ISSN 0976 – 3333

Available Online at www.ijpba.info

International Journal of Pharmaceutical & Biological Archives 2016; 7 (4): 1 - 12

REVIEW ARTICLE

Orodispersible Tablets: A splendid Form of Oral Drug Delivery System- An Updated Review

Ritesh Kumar[1*], Sakshi Garg[1], Amrish Chandra[2], Vijay Kumar Sharma[1]

[1]*Dr. K. N. Modi Institute of Pharmaceutical Education and Research, Modinagar, 201204, Uttar Pradesh, India*
[2]*Amity Institute of Pharmacy, Amity University, Noida-201313, Uttar Pradesh, India*

Received 28 Mar 2016; Revised 11 June 2016; Accepted 21 June 2016

ABSTRACT

Orodispersible tablets (ODTs) are solid dosage forms that disintegrate or dissolve in the oral cavity in less than 60 seconds without water and chewing. They were first introduced to the market in the 1980s, and become one of the fastest growing subdivisions of the oral drug delivery industry and their products are developing at a great rate. New orodispersible tablet technologies address many pharmaceutical and need of patients, ranging from enhanced life-cycle management for suitable dosing for pediatric, geriatric and psychiatric patients with dysphagia. This is seen to affect about 35% of the general population and associated with a number of diseases like Parkinsonism, mental disability, motion sickness, unconsciousness, water unavailability etc. Other groups that may face problems using conventional oral dosage forms include the mentally ill, the partially developed patients, and some patients who are uncooperative, on reduced liquid intake, or are nauseated. To overcome such difficulties, orodispersible tablets have been developed. This property in dosage form can be reached by the addition of different excipients, from which super disintegrant is the key adjuvant. This has motivated both academia and industry to generate new orally dispersible formulations and technological approaches in the field. Among the dosage forms developed to facilitate for easy medication, the Orodispersible tablets (ODTs) are one of the most widely implemented commercial products. The aim of this review article is to give knowledge of desired characteristics, advantages, preparation methodologies, patented technologies, evaluation and industrial applications of ODTs formulation.

Key words: ODT, Super disintegrants, Dysphagia, Parkinsonism, Patented.

INTRODUCTION

Orodispersible tablets (ODT) are oral unit solid dosage forms that disintegrate in the oral cavity in easy swallow residue. Mouth dissolving tablets, Orally disintegrating tablets, Melt- in- mouth tablets, Fast dissolving drug delivery, Porous tablets, Quick dissolving tablets are also known as Orodispersible tablets.

Recently, ODT has started to gain popularity as a new drug delivery system, because they are easy to administer and lead to enhanced patient compliance mainly in pediatric and geriatric patients. In order to allow fast dissolving tablets to disperse in the oral cavity, they are made either very porous and soft- molded matrices or compressed into tablets that are made by very low compression force, which make the tablets friable and/or brittle, which are difficult to handle, so they need specialized peel-off blister packaging. A key reason that companies choose ODTs over other delivery technologies is that it is a comparatively easy and less risky delivery option to develop. Since, the route of administration remains the same; ODTs are formulated as generic versions of an existing oral dosage form have very less clinical requirements to gain approval[1]. Their growing popularity was underlined recently when European pharmacopoeia accepted the term "Orodispersible tablet, " as a tablet that to be placed in the mouth where it dissolves rapidly before swallowing. According to EP, the ODT should disperse or disintegrate in less than 3 minutes. The basic perspective in the development of ODT is the use of super disintegrants i.e. croscarmellose, sodium starch glycolate (primogel, exploited), polyvinylpyrrolidone (polyplasdone) etc., which provide rapid

***Corresponding Author:** Ritesh Kumar, **Email:** ritesh_pharma@rediffmail.com

dispersion of the tablet after putting in the mouth, so that the drug rapidly release in saliva [2].

