



A REVIEW ON FAST DISSOLVING TABLETS

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ABSTRACT

Oral delivery is currently the gold standard in the pharmaceutical industry where it is regarded as the safest, most convenient and most economical method of drug delivery having the highest patient compliance.

Oral dosage form and oral route are the most preferred route of administration for various drugs has limitations like first-pass metabolism, psychiatric patients, bedridden and uncooperative patients. FDTs are disintegrating or dissolve quickly in the saliva without a need of water. Fast dissolving tablets are designed to dissolve in saliva remarkably faster, within a few seconds (less than 60 seconds), and those are real fast-dissolving tablets. FDTs formulations contain super disintegrants to enhance the disintegration rate of a tablet in the buccal cavity. FDTs have disintegrated quickly, absorb faster so, *in vitro* drug release time improve and this property of drugs (dosage form) enhanced bioavailability. In this review contain brief information about FDTs including definition, advantages, salient features of FDTs, limitations, challenges to developing FDT, technologies, evaluation parameters, marketed formulations of fast dissolving tablets, etc.

KEYWORD: - Fast dissolving tablets, Superdisintegrants, Evaluation of fast dissolving tablets, Fast dissolving technologies.

INTRODUCTION

Fast dissolving drug delivery systems were first developed in the late 1970s as an alternative to conventional dosage forms for the pediatric and geriatric patient. These tablets are designed to dissolve or disintegrate rapidly in the saliva generally less than 60 seconds.^[20] To fulfill these medical needs, pharmaceutical technologists have developed a novel oral dosage forms known as orally disintegrating (dispersible) tablets (ODTs) or Fast disintegrating (dissolving) tablets (FDTs) or mouth melting tablets (MMTs) or mouth dissolving tablets (MDTs), immediate release tablets which disintegrate rapidly in saliva, usually in a matter of seconds, without the need to take water.

United States Food and Drug Administration (USFDA) defined fast dissolving tablet (FDT) as "a solid dosage form containing a medicinal substance or active ingredient which disintegrate rapidly usually within a matter of seconds when placed upon the tongue".^[18]

The oral route of administration is considered as the most widely accepted route because of its convenience of self-medication, compaction, ease of manufacturing, ease of administration, accurate dose, safest and economical route.^[2-3]

Recent market studies indicate that more than half of the patient population prefers FDTs to other dosage forms. Mouth dissolving tablets are formulated mainly by two techniques first use of super disintegrants like Croscarmellose sodium, sodium starch glycolate and crospovidone. Another method is maximizing pore structure of the tablets by freeze drying and vacuum drying.^[20] In all methods, direct compression is preferred because of its effortlessness, quick procedure and cost-effectiveness.^[19]

Advantages Of Fast Dissolving Tablets^[21,22]

- No need of water to swallow the tablet.
- FDTs can be easily administered to pediatric, elderly and mentally disabled patients.
- Accurate dosing as compared to liquids.
- Dissolution and absorption of the drug is fast, offering rapid onset of action.
- Bioavailability of drugs is increased as some drugs are absorbed from mouth, pharynx and esophagus through saliva passing down into the stomach.
- Advantageous over liquid medication in terms of administration as well as transportation.
- First pass metabolism is reduced, thus offering improved bioavailability and thus reduced dose and side effects.
- offering improved safety.

- Allows high drug loading.

Ideal Characteristics Of Fast Dissolving Tablets

They should not require water for administration, yet dissolve or disintegrate in the mouth within a few seconds,^[23, 24]

- should compatible with sweetening agents for masking of taste
- should have acceptable taste
- should leave minimal residue in the mouth after its administration
- should compatible for high drug loading
- should withstand to humidity and temperature
- Manufacturing and packaging should be economic

Limitations of Fast Dissolving Tablets^[25, 26]

- The major disadvantages of FDTs are related to the mechanical strength of tablets.
- FDT are very porous and soft molded metrics or compressed in a tablet with low compression, which makes tablet friable and brittle which difficult to handle.
- Bad tastes drugs are difficult to formulate as FDT; special precaution should have to be taken before formulate such kind of drug.
- Several FDT are hygroscopic cannot maintain physical integrity under normal condition from humidity which requires specialized package.
- Dryness of the mouth due to decreased saliva production may not be good candidates for these tablet formulations.
- Rate of absorption from the saliva solution and overall bioavailability

Challenges in Formulation of Fast Dissolving Tablets

1) Mechanical strength and disintegration time

FDTs are formulated to obtain disintegration time usually less than a minute. While doing so, maintaining good mechanical strength is a prime challenge. Many FDTs are fragile and there are many chances that such a fragile tablet will break during packaging, transport or handling by the patients. Tablets based on technologies like zydis need special type of packaging. It is very natural that increase in the mechanical strength will delay disintegration time.

