Journal of Advanced Drug Delivery (JADD)
Volume 3, Issue 3 May- June -2016

ISSN NO: 2348-3278

ISRA IMPACT FACTOR: 0.46

A REVIEW ON ORODISPERSIBLE TABLETS

Sangale S.S ,*[1] Borse G.C; Bhuktar D.B Mahale N.B; Chaudhari S.R·

Abstract: Orodispersible tablet (ODTs) are an innovative dosage forms overcomes the problems of swallowing and gives onset of action. In recent decades, a variety of pharmaceutical research has been conducted to develop new dosage forms. Among the dosage forms developed to facilitate ease of medication, the rapid disintegrating (RDT) is one of the most widely employed commercial products. This review describes the various formulation technologies developed for ODTs, patented technology and marketed formulations. Recent developments in the dosage form technology resulted in the development of ODTs with improved patient compliance and convenience. ODTs are also known as fast melt, quick melts, fast disintegrating have the unique property of disintegrating in the mouth in seconds without chewing and the need of water. Orally disintegrating tablets provide an advantage particularly for pediatric 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.

KEY WORDS: Orally disintegrating tablets, Formulation and evaluation methods, patented technologies

1 INTRODUCTION [1,2,3]

Orally disintegrating tablets are also called as orodispersible tablets (ODTs), quick disintegrating tablets, mouth dissolving tablets, fast disintegrating tablets, fast dissolving tablets, rapid dissolving tablets, porous tablets, and rapid melts. However, of all the above terms, United States Pharmacopoeia (USP) approved these dosage forms as ODTs. Recently, European Pharmacopoeia has used the term orodispersible tablet for tablets that disperses readily and within 3 min in mouth before swallowing. United States Food and Drug Administration (FDA) defined ODT as "A solid dosage form containing 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. The concept of Orodispersible tablet Drug Delivery System emerged from the desire to provide patient with more conventional means of taking their medication. It is difficult for many patients to swallow tablets and hard gelatin capsules. Hence they do not comply with prescription, which results in high incidence of non-compliance and in effective therapy. In some cases such as motion sickness, sudden episodes of allergic attacks or coughing and unavailability of water, swallowing conventional tablets may be difficult. Particularly the difficulty is experienced by pediatric and geriatric patients. Such problems can be resolved by means of ODTs. When put on tongue, this tablet disintegrates instantaneously, releasing the drug, which dissolves or disperses in the saliva.

****

Sangale S.S ,*[1] Borse G.C; Bhuktar D.B Mahale N.B; Chaudhari S.R· Department of Pharmaceutics, Amrutvahini College of Pharmacy, Sangamner-422608, Dist-Ahmednagar, (M.S), India.

The center for drug Evaluation and Research states an ODT to be: "A solid dosage form containing medicinal substances, which disintegrate rapidly, usually within a matter of seconds, when placed upon the tongue." These tablets are distinguished from Conventional sublingual tablets, lozenges and buccal tablets which require more than a minute to dissolve in the mouth. In the literature these are also called orally disintegrating, Orodisperse, Mouth dissolving, Quick dissolving, Fast-melt and rapidly disintegrating tablets and freeze- dried wafers. Currently these tablets are available in the market for treating many disease conditions like hypertension, migraine, dysphasia, nausea, vomiting, Parkinson's disease, schizophrenia and pediatric emergency.

2 TYPES OF ODTS [2]

For ease of comparison, ODTs may be categorized into two main groups

1) Lyophilized formulations
2) Loosely compressed tablets

Advantages

1. **Clinical benefits**
   a. Improved oral absorption.
   b. Faster onset of action.
   c. Minimized first pass effect.
   d. Improved bioavailability.
2. **Medical / Patient benefits**
   a. Better taste.
   b. No water required.
   c. Improved safety and efficacy.
   d. Improved compliance.
3. **Technical benefits**
   a. Accurate dosing compared to liquid products.
   b. Contains sugars and GRAS (Generally Regarded As Safe) excipients.
   c. Improved stability due to better packaging.
   d. Employ common process and convenient equipments.

4. Business benefits

a. Unique product differentiation
b. Provide exclusive marketing
c. Extend patent protection.

