



AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: <http://www.ajptr.com/>

Patented Technologies in Fast Dissolving Tablets: A Review

Pavithra Putta, Saikrishna Mundra & Bhavani Boddeda*

Koringa College of Pharmacy, Korangi, Tallarevu, East Godavari, AP

ABSTRACT

Improvement of patient's compliance has always a challenge towards the development of oral drug delivery system. Different dosage forms are available in the market among all oral dosage form is preferred one. However, the incompliance of pediatric & geriatric patients the scientists worked towards fast dissolving solid dosage form to encounter existing drawbacks with unique palatability and rapid disintegration. The concept of fast dissolving tablet came into existence in late 1970s. Recently, fast dissolving drug delivery systems have started gaining popularity and acceptance as new drug delivery system, because they are easy to administer and lead to better patient compliance. For further improvement in existing technologies and newer technologies has been succeeded and still research is going on in improvement with its preparation methodologies all over the globe. Fast dissolution tablets have faster disintegration and dissolution rate and release within 30 seconds as they come in contact with saliva. These systems also obviate the requirement of carry water during drug administration. As fast dissolving tablets falls under desired expectation of safer, convenient and economical solid dosage forms, several techniques have been developed to improve disintegration quality in the recent past years. This article mainly focuses on patented technologies with recent advancement made so far in the field of the fast dissolving tablets.

Keywords: Fast dissolving tablets, Patent, Technologies

*Corresponding Author Email: bhavani2008@gmail.com

Received 01 October 2019, Accepted 10 October 2019

Please cite this article as: Boddeda B *et al.*, Patented Technologies in Fast Dissolving Tablets: A Review. American Journal of PharmTech Research 2019.

INTRODUCTION

Recent developments in technology have presented viable dosage alternatives for patients who may have difficulty swallowing tablets or liquids. Traditional tablets and capsules administered with a glass of water may be inconvenient or impractical for some patients. For example, a very elderly patient may not be able to swallow a daily dose of antidepressant. An eight year-old with allergies could use a more convenient dosage form than an antihistamine syrup. A schizophrenic patient in the institutional setting can hide a conventional tablet under his or her tongue to avoid their daily dose of an atypical antipsychotic. A middle aged woman undergoing radiation therapy for breast cancer may be too nauseous to swallow her H₂-blocker. Fast-dissolving/disintegrating tablets (FDDTs) are a perfect fit for all of these patients. FDDTs disintegrate and/or dissolve rapidly in the saliva without the need for water. Some tablets are designed to dissolve in saliva remarkably fast, within a few seconds, and are true fast-dissolving tablets. Others contain agents to enhance the rate of tablet disintegration in the oral cavity, and are more appropriately termed fast disintegrating tablets, as they may take up to a minute to completely disintegrate. A fast-dissolving drug delivery system, in most cases, is a tablet that dissolves or disintegrates in the oral cavity without the need of water or chewing. Most fast dissolving delivery system films must include substances to mask the taste of the active ingredient.

Numerous of researches are going on the medicaments to improve the patient compliance, quick onset of action, easy to handle and cost effective. The experimentation on different aspects such as improving solubility, method of preparation techniques, usage of newer additives taking place simultaneously balancing the patient comfort with affordable cost. Patenting the innovative technologies for exhibiting greater benefit for healthy environment. Patients with persistent nausea, who are traveling, or who have little or no access to water are also good candidates for FDDTs.¹

Patented Technologies for Fast Dissolving Tablets²

Rapid dissolving characteristics of FDT is generally attributed to fast penetration of water into tablet matrix resulting in its fast disintegration. Several technologies have been developed on the basis of formulation aspects and different process and patented by several pharmaceutical companies. Patented technology is described below and showed in Table 1-4.

- Zydis technology
- Durasolv technology
- Orasolv technology

- Wow tab technology
- Flashdose technology/Cotton candy process
- Flashtab technology
- Oraquick technology

Zydis technology^{2,3,4}

Catalent Pharma has the patent for Zydis technology and best known of the fast dissolving/disintegrating tablet preparations, was the first marketed new technology tablet. This 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. Thirteen products are currently available using Zydis technology. In the U.S., they include: Claritin Reditab, Dimetapp Quick Dissolve, Feldene Melt, Maxalt-MLT, Pepcid RPD, Zofran ODT and Zyprexa Zydis. On the worldwide market, other Zydis formulations are available for oxazepam, lorazepam, loperamide, and enalapril.

A Zydis tablet is produced by lyophilizing or freeze drying the drug in a matrix usually consisting of gelatin. The product is very lightweight and fragile, and must be dispensed in a special blister pack. Patients should be advised not to push the tablets through the foil film, but instead peel the film back to release the tablet. The Zydis product is made to dissolve on the tongue in 2 to 3 seconds. The Zydis formulation is also self-preserving because the final water concentration in the freeze-dried product is too low to allow for microbial growth. The Zydis formulation utilizes flavors and sweeteners to optimize the taste of the dosage form. In addition, it utilizes microencapsulation with specialized polymers or complexation with ion exchange resins to mask the bitter tasting drug. The combination of lyophilization and taste masking creates a product that is both pleasing to the eye and also to the senses of taste and touch. A major claim of the Zydis

product is increased bioavailability compared to traditional tablets. Because of its dispersion and dissolution in saliva while still in the oral cavity, there can be a substantial amount of pregastric absorption from this formulation. Buccal, pharyngeal and gastric regions are all areas of absorption of the Zydis formulation. Any pre-gastric absorption avoids first-pass metabolism and can be an advantage in drugs that undergo a great deal of hepatic metabolism. However, if the amount of swallowed drug varies, there is the potential for inconsistent bioavailability. While the claimed increase in bioavailability is debatable, it is clear that the major advantage of the Zydis formulation is convenience. There are some disadvantages to the Zydis technology.

