

## **FORMULATION AND EVALUATION OF MOUTH DISSOLVING TABLETS**

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### **ABSTRACT**

Mouth dissolving drug delivery is rapidly gaining acceptance as an important new drug delivery technology. The aim the study was to prepare and characterize fast dissolving tablets (MDT). Orally disintegrating tablets provide an advantage particularly for paediatric and geriatric populations who have difficulty in swallowing conventional tablets and capsules. Literature on ODTs, their formulation and evaluation methods, patented technologies along with recent research in this area is reviewed in this article.

**KEYWORDS:** Mouth dissolving tablets, formulation, evaluation.

### **INTRODUCTION**

The oral route of administration is considered as the most widely accepted route. But the most evident drawback of the commonly used oral dosage forms like tablets and capsules is difficulty in swallowing, leading to patients' in compliance particularly in case of paediatric and geriatric patients.<sup>[1]</sup> Recently fast dissolving drug delivery systems have started gaining popularity and acceptance as one such example with increased consumer choice, for the reason of rapid disintegration or dissolution, self administration even without water or chewing. Fast dissolving tablets are also applicable when local action in the mouth is desirable such as local anaesthetics for toothaches, oral ulcers, cold sores, or teething, and to those who cannot swallow intact sustained action tablets/capsules.<sup>[2]</sup>

Fast dissolving tablets are also known as melt in-mouth tablets, mouth dissolving tablets, repimelts, porous tablets, orodispersible, quick dissolving or rapid disintegrating tablets<sup>[3]</sup>, Effervescent drug absorption system, Orosolv, Zydis etc.

Fast dissolving technology is one of the best opportunities to improve bioavailability, immediate relief and patient compliance in comparison to conventional tablets. Fast dissolving drug delivery can be achieved by various conventional methods like direct compression, wet granulation, moulding, spray drying, freeze drying and sublimation. In order to allow fast dissolving tablets to dissolve in the mouth, they are made of either very porous and soft-moulded matrices or compressed into tablets with very low compression force, which makes the tablets friable or brittle, which are difficult to handle, often requiring specialized peel off blister packaging. Fast dissolving tablets disintegrate or dissolve rapidly in the saliva without the need for water. They 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. When put on the tongue, this tablet disintegrates instantaneously, releasing the drug, which dissolves or disperses in the saliva.<sup>[4]</sup>

Currently these tablets are available in the market for treating many disease conditions like hypertension, migraine, dysphasia, nausea, vomiting, Parkinson's disease, schizophrenia and paediatric emergency.<sup>[5-9]</sup> Several drugs belonging to various pharmacological categories.<sup>[10,11]</sup>

### **Ideal Characteristics of Orodispersible Tablets<sup>[12]</sup>**

#### **Mouth Feel**

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

#### **Hygroscopicity**

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

**Friability**

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

Orally disintegrating tablets offer all advantages of solid dosage forms and liquid dosage forms along with special advantages, which include.

- i. As ODTs are unit solid dosage forms, they provide good stability, accurate dosing, easy manufacturing, small packaging size, and easy to handle by patients.<sup>[13, 14, 15, 16, 17]</sup>
- ii. No risk of obstruction of dosage form, which is beneficial for travelling patients who do not have access to water.
- iii. Easy to administer for pediatric, geriatric and institutionalized patients (specially for mentally retarded and psychiatric patients)
- iv. Rapid disintegration of tablet results in quick dissolution and rapid absorption which provide rapid onset of action.<sup>[18]</sup>
- v. Medication as "bitter pill" has changed by excellent mouth feel property produced by use of flavours and sweeteners in ODTs.
- vi. Bioavailability of drugs that are absorbed from mouth, pharynx, and oesophagus is increased.<sup>[19, 20, 21]</sup>
- vii. Pre-gastric absorption of drugs avoids hepatic metabolism, which reduces the dose and increase the bioavailability.<sup>[22]</sup>

