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A Review on Orodispersible Tablet

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ABSTRACT

Systemic effect producing medicinal and other curative agents can be taken by several route of administration but oral route is considered to be more effective route and possess high degree of patient compliance. Orodispersible tablet is the solid unit dosage form containing super disintegrates which impart the quality of quick disintegration in the presence of saliva and without producing any difficulty in swallowing of tablet. ODTs have very porous structure and highly soluble composition which get dispersed even in small presence of water such as saliva because this dosage form has been developed mainly for geriatric, pediatric and bedridden or disabled patients. For Rapid drug delivery ODTs are considered to be preferred dosage form.

Keywords: ODTs, Medication, Disintegration, Dissolution, Pharmacopoeia.

1. INTRODUCTION

Systemic effect producing medicinal and other curative agents can be taken by several route of administration but oral route is considered to be more effective route and possess high degree of patient compliance.[1] A new term has been introduced by European Pharmacopoeia- "Orodispersible tablets". These are uncoated tablets which when taken into mouth get easily disperse within 3 min before swallowing.[2] These tablets are also known as orally disintegrating tablets, mouth-dissolving tablets, rapid dissolving tablets, fast-disintegrating tablets, fast-dissolving tablets.

Orodispersible tablet is the solid unit dosage form containing super disintegrates which impart the quality of quick disintegration in the presence of saliva and without producing any difficulty in swallowing of tablet. As soon as the tablet gets disintegrated into mouth, the drug is released, then it is dissolved or dispersed in saliva and is absorbed sublingually. This results in greater bioavailability. Due to effectiveness of this kind of dosage form the United States Pharmacopoeia has also approved these dosage forms as Orodispersible tablets. [3-6]

ODTs have very porous structure and highly soluble composition which get dispersed even in small presence of water such as saliva because this dosage form has been developed mainly for geriatric, pediatric and bedridden or disabled patients. Patients with persistent nausea, who are traveling, or who have little or no access to water are also considered for this dosage form.[7] Composition of this dosage form demands incorporation of appropriate disintegrants along with water-soluble excipients. [8]

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1.1 Advantages Of Orodispersible Tablet

1. Ease of administration is major advantage for those patients who have problem with swallowing of drugs (patients in shock state, stroke victims and bedridden patients) or suffer from renal failure and who refuse to swallow drugs like pediatric, geriatric and psychiatric patients [9, 10]
2. For Rapid drug delivery ODTs are considered to be preferred dosage form.
3. Drug is released quickly from this dosage form and gets dissolve in GIT tract without getting into stomach, increased bioavailability can be achieved. [10,11]
4. ODTs are very convenient for administrating to various classes of patients from disabled, travelers and busy people, who do not always have access to water.
5. It produces good mouth feel property, which helps to change the perception of medication. This factor is useful while preparing dose for pediatric patients. [12]

1.2 Disadvantages of Orodispersible Tablets [13, 14]

1. These are highly hygroscopic, so care has to be taken while storage.
2. Drugs with relatively larger doses are difficult to formulate into ODTs e.g. antibiotics like ciprofloxacin with adult dose tablet containing about 500 mg of the drug.
3. Due its porous structure ODTs are highly fragile sometimes.
4. ODTs require special packaging for proper stabilization & safety of stable product.
5. After taking ODTs special precautions must be taken, like eating and drinking may become restricted for some time.

1.3 Characteristic of an Ideal Orodispersible Tablet [15]

An Orally disintegrating drug delivery system should possess following characteristics:

1. Method of production should be cost effective.
2. It must not need water for oral administration. It should disintegrate when come in contact with saliva.
3. Time to get dissolve or disperse or disintegrate should be less than a minute.
4. ODTs should produce pleasing, acceptable mouth feel and taste masking of drug incorporated.
5. It should have proper friable structure with sufficient hardness.
6. It should not leave any or minimal residue in mouth after administration.
7. Preparation and packaging must be done through conventional methods.

1.4 Constraints in the formulation of Orodispersible tablets

1.4.1 Mechanical strength and disintegration time

ODTs are formulated to obtain disintegration time usually less 3 minute. While doing so, maintaining a good mechanical strength is a prime challenge. Many ODTs are fragile and there are many chances that tablet will break during packing, transport or handling. Tablets based on technologies like Zydis need special type of packaging. It is very natural that increasing the mechanical strength will delay the disintegration time. So a good compromise between these two parameters is always essential.

