



## Review Article

# Fast Dissolving Tablets as A Novel Boon: A Review

Ujjwal Nautiyal\*, Satinderjeet Singh, Ramandeep Singh, Gopal, Satinder Kakar

Department of Pharmacy, Himachal Institute of Pharmacy, Paonta Sahib (H.P), India.

\* **Corresponding author:** Nautiyal Ujjwal **Email:** [ujjwal\\_nautiyal@rediffmail.com](mailto:ujjwal_nautiyal@rediffmail.com)

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### ABSTRACT

Novel drug delivery system assists to achieve better patient compliance. Fast dissolving tablets are one of them. FDT have benefits such as accurate dosing, easy portability and manufacturing, good physical and chemical stability and an ideal alternative for pediatric and geriatric patients. FDDT formulation combines the advantage of both liquid and conventional tablet formulation while also offering advantage over both traditional dosage forms. This review gives a view of advantages, limitations, need for formulating FDTs, Formulation factors, excipients used, methodology and evaluation parameters.

**Keywords:** Melting, Fast dissolving tablets, evaluation

### INTRODUCTION

Recent advances in novel drug delivery system (NDDS) aim to enhance safety and toxicity of drug molecules by formulating a convenient dosage form for administration and to achieve better patient compliance. One such approach led to development of fast dissolving tablets.[1,2] Fast dissolving drug-delivery systems were first developed in the late 1970s as an alternative to conventional dosage forms for pediatric and geriatric patient. Traditional tablets and capsules administered with an 8-oz. glass of water may be inconvenient or impractical for some patients who experience difficulties in swallowing traditional oral solid-dosage forms. These tablets

are designed to dissolve or disintegrate rapidly in the saliva generally less than 60 seconds. Fast dissolving/disintegrating tablets (FDDTs) are a perfect fit for all of these patients. The FDT is also known as fast melting, fast dispersing, rapid dissolve, rapid melt, and or quick disintegrating tablet. All FDTs approved by the Food and Drug Administration (FDA) are classified as orally disintegrating tablets. Recently, the European Pharmacopoeia adopted the term "Orodispersible Tablet" as a tablet that is to be placed in oral cavity where it disperses rapidly before swallowing. The major advantage of FDDT formulation is that it combines the advantage of both liquid and conventional tablet formulation

while also offering advantage over both traditional dosage forms. It provides the convenience of a tablet formulation, while also allowing the ease of swallowing provided by a liquid formulation. FDDTs allow the luxury of much more accurate dosing than the primary alternative, oral liquids [3].

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 [4-6]. It is the duty of the health care provider to administer bitter drugs orally with acceptable level of palatability especially with pediatric and geriatric patients [7]. The most evident drawback of the commonly used oral dosage forms like tablets and capsules is swallowing, particularly in case of pediatric and geriatric patients [5]. To fulfill these medical needs, pharmaceutical technologists have developed a novel oral dosage forms known as orally disintegrating tablets (ODTs) or Fast disintegrating tablets (FDTs) or mouth melting tablets(MMTs) or mouth dissolving tablets(MDTs) which disintegrate rapidly in saliva, usually in a matter of seconds, without the need to take water. Drug dissolution and absorption as well as onset of clinical effect and drug bioavailability may be significantly greater than those observed from conventional dosage forms.[8,9] When such tablets are placed in oral cavity, saliva quickly penetrates into the pores to cause rapid tablet disintegration [10]. 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 superdisintegrants like croscarmellose sodium, sodium starch glycolate and crosspovidone. Another method is maximizing pore structure of the tablets by freeze drying and vacuum drying. The bioavailability of some drugs may be increased due to absorption of drugs in oral

cavity and also due to pregastric absorption of saliva containing dispersed drugs that pass down into the stomach. Moreover the amount of drug that is subjected to first pass metabolism is reduced as compared to standard tablets [11, 12].

Drug delivery systems (DDS) are a strategic tool for expanding markets, extending product life cycles and generating opportunities. Oral administration is the most popular route for systemic effects due to its ease of ingestion, pain avoidance, versatility and most importantly, patient compliance. Also solid oral delivery systems do not require sterile conditions and are therefore, less expensive to manufacture. Patient compliance, high-precision dosing, and manufacturing efficiency make tablets the solid dosage form of choice. Excipients and equipments choices will be significantly affected should solid dosage form technologies change in response to the unprecedented shifts in the drug discovery such as genomics. Injections generally are not favored for use by patients unless facilitated by sophisticated auto injectors. Inhalation is one good alternative system to deliver these drugs, but the increased research into biopharmaceuticals so far has generate predominantly chemical entities with low molecular weights. The development of enhanced oral protein delivery technology by Fast dissolving Tablets which may release these drugs in the mouth are very promising for the delivery of high molecular weight protein and peptide . The oral route remains the perfect route for the administration of therapeutic agents because the low cost of therapy, manufacturing and ease of administration lead to high levels of patient compliance [13-20].

