



FAST DISINTEGRATING TABLETS – AN EMERGING TREND

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ABSTRACT

Fast disintegrating tablets (FDTs) have received ever-increasing demand during the last decade and the field has become a rapidly growing area in the pharmaceutical industry. Upon introduction into the mouth, these tablets dissolve or disintegrate in the mouth in the absence of additional water for easy administration of active pharmaceutical ingredients. Such tablets readily dissolve or disintegrate in the saliva generally within <60 seconds. Fast or mouth dissolving tablets have been formulated for pediatric, geriatric, bedridden patients and for active patients who are busy and traveling and may not have access to water. Such formulations provide an opportunity for product line extension in the many elderly persons will have difficulties in taking conventional oral dosage forms (viz., solutions, suspensions, tablets, and capsules) because of hand tremors and dysphasia.

Keywords: Fast disintegrating tablets, Superdisintegrants, Direct compression, wetting time.

INTRODUCTION

The tablet is the most widely used dosage form because of its convenience in terms of self administration, compactness and ease in manufacturing. However, many patients especially children and elderly have difficulty in swallowing tablets and capsules and consequently unable to take medicine as prescribed. Almost 50% of the population is affected by such problem, resulting in the high incidence of non compliance and infective therapy.

To overcome such problems, fast disintegrating tablets or orally disintegrating tablets have emerged as an alternative dosage forms. These tablets are also known as quick dissolve, fast dissolving, rapid disintegrating, mouth dissolving, melt in mouth, orodispersible or orally disintegrating tablets.^{1, 2, 3}

Recently Orally Disintegrating (OD) Tablet technology has been approved by United States Pharmacopoeia (USP), Centre for Drug Evaluation and Research (CDER). USFDA defined OD tablet as "A solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue".^{4, 5, 6}

Requirements of Fast disintegrating tablets

- It should require no water for oral administration, yet dissolve/disperse/disintegrate in mouth in a matter of seconds.
- Have a pleasing mouth feel.
- Have an acceptable taste masking property.
- Should be harder and friable.
- Leave minimal or no residue in the mouth after oral administration.
- Exhibit low sensitivity to environmental conditions such as humidity and temperature.⁷

Salient features of Fast disintegrating tablets

- This system provides rapid dissolution of drug and absorption which may produce rapid onset of action.
- Ease of administration to patients who refuse to swallow a tablet such as pediatric, geriatric patients and psychiatric patients.
- No need of water to swallow the dosage form, which is highly convenient especially for patients who are traveling and do not have immediate access to water.
- Convenience of administration and accurate dosing as compared to liquids.
- Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach; in such cases bioavailability of drugs is increased.

Conventional methods used for the preparation of Fast disintegrating tablets:

Addition of superdisintegrants: A disintegrant is a substance in a tablet formulation that enables the tablet to break up into smaller fragments upon contact with gastrointestinal fluids.⁸ Superdisintegrants are used at a low level in the solid dosage form, typically 1–10% by weight relative to the total weight of the dosage unit. Examples of superdisintegrants are croscarmellose, crospovidone and sodium starch glycolate, which are a cross linked cellulose, cross linked polymer and a cross linked starch respectively. The proper choice of disintegrant and its consistency of performance are critical to formulation development of such tablets.⁹

Microcrystalline cellulose and low substituted hydroxypropylcellulose were used as disintegrating agents in the range of 8:2 – 9.1 to prepare fast dissolving



tablet. Agar powder is used as disintegrant for the development of rapidly disintegration tablets by enhancing the porosity of agar by water treatment. Sodium starch glycolate, crospovidone and croscarmellose are some of the popular superdisintegrants.

Direct compression: It is one of the easiest ways to manufacture tablets. Conventional equipments, commonly available excipients and a limited number of processing steps are involved in direct compression. Sawant K et al. prepared orodispersible tablets of ondansetron HCl by direct compression using superdisintegrants and they reported that in vitro dispersion time of these tablets has been found to be 5 minutes where as conventional tablets have shown 30-35 minutes.¹⁰

Freeze drying or Lyophilization: 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 rapidly. A typical procedure involved in the manufacturing of ODT using this technique is mentioned here. The active drug 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 passed through liquid nitrogen freezing tunnel to freeze the drug solution or dispersion. Then the frozen blister packs are placed in refrigerated cabinets to continue the freeze-drying.