The process of freeze-drying is a relatively expensive manufacturing process. As mentioned earlier, the Zydis formulation is very lightweight and fragile, and therefore should not be stored in backpacks or the bottom of purses. Finally, the Zydis formulation has poor stability at higher temperatures and humidities. It readily absorbs water, and is very sensitive to degradation at humidities greater than 65%. If there is any pinhole or minor damage to the package, the patient may find the lyophilized product has collapsed due to absorption of moisture. As with most other drugs, patients should be advised to avoid storing the Zydis technology in the medicine cabinet in the bathroom. Patients should use their Zydis formulation within six months of opening the laminated foil pouch and immediately after opening its individual blister packaging.

Limitations

- The amount of drug could be incorporated should generally be less than 400 mg for insoluble drugs and less than 60 mg for soluble drugs.
- The particle size of the insoluble drugs should not be less than 50 μm and not more than 200 μm to prevent sedimentation during processing.

Advantages

- Buccal pharyngeal and gastric regions are all areas of absorption from this formulation. Any pre-gastric absorption avoids first-pass metabolism and can be an advantage in drugs that undergo a great deal of hepatic metabolism.
- The Zydis formulation self-preserving because the final water concentration in the freeze-dried product is too low to allow for microbial growth.
- Patients who have difficulty swallowing oral medication due to dysphagia, stroke or medical conditions such as gastroesophageal reflux disease, multiple sclerosis or Parkinson's disease.

Disadvantages

- The process of freeze-drying is a relatively expensive manufacturing process.
- The formulation is very lightweight and fragile, and therefore should not be stored in backpacks or the bottom of purses.
- It has poor stability at higher temperatures and humidities.
- A water insoluble drug can be incorporated only up to 400 mg per tablet or less. On the other hand water, the soluble drug can be incorporated only up to 60 mg.

OraSolv Technology^{2,3,5,6} (Cima Labs, Inc.)

OraSolv was Cima's first fast-dissolving/disintegrating dosage form. The OraSolv technology, unlike Zydis, disperses in the saliva with the aid of almost imperceptible effervescence. The OraSolv technology is best described as a fast-disintegrating tablet; the tablet matrix dissolves in less than one minute, leaving coated drug powder. The taste-masking associated with the OraSolv formulation is two-fold. The unpleasant flavour of a drug is not merely counteracted by sweeteners or flavors; both coating the drug powder and effervescence are means of taste-masking in OraSolv. This technology is frequently used to develop over-the-counter formulations. In this system active medicament is taste masked. It also contains effervescent disintegrating agent. Tablets are made by direct compression technique at low compression force in order to minimize oral dissolution time. Conventional blenders and tablet machine is used to produce the tablets. The tablets produced are soft and friable. The major disadvantage of the OraSolv formulations is its mechanical strength. The OraSolv tablet has the appearance of a traditional compressed tablet. However, the OraSolv tablets are only lightly compressed, yielding a weaker and more brittle tablet in comparison with conventional tablets. For that reason, Cima developed a special handling and packaging system for OraSolv. An advantage that goes along with the low degree of compaction of OraSolv is that the particle coating used for taste masking is not compromised by fracture during processing. Lyophilization and high degrees of compression, as utilized in OraSolv's primary competitors, may disrupt such a taste masking approach. The OraSolv technology is utilized in six marketed products: four Triaminic Softchew formulations, Tempra FirsTabs, and Remeron SolTab.

Advantages

- The orosolv formulations are not very hygroscopic.
- The formulation can accommodate high doses
- It also provides a distinct, pleasant sensation of effervescence in the mouth.

- Taste – masking is two –fold, quick dissolution. This technology has been for drug strength in the range of 1 mg to 750 mg. Depending on formulation and tablet size, the disintegration time of the tablet can be designed in the range of 10 to 40 seconds
- As tablets are compressed under low compression force, coated particles for taste masking of drug escape from fracture during tablet compression.

Disadvantages

- Tablets obtained have less mechanical strength and brittle in nature
- Special handling and packaging system required for orsolv as these tablets are more brittle and weaker than conventional tablets.
- They are sensitive to moisture due to the presence of the effervescent system and must be packaged appropriately.
- Low mechanical strength
- The cost of fast dissolving tablets is higher than the cost of standard tablets made by direct compression. Manufacturing requires a controlled environment at low relative humidity.

Durasolv Technology^{2,3,5,7} (Cima Labs, Inc.)

DuraSolv is Cima's second-generation fast dissolving/ disintegrating tablet formulation. Produced in a fashion similar to OraSolv, DuraSolv has much higher mechanical strength than its predecessor due to the use of higher compaction pressures during tableting. The DuraSolv product is thus produced in a faster and more cost-effective manner. DuraSolv is so durable that it can be packaged in either traditional blister packaging or vials.

