Recent Trends in Orodispersible Tablets – An Overview of Formulation Technology and Future Prospects

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Abstract

Orodispersible tablet is advanced and convenient drug delivery system, now days acquiring the most widely accepted dosage form. The recent advance in novel drug delivery system aimed for the development of dosage forms convenient to manufacturing and administration, offering immediate release and increased bioavailability. Difficulty in swallowing (Dysphasia) is common among all age groups especially in aged patients and children's. As our society is becoming increasingly aged, there is need to development of an appropriate dosage form for the elderly patients are mostly desirable. A novel orodispersible tablet was investigated in this study as a user-friendly dosage form for the elderly patients and also for children's. Advance development in fast disintegrating technology mainly works to improve the disintegration quality of these delicate dosage forms without affecting their integrity. This article focuses on the patented technologies available and the advancements made so far in the field of fabrication of orodispersible tablets. Apart from the conventional methods of formulation, this review also provides the detailed concept of some unique technologies like freeze drying, direct compression, spray drying, tablet molding, sublimation, fast dissolving films cotton candy process, along with their advantages and limitations.

Keywords: Orodispersible tablet, Increased bioavailability, Dysphasia, Integrity, Patented technologies.

INTRODUCTION

Due to society that is becoming increasingly aged, the development of an appropriate dosage form for the aged patients is most desirable. Because the changes in various physiological functions related with aging including difficulty in swallowing, current dosage forms, like capsules, are impractical. The most desirable formulation for use by the elderly patients is one that is easy to swallow and easy to handle. Taking these requirements into consideration, attempts have been made to develop an orodispersible tablet [1]. Oro dispersible tablets (ODT) are solid single-unit dosage forms that are placed in the mouth, allowed to disperse/dissolve in the saliva and then swallowed without the need for water (European Pharmacopoeia 4.1, 2002) [2]. Difficulty in swallowing (dysphasia) is common among all age groups, especially in elderly, and is also seen in swallowing conventional tablets and capsules. This disorder is associated with many medical conditions, including stroke, Parkinson's, AIDS, thyroidectomy, head and neck radiation therapy, and other neurological disorders, including cerebral palsy .One study showed that 26% of 1576 patients experienced orally disintegrating tablets have been developed, which combine hardness, dosage uniformity, stability and other parameters, with extremely easy administration since no water is required for swallowing the tablets [3]. They are thus suitable for geriatric, pediatric and traveling patients [4]. The solution containing the active ingredients is swallowed, and the active ingredients are then absorbed through the gastrointestinal epithelium to reach the target and produce the desired effect. In addition to improving patient compliance, ODTs have been investigated for their potential in increasing the bioavailability of poorly water soluble drug through enhancing the dissolution profile of the drug. Moreover, pharmaceutical companies also have commercial reasons for developing ODTs. As a drug formulation comes to the end of its patent, the development and formulation of the drug into new dosage forms allows pharmaceutical companies to extend the patent life and 'market exclusivity' . This allows pharmaceutical companies to attract new consumers through advertisement and product promotion plans, and increase profits in the long term [5]. However, due to the rapid ODT disintegration, the active substance comes in contact with the taste buds and the need for a pleasant taste becomes a key aspect for patient palatability. Thus the taste-masking of bitter active substances is a critical hurdle to overcome for the successful development of ODT formulations. In general, oral administration of bitter active substances through ODT formulations should provide an improved degree of palatability, increased patient