1.4.2 Taste masking

Many drugs are bitter in taste. A tablet of bitter drug, dissolving/disintegration in mouth will seriously affect patient acceptability for the dosage form. So effective taste masking of the bitter drugs must be done so that the unpleasant taste of the drug is not felt in the oral cavity.

1.4.3 Disintegration pattern and additives

The ODTs should not disintegrate into large particles in the oral cavity. The particles generated after disintegration of the ODTs should be as small as possible. ODTs should leave minimal or no residue in mouth after oral administration. More over, addition of flavors and cooling agents like menthol improve the mouth feel.

1.4.4 Sensitivity to environmental conditions

ODTs generally should exhibit low sensitivity to environmental conditions such as humidity and temperature, as most of the materials used in ODTs are meant to dissolve in minimum quantity of water.

1.4.5 Cost

The technology used for ODTs should be economic in terms of cost of the final product. Methods like Zydis and Orasolv that require special technologies and specific packaging, which increase the cost to a remarkable extent.

2. VARIOUS TECHNIQUES USED IN PREPARATION OF ORODISPERSIBLE TABLETS

2.1 Conventional Technology

2.1.1 Freeze Drying

Commonly used methods for preparation of ODTs are freeze-drying or lyophilization that produces very porous structure of dosage form due to which it disintegrates or dissolves quickly when come in contact with saliva in oral cavity. This preparation method requires the material to be freezed less than its eutectic point. Then drying is done to reduce the amount of bound moisture to the required volume. By using lyophilization, bulking agent and even drug gets glossy amorphous structure and thus, extent of dissolution is enhanced.[26, 27] But freeze-drying is costly method, requiring costly equipment and processing. But without freeze-drying, tablets produced are with low mechanical strength and show poor stability at higher temperature and humidity.

Advantages*:* More rapid dissolution than other available solid products.

Disadvantages: High cost of the equipments & lack of physical resistance in blister packs.

2.1.2 Sublimation

In this process, excipients used have high volatility and are chemically inert like urea, urethane, naphthalene, camphor, menthol, ammonium bicarbonate. These are added with compression of blend into tablet. When these volatile substances get removed by sublimation process, pores in the tablet structure are left. This helps to impart high dissolution property into tablet when come in contact with saliva [28]. Mouth dissolving Tablets with highly porous structure and good mechanical strength can be developed by this method.

Advantage: Tablets dissolve in 10-20 sec. and exhibit sufficient mechanical strength.

2.1.3 Molding

Quick disintegrating tablets are prepared by this method. Tablets made by this method contain the matrix. The drug can exist as discrete particles or micro particles in the matrix. Molded tablets are less compact than compressed tablets. These molded tablets also have porous structure that facilitates rapid disintegration and easy dissolution. Dispersion matrix of molded tablets contains water-soluble sugars that make these tablets more acceptable in taste. But molded tablets do not possess good mechanical strength and can undergo breakage or erosion during handling and opening of blister packs. For enhancing mechanical strength of these molded tablets, sucrose, acacia or polyvinyl pyrrolidone can be added. [8, 29, 30]

Advantages: Moulded tablets disintegrate more rapidly and offer improved taste because the dispersion matrix is, in general made from water soluble sugars.

Disadvantages: Moulded tablets do not possess great mechanical strength. Erosion & breakage occur during handling & opening of blister packages.

2.1.4 Spray Drying

This technique is based on a particulate support matrix, which is prepared by spray drying of an aqueous composition containing support matrix and other components to form a highly porous and fine powder. Then this is mixed with active ingredients and compressed into tablets. For getting immediate dissolution (<20 sec) this method is used , but this approach involves both high cost and time of production and produce tablets of very poor mechanical strength. [31]

Advantages: Rapid disintegration of tablets.