The newest DuraSolv formulation, NuLev, is actually dispensed in a conventional stock bottle. Pharmacists are advised to take care when dispensing such DuraSolv formulations from stock bottles to ensure they are not exposed to high levels of moisture or humidity. Excess handling of tablets can introduce enough moisture to initiate dissolution of the tablet matrix. One disadvantage of DuraSolv is that the technology is not compatible with larger doses of active ingredients, because the formulation is subjected to such high pressures on compaction. Unlike OraSolv, the structural integrity of any taste masking may be compromised with high drug doses. The drug powder coating in DuraSolv may become fractured during compaction, exposing the bitter-tasting drug to a patient's taste buds. Therefore, the DuraSolv technology is best suited for formulations including relatively small doses of active compound. DuraSolv is currently available in two products: NuLev and Zomig ZMT. 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. Durasolv is an appropriate technology for product requiring low amounts of active ingredients.

Advantages

- DurSolv technology is good for tablets having a low amount (125 mcg to 500mg) of active ingredients and tablets are compressed to a greater hardness of 15-100N, resulting in a more durable ODT. As a result, this technology enables packaging flexibility, tablets can be bottled and blistered.
- Durasolv has much higher mechanical strength than Orasolv due to the use of higher compaction pressures during tableting.
- The Durasolv product is thus produced in a faster and more effective manner.
- For packing, conventional packing like blister packs can be used.

Disadvantages

- This technique is not suitable for high amounts of active ingredients because the formulation is subjected to high pressure during compaction.
- The drug powder coating may fractured during compaction, exposing the bitter tasting drug to patient's taste buds

Wow tab Technology^{2,3,5,7-9} (Yamanouchi Pharma Technologies, Inc.)

Wow tab technology is patented by Yamanouchi Pharmaceutical Co. WOW means "Without Water". In this process, combination of low mouldability saccharides and high mouldability saccharides is used to obtain a rapidly melting strong tablet. The active ingredient is mixed with a low mouldability saccharide (eg. lactose, glucose, and mannitol) and granulated with a high mouldability saccharide (eg. Maltose, oligosaccharides) and compressed into tablet. The WOWTAB fast-dissolving/disintegrating tablet formulation has been on the Japanese market for a number of years. It has just recently been introduced into the U.S. The WOWTAB technology utilizes sugar and sugar-like (e.g., mannitol) excipients. The two different types of saccharides are combined to obtain a tablet formulation with adequate hardness and fast dissolution rate. Due to its significant hardness, the WOWTAB formulation is a bit more stable to the environment than the Zydis or OraSolv. It is suitable for both conventional bottle and blister packaging. The taste masking technology utilized in the WOWTAB is proprietary, but claims to offer superior mouthfeel due to the patented SMOOTHMELT action. The WOWTAB product dissolves quickly in 15 seconds or less. The WOW in WOWTAB signifies the tablet is to be given With Out Water.

Two WOWTAB formulations currently on the U.S. market are Benadryl Allergy & Sinus FASTMELT and Children's Benadryl Allergy & Cold FASTMELT.

Advantages

- Offers superior mouthfeel due to the smooth melt action
- It is suitable for both conventional bottle and blister packaging
- Comparatively more stable to the environment than the zydis and orsolv
- Adequate dissolution rate and hardness

Disadvantages

- No significant change in bioavailability of the drug

OTHER TECHNOLOGIES NOT YET ON THE U.S. MARKET

FlashDose (Fuisz Technologies, Ltd.), Flashtab (Prographarm Group), and OraQuick (KV Pharmaceutical Co., Inc.) are three formulations on the worldwide market which will likely reach the United States in the near future. Biovail Corp. Recently announced the filing of an NDA for a FlashDose version of zolpidem tartrate. These technologies are similar to Zydis, WOWTAB, OraSolv and DuraSolv in that they dissolve or disperse on the tongue within a minute. However, each also has unique characteristics to differentiate itself from the competition. Table 5 & 6 showed the marketed/commercial fast dissolving products available in India market and International market.

Flash Dose Technology^{2,3,7,8,10} (Fuisz Technologies, Ltd.)

Flash dose technology has been patented by fuisz. Nurofen meltlet, a new form of ibuprofen as melt in mouth tablets prepared using flash dose technology is the first commercial product launched by biovail corporation. Flash dose tablets consist of self-binding shear form matrix termed as “floss”. Shear form matrices are prepared by flash heat processing. Fuisz Technologies has three oral drug delivery systems that are related to fast dissolution. The first two generations of quick-dissolving tablets, Soft Chew and EZ Chew, require some chewing. However, these paved the way for Fuisz's most recent development, FlashDose. The FlashDose technology utilizes a unique spinning mechanism to produce a floss-like crystalline structure, much like cotton candy. This crystalline sugar can then incorporate the active drug and be compressed into a tablet. This procedure has been patented by Fuisz and is known as Shearform. The final product has a very high surface area for dissolution. It disperses and dissolves quickly once placed onto the tongue. Interestingly, by changing the temperature and other conditions during production, the characteristics of the product can be altered greatly. Instead of a floss-like material, small spheres

of saccharides can be produced to carry the drug. The process of making microspheres has been patented by Fuisz, and is known as CEFORM1 and serves as an alternative method of taste masking.