compliance and a concomitantly beneficial therapeutic effect. In the past, the methods of taste-masking in orodispesible tablets included sweeteners and flavors. Nevertheless, these additives were not a sufficient means for complete taste-masking. Recent advances in technology have presented viable dosage alternatives to taste-mask bitter drugs. Several approaches have been reported which involve complexation, freeze-drying, micro encapsulation, fluidized-bed coating and supercritical fluids for taste-masking purposes [6]. Recently the European Pharmacopoeia adopted the term orodispersible tablet as a tablet to be placed in the oral cavity where it disperses rapidly before swallowing and which disintegrates in less than 3 min. There was no specification concerning neither the hardness nor the friability of this kind of tablets. That is why we find certain ODT in the market that disintegrate in less than 1min or maybe 30 s. Commercially available ODT are prepared by various techniques, mainly lyophilisation, moulding and direct compression. The lyophilisation and molding techniques produce ODT which disintegrate within about 30 s, but that have low physical resistance and high friability. On the other hand, tablets obtained by direct compression are less friable but disintegrate in a longer time [7]. Recently, there is developed the new preparation method for orodispersible tablets, the crystalline transition method (CT method), utilizing the crystalline transition of amorphous sucrose. The ODT tablets of diluent and amorphous saccharide mixture are prepared at low compression pressure and stored for the crystalline transition. The diluents and amorphous saccharides include mannitol, erythritol, xylitol, microcrystalline cellulose etc. and sucrose, maltose, lactose, etc., respectively. As an alternative technique for preparing ODTs, molded tableting technique that compresses wet granules at low compression force has been developed to achieve rapid disintegration in conjunction with high tablet hardness compared with those prepared by standard compression method. Molded tablets have high porosity; thereby allowing greater water penetration into the tablets and accelerating tablet disintegration [8]. This review discusses the method of preparation, properties, advantages, mechanisms; drugs to be incorporated in the mouth dissolving tablet and evaluation of the mouth dissolving tablet are emphasized.The objectives of this study are to produce a orodispersible tablet, which has sufficient hardness for handling and can be and equipment manufactured by commonly used production methods [9].

IDEAL PROPERTIES OF ODTs

Orodispersible tablet should:

1. Require no water for oral administration.
2. Easily dissolve or disperse in saliva within a few seconds.
3. Have a pleasing taste.
4. Leave negligible or no residue in the mouth when administered.
5. Portable and easy to transport.
6. Able to be manufactured in a simple conventional manner within low cost.
7. Be less sensitive to environmental conditions like temperature, humidity etc.
8. Permit the manufacture of tablet using conventional processing.
9. It should be compatible with taste masking.

ADVANTAGES OF ORODISPERSIBLE TABLETS

Orodispersible technology offers:

- Ease of administration to patients who cannot swallow, such as the aged, stroke victims and bedridden patients; patients who should not swallow, such as renal failure patients; and who refuse to swallow, such as pediatrics, geriatric and psychiatric patients.
- Improved compliance.
- Better Patient’s compliance for disabled bedridden patients and for travelling and busy people, who do not have ready access to water.
- No water needed.
- No chewing needed.
- Better taste.
- Improved stability.

- Suitable for controlled/sustained release actives.
- Allows high drug loading.
- Ability to provide advantages of liquid medication in the form of solid preparation.
- Cost effective.
- Rapid drug therapy intervention.
- Best for patent with oesophageal problems and have difficulties of deglutition tablets.
- High drug loading is possible.
- Have acceptable taste and pleasant mouth feeling.
- Leave minimum residue.

LIMITATIONS OF ORODISPERSIBLE TABLETS

- These tablets usually have insufficient mechanical strength i.e. hence, careful handling required.
- These tablets may leave unpleasant taste and/or grittiness in mouth if not formulated properly.

CHALLENGES TO DEVELOP ODTs

- Rapid disintegration of tablet.
- Avoid increase in tablet size.
- Have sufficient mechanical strength.
- Minimum or no residue in mouth.
- Protection from moisture.
- Good package design.
- Compatible with taste masking technology.
- Not affected by drug properties [10-12].

EXCIPIENTS USED IN PREPARATION OF ODTs

The following excipients are used in preparation of ODT:

1. Superdisintegrants:

As day's passes, demand for faster disintegrating formulation is increased. So, pharmacist needs to formulate disintegrants i.e. Superdisintegrants which are effective at small concentration and have greater disintegrating capacity and they are more effective intragranularly. This superdisintegrants act by swelling and as result of swelling pressure exerted in the outer direction or radial direction, it causes tablet to burst or the accelerated absorption of water leading to an enormous increase in the volume of granules to promote disintegration. The mechanism of disintegration is as shown in Figure no. (1).