Table No:- 1 Category allowing with Drug as ODTs ; Formulated as orodispersible tablets (ODTs).

Sr no	Category	Drug
1	Analgesics & Antiinflammatory Agents	Fenbufen, Flurbiprofen, Ibuprofen, Indomethacin, Mefenamic acid, Nabumetone, Piroxicam, Sulindac
2	Anthelmintics	Albendazole, Cambendazole, Praziquantel, Pyrantelembonate, Thiabendazole
3	Anti- Arrhythmic	Amiodarone, Disopyramide, Flecainide acetate, Quinidine sulphate
4	Anti- Epileptics	Carbamazepine, Paramethadione, Phenobarbitone, Phenytoin, Valproic acid
5	Anti- Hypertensives	Amlodipine, Carvedilol, Diltiazem, Felodipine, Nicardipine, Nifedipine, Reserpine
6	Anti-protozoals	Diloxanide Furoate, Metronidazole, Nitrofurazone, Omidazole, Tinidazole
7	Anxiolytics, Sedatives, Hypnotics and Neuroleptics	Alprazolam, Barbitone, Bromazepam, Chlormethiazole, Chlorpromazine, Flupenuiixol decanoate, Lorazepam, Methaqualone, Nitrazepam, Zopiclone.

3 DRUG SELECTION CRITERIA FOR ORODISPERSIBLE TABLET [2,4,5]

The ideal characteristics of a drug for oral dispersible tablet include

1) Ability to permeate the oral mucosa.
2) At least partially non-ionized at the oral cavity pH.
3) Have the ability to diffuse and partition into the epithelium of the upper GIT.
4) Small to moderate molecular weight.
5) Low dose drugs preferably less than 50mg.
6) Short half life and frequent dosing drugs are unsuitable for ODT.
7) Drug should have good stability in saliva and water.
8) Mechanical strength of final product.
9) Taste, good mouth feel.
10) Rate of absorption from the saliva solution.
11) Overall bioavailability.
12) Require no water for oral administration.
13) Have an acceptable taste masking property.
14) Be harder and less friable.

LIMITATIONS OF ODTS [6]

1) Difficult to formulate for those drugs with relatively larger doses. E.g. Antibiotics

2) Not suitable for patients with dryness of mouth due to decreased saliva production

4 EXCIPIENTS COMMONLY USED FOR ODTs FORMULATION [7]

Excipients used in ODTs contain at least one superdisintegrant, a diluent, a lubricant and optionally a swelling agent, a permeabilizing agent, sweeteners and flavorings.

Table 2: **Name and weight percentage of various excipients** [7]

Excipients	Percentage used
Superdisintegrants	1-15 %
Binder	5-10 %
Antistatic agent	0-10 %
Diluents	0-85

Superdisintegrants

In recent years, several newer agents have been developed known as "Superdisintegrants". A "Superdisintegrants" is an excipient, which is added to tablet or capsule blend to aid in the breakup of the compacted mass, when put into a fluid environment. This is especially important for immediate release product where rapid release of the product is required. These newer substances are more effective at lower concentrations with greater disintegrating efficiency and mechanical strength. The use of superdisintegrants is the basic approach in the development of Oral disintegrating tablets (ODTs). Superdisintegrants plays a major role in the dissolution and disintegration of the tablets.

Table 3: List of super disintegrants [8]

Superdisintegrants	Example	Mechanism Of Action	Special comment
Crosscarmellose® Ac-Di-Sol® .Nymce ZSX® Primellose® Solutab® Vivasol® L-HPC	Crosslinked cellulose	Swells 4-8 folds in < 10 seconds. Swelling and Wicking both.	-Swells in two dimensions. -Direct compression or granulation -Starch free
Crosspovidone Crosspovidon M® 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
SodiumStarch 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 products.
Calcium silicate		Wicking Action	Highly porous, Optimum concentration is b/w 20-40%

Binders:

The choice of a binder is critical in a fast- dissolving formulation for achieving the desired sensory and melting characteristics, and for the faster release of active ingredient. Binders can either be liquid, semi solid, solid or mixtures of varying molecular weights such as polyethylene glycol. Main role of Binders is to keep the composition of these fast-melting tablets together during the compression stage. Binders commonly used are cellulosic polymers, povidones, polyvinyl alcohols, and acrylic polymers. Among the cellulosic polymers it will be advantageous to select ethylcellulose, hydroxypropylcellulose (HPC), and hydroxyl propyl methyl cellulose (HPMC), alone or in admixtures, and the most commonly acrylic polymer used are the ammonia-methacrylate copolymer (Eudragit RL and RS), polyacrylate (Eudragit NE), and polymethacrylate (Eudragit E). The temperature of the excipient should be preferably around 30–35ºC for faster melting properties. Further, its incorporation imparts smooth texture and disintegration characteristics to the system.