Oral route of drug administrations has broad acceptance up to 50-60% of the total dosage form. Solid dosage forms are popular because of easy administration, self-medications, and most importantly the patient compliance [3]. The tablet is still most conventional dosage form exists today due to ease of self-administration, compact in nature, easy to manufacture and it can be given inaccurate dose. One main drawback of solid dosage forms is the difficulty in swallowing (dysphagia) or chewing for some patients mainly in pediatric and geriatric patients. The problem of swallowing is a common experience in geriatric patients due to choking fear, hand tremors, dysphasia and in young individuals due to undeveloped muscular and nervous system and in schizophrenic patients which leads to poor patient compliance [4]. Difficulties in swallowing of tablets and capsules are also occurring when water is not available, in diarrhea, common cold associated with coughing, allergic condition and bronchial infection [5]. Approximately one-third of the population (mainly pediatric and geriatric) has problems in swallowing, resulting in poor compliance with oral tablet drug therapy which reduced overall therapy effectiveness.

During the past decade, the ODT (Orodispersible technology), which makes tablets dissolve or disintegrate or disperse in the mouth without water intake, has drawn a great deal of attention [6]. The time of disintegration of fast disintegrating tablets is mainly considered to be less than one minute[7-10]. The fast dissolving solid dosage form turns into a soft paste or liquid form which make swallowing easier, and thus it is free of risk of choking [11,12]. In recent years, a variety of improved techniques for delivering drugs have been developed with the aim of enhancing bioavailability, convenience of patient and patient compliance.

Advantages of Orodispersible Tablets [13-18]:

- It does not need chewing.
- Its improved stability.
- It is Suitable for control as well as fast release activities.
- It is improved compliance/ added convenience.
- It has no water needed.
- It has Better taste.
- Benefit of liquid medication in the form of solid preparation.
- Patient's compliance for disabled bed ridden patients and for travelling and busy people, who do not have ready access to water.

Ideal Properties of Orodispersible Tablets [19]:

The performance of ODTs depends on the technology, which is used during their manufacturing process. The important property of these tablets is the ability to disintegrate rapidly and dissolve in saliva, thereby obviating the need for water. Various technologies have been developed that allow tablet to perform this unique property. An ideal ODT should meet the following criteria:

- It does not require water for oral administration yet disintegrates and dissolve in few seconds.
- It must have sufficient strength to withstand the situations of stiffness of the manufacturing process and post-manufacturing handling.
- It must allow high drug loading.
- It must have a pleasant mouth feel.
- It is insensitive to environmental conditions.
- Show low sensitivity to environmental conditions (temperature and humidity).
- It is more accurate dosing, and lower volume and weight**.**
- It should be portable without friability concern.
- Have a pleasant mouth feel.
- Leave minimum or no residue on the tongue after oral administration.
- Ensure a low sensitivity to environmental condition such as temperature and humidity.
- Allow the manufacturing of the tablet using conventional processing and packaging, and low-cost equipment.
- Mouthfeel- Mouthfeel is critical property, and patients should receive a product that feels pleasant and sweet.
- Some large particles from the disintegrating tablets those are insoluble or slowly soluble in saliva may lead to an unpleasant gritty feeling. This can be overcome by keeping most of the particles under the detectable size limit. In some cases, certain flavors can be improved mouth-feel perception, resulting in a product that is received as being less gritty, even if the only change is the

flavor or taste. Effervescence can be added to aid disintegration and mouth feel can be improved by reducing the "dryness" of a product [20].

- Friability- In order to allow orodispersible tablets to dissolve in the mouth, they are made up of either very porous or soft molded matrices or compressed into tablets by applying very low compression force, which makes the tablets friable which are difficult to handle, often need specialized peel-off blister packing. To overcome this type of problem, some companies introduced more durable forms of fast dissolving tablets, such as Wowtab and Dura Solve [21].

Mechanisms [2, 22]:

- **Swelling:** The most widely accepted general mechanism of action for tablet disintegration is swelling. Tablets of high porosity show poor disintegration due to lack of sufficient swelling force. It is worthwhile to note that if the packing fraction is very high, so the fluid is unable to penetrate in the tablet and disintegration is again slow down
- **Porosity and Capillary Action:** When we put the tablet in suitable aqueous medium, the medium penetrates into the tablet and replace the air adsorbed on the particles, which weakens the intermolecular bond and breaks the tablet into fine particles. Water uptake by tablet depends on the hydrophilicity of the drug /excipient and on tablet conditions. For these types of disintegrating agents, maintenance of porous structure and low interfacial tension towards fluid is necessary which helps in disintegration with developing a hydrophilic network around the drug particles.
- **Due to Disintegrating Particle or Particle Repulsive Forces:** Another mechanism of disintegration attempts to explain the swelling of tablets made with non-swellable disintegrants. Goyt-Hermann has proposed a particle repulsion theory based on the observation that non-swellable particle also causes disintegration of tablets.
- **Due to Deformation:** During tablet compression, disintegrated particles get deformed and these deformed particles get into their original structure when they come in contact with aqueous media or water. Occasionally, the swelling capacity of starch is improved when granules are extensively deformed at the time of compression. This increase in size of the deformed particles produces a fracture of the tablet. This may be a mechanism of starch and has only recently begun to be studied.