Various types of Superdisintegrants used are as follows:

- Crosspovidone
- Microcrystalline cellulose
- Sodium starch glycolate
- Sodium carboxy methyl cellulose or cross carmellose sodium
- Pregelatinzed starch
- Calcium carboxy methyl cellulose
- Modified corn starch, Sodium starch glycolate has good flowability than Cross carmellose sodium.

Factors to be considered for selection of superdisintegrants for use:

- It should produce mouth dissolving when tablet meets saliva in the mouth
- It should be compactable as enough to produce less-friable tablets.
- It should able to produce good mouth feel to the patient. Thus, small particle size is preferred to acquire patient compliance.
- It should have good flow since it improve the flowability of the total blend.

2. Taste masking agents:

These agents are used for masking the bitter taste of drug. Taste-masking of bitter or with objectional-tasting drug substances is critical for any orally-administered dosage form drugs for ODT. Less commonly, active pharmaceutical ingredients to be incorporated are tasteless and do not require taste masking. Sugar based excipient are used for taste masking and as bulking agents. Most of the drugs are having unpleasant or bitter taste. And the basic requirement for designing ODTs is that the drug should not have disagreeable taste. So taste masking is necessary in most of the cases, Sorbitol, mannitol, xylitol, dextrose, fructose, etc. are mainly used. There are various approaches of taste masking of bitter drugs for ODT.

3. Binders:

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, hydroxyl propyl cellulose (HPC), and (HPMC), alone or in admixtures, and the most commonly acrylic polymers are used are the ammonio-methacrylate copolymer (Eudragit RL and RS), polyacrylate (Eudragit.NE), and polymethacrylate (Eudragit E). The right selection of a binder or combination of binders is essential to maintain the integrity and stability of the tablet. The temperature of the excipient should be preferably around 30–35^0 C for faster melting properties. Further, its addition imparts smooth texture and disintegration characteristics to the system [13].

METHODS USED FOR PREPARATION OF ODTs

1. Melt Granulation:

Melt granulation technique is a process by use of which pharmaceutical powders are efficiently agglomerated by a meltable binder. The advantage of this technique compared to a conventional granulation technique is that no water or organic solvents are required. Because there is no drying step involved, the process is less time consuming and uses less energy than wet granulation. It is a useful technique to increase the dissolution rate of poorly water-soluble drugs, such as griseofulvin. This approach to prepare ODT with sufficient mechanical integrity, involves the use of a hydrophilic waxy binder (Superpolystate©, PEG – 6 – stearate). Superpolystate© is a waxy material with a melting point of 33–37°C and a HLB value of 9. So it will not only act as a binder and enhance the physical resistance of tablets but will also help the disintegration of the tablets as it melts in the mouth and solublises rapidly leaving no residues.

2. Effervescent Method:

Orodispersible tablets are also prepared by effervescent method by mixing sodium bicarbonate and tartaric acid or citric acid of concentration 12% (w/w) along with super disintegrants like pregelatinized starch, sodium starch glycolate, crospovidone, and croscarmellose. First, sodium bicarbonate and tartaric acid were preheated at a temperature of 80°c to remove absorbed/residual moisture and thoroughly mixed in the motor. Finally, the blends are compressed in the punch [14].

3. Cotton candy process:

In this process Shearform technology is used in the preparation of a matrix known as FLOSS, made from the combination of the recipients either alone or with the drugs. The fibrous nature of the floss is similar to the cotton-candy fibers. The floss is commonly made of saccharides such as sucrose, dextrose, lactose and fructose at temperatures ranging between 180–260 °F. Other polysaccharides such as polymaltodextrins and polydextrose can be converted into fibers at 30- 40% lower temperature range.