Sublimation: To generate a porous matrix, volatile ingredients are incorporated in the formulation that is later subjected to a process of sublimation. Highly volatile ingredients like ammonium bicarbonate, ammonium carbonate, benzoic acid, camphor, naphthalene, urea, urethane and phthalic anhydride may be compressed along with other excipients into a tablet. Ex: Ravikumar et al. prepared aceclofenac fast dissolving tablets by sublimation method using camphor as subliming agent and sodium starch glycolate together with croscarmellose sodium as superdisintegrants.¹¹

Mass extrusion: In this method active blend is softened using the solvent mixture of water-soluble polyethylene glycol and methanol and then subsequent expulsion of softened mass through the extruder or syringe is made 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.

Spray drying: In this technique, gelatin can be used as a supporting agent and as a matrix, mannitol as a bulking agent and sodium starch glycolate or croscarmellose or crospovidone are used as superdisintegrants. Tablets manufactured from the spray-dried powder have been reported to disintegrate in less than 20 seconds in aqueous medium.

Challenges in formulating Fast disintegrating tablets

Palatability: As most drugs are unpalatable, rapid disintegrating drug delivery systems usually contain the medicament in a taste-masked form. Delivery systems disintegrate or dissolve in patient's oral cavity, thus releasing the active ingredients which come in contact with the taste buds; hence, taste-masking of the drugs becomes critical to patient compliance.^{12,13}

Mechanical strength: The major criteria for fast dissolving tablets is to disintegrate in oral cavity is that they should be made of either very porous and soft-molded matrices or compressed into tablets with very low compression force, which makes the tablets friable, brittle, difficult to handle and often requiring specialized peel-off blister packing that may add to the cost.^{14,15,16}

Hygroscopicity: Several orally disintegrating dosage forms are hygroscopic and cannot maintain physical integrity under normal conditions of temperature and humidity. Hence, they need protection from humidity which calls for specialized product packaging.¹⁷

Amount of drug: The application of technologies used for ODTs is limited by the amount of drug that can be incorporated into each unit dose. For lyophilized dosage forms, the drug dose must be lower than 400 mg for insoluble drugs and less than 60 mg for soluble drugs. This parameter is particularly challenging when formulating a fast-dissolving oral films or wafers.¹⁸

Aqueous solubility: Water-soluble drugs pose various formulation challenges because they form eutectic mixtures, which result in freezing-point depression and the formation of a glassy solid that may collapse upon drying because of loss of supporting structure during the sublimation process.^{19,20}

Size of tablet: The degree of ease when taking a tablet depends on its size. It has been reported that the easiest size of tablet to swallow is 7-8 mm while the easiest size to handle was one larger than 8 mm.²¹

Patented technologies for Fast disintegrating tablets

Zydis technology: Zydis, the best known of the fast-dissolving/disintegrating tablet preparations was the first marketed new technology tablet. The tablet dissolves in the mouth within seconds after placement on the tongue. A Zydis tablet is produced by lyophilizing or freeze drying the drug in a matrix usually consisting of gelatin.²²

Durasolv technology: Durasolv is the patented technology of CIMA labs. The tablets made by this technology consist of a drug, fillers and a lubricant. Tablets are prepared by using conventional tableting equipment and have good rigidity. Durasolv is an appropriate technology for products requiring low amounts of active ingredients.²³

Orasolv technology: Orasolv Technology has been developed by CIMA labs. It uses an effervescent disintegration pair that releases gas upon contact with



water. The widely used effervescent disintegration pairs usually include acid sources like include citric acid, tartaric acid, malic acid, fumaric acid, adipic acid and a carbonate source include sodium bicarbonate, sodium carbonate, potassium bicarbonate and potassium carbonate. The amount of effervescent agent is in general about 20–25% of the total weight of the tablet.^{23, 24}

Flashtab technology: The Flashtab technology is yet another fast dissolving/disintegrating tablet formulation. Prographarm laboratories have patented the Flashtab technology. 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 less than one minute.²⁵

Advatab technology: 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.^{26,27,28}

List of commercially available Fast disintegrating 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

Evaluation of Fast disintegrating tablets

Tablets from all the formulation were subjected to following quality control test.