Potential Candidate for Orodispersible Tablets[23-30]:

Analgesics, anti-arrhythmic, anti-inflammatory agents, anthelmintics, antibacterial agents, anti-coagulants, anti-depressants, anti-diabetics, anti-epileptics, anti-fungal agents, anti-gout agents, anti-hypertensive agents, anti-malarias, anti-migraine agents, anti-muscarinic agents, anti-neoplastic agents, immunosuppressants, anti-protozoal agents, anti-thyroid agents, anxiolytic, sedatives, hypnotics and neuroleptics, cardiac inotropic agents, nitrates, anti-anginal agents and oral vaccines.

Techniques of Orodispersible Tablets [2]:

Many techniques have been reported for the preparation of mouth dissolving tablets or tablets.

- **Freeze Drying/ Lyophilization:** Freeze drying is the process in which water is sublimated after the product has been freezed. This technique creates an amorphous porous structure that can dissolve rapidly. A typical procedure involved in the manufacturing of ODTs using this technique is mentioned here-The active drug is dissolved or dispersed in an aqueous solution of a carrier or polymer. The weighted mixture is poured into the walls of the preformed blister packs. The trays holding the blister packs pass through liquid nitrogen freezing tunnel to freeze the drug solution. Then the frozen blister packs are settled in refrigerated chambers for continuation of the freeze-drying process. After freeze-drying, the aluminium foil covering is applied to a blister-sealing machine. Finally the blisters are packaged and shipped. The freeze-drying technique has indicated an enhanced absorption and increase in bioavailability. The major disadvantages of the freeze-drying technique are that it is an expensive and time-consuming process; fragility makes conventional packaging unsuitable for these types of products and

poor stability under stressed conditions. The process had to go through various modifications to pass drugs with different physicochemical characteristics, drug loading and particle size, and matrix alterations to result in a suitable dosage form [24-30].