4. Direct Compression:

It is the simplest and most cost effective tablet manufacturing technique for ODTs as they can be fabricated using conventional tablet manufacturing and packaging machinery and also due to availability of tableting excipients with improved flow, compressibility and disintegration properties, especially tablet disintegrants, effervescent agents and sugar based excipients. A type of disintegrant and its proportion are of prime importance. There are number of factors which affect disintegration like particle size distribution, contact angle, pore size distribution, tablet hardness, water absorption capacity and type and

proportion of disintegrants. FLASHTAB, a DC based technology contains coated crystals of drug and micro granules along with disintegrants. In this technology, two types of disintegrants are used: a disintegrating agent (e.g., modified cellulose), which has a high swelling force and a swelling agent (e.g., starch, etc.) which has a low swelling force. A rapidly disintegrable multi particular tablet was prepared using carboxymethyl cellulose as disintegrating agent and swelling agent consisting of modified starch or microcrystalline cellulose. The disintegration time of this tablet was 60 sec (Cousin, et al, 1995).The evolution of carbon dioxide as a disintegrating mechanism forms the basis of another DC based technology called as ORASOLV. One of the processes describes the use of alginic acid and a water-soluble metal carbonic acid to prepare tablets (J. Machalson, 1983). An acidbase reaction occurs when they are dissolved in water. The salt causes the tablet to swell and the carbonic acid produced carbon dioxide within the swelling tablet so that rapid disintegration can be possible. Similarly, the use of sugar-based recipients like dextrose, fructose, isomalt, lactitol, maltitol, maltose, mannitol, sorbitol, starch hydrolysate, polydextrose and xylitol is appreciated in masking the bad taste of the tablets and impart sweetness while formulating OD tablets. A process, in which water is sublimated from the product after freezing, is called freeze drying. Freeze - dried forms provides more rapid dissolution than other available solid products. The lyophilization process imparts glossy amorphous structure to the bulking agent and sometimes to the drug, thereby enhancing the dissolution characteristics of the formulation [15].

5. Tablet Molding:

Tablets produced by molding are solid dispersions. Physical form of the drug in the tablets depends whether and to what extent, it dissolves in the molten carrier. The drug can exist as discrete small particles or micro particles dispersed in the matrix. It can dissolve totally in the molten carrier to produce solid solution or dissolve partially in the molten carrier and the remaining particles stay undissolved and dispersed in the matrix. Disintegration time, drug dissolution rate and mouth feel will depend on the type of dispersion or dissolution [16].

6. Sublimation:

The key to rapid disintegration for orodispersible tablets is the presence of a porous structure in the tablet matrix. Conventional compressed tablets that contain highly water-soluble ingredients often fail to dissolve rapidly because of low porosity of the matrix. Hence, to produce porous matrix, volatile ingredients are used that are later subjected to a process of sublimation. Sublimation is a process in which water passes directly from solid state to vapour state without passing through liquid state. This process involves addition of some inert volatile substances like urea, urethane, naphthalene, camphor, menthol, etc to otherexcipients and the compression of blend into tablet. Removal of volatile constituent by sublimation creates pores in tablet structure, due to which tablet dissolves when comes in contact with saliva. Additionally many solvents like cyclohexane, benzene etc can also be used as pore forming agents. Various steps involved in sublimation technique for preparation of ODT are shown in Figure no. (2).

7. Phase Transition:

MDTs 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 also increased. The increase of tablet hardness associated with heating and storage did not depend on the crystal state of the lower melting point sugar alcohol [17].

8. Freeze Drying:

Freeze drying is the process in which water is sublimed from the product after it is frozen. This technique creates an amorphous porous structure that can dissolve or disperse rapidly. A typical procedure involved in the formulation of ODT using this technique is mentioned here. The active drug constituent is dissolved or dispersed in an aqueous solution of a carrier/polymer. The mixture is done by weight and poured in the walls of the preformed blister packs. The trays holding the blister packs are transfer through liquid nitrogen freezing tunnel to freeze the drug solution or dispersion. Then the frozen blister packages are placed in refrigerated cabinets to continue the freeze - drying process. After freeze-drying the aluminum foil backing is applied on a blister-sealing machine. Finally the blisters are packaged and shipped. The freeze-drying method has demonstrated

improved absorption and increase in bioavailability of drug. The major disadvantages of lyophillization method are that it is expensive method and time consuming; fragility makes conventional packaging unsuitable for these products and poor stability under stressed conditions.

