INTERNATIONAL RESEARCH JOURNAL OF PHARMACY **ISSN 2230 – 8407**
Available online http://www.irjponline.com
Review Article

FAST DISSOLVING TABLETS: AN UPDATE

Darna Bikshapathi[1], Kandikonda Saikrishna*[1], Uppuluru Ashok Kumar[1], Gade Sabitha[1], Bhupathi Saikumar[2]
[1]Trinity College of Pharmaceutical Sciences, Peddapalli, Karimnagar (Dist.), AP-505172, India
[2]Matrix Laboratories Limited, City, Nasik, Maharashtra, India

Article Received on: 12/04/2011 Revised on: 22/05/2011 Approved for publication: 10/06/2011

*Kandikonda Saikrishna, Trinity College of Pharmaceutical Sciences, Peddapalli, Karimnagar (Dist.), AP-505172, Email: sai1985_pharma@yahoo.in

ABSTRACT
Fast dissolving tablets are dissolving 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. Other ingredients 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. Fast or mouth dissolving tablets have been formulated for pediatric, geriatric, and bedridden patients and for active patients who are busy and traveling and may not have access to water. Fast dissolving tablets (FDTs) have received ever-increasing demand during the last decade, and the field has become a rapidly growing area in the pharmaceutical industry. This article describes various formulations and technologies developed to achieve fast dissolution/dispersion of tablets in the oral cavity. In this review describes in detail about FDT technologies based on lyophilization, molding, sublimation, spray drying, mass extrusion and direct compression. Several techniques have been developed in the recent past, to improve the disintegration quality of these delicate dosage forms without affecting their integrity. This article focuses on the technologies available and the advances made so far in the field of fabrication of fast dissolving tablets. Apart from the conventional methods of fabrication, this review also provides the detailed concept of some unique patented technologies like Zydis, Orasolv, Durasolv, Flashtab, Flash dose and Wowtab, Lyoc, Pharmaburst technology, Frosta technology, OraQuick, Quick-Dis Technology, Sheaform Technology, Ceform Technology, Nano technology, Advatab.
KEYWORDS: Fast dissolving, Patented technologies, Superdisintegrants, Evaluation technique, Drug delivery system.

INTRODUCTION

A solid dosage forms are more popular because of ease of administration, accurate dosage, self medication, pain avoidance and most importantly the patient compliance. The most popular solid dosage forms are being tablets and capsules; one important drawback of this dosage forms for some patients are difficulty to swallow. Drinking water plays an important role in the swallowing of oral dosage forms[1,2]. Often times people experience inconvenience in swallowing conventional dosage forms such as tablet when water is not available, in the case of the motion sickness (kinetosis) and sudden episodes of coughing during the common cold, allergic condition and bronchitis. For these reason, tablets that can rapidly dissolve or disintegrate in the oral cavity (Table1) have attracted a great deal of attention. Oro dispersible tablets are not only indicated for people who have swallowing difficulties, but also are ideal for active people[3]. Fast dissolving tablets are also called as mouth-dissolving tablets, melt-in mouth tablets, Orodispersible tablets, rapimelts, porous tablets, quick dissolving etc. Fast dissolving tablets are those when put on tongue disintegrate instantaneously releasing the drug which dissolve or disperses in the saliva[4]. According to European pharmacopoeia, the ODT should disperse /disintegrate in less than three minutes. The basic approach in development of FDT is the use of superdisintegrants like cross linked carboxymethyl cellulose (croscarmellose), sodium starch glycolate (primogel, explotab), polyvinylpyrollidone (polyplasdone) etc, which provide instantaneous disintegration of tablet after putting on tongue, their by release the drug in saliva. The bioavailability of some drugs may be increased due to absorption of drug in oral cavity and also due to pregastric absorption of saliva containing dispersed drugs that pass down into the stomach.

DEFINITION

The Center for Drug Evaluation and Research (CDER), US FDA defined Oral Disintegrating Tablets (ODT) as "A solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue." A fast dissolving tablet can be defined as a solid dosage form that can disintegrates into smaller granules which slowly dissolve in the mouth. The disintegration time for fast

dissolving tablet varies from a few seconds to more than a minute depending on the formulation and the size of the tablet[5,6].