Antistatic agent and diluents

The most common antistatic agents used are colloidal silica (Aerosil), precipitated silica (Sylod.FP244), micronized or non- micronized talc etc. Magnesium stearate, stearic acid, sodium stearyl fumarate, micronized polyoxyethylene glycol (micronized Macrogol 6000), leucine, sodium benzoate are used as lubricant. An additional thickening agent, generating a stabilized suspension, is added to avoid settling of the particles and moreover provide a pleasant mouth feeling. Commonly used Diluents are most commonly selected from cellulose derivatives and preferably microcrystalline cellulose, maltodextrins, beta-cyclodextrins, starches, lactose, polyols and preferably mannitol.

5 CRITERIA FOR EXCIPIENT USED IN FORMULATION OF ODTS [9]

- It must be able to disintegrate quickly.
- Their individual properties should not affect the ODTs.
- It should not have any interaction with drug and other excipients.
- It should not interfere in the efficacy and organoleptic properties of the product.
- When selecting binder (a single or combination of binders) care must be taken in the final integrity and stability of the product.
- The melting point of the excipients used should be in the range of 30-35oC.
- The binder may be in liquid, semi solid, solid or polymeric in nature.

6 TECHNIQUES USED IN THE PREPARATION OF ODTS [10,11,12]

1) Freeze-Drying or Lyophilization
2) Tablet Molding
3) Spray Drying
4) Mass-Extrusion
5) Cotton Candy Process
6) Melt Granulation
7) Phase Transition
8) Sublimation
9) Direct compression

1) Freeze-Drying or Lyophilization [10]

Freeze-drying orlyophilization is a process in which solvent is removedfrom a frozen drug solution or suspension containing structure-forming excipients. This

technology consists of three phases: Freezing to bring the material below its eutecticzone Sublimation or primary drying to reduce moistureto around 4 % w/w of dry product. Desorption or secondary drying to reduce boundmoisture to the required final value. The tablets prepared by lyophilization disintegraterapidly in less than 5 seconds due to quick penetration of saliva in pores when placed in the oral cavity. Lyophilization is useful for heat sensitive drugs. i.e. thermolabile substances.

2) Tablet Molding [10]

Powdered blend (containing drug and excipients likebinding agents e.g., sucrose, acacia, polyvinyl pyrrolidoneetc.) is pushed through a very fine screen (to ensureRapid dissolution) and then moistened with a hydro-alcoholicsolvent and molded into tablets under pressure lower than employed for conventional compressed tablets. The solvent is later removed by air-drying. Different molding techniques can be used to prepare ODTs

- **Compression molding**:

The manufacturing processinvolves moistening the powder blend with a hydro alcoholisolvent followed by compressing into moldplates to form a wetted mass, which is, then airdried to remove the solvent.

- **Heat molding:**

A molten matrix in which drug is dissolved or dispersed can be directly molded into ODTs. The tablets prepared using heat molding process involves settling of molten mass that contain a dispersed or dissolved drug. In this process, the suspension or solution of drug, agar, and sugar is prepared and then poured into the blister packaging. Then it is solidified at room temperature to form ajelly and dried at 30°C under the vacuum.

3) Spray drying [12]

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.The formulations that were produced contained hydrolyzed and unhydrolyzed gelatine as a support agent for the matrix, mannitol as a bulking agent, and sodium starch glycolate or crosscarmellose as a disintegrant. Disintegration and dissolution was further enhanced by adding an acid (e.g., citric acid) or an alkali (e.g., sodium bicarbonate). The formulation was spray dried to yield a porous powder. Tablets manufactured from this powder disintegrated in less than 20 second in an aqueous medium.