9. Mass-Extrusion:

This technology involves softening the active blend using the solvent mixture of water-soluble polyethylene glycol and methanol and subsequent expulsion of softened mass through the extruder or syringe to get a cylinder of the product into even segments using heated blade to form tablet. The dried cylinder can also be used to coat granules for bitter drugs and thereby achieve taste masking [18].

IMPORTANT PATENTED TECHNOLOGIES OF ODTs

1. Zydis Technology:

Zydis formulation is a unique freeze dried tablet in which drug is physically entrapped or dissolved within the matrix of fast dissolving carrier material. When zydis units are put into the mouth, the freeze-dried structure disintegrates instantaneously and does not require water to aid swallowing. The zydis matrix is composed of many material designed to achieve a number of objectives. To impart strength and resilience during handling, polymers such as gelatin, dextran or alginates are incorporated. These form a glossy amorphous structure, which imparts strength. To obtain crystallinity, elegance and hardness, saccharides such as mannitol or sorbitol are incorporated. Water is used in the manufacturing process to ensure production of porous units to achieve rapid disintegration while various gums are used to prevent sedimentation of dispersed drug particles in the manufacturing process. Collapse protectants such as glycine prevent the shrinkage of zydis units during freeze-drying process or long-term storage. Zydis products are packed in blister packs to protect the formulation from moisture in the environment.

2. Durasolv Technology:

Durasolv is the patented technology of CIMA labs. The tablets made by this technology consist of drug, filler and a lubricant. Tablets are prepared by using conventional tableting equipment and have good rigidity. These can be packaged into conventional packaging system like blisters, strips. Durasolv is an appropriate technology for product requiring low amounts of active ingredients i.e. potent drugs.

3. Dispersible tablet Technology:

It offers formulation of ODT with improved dissolution rate by incorporating 7-10 % of organic acids and disintegrating agents. Disintegrate include starch, modified starches, microcrystalline cellulose, alginic acid, cross-linked sodium carboxymethyl cellulose and cyclodextrins [19].

4. Orasolv Technology:

OraSolv was Cima's first orodispersible / disintegrating dosage form. In this system active medicament is taste masked, contains disintegrating agent. The disintegration 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 acarbonate source (sodium bicarbonate, sodiumcarbonate, 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.

5. 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.

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 [20].

7. Flashtab Technology:

Flashtab technology (Ethypharm, France) produces tablets by compression of granular excipients (Cousin et al., 1995). This technology uses almost the same excipients as do conventional compressed tablets. Excipients used in this technology comprise two groups of components: disintegrating agents, such as carboxymethylcellulose or insoluble reticulated polyvinyl pyrrolidone; and swelling agents, such as carboxymethylcellulose, starch, modified starch, carboxymethylated starch, microcrystalline cellulose, and possibly directly compressible sugars. The mixture of excipients is prepared by either dry or wet granulation methods. The produced tablets are known to have satisfactory physical resistance and disintegrate in the mouth within 1 minute.