#### **ADVANTAGES OF FDTs**

- Ease of administration to geriatric, pediatric, mentally disabled, and bed-ridden patients, who have difficulty in swallowing the tablet.

- The FDTs do not need water for swallowing unlike conventional dosage forms. This is very convenient for patients who are travelling or do not have immediate access to water, and thus, provide improved patient compliance.
  - Being unit solid dosage forms, provide luxury of accurate dosing, easy portability and manufacturing, good physical and chemical stability and an ideal alternative for pediatric and geriatric patients.
  - Bioavailability of drugs is enhanced due to absorption from mouth, pharynx, and oesophagus.
  - Pre-gastric absorption can result in improved bioavailability and because of reduced dosage, improved clinical performance through a reduction of unwanted effects.
  - Rapid onset of therapeutic action as tablet is disintegrated rapidly along with quick dissolution and absorption in oral cavity.
  - Good mouth feels, especially for pediatric patients as taste-masking technique is used to avoid the bitter taste of drugs.
  - Minimum risk of suffocation in airways due to physical obstruction, when ODTs are swallowed, thus they provide improved safety and compliance with their administrations.
  - Rapid drug therapy intervention is possible.
  - Conventional processing and packaging equipments allow the manufacturing of tablets at low cost.
  - No specific packaging is required. It can be packaged in push through blisters.
  - Provide new business opportunities in the form of product differentiation, patent-life extension, uniqueness, line extension, and life-cycle management, and exclusivity of product promotion [21, 22].
- Patients who concurrently take anti-cholinergic medications may not be the best candidates for FDTs.
  - Tablets usually have insufficient mechanical strength. Hence, it requires careful packaging and handling.
  - Tablets may leave unpleasant taste and/or grittiness in mouth if not formulated properly.
  - They are more susceptible to degradation by humidity and temperature.[23]
  - Fast dissolving tablet is hygroscopic in nature so must be kept in dry place.
  - Some time it possesses mouth feeling.
  - MDT requires special packaging for proper stabilization & safety of stable product.[24]
  - Drugs difficult to formulate into FDT with relatively larger doses.
  - Drugs with short half-life and frequent dosing and those whom require controlled or sustained release are unsuitable candidates of FDTs [25,26].

### THE NEED FOR DEVELOPMENT OF FAST DISINTEGRATING TABLETS [27]

**Patient factors:** Fast disintegrating dosage forms are particularly suitable for patients, who for one reason or the other; find it inconvenient to swallow traditional tablets and capsules with an 8-oz glass of water. These include the following: Geriatric patients mainly suffering from conditions like hand tremors and dysphasia. Pediatric patients who are unable to swallow easily because their central nervous system and internal muscles are not developed completely. Traveling patients suffering from motion sickness and diarrhea that do not have easy access to water.

**Effectiveness factor:** Increased bioavailability and faster onset of action are a major claim of these formulations. Dispersion in saliva in oral cavity causes pre-gastric absorption from some

### LIMITATIONS TO FDT

- Drugs with relatively large doses are difficult to formulate into FDTs.

formulate ions in those cases where drug dissolves quickly. Buccal, pharyngeal and gastric regions are all areas of absorption for many drugs. Any pre-gastric absorption avoids first pass metabolism and can be a great advantage in drugs that undergo hepatic metabolism. Furthermore, safety profiles may be improved for drugs that produce significant amounts of toxic metabolites mediated by first-pass liver metabolism and gastric metabolism, and for drugs that have a substantial fraction of absorption in the oral cavity and pre-gastric segments of GIT.

## FORMULATION

### CHALLENGES IN FORMULATION OF FAST DISSOLVING TABLETS (FDTs)

#### ➤ **Mechanical strength and disintegration time:**

It is obvious that increasing the mechanical strength will delay the disintegration time. So a good compromise between these two parameters is always essential. FDTs are formulated to obtain disintegration time usually less than a minute. While doing so, maintaining a good mechanical strength is a prime challenge [28].

➤ **Taste masking:** 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 [29,30].

➤ **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. Such collapse

sometimes can be prevented by using various matrix-forming excipients such as mannitol than can induce crystallinity and hence, impart rigidity to the amorphous composite [31,32].

➤ **Hygroscopicity:** Hygroscopicity is, of course, an important characteristic of a powder. It can be shown, roughly, for a fairly soluble compound that the hygroscopicity is related to its solubility. FDTs should have low sensitivity to humidity. This problem can be especially challenging because many highly water-soluble excipients are used in formulation to enhance fast-dissolving properties as well as to create good mouth feel. Those highly water-soluble excipients are susceptible to moisture; some will even deliquesce at high humidity. A good package design or other strategy should be created to protect FDTs from various environmental conditions [33-35].