4) Mass Extrusion [1]

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 tablets.

5) Cotton Candy Process [11]

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 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.

6) Melt granulation [10]

Melt granulation is a process in which pharmaceutical powders are efficiently agglomerated by the use of binder that can be a molten liquid, a solid, or a solid that melts during the process. For accomplishing this process, high shear mixers are utilized, where the product temperature is raised above the melting point of binder by a heating jacket or by the heat of friction generated by impeller blades. Abdel bary et al. prepared orally disintegrating tablet by incorporating a hydro philicwaxy binder PEG 6-stearate (Superpolystate®) in theformulation. It has melting point of 33-37°C and HLB value of nine. It acts as a binder and increases the physical resistance of tablet. It helps for fast disintegration of tablet**.** when place in mouth and leaving no residue in oral cavity. The granules were prepared by using polyethylene glycol (PEG-4000) as a melting binder and lactose monohydrateas hydrophilic filler without using solvents or water.

7) Phase Transition[10]

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 combination of low and high melting point sugar alcohols, as well as a phase transition in the manufacturing process, is important for making ODTs without any special apparatus. Here, tablet produced by compressing the powder containing two sugar alcohols of high and low melting point and subsequently heating at temperature between their two melting points. Orally disintegrating tablets were produced by compressing powder containing erythritol (melting point: 122°C) and xylitol (melting point: 93-95°C), and then heating at about 93 °C for 15 min. After heating, the median pore size of the tablets was increased and tablet hardness was increased. The increase of tablet hardness with heating and storage did not depend on the crystalstate of the lower melting point sugar alcohol

8)Sublimation[10]

This technique is based on the use of volatile ingredients (e.g. camphor, ammonium bicarbonate, Naphthalene, urea, urethane etc.) to other tablet

excipients and the mixture is then compressed into tablets. Entrapped volatile material is then removed via sublimation, which leads to formation of a porous structure. These compressed tablets which have high porosity (approximately 30 %) rapidly dissolved within 15 seconds in saliva. They used a mixture containing active ingredient and carbohydrates (glucose, mannitol, xylitol etc) which then moistened with water (1-3 % w/w) and compressed into tablets. Then water was removed, yielding highly porous tablet.

9) Direct compression method[10]

Among the above technologies direct compression is most convenient and cheap way to produce tablets with sufficient structural integrity. Direct compression (DC) is the most preferred because of simplicity, rapidity, economic reasons and stability . Hence for any active pharmaceutical ingredient (API), ultimately the formulator strives to develop in DC tablet form. Formerly only crystalline materials were thought to be eligible for DC; now the scenario is changing and this technique is being applied for many non crystalline materials. The approach mainly employs impartation or modification of certain physical properties of the material under consideration, such as cohesiveness, compactness and flow properties. Main reason for shifting from conventional wet granulation method to DC despite the farmer's advantages like content uniformity, increased segregation resistance and more hydrophilic nature of compact and the disadvantages of wet granulation like stability problems due to exposure to moisture, involvement of too many steps in processing, long processing time and ultimately higher tablet manufacturing cost. The weakening of microcrystalline cellulose (MCC) tablets and browning of lactose on exposure to high moisture level are examples that justify the need of Direct Compression. Now, a number of excipients are available commercially, which turn the non-compressible APIs into directly compressible material. The widely used ones are microcrystalline cellulose, ethyl cellulose and metal phosphates and carbonates.

7 PATENTED TECHNOLOGIES FOR ODTs [15]

1) Zydis Technology.
2) Orasolv Technology
3) Durasolv Technology.
4) Wow tab technology
5) Cotton candy technology
6) Nanocrystal technology
7) Nanocrystal technology
8) Shearform technology
9) Pharmaburst technology
10) Frosta technology