2.1.5 Mass Extrusion

In this technique, a blend of active drug and other ingredients is softened using solvent mixture of water soluble polyethylene glycol, using methanol and then the softened mass is extruded through the extruder or syringe to get a cylindrical structured product, which is finally cut into even segments with the help of heated blades to get tablets. The dried cylinder can be used to coat the granules of bitter tasting drugs and thereby masking their bitter taste. [12, 32]

2.2 Patented Technologies

2.2.1 Zydis Technology

Zydis formulation is a unique freeze drying method which produces tablet in which drug is physically entrapped or dissolved within the tablet matrix. The matrix consist the fast dissolving carrier material. When Zydis OTDs are taken orally, this freeze-dried structure disintegrates instantly and does not require water to aid swallowing. Composition of Zydis matrix is being done with special material to achieve a number of objectives, e.g, imparting strength and resilience during handling by using polymers such as gelatin, dextran or alginates. Due to the use of these polymers, tablet gets a glossy amorphous structure, which imparts strength [33]. By use of saccharides such as mannitol or sorbitol high crystalline structure, elegance and hardness are being achieved. For getting porous structure water is used in the manufacturing process. This is to achieve rapid disintegration.

2.2.2 Flashtab Technology

Flashtab technology is used by Prographarm laboratory and they patented this method. In this technology, rapidly disintegrating tablets are prepared in the form of microcrystals with active ingredient by using the many conventional techniques like coacervation, extrusion-spheronization, simple pan coating methods and microencapsulation by which drug microgranules may be prepared. These microcrystals of microgranules of the active ingredient are then added to the granulated mixture of excipients which is prepared by wet or dry granulation, and compressed into tablets. Whole processing operates through conventional tableting technology. Prepared tablets are found to have good mechanical strength and disintegration time less than one minute by experts. [34]

2.2.3 Nanocrystal Technology

For rapid disintegration of tablet matrix good pharmacokinetic quality is required. Orally administered nanoparticles (<2 microns) are taken in the form of a rapidly disintegrating tablet matrix. The basis of product differentiation is combination of proprietary and patent-protected technology elements. Manufacturing process which is cost-effective must utilize conventional, scalable unit operations. Durability of drug must be exceptional that enable use of conventional packaging, equipment and formats (i.e., bottles and/or blisters). Wide range of doses (up to 200mg of API per unit) is available. Inactive components that are used must be of conventional compendia. Nanocrystal colloidal dispersions of drug substance are combined with water-soluble GRAS (Generally Regarded as Safe) ingredient which are filled into blisters, and lyophilized. Wafers made by this procedure are extraordinarily tough, still gets dissolve in very small quantities of water in seconds. For handling potent or hazardous materials, this method is very effective as it does not involve rigorous manufacturing operations like granulation, blending, and tableting. All these steps generate large quantities of aerosolized powder and present much higher risk of exposure. When drug quantity available is very less, by freeze-drying approach that also can be converted into ODT dosage forms because losses due to manufacturing are minor.[35]

2.2.4 Wowtab Technolgy

Japanese market has been massive user of the Wowtab fast-dissolving/disintegrating tablet formulation technique for long time. This technique is patented by Yamanouchi Pharmaceutical Co. The WOW in Wowtab signifies the tablet is to be given *"With out Water".* It has just recently been introduced into the U.S. In this technology, sugar and sugar-like (e.g., mannitol) excipients are needed. In this method a combination of low mouldable saccharides (property of rapid dissolution) and high mouldable saccharides (property of good binding property) is used. By combination of two different types of saccharides adequate hardness and fast dissolution rate in the formulation can be achieved. Thus, Wowtab formulation is a bit more stable to the environment than the Zydis or OraSolv because of its significant hardness. Formulation made by this method can be easily packed into conventional bottle and blister packaging. Good taste masking agent is used and also produce best mouth feel due to use of patented SMOOTHMELT action. Dissolution time is very less upto 15 seconds.[36, 37]

2.2.5 Durasolve Technology

Cima's second-generation fast-dissolving/disintegrating tablet formulation is DuraSolv. During tableting higher compaction pressure is used in Durasolv Technology, due to this high mechanical strength formulations are produced than Orasolv. These tablets are made by conventional tableting equipment and have good rigidity (friability less than 2%). Thus, products are produced with a faster rate and in more cost effective manner. Traditional blister packaging, pouches or vials are used for packing DuraSolv tablets [38].