Advantages

- Fast dissolving tablets produced by this technology can accommodate drug up to 600 mg
- Tablets produced by this technology have very large surface area for dissolution and this disperse and dissolve once placed on the tongue.
- High surface area for dissolution

Disadvantages

- High temperature required to melt the matrix can limit the use of heat-sensitive drugs, sensitive to moisture and humidity.
- The dosage form can accommodate only up to 600 mg of drug
- Tablets produced are highly friable, soft and moisture sensitive. Therefore specialized packaging is required
- High friable, soft and moisture sensitive tablets are the major drawbacks

Flash tab Technology^{2,3,11,12} (Prographarm Group)

Prographarm laboratories have patented the Flash tab technology. Tablet prepared by this system consists of an active ingredient in the form of micro crystals. Drug micro granules may be prepared by using the conventional techniques like coacervation, micro encapsulation and extrusion spheronisation. All the processing utilized conventional tableting technology. The Flashtab technology is yet another fast dissolving/ disintegrating oral tablet formulation. It utilizes most of the same excipients as in conventional compressed tablets. A disintegrating agent and a swelling agent are used in combination with coated drug particles in this formulation to produce a tablet that disintegrates in the mouth in under one minute.

Advantages

Tablets obtained have good physical resistance and disintegrates in the mouth less than one minute.

ORAQUICK^{8,13} (KV Pharmaceutical Co., Inc.)

The OraQuick fast-dissolving/disintegrating tablet formulation utilizes a patented taste masking technology. KV Pharmaceutical claims its microsphere technology, known as MicroMask, has superior mouthfeel over taste masking alternatives. The taste masking process does not utilize solvents of any kind, and therefore leads to faster and more efficient production. Also, lower heat

of production than alternative fast-dissolving/disintegrating technologies makes OraQuick appropriate for heat sensitive drugs. KV Pharmaceutical also claims that the matrix that surrounds and protects the drug powder in microencapsulated particles is more pliable, meaning tablets can be compressed to achieve significant mechanical strength without disrupting taste-masking. OraQuick claims quick dissolution in a matter of seconds, with good taste-masking. There are no products using the OraQuick technology currently on the market, but KV Pharmaceutical has products in development such as analgesics, scheduled drugs, cough and cold, psychotropics, and anti-infectives.

Advantage

- Appropriate for heat sensitive drugs due to its lower heat of production
- Tablets obtained have significant mechanical strength fast dissolution with good taste masking.

ADVANTOL™ 200

Advantol™ 200 is a directly compressible excipient system offering "Soft-Melt" functionality and specially formulated for nutraceutical applications. SPI Pharma's Advantol platform uses proprietary co-processing technology.¹⁴ Advantol requires no special manufacturing equipment or tooling. Advantol formulations utilize a standard rotary tablet press with standard tooling under normal tableting temperature and humidity conditions to make robust "soft-melt" tablets.

ADVATAB¹⁴

AdvaTab tablets disintegrate rapidly in the mouth, typically in less than 30 seconds, to allow for convenient oral drug administration without water. These tablets are especially suited to those patients that experience difficulty in swallowing capsules and tablets. AdvaTab is distinct from other ODT technologies as it can be combined with Eurand's complimentary particle technologies like its world leading Microcaps® taste masking technology and its Diffucaps® , controlled release technology. The pairing of AdvaTab with Microcaps creates products that offer the dual advantage of a patient preferred dosage form, together with a superior taste and smooth mouth feel. This is a critical advantage as the unpleasant taste of drugs is a significant restriction in the application of other ODT technologies

Dispersible tablet technology⁵

Lek in Yugoslavia was issued patents for dispersible tablets of dihydroergotamine and cimetidine, which were claimed to disintegrate in less than 1 minute when in contact with water at room temperature. Dihydroergotamine is poorly soluble in water in the free base form. An improved

dissolution rate of dihydroergotamine methanesulphonate was observed with dispersible tablets containing 0.8-10%, preferably about 4% by weight, of organic acids. One of the essential excipients in the cimetidine formulate is a disintegrating agent. It provides rapid swelling and/or good wetting capability to the tablets and thereby a quick disintegration. The disintegrating agents include starch or modified starches, microcrystalline cellulose, alginic acid, cross-linked sodium carboxymethyl cellulose, and cyclodextrin polymers. A combination of two or more disintegrating agents produced better disintegration results.

Nanocrystal technology^{5,8,15}

For fast dissolving tablets, elan's 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 in dissolution rate. This can be accomplished predictably and efficiently using nanocrystal technology. Nanocrystal particles are small particles of drug substance, typically less than 1000 nanometers (nm) in diameter, which are produced by milling the drug substance using a proprietary wet milling technique.

Advantages

- Pharmacokinetic benefits of orally administered nanoparticles (<2 microns) in the form of a rapidly disintegrating tablet matrix.
- Product differentiation based upon a combination of proprietary and patent protected technology elements.
- Cost-effective manufacturing processes that utilize conventional, scalable unit operations.

Pharmaburst technology^{5,15}

Pharmaburst technology is being patented by SPI pharma. The tablet manufactured by this process involves a dry blend of a drug, flavors, and lubricant then followed by compression into tablets which then dissolve within 30-40 seconds. Tablets manufactured by this methodology have sufficient strength can be packed in blister packs and bottles.