➤ **Amount of drug:** The application of technologies used for FDTs 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 [36].

➤ **Size of tablet:** It has been reported that the easiest size of tablet to swallow is 7-8 mm while the easiest size to handle was larger than 8 mm. Therefore, the tablet size that is both easy to take and easy to handle is difficult to achieve [37].

➤ **Mouth feel:** FDTs should not disintegrate into larger particles in the oral cavity. The particles generated after disintegration of the FDTs should be as small as possible. Moreover addition of flavours and cooling agents like menthol improve the mouth feel [38].

➤ **Sensitivity to environmental conditions:** FDTs should exhibit low sensitivity to environmental conditions such as humidity and temperature as

most of the materials used in FDTs are meant to dissolve in minimum quantity of water [38].

### CRITERIA FOR EXCIPIENT USED IN FORMULATION OF FDTs

- It must be able to disintegrate quickly.
- Their individual properties should not affect the ODTs.
- It should not have any interaction with drug and other excipients.
- It should not interfere in the efficacy and organoleptic properties of the product.
- When selecting binder (a single or combination of binders) care must be taken in the final integrity and stability of the product.
- The melting point of the excipients used should be in the range of 30-35°C.
- The binder may be in liquid, semi solid, solid or polymeric in nature [39-41].

### EXCIPIENTS USED IN FDT'S PREPARATION

Excipients used in FDTs contain at least one superdisintegrant, a diluent, a lubricant and optionally a swelling agent, a permeabilizing agent, sweeteners and flavourings.

**Table 1 Name and weight percentage of various excipients [42]**

Name of the Excipients	% used
Superdisintegrants	1-15%
Binders	5-10%
Antistatic agent	0-10%
Diluents	0-85%

### SUPER DISINTEGRANTS

As day's passes, demand for faster disintegrating formulation is increased. So, pharmacist needs to formulate disintegrants i.e. Superdisintegrants which are effective at low concentration and have greater disintegrating efficiency and they are more effective intragranularly. This superdisintegrants act by swelling and due to swelling pressure exerted in the outer direction or radial direction, it causes tablet to burst or the accelerated absorption of water leading to an enormous increase in the volume of granules to promote disintegration [43-45].

### FACTORS TO BE CONSIDERED FOR SELECTION OF SUPERDISINTEGRANTS

- **Disintegration:** The disintegrant must quickly wick saliva into the tablet to generate the volume expansion and hydrostatic pressure necessary to provide rapid disintegration in the mouth.
- **Compactibility:** It is desirable to have ODT with acceptable hardness and less friability at a given compression force to produce robust tablets that avoid the need to use specialized packaging while maximizing production speed.
- **Mouth feel:** Large particles can result in a gritty feeling in mouth. Thus, small particles are preferred. If the tablet forms a gel-like consistency on contact with water, However, it produces a gummy texture that many consumer find objectionable.
- **Flow:** In typical tablet formulation, superdisintegrants are used at 2-5 wt % of the tablet formulation. With ODT formulation, disintegrant level can be significantly higher [46].

**Table 2. List of Superdisintegrants [47]**

Superdisintegrants	Example	Mechanism Of Action	Special comment
Crosscarmellose® Ac-Di-Sol® Nymce ZSX® Primellose® Solutab® Vivasol® L-HPC	Crosslinked cellulose	-Swells 4-8 folds in < 10 seconds. -Swelling and Wicking both.	-Swells in two dimensions. -Direct compression or granulation -Starch free
Crosspovidone Crosspovidon M® Kollidon® Polyplasdone®	Crosslinked 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®	Crosslinked alginic acid	-Rapid swelling in aqueous medium or wicking action	-Promote disintegration in both dry or wet granulation
Soy polysaccharides Emcosoy®	Natural super disintegrant		-Does not contain any starch or sugar. Used in nutritional Products
Calcium silicate		-Wicking Action	Highly porous, Optimum concentration is b/ 20-40%

### BULKING MATERIALS

Bulking materials are significant in the formulation of fast-dissolving tablets. The material contributes functions of a diluents, filler and cost reducer. Bulking agents improve the textural characteristics that in turn enhance the disintegration in the mouth, besides adding bulk also reduces the concentration of the active in the composition. The recommended bulking

agents for this delivery system should be more sugar-based such as mannitol, polydextrose, lactitol, DCL (direct compressible lactose) and starch hydrolystate for higher aqueous solubility and good sensory perception. Mannitol in particular has high aqueous solubility and good sensory perception. Bulking agents are added in the range of 10 percent to about 90 percent by weight of the final composition.