One disadvantage of DuraSolv is that the technology is not compatible for large doses of active ingredients, because the formulation is subjected to such high pressures on compaction. Unlike OraSolv, the structural integrity of any taste masking may be compromised with high drug doses. The drug powder coating in DuraSolv technology may become fractured during compaction, exposing the bitter-tasting drug to a patient's taste buds. Therefore, the DuraSolv technology is best suited for formulations including relatively small doses of active compound.[39]

2.2.6 Orodis Technology

Orodis® is compressed technology. It produce tablets with a fast disintegration time in the mouth (15 to 30 seconds). It has many advantages against other technologies.

1. It produces hard tablets, not fragile so formulations are easy to handle.
2. Tablets produced don't require specific packing. They can be packaged in push -through blisters.
3. Tablets give smooth mouth feel.
4. Due to use of taste masking agents and flavors, tablets are of pleasant taste.
5. All the materials used in this method meet USP and EP standards.

6. Conventional manufacturing equipment – not difficult to transfer to final production site.
7. Cost effective.[40]

3. INGREDIENTS USED FOR ORODISPERSIBLE TABLETS [41,42]

Formulation of Orally disintegrating tablets require use of ingredients which enhance dissolution of dosage form and results in quick release of drug. This includes both the active and inactive ingredients.

3.1 Binders

Binder selected should possess desired binding quality and proper melting characteristics and produce fast release of active ingredients. Binders keep the composition of these fast dissolving tablets together during the compression stage. To maintain the integrity and stability of the tablet selection of a right binder or combination of binders is essential. Binders can be in any form like liquid, semi solid, solid or mixtures of varying molecular weights such as polyethylene glycol.

3.2 Lubricants

Lubricants are used for to reduce the friction during compaction and ejection of tablets. Eg. magnesium stearte and talc.

3.3 Bulking agent

The materials function as diluent, filler and cost reducer. Bulking agents improve the textural characteristics that in turn enhance the disintegration in the mouth. Besides, adding bulk also reduces the concentration of the active ingredient in the composition. The recommended bulking agents for this delivery system should be more sugar-based such as mannitol, polydextrose, lactate and starch hydrolysate for higher aqueous solubility and good sensory perception.

3.4 Emulsifying agents

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 disintegrating tablet formulation, including alkyl sulfates.

3.5 Flavours and sweetners

The addition of these ingredients assists in overcoming bitterness and undesirable tastes of some active ingredients. Formulators can choose from a wide range of sweeteners including sugar, dextrose and fructose, as well as non-nutritive sweeteners such as aspartame, sugar alcohols and sucralose.

3.6 Superdisintegrants

As demand for faster disintegrating formulation is increased, so pharmacist needs to formulate disintegrants i.e. Superdisintegrants which are effective at low concentration and have greater disintegrating efficiency and they are more effective intragranularly. But they have one drawback that they are hygroscopic. Therefore not used with moisture sensitive drugs.

4. MECHANISM OF ACTION OF SUPERDISINTEGRANTS [43,44,45]

Following are the primary mechanism by which a tablet can disintegrate into its primary particles:

4.1 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 slowed down.

4.2 Capillary Action

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 and excipient and on tablet manufacturing 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.

4.3 Repulsive Force between Particles

Another mechanism of disintegration attempts to explain the swelling of tablet made with ‘nonswellable’ 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.

4.4 Release of Gases

As tablet wets, carbon dioxide is released within it due to interaction between carbonates and bicarbonates with tartaric or citric acid. A pressure is generated between tablet due to this gas. This mixture of carbonates and citric acid is also used for effervescent tablets which show rapid disintegration.

As these disintegrants are highly sensitive to small changes in humidity level and temperature, strict control of environment is required during manufacturing of the tablets. The effervescent blend is either added immediately prior to compression or can be added in two separate fraction of formulation.

4.5 Enzymatic Reaction

For a tablet, body enzymes act as disintegrating agent. They disintegrate tablet by reducing the binding action of binder and thus, works as disintegrating agent.

4.6 Deformation

Hess had proved that 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 breakup of the tablet. This may be a mechanism of starch and has only recently begun to be studied.