BENEFITS OF FAST DISSOLVING TABLETS

1. Administered without water, anywhere, any time.
2. Suitability for geriatric and pediatric patients, who experience difficulties in swallowing and for the other groups that may experience problems using conventional oral dosage form, due to being mentally ill, the developmentally disable and the patients who are un-cooperative, or are on reduced liquid intake plans or are nauseated.
3. Beneficial in cases such as motion sickness and coughing where an ultra rapid onset of action required.
4. An increased bioavailability, particularly in cases of insoluble and hydrophobic drugs, due to rapid disintegration and dissolution of these tablets.
5. Stability for longer duration of time, since the drug remains in solid dosage form till it is consumed. So, it combines advantage of solid dosage form in terms of stability and liquid dosage form in terms of bioavailability[7].

SALIENT FEATURES OF FAST DISSOLVING TABLETS

1. Ease of administration to patients who refuse to swallow a tablet, such as pediatric and geriatric patients and psychiatric patients.
2. Convenience of administration and accurate dosing as compared to liquids.
3. No need of water to swallow the dosage from, which is highly convenient feature for patients who are traveling and do not have immediate access to water.
4. Good mouth feels properly of MDDS helps to change the basic view of medication as "bitter pill", particularly for pediatric patients.
5. Rapid dissolution of drug and absorption which may produce rapid, onset of action. Some drugs are absorbed from the month pharynx and oesophagus as the saliva passes down into the stomach, in such cases bioavailability of drugs is increased.
6. Ability to provide advantages of liquid medication in the form of solid preparation. Pregastric absorption can result in improved bioavailability and as a result of reduced dosage, improved clinical performance through a reduction of unwanted effects[8].

TECHNIQUES FOR PREPARING FAST DISSOLVING TABLETS

The basic approaches to developing fast dissolving tablets include maximizing the porous structure of the tablet matrix, incorporating the appropriate disintegrating agent and using highly water-soluble excipients in the formulation[1,8,9,10,11,12].

Various technologies used in the manufacture of Fast dissolving tablets include

1. Freeze drying Technology or lyophilization
2. Tablet Moulding
3. Spray drying
4. Direct compression
5. Sublimation Technique
6. Mass extrusion

FREEZE DRYING TECHNOLOGY (ZYDIS TECHNOLOGY)

Lyophilization can be used to prepare tablets that have very porous open matrix network into which saliva rapidly moves to disintegrate lyophilized mass after it is placed in mouth. The drug is entrapped in a water soluble matrix which is freeze dried to produce a unit which rapidly disperses when placed in mouth. Apart from the matrix and active constituents, the final formulation may contain other excipients, which improve the process characteristics or enhance the quality of final product. These include suspending agents, wetting agents, preservatives, antioxidants, colors and flavors. The preferred drug characteristics for freeze drying formulations are water insoluble, low dose, chemically stable, small particle size and tasteless.

Corveleyn and Remon was studied the influence of various formulation and process parameters on the characteristics of rapidly disintegrating tablets in lyophilized form using hydrochlorthiazide as a model drug. They have concluded that maltodxtrins are useful in the formulation of fast dissolving tablets made by freeze-drying. Lyophilization is relatively expensive and time consuming manufacturing process. Other drawback includes fragility, which make the use of conventional packing difficult and poor stability during storage under stressful condition.

TABLET MOULDING

In this technology, water-soluble ingredients are used so that tablet disintegrate and dissolve rapidly. The powder blend is moistened with a hydro alcoholic solvent and is molded in to tablet using compression pressure lower than used in conventional tablets compression. The solvent is then removed by air-drying. Molded tablets have a porous structure that enhances dissolution. Two problems commonly encountered are mechanical strength and poor taste masking characteristics. Using binding agents such as sucrose, acacia or poly vinyl pyrrolidone can increase the mechanical strength of the tablet. To overcome poor taste masking characteristic Van Scoik incorporated drug containing discrete particles, which were formed by spray congealing a molten mixture of hydrogenated cottonseed oil, sodium bicarbonate, lecithin, polyethylene glycol and active ingredient into a lactose based tablet triturate form.