2) Taste masking

Many drugs are bitter in taste. A tablet of better drug dissolving, disintegration in mouth will seriously affect patient compliance and acceptance for the dosage form. So effective taste masking of the bitter drugs must be done so that the taste of the drug is not felt in the oral cavity.

3) Mouth feel

FDT should disintegrate into larger particles in the oral cavity. The particles generated after disintegration of the FDTs should be as small as possible. FDTs should leave minimal or no residue in mouth after oral administration.

More over addition of flavor's and cooling agents like menthol improve the mouth feel.

4) Cost

The technology used for FDTs should be acceptable in terms of cost of the final product method like Zydis and Orasolv that require remarkable.^[4, 5]

Technologies Used For Manufacturing Fast Disintegrating Tablets

Various technologies used in the manufacture of FDT include:

1. Freeze drying/ Lyophilisation
2. Tablet moulding
3. Spray drying
4. Direct Compression
5. Sublimation
6. Mass Extrusion

1) Freeze-Drying or Lyophilisation-

It is one of the first generation techniques for preparing FDT, in which sublimation of water takes place from the product after freezing. Lyophilisation is a pharmaceutical technology which allows drying of heat sensitive drugs and biological at low temperature under conditions that allow removal of water by sublimation.

Freeze drying process normally consists of three steps:

- Material is frozen to bring it below the eutectic point.
- Primary drying to reduce the moisture around 4% w/w of dry product.
- secondary drying to reduce the bound moisture up to required final volume.

Due to lyophilisation, bulking agent and sometimes drug acquire glossy amorphous structure and thus dissolution is enhanced. The tablets prepared by freeze drying or lyophilisation are very porous in nature and disintegrate or dissolve rapidly when come in contact with saliva.^[6,7]

2) Molding

Tablets produced by molding are solid dispersion. Molded tablets disintegrate more rapidly and offer improved taste because the dispersion matrix is generally made from water soluble sugars. There are two types of molding process:

a) Solvent method

Solvent method involves moistening the powder blend with a hydro alcoholic solvent followed by compression at low pressure in molded plates to form a wetted mass. Air drying is done to remove the solvent. Such tablets are less compact than compressed tablets and possess a powder structure that hastens dissolution.

b) Heat method

In the heat molding process a suspension is prepared that contains a drug, agar and sugar (mannitol or lactose). This suspension is poured in the blister packaging wells, and then agar is solidified at the room temperature to

form a jelly and dried at 30°C under vacuum. The main concern about these molded tablets is their mechanical strength, which can be achieved by using binding agents.^[8]

3) Spraydrying

Pharmaceutical Industry to Produce Highly Porous Powders. Allen Et Al. Have Used Spray Drying For The Production Of FDT's. The Formulations Contained Hydrolyzed And Nonhydrolysed Gelatin As A Supporting Agent For The Matrix, Mannitol As A Bulking Agent And Sodium Starch Glycol As Or Croscarmellose As A Disintegrant. By Adding An Acid (Eg: Citric Acid) Spray Or An Alkali (Eg: Sodium Bicarbonate) Disintegration And Dissolution Were Further Enhanced. Tablets Manufactured By This Method Show Disintegration Time < 20 Sec In An Aqueous Medium.^[7]

4) Sublimation

This process involves addition of some inert volatile substances like urea, urethane, camphor etc. to other excipients and the compression of blend into tablet. Removal of volatile material by sublimation creates pores in the tablet structure, due to which tablet dissolves when comes in contact with saliva. Additionally several solvent like cyclohexane, benzene etc. can also be used as pore forming agents. Fast dissolving tablets with highly porous structure and good mechanical strength have been developed by this method.^[9,10]

5) Mass extrusion

This technology involves softening the active blend using the solvent, mixture of water soluble polyethylene glycol using methanol and expulsion of softened mass through the extruder or syringe to get a cylinder of the product and cutting into even segments up to heated blade to form tablets.^[11]

6) Direct Compression

Direct compression represents the most cost effective and simplest tablet manufacturing technique. Because of the accessibility of improved excipients especially superdisintegrants and sugar based excipients, this technique can now be utilized for preparation of Fast Dissolving Tablets.^[8]

A. Superdisintegrants

Superdisintegrants are the principally affecting disintegration and ultimately dissolution of the fast dissolving tablets, mainly for direct compression techniques. The presence of other ingredients such as water-soluble excipients and effervescent agents further hastens the disintegration process.