5. EVALUATION OF ORODISPERSIBLE TABLETS

5.1 Tablet thickness

Tablet thickness is an important characteristic in reproducing appearance. Thickness was determined for 6 tablets of each batch and the average thickness was determined in mm. The tablet thickness should be controlled within a ± 5% variation of a standard.

Thickness was recorded using vernier calliper. [47,48]

5.2 Weight variation

20 tablets were selected randomly from the lot and weighted individually to check for weight variation. Weight variation specification as per I.P. is shown in Table.[47,49]

Table 1: Weight Variation Specification as per IP

Average Weight of Tablet	% Deviation
80 mg or less	±10
More than 80 mg but less than 250 mg	±7.5
250 mg or more	±5

5.3 Friability [50]

Friability is a measure of mechanical strength of the tablet. It 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 and shock in packaging, handling and transport. If a tablet has more friability it may not remain intact during packaging, transport or handling. Roche friabilator is used to determine the friability by following procedure. Pre weighed tablets are 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 are rotated in the friabilator for at least 4 minutes. At the end of test tablets are dusted and reweighed; the loss in the weight of tablet is the measure of friability and is expressed in percentage as:

$$\% \text{ Friability} = [(W_0 — W_f) / W_0] \times 100$$

W_0 = Initial weight of tablets
W_f = Final weight of tablets
Limit- less than 1%

5.4 Hardness (Crushing strength)

The hardness of tablet is an indication of its strength.

Measuring the force required to break the tablet across tests it. Hardness of 10 tablets from each formulation is determined by Monsanto hardness tester, Pfizer hardness tester etc. A tablet is placed in the hardness tester and load required to crush the tablet is measured. 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. [51,52]

5.5 Water absorption ratio [50,53]

A small piece of tissue paper folded twice is placed in a small petridish containing 6 ml of water. Put a tablet on the paper and the time required for complete wetting is measured. The wetted tablet is then weighed again. Water absorption ratio, R is determine by using following formula

$$R = 100 \times Wa - Wb / Wb$$

Where,
Wb - weight of tablet before water absorption
Wa - weight of tablet after water absorption

5.6 Uniformity of dispersion

Keep the Two tablets in 100ml water and stir gently for 2 minutes. The dispersion is passed through 22 meshes. The tablets will consider passing the test if no residue remained on the screen. [53]

5.7 Wetting time

Five circular tissue papers of 10 cm diameter are placed in a petridish with a 10 cm diameter. Ten millimeters of water containing Eosin, a water-soluble dye, is added to petridish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as a wetting time. [50]

5.8 Disintegration time

According to the European pharmacopoeia, the fast disintegrating or orodispersible tablets should disintegrate within 3 minutes without leaving any residue on the screen. However it is difficult to assess the disintegration rate even in small amounts of water. Further the conventional test employs a volume of 900 ml of distilled water compared to the volume of saliva in humans, which is limited to a few ml. Thus, the disintegration rate obtained from conventional test does not appear to reflect the actual disintegration rate in human mouth. To overcome these problems, several new methods have been proposed. One of these methods uses a Charge Couple Device (CCD) camera or texture analyzer to evaluate the disintegration time of tablets. In another method, a modified DT apparatus is used. Here a wire basket of 3cm height and 2 cm diameter and mesh size of #10 is placed above a beaker containing 900 ml of simulated saliva. The basket is so positioned in the liquid that it contains only 6 ml of the liquid. The assembly is supported with a heater to maintain temperature at 37°C and a magnetic stirrer. DT is noted at 25 rpm. One of the simplest methods is to take 6ml of simulated saliva in a measuring cylinder and place the tablet in it. The liquid is neither shaken nor stirred and DT is noted. [54]

5.9 *In vivo* disintegration time

In vivo disintegration time is determined using a panel of healthy human volunteers. The test is carried out on 2 or 3 tablets in the mouth and the time (in seconds) taken for complete disintegration of the tablet is measured. The Disintegration time is noted. [53]

5.10 Taste/ Mouth sensation

Mouth-feel is critical, and patients should receive a product that feels pleasant. One tablet from each batch is tested for the sensation by placing the tablet on the tongue. The healthy human volunteers are used for evaluation of mouth feel. Taste evaluation is done by a panel of 5 members using time intensity method. Sample equivalent to 40 mg i.e. dose of drug is put in mouth for 10 seconds and record taste instantly and then after 10 sec, 1, 2, 4 and 6 minutes. Volunteer's opinion for the taste is rated by giving different score values i.e.