Frosta technology (Akina)^{5,15,16}

This technology is patented by Akina. Frosta technology utilizes the core concept of formulating plastic granules and compressing at low pressure to produce strong tablets with high porosity. The process involves mixing the porous plastic material with water penetration enhancer and followed by granulating with a binder. The technology can be used for almost any drugs including market place and extension of patent term innovator.

Lyo (Pharmalyoc)^{5,15,16}

Oil in water emulsion is prepared and placed directly into blister cavities followed by freeze-drying. Non-homogeneity during freeze-drying is avoided by incorporating inert filler to increase the viscosity finally the sedimentation. A high proportion of filler reduces the porosity of tablets due to which disintegration is lowered.

Sheaform technology⁵

The technology is based on the preparation of floss that is also known as, shear from matrix, which is produced by subjecting a feed stock containing a sugar carrier by flash heat processing. In this process, the sugar is simultaneously subjected to centrifugal force and to a temperature gradient, which raises the temperature of the mass to create an internal, flow condition, which permits part of it to move with respect of the mass.

Quick- Dis technology^{5,17,18}

Lavipharm laboratories Inc. (Laviparm) has invented an ideal intraoral fast dissolving drug delivery system, which satisfies the unmet needs of the market. The novel intraoral drug delivery system, trade marked Quick-dissolving film. The film is packaged ranging from unit-dose pouches to multiple-dose blister packages.

OraQuick technology^{2,5,19}

The OraQuick fast dissolving / disintegrating tablet formulation utilizes a patented taste masking technology. KV Pharmaceuticals claims its microsphere technology, known as Micro Mask, has superior mouthfeel over taste-masking alternatives. The taste masking process does not utilize solvents of any kind, and therefore leads to faster and more efficient production. Also, lower heat of production than alternative fast dissolving/disintegrating technologies makes OraQuick appropriate for heat-sensitive drugs. KV Pharmaceuticals also claims that the matrix that surrounds and protects the drug powder in microencapsulated particles is more pliable without disrupting taste masking. Oraquick claims quick dissolution in a matter of seconds, with good taste-masking. There are no products using the Oraquick technology currently in the market, but KV Pharmaceuticals has products in development such as analgesics , psychotropics and anti-infectives.

PATENTS ON FAST DISSOLVING TECHNOLOGIES

- Ahmed, Salah U Gorukanti, *et al* (2008) received US patent for Ondansetron orally disintegrating tablets²⁰.
- Moreau, Marinette et al (2008) filled US patent application for Methods for Obtaining a Fast Dissolving Imidapril Powder²¹.

- Nakatani, Manabu Yokoyama *et al* (2008) filled US patent application for bilayer tablet comprising telmisartan and diuretic²².
- Withiam, Michael C *et al* (2007) filled US patent application for Rapidly dissolving tablets comprising low surface area titanium dioxide²³.
- Fu, Yourong Jeong *et al*(2006) received US patent for Mannose-based fast dissolving tablets in which Fast dissolving pharmaceutical tablets comprising mannose²⁴.
- Yousef, Abdul Razzaq *et al* (2005) received US patent for Instant dissolving tablet composition for loratidine and desloratidine²⁵.
- Wang, Wen-Che *et al* (2005) received US patent for Fast dissolving tablet and method of preparing fast dissolving tablet²⁶.
- Kohlrausch *et al* (2005) received US patent for Multilayer tablet in which tablet comprises a first layer formulated for instant release of the angiotensin II receptor, a second layer formulated for instant release of the angiotensin converting enzyme inhibitor ramipril and optionally a diuretic from a disintegrating tablet matrix, and, optionally, a third layer formulated for instant release of a diuretic like hydrochlorothiazide from a fast disintegrating tablet matrix²⁷.
- Purdy, David F *et al* (2005) received US patent for Dual layer tablet, method of making and use thereof in which a method for treating a recirculating water system which comprises introducing into water system to form multifunctional, multilayer tablet²⁸.
- Danilovski, Aleksandar *et al* (2005) received US patent for Single dose fast dissolving azithromycin²⁹.
- Fu, Yourong Pai, Chaul Min *et al* (2005) received US patent for highly plastic granules for making fast melting tablets³⁰.
- Abu-Izza, Khawla A *et al* (2004) received US patent for fast dissolving tablet³¹.
- Thombre, Avinash G *et al* (2002) received US patent for rapidly disintegrating and fast-dissolving solid dosage form which is Described are non-friable, rapidly disintegrating, fast-dissolving solid dosage forms that are produced from pharmaceutically acceptable steam extruded polymers³².
- Liu, Fang-yu. *et al* (2002) received US patent for water soluble polymer-based rapidly dissolving tablets and production processes thereof³³.

- Khankari, Rajendra K *et al* (2001) received US patent for rapidly dissolving robust dosage form. The invention relates to a hard, compressed, rapidly dissolvable dosage form adapted for direct oral dosing³⁴.
- Allen, Loyd V *et al* (2001) received US patent for Particulate support matrix for making a rapidly dissolving dosage form³⁵.
- Herreid, Richard M *et al* (2000) received US patent for Method for making fast dissolving bouillon cubes in which method for producing a fast dissolving low fat bouillon cube includes providing a bouillon powder which is free-flowing to a die having a residual of water on a surface³⁶.