1) Zydis technology

Zydis was the first marketed technology developed by R.P.Scherer,Inc. for formation of new generation tablets. Zydis, the best known of the fast dissolving/ disintegrating tablet preparations was the first marketed new technology tablet. The tablet dissolves in the mouth within seconds after placement on the tongue. Zydis formulation is a unique freeze dried tablet in which drug is physically entrapped or dissolve in a matrix composed of two components, a saccharide e.g. mannitol and a polymer. When Zydis units are kept in the mouth the freeze dried structure disintegrates instantaneously and does not require water for swallowing. Polymers such as gelatin, dextran or are incorporated to impart strength during handling. Mannitol or sorbitols are incorporated, to obtain crystallanity, elegance and hardness. Flocculating agents (e.g, xanthan gum and acacia) to provide uniform dispersion of drug particles; preservatives (e.g., parabens) to prevent microbial growth; permeation enhancers(e.g., sodium lauryl sulphate) to improve transmucosal permeability; pH adjusters (e.g, citric acid) to optimize chemical stability; flavours and sweetners to improve patient compliance Water is used in the manufacturing process to ensure production of porous units to achieve rapid disintegration. Gums prevent the sedimentation of dispersed particles in manufacturing process. Collapse protectants like gelatin prevents the shrinkage of Zydis units during freeze-drying process or on long term storage. The product is very light weight and fragile, and must be dispensed in a special blister pack.

2) Orasolv technology

OraSolv was Cima's first fastdissolving/ disintegrating dosage form. In this system active medicament is taste masked, contains disintegrating agent. The isintegration of ODT in the mouth is cause by the action of an effervescent agent, activated by saliva. The amount of effervescent agent is in general about 20-25% of the total weight of the tablet. The widely used effervescent disintegration pair usually include an acid source (citric, tartaric, malic, fumeric, adipic and succinics) and a carbonate source (sodium bicarbonate, sodium carbonate, potassium bicarbonate and potassium carbonate, magnesium carbonate).The microspheres are loosely compressed to maintain the integrity of the coating.The major disadvantage of the OraSolv formulations is its mechanical strength. For that reason, Cima developed a special handling and packaging system for OraSolv. Manufacturing requires a controlled environment at low relative humidity and protection of the final tablets with moisture impermeable blisters.

3) Durasolv technology

Durasolv is CIMA's second generation fast dissolving or disintegrating tablet formulation to produce stronger tablets for packing in conventional blisters or bottles. Durasolv has much higher mechanical strength due to use of the higher compaction pressure during tabletting. One disadvantage of Durasolv is that the technology is not compatible with larger doses of active ingredients, because the formulation is subjected to high pressure during compaction. The drug powder coating in Durasolv may become fractured during compaction, exposing the bitter tasting drugs to the patient taste

buds. So This technology is good for tablets having low amount of active ingredients.

4) Wow tab technology

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. Due to the significant hardness the WOWTAB formulation is more stable to the environment than the Zydis and Orasolv. Erythritol was found to be the best sugar for this type of formulation, showing rapid disintegration which is unaffected by tablet hardness.

5) Cotton candy technology

This process is so named as it utilizes an inimitable spinning mechanism to produce floss like crystalline structure, which mimics cotton candy. The cotton candy process also known as the candy floss process. A mouth dissolving tablet is formed using candy floss or shear form matrix. It involves the formation of matrix of polysaccharides or saccharides by simultaneous action of flash melting and spinning. The matrix formed is partially recrystallised to have improved flow properties and compressability. This candy floss matrix is then milled and blended with active ingredients, excipients and subsequently compressed to ODT. This process can accommodate larger drug doses and offer improved mechanical strength. However, high process temperature limits the use of this process.

6) 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 matter of seconds.

7) Nanocrystal technology

NanoCrystal™ Fast dissolving technology provides for: Pharmacokinetic benefits of orally administered nanoparticles (<2 microns) in the form of a rapidly disintegrating tablet matrix.Nano Crystal colloidal dispersions of drug substance are combined with water-soluble GRAS (Generally Regarded As Safe) ingredients, filled into blisters, and lyophilized. This method avoids manufacturing process such as granulation, blending and tabletting which is more advantages for highly potent and hazardous drugs.For fast dissolving tablets, Elans proprietary Nanocrystal technology can enable formulation and improve compound activity and final product characteristics. Decreasing particle size increases the surface area,which leads to an increase dissolution rate.