0 = good, 1 = tasteless, 2 = slightly bitter, 3 = bitter, 4 = awful. [50]

5.11 Dissolution test

The dissolution method for oral disintegrating tablets is the same as that of conventional tablets. USP type II paddle apparatus is most suitable and common choice for dissolution test of oral disintegrating tablets, where the paddle speed is 50 rpm is used. The USP 1 (basket) apparatus may have certain application for such tablets but is used less frequently due to specific physical properties of tablets. [50,53]

6. CONCLUSION

The introduction of orodispersible tablets has solved some of the problems encountered in administration of drugs to the pediatric and elderly patient, which constitutes a large proportion of the world's population. ODTs are solid unit dosage form containing super disintegrants which imparts the quick disintegration in the presence of saliva and without producing any difficulty in swallowing of tablet. As soon as the tablet gets disintegrated into mouth, the drug is released, then it is dissolved or dispersed in saliva and is absorbed sublingually. This results in greater bioavailability. ODTs offers the advantage such as self administration, quick or immediate onset of action, no water required for swallowing, reduced changes of ulceration, avoids first pass metabolism of drug and increased bioavailability. Thus, ODTs can be used as an appreciable alternative in the near future.

Table 2: List of comman superdisintegrants[46]

Superdisintegrants	Example of	Mechanism of action	Special comment
Crosscarmellose® Ac-Di-Sol®	Crosslinked cellulose	-Swells 4-8 folds in < 10 seconds. -Swelling and wicking both.	-Swells in two dimensions. -Direct compression or granulation
Crosspovidone Crosspovidon M® Kollidon® Polyplasdone®	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® Primogel®	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®	Crosslinked alginic Acid	-Rapid swelling in aqueous medium or wicking action	-Promote disintegration in both dry or wet granulation
Soy polysaccharides Emcosoy®	Natural super Disintegrant	----------	-Does not contain any starch or sugar. Used in nutritional Product
Calcium silicate		-Wicking action	-Highly porous, -light weight -optimum concentration is between 20-40%