Table 1: Some patented fast dissolving technologies

Technology	Company's Name	Technology Base
Zydis	R P Scherer, Inc.	Freeze dried wafers
Orasolv, Durasolv	CIMA Labs Inc.	Molding
Wow Tab	Yamanouchi pharma	Molding
Flash Tab	Ethypharm	Molding
Flash Dose	Fuisz Technology, Ltd.	Cotton –candy Process

Table 2: Comparing fast dissolving techniques

ZYDIS (R.P. SCHERER, INC.)		
Novelty	Handling/Storage	Drug Release/Bioavailability
First to market	Do not push tablet through foil	Dissolves in 2 to 10 seconds
Freeze Dried	Do not use dosage form from damaged package Sensitive to degradation at humidities >65%	May allow for pre-gastric absorption leading to enhanced bioavailability
ORASOLV (CIMA LABS, INC.)		
Novelty	Handling/Storage	Drug Release/Bioavailability
Unique taste masking	Packaged in patented foil packs	Disintegrates in 5 to 45 seconds depending upon the size of the tablet
Lightly compressed		No significant change in drug bioavailability
DURASOLV (CIMA LABS, INC.)		
Novelty	Handling/Storage	Drug Release/Bioavailability
Similar to Orasolv, but with better mechanical strength	Packaged in foil or bottles If packaged in bottles, avoid exposure to moisture or humidity	Disintegrates in 5 to 45 seconds depending upon the size of the tablet No significant change in drug bioavailability
WOWTAB (YAMANOUCHI PHARMA TECHNOLOGIES, INC.)		
Novelty	Handling/Storage	Drug Release/Bioavailability
Compressed dosage form	Package in bottles	Disintegrates in 5 to 45 seconds depending upon the size of the tablet
Proprietary taste masking	Avoid exposure to moisture or	No significant change in drug

	humidity	bioavailability
FLASHDOSE (Fuisz Technologies, Ltd.)		
Novelty	Handling/Storage	Drug Release/Bioavailability
Unique spinning mechanism to produce a floss-like crystalline structure, much like cotton candy	Avoid exposure to moisture or humidity Require specialized packaging	Dissolves within 1 minute Enhanced bioavailability
FLASHTAB (Prographarm Group)		
Novelty	Handling/Storage	Drug Release/Bioavailability
Compressed dosage form containing Drug as microcrystals	Avoid exposure to moisture or humidity	Dissolves within 1 minute

Table 3: Fast dissolving tablets available in the market based on their technology⁵⁶

Product	Examples	Active ingredient	Therapeutic Indication	Manufactured by
Zydis	Feldene Melt 20mg	Piroxicam	Osteoarthritis, rheumatoid arthritis or spondylitis	Pfizer Limited
Orosolv Technology	Fazacllo®	Clozapine	Antipsychotic drug	Cima Labs
Dursolv Technology	Parcopa	Levodopa and Carbidopa	Parkinson's disease	Sun Pharma
WowTab Technology	Benadryl fast melt tablet	Diphenhydramine Hydrochloride	Antihistamine, allergy, sinus	Pfizer Limited
Flash dose Technology	Ralivia	Tramadol	Opiod analgesic	Biovail
Flash Tab Technology	Flashdose® Nurofen® Flashtab®	Hydrochloride Ibuprofen	NSAID	Athena
Oraquick Technology	Hyoscyamine sulphate ODT	Hyoscyamine sulphate	Used in diarrhea, gastrointestinal ulcers, irritable bowel syndrome	Ethex corporation
Advatab Technology	Advatab Cetirizine	Cetirizine	Anthistamine used to relieve allergy symptoms such as watery eyes, runny nose, itching eyes/nose, sneezing and hives	ADARE Pharmaceuticals
Lyoc Technology	Sparfon Lyoc	Phloroglucinol hydrate	Antispasmodic, reduce spasmodic pain, abdominal pain, and visceral pain of the lower abdomen	Cephalon
Ziplet Technology	Cibalgina duefast	Ibuprofen	NSAID	Novartis

Table 4: Available fast dissolving drugs in the market with their trade names

Trade Name	Active Drug	Manufacturer
Felden fast melt	Piroxicam	Pfiser Inc., NY, USA
Claritin redi Tab	Loratidine	Schering plough Corp., USA
Maxalt MLT	Rizatriptan	Merck and Co., NJ, USA
Zyprexa	Olanzapine	Eli lilly, Indianapolis, USA
Pepcid RPD	Famotidine	Merck and Co., NJ, USA

Zofran ODT	Ondansetron	Glaxo Wellcome, Middlesex, UK
Zoming-ZMT	Zolmitriptan	AstraZeneca, Wilmington, USA
Zeplar TM	Selegiline	Amarin Corp., London, UK
Tempra Quiclets	Acetaminophen	Bristol myers Squibb, NY, USA
Febrectol	Paracetamol	Prographarm, Chateaufneuf, France
Nimulid MDT	Nimesulide	Panacea Biotech, New delhi , India
Torrox MT	Rofecoxib	Torrent pharmaceuticals , India
Olanex instab	Olanzapine	Ranbaxy lab. Ltd. New-delhi, India
Romilast	Montelukast	Ranbaxy lab. Ltd. New-delhi, India
Benadryl Fastmelt	Diphenhydramine and pseudoephedrine	Warner Lambert, NY, USA