- **Tablet Molding:** Molding process is of two type's i.e. solvent method and heat method. The solvent method involves wetting the powder blends with a hydroalcoholic solvent proceeded by compression at low pressures in molds to form a wetted material (compression molding). The solvent is then removed by air-drying. The tablets manufactured in this manner are less rigid than compressed tablets and posses a porous structure that fastens dissolution. The heat method involves a preparation of a suspension that contains a drug, agar and sugar (e.g. Mannitol or lactose) and transfers the suspension in the blister packaging molds, solidifying the agar at the room temperature to form a jelly and drying at 30^{o}C under vacuum. The mechanical strength of molded tablets is a matter of serious concern. Binding agents, which increase the strength of the tablets, need to be added. Taste masking is an added problem for this technology. The taste-masked drug particles were made by spray congealing; a molten triturated mixture of hydrogenated cottonseed oil, lecithin, sodium carbonate, polyethylene glycol and an active ingredient are compressed into a lactose based tablet. Compared to the lyophilization technique, tablets developed by the molding technique are easier to scale up for industrial manufacture [31].
- **Spray Drying** [23, 32, 33]**:** Spray dryers are mainly used in pharmaceuticals and biochemical processes. Due to the solvent is evaporated very rapidly; spray drying can make highly porous, fine powder. Spray drying can be used to prepare rapidly dispersible tablets. This technique is based on a particulate support matrix, which is made by spray drying, an aqueous composition containing support matrix and other components to produce a highly porous and fine powder. Then this is mixed with active ingredients and compressed into tablets. Tablets made by this technology are meant to disintegrate within 20 seconds.
- **Sublimation Technique** [23, 34]**:** The sublimation technique to prepare extremely porous compressed tablets that are quickly soluble in saliva. Mannitol and camphor are mainly used as a tablet matrix material and subliming the material respectively. Camphor is followed by subliming in vacuum at 80^{0}C for 30 minutes to develop pores in the tablets. A mixture containing active ingredients and carbohydrates (glucose, mental, Xylitol etc.) is moistened with water (1- 3 %w/w) and compressed into tablets. Then remove the water, which yields to the highly porous tablet that exhibit excellent bioavailability.
- **Direct Compression Method** [23, 35, 36]**:** In this method, tablets are compressed directly from the triturated mixture of the drug and excipients without any pre-treatment. The triturated mixture to be compressed must have adequate flow properties and bind under pressure, thus granulation is unnecessary. Few drugs can be directly compressed into tablets with acceptable qualities. A type of disintegrant and its proportion hold a prime importance in this method. The other main factors to be considered are particle-size distribution, pore size distribution, contact angle, tablet hardness and water absorption capability. All these factors mainly used to determine the disintegration. The disintegrant addition technology is cost effective and very easy to process at industrial level. Carboxymethylcellulose as disintegrating agent and one swelling agent consisting of modified starch or microcrystalline cellulose can form quickly dispersible tablets. The tablets disperse in the mouth in less than 60 seconds by this method.
- **Mass-Extrusion (Mass-Extrusion)** [23, 37]**:** This technology involves palliating the active blend using the solvent mixture of water-soluble polyethylene glycol, methanol and subsequent expulsion of palliated mass through the extruder or syringe to get a cylinder of the product into even segments using a blade that is heated to form tablets. The dried cylinder can also be used to coat granules for bitter drugs to achieve the taste masking.

- **Nanonization:** A newly developed Nanomelt technology involves particle size reduction of drug to nanosize through milling the drug using a proprietary wet-milling process. The nanocrystals are stabilized against agglomeration through surface adsorption on selected stabilizers, which are then compress to form ODTs. This technique is especially for water insoluble drugs. Other advantages of this technology include fast disintegration/ dissolution of nanoparticles for increased absorption and hence high bioavailability and dose reduction, manufacturing process is cost-effective, conventional packaging due to rare durability and wide range of doses (up to 200 mg of drug per unit) [23].

Patented Technologies of Orodispersible Tablets [23]:

Following are the patented technologies of Orodispersible Tablets:-

- **Zydis Technology [23,38]:** Zydis formulation is an isolated freeze dried tablet in which drug is physically dissolved with the fast-dissolving carrier material. When zydis formulations are situate into the mouth, the freeze-dried structure disintegrates instantaneous and does not require water for swallowing. To provide strength during handling, polymers such as gelatin, dextran or alginates are added. To obtain crystallinity, elegance and hardness, saccharides such as mannitol or sorbitol are added. Water is used in the manufacturing process to ensure production of porous units to attain faster disintegration. Various gums are used to prevent sedimentation of dispersed drug particles in the manufacturing process. Glycine is added to prevent the shrinkage of zydis units during freeze drying process. Zydis products are packed in blister packaging to protect the formulation from moisture in the environment.
- **Durasolv Technology [23, 37]:** Durasolv is a patented technology of CIMA labs. The units made by this technology consist of a drug, fillers and lubricant. Units are prepared by using conventional tableting machine and must have good rigidity. Units can be packed into blister packaging. Durasolv is an excellent technology for products requiring low amounts of API.
- **Orasolv Technology [23, 38, 39]:** Orasolv Technology has also been developed by CIMA labs. In this system API is taste masked. It also contains effervescent disintegrating agent. Tablets are produced by direct compression technique at low compression force for minimizing oral disintegration time. Conventional blenders and tablet machine are used to produce the tablets. The produced tablets are soft, friable and packed in specially designed pick and place system.
- **Wowtab Technology [35, 40]:** Wowtab Technology has been patented by Yamanouchi Pharmaceutical Co. WOW stands for "Without Water". In this process, combination of low moldability saccharides and high moldability saccharides are used to acquire a rapidly disintegrating strong tablet. The API is mixed with a low moldability saccharide and granulated with a high moldability saccharide and then compressed into tablet.
- **Flash Dose Technology [23, 31, 38]:** Flash dose technology is patented by Fuisz Nurofen meltlet, a new form of ibuprofen named melt-in-mouth tablets are prepared by using flash dose technology is the first marketed product launched by Biovail Corporation. Flash dose tablets/units consist of self binding shear form matrix named as "floss". Shear form matrices are made by flash heat processing.
- **Flashtab Technology [23, 31, 38]:** Prographarm laboratories have been patented the Flashtab technology. Tablets/Units prepared by this technology consist of an API in the form of microcrystals. Drug microgranules are prepared by using the simple techniques like coacervation, microencapsulation, and extrusion- spheronisation. All processing needs conventional tabletting technology.
- **Oraquick Technology [23, 38, 41]:** KV Pharmaceutical claims its microsphere technology, known as Micro Mask, has superior mouth feel over taste-masking alternatives. The taste masking process does not use any kind of solvents; therefore it leads to faster and more successful production. Also, lower heat of production than alternative fast-disintegrating technologies makes