SPRAY DRYING

Spray dryers are widely used in pharmaceuticals and biochemical processes. Due to processing solvent is evaporated rapidly; spray drying can produce highly

porous, fine powder. Spray drying can be used to prepare rapidly disintegrating tablets. This technique is based on a particulate support matrix, which is prepared by spray drying an aqueous composition containing support matrix and other components to form a highly porous and fine powder. This is then mixed with active ingredients and compressed into tablets. Allen et al used a spray drying technique to prepare fast dissolving tablets. The tablets made from this technology are claimed to disintegrate within 20 seconds.

DIRECT COMPRESSION METHOD

In this method, tablets are compressed directly from the mixture of the drug and excipients without any preliminary treatment. The mixture to be compressed must have adequate flow properties and cohere under pressure thus making pretreatment as wet granulation unnecessary. Few drugs can be directly compressed into tablets of acceptable quality. A type of disintegrants and its proportion are of prime importance. The other factors to be considered are particle size distribution, contact angle, pore size distribution, tablet hardness and water absorption capacity. All these factors determine the disintegration. The disintegrant addition technology is cost effective and easy to implement at industrial level.

Cousin et al, using carboxymethyl cellulose as disintegrating agent and one swelling agent consisting of modified starch or microcrystalline cellulose formulated rapidly disintegrable multi particular tablets. The tablets disintegrate in the mouth in less than 60 seconds. Gas Evolving disintegrants have been used to formulate fast dissolving tablets. The evolution of carbon dioxide as a disintegration mechanism called OROSOLV and DURASOLV have been described in two US Patents assigned to CIMA Labs. J. Michaelson described the use of intimate mixture of alginic acid and a water-soluble metal carbonic acid to prepare tablets. When tablet was placed in water, an acid base reaction takes place forming a metal alginic acid salt and carbonic acid. The salt caused the tablet to swell and the carbonic acid produced carbon dioxide within the swelling tablet whereby rapid disintegration of tablet was effected.

SUBLIMATION TECHNIQUE

The basis of this technique is to add inert solid ingredients that volatilize readily, (e.g. camphor, ammonium bicarbonate, naphthalene, urea, urethane etc) to other tablet excipients and the mixture is then compressed into tablets. Volatile material is then removed via sublimation, which generate a porous structure. Koizumi et al applied the sublimation technique to prepare highly porous compressed tablets that were rapidly soluble in saliva. Mannitol and camphor were used as a tablet matrix material and subliming the material respectively. Camphor was iminated by subliming in vacuum at 80^0C for 30 minutes to develop pores in the tablets.

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 tablets. The dried cylinder can also be used to coat granules for bitter drugs and thereby achieve taste masking.

IMPORTANT PATENTED TECHNOLOGIES FOR FAST DISSOLVING TABLETS

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[1,13,14]

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.

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 tabletting 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.

ORASOLV TECHNOLOGY

CIMA labs have developed Orasolv Technology. 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.

FLASH DOSE TECHNOLOGY

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.

WOW TAB TECHNOLOGY

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.

FLASH TAB TECHNOLOGY

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 tabletting technology.

LYOC (Laboratories L. Lafon, Maisons Alfort, France)

Lyoc utilizes a freeze drying process but differ from Zydis in that the product is frozen on the freeze dryer shelves. To prevent in homogeneity by sedimentation during this process, these formulations require a large proportion of undissolved inert filler (mannitol), to increase the viscosity of the suspension. The high proportion of filler reduces the potential porosity of the dried dosage form and results in denser tablets with disintegration rates that are comparable with the loosely compressed fast melt formulations.

PHARMABURST TECHNOLOGY

Pharmaburst is a "Quick Dissolve" delivery system patented by SPI Pharma. Pharmaburst is a co-processed excipient system with specific excipients, which allows rapid disintegration and low adhesion to punch faces mouldability saccharides are used to obtain rapid melting strong tablet. The active ingredient mixes with low mouldability saccharides.

FROSTA TECHNOLOGY

Akina patents this technology. It utilizes the concept of formulating plastic granules and compressing them at low pressure to produce strong tablets with high porosity. Plastic granules composed of porous and plastic material, water penetration enhancer, and binder. The process involves mixing the porous plastic material with water penetration enhancer followed by granulating with binder. The tablets obtained have excellent hardness and rapid disintegration time ranging from 15 to 30 sec depending on size of tablet.

ORAQUICK

The OraQuick fast-dissolving/disintegrating tablet formulation utilizes a patented taste masking technology. KV Pharmaceutical claims its microsphere technology, known as Micro Mask, has superior mouth feel 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.