REFERENCES

1. Valleri M, Mura P, Maestrelli F, Cirri M, Ballerini R. Development and evaluation of glyburide fast dissolving tablets using solid dispersion technique. Drug Dev Ind Pharm 2004;30(5): 525-534.
2. Fu Y, Yang S, Jeong SH, Kimura S, Park K. Orally fast disintegrating tablets: Developments, technologies, taste masking and clinical studies. Crit Rev Ther Drug Carrier Syst 2004; 21: 433–76.
3. Ghosh TK, Pfister WR. Quick dissolving oral dosage forms: Scientific and regulatory considerations from a clinical pharmacology and biopharmaceuticals perspective; In: Drug delivery to the oral cavity: Molecules to market. New York, CRC Press 2005; 337-356.
4. Dobetti L. Fast melting tablets: Developments and technologies. Pharm Technol Drug Deliv Suppl . 2001;44-50.
5. Deepak K. Orally disintegrating tablets. Tablets and Capsule 2004; 7: 30-35.
6. Brown D (2001). Orally disintegrating tablets: Taste over speed. Drug Deliv Technol 2001; 3: 58-61.
7. Robin H. Bogner, Wilkosz. Fast dissolving tablets. US Pharmacist. A Jobson Publications 2002;72:23.
8. Parakh SR, Gothoskar AV. A review of mouth dissolving tablet technologies. Pharm Tech 2003; 27: 92-98.
9. Wilson CG, Washington N, Peach J, Murray GR, Kennerley J. The behavior of a fast dissolving dosage form (Expidet) followed by g-scintigraphy. Int J Pharm 1987; 40: 119–123.
10. Fix JA. Advances in quick-dissolving tablets technology employing Wowtab. Paper Presented at: IIR Conference on Drug Delivery Systems. 1998; Washington DC, USA.
11. Virely P, Yarwood R. Zydis – a novel, fast dissolving dosage form. Manuf Chem 1990; 61: 36–37.
12. Shukla D, Chakraborty S, Singh S, Mishra B. Mouth Dissolving Tablets I:An Overview of Formulation Technology. Scientia Pharmaceutica Sci Pharm 2009; 77: 309–326.
13. Chang RK, Guo X, Burnside BA, Cough RA. Fast dissolving tablets. Pharm Tech 2000; 24: 52-58.
14. Reddy LH, Ghosh B, Rajneesh. Fast dissolving drug delivery systems: a review of the literature. Indian JPharm Sci 2002*;* 64(4): 331-336.
15. Bradoo R. Fast Dissolving Drug Delivery Systems. J Am Med Asso2001*;* 4: 27-31.
16. Bandari S, Mittapalli RK, Gannu R, Rao YM. Orodispersible tablets: An overview. Asian J Pharm2008*;* 2(1): 2-11.
17. O'Connor R, Schwartz J. Extrusion and spheronization technology. In Pharmaceutical Pelletization Technology. Marcel Dekker Inc., New York 1989; 37: 187.
18. Agarwal V, Kothari BH, Moe DV, Khankari RK. Drug delivery: Fast-dissolve systems. In: Swarbrick J, Encyclopedia of pharmaceutical technology. New York, USA: Informa Healthcare Inc. 2006; 1104 – 1114.
19. Fini A, Valentina B, Gian CC, Celestino R, Carlos A, Fonseca de M. Fast dispersible/slow releasing ibuprofen tablets. Eur J Pharm Biopharm 2008; 69: 335–341.
20. Masters K. Spray Drying Fundamentals: Process stages and Layouts. In: Spray Drying Handbook. USA: Longman Scientific and Technical, New York, 5th ed. 1991: 23–64.
21. Hughes L. Selecting the right ion exchange resin. Pharma Quality 2005*;*1: 54–56.
22. Jeong SH, Park K. Development of sustained release fast-disintegrating tablets using various polymercoated ion-exchange resin complexes. Int J Pharm 2008; 353: 195–204.
23. Prasad N, Straus D, Reichart G. Cyclodextrin flavor delivery systems. US Patent 6, 1999; 287,603.
24. Venkatesh DP, Geetha Rao CG. Formulation of taste masked orodispersible tablets of ambroxol hydrochloride. Asian J Pharm 2008; 2: 261-264.
25. Ohwavworhu F, Adelakun T. Phosphoric acidmediated depolymerization and decrystallization of α- Cellulose obtained from Corn Cob: Preparation of Low Crystallinity Cellulose and some Physicochemical Properties. Tropical. J Pharm Res 2004; 4(2): 509-516.
26. Virely P, Yarwood R. Zydis – a novel, fast dissolving dosage form. Manuf Chem 1990; 36-37.