8. Quick –Dis Technology:

Lavipharm Laboratories Inc. (Lavipharm) has invented an ideal intraoral fast-dissolving drug delivery system, which satisfies the unmet needs of the market. The novel intraoral drug delivery system, trademarked Quick-Dis™, is Lavipharm's proprietary patented technology and is a thin, flexible, and quick-dissolving film. The film is placed on the top or the floor of the tongue. It is retained at the site of application and rapidly releases the active agent for local and/or systemic absorption. The Quick-Dis™ drug delivery system can be provided in various packaging configurations, ranging from unit-dose pouches to multiple-dose blister packages. The typical disintegration time, which is defined as the time at which the film begins to break when brought into contact with water, is only 5 to 10 seconds for the Quick-Dis™ film with a thickness of 2 mm. The dissolving time, which is may be defined as the time at which not less than 80% of the tested film is dissolved in aqueous media, is around 30 seconds for Quick Dis™ film with a thickness of 2 mm. The typical release profile of an active ingredient exhibited by a Quick-Dis™ drug delivery system is 50% released within 30 seconds and 95% within 1 minute.(Dobetti., 2001 and Rish., 2004) [21] .

9. Frosta Technology:

This technology patents by Akina. It uses the concept of formulating plastic granules and compressing at low pressure to develop strong tablets with high porosity. Plastic granules are composed of: Porous and plastic material, Water penetration enhancer and binder. The process involves usually mixing the porous plastic material with water penetration enhancer and followed by granulating with binder material. The tablets obtained have better hardness and rapid disintegration time ranging from 15 to 30 s depending on size of tablet.

10. Pharmaburst Technology:

SPI Pharma, New Castle, patents this technology. It utilizes the co-processed excipients to develop ODTs, which dissolves within 30-40 s. This technology involves dry blending of drug, flavour, and lubricant followed by compression into tablets. Tablets obtained have sufficient strength so they can be packed in blister packs and bottles [22].The marketed products of ODTs are given in Table no. (1).

EVALUATION OF ODTs

1. Hardness / Crushing strength:

It is the force required to break a tablet by compression in the radial direction, it is an important parameter in formulation of mouth dissolve tablets because excessive crushing strength significantly reduces the disintegration time. In the present study the crushing strength of the tablet was measured using Pfizer hardness testers. An average of three observations is reported.

2. Thickness:

Tablet thickness can be measured using a simple procedure. 5 tablets were taken and their thickness was measured using Varnier calipers [23].

3. Friability:

Friability indicates the ability of a tablet to withstand mechanical shocks while handling. Friability of the tablets were determined using Roche Friabilator and is expressed in percentage (%). Ten tablets were initially weighed (W initial) and placed into the friabilator. The friabilator was operated at 25 rpm for 4 minutes or run up to 100 revolutions and then the tablets were weight again (W final). The loss in tablet weight due to abrasion or fracture was the measure of tablet friability. Percent friability (f) was calculated by using the following formula.

$$F = \frac{W\ (initial) - W\ (final)}{W\ (initial)} \times 100$$

% friability of less than 1 % is considered acceptable [24].

4. Water absorption ratio:

Water absorption ratio was measured by keeping a tablet on a piece of tissue paper folded twice in a small culture dish containing 6 ml of phosphate buffer pH 6.8 and water respectively. The time required for water to reach the upper surface of the tablet was measured as the wetting time [25].

5. Wetting time:

Piece of tissue paper folded twice was placed in small Petri dish containing 6 ml of water. A tablet was put on the paper and the time required for complete wetting of tablet was noted. Schematic diagram of determination of wetting time is shown in Figure no. (3).

6. In vitro disintegration time:

In vitro disintegration time was measured by using 200ml distilled water in 250 ml beaker at 37± 0.5^{o}C temperature. Time required for disintegration of the tablets was noted [26].

7. Mouth feel:

To know mouth feel of these tablets, selected human volunteers were given placebo tablets and the taste sensation felt was evaluated.

8. Weight variation:

20 tablets were selected randomly and weighted individually to check for weight variation. Weight variation specification as per I.P. is shown in Table no. (2).

9. Tablet Porosity:

The mercury penetration porosimeter can be used to measure the tablet porosity. The tablet porosity (ε) can be calculated by using following equation,

$\varepsilon = 1\text{-}m / (\rho t V)$

Where ρt is the true density, and m and V are the weight and volume of the tablet, respectively [27].

