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Review Article

# ORODISPERSIBLE TABLETS: A REVIEW

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**ABSTRACT**

Orally disintegrating tablets (ODTs) are solid dosage forms containing drugs that disintegrate in the oral cavity within less than 1 minute leaving an easy-to-swallow residue. The European Pharmacopeia adopted the term orodispersible tablet for a tablet that disperses or disintegrates within <3 minutes in the mouth before swallowing. ODT is a good choice of drug delivery for pediatric and geriatric patients because it troubleshoots the problem of dysphagia. The current article is focused on ideal characteristics, advantages and disadvantages, various technologies developed for ODT, evaluation methods along with recent research and future potential.

**Keywords:** Orodispersible tablets, Mechanism of disintegration, Fast dissolving films, Recent research.

## INTRODUCTION

Solid dosage forms are popular because of low cost, ease of administration, accurate dosage self-medication, pain avoidance, and the most importantly the patient compliance. The most popular solid dosage forms are being tablets and capsules [1,2]. One important drawback of such dosage forms is Dysphagia, or difficulty in swallowing is common among all age groups. Common complaints about the difficulty in swallowing tablets are size, surface, and taste of tablets. Geriatric and pediatric patients and traveling patients, who may not have ready access to water, are most in need of easy swallowing dosage forms [3]. To fulfill these medical needs, pharmaceutical technologists have developed a novel oral dosage form known as ODTs which disintegrate rapidly in saliva, usually within a matter of seconds, without the need to take it water. Drug dissolution and absorption, as well as onset of clinical effect and drug bioavailability, may be significantly greater than those as compared with conventional dosage forms [4-6]. ODTs releases the medicament in the mouth for absorption through local oromucosal tissue and through pre-gastric (oral cavity, pharynx, and esophagus), gastric (stomach), and post-gastric (small and large intestine) segments of gastrointestinal tract (GIT) [7].

ODTs are also called as orodispersible tablets, quick disintegrating tablets, mouth dissolving tablets, fast disintegrating tablets, fast dissolving tablets, rapid dissolving tablets, porous tablets, and rapidmelts. However, of all the above terms, United States pharmacopoeia (USP) approved these dosage forms as ODTs. The European Pharmacopoeia has used the term orodispersible tablet for tablets that disperses readily within 3 minutes in the mouth before swallowing [3]. United States Food and Drug Administration defined ODT as "A solid dosage form containing a medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue." The disintegration time for ODTs generally ranges from several seconds to about a minute [8].

## IDEAL PROPERTIES OF ORODISPERSIBLE TABLETS [9]

- Not require water to swallow and should dissolve or disintegrate in the mouth within a few seconds
- High drug loading
- Be compatible with taste masking and other excipients
- Have a pleasing mouth feel
- Leave minimal or no residue in the mouth after oral administration
- Exhibit low sensitivity towards environmental conditions such as humidity and temperature
- Be adaptable and amenable to existing processing and packaging machinery.

## ADVANTAGES OF ORODISPERSIBLE TABLETS [10]

- Administration to patients who cannot swallow, like the elderly, stroke victims and bedridden patients; patients who should not swallow, like renal failure patients; and patients who refuse to swallow, such as pediatrics, geriatric and psychiatric patients
- Patient's compliance for disabled bedridden patients and for traveling and busy people, who do not have ready access to water
- Good mouth feel property helps to change the basic view of medication as "bitter pill," particularly for pediatric patients due to improved taste of bitter drugs
- The 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 esophagus which may produce rapid onset of action
- Pregastric 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.

## DISADVANTAGE OF ORODISPERSIBLE TABLETS [9,11]

- Orodispersible is hygroscopic in nature so must be keep in dry place
- Sometime it possesses mouth feeling
- ODT requires special packaging for properly stabilization and safety of stable product
- Dose uniformity is a technical challenge.