8) Shearform technology

In this technology, a shearform matrix, 'Floss' is prepared. Feedstock prepared with a sugar carrier is subjected to flash heat processing. In this process, sugar is simultaneously subjected to centrifugal force and to a temperature gradient, which causes the temperature of the mass to rise and hence an internal flow condition is created, permitting part of it to move with respect of the mass. This is followed by its exit through the spinning head that flings the floss under centrifugal force and draws into long and thin floss fibres, which are usually amorphous in nature. the floss so produced is further chopped and recrystallised to provide a uniform flow, thus facilitate blending. Then the recrystallised matrix, active drug and other excipients are blended together and finally compressed into tablets. Active drug and other excipients may be blended with the floss before recrystallising it. The tablets manufactured by this process are highly porous in nature and offer very pleasant mouth feel due to rapid solubilisation of sugars in presence of saliva.

9) Pharmaburst technology

Pharmaburst technology is patented by SPI pharma. Pharmaburst technology uses off the shelf coprocessed excipients to create an ODT that, depending on the type of active ingredients and loading, dissolves within 30- 40 seconds. The quantity of pharmaburst required in a formulation depends on the active ingredients in the tablet. The process involves a dry blend of a drug, flavor and lubricant that are compressed into a tablet on a standard tablet press with stock tooling. The manufacture process can be carried out under normal temperature and humidity conditions. The tablets can be packaged in blister packs or bottle.

10 Frosta technology

Akina patents this technology. The core concept of Frosta technology is compressing highly plastic granules at low pressure to produce strong tablets with high porosity. The highly plastic granules comprise three classes of components: a porous and plastic material, a water penetration enhancer, and a binder. The process involves mixing the porous plastic material with water penetration enhancer followed by granulating with binder. The technology can be used for almost any drugs including aspirin, loratidine, caffeine, and folic acid, vitamins and dietary supplements. The highly plastic granule approach produces fast melting pharmaceutical tablets with excellent hardness and fast disintegration time ranging from several seconds to 30 seconds, depending on the size of the tablets.

8 MARKET POTENTIAL FOR ODTs [4,10,13.14]

About 92% of the ODT world market is divided in three therapeutic categories-

1. **Central nervous system** (50% market share) with the greatest potential for success with ODTs are treatments for GERD, pain, schizophrenia and other CNS diseases, Parkinson's disease, migraine, nausea and sleep nervous system.
2. **Gastrointestinal system** (29%), and
3. **Oncology system** (13%).

A key reason that companies choose an ODT over other delivery technologies is that it is relatively easy and often less risky delivery option to develop. Since the route of administration remains the same, ODTs that are formulated as bioequivalent line extensions or generic versions of an existing oral dosage form have minimal clinical requirements to gain approval. Using ODT technology to extend the patent life and market exclusivity of an established drug boosts the value of a brand, fending off generic erosion and thereby increasing revenues.

9 EVALUATION OF ODTs [1,5,16,17,18]

Hardness[18]

Hardness or tablet crushing strength (kg) is the force required to break a tablet in a diametric compression and is measured using Monsanto tablet hardness tester(eg. Monsanto).It is an important parameter in formulation of mouth dissolve tablets because excessive crushing strength significantly reduces the disintegration time. Hardness is expressed in kg/cm2.

Friability [18]

Friability of the tablet determined using Roche friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at a height of 6 inches in each revolution. Pre weighted sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. Tablets were dusted using a soft muslin cloth and reweighed. The friability (F) is given by the formula.

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

Weight Variation [17]

Randomly, twenty tablets were selected after compression and the mean weight was determined.None of the tablets deviated from the average weight by more than ±7.5% (USPXX).

Thickness [18]

Tablet thickness can be measured using a simple procedure. 5 tablets are taken and their thickness is measured using Vernier calipers.

Wetting time and water absorption ratio [1]

Wetting time of dosage form is related with the contact angle. Wetting time of the ODT is another important parameter, which needs to be assessed to give an insight into the disintegration properties of the tablet. Lower wetting time implies

The wetting time of the tablets can be measured using a simple procedure, five circular tissue papers of 10 cm diameter are placed in a petridish with a 10-cm diameter. Ten milliliters of water-soluble dye (eosin) solution 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 the wetting time. For measuring water absorption ratio the weight of the tablet before keeping in the petri dish is noted (W b). The wetted tablet from the petridish is taken and reweighed (W a). The water absorption ratio, *R* can be then determined according to the equation:

$$R = 100 (W_a - W_b) / W_b.$$

Disintegration test [1]

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 [1]

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 I and II can be used. USP I 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. Proposed USP II Paddle apparatus, which is the most suitable and common choice for ODTs, with a paddle speed of 50 rpm commonly used. Typically, the dissolution of ODT is very fast when using USP monograph conditions; hence, slower paddle speeds may be utilized to obtain a profile. The USP II 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 flavors and sweetener. Excipient to drug ratio may be higher since the formulation is designed to have good taste and mouth feel, decreasing the detection of the drug to background (excipient) in the UV spectrophotometer.