Oraquick suitable for heat-sensitive drugs. KV Pharmaceutical also claims that the matrix which surrounds and protects the drug powder in microencapsulated particles is more compressible, meaning tablets can be compressed to attain significant mechanical strength without disrupting taste-masking. Oraquick claims quick disintegration in seconds also with good taste-masking. There are no marketed products using the Oraquick technology currently but KV pharmaceutical has products in development stages such as analgesics, scheduled drugs, cough and cold medicines, psychotropics, and anti-infectives.

Material Properties for Making Orodispersible Tablets:

Orodispersible tablets (ODTs) are prepared by several different methods including crystalline transition, phase transition, sublimation, spray drying, and direct compression.

- **Direct Compression Method** [42, 43]**:** Direct compression method is used most commonly because of its low cost and ease of manufacturing. Research on ODTs prepared by the compression method has mainly focused on decreasing the disintegration time of the tablets in the saliva, while maintaining necessary mechanical strength for handling during manufacturing, packaging, and transportation. The main point to developing a successful ODT formulation by the compression method is to select the appropriate excipients and the appropriate processing techniques.
- **Crystalline Transition Method:** The crystalline transition method (CTM) makes use of the phase transition of pharmaceutical excipients mainly sugars, from the amorphous maintaining porosity. Amorphous forms of sugars have higher compressibility than crystalline forms[44, 45], so they can contribute to high tablet porosity. However, amorphous sugars have a tendency to absorb more moisture than crystalline ones, which means that the tablets containing amorphous sugars are more sensitive to moisture. A blend of the two was compressed at varying compaction pressure and exposed to various conditions of temperature and humidity to induce phase transition [46]. The storage temperature and humidity affected the rate of crystalline transition and it was shown that the faster the crystalline transition, the faster the rate of increase in tablet tensile strength [46-48]. The mechanism of the CTM can be understood by using the moisture sorption model of amorphous sucrose [49]. The absorbed water can act as a plasticizer and also influence free volume due to breakage of hydrogen bonds between the molecules in the solid. This can lower the glass transition temperature (Tg) to, or below, the operation temperature changing it from a glassy to a rubbery state[50]. The hydrated amorphous sucrose in an ODT can be converted into the crystalline form and the crystalline sucrose forms new internal contact points in the tablet [46,47].When ODTs are prepared by CTM, a level of 10–20% amorphous sucrose in the tablet is suggested. The tensile strength increases with an increasing percentage of amorphous sucrose due to its good compatibility. However, the higher amorphous content causes a longer disintegration time in the mouth [47]. The tensile strength of the tablet remarkably increased during storage, although the porosity of the tablet seemed hardly changed. Conditioning of tablets a certain temperature and humidity was also investigated, and involved different kinds of pharmaceutical polymers, such as polyvinylpyrrolidone (PVP), or other excipients[50-53]. For example, highly water-soluble polymers absorb moisture and form new contact points as the amorphous sugars described above do, although crystal transi- tion seems a rare occurrence in the case of polymers[50]. Similar to the CTM, the mechanical strength of the tablets can be increased significantly with humidity conditioning. This increase might be due to the formation of liquid bridges in the presence of moisture, and then formation of solid bridges after drying [53, 54].
- **Phase Transition Method (PTM):** Saccharides and sugar alcohols can be classified not only by compressibility but also by melting point. Based on the melting point, they are divided into two

groups and investigated using conventional granulation and compression apparatus[55]. Erythritol is the high melting (122 C) and xylitol the low melting (9395 C) sugar alcohol. Erythritol and xylitol are used as a diluents and a binder, respectively for fluid bed granulation. After compression, Place the resulting tablets in a drying oven and heat at a temperature near to the melting point of xylitol (approximately 93^{o}C). Maintain conditions for a certain period of time and then allow the tablets cooling to room temperature.