The advantage of mouth dissolving dosage forms are increasingly being recognised in industry and academics, in both.<sup>[23]</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. 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, their by release the drug in saliva. More ever, the amount of drug that is subjected to first pass metabolism is reduced as compared to standard tablet. Recently

Orally disintegrating (OD) tablet technology has been approved by United States Pharmacopoeia (USP), Centre for Drug Evaluation and Research (CDER). USFDA defined OD tablet as “A solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue”.<sup>[23]</sup>

#### **Advantages of mouth dissolving tablets<sup>[24-26]</sup>**

- 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 pediatrics, 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.
- Good mouth feel property of mouth dissolving drug delivery system helps to change the basic view of medication drugs.
- 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.
- Pre-gastric absorption can result in improved bioavailability, reduced dose and improved clinical performance by reducing side effects.
- New business opportunities: product differentiation, line extension and life-cycle management, exclusivity of product promotion and patent-life extension.<sup>[27,28]</sup>

#### **Formulation**

##### **Excipients commonly used in formulation of mouth dissolving tablets<sup>[29-32]</sup>**

Mainly seen excipients in FDT are disintegrant, a diluent, a lubricant and optionally, a swelling agent, a permeabilizing agent and flavourings.

**Disintegrants**, are an essential component to tablet formulations. They are agents which are added to tablet and some encapsulated formulations to promote the breakup of the tablet and capsule “slugs” into smaller fragments in an aqueous environment thereby increasing the available surface area and promoting a more rapid release of the drug substance. The ability to interact strongly with water is essential to disintegrate function. The major function to oppose the efficiency of the tablet binder and the physical forces that act under compression to form the tablet. The stronger the binder, the more effective must be the disintegrating agents in order for the tablet to release its medication. They promote moisture penetration and

dispersion of the tablet matrix.<sup>[33]</sup> Ideally, it should cause the tablet to disrupt, not only into the granules from which it was compressed, but also into powder particles from which the granulation was prepared. It is essential to choose a suitable disintegrant, in an optimum concentration so as to ensure quick disintegration and high dissolution rates. Super disintegrant provide quick disintegration due to combined effect of swelling and water absorption by the formulation. Due to swelling of super disintegrant, the wetted surface of the carrier increases; this promotes the wettability and dispersibility of the system, thus enhancing the disintegration and dissolution. Super disintegrates are selected according to critical concentration of disintegrant. Below this concentration, the tablet disintegration time is inversely proportional to the concentration of the super disintegrant, whereas if concentration of super disintegrant is above critical concentration, the disintegration time remains almost constant or even increases.

There are three methods of incorporating disintegrating agent into the tablet.<sup>[34,35]</sup>

- (i). Internal addition (Intragranular)
- (ii). External addition (Extragranular)
- (iii). Partly internal and external.

**Table 1. Some examples of enzymes as disintegrating agents are.**

Enzyme	Binder
Amylase	Starch
Protease	Gelatin
Cellulose	Cellulose and its derivatives

### Types of super disintegrants

Natural, These are various plant based material. Plant based material serve as an alternative to synthetic products because of following reasons.

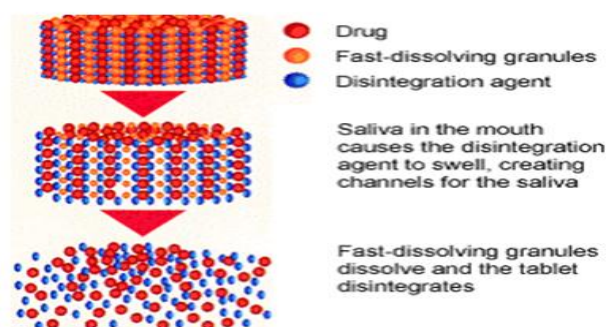
- Local accessibility
- Eco-friendly
- Bio-acceptable
- Renewable source and low price as compared to synthetic products
- Example: Lepidus sativum, Locust bean gum, Isapgula Husk (Plantago ovata), Hibiscus rosa sinensis linn. Mucilage etc.