Moisture uptake studies [1]

Moisture uptake studies for ODT should be conducted to assess the stability of the formulation. Ten tablets from each formulation are kept in a desiccator over calcium chloride at 37°C for 24 h. The tablets are then

weighed and exposed to 75% relative humidity, at room temperature for 2 weeks. Required humidity is achieved by keeping saturated sodium chloride solution at the bottom of the desiccator for 3 days. One tablet as control (without superdisintegrant) is kept to assess the moisture uptake due to other excipients. Tablets are weighed and the percentage increase in weight is recorded.

10 CONCLUSION

ODTs offer numerous significant advantages over conventional dosage forms because of improved efficacy, bioavailability, rapid onset of action, better patient compliance, and acceptance. MDTs may be more suitable for the oral delivery of drugs such as protein and peptide-based therapeutics that have limited bioavailability when administered by conventional preparations. Some fast dissolving technologies could be used to produce stable freeze dried solid tablets and deliver these biomolecules pregastrically in a form that allows rapid dissolution in mouth. The development of enhanced oral protein delivery technology by Fast dissolving Tablets which may release these drugs in the mouth are very promising for the delivery of high molecular weight protein and peptide.

Table No.4: ODT products in Indian market [4,14]

Brand Name	Active Ingredients	Company
Nimulid-MD	Nimesulide	Panacea
Biotech Zyrofmeltab	Rofecoxib	Zydus Cadila
MOSID-MD	Mosapride Citrate	Torrent Pharmaceuticals
Feledine Melt	Piroxicam	Pfizer
Maxalt ODT	Famotidine	Merck
Remeron Sol Tab	Mirtazapine	Organon
Romilast	Montelukast	Ranbaxy
Manza BDT	Olanzepine	Orchid
Olanexinstab	Olanzepine	Ranbaxy
Valus	Valdecoxib	Glenmark
Rofaday MT	Rofecoxib	Lupin
Torrox MT	Rofecoxib	Torrent

Table No.5: ODT products available in International market [4,13]

Product	Manufactured by/for	Active ingredient	Category	Indication
Abilify Discmelt	Otsuka	Aripiprazole	Atypical Antipsychotics	Schizophrenia, Bipolar disorder
Allegra	Sanofi Aventis	Fexofenadine	Anti-histamine	Allergic rhinitis
Aricept	Eisai Co.	Donepzil	ACE Inhibiter	Alzheimer's dis
Benadryl Fast Melt	Pfizer	Diphenhydramine	Anti-histamine	Allergy
Calpol fast Melt	McNeil Healthcare UK	Paracetamol	Analgesics	Pain
Clonazepam ODT	Par Pharmaceutical	Clonazepam	benzodiazepines	Anxiety,Seizure Disorder
Loratadine Redidose	Ranbaxy	loratadine	Anti-histamine	Allergy
Maxalt-Mlt	Merk& Co.	Rizatriptan	5-HTAntagonist	Acute Migraine
Mirtazapine ODT	Teva Pharmaceuticals	Mirtazapine	Antidepressant	MajorDepressive Disorder
NurofenMeltlets	Reckitt Benckiser	Ibuprofen	NSAIDs	Pain, fever, Inflammation
Ondensetron ODT	Teva Pharmaceuticals	Ondensetron	Antiemetics	Nausea, Vomiting
Parcopa	Schwarz Pharma	Carbidopa / Levodopa	DDC Inhibitors [Carbidopa]	Parkinson's Disease