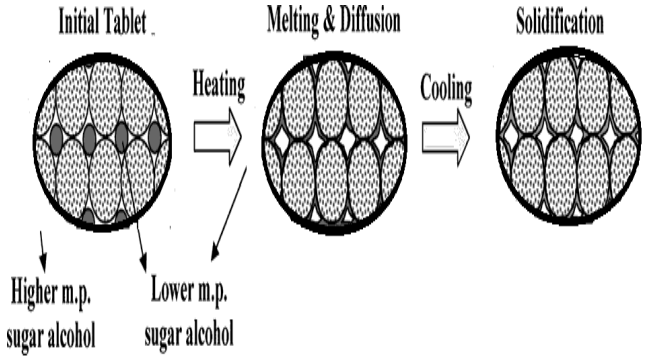

Figure 1: Schematic Illustration of a Orodispersible Tablet Prepared By The Phase Transition Method Using A Higher Melting (Erythritol) And A Lower Melting (Xylitol) Sugar Alcohol

It shows that hardness of tablet will increase with increase in xylitol concentration.

Heating process primarily affects the tablet hardness and disintegration time, but also by the content of saccharides or sugar alcohols. Heating increases pore size of the tablets. It is suggested that the diffusion of xylitol in the tablets causes increase in tablet hardness with increasing pore size. Xylitol melted, diffused, and solidified again in the heated tablets resulting in a greater bonding surface area between the powder particles and increasing hardness. Tablets containing about 5% xylitol shows hardness of 4 kp and an oral disintegration time of <30s. It is also suggested that increasing tablet hardness by heating and storage will not dependent on the crystal state of the sugar alcohols, but related to the formation of inter-particle bonds or the increased bonding surface area induced by the melting of xylitol particles and their subsequent solidification upon cooling. Other pharmaceutical materials, such as polyethylene glycol, and wax, have been also applied to the PTM [56, 57].

- **Sublimation Methods:** The low porosity of compressed tablets may reduce water penetration into the tablet matrix resulting in slow disintegration or dissolution because these processes only occur at the surface.

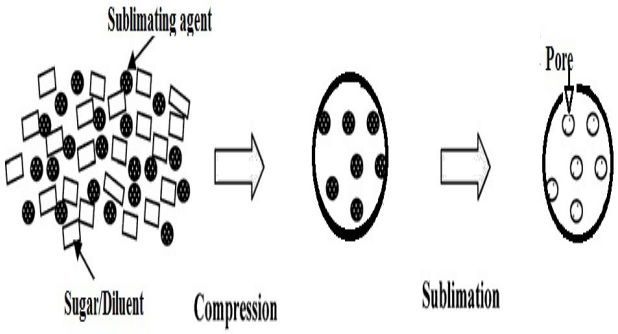

Figure 2: Sublimation Method

- However, when volatile solids are compressed into tablets using a conventional method, they can be removed by sublimation to produce highly porous structures. Typical materials used for this purpose include camphor, menthol, thymol, urea, ammonium carbonate, and ammonium bicarbonate [58, 59].
- **Addition of Super Disintegrants [**60, 61, 62]**:** A disintegrant helps the tablet to break up into granules upon contact with aqueous solution. Fast disintegration of a tablet matrix in the oral cavity easier swallowing and increases the surface area of the tablet granules, which increases the rate of absorption of the API to attain the desired therapeutic effect.Disintegration starts when a small amount of water or saliva contacts the dosage form, then wetting is start and saliva penetrates the tablet matrix by capillary action. Therefore, the material properties of pharmaceutical excipients need to be considered for successful formulation development. There are various number of disintegrants and super-disintegrants in the market and most of them can be considered for use in ODTs. Typical examples include crospovidone (crosslinked PVP), croscarmellose (crosslinked cellulose), sodium starch glycolate (SSG), and low-substituted hydroxypropyl- cellulose. Crospovidone is a synthetic and water insoluble crosslinked homopolymer with the chemical structure of N-vinyl-2-pyrrolidone. A unique one-