Synthetic, Advantages of synthetic superdisintegrants:

- Effective in lower concentrations than starch.

- Less effect on compressibility and flow ability.
- More effective intragranularly

Co processing, is defined as combining two or more established excipients by an appropriate process.<sup>[36,37]</sup> Co-processing is a process in which two or more excipients interacting at the sub particle level, the objective of which is to provide a synergy of functionality improvements as well as masking the undesirable properties of individual excipients. The main aim of co processing is to obtain a product with added value related to the ratio of its functionality price. Co processing is interesting because the products are physically modified in a special way without altering the chemical structure. A fixed and homogenous distribution for the components is achieved by embedding them within mini granules. The use of the co-processed excipient combines the advantages of wet granulation with direct compression.<sup>[38]</sup> Most important characteristics are binding and blending properties of the co processed excipients, which must be better than those of a physical mixture of the starting materials. Cost is another factor to be considered in the selection of co processed product. Co-processing of excipient could lead to formation of excipients with superior properties compared with the simple physical mixture of their components or with individual components. A large number of co-processed diluents are commercially available. The representative examples are ludipress, cellactose and starlac. The use of coprocessing is a totally unexplored avenue in disintegrants. The widely used superdisintegrants are sodium starch glycolate, crospovidone and croscarmellose sodium. Like diluents each superdisintegrant has strengths and weaknesses. One of the reasons for preparing the coprocessed superdisintegrant was to avoid the problem of segregation. A blend of swelling and wicking types of excipient may also prove to be efficient because the medium (usually water) required for swelling will be brought into the tablet more easily if a wicking (hydrophilic) type of superdisintegrant is also present.<sup>[39,40]</sup>



**Fig 1. Mechanism of disintegration.**

**Emulsifying Agents**, are important excipients for formulating fast-melting tablets they aid in rapid disintegration and drug release without chewing, swallowing or drinking water. In addition, incorporating emulsifying agents is useful in stabilizing the immiscible blends and enhancing bioavailability. A wide range of emulsifiers is recommended for fast tablet formulation, including alkyl sulfates, propylene glycol esters, lecithin, sucrose esters and others. These agents can be incorporated in the range of 0.05 percent to about 15 percent by weight of the final composition.

**Lubricants**, though not essential excipients, can further assist in making these tablets more palatable after they disintegrate in the mouth. Lubricants remove grittiness and assist in the drug transport mechanism from the mouth down into the stomach.

**Flavours and Sweeteners**, flavours and taste-masking agents make the products more palatable and pleasing for patients. The addition of these ingredients assists in overcoming bitterness and undesirable tastes of some active ingredients. Both natural and synthetic flavors can be used to improve the organoleptic characteristic of fast-melting tablets. Formulators can choose from a wide range of sweeteners including sugar, dextrose and fructose, as well as non-nutritive sweeteners such as aspartame, sodium saccharin, sugar alcohols and sucralose. The addition of sweeteners contributes a pleasant taste as well as bulk to the composition.<sup>[41]</sup>

### Techniques

Many techniques have been reported for the formulation of Fast dissolving tablets or Oro dispersible tablets.

- I. Freeze drying/lyophilization
- II. Tablet Moulding
- III. Spray drying
- IV. Sublimation
- V. Direct compression
- VI. Mass extrusion
- VII. Cotton candy process
- VIII. Fast dissolving Films.



**I. Freeze-drying or lyophilisation<sup>[13,42-44]</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. According to general procedure, 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 aluminium foil backing is applied on a blister-sealing machine. Finally the blisters are packaged and shipped. 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.

**II. Tablet molding**

Molding process is of two type's 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. 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 300C 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.<sup>[45]</sup>

**III. Spray drying**

In this technique, gelatin can be used as a supporting agent and as a matrix, mannitol as a bulking agent and sodium starch glycolate or croscarmellose or crospovidone are used as



super disintegrants. Tablets manufactured from the spray-dried powder have been reported to disintegrate in less than 20 seconds in aqueous medium. This spray-dried powder, which compressed into tablets showed rapid disintegration and enhanced dissolution.