## LUBRICANTS

Though not essential excipients can further assist in making these tablets more palatable after they disintegrate in the mouth. Lubricants remove grittiness and assist in the drug transport mechanism from the mouth down into the stomach.

## TASTE MASKING

The materials for taste-masking purpose have often been classified depending upon the basic taste. Flavoring and perfuming agents can be obtained from either natural or synthetic sources. Natural products include fruit juices, aromatic oils such as peppermint and lemon oils, herbs, spices, and distilled fractions of these. They are available as concentrated extracts, alcoholic or aqueous solutions, syrups, or spirit. Apart from these conventional materials, many compositions have been found to show effective taste-masking abilities with improved flavor such as alkaline earth oxide, alkaline earth hydroxide, or an alkaline hydroxide. Another composition includes phosphorylated amino acid such as phosphotyrosine, phosphoserine, and phosphothreonine and mixtures thereof. Anethole effectively masked bitter taste as well as the aftertaste of zinc, which is used in treating the common cold. Clove oil and calcium carbonate, which has been found to be particularly useful to mask the unpalatable active in formulations which are intended to be chewed or dissolve in mouth prior to ingestion in solution [48-53].

## EMULSIFYING AGENT

Emulsifying agents are important excipients for formulating fast-melting tablets they aid in rapid disintegration and drug release without chewing, swallowing or drinking water. In addition, incorporating emulsifying agents is useful in stabilizing the immiscible blends and enhancing

bioavailability. A wide range of emulsifiers is recommended for fast dissolving tablet formulation, including alkyl sulfates, propylene glycol esters, lecithin, sucrose esters and others. These agents can be incorporated in the range of 0.05 percent to about 15 percent by weight of the final composition [54].

## METHODOLOGY

### TECHNIQUES FOR PREPARING FAST DISSOLVING TABLETS:

#### Conventional Technologies

**Freeze Drying/Lyophilization [55]:** A process, in which water is sublimated from the product after freezing, is called freeze drying. Freeze-dried forms offer more rapid dissolution than other available solid products. The lyophilization process imparts glossy amorphous structure to the bulking agent and sometimes to the drug, thereby enhancing the dissolution characteristics of the formulation.

**Tablet Molding:** Compression molding is a process in which tablets are prepared from soluble ingredients such as sugars by compressing a powder mixture previously moistened with solvent (usually ethanol or water) into mold plates to form a wetted mass. The advantages of molded tablet are that these tablets disintegrate more rapidly and offer improved taste as these tablets are made from water-soluble sugars. Dispersion matrix is made from water-soluble sugars; molded tablets disintegrate more rapidly and offer improved taste. These properties are enhanced when tablets with porous structures are produced or when components that are physically modified by the molding process are used. In comparison with lyophilization process, tablets produced by molding technique are easier to adapt to the industrial scale. The lyophilization and molding techniques produce RDT which disintegrate within about 30 seconds, but that have low physical resistance and high friability. On the

other hand, tablets obtained by direct compression are less friable but disintegrate in a longer time [56, 57].

**Direct Compression Method:** Direct compression represents the simplest and most effective tablet manufacturing technique.

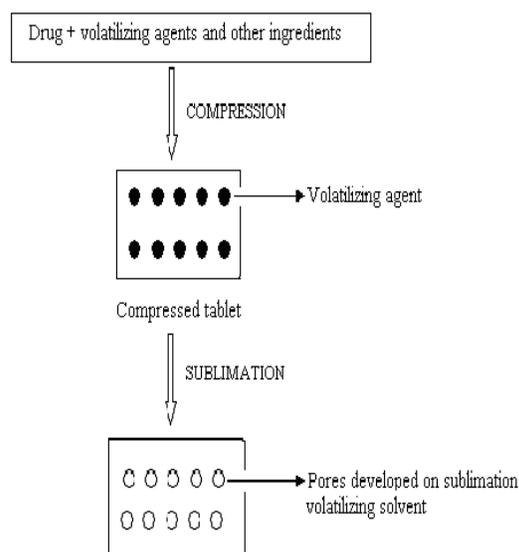
FDT can be prepared by using this technique because of the availability of improved excipients especially superdisintegrants and sugar based excipients.

**(a) Superdisintegrants:** Tablet disintegration time can be optimized by concentrating the disintegrants. Below critical concentration tablet disintegration time is inversely proportional to disintegrants concentration. Above the critical concentration level, however, disintegration time remains approximately constant or even increases. Microcrystalline cellulose, cross linked carboxymethyl cellulose sodium, cross linked polyvinyl pyrrolidone and partially substituted hydroxypropyl cellulose, though water insoluble, absorbs water and swells due to capillary action and are considered as effective disintegrants in the preparation of fast dissolving tablets. Fast disintegration of tablets can also be achieved by incorporating effervescent disintegrating agents, which generates carbon dioxide. This phenomenon also resulted in partial taste masking of unacceptable taste of the drug. The major drawback of effervescent excipients is their hygroscopicity. Hence their manufacture requires control of humidity conditions and protection of the final product. This is reflected by the overall cost of the product[58].