Table 5: Fast dissolving tablets products available in Indian market

Brand (Trade) name	Active drug	Manufacturer/Company
Acepod-O	Cefpodoxime	ABL Lifecare, India
Acufix DT-TAB	Cefixime	Macleods, India
Alepan	Amoxicillin trihydrate and Potassium clavulanate	Scoshia Remedy, India
Bigcef DT-TAB	Cefuroxime	Bestochem, India
Clonazepam ODT	Clonazepam	Par Pharmaceutical
Dompan	Pantoprazole and Domperidone	Medley pharmaceuticals, India
Mosid-MT	Mosapride citrate	Torrent Pharmaceuticals, Ahmedabad, India
Minoclav DT-TAB	Amoxicillin trihydrate and Potassium clavulanate	Minova life Sciences, India
Nulev	Hyoscyamine sulfate	Schwarz Pharma, India
Nimulid MDT	Nimesulide	Panacea Biotech, New delhi, India
Numoxylin CV DT	Amoxicillin trihydrate and Potassium clavulanate	Gepach international, India
Zyrof Meltab	Rofecoxib	Zydus, Cadila, India
Romilast	Montelukast	Ranbaxy Labs Ltd., New Delhi, India
Torrox MT	Rofecoxib	Torrent Pharmaceuticals, Ahmedabad, India
Olanex Instab	Olanzapine	Ranbaxy Labs Ltd., New Delhi, India
Kemstro	Baclofen	Schwarz Pharma, India
Romilast	Montelukast	Ranbaxy Lab. Ltd. Delhi, India
Rofaday MT	Rofecoxib	Lupin., India
Valus	Valdecoxib	Glenmark, India
Zinase-Clav	Amoxicillin trihydrate and Potassium clavulanate	Rapross Pharmaceuticals Pvt Ltd, India

Table 6: Fast dissolving tablets products available in international market

Brand (Trade) name	Active drug	Manufacturer/company
Benadryl Fastmelt	Diphenhydramine and Pseudoephedrine	Warner-Lambert, NY, USA
Claritin redi Tab	Loratidine	Schering-Plough Corp.,USA
Domperidon Ebb	Domperidon	Ebb medical, Sweden

Domperon	Domperidon	Astra Pharma, Bangladesh
Feldene Fast Melt	Piroxicam	Pfizer Inc., NY, U. S. A
Febrectol	Paracetamo	Prographarm, Chateaneuf, France
Gaster D	Famotidine	Yamanouchi
Imodium Istant Melts	Loperamide HCL	Janssen, UK
Maxalt MLT	Rizatriptan	Merck and Co., NJ, U. S. A
Nasea OD	Ramosetoron HCl	Yamanouchi
Klonopin Wafers	Clonaxepam	Roche Laboratories
Pepcid RPD	Famotidine	Merck and Co., NJ, U. S. A
TemptraQuiclets	Acetaminophen	Bristol-Myers Squibb NY, USA
Zelapar TM	Selegiline	Amarin Corp., London, UK
Zyprexa	Olanzapine	Eli Lilly, Indianapolis, USA
Zoming-ZMT	Zolmitriptan	AstraZeneca, Wilmington, USA
Zofran ODT	Ondansetron	Glaxo Wellcome, Middlesex, UK

CONCLUSION

Fast dissolving tablets are innovative dosage forms developed and specially designed to overcome some of the problems that seen in conventional solid dosage form i.e. difficulty in swallowing of the tablet in geriatric and pediatric patients. Fast dissolving tablets are designed to dissolve or disintegrate quickly in the saliva generally within less than 60 seconds (range of 5-60 seconds). Fast dissolving tablets have better patient compliance and acceptance may improve biopharmaceutical properties, bioavailability improved efficacy, convenience, and better safety compared with conventional oral dosage forms. The popularity of FDTs has increased fabulously over the last decade. FDTs need to be formulated for psychotic patients, bedridden, geriatric, pediatric patients, for those patients who may not have access to water, patients who are busy in traveling. FDTs formulations formulated by some of these patent technologies have sufficient mechanical strength, quick disintegration/dissolution without water.

REFERENCES

1. Shailesh sharma, new generation of tablet: fast dissolving tablet,pharmainfo.net, vol. 6 issue 1, 2008
2. Seager, H., J.Pharma . Pharmacol., 1998;50:375-382.
3. Shangraw, R., Mitrevej, A. and Shah, M., Pharma . Tech., 1980;4(10): 49-57
4. Keshari R, Bharkatiya M, Rathore KS, Shyama S, Kumar, Sirvi G, somani N, *et al.* Fast dissolving tablet drug delivery system-an overview. Int J Pharm 2015;5:577-89.
5. Nautiyal U, Singh S, Singh R, Gopal, Kakar S. Fast dissolving tablets as a novel boon: a review. J Pharm Chem Biol Sci 2014;2:5-26.