## SELECTION OF THE ODTS DRUG CANDIDATES [12]

Several factors must be considered when selecting drug candidates for delivery as ODT dosage forms:

- The drugs which have significantly different pharmacokinetic profiles compared with the same dose administered in a conventional dosage form. E.g., selegiline, apomorphine, buspirone, etc.
- The drugs that produce a significant amount of toxic metabolites mediated by first pass liver metabolism and gastric metabolism and for drugs that have a substantial fraction of absorption in the oral cavity and segments of the pre-gastric GIT
- Drugs are having the ability to diffuse and partition into the

epithelium of the upper GIT (log P > 1, or preferable > 2); and those able to permeate oral mucosal tissue are considered ideal for ODT formulations
- Patients who concurrently take anticholinergic medications may not be the best candidates for these drugs
- Patients with Sjogren's syndrome or dryness of the mouth due to decreased saliva production may not be good candidates for ODT formulations
- Drugs which are having a short half-life and needs frequent dosing, which are very bitter or either having unacceptable taste whose taste masking cannot be achieved or which require controlled or sustained release are inappropriate for ODT formulation.

## CHALLENGES IN THE FORMULATION OF ODTS

**Mechanical strength and disintegration time**
ODTs are formulated to obtain disintegration time usually less than a minute. While doing so, maintaining a good mechanical strength is a prime challenge. Many ODTs are fragile, and there are many chances that such fragile tablet will break during packing, transport or handling by the patients. It is very natural that increasing the mechanical strength will delay the disintegration time. Hence, a good compromise between these two parameters is always essential [13].

**Tastes masking**
Many drugs are bitter in taste. A tablet of bitter drug dissolving/ disintegration in the mouth will seriously affect patient compliance and acceptance for the dosage form. Hevce, effective taste masking of the bitter drugs must be done so that the taste of the drug is not felt in the oral cavity [13].

**Aqueous solubility**
Water-soluble drugs pose various formulation challenges because they form eutectic mixtures, which result in freezing-point depression and the formation of a glassy solid that may collapse upon drying because of loss of supporting structure during the sublimation process. Such collapse sometimes can be prevented using various matrix-forming excipients such as mannitol that can induce crystallinity and hence, impart rigidity to the amorphous composite [14].

**Size of tablets**
The degree of ease when taking tablets depends on its size. It has been reported that the easiest size of tablet to swallow is 7-8 mm while the easiest size to handle was one larger than 8 mm. Therefore, the tablet size that is both easy to take and easy to handle is difficult to achieve [14].

**Amount of drug**
The application of technologies used for ODTs is limited by the amount of drug that can be incorporated into each unit dose. According to USP generally, the ODT tablet weight should not exceed 500 mg. For lyophilized dosage form, the drug dose should be lower than 400 mg for insoluble drug and <60 mg for soluble drug. This parameter is particularly challenging when formulating a fast-dissolving oral films or wafers [9].

**Hygroscopicity**
Several orally disintegrating 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 [9].

**Mouth feel**
ODTs should not disintegrate into larger particles in the oral cavity. The particles generated after the disintegration of the ODTs should be as small as possible. Moreover, addition of flavors and cooling agents like menthol improve the mouth feel [13].

**Good packaging design**
For the protection of ODTs from moisture and other environmental hazards, the package design should be considered early in the development stages [14].

## TECHONOLOGIES FOR PREPARING ORODISPERSIBLE TABLETS

Various technologies used in the manufacture of orodispersible tablets include:
- Freeze-drying or lyophilization
- Tablet Molding
- Spray drying
- Sublimation
- Melt granulation
- Cotton candy process
- Mass extrusion
- Phase transition
- Nanonization
- Fast dissolving films
- Direct compression.

**Freeze drying or lyophilization**
Freeze drying or lyophilization is a process in which solvent is removed from a frozen drug solution or suspension containing structure forming excipients. Tablets formulated by this technique are usually very light and porous in nature which allows their rapid dissolution. The glassy amorphous porous structure of excipients, as well as the drug substance produced with freeze drying, results in enhanced dissolution. Freeze drying process normally consists of three steps:
- Material is frozen to bring it below the eutectic point
- Primary drying to reduce the moisture around 4% w/w of dry product
- Secondary drying to reduce the bound moisture up to required final volume.

Entire freeze drying process is carried out at non-elevated temperature; therefore, nullifying adverse thermal effects that may affect drug stability during processing [15].

**Tablet molding**
The major components of molded tablets typically are water-soluble ingredients. The powder mixture is moistened with a solvent (usually ethanol or water), and then the mixture is molded into tablets under pressures lower than those used in conventional tablet compression. (This process is known as compression molding). Then the solvent can be removed by air drying. Because molded tablets are usually compressed at a lower pressure than are conventional compressed tablets, a higher porous structure is created to enhance the dissolution. To improve the dissolution rate, the powder blend usually has to be passed through a very fine screen. Recently, the molded forms have also been prepared directly from a molten matrix in which the drug is dissolved or dispersed (known as heat molding) or by evaporating the solvent from a drug solution or suspension at ambient pressure (novacuum lyophilization) [16].

