

FAST DISSOLVING TABLET- BENEVOLENCE FOR THE SOCIETY

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ABSTRACT

Fast dissolving tablets (FDT's) are becoming more trendy in geriatric patients as it provides better patient-compliance, fast-action, and moreover; easy to administer even without water. Even they have played an emerging role in pediatrics patients because of incomplete development of muscular and nervous system. FDT's are disintegrating or dissolve quickly in the saliva providing rapid onset of action. With the aid of superdisintegrants (excipients), the normal tablets/ capsules pharmacological-action has been enhanced; leading to what we say fast dissolving tablets. FDTs have advantages such as easy portability and manufacturing, accurate dosing, good chemical and physical stability and an ideal alternative for geriatric and pediatric patients. FDTs have disintegrated quickly, absorb faster so, *in vitro* drug release time improve and this property of drugs (dosage form) enhanced bioavailability. FDT formulations have the advantage of both conventional tablet formulation and liquid dosage form. There are several technologies that are conventional or patented based on spray drying, cotton candy process, sublimation, melt granulation, direct compression freeze drying/lyophilization, phase transition process, mass extrusion, etc. have been developed for manufacturing of FDTs. In this review contain brief information about FDTs including definition, advantages, needs or requirements of FDTs, salient features of FDTs, limitations, challenges to developing FDT, marketed formulations of fast dissolving tablets, etc.

Keywords - Fast dissolving tablets, FDTs, Superdisintegrants, Manufacturing factors, Patent technologies, marketed preparations etc.

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. Fast dissolving drug-delivery systems were first developed in the late 1970s as an alternative to conventional dosage forms for pediatric and geriatric patient. The tablet is the most widely used dosage form existing today because of its convenience in terms of self-administration, compactness and ease in manufacturing. However, geriatric, pediatric and mentally ill patients experiences difficulty in swallowing conventional tablets, which leads to poor patient compliance. To overcome these problems, scientists have developed innovative drug delivery system known as mouth dissolving/disintegrating tablets (MDTs