#### **IV. 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.

#### **V. 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.

a. Super disintegrants, 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. This is another approach to manufacture ODT by direct compression.

b. Sugar based excipients, the use of sugar based excipients especially bulking agents like dextrose, fructose, isomalt, lactitol, 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.

#### **VI. Mass-extrusion<sup>[46]</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.

## VII. Cotton Candy Process

This process is so named as it utilizes a unique spinning mechanism to produce floss-like crystalline structure, which mimic cotton candy. Cotton candy process<sup>[47]</sup> involves formation of matrix of polysaccharides or saccharides by simultaneous action of flash melting and spinning. The matrix formed is partially recrystallized to have improved flow properties and compressibility. This candy floss matrix is then milled and blended with active ingredients and excipients and subsequently compressed to ODT. This process can accommodate high doses of drug and offers improved mechanical strength. However, high-process temperature limits the use of this process.

## VIII. Fast dissolving films

In this technique, a non-aqueous solution is prepared containing water soluble film forming polymer (pullulan, carboxy methylcellulose, hydroxypropyl methylcellulose, hydroxyl ethylcellulose, hydroxyl propylcellulose, polyvinyl pyrrolidone, polyvinyl alcohol or sodium alginate, etc.) drug and other taste masking ingredients, which is allowed to form a film after evaporation of solvent. In case of a bitter drug, resin adsorbate or coated microparticles of the drug can be incorporated into the film<sup>30</sup>. This film, when placed in mouth, melts or dissolves rapidly, releasing the drug in solution or suspension form. The features of this system include paper thin films of size less than 2 x 2 inches, dissolution in 5 sec, instant drug delivery and flavored after taste.

Conventional methods for formulating tablets such as dry granulation<sup>[48]</sup>, wet granulation<sup>[49]</sup> and direct compression methods were adapted to produce ODTs.

## Patented Technologies<sup>[50,51]</sup>

### Zydis technology

Using the concept of Gregory et al., R.P. Scherer has patented zydis technology. Zydis is a unique freeze-dried oral solid dosage form that can be swallowed without water as it dissolves instantly on tongue in less than 5 seconds. The drug is physically trapped in a water-soluble matrix and then freeze-dried to produce a product that rapidly dissolves. The matrix consists of water soluble saccharides and polymer (gelatin, dextran, alginates) to

provide rapid dissolution and to allow sufficient physical strength to withstand handling. Water is used during the process to produce porous units for rapid disintegration. Various gums are used to eliminate the sedimentation problem of dispersed drugs. Glycine is used to prevent the shrinkage of zydis unit during the process and in long-term storage. As the zydis dosage form is weak in physical strength, unit is contained in peelable blister pack, which allows removal of product without damaging it.

### **Orasolv technology**

CIMA labs have developed Orasolv technology. The system essentially makes tablets that contain taste masked active ingredients and effervescent disintegrating agent which on contact with saliva, rapidly disintegrates and releases the taste mask active ingredient. The tablets made by direct compression at very low compression force in order to minimize oral dissolution time. The tablets so produced are soft and friable and are packaged specially designed pick and place system. The taste masking associated with Orasolv formulation is two folds. The unpleasant flavour of a drug is not merely counteracted by sweeteners or flavours; coating the drug powder and effervescence are means of taste masking in Orasolv.

### **Durasolv technology**

Durasolv is CIMA's second generation fast dissolving tablet formulation. Produced in a similar fashion to that of orasolv, durasolv has much higher mechanical strength than its predecessor due to the use of higher compaction produced during tableting. The durasolv product is thus produced in a faster and more cost effective manner. One disadvantage of durasolv is that the technology is not compatible with larger doses of active ingredients, because formulation is subjected to high pressures on compaction. Durasolv is currently available in two products nulev and zorlip.