**Spray drying**
Spray drying is a process by which highly porous, fine powders can be produced. Spray dryers are invariably used in the pharmaceutical industry to produce highly porous powders. Allen *et al.* have reported applying this process to the production of fast dissolving tablets [16].

The main aim of drying is to obtain dry particles with desired properties. Orally disintegrating tablets are made up of hydrolyzed or unhydrolyzed gelatin as supporting agent for the matrix, mannitol as a bulk agent, and sodium starch glycolate and croscarmellose sodium as a disintegrating agent. Sometimes in order to improve the disintegration and dissolution, citric acid and sodium bicarbonate are used. Finally, the formulation is spray-dried in a spray drier. ODTs prepared through this method are disintegrated in <20 seconds [17]. Maximum drug release and minimum disintegration time were observed with kollidon CL excipient base as compared to tablets prepared by direct compression, showing the superiority of the spray dried excipient base technique over direct compression technique [10].

**Sublimation**
The slow dissolution of the compressed tablet containing even highly water-soluble ingredients is due to the low porosity of the tablets. Inert solid ingredients that volatilize readily (e.g., urea, ammonium carbonate, ammonium bicarbonate, hexamethelenetetramine, camphor, etc.) were added to the other tablet ingredients, and the mixture is compressed into tablets. The volatile materials were then removed via sublimation, which generates porous structures. In addition, several solvents (e.g., cyclohexane, benzene) can also be used as pore forming agents [11].

Tablets manufactured by this technique are reported to usually disintegrate in 10-20 seconds. Mannitol and camphor were used, respectively, as tablets matrix and subliming material. Camphor was vaporized by subliming in vacuum at 80°C for 30 minutes to develop pores in the tablets [12].

**Melt granulation**
Melt granulation technique is a process by which pharmaceutical powders are efficiently agglomerated by a meltable binder. The advantage of this technique compared to conventional granulation is that no water or organic solvents are needed. For accomplishing this process, high shear mixers are utilized, where the product temperature is raised above the melting point of the binder by a heating jacket or by the heat of friction generated by impeller blades. This approach to prepare FDT with sufficient mechanical integrity involves the use of a hydrophilic waxy binder (Superpolystate©, PEG-6-stearate). Superpolystate© is a waxy material with a melting point of 33-37°C and an HLB value of 9. So it will not only act as a binder and increase the physical resistance of tablets but will also help the disintegration of the tablets as it melts in the mouth and solublises rapidly leaving no residues [18].

**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. It is also known as the candy floss process [18].

Cotton candy process 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 [19].

**Mass extrusion**
It involves softening the active blend using the solvent mixture of water soluble polyethylene glycol, using methanol and expulsion of softened mass through the extruder or syringe to get a cylinder of the product into even segments using the heated blade to form tablets [14].

**Phase transition**
A novel method to prepare ODTs with sufficient hardness by involving the phase transition of sugar alcohol. In this technique, ODTs are produced by compressing and subsequently heating tablets that contain two sugar alcohols, one with high and other with a low melting point. The heating process enhances the bonding among particles leading to sufficient hardness of tablets which was otherwise lacking owing to low/little compatibility [19].

**Nanonization**
A recently developed Nanomelt technology involves a reduction in the particle size of drug to nanosize by milling the drug using a proprietary wet-milling technique. The nanocrystals of the drug are stabilized against agglomeration by surface adsorption on selected stabilizers, which are then incorporated into ODTs. This technique is, especially advantageous for poorly, water soluble drugs. Other advantages of this technology include fast disintegration/dissolution of nanoparticles leading to increased absorption and hence higher bioavailability and reduction in dose, cost effective manufacturing process, conventional packaging due to exceptional durability, and wide range of doses (up to 200 mg of drug per unit) [10].

**Fast dissolving films**
It is a new frontier in ODTs that provides a very convenient means of taking medications and supplements. In this technique, a non-aqueous solution is prepared containing water soluble film forming polymer (pullulan, carboxymethylcellulose, 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. 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 <2×2 inches, dissolution in 5 seconds, instant drug delivery and flavored after taste [20].