B. Sugar Based Excipients

This is another route to approach the direct compression technique. The use of sugar based excipients especially bulking agents like lactitol, dextrose, is malt, fructose, multirole, maltose, mannitol, sorbitol, polydextrose,

xylitol, and starch hydrolysate which display high aqueous solubility and sweetness, and hence impart taste masking property and a pleasant mouth feel. Manumit et al have categorized sugar-based excipients into two types on the basis of molding and dissolution rate.

Type 1 saccharides (mannitol and lactose) exhibit low mould-ability but high dissolution rate.

Type 2 saccharides (mannitol and maltose) exhibit high mould-ability and low dissolution rate^[24]

Patented Technologies For Fast Dissolving Tablets

1) Zydis Technology

Zydis formulation is a unique technology of preparing fast dissolving tablet. It is freeze dried tablet technology in which drug materials are physically entrapped or dissolved within the matrix of fast dissolving carrier materials. Water is not required for swallowing because when "zydis unit" is put in mouth then the freeze dried structure disintegrates rapidly. Zydis material is composed of so many substances to achieve a number of objectives.^[27] To provide strength during handling polymers such as dextran, alginate and gelatin are incorporated. Saccharides such as sorbitol or mannitol are incorporated to obtain good elegance, hardness and crystallinity. To prevent the shrinkage of "zydis unit" during freeze drying process or long term storage glycine is generally used as collapse protectants. To protect the formulation from the moisture it should be packed in a blister.^[28]

2) Durasolv Technology

It is patented technology of CIMA LAB (US patent no.6, 024,981) and is based on direct compression technology which uses suitable excipients with improved properties, especially superdisintegrants that accelerate the rate of disintegration and hence dissolution.^[30] This technology is based on employment of conventional non-direct compression fillers (such as dextrose, mannitol, sorbitol etc.) in the form of fine particles that quickly dissolve without producing a gritty or sandy sensation in the mouth. The water soluble and sometimes effervescent agents can also be used that assist in the disintegration process. The DuraSolv technology is designed to provide stronger tablets without packaging precautions and can be packed in blisters. In this technology the tablet consists of drug materials, lubricants and fillers.^[29]

3) Orasolv Technology

CIMA LAB has developed Orasolv technology. Orasolv is an effervescent direct compression tablet that disperses in mouth's saliva with the aid of almost hardly noticeable effervescence and dissolves in less than one minute, leaving the coated drug powder. The unpleasant flavor of the drug is addressed by coating of the drug powder and effervescence. The major disadvantage of Orasolv is its mechanical strength due to light compression. In Flash dose technology the matrices are prepared by flash heat processing. This technique is patented by fuisz. E.g.

Nurofen is the first commercial product by this technology launched by Biovil Corporation.^[30]

4) Wow Technology

It is patented by Yamanouchi Pharmaceutical Corporation where wow tends for “without water”. In this process high mouldability saccharide like oligosaccharide, mannitol is mixed with low mouldability saccharide like glucose, lactose and mannitol to obtain rapidly melting strong tablet.^[31]

5) Shear Form Technology

The core of this technology is preparation of floss. Floss is prepared by subjecting feed stock containing sugar carrier to flash heat process. Sucrose plus either mannitol or dextrose is mixed with surfactant and blended well. This is the primary floss mixture. In flash heat process, the carrier materials show an internal flow condition, which is heat induced and exits via spinning head, and simultaneously under centrifugal force, the floss is flinged. The floss produced by the above way are longer fibers and are further chopped converting them into smaller particles via a high shear mixer granulator. Recrystallization is completed by use of ethanol treatment (1%), spraying out floss, which subsequent evaporation, which increases flow and cohesive properties. This recrystallized matrix is then mixed with drugs and other excipients and subjected to compression. Tablets produced by this process are highly porous, have a good mouth feel, and have an immediate solubilisation of sugar as it comes in contact with saliva.^[31]

6) Flash dose Technology

This technology is much like cotton candy, using a unique spinning mechanism to produce crystalline floss structure. The drug can then be incorporated into this crystalline sugar and compressed into a tablet. Such product has a high surface area for dissolution, dissolving rapidly on tongue and easy dispersion. The Flash dose tablets consist of self-binding shear form matrix termed as “floss”.^[33]

