be a mechanism of starch and has only recently begun to be studied.

DEFORMATION



Particles swell to precompression  
Size and break up matrix

REPULSION



Water is drawn into pores and  
particles repel each other because of  
Resulting electrical force.

#### ➤ LIST OF SUPERDISINTEGRANTS

Superdisintegrants	Example	Mechanism Of action	Special comment
Crosscarmellose <sup>®</sup> Ac-Di-Sol <sup>®</sup> Nymce ZSX <sup>®</sup> Primellose <sup>®</sup> Solutab <sup>®</sup> Vivasol <sup>®</sup> L-HPC	Crosslinked cellulose	-Swells 4-8 folds in < 10 seconds. -Swelling and wicking both.	-Swells in two dimensions. -Direct compression or granulation -Starch free
Crosspovidone Crosspovidon M <sup>®</sup> Kollidon <sup>®</sup> Polyplasdone <sup>®</sup>	Crosslinked PVP	-Swells very little and returns to original size after compression but act by capillary action	-Water insoluble and spongy in nature so get porous tablet
Sodium starch glycolate Explotab <sup>®</sup> Primogel <sup>®</sup>	Crosslinked starch	-Swells 7-12 folds in < 30 seconds	-Swells in three dimensions and high level serve as sustain release matrix
Alginic acid NF Satialgine <sup>®</sup>	Crosslinked alginic acid	-Rapid swelling in aqueous medium or wicking action	-Promote disintegration in both dry or wet granulation
Soy polysaccharides Emcosoy <sup>®</sup>	Natural super disintegrant		-Does not contain any starch or sugar. Used in nutritional products.
Calcium silicate		-Wicking action	Highly porous, Optimum concentration is between 20-40%

## Conclusion

Conventional tablets available in market are not suitable where quick onset of action is required. Besides, the conventional tablets also show poor patient compliance particularly by the geriatric and pediatric patients who experience difficulty in swallowing, and by those who are bed ridden or who are traveling and do not have an easy access of water. To provide the patients with the most conventional mode of administration, there was a need to develop rapidly disintegrating dosage form, particularly one that disintegrants and dissolves/disperses in saliva and can be administered without need of water, anytime, anywhere, such tablets are called as mouth dissolving tablets.

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