step polymerization process known as ‘‘popcorn’’ polymerization is used to synthesize crospovidone polymers. Crosslinking chemically ‘‘entangles’’ the polymer chains and is a major determinant of the product’s properties. This process results in a porous structure with densely cross linked polymers and a morphology that rapidly wicks liquids into the particle to enhance swelling and disintegration. Crospovidone polymers are nonionic so their disintegration properties are independent of pH changes in the gastrointestinal tract. Moreover, they do not form gels. Different grades of Kollidon and Polyplasdone are crospovidone products of BASF and ISP, respectively. Ac-Di-Sol (Croscarmellose sodium) is an internally crosslinked sodium carboxymethylcellulose. Primojel is SSG produced by cross linking and carboxymethylation of potato starch. Both exhibit good water uptake with high capillary action and rapid swelling. The high swelling capacity together with high water penetration leads to fast tablet disintegration. Disintegrants are mainly water-insoluble materials that swell on contact with moisture; therefore the addition of excess disintegrant can lead to grittiness after tablet disintegration. Moreover, tablets containing glycine showed faster disintegration than those without glycine, mainly due to the fine wetting nature of this amino acid. This result is reported for some amino acids which act as disintegration accelerators. In another example of famotidine ODTs, croscarmellose sodium was superior to crospovidone, Indion 414, and sodium starch glycolate. Crospovidone can work as an efficient disintegrant with fast swelling properties. When mannitol and crospovidone were formulated by a direct compression method, the effects of the amount of mannitol and crospovidone as well as the compression force on the characteristics of the tablet were investigated.More polar amino acids have a stronger affinity to water so wetting is faster. A linear trend is observed between tablet wetting time and the polar component of the amino acids. When the polar component of the amino acid is large or the dispersion component has a small value, faster wetting of the tablet is observed. ODTs were prepared by direct compression using microcrystalline cellulose (MCC) and low-substituted hydroxypropyl cellulose (L-HPC) as disintegrants.

Evaluation of Mouth Dissolving Tablets [1, 2]:

Evaluation parameters of tablets mentioned in the Pharmacopoeias, along with some special tests are as following:

- **Weight variation:** Select 20 tablets randomly from the lot and weigh individually for weight variation. Weight variation specification as per I.P. is shown in (**Table 1**) [63].

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

- **Hardness/Crushing Strength:** A significant strength of ODT is difficult to attain due to the specialized processes and ingredients such as super disintegrants used in the manufacturing. The limit of crushing strength for an ODT is usually kept in a lower range to accelerate early disintegration in the mouth/Saliva. It is expressed in kg/cm^2. The crushing strength/hardness of the tablet may be measured using conventional hardness testers such as Monsanto tablet hardness tester [63].
- **Friability (F):** To attain % friability within limits for an ODT is a difficult task to the developer since all methods of manufacturing of ODT are reasonable for increasing the % friability. Thus, it is important that this parameter should be evaluated and the results are within the prescribed limits (0.10.9%) [64].
- **Wetting Time:** Wetting time of tablet is mainly related with the contact angle. Wetting time of the ODT is an important parameter, which needs to be evaluated to give an understanding of disintegration properties of the tablet. Lower wetting time means a quicker disintegration of the tablet.The wetting time of the tablets can be measured using a simple procedure. Place five circular tissue papers/ whatman’s filter paper of 10 cm diameter in a petridish with a 10cm diameter. Add

ten millilitres of water soluble dye (eosin/amaranth color) solution to Petri dish. Place the tablet carefully on the surface [65].