7) Ceform Technology

The crux of this process is placing a dry powder containing pure drug and excipients into a rapidly spinning machine. Centrifugal force of the rotating head of this ceform machine, through small heated opening at high speed blends dry drug powder. This drug blend is liquefied to form a sphere, owing to the microburst of heat attained by carefully controlled temperature. This does not affect the stability of the drug. In the preselected

oral dosage format the microspheres are blended and/or compressed.^[34]

8) Flashtab Technology

This technology aims to make the drug have rapid release in GIT, micro encapsulated drug with effervescence, and easily flash dispersal tablet. Usually the polymer used is Eudragit for rapid release. This technology uses conventional approach of wet/dry granulation follow by classical method of compression. Micro-granules of drug, taste masking agents, disintegrating agent, and swelling agents are used to formulate drugs.^[35] These tablets have good physical resistance, and highly suggested for hygroscopic materials for blister packing as materials like polyvinyl chloride/aluminum foils cater better moisture protection in comparison to conventional polyvinyl chloride or polypropylene foils.

9) Nanocrystal Technology

The technology enhances dissolution rate by decreasing particles size and increasing surface area. Nano-crystal particles are drug particles (less than 1000 nm in diameter), produced by milling the drug substance, and obtained via wt. milling technique. Nanocrystal fast dissolving technology provides, Wide range of doses per unit (up to 200 mg of API per unit), Based on proprietary and patent-protected technology elements products can be well classified. Enhanced Pharmacokinetics of oral drug. Utilization of non-moisture sensitive in actives, and is economic and Cost-effective. Combining drug Nano crystal colloidal dispersions and water-soluble GRAS (Generally Regarded as Safe) ingredients, then filled into blisters, and lyophilized product wafers are formed. They are highly robust; yet dissolve in very small quantities of water in seconds which is agreeable when working with highly potent or hazardous materials reducing operations, like granulation, blending, and tableting. This approach is also enables small quantity of drugs to be converted into fast dissolving tablets because manufacturing loss is negligible.^[36]

10) Advantol 200

Specially formulated for nutraceutical applications Advantol 200 is a directly compressible excipient system offering "Soft-Melt" functionality and it requires no special manufacturing equipment or tooling. To make robust “softmelt” tablets it requires standard rotary tablet press with standard tooling under normal tableting temperature and humidity conditions.

Evaluation parameters for FDTs.

Parameters	Criteria
Weight variation	Weight variation tests are carried out according to either USP, IP, BP.
Hardness	Hardness of the tablet should be lesser conventional tablet falling in the range of 3-4 kg/cm ²
Friability	Friability should be within the range of 0.1-0.9%
Mechanical Strength	Should possess adequate mechanical strength to absorb the transportation shock and avoid breakage of tablet

Tablet Porosity	Is conducted(as per ICH guideline)
Wetting time and Water absorption	Use of simulated saliva to check the wetting time of tablet as well as water absorption.
In-vitro Dispersion time	At optimum & fixed PH & temp,time taken for dispersion of tablet in media is determine
Disintegration Studies	The time period at which the tablet starts to disintegrate in given aq.media is determined.
Dissolution Studies	Dissolution studies carried out according to USP,IP,BP.
Stability Studies	Stability studies (including Accelerated stability studies) are conducted according to the ICH guidelines.
Content informality	According to either USP,IP,BP.

Fast dissolving marketed drugs

Sr.no	Brand name	Active agent	Category
1)	Alavert Quick dissolving tablet	Loratadine	Anti-histamine
2)	Benadry fast melt	Diphenhydramine	Anti-histamine
3)	Claritin Red tabs	Loratadine	Anti-histamine
4)	Flazaclo	Clozapine	Anti-psychiatric
5)	Feldene fast melt	Piroxicam	Anti-rheumatic
6)	Meloxicam 7.5&15 mg	Meloxicam	NSAIDs
7)	Mirtazapine quick dissolving tablet	Mirtazapine	Anti-depressant
8)	Nurofenmeltlets	Ibuprofen	NSAIDs
9)	Romilast	Montelukast	Anti-allergic

CONCLUSION

Fast dissolving tablets have better patient compliance and acceptance may improve biopharmaceutical properties, bioavailability compared with conventional oral dosage form. Fast dissolving tablets need to formulate for psychotic patients, bedridden, geriatric, pediatric patients. Larger number of drugs belonging to different categories can be easily formulated in fast dissolving tablet. In FDTs, not only single drug formulated but also combination of drugs can be formulated.

FDTs provide rapid onset of action, better patient's compliance and more advantages .FDTs also provide wide marketing also which makes the dosage form successful in the market. Many drugs will be formulated as fast dissolving tablets in future for its market potential.

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