### **WOWTAB technology**

WOWTAB technology is patented by Yamanouchi Wow means "without water". WOWTAB is an intrabuccally soluble, compressed tablet consisting of granules made with saccharides of low and high mouldability. The combination of high and low mouldability is used to obtain a tablet of adequate hardness and fast dissolution rate. Mouldability is the capacity of the compound to be compressed. Low mouldability means the compounds show reduced compressibility for tableting and rapid dissolution rate. But in case of high mouldability compounds this context is reversed. In this the active ingredient is mixed with low mouldability saccharides and granulated with high mouldability saccharides and then

compressed into tablet. The wowtab formulation is stable to environment due to its significant hardness than Zydis or Orasolv. WOWTAB product is suitable both for conventional bottle and blister packaging.

#### **Flash dose technology (Fuisz Technologies, Ltd.)**

Fuisz has patented the Flash Dose technology. The Flash Dose technology utilizes a unique spinning mechanism to produce floss like crystalline structure, much like cotton candy. This crystalline sugar can then incorporate the active drug and be compressed into a tablet. Flash Dose tablet consists of self-binding sheaform matrix termed “floss”. The procedure has been patented by Fuisz and known as “Shearform”. Interestingly, by changing the temperature and other conditions during production, the characteristics of the product can be altered greatly. Instead of floss- like material, small spheres of saccharide can be produced to carry the drug. The procedure of making microspheres has been patented by Fuisz and known as “Ceform”.

#### **Shearform technology TM**

The technology is based on the preparation of floss that is also known as ‘Shearform Matrix’, which is produced by subjecting a feed stock containing a sugar carrier by flash heat processing. In this process, the sugar is simultaneously subjected to centrifugal force and to a temperature gradient, which raises the temperature of the mass to create an internal, flow condition, which permits part of it to move with respect of the mass. The floss so produced is amorphous in nature so it is further chopped and recrystallised by various techniques to provide aciform flow properties and this facilitate blending the recrystallised matrix is then blended with other tablet excipients and an active ingredient. The resulting mixture is compressed into tablet.

#### **Ceform technology TM**

In ceform technology microspheres containing active ingredient are prepared. The essence of ceform microsphere manufacturing process involves placing a dry powder, containing substantially pure drug material or a special blend of drug materials plus other pharmaceutical compounds, and excipients into a precision engineered and rapidly spinning machine. The centrifugal force of the rotating head of the ceform machine throws the dry drug blend at high speed through small heated openings. The microspheres are then blended and/or compressed into the pre-selected oral delivery dosage format. The ability to simultaneously process both drug and excipient generates a unique microenvironment in

which materials can be incorporated into the microsphere that can alter the characteristics of the drug substance.

### **Oraquick technology**

The oraquick fast dissolving tablet formulation utilizes a patented taste masking technology by K. V. Pharmaceutical Company, who claim that its taste masking technology i.e. microsphere technology (micromask) has superior mouth feel over taste masking alternatives. The taste masking process does not utilize solvents of any kind and therefore leads to faster and more efficient production. Tablet with significant mechanical strength without disrupting taste masking are obtained after compression.

### **Fastwrap system**

Bio Progress had developed novel tablet cores with a high disintegration profile that were easily coated using the Tab Wrap finishing process. The Fast Wrap system combines the Tab Wrap process with the company's patented novel tablet core technology to create coated tablets that can rapidly disintegrate and dissolve, allowing for a faster onset of action. The Fast Wrap technology can also be used to manufacture film-flavoured orally disintegrating tablets. As standard coating techniques tend to involve spraying on a coating that has been dissolved in liquid, they have run into problems with tablets that incorporate highly moisture sensitive superdisintegrants or excipients. The Tab Wrap system, on the other hand, is a completely dry coating process.

### **Nano crystal technology**

RDT, Elan's proprietary Nano Crystal technology can enable formulation and improve compound activity and final product characteristics. Decreasing particle size increases the surface area, which leads to an increase in dissolution rate. This can be accomplished predictably and efficiently using Nano Crystal technology. Nano Crystal particles are small particles of drug substance, typically less than 1000 nanometers (nm) in diameter, which are produced by milling the drug substance using a proprietary wet milling technique.