Zofran ODT	GlaxoSmithKline	Ondansetron	Antiemetics	Nausea,Vomiting

11 REFERENCES:

1) Chowdary.K.P.R, K. Ravi Shankar,and B. Suchitra. Recent Research On Orodispersible Tablets – A Review. International Research Journal of Pharmaceutical and Applied Sciences. 2014; 4(1): 64-73.
2) SivaSankar G.V, K. Sasikanth, Sreekanth Nama, B. Brahmaiah, G. Krishna Chaitanya A Review On Oral Disintegrating Tablets. International Journal of Advanced Pharmaceutics. 2013; 3(2): 59-64.
3) Chowdary,K.P.R, and Aishwarya, K. V. N. R., Recent research on fast dissolving tablets –A review, Journal of Global Trends in Pharmaceutical Sciences. 2013; 4(1): 940-954.
4) Sunitha H. S, S. Parthiban, G. P. Senthil Kumar, T. Tamiz Mani. A Recent Review On Technological Advancement And The Use Of Natural Superdisintegrant In The Formulation Of Fast Disintegrating Tablet. Asian Journal of Research in Pharmaceutical Sciences and Biotechnology. 2014; 2(2): 31 – 37.
5) Khairnar Dhiraj A, Anantwar Sanjay P, Chaudhari Chetan S, Valavi Ashish B. Orodispersible Tablets – An Overview. International Journal Of Pharmaceutical Research And Bio-Science.Ijprbs. 2013; 2(6): 305-331.
6) Mudgal V, Sethi P, Kheri R, Saraogi GK, Singhai AK. Orally Disintegrating Tablets: A Review. International Research Journal of Pharmacy. 2011; 2(4): 16-22.
7) Sharma Deepak, Kumar Dinesh, Singh Mankaran, Singh Gurmeet, Rathore M.S. fast disintegrating tablets: a new era in novel drug delivery system and new market opportunities. Journal of Drug Delivery & Therapeutics.2012; 2(3): 74-86
8) Bhowmik D, Chiranjib B, Krishnakanth, Pankaj, Chandira MR, Fast Dissolving Tablet: An Overview, Journal of Chemical and Pharmaceutical Research, 2009;1(1): 163-177.
9) Ujjwal Nautiyal, Satinderjeet Singh, Ramandeep Singh, Gopal, Satinder Kakar. Fast Dissolving Tablets as A Novel Boon: A Review. Journal of Pharmaceutical, Chemical and Biological Sciences.2014;2(1): 05-26.
10) Shiv kumar srivastava, ravendra verma, vikash chandra, shobhit prakash srivastava. Orally disintegrating tablets; a dosage form that extends the market exclusivity and patent protection. World journal of pharmacy and pharmaceutical sciences. 2014; 3(7); 526-546.
11) Tejvir Kaur, Bhawandeep Gill, Sandeep Kumar, G.D. Gupta. Mouth Dissolving Tablets: A Novel Approach To Drug Delivery, International Journal of Current Pharmaceutical Research. 2011; 3(1): 08-17.
12) Tanmoy ghosh, Amitava ghosh and Devi prasad. A review on new generation orodispersible tablets and its future Prospective.international journal of pharmacy and pharmaceutical sciences. 2011; 3(1):1-7
13) www.wikipedia.com.
14) Amrita A, Kagalkar, Basavaraj K, Bagli R S. Development and evaluation of herbal fast dissolving tablet. International journal of pharma research and review.2014; 3(1): 6-14.
15) Velmurugan S and Sundar V. Oral Disintegrating Tablets: An Overview. International Journal Of Chemical And Pharmaceutical Sciences. 2010; 1(2): 1-12.
16) Chang R.K, Guo X, Burnside B.A, Couch R. Fast dissolving tablets. Pharma Tech. 2008; 24(6): 52-58.
17) Rathod C.P, Dhadwe A.K, Patil K.G, Bhosale P.H, M.Rajurkar. .Formulation And Evaluation Of Orodispersible Tablet Of Sumatriptan Succinate By Sublimation Method. World journal of pharmacy and pharmaceutical sciences. 2013; 2(6): 6178-6188.
18) Bankar S.K, Chaudhari A.V, Mahale N.B, Chaudhari S.R. A Review on Orodispersible Tablets Prepared Using Spray Dried Sustained Release Microparticles. Journal of Advanced Drug Delivery. 2014; 1(2); 82-95.