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 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.

SHEAFORM TECHNOLOGY

This technology make Sheaform matrix consisting of floss preparation. Floss is produced by subjecting to a feed shock containing a sugar to flash heat processing.

CEFORM TECHNOLOGY

In this technology microspheres containing active ingredient are prepared. Basic requirement of this technology is placing dry powder containing either pure drug or special blend of drug and excipients. The microspheres then mixed and compressed into previously selected oral dosage form.

NANO TECHNOLOGY

For fast dissolving tablets, Elan's proprietary Nanocrystals 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 Nano Crystal technology.

Nano Crystal Fast dissolving technology provides for:

1. 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
2. Cost-effective manufacturing processes that utilize conventional, scalable unit operations
3. Exceptional durability, enabling use of conventional packaging equipment and formats (i.e., bottles and/or blisters)
4. Wide range of doses (up to 200mg of API per unit)
5. Use of conventional, compendial inactive components
6. Employment of non-moisture sensitive inactives

ADVATAB

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.

SUPERDISINTEGRANTS

In many orally disintegrating tablet technologies based on direct compression, the addition of superdisintegrants principally affects the rate of disintegration and hence the dissolution. The presence of other formulation ingredients such as water-soluble excipients and effervescent agents further hastens the process of disintegration (Table No. 2).

MECHANISM OF SUPERDISINTEGRANTS

There are four major mechanisms for tablets disintegration as follows[1,15]

Swelling

The general mechanism of action for tablet disintegration is swelling (Figure 1). Tablets with high porosity show poor disintegration due to lack of adequate swelling force. On the other hand, sufficient swelling force is exerted in the tablet with low porosity. It is worthwhile to note that if the packing fraction is very high, fluid is unable to penetrate in the tablet and disintegration is again slows down.

Porosity and capillary action (Wicking)

Disintegration by capillary action is always the first step (Figure 1). When we put the tablet into suitable aqueous medium, the medium penetrates into the tablet and replaces the air adsorbed on the particles, which weakens the intermolecular bond and breaks the tablet into fine particles. Water uptake by tablet depends upon hydrophilicity of the drug /excipient and on tabletting conditions. For these types of disintegrants maintenance of porous structure and low interfacial tension towards aqueous fluid is necessary which helps in disintegration by creating a hydrophilic network around the drug particles.

Due to disintegrating particle/particle repulsive forces

In this another mechanism of disintegration attempts to explain the swelling of tablet made with 'nonswellable' disintegrants. Guyot-Hermann has proposed a particle repulsion theory based on the observation that nonswelling particle also cause disintegration of tablets (Figure 2). The electric repulsive forces between particles are the mechanism of disintegration and water is required for it. Researchers found that repulsion is secondary to wicking.

Due to deformation

During tablet compression, disintegrated particles get deformed and these deformed particles get into their normal structure when they come in contact with aqueous media or water (Figure 2). Occasionally, the swelling capacity of starch was improved when granules were extensively deformed during compression. This increase in size of the deformed particles produces a breakup of the tablet. This may be a mechanism of starch and has only recently begun to be studied.

PREFORMULATION STUDIES FAST DISSOLVING TABLET

Preformulation study relates to pharmaceutical and analytical investigation carried out proceeding and supporting formulation development efforts of the dosage form of the drug substance. Preformulation yields basic knowledge necessary to develop suitable formulation for the toxicological use. It gives information needed to define the nature of the drug substance and provide frame work for the drug combination with pharmaceutical excipients in the dosage form. Hence, the following preformulation studies were performed on the obtained sample of drug[1].

IDENTIFICATION OF DRUG SAMPL

It was confirmed by melting point determination and also by FT-IR spectral analysis

DRUG EXCIPIENT COMPATIBILITY STUDY

Compatibility of the drug with excipients was determined by FT-IR spectral analysis, this study was

carried out to detect any changes on chemical constitution of the drug after combined it with the excipients. The samples were taken for FT-IR study.

EVALUATION OF BLEND

There are five parameters for evaluation of blend as follows[8,17,18,19,20]

1. Angle of repose
2. Bulk density
3. Tapped density
4. Carr's index
5. Hauser's ratio

Angle of repose

The angle of repose was determined by using funnel method. The accurately weighed blend was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of blend. The drug (as solid dispersion)-excipient blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation.

$$\mathbf{Tan\ \Theta = h/r}$$

Where h and r are the height and radius of the powder conc.