**Direct compression**
Direct compression represents the simplest and the most cost-effective tablet manufacturing technique for ODTs as they can be fabricated using conventional tablet manufacturing and packaging machinery and also due to availability of tableting excipients with improved flow, compressibility and disintegration properties, especially tablet disintegrants, effervescent agents and sugar based excipients [20].

**Superdisintegrants**
In many ODT 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 [20].

**Effervescent agents**
The evolution of $CO_2$ as a disintegrating mechanism forms the basis of the patented Orasolv technology (OT) and is frequently used to develop over-the counter formulations. The product contains microparticles and is slightly effervescent in nature. Saliva activates the effervescent agent which causes the tablet to disintegrate [20].

**Sugar based excipients**
This is another approach to manufacture ODT by direct compression. The use of sugar-based excipients is 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 mouth feel [12]. Mizumito *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 maltilol) exhibit high mouldability and low dissolution rate [12].

**PATENTED TECHNOLOGIES FOR ORODISPERSIBLE TABLETS**

There are number of patented technologies which were developed for the formation of orodispersible tablets and are described as under:

**Zydis technology**
Zydis® technique is owned by Scherer, a subsidiary of Cardinal Health [21]. This technology uses freeze drying process for manufacturing of the tablets, in which the active drug is incorporated in a water-soluble matrix, which is then transformed into blister pockets and freeze dried to remove water by sublimation. Matrix is made up of a number of ingredients like gelatin, dextran or alginates to impart

strength during handling these form a glossy and amorphous structure, mannitol or sorbitol is added to impart crystallinity, elegance, and hardness, various gums may be added to prevent sedimentation of dispersed drug particles. Collapse protectants like glycine may be used to prevent shrinkage of dosage form during freeze drying and long-term storage [14]. The Zydis product is made to dissolve on the tongue in 2-3 seconds. Zydis formulation is very lightweight, fragile and has poor stability at higher temperatures and humidities. It readily absorbs water and is very sensitive to degradation at humidity >65% [22].

**Quick-dis technology**

The novel intra-oral drug delivery system, trademarked as Quick-Dis™, is Lavipharm's proprietary patented technology and is a thin, flexible, and quick-dissolving film. When the film is placed on the top or the floor of the tongue, it is retained at the site of application and rapidly releases the active agent for local or systemic absorption. The typical disintegration time is only 5-10 seconds for the Quick-Dis™ film with a thickness of 2 mm [22].

**Oraquick technology**

The Oraquick fast dissolving/disintegrating tablets formulation utilizes a patented taste masking technology. This taste masking process does not utilize solvents of any kind, so leads to faster and more efficient production. During processing low-heat is produced so this technique is suitable for heat sensitive drugs. KV Pharmaceuticals also claims that the matrix that surrounds and protects the drug powder in microencapsulated particle is more pliable. This technique gives tablets with good taste masking and quick dissolution in a matter of seconds [23].

**Durasolv technology**

Durasolv® is Patented technology of CIMA lab's second-generation ODT tablet formulation, produced in a fashion similar to OraSolv, Which requiring low amounts of active ingredients and the tablets consist of drug, filler and a lubricant. Tablets are prepared using conventional tableting equipment and have good rigidity (friability less than that 2%). These can be packaged into conventional packaging system like blisters, pouches or vials. Much higher mechanical strength than its predecessor due to the use of higher compaction pressures during tableting [22]. The newest Durasolv® formulation, NuLev®, is actually dispensed in stock bottles [21].

**OT**

CIMA labs have developed OT. In this system, active medicament is taste masked. It also contains the 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 [19].

**Shearform technology**

This technology is based on the preparation of floss that is also known as "Shearform Matrix," which is produced by subjecting a feedstock containing a sugar carrier by flash heat processing. In this procedure, 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 recrystallized. The recrystallized matrix is then blended with other tablet excipients and an active ingredient. The resulting mixture is compressed into tablets [9].

**Flash dose technology**

Flash dose technology has been patented by Fuisz. Nurofenmeltlet, a new form of ibuprofen as melt-in mouth tablets, prepared using flash dose technology is the first commercial product launched by Biovail Corporation [22]. The Flash Dose technology uses a unique spinning mechanism so as to produce a floss-like crystalline structure, much like cotton candy. This crystalline sugar can then incorporate the drug and be compressed into a tablet. The Flash dose tablets consist of self-binding shear form matrix termed as "floss." Shear form matrices are prepared by flash heat processing [14].