6. Pagar R, Ahirrao S, Yallatkar T, Wagh M. Review on orodispersible tablets. *Int J Res Dev Pharm L Sci* 2014;3:949-58.
7. Gupta DK, Bajpai M, Chatterjee DP. Fast mouth is dissolving disintegrating tablet and patient counselling points for FDDTS-a review. *Int J Res Dev Pharm L Sci* 2014;3:949-58.
8. Gohel M, Patel M, Amin A, Agrawal R, Dave R, Bariya N. Formulation design and optimization of mouth dissolve tablets of nimesulide using vacuum drying technique. *AAPS PharmSciTech* 2004;5:36
9. Khan AB, Tripuraneni A. Fast dissolving tablets—a novel approach in drug delivery. *Rguhs J Pharm Sci* 2014;1:7-16.
10. Takagi H, Kajiyama A, Yanagisawa M. Rapidly disintegrable pharmaceutical composition. *U. S. Patent*; 2005;6:899.
11. Divate S., Kunchu K, Sockan GN. Fast disintegrating tablets—an emerging trend. *Int J Pharm Sci Rev Res* 2011;2:18-22
12. Mohan SC, Margret CR. Recent advances in orodispersible tablets: a review. *Int J Drug Discovery Herbal Res* 2011; 2:78-83.
13. Divate S., Kunchu K, Sockan GN. Fast disintegrating tablets—an emerging trend. *Int J Pharm Sci Rev Res* 2011;2:18-22.
14. Kuchekar BS, Badha AC, Mahajan HS. Mouth dissolving tablets: a novel drug delivery system. *Pharmatimes* 2003;35:7-9.
15. Sharma S. New generation of the tablet: fast dissolving tablet. *Latest Rev Pharmainfo Net*; 2008. p. 6.
16. Yoshio, K., Masazumi, K., Shuichi A., and Hiroaki N.,2005, Evaluation of rapidly disintegrating tablets manufactured by phase transition of sugar alcohols, *J. Control. Release*, 105(1-2), 16-22.
17. Sri KV, Raj GB, Ravishanker D, Kumar CA. Preparation and evaluation of montelukast oral dispersible tablets by direct compression method. *Int Res J Pharm* 2012;7:315-8.
18. Yang D, Kulkarni R, Behme RJ, Kotiyan PN. Effect of the melt granulation technique on the dissolution characteristics of griseofulvin. *Int J Pharm* 2007;329:72-80.
19. Yoshio, K., Masazumi, K., Shuichi A., and Hiroaki N.,2005, Evaluation of rapidly disintegrating tablets manufactured by phase transition of sugar alcohols, *J. Control. Release*, 105(1-2), 16-22.
20. Ahmed, salah u. Gorukanti, sudhir r. Chowdhury, tahseen a., ondansetron orally disintegrating tablets, us patent 7390503, june 24, 2008

21. Moreau, marinette ,grellety, sebastien, methods for obtaining a fast dissolving imidapril powder, us patent application 20080167358, july 10, 2008.
22. Nakatani, manabu,yokoyama, kazutoshi sawada, takeshi, bilayer tablet comprising telmisartan and diuretic, us patent application 20080113023,may 15, 2008 8.
23. withiam, michael c.,mehra, dev k.,cornelius, john m, rapidly dissolving tablets comprising low surface area calcium phosphates, us patent application 20070196477,august 23, 2007
24. Fu, yourong ,jeong, seong hoon,kim, jeanny,callihan, jacqueline a park, kinampai, chaul minpark, sang yeobseomoon, mannosebased fast dissolving tablets, us patent application 20060134195,june 22, 2006
25. Yousef, abdul razzaq,zaman, quamar, instant dissolving tablet composition for loratidine and desloratidine, us patent application 20050214365,september 29, 2005
26. wang, wen-che, chen, hui-yu,yang, chih-chiang, fast dissolving tablet and method of preparing the same, us patent application 20050196438,september 8, 2005
27. Nakatani, manabu, Yokoyama, Kazutoshisawada, takeshi, bilayer tablet comprising telmisartan and diuretic, us patent application 20080113023,may 15, 2008
28. Davis f purbi,dual layer tablets-method of using and therof,us patent no-6863830,march 8,2005.
29. Danilovski, aleksandar, zdravka, knezevic, single dose fast dissolving azithromycin, us patent application 20050026851, february 3, 2005
30. Fu, yourong,pai, chaul minpark, sang yeob,seomoon, gun,park, kinam, highly plastic granules for making fast melting tablets, us patent application 20050013857, january 20, 2005
31. Abu-izza, khawla a.li, vincent h.look, jee l.parr, graham d.schineller, matthew k., fast dissolving tablet, us patent 6733781, may 11, 2004
32. Thombre g, avinash,rapidly disintegrating and fast dissolving solid dosage form,patent no6494899, december 24,2002
33. Liu, fang-yu,he, min michael,nyshadham, janaki ram, sharma,kuldeepak,chu, james shunnan,fix, joseph a. Water soluble polymer-based rapidly dissolving tablets and production processes thereof, us patent 6465009,october 15, 2002
34. Khankari, Rajendra k.,hontz, john,chastain, sara j,katzner, leo, rapidly dissolving robust dosage form us patent 6024981february 15, 2000
35. Allen, loyd v,wang, Bingnan, particulate support matrix for making a rapidly dissolving dosage form us patent 6177104,january 23, 2001

36. Herreid, richard m.,lippert, vernon e., method for making fast dissolving bouillon cubes, us patent 6126979,october 3, 2000

AJPTR is

- Peer-reviewed
- bimonthly
- Rapid publication

Submit your manuscript at: editor@ajptr.com