10. Dissolution test:

The dissolution methods for FDT are practically identical to conventional tablet when FDT does not utilize taste masking. Commonly the drugs may have dissolution conditions as in USP monograph. 0.1N HCl, pH 4.5 and pH 6.8 buffers should be used for evaluation of FDT in the same way as their ordinary tablet counterparts. USP 2 paddle apparatus is most suitable and common choice for dissolution test of FDT tablets as compared to USP1 (basket) apparatus due to specific physical properties of tablets. In paddle apparatus the

paddle speed of 25-75 rpm is commonly used. Since the dissolution of FDTs is very fast when using USP monograph conditions hence slower paddle speeds may be utilized to obtain a comparative profile. Large tablets (≥1gram) may produce a mound in the dissolution vessel which can be prevented by using higher paddle speeds [28].

FUTURE PROSPECTS

These dosage forms may be suitable for the oral delivery of drugs such as protein and peptide based therapeutics those have limited bioavailability when administered by conventional tablets. These products usually degrade rapidly in the stomach and next generation drugs may be pre dominantly protein or peptide based, tablets may no longer be the dominant format for dosing such moieties. Injections generally are not favored for use by patients unless facilitated by sophisticate auto injectors. Inhalation is one good alternative system to deliver these drugs, but the increased research into biopharmaceuticals so far has generated predominantly chemical entities with low molecular weights. The developments of enhanced oral protein delivery technology by ODTs which may release these drugs in the oral cavity are very promising for the delivery of high molecular weight protein and peptide.

CONCLUSION

ODT concept evolved to overcome some of the problems that existed in conventional solid dosage form i.e. difficulty in swallowing of tablet in pediatric and geriatric patients who constitute a large proportion of world's population. ODT may lead to improve efficacy, bioavailability, rapid onset of action, better patient compliance due to its quick absorption from mouth to GIT as the saliva passes. Fast dissolving tablet acts like solid dosage form when outside the body and solution when administered. In future ODT may be most acceptable and prescribed dosage form due to its fast action (within minute). Their characteristic advantages such as administration without water needed, anywhere, at anytime lead to their enhanced patient compliance in today's scenario of hectic life. Considering the many benefits of ODTs, a number of formulations are prepared in ODT forms by most of the pharmaceutical companies. Because of increased patient demand, popularity of these dosage forms will surely expand in future.

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Table no. (1): Marketed products of ODTs

Brand name	**Active ingredient**	**Application**	**company**
Claritin® RediTabs®	Loratadine	Antihistamine	Scherig corporation
Feldene Melt®	Piroxicam	NSAIDs	Pfizer
Maxalt® -MLT®	Rizatritpan benzoate	Migrane	Merck
Pepeid® ODT	Femotidene	Anti-ulcer	Merck
Zyperxa®	Olazepine	Psychotropic	Eli Lilly
Zofran® ODT	Olandansetron	Antiemetic	Galaxo Smith kline
Resperdal® M-TabTM	Resperidone	Schizophrenia	Janssen
ZubrinTM (Pet drug)	Tepoxelin	Canine NSAIDs	Scherig corporation
ZelaparTM	Selegiline	Parkinsons disease	Elanl Amarin corporation
Klonopin® wafer	Clonazepam	Sedation	Roche
Childrens Dimetapp® ND	Loratadine	Allergy	Wyeth consumer Healthcare
Imodium Istant Melts	Loperamide HCL	Antidiarrheal	Jannsen
Propulsid® Quicksolv ®	Cisapride Monohydrate	Gastrointestinal prokinetic Agent	Jannsen
Tempra Quicksolv®	Acetaminophen	Analgesic	Bristol-Mters squibb
Remeron® Soltab®	Mirtazapine	Anti-dipression	Organon Inc.
Triaminic® Softchews®	Various combination	Pediatric cold cough,Allergy	Novartis consumer Health

Table no. (2): Average weight of tablet and % accepted deviation

Average weight of tablet	% Accepted deviation
80 mg or less	10
More than 80 mg but less than 250 mg	7.5
250 mg or more	5