**Flashtab technology**

Prographarm laboratories have patented the Flash tab technology. Tablet prepared by this system consists of an active ingredient in the form of microcrystals. Drug microgranules may be prepared using the conventional techniques such as coacervation, micro encapsulation, simple pan coating methods and extrusion spheronization. All the processing utilized conventional tableting technology. The microcrystals of microgranules of the active ingredient are added to the granulated mixture of excipients prepared by wet or dry granulation, and compressed into tablets. The tablets produced are reported to have good mechanical strength and disintegration time <1 minute [22].

**Wowtab technology**

Wowtab® technology was developed by Yamanouchi Pharma Technologies, USA [21]. The WOW in the WOWTAB signifies the tablet is to be given without water. This technology utilizes sugar and sugar-like excipients. The two different types of saccharides are combined to obtain a tablet formulation with adequate hardness and fast dissolution rate. The two different saccharides are those with high moldability like maltose, mannitol, sorbitol, and oligosaccharides (good binding property) and low moldability like lactose, glucose, mannitol, xylitol (rapid dissolution). Tablets produced from this technology will have sufficient hardness to maintain the physical characteristics of the dosage form during production until it comes in contact with moisture such as saliva in mouth. Erythritol was found to be the best sugar for this type of formulation, showing rapid disintegration which is unaffected by tablet hardness [23].

**Nanocrystal technology**

This is patented by Elan, King of Prussia. Nanocrystal technology includes lyophilization of colloidal dispersions of drug substance and water-soluble ingredients filled in to blister pockets. This method avoids manufacturing process such as granulation, blending, and tableting, which is more advantageous for highly potent and hazardous drugs. As manufacturing losses are negligible, this process is useful for small quantities of drug [24].

**Lyoc**

Lyoc technology is owned by Cephalon Corporation. CIMA is a subsidiary of Cephalon, and currently manages the Lyoc R and D efforts [24]. This was the first freeze drying- based technology introduced for ODTs. Oil in water emulsion is prepared and placed directly into blister cavities followed by freeze-drying. Non-homogeneity during freeze-drying is avoided by incorporating inert filler to increase the viscosity finally the sedimentation. High proportion of filler reduces porosity of tablets due to which disintegration is lowered [25].

**Ziplet technology**

This technology is patented by passano con Barnago, Italy [24]. In ziplet technology water insoluble drug(s) as coated micro particles are used. The addition of suitable amount of water soluble inorganic excipients combination with disintegrants are impart an excellent physical resistance to the ODT and simultaneously maintained optimal disintegration. The use of water soluble inorganic excipients offer better enhancement of disintegration in comparison to the most commonly used water soluble sugars or salts. Tablets primarily contain water soluble components often tend to dissolve rather than disintegrate and concentrated viscous solution is formed reduces the rate of water diffusion into the tablet core [22].

**Pharmaburst technology**

Pharmaburst™ is a "Quick Dissolve" delivery system patented by SPI Pharma. Pharmaburst is a co-processed excipient system which involves a dry blend of a drug, flavors, and lubricant then followed by

compression into tablets which then dissolve within 30-40 seconds. Tablets manufactured by this methodology have sufficient strength can be packed in blister packs and bottles [24].

**Frosta technology**

Akina patents this technology. It utilizes the concept of formulating plastic granules and compressing them at low pressure to produce strong tablets with high porosity. Plastic granules composed of porous and plastic material, water penetration enhancer, and binder. The tablets obtained have excellent hardness and rapid disintegration time ranging from 15 to 30 seconds depending on size of tablet [25].

## MECHANISM OF TABLET DISINTEGRATION

The major mechanisms for tablet disintegration are as follows:

- Swelling
- Porosity and capillary action (Wicking)
- Deformation
- Due to disintegrating particle/particle repulsive forces
- Enzymatic reaction·
- Chemical reaction (acid-base reaction).

**Swelling**

Swelling is believed to be a mechanism in which certain disintegrating agents (such as starch) impart the disintegrating effect. By swelling in contact with water, the adhesiveness of other ingredients in a tablet is overcome causing the tablet to fall apart (Fig. 1). E.g., Sodium starch glycolate, Plantago Ovata [26].