### **Evaluation**<sup>[52,53]</sup>

MDTs formulations have to be evaluated for the following evaluation test.

### **Size and shape**

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

**Tablet thickness**

Tablet thickness is an important characteristic in reproducing appearance and also in counting by using filling equipment. Some filling equipment utilizes the uniform thickness of the tablets as a counting mechanism. Ten tablets were taken and their thickness was recorded using micrometer.

**Uniformity of weight**

As per I.P. procedure for uniformity of weight was followed, 20 tablets were taken and their weight was determined individually and collectively on a digital Weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of determining the drug content uniformity.

**Tablet hardness**

Hardness of tablet is defined as the force applied across the diameter of the tablet in the order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. Hardness of the tablet of each formulation was determined using Monsanto Hardness tester.

**Friability**

It is measured of mechanical strength of tablets. Roche friabilator was used to determine the friability by following procedure. A pre weighed tablet was placed in the friabilator. Friabilator consist of a plastic-chamber that revolves at 25 rpm, dropping those tablets at a distance of 6 inches with each revolution. The tablets were rotated in the friabilator for at least 4 minutes. At the end of test tablets were dusted and reweighed, the loss in the weight of tablet is the measure of friability and is expressed in percentages:

$$\% \text{ Friability} = \text{loss in weight} / \text{Initial weight} \times 100$$

**Wetting time**

The method reported by Yunixia et al., was followed to measure tablet wetting time. A piece of tissue paper (12 cm X 10.75 cm) folded twice was placed in a small petridish (ID = 6.5 cm) containing 6 ml of Sorenson's buffer pH 6.8. A tablet was put on the paper and the time for complete wetting was measured. Three trials for each batch and the standard deviation were also determined.

**Moisture uptake studies**

Moisture uptake studies for ODT should be conducted to assess the stability of the formulation. Ten tablets from each formulation were kept in a desiccator over calcium chloride at 37°C for 24 h. The tablets were then weighed and exposed to 75% relative humidity, at room temperature for 2 weeks. Required humidity was achieved by keeping saturated sodium chloride solution at the bottom of the desiccator for 3 days. One tablet as control (without superdisintegrant) was kept to assess the moisture uptake due to other excipients. Tablets were weighed and the percentage increase in weight was recorded.

**Disintegration test**

The time for disintegration of ODTs is generally <1 min and actual disintegration time that patient can experience ranges from 5 to 30 s. The standard procedure of performing disintegration test for these dosage forms has several limitations and they do not suffice the measurement of very short disintegration times. The disintegration test for ODT should mimic disintegration in mouth with in salivary contents.

**Dissolution test**

The development of dissolution methods for ODTs is comparable to the approach taken for conventional tablets and is practically identical. Dissolution conditions for drugs listed in a pharmacopoeia monograph, is a good place to start with scouting runs for a bioequivalent ODT. Other media such as 0.1 N HCl and buffers (pH - 4.5 and 6.8) should be evaluated for ODT much in the same way as conventional tablets.

USP dissolution apparatus 1 and 2 can be used. USP 1 Basket apparatus may have certain applications, but sometimes tablet fragments or disintegrated tablet masses may become trapped on the inside top of the basket at the spindle where little or no effective stirring occurs, yielding irreproducible dissolution profiles.

The USP 2 Paddle apparatus at 50-100 rpm is suitable for dissolution testing of taste-masked drug as well. The media used for the taste-masked drug should match that of the finished product to maximize the value of the test. High performance liquid chromatography (HPLC) is often required to analyze dissolution aliquots due to presence of UV absorbing components, specifically flavours and sweetener.



## CONCLUSION

Orodispersible tablets (ODTs) are innovative drug delivery systems and have potential advantages over conventional dosage forms, with their improved patient compliance, convenience, bioavailability and rapid onset of action.

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