Bulk density

Apparent bulk density was determined by pouring a weighed quantity of blend into graduated cylinder and measuring the volume and weight.

BD =Weight of the powder / Volume of the packing.

Tapped density

It was determined by placing a graduated cylinder, containing a known mass of drug-excipients blend. The cylinder was allowed to fall under its own weight onto a hard surface from the height of 10cm at 2- second intervals. The tapping was continued until no further change in volume was noted.

TBD =Weight of the powder / volume of the tapped packing.

Compressibility index

The Compressibility Index of the blends was determined by Carr's compressibility index.

Carr's compressibility index (%) = [(TBD-LBD) X 100] / TBD

Hausner's

Hauser's ratio = Tapped density/ Poured density

Hausner's ratio <1.25 – Good flow = 20% Carr

1.25 – Poor flow =33% Carr's

EVALUATION OF FAST DISSOLVING TABLETS

There are various evaluation parameters for tablets as follows[1,18,19,20,21]

Weight variation

The weight variation can be performed to select 20 tablets randomly from the lot and weighted individually to check for weight variation. Weight variation specification as per I.P. is shown in table No.3

Hardness

The Hardness or tablet crushing strength (fc), the force required to break a tablet in a diametric compression was measured using Monsanto tablet hardness tester. It is expressed in kg/cm2.

Friability (F)

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

$$F = \frac{W_{initial} - W_{final}}{W_{initial}} X100$$

WETTING TIME

In this the Wetting time is closely related to the inner structure of the tablets and to the hydrophilicity of the excipient. According to the following equation proposed by Washburn E.W (1921), the water penetration rate into the powder bed is proportional to the pore radius and is affected by the hydrophilicity of the powders.

$$\mathbf{dl/dt = r\ \Theta\ cos\ \Theta\ /(4Xl)}$$

Where l is the length of penetration, r is the capillary radius, is the surface tension, is the liquid viscosity; t is the time, and Θ

pores size becomes smaller and wetting time increases with an increase in compression force or a decrease in porosity. A linear relationship exists between wetting time and disintegration time. Thus wetting is the important step for disintegration process to take place.

A piece of tissue paper folded double was placed in a Petri plate (internal diameter is 6.5 cm) containing 6ml of water. The tablet was placed on the paper and the time for complete wetting of the tablet was measured in seconds. The method was slightly modified by maintaining water at 37^0c. Wetting time corresponds to the time taken for the tablet to disintegrate when kept motionless on the tongue.

IN-VITRO DRUG RELEASE

Generally the release of the drug *in vitro* was determined by estimating the dissolution profile.

Dissolution test

Here, USP 2 Paddle apparatus was used and paddle was allowed to rotate at 50 rpm .phosphate buffer (PH 6.8) (900 ml) was used as a dissolution medium.

MECHANICAL STRENGTH

Tablets should possess adequate strength to withstand mechanical shocks of handling in manufacturing, packaging and shipping. Crushing strength and friability are two important parameter to evaluate a tablet for its mechanical strength.

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.

Friability Testing

The crushing test may not be the best measure of potential behavior during handling and packaging. The resistance to surface abrasion may be a more relevant parameter. Friability of each batch was measure in "Electro lab friabilator". Ten preweighed tablets were rotated at 25 rpm for 4 min, the tablets were then re weighed and the percentage of weight loss was calculated.

RAPIDLY DISINTEGRATING PROPERTY

To evaluate the tablets for their rapid disintegration properties, following tests were carried out.

Wetting Time

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

Modified Disintegration Test

The standard procedure of performing disintegration test for these dosage forms has several limitations and they do not suffice the measurement of very short disintegration times. The disintegration time for ODT needs to be modified as disintegration is required without water, thus the test should mimic disintegration in salivary contents. For this purpose, a petridish (10 cm diameter) was filled with 10 ml of water. The tablet was carefully put in the center of petridish and the time for the tablet to completely disintegrate into fine particles was noted.

DISINTEGRATION IN ORAL CAVITY

The time required for complete disintegration of tablets in oral cavity was obtained from six healthy volunteers, who were given tablets from the optimum formulation.