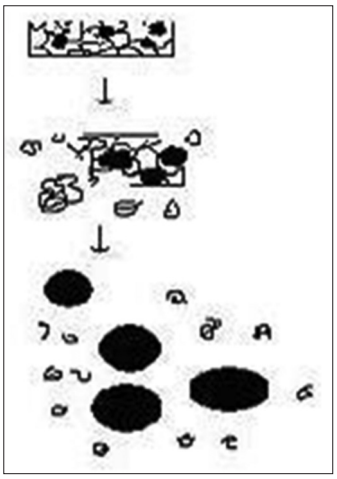

**Fig. 1: Steps involved in swelling**

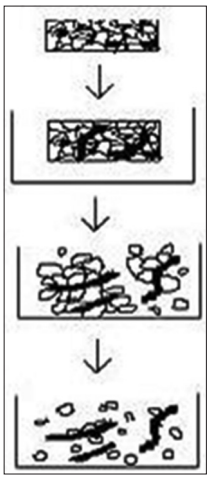

**Fig. 2: Steps involved in wicking**

**Porosity and capillary action (wicking)**

Tablet porosity provides pathways for the penetration of fluid into tablets. The disintegrant particles (with low cohesiveness and compressibility) themselves act to enhance porosity and provide these pathways into the tablet. Liquid is drawn up or "wicked" into these pathways through capillary action and rupture the interparticulate bonds causing the tablet to break apart (Fig. 2). e.g., Crospovidone, Croscarmellose [26].

**Deformation**

Starch grains are generally thought to be "elastic" in nature meaning that grains that are deformed under pressure will return to their original shape when that pressure is removed. But with the compression forces involved in tableting, these grains are believed to be deformed more permanently and are said to be "energy rich" with this energy being released upon exposure to water. In other words, the ability for starch to swell is higher in "energy rich" starch grains than it is for starch grains that have not been deformed under pressure [26] (Fig. 3).

**Due to disintegrating particle/particle repulsive forces**

Another mechanism of disintegration attempts to explain the swelling of tablet made with "non-swellable" disintegrants. Guyot-Hermann has proposed a particle repulsion theory based on the observation that non-swelling 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 [26] (Fig. 4).

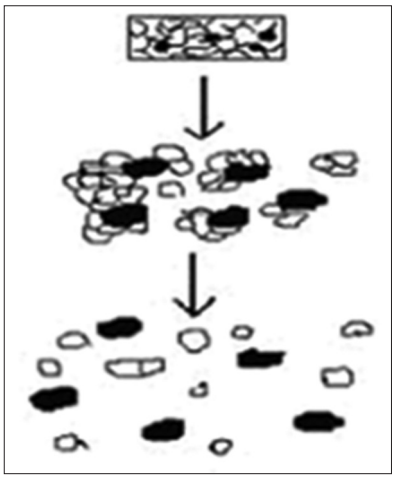

**Fig. 3: Steps involved in deformation**

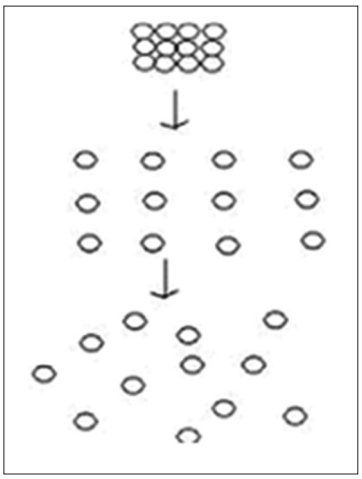

**Fig. 4: Steps involved in repulsion**

**Enzymatic reaction**
Enzymes present in the body also act as disintegrants. These enzymes dearth the binding action of binder and helps in disintegration. Due to swelling, the pressure is exerted in the outer direction that causes the tablet to burst, or the accelerated absorption of water leads to an enormous increase in the volume of granules to promote disintegration [26].

**Chemical reaction (acid-base reaction)**
The tablet is quickly broken apart by internal liberation of $CO_2$ in water due to interaction between tartaric acid and citric acid (acids) with alkali metal carbonates or bicarbonates (bases) in presence of water. The tablet disintegrates due to generation of pressure within the tablet. Due to liberation in $CO_2$ gas, the dissolution of active pharmaceutical ingredients in water as well as taste masking effect is enhanced. As these disintegrants are highly sensitive to small changes in humidity level and temperature, strict control of environment is required during preparation of the tablets. The effervescent blend is either added immediately prior to compression or can be added in two separate fraction of the formulation [27].