General Appearance: The general appearance of a tablet, its visual identity and over all "elegance" is essential for consumer acceptance and tablet's size, shape, colour, presence or absence of an odour, taste, surface texture, physical flaws and consistency and legibility of any identifying marking.

Size and Shape: The size and shape of the tablet can be dimensionally described, monitored and controlled.

Tablet thickness: Tablet thickness is an important characteristic in reproducing appearance and also in counting by using filling equipment. Some filling equipment utilizes the uniform thickness of the tablets as a counting mechanism. Ten tablets were taken and their thickness was recorded using micrometer.

Weight variation: 20 tablets were selected randomly from the lot and weighted individually to check for weight variation. Weight variation specification as per I.P. is shown in following table.

Average Weight of Tablet	% Deviation
80 mg or less	±10
More than 80 mg but less than 250 mg	±7.5
250 mg or more	±5

Hardness: Hardness of tablet is defined as the force applied across the diameter of the tablet in the order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. Hardness of the tablet of each formulation was determined using Monsanto Hardness tester.

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 height of 6 inches in each revolution. Pre weighted sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. The friability (F) is given by the formula.

$$F = \frac{W_{int} - W_{fn}}{W_{int}}$$



Where, W_{int} - Weight of tablets before friability.

W_{fin} - Weight of tablets after friability.

Wetting Time and Water Absorption Ratio: Wetting time of dosage form is related to the contact angle. It needs to be assessed to give an insight into the disintegration properties of the tablets; a lower wetting time implies a quicker disintegration of the tablet. For this purpose, a tablet is placed on a piece of tissue paper folded twice and kept in a small Petri dish (ID = 6.5 cm) containing 6 ml of water, and the time for complete wetting is measured.

Water absorption Ratio: A piece of tissue paper folded twice was placed in a small Petridish 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,

$$R = 10 (w_a/w_b)$$

Where, w_a is weight of tablet before water absorption & w_b is weight of tablet after water absorption.

In vitro dispersion time: In vitro dispersion time was measured by dropping a tablet in a beaker containing 50 ml of Sorenson's buffer pH 6.8. Three tablets from each formulation were randomly selected and in vitro dispersion time was performed.

In vitro Dissolution test: The development of dissolution methods for FDTs is comparable to the approach taken for conventional tablets and is practically identical. Dissolution conditions for drugs listed in a pharmacopoeia monograph, is a good place to start with scouting runs for a bioequivalent FDT. Other media such as 0.1 M HCl and buffer (pH 4.5 and 6.8) should be evaluated for FDT much in the same way as their ordinary tablet counterparts. It has been suggested that USP 2 paddle apparatus is the most suitable and common choice for orally disintegrating tablets, with a paddle speed of 50 rpm commonly used.

Stability testing of drug (temperature dependent stability studies)

The fast dissolving tablets are packed in suitable packaging and stored under the following conditions for a period as prescribed by ICH guidelines for accelerated studies.

(1) $40 \pm 1^\circ\text{C}$

(2) $50 \pm 1^\circ\text{C}$

(3) $37 \pm 1^\circ\text{C}$ and RH $75\% \pm 5\%$

The tablets were withdrawn after a period of 15 days and analyzed for physical characterization (Visual defects, Hardness, Friability, Disintegrations and Dissolution etc.) and drug content. The data obtained is fitted into first order equations to determine the kinetics of degradation. Accelerated stability data are plotting according Arrhenius equation to determine the shelf life at 25°C .^{29,30}

CONCLUSION

Fast disintegrating tablets have better patient compliance and may offer improved biopharmaceutical properties, improved efficacy and better safety compared with conventional oral dosage forms. Today, fast disintegrating tablets are more widely available as over-the-counter products for the treatment of allergies, cold and flu symptoms. The target population has expanded to those who want convenient dosing anywhere, anytime, without water. The future potential for these products is promising because of the availability of new technologies combined with strong market acceptance and patient demand. Future possibilities for improvements in Rapid disintegrating and drug delivery are bright, but the technology is still relatively new. Several drug delivery technologies that can be leveraged on improving drug therapy from these dosage forms.

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