**(b) Sugar based excipients:-**This is another approach to manufacture FDT by direct compression. The use of sugar based excipients especially bulking agents like dextrose, fructose, isomalt, lactitol, maltitol, sorbitol, starch hydrolysate, polydextrose and xylitol which display high aqueous solubility and sweetness and hence impart taste masking property and a pleasing mouth feel [59-61].

**Spray Drying:** Spray drying was used for the preparation of the microspheres. Spray drying is widely used in pharmaceutical processing because it requires only a one-step process and can be easily controlled and scaled up. Spray drying is widely used in pharmaceutical and biochemical fields and the final particle size is controlled by a number of factors including the size of the nozzle used in the processing [62-65].

**Sublimation:** Sublimation has been used to produce FDTs with high porosity. A porous matrix is formed by compressing the volatile ingredients along with other excipients into tablets, which are finally subjected to a process of sublimation. Inert solid ingredients with high volatility (e.g., ammonium bicarbonate, ammonium carbonate, benzoic acid, camphor, hexamethylene-tetramine, naphthalene, phthalic anhydride, urea and urethane) have been used for this purpose.[66] Solvents such as cyclohexane and benzene were also suggested for generating the porosity in the matrix.



**Phase Transition Process:** It is concluded that a combination of low and high melting point sugar alcohols, as well as a phase transition in the manufacturing process, are important for making FDTs without any special apparatus. FDT were

produced by compressing powder containing erythritol (melting point: 122 degC) and xylitol (melting point: 93 95 degC), and then heating at about 93 degC for 15 min. After heating, the median pore size of the tablets was increased and tablet hardness was also increased. The increase of tablet hardness with heating and storage did not depend on the crystal state of the lower melting point sugar alcohol [67].

**Melt Extrusion Method:** The drug/carrier mix is typically processed with a twin-screw extruder. The drug/carrier mix is simultaneously melted, homogenized and then extruded and shaped as tablets, granules, pellets, sheets, sticks or powder. The intermediates can then be further processed into conventional tablets. An important advantage of the hot melt extrusion method is that the drug/carrier mix is only subjected to an elevated temperature for about 1 min, which enables drugs that are somewhat thermo labile to be processed [68].

**Melt Granulation:** Melt granulation technique is a process by which pharmaceutical powders are efficiently agglomerated by a meltable binder. The advantage of this technique compared to a conventional granulation is that no water or organic solvents is needed. Because there is no drying step, the process is less time consuming and uses less energy than wet granulation. It is a useful technique to enhance the dissolution rate of poorly water-soluble drugs, such as griseofulvin [69].

**Nanonozation:** A recently developed Nano melt technology involves reduction in the particle size of drug to nano size by milling the drug using a proprietary wet-milling technique. The nano crystals of the drug are stabilized against agglomeration by surface adsorption on selected stabilizers, which are then incorporated into FDTs. This technique is especially advantageous for poor water soluble drugs. Other advantages

of this technology include fast disintegration/dissolution of nano particles leading to increased absorption and hence higher bioavailability and reduction in dose, cost effective manufacturing process, conventional packaging, due to exceptional durability and wide range of doses (up to 200 mg of drug per unit) [70].

**Cotton Candy Process:** This process is so named as it utilizes a unique spinning mechanism to produce floss-like crystalline structure, which mimic cotton candy. Cotton candy process involves formation of matrix of polysaccharides or saccharides by simultaneous action of flash melting and spinning. The matrix formed is partially recrystallized to have improved flow properties and compressibility. This candy floss matrix is then milled and blended with active ingredients and excipients and subsequently compressed to FDT. This process can accommodate larger drug doses and offers improved mechanical strength. However, high-process temperature limits the use of this process [71].

## PATENTED TECHNOLOGIES

**Zydis Technology:** Zydis technology is the first mouth dissolving dosage form in the market. It is a unique freeze dried tablet in which the active drug is incorporated in a water soluble matrix, which is then transformed in to blister pockets and freeze dried to remove water by sublimation. 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. Polymers such as gelatin, dextran or alginates are added to impart strength during handling. These form a glossy and amorphous structure. Mannitol or sorbitol is added to impart

crystallinity, elegance and hardness. Water is used as a medium to ensure the formation of a porous dosage form. Collapse protectants like glycine may be used to prevent shrinkage of dosage form during freeze drying and long term storage [72, 73].