- **Water Absorption Ratio:** First weigh a tablet, and then fold a piece of tissue paper twice and place in a small Petri dish containing 6 ml of water. Put a tablet on the paper & Measure the time required for complete wetting. Reweigh the tablet. Determine the Water absorption ratio R, by using following equation,
  $R=10(w_a/w_b)$ where,W_b weight of tablet before water absorption & wa is weight of tablet after water absorption [66].
- **Modified Disintegration Test:** The standard procedure of carrying out disintegration test for these types of dosage forms has several limitations and they do not adequate the measurement of very short disintegration times. The disintegration time for ODT needs to be modified as disintegration is required in absence of water, thus the test should resemble disintegration in salivary contents. For this purpose, fill a petridish (10 cm diameter) with 10 ml of water. Carefully put the tablets in the center of petridish and note the time for the tablet to completely disintegrate into fine particles [67, 68].
- ***In-vitro* Dispersion Time:** Add tablet to 10 ml of phosphate buffer solution, ph 6.8 at 37+0.5ºc, Measure the time required for complete dispersion of a Tablet [69, 70].
- **Dissolution Test:** Most suitable and common choice of apparatus is USP 2 paddle apparatus for dissolution of orodispersible tablets, with a rotation speed of 50 rpm. Mainly phosphate buffer (PH 6.8) (900 ml) is used as a dissolution medium [71].

Marketed Products of Orodispersible Tablets [72]:

Table 2: List of Marketed Products of Orodispersible Tablets.

Brand name	Drug	Pharmaceutical company
Benadryl Fastmelt	Diphenhydramine	Pfizer
Benadryl Fast melt	Diphenhydramine	Warner Lambert
Cibalginadue FAST	Ibuprofen	Novartis Consumer Health
Domray MD	Domperidone	Ray Remedies
Dolib MD	Rofecoxib	Panacea
Feldene melt	Piroxicam	Pfizer
Febrectol	Paracetamol	Prographarm
Orthoref MD	Rofecoxib	Biochem
Olanex Instab	Olanzepine	Ranbaxy
Pepcid ODT	Famotidine	Merck
Rofaday MT	Rofecoxib	Lupin
Torrox MT	Rofecoxib	Torrent
Valus	Valdecoxib	Glenmark
Zotacet MD	Cetrizine Hcl	Zota Pharma
Zyprexa	Olanzapine	Elililly
Zofran ODT	Ondansetron	GSK
Claritin redi Tab	Loratidine	Schering plough Corp., USA

Future Potentials of Orodispersible Tablets [73-77]:

A number of ODTs are commercially available using technologies developed by pharmaceutical companies such as Cardinal Healthcare, Jannsen Pharmaceutical, Bioavail, and Eurand, Yamanouchi. However, these technologies use expensive processing technology producing friable tablets that require costly specialised packaging and some use conventional tableting procedures which give longer than desired disintegration time & those still require specialised packaging. Dr Zeibun Ramtoola and her entire team at the Royal College of Surgeons in Ireland have labelled the above disadvantages by developing a novel, cost effective ODTs manufacturing process using conventional tabletting procedures for the formulation of durable tablets suitable for conventional packaging. This patented technology is applicable to a wide range of APIs including generics.

ODTs technologies entered the market in the 1980s, they have grown rapidly in demand and importance, and their product pipeline is rapidly increasing. In 2004, ODTs products generated revenues of well over $2 billion, an increase of 20% after 2003, according to a 2005 report by TCI. With multiple new consumer health and prescription product launches in recent years, the ODTs market was predicted to easily reach $3 billion in 2006, including brands and generics. The market continues to increase 20% each year, with a growing perforation of generic ODTs.

CONCLUSION

The clinical studies show ODTs can improve patient compliance, provide a rapid onset time of action, and increase bioavailability. Considering the many benefits of ODTs, it is only a matter of time until a majority of oral formulations are prepared in ODT forms. By paying close attention to advances in technologies, pharmaceutical companies can take advantage of ODTs for product line perpetuation or for first-to-market products. With continued development of new API, one can expect the emergence of more novel technologies for ODTs in the days to come. The

successful marketed ODTs have good taste and rapid disintegration properties. With rapid acceptance of ODTs by patients and pharmaceutical companies, the market for this dosage form will surely increase, and the product pipeline continues to grow.

ACKNOWLEDGEMENT

We would like to express our grateful thanks to our beloved parents for their blessings, our teacher's and friends for their help and wishes for the prosperous completion of this review article.

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