## EVALUATION OF ORODISPERSIBLE TABLETS

**Content uniformity**
The test for uniformity of content is based on the assay of the individual content of drug substance(s) in a number of individual dosage units to determine whether the individual content is within the limit. The test for content uniformity is required for tablets containing <25 mg or <25% of one tablet. The content of active ingredient is determined in each of 10 dosage units taken at random using method described in assay. The preparation complies with the test if individual content is 85-115% of average content [28].

**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 the 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 [29]. The hardness of ODTs is generally kept lower than conventional tablets as increased hardness delays the disintegration of the tablet. The force is measured in kg and the hardness of about 3-5 kg/cm$^2$ is considered to be satisfactory for uncoated tablets [24].

**Uniformity of weight**
Weight variation test is done by weighing 20 tablets individually and calculating the average weight of tablet, and then comparing the individual tablet weight to the average weight [28] (Table 1).

**Friability test**
Friability is the loss of weight of tablet in the container due to removal of fine particles from the surface. Friability test is carried out to access the ability of the tablet to withstand abrasion in packaging, handling and transport. Roche friabilator is employed for finding the friability of the tablets [30]. Friabilator consist of a plastic chamber that revolves at 25 rpm and dropping the tablets at a height of 6 inches in each revolution. Pre-weighed sample of tablets was placed in the friabilator and were subjected to 100 revolutions [31]. Tablets were de-dusted utilizing a soft muslin cloth and reweighed, the loss in the weight of tablet is the measure of friability and is expressed in percentage as [29].

$$\% \text{ Friability} = \frac{\text{Loss in weight}}{\text{Initial weight}} \times 100$$

**Table 1: Weight variation specification as per IP/BP and USP [28]**

| Monograph | Average weight | Deviation (%) |
|---|---|---|
| IP/BP | <80 mg | 10 |
| | Between 80 and 250 mg | 7.5 |
| | >250 mg | 5 |
| USP | <130 mg | 10 |
| | Between 130 and 325 mg | 7.5 |
| | >325 mg | 5 |

**Thickness**
The thickness and diameter of the tablets was determined using a Micrometer screw gauge. Five tablets from each type of formulation were used and average values were calculated. It is expressed in mm [32].

**Water absorption ratio**
A piece of tissue paper folded twice was placed in a small Petri dish containing 6 ml of water. A tablet was put on the paper and the time required for complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio (R), was determined using following equation,

$$R = 10 \times \frac{Wa}{Wb}$$

Where, Wb is weight of tablet before water absorption and Wa is weight of tablet after water absorption [30].

**Disintegration time**
The test was carried out on 6 tablets using the apparatus specified in I.P.-1996 distilled water at 37°C ± 2°C was used as a disintegration media and the time in the second taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured in seconds [11,12].

**Modified disintegration test**
Many reports suggest that conventional disintegration test apparatus may not give correct values of disintegration Test for ODTs. The amount of saliva available in the oral cavity is very inhibited (<6 ml) whereas the conventional disintegration test apparatus utilizes a substantial amount of dihydrogen monoxide with very rapid up and down forms of kineticism. In the simplest method to surmount this quandary, 6 ml of phosphate buffer of pH 6.8 was taken in a 25 ml quantifying cylinder. Temperature was maintained at 37± 2°C. An ODT was put into it and time required for consummate disintegration of tablet was noted [31].

**Wetting time**
A piece of tissue paper (12 cm × 10.75 cm) folded twice was placed in a small Petridish (ID = 9 cm) containing 6 ml pH 6.8 phosphate buffer, a tablet was placed on the paper and the time taken for complete wetting was noted. Three tablets from each formulation were randomly selected and the average wetting time was noted [32].

**Dissolution test**
It is an important test as the drug-release profile can be obtained by performing this test. Both the USP dissolution test apparatus can be used. Dissolution of orodispersible tablets is very fast. Therefore, USP 2 Paddle-type apparatus at 50-100 r/minutes is used for dissolution testing. USP Type I basket apparatus have certain application in the case of orodispersible tablets, but tablet fragments or disintegrated tablet masses may become trapped on the inside top of the basket at the spindle. An erroneous-dissolution profile is obtained, where little or no effective stirring occurs. Thus, Type II is more preferred due to reproducible-dissolution profile [33].