**Orasolv Technology (Cima Labs):** This includes use of effervescent disintegrating agents compressed with low pressure to produce the FDTs. This evolution of carbon dioxide from the tablet produces fizzing sensations, which is a positive organoleptic property. Concentration of effervescent mixture usually employed is 20-25% of tablet weight. As tablets are prepared at low compression force, they are soft and fragile in nature. This initiated to develop pakslov, a special packing to protect tablets from breaking during storage of transport. Paksolv is a dome-shaped blister package, which prevents vertical movement of tablet within the depression. Paksolv offers moisture, light and child resistance packing [74].

**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. These can be packaged into conventional packaging system like blisters. Durasolv is an appropriate technology for products requiring low amounts of active ingredients [75, 76].

**Wowtab Technology:** Yamanauchi pharmaceutical company patented this technology. 'wow' means 'without water'. The active ingredients may constitute upto 50% w/w of the tablet. In this technique, saccharides of both low and high mouldability are used to prepare the granules. Mouldability is the capacity of a compound to be compressed. Highly mouldable substance has high compressibility

and thus shows slow dissolution. The combination of high and low mouldability is used to produce tablets of adequate hardness. Active ingredients are mixed with low mouldability saccharides and then granulated with high mouldability saccharides and then compressed into tablet. The Wowtab product dissolves quickly in 15 s or less. Wowtab product can be packed in both into conventional bottle and blister packs [77].

**Flashtab Technology (Ethypfarm France):** This technology includes granulation of recipients by wet or dry granulation method and followed by compressing into tablets. Excipients used in this technology are of two types. Disintegrating agents include reticulated polyvinylpyrrolidone or carboxy methylcellulose. Swelling agents include carboxy methylcellulose, starch, modified starch, microcrystalline cellulose, carboxy methylated starch, etc. These tablets have satisfactory physical resistance. Disintegration time is within 1 min [78, 79].

**Oraquick Technology:** The Oraquick fast dissolving/disintegrating tablet formulation utilizes a patented taste masking technology. KV Pharmaceutical claims its micro sphere 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, psychotropic, and anti-infective [80].

**Nanocrystal Technology:** For fast disintegrating tablets, Elan's proprietary Nano crystal 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 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.

Nano Crystal Fast dissolving technology provides for:

- Pharmacokinetic benefits of orally administered nano particles (<2 microns) in the form of a rapidly disintegrating tablet matrix.
- Product differentiation based upon a combination of proprietary & patent-protected technology elements.
- Cost-effective manufacturing processes that utilize conventional, scalable unit operations.
- Exceptional durability, enabling use of conventional packaging equipment & formats (bottles &/or blisters).
- Wide range of doses (up to 200mg of API per unit).
- Use of conventional, compendial inactive components.
- Employment of non-moisture sensitive inactives [81, 82].

**Quicksolv:** In Quicksolv porous solid dosage forms are obtained by freezing an aqueous dispersion/solution of the drug-containing matrix and then drying it by removing the water using excess of alcohol by solvent extraction. The final form disintegrates very rapidly, but is limited to

low drug content and can be used only for those drugs that are insoluble in the extraction solvent. The ideal drug characteristics required for this technology are relative low aqueous solubility, fine particle size <50  $\mu\text{m}$ , and good aqueous stability in the suspension [83, 84].

**Frosta Technology (Akina):** It utilizes the concept of formulating plastic granules and compressing 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 usually mixing the porous plastic material with water penetration enhancer and followed by granulating with binder. The tablets obtained have excellent hardness and rapid disintegration time ranging from 15 to 30s depending on size of tablet 30. filler reduces porosity of tablets due to which disintegration is lowered [85].

**Dispersible Tablet Technology:**

Lek in Yugoslavia was issued patents for dispersible tablets of dihydroergotoxine and cimetidine, which were claimed to disintegrate in less than 1 minute when in contact with water at room temperature. Dihydroergotoxine is poorly soluble in water in the free base form. An improved dissolution rate of dihydroergotoxine methanesulphonate was observed with dispersible tablets containing 0.8-10%, preferably about 4% by weight, of an organic acids. One of the essential excipients in the cimetidine formulate ion was 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 [86, 87].

**Pharmaburst Technology (Spi Pharma, New Castle):** It utilizes the co processed recipients to develop FDTs, which dissolves within 30-40s. This technology involves dry blending of drug, flavour, and lubricant followed by compression into tablets. Tablets obtained have sufficient strength so they can be packed in blister packs and bottles [88].

**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 [89-91].

**Lyo (Pharmalyoc):** Oil in water emulsion is prepared and placed directly into blister cavities followed by freeze-drying. Nonhomogeneity during freeze-drying is avoided by incorporating inert filler to increase the viscosity finally the sedimentation. High proportion of filler reduces porosity of tablets due to which disintegration is lowered [92].