27. Seager H. Drug delivery product and the Zydis fast-dissolving dosage form. J Pharm Pharmacol 1998;50: 375- 382.
28. Koizumi K, Watanabe Y, Morita K, Utoguchi N, Matsumoto M. New method of preparing high porosity rapidly saliva soluble compressed tablets using mannitol with camphor, a subliming material. Int J Pharm1997; 152(1): 127-31.
29. Masaki K. Intrabuccally disintegrating preparation and production thereof. US Patent 5,1995; 466,464.
30. Pebley WS, Jager NE, Thompson SJ. Rapidly disintegrating tablet. US Patent 5,1994; 298, 261.
31. Mishra DN, Bimodal M, Singh SK, Vijaya Kumar SG. Spray dried excipient base: a novel technique for the formulation of orally disintegratinuhg tablets. Chem Pharm Bull 2006; 54(1): 99-102.
32. Kumar R., Patil M.B., Patil S.R., Paschpura M.S. Development & characterization of melt-in-tablets of Haloperidol by sublimation technique. Int J Pharm Pharm Sci 2009; 1(1): 65-73.
33. DeRoche CC. Consumer preference for orally disintegrating tablets over conventional forms of medication: Evolving methodology for medication intake in dysphagia. Lecture presented at the 12th Annual Meeting of the Dysphagia Research Society, San Francisco, CA, 2-4 Oct.,2003, Dysphagia.2005; 20 (1): 77- 86.
34. Pebley WS, Jager NE, Thompson SJ. Rapidly Disintegrating Tablets. US Patent 5, 1994; 298, 261.
35. Kaushik D, Dureja H, Saini TR. Orally disintegrating tablets: An overview of melt-in mouth tablet technologies and techniques. Tablets Capsules2004; 2: 30-6.
36. Rish RK. A review on fast dissolving tablets techniques. The Pharma Review 2004; 2: 32.
37. Allen LV, Wang B, Davis JD, et al. US patent 5,1998; 807, 567.
38. Gohel M, Patel M, Agarwal R, Amin A, Dev R, Bariya N. Formulation design and optimization of mouth dissolve tablets of nimesulide using vacuum drying technique. AAPS Pharm Sci Tech 2004; 5(36): 1-6.
39. Adel M, Semreen MK, Qato KM, et al. fast dissolving dosage forms-technique. Pharm Tech 2005; 2: 68-75.
40. Ghosh T, Ghosh A, Prasad D. A Review on New Generation Orodispersible Tablets and its future prospective. Int Journ Pharm Pharm Sci 2011.
41. More SA et al. Orodispersible Tablet- A Novel Drug Delivery System. J Pharm Sci Tech 2012; 4 (1): 798 -806.
42. Yoshio K, Masazumi K, Shuichi A, Hiroaki N. Evaluation of rapidly disintegrating tablets manufactured by phase transition of sugar alcohols. J Control Release 2005;105 (1-2): 16-22.
43. Rasheed SH, Arief M, Gajavalli SR, Vani PS, Rao KS, Kumar S, Rao T, Hussain SS. A Comparison of different superdisintegrants in designing of fast dissolving tablets of salbutamol sulphate. Res J Pharm Bio Chem Sci 2011; 2(2): 155- 163.
44. Mukesh, Ratnaparkhi P, Mohant GP, Upadhyay L. Fast Dissolving Tablet. J Pharm Res 2009; 2(1): 5- 12.
45. Biradar S.S, Bhagwati S.T. and Kuppasad I.J., Fast Dissolving Drug Delivery System: A Brief Overview, International Journal of Pharmacology,2006,2(4)
46. Bhowmik D, Chiranjib B, Pankaj K, Chandira RM. Fast Dissolving Tablet: An Overview. Journal of Chemical and Pharmaceutical Research 2009; 1(1): 163-177.
47. Peera N, Lohithasu D, Sahoo SK, Naidu MS. Formulation development and evaluation of oral disintegrating tablets of Zolmitriptan. Der Pharmacia Lettre, 2013, 5 (2):324-332.
48. Mukesh, Ratnaparkhi P, Mohant GP, Upadhyay L. Fast Dissolving Tablet. Journal of Pharmacy Research. 2009; 2(1): 5-12.
49. Patil B, Kulkarni U, Parik B, Srinivas R S, Korwar P. Formulation and evaluation of mouth dissolving tablets of Nimesulide by new coprocessed technique. Research Journal of Pharmaceutical, Biological and Chemical Sciences ISSN: 0975-8585:587- 592.
50. Nagar P, Singh K, Chauhan I. Orally disintegrating tablets: formulation, preparation techniques and evaluation. Journal of Applied Pharmaceutical Science.2011; 01 (04): 35-45.
51. Liberman H.A, Lachman L, Schawstr JB. Pharmaceutical Dosage Forms: Tablets. 1989;2: 173-177.
52. Daharwal S, Jangde R, Saraf S, Saraf S. Taste masking method for bitter drug and tasteless dispersible tablet: An overview. Famvita Net Journal. 2008:1-3.

53. Arora P, Sethi V. Orodispersible tablets: A comprehensive review. International Journal of Research and Development in Pharmacy and Life Sciences. 2013; 2(2): 270-284.

54. Paul Y, Tyagi S, Singh B. Formulation and evaluation of oral dispersible tablets of Zidovudine with different superdisintegrants. International Journal of Current Pharmaceutical Review and Research. 2011; 2 (2): 81-91.