**Moisture-uptake studies**
It is an important study in the case of orodispersible tablets. This study is carried out in order to assess the stability of the tablets. 10 tablets were kept in the desiccators over calcium chloride at 37°C for

**Table 2: Summary of recent research on ODTs**

| Drug | Method used | Excipients used | Result | Reference |
|---|---|---|---|---|
| Candesartan cilexetil | Direct compression | Indion 204, tulsion 339, primogel, micro crystalline cellulose, magnesium stearate | Better patient compliance | [34] |
| Lovastatin | Direct compression | Sodium starch glycolate, crosspovidone, crosscarmellose | Rapid dissolution rapid onset of action | [35] |
| Lavocetrizine dihydrochloride | Direct compression | Kyron T-134, talc, colloidal silicon dioxide, sodium starch glycolate, microcrystalline cellulose, crospovidone | 99.73% of drug is released within 10 minutes | [36] |
| Primaquine phosphate | Direct compression | β-cyclodextrine, lactose, dextrose, cross povidone, sodium starch glycolate, Magnesium stereate, PVP | Less disintegration time | [37] |
| Diclofenac sodium | Direct compression | Mannitol, crospovidone, microcrystalline cellulose, sodium starch glycolate, aspartame | Better bioavailability and improved drug release | [38] |
| Triphala | Direct compression | Embelica officinalis, terminalia belerica, terminala chebula | Less dispersible time | [39] |
| Meclizine HCL | Direct compression | Explotab, tulsion 334, Eudragit E100 | 99.4% drug is release within 2 minutes | [40] |
| Quetiapine Fumarate | Sublimation | Pearlitol SD-200, magnesium stearate, camphor, Indion 414, sucralose | Less disintegration time and greater drug release | [41] |
| Cyproheptadine HCL | Direct compression | Microcrystalline cellulose, magnesium stearate, mannitol | 98.64% drug is release within 30 minutes | [42] |
| Cinnarizine | Direct compression | Polyplasdone XL, Indion 414 | High patient compliance | [43] |
| Efavirenz | Direct compression | Crospovidone, aspartame, croscarmellose sodium, sodium starch glycolate, magnesium stearate, microcrystalline cellulose pH 102 | Faster drug release | [44] |

PVP: Poly vinyl pyrolidone

24 h. The tablets were then weighted 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 desiccators for 3 days. One tablet as control (without super disintegrant) was kept to assess the moisture uptake due to other excipients. Tablets are weighed and the percentage increase in weight is recorded [33].

**Packaging**

Packaging special care is required during manufacturing and storage to protect the dosage of other fast-dissolving dosage forms. Quick-dispersing and/or dissolving oral delivery systems, the system can be packaged using various options, such as single pouch, blister card with multiple units, multiple unit dispenser, and continuous roll dispenser, depending on the application and marketing objectives [11].

## RECENT RESEARCH ON ODTS

Several studies reported the formulation and evaluation of ODTs of various drugs for different purposes. Recent research on ODTs is summarized in (Table 2).

## FUTURE PROSPECTIVE FOR ORODISPERSIBLE TABLETS

Future challenges for many ODT manufacturers include reducing costs by finding ways to manufacture with conventional equipment, using versatile packaging, improving mechanical strength and taste-masking capabilities. ODTs may be suitable for the oral delivery of drugs such as protein and peptide-based therapeutics that have limited bioavailability when administered by conventional tablets because these products usually degrade rapidly in the stomach. Furthermore, there is a scope to develop controlled release ODTs prepared using different drug carriers [28,45].

## CONCLUSION

The popularity of ODTs has increased tremendously over the last decade. Based on the literature surveyed, it may be concluded that Orodispersible tablets are particularly beneficial to the pediatric, geriatric, bedridden, and psychotic patients affected by dysphagia. These tablets get converted into a suspension with the salivary fluid in the oral cavity thereby showing rapid onset of action with improved bioavailability, better patient acceptance and offer better safety as compared to conventional oral dosage forms. Today, Orodispersible tablets are more widely available as over-the-counter products for the treatment of allergies, cold and flu symptoms. All the information's collected above about the ODT gives a better scientific based understanding. With continued research and development of new pharmaceutical excipients, one may expect some new technology for a more novel orodispersible tablets in the future.

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