**Sheaform Technology:** The technology is based on the preparation of floss that is also known as, Sheaform 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. The floss so produced is amorphous in nature so it is further chopped and recrystallised by various techniques

to provide aciform flow properties and this facilitate blending the re-crystallised matrix is then blended with other tablet excipients and an active ingredient. The resulting mixture is compressed into tablet [93].

**Ceform Technology:** In ceform technology microspheres containing active ingredient are prepared. The essence of ceform microsphere manufacturing process involves placing a dry powder, containing substantially pure drug material or a special blend of drug materials plus other pharmaceutical compounds, and excipients into a precision engineered and rapidly spinning machine. The centrifugal force of the rotating head of the ceform machine throws the dry drug blend at high speed through small heated openings. The microspheres are then blended and/or compressed into the pre-selected oral delivery dosage format. The ability to simultaneously process both drug and excipient generates a unique microenvironment in which materials can be incorporated into the microsphere that can alter the characteristics of the drug substance [94].

## EVALUATION

### PREFORMULATION STUDIES FAST DISSOLVING TABLET

**Angle of Repose:** The angle of repose was determined using funnel method. Funnel that can be fit vertically with stand at 6.3 cm. height. The opening end of funnel is closed with thumb until drug is poured. The 5 gm of powder was poured into funnel that can be raised vertically until a maximum cone height (h) was obtained. Radius of the heap (r) was measured and the angle of repose (q) was calculated using the formula [95, 96].

$$\tan \theta = h / r$$

$$\text{Therefore } \theta = \tan^{-1} h/r$$

Where  $\theta$  = Angle of repose

**Bulk Density (Db):** It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weight powder (passed through standard sieve # 20) into a measuring cylinder and initial weight was noted. This initial volume is called the bulk volume. From this the bulk density is calculated according to the formula mentioned below. It is expressed in g/ml and is given by

$$Db = M / Vb$$

Where, M is the mass of powder

Vb is the bulk volume of the powder.

**Tapped Density (Dt):** It is the ratio of total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder for 750 times and the tapped volume was noted if the difference between these two volumes is less than 2%. If it is more than 2%, tapping is continued for 1250 times and tapped volume was noted. Tapping was continued until the difference between successive volumes is less than 2 % (in a bulk density apparatus). It is expressed in g/ml and is given by

$$Dt = M / Vt$$

Where, M is the mass of powder

Vt is the tapped volume of the powder.

**Carr's Index (Or) % Compressibility:** It indicates powder flow properties. It is expressed in percentage and is give (Table 3)

$$I = (Dt - Db) / Dt \times 100$$

Dt is the tapped density of the powder

Db is the bulk density of the powder.

**Table 3: Relationship between % compressibility and flow ability [97, 98]**

% Compressibility	Flow ability
5-10	Excellent
12-16	Good
18-21	Fair Passable
23-25	Poor
33-38	Very Poor
<40	Very Very Poor

**Hausner Ratio [99]:** Hausner ratio is an indirect index of ease of powder flow. It is calculated by the following formula

$$\text{Hausner ratio} = \tilde{n}t / \tilde{n}d$$

Where,  $\tilde{n}t$  = tapped density

$\tilde{n}d$  = bulk density.

Lower Hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25).

#### EVALUATION OF FAST DISSOLVING TABLETS BY WEIGHT VARIATION

20 tablets are selected randomly from the lot and weighted individually to check for weight variation. Weight variation specification as per I.P. [100]

**Table 4. Weight variation specification as per I.P [101, 102]**

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

**TABLET 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 or Pfizer hardness tester [103].

**Uniformity of Weight [104]:** I.P. procedure for uniformity of weight was followed, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of determining the drug content uniformity dropped in it. Time required for complete dispersion was determined.

**Table 5.**

Average weight of Tablets (mg)	Maximum percentage difference allowed
130 or less	10
130-324	7.5
More than 324	5

**Accelerated Stability Study [105]:** The Orally disintegrating tablets are packed in suitable packaging and stored under the following conditions for a period as prescribed by ICH guidelines for accelerated studies.

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

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

(iii)  $37 \pm 1^\circ\text{C}$  and Relative Humidity =  $75\% \pm 5\%$

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  $25^\circ\text{C}$ .

**Friability:** Friability test is performed to assess the effect of friction and shocks, which may often cause tablet to chip, cap or break. Roche friabilator was used for the Purpose. This device subjects a number of tablets to the combined effect of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm dropping the tablets at a distance of 6 inches with each revolution. Pre weighed sample of tablets was placed in the friabilator, which was then operated for 100 revolutions. Tablets were dusted and reweighed. Compressed tablets should not loose more than 1% of their weight [106].

$$F = \frac{\text{Wt initial} - \text{Wt final}}{\text{Wt initial}} \times 100$$

**Wetting Time [107]:** 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.

$$dl/dt = r \cos \theta / (4\eta l)$$

Where  $l$  is the length of penetration,  $r$  is the capillary radius,  $\theta$  is the surface tension,  $\eta$  is the liquid viscosity,  $t$  is the time, and  $q$  is the contact angle.