Water Absorption Ratio

A piece of tissue paper folded twice was placed in a small Petri dish containing 6 ml of water. A tablet was put on the paper & the time required for complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio, R, was determined using following equation,

$R=10(wa/wb)$ where,

Wb is weight of tablet before water absorption & wa is weight of tablet after water absorption.

***In-Vitro* Dispersion Time**

Tablet was added to 10 ml of phosphate buffer solution, ph 6.8 at 37+0.5ºc, Time required for complete dispersion of a Tablet was measured.

CONCLUSION

Fast dissolving tablets constitute an innovative dosage form, which overcomes the problem of swallowing and provides a quick onset of action. The pediatric and geriatric populations are the primary. These tablets are designed to dissolve or disintegrate rapidly in the saliva generally within <60 seconds (range of 5- 50seconds). Due to the constraints of the current FDDT technologies as highlighted above, there is an unmet need for improved manufacturing processes for fast dissolving tablets that are mechanically strong, allowing ease of handling and packaging and with production costs similar to that of conventional tablets. To fulfill these medical needs, formulators have devoted considerable effort to developing a novel type of tablet dosage form for oral administration, one that disintegrates and dissolves rapidly in saliva without the need for drinking water. The development of a fast-dissolving tablet also provides an opportunity for a line extension in the market place; a wide range of drugs (e.g., neuroleptics, cardiovascular drugs, analgesics, antihistamines, and drugs for erectile dysfunction) can be considered candidates for this dosage form. Pharmaceutical marketing is another reason for the increase in available fast dissolving/ disintegrating products. The basic approach followed by all the currently available technologies engaged in the formulation of Fast dissolving tablets is to maximize the porous structure of the tablet matrix and incorporate super disintegrating agents in optimum concentration so as to achieve rapid disintegration and instantaneous dissolution of the tablet along with good taste masking properties and excellent mechanical strength The availability of the various technologies and manifold advantages of Fast dissolving tablets will surely increase its popularity in the near future.

REFERENCES

1. Debjit Bhowmik, Chiranjib B, Krishnakanth, Pankaj, Margret Chandira R. Fast Dissolving Tablet: An Overview. Journal of Chemical and Pharmaceutical Research 2009; 1(1): 163-177.
2. Yourong Fu, Shicheng Yang, Seong Hoon Jeong, Susumu Kimura & Kinam Park. Orally Fast Disintegrating Tablets: Developments, Technologies, Taste-Masking and Clinical Studies. Critical Reviews in Therapeutic Drug Carrier Systems 2004; 21(6):433–475.
3. Seager H. Drug delivery products and zydis fast dissolving dosage form. J. Pharm. Phamacol. 1998; 50: 375-382.
4. Renon JP, Corveleyn S. Freeze-dried rapidly disintegrating tablets. US Patent No.6, 010,719, 2000.
5. Rajeshree panigrahi, Saiprasanna behera. A review on fast dissolving tablets. Webmed Central Quality and patient safety 2010; 1(9): WMC00809.