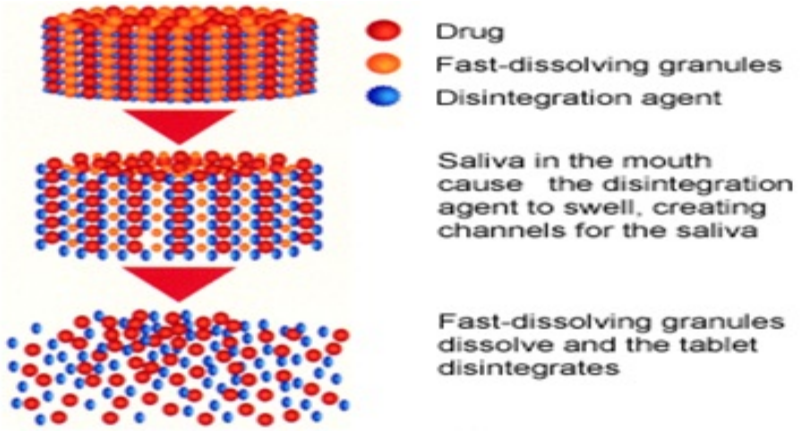

Figure no. (1): Mechanism of disintegration

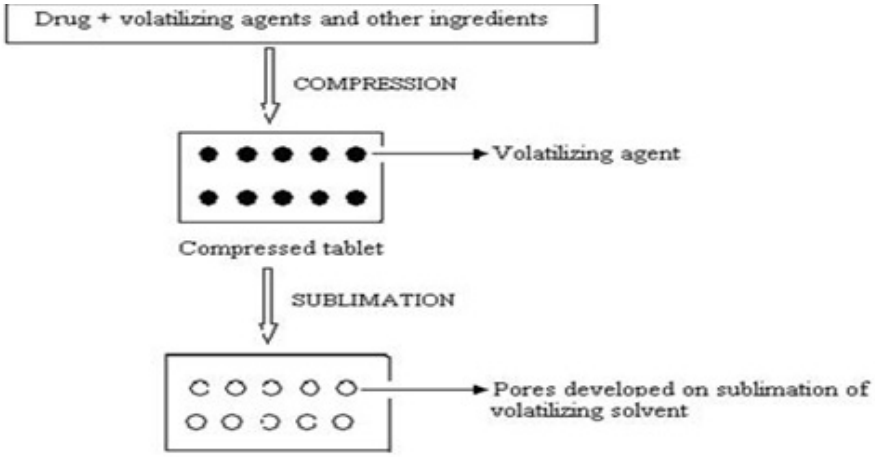

Figure no. (2): Schematic diagram of sublimation technique

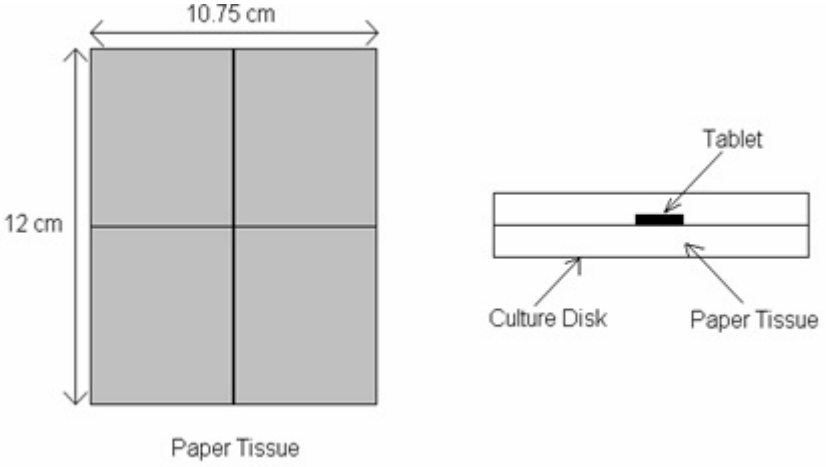

Figure no. (3): Determination of wetting time