**Dissolution Test:** The development of dissolution methods for ODTs is comparable with 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 ODT. Other media such as 0.1N HCl and buffers (pH - 4.5 and 6.8) should be evaluated for ODT much in the same way as conventional tablets [108].

**Thickness Variation:** Ten tablets from each formulation were taken randomly and their thickness was measured with a digital screw gauge micrometer. The mean SD values were calculated [109].

**Disintegration Time:** The test was carried out on 6 tablets using the apparatus specified in I.P.-1996 distilled water at  $37^{\circ}\text{C} \pm 2^{\circ}\text{C}$  was used as a disintegration media and the time in second taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured in seconds 28.

**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 FDT 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 [110].

**In-Vitro Dispersion Time Test:** To determine dispersion time 10 ml measuring cylinder was taken in which 6 ml distilled water was added and tablet was dropped in it. Time required for complete dispersion was determined [111].

**Packaging:** The products obtained by lyophilization process including various technologies such as Quicksolv, Nanocrystal, Zydis, and Lyoc are porous in nature, have less physical resistance, sensitive to moisture, and may degrade at higher humidity conditions. For the above reasons products obtained require special packing. Zydis units are generally packed with peelable backing foil. Paksolv is a special packaging unit, which has a dome-shaped blister, which prevents vertical movement of tablet within the depression and protect tablets from breaking during storage and transport, which is used for Orasolv tablet. Some of the products obtained from Durasolv. WOW Tab, Pharmaburst oraquick, Zipllets, etc. technologies have sufficient mechanical strength to withstand transport and handling shock so they are generally packed in push through blisters or in bottles [112, 113].

**MARKETED PRODUCTS: [114]****Table 6:** Marketed product of MDTs

Brand name	Active ingredient	Application	Company
Claritin® RediTabs®	Loratadine	Antihistamine	Schering corporation
Feldene Melt®	Piroxicam	NSAIDs	Pfizer
Maxalt –MLT	Rizatriptan benzoate	Migrane	Merck
Pepeid® ODT	Femotidene	Anti-ulcer	Merck
Zyperxa®	Olazepine	Psychotropic	Eli Lilly
Zofran® ODT	Olandansetron	Antiemetic	Galaxo Smith kline
Resperdal® M-Tab™	Resperidone	Schizophrenia	Janssen
Zubrin™ (Pet drug)	Tepoxelin	Canine NSAIDs	Schering corporation
Zelapar™	Selegiline	Parkinsons disease	Elanl Amarin corporation
Klonopin® wafer	Clonazepam	Sedation	Roche
Childrens Dimetapp® ND	Loratadine	Allergy	Wyeth consumer Healthcare
Imodium Istant Melts	Loperamide HCL	Antidiarrheal	Janssen
Propulsid® Quicksolv®	Cisapride Monohydrate	Gastrointestinal prokinetic Agent	Janssen
Tempra Quicksolv®	Acetaminophen	Analgesic	Bristol-Mters squibb
Remeron® Soltab®	Mirtazapine	Anti-dipression	Organon Inc.
Triaminic® Softchews®	Various combination	Pediatic cold cough,Allergy	Novartis consumer Health
Zomig-ZMT® and Rapimelt®	Zolmitriptan	Anti-migraine AstraZeneca	AstraZeneca Alavert® Loratadine Allergy
DuraSolv® Alavert®	Loratadine	Allergy	Wyeth consumer Healthcare
NuLev®	Hyoscyamine sulfate	Anti-ulcer	Schwarz Pharma
Kemstro™	Baclofen	Anti-spastic Analgesic	Schwarz Pharma
Benadryl® Fastmelt®	Diphenhydramine Citrate	sinus pressure relief	Pfizer
Nasea OD	Ramosetoron HCl	Anti-emetic	Yamanouchi
Gaster D	Famotidine	Anti-ulcer	Yamanouchi
Excedrin® QuickTabs	Acetaminophen	Pain reliever	Bristol-Myers Squibb

**CONCLUSION**

FDT concept evolved to overcome some of the problems that existed in conventional solid dosage form i.e. difficulty in swallowing of tablet

in pediatric and geriatric patients. FDT may lead to improve efficacy, bioavailability, rapid onset of action, better patient compliance due to its quick absorption from mouth to GIT as the saliva

passes. In future FDT may be most acceptable and prescribed dosage form due to its quick action (within minute).

### CONFLICT OF INTEREST STATEMENT

We declare that we have no conflict of interest. The authors alone are responsible for the content and writing of the paper.

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