6. Leon Lachmann , Herbert A , Liberman , Joseph L.Kaing , The theory and practice of Industrial Pharmacy, 3rd ed. New York: Marcel Dekker Inc; 2008.
7. Hamilton EL, Luts EM. Advanced Orally disintegrating tablets bring significant benefits to patients and product life cycle. Drug Deliv Technol 2005; 5(1): 34-37.
8. Mukesh P, Ratnaparkhi, Mohanta GP, Lokesh Upadhyay. Review On: Fast Dissolving Tablet. Journal of Pharmacy Research 2009; 2(1): 5-12.
9. Indurwade NH.et al., Novel approach – Fast Dissolving Tablets. Indian drugs. August 2002; 39(8):405-409.
10. Lailla JK, Sharma AH. Freeze-drying and its applications. Indian Drugs 1993; 31:503 513.
11. Amin AF, Shah TJ, Bhadani MN, Patel MM. Emerging trends in orally disintegrating tablets. www. Pharminfo.net. 2005.
12. Jaysukh J Hirani, et al. Orally Disintegrating Tablets: A Review. Tropical Journal of Pharmaceutical Research April 2009; 8 (2): 161-172.
13. Patricia VA. Outsourcing solid-dosage manufacturing. Pharm Tech2006; 30 (6): 44-52.
14. Seager H. Fast dissolving 051104 (1998) available from http;// www. Pharmacist.com/patents100/Yr2004 /051104/6733781. Htm. J. Pharma 50: 375-382.
15. Yoshio K, Masazumi K, Shuichi A, Hiroaki N. Evaluation of rapidly disintegrating tablets manufactured by phase transition of sugar alcohols. J. Control. Release 2005; 105(1-2):16-22.
16. Reddy L H et al., "Fast dissolving drug delivery systems: A review of the literature. IJPS July 2002; 331-336.
17. Indurwade N H et al., "Novel approach – Fast Dissolving Tablets. Indian drug August 2002; 39(8):405-409.
18. Kuchekar B S. et al., "Mouth Dissolving Tablets: A Novel Drug Delivery System. Pharma timesJune 2003:35.
19. Lalla J K, Mamania H M. Fast dissolving rofecoxib tablets. Indian J. Pharm. Sci 2004; 59(4): 23-26.
20. Chang R, Guo X, Burnside B A, Couch R. Fast-dissolving tablets. Pharm. Tech2000; 24(6):52- 58.
21. Brown D, Orally disintegrating tablets-taste over speed. Drug Del Tech2003; (3)58-61.
22. Dobetti L, Fast disintegrating tablets US patent. 6, 2003,311.
23. Makino T, Yamada M, Kikuta J. Fast dissolving tablet and its production. European Patent1993; 0553777 A2.

TABLE 1: LIST OF COMMERCIALLY AVAILABLE FAST DISSOLVING TABLETS

Trade Name	Active Drug	Manufacturer
Felden fast melt	Piroxicam	Pfizer Inc., NY, USA
Claritin redi Tab	Loratidine	Schering plough Corp., USA
Maxalt MLT	Rizatriptan	Merck and Co., NJ, USA
Zyprexia	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	Selegilline	Amarin Corp., London, UK
Tempra Quiclets	Acetaminophen	Bristol myers Squibb, NY, USA
Febrectol	Paracetamol	Prographarm, Chateauneuf, 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 2: LIST OF SUPER DISINTEGRANTS

Superdisintegrants	Example	Mechanism Of action	Special comment
Croscarmellose® Ac-Di-Sol® Nymce ZSX® Primellose®Solutab® Vivasol®L-HPC	Cross linked cellulose	-Swells 4-8 folds in < 10 seconds. -Swelling and wicking both.	-Swells in two dimensions. -Direct compression or granulation -Starch free
Crosspovidone Crosspovidone M® Kollidon® Polyplasdone®	Cross linked PVP	-Swells very little and returns to original size after compression but act by capillary action	-Water insoluble and spongy in nature so get porous tablet.
Sodium starch glycolate Explotab® Primogel®	Cross linked starch	-Swells 7-12 folds in <30 seconds	-Swells in three dimensions and high level serve as sustain release matrix.
Alginic acid NF Satialgine®	Cross linked alginic acid	-Rapid swelling in aqueous medium or wicking action	-Promote disintegration in either dry or wet granulation.

TABLE NO 3: 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**

WICKING SWELLING

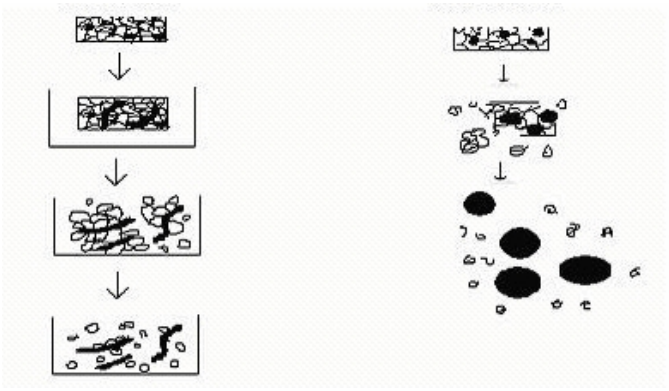

Figure 1 **Water is pulled by disintegrants and reduced the physical bonding force between particles** **Particles swell and break up the matrix from within**

DEFORMATION REPULSION

Figure 2 **Particles swell to precompression size and break up matrix particles** **Water is drawn into pores and repel each other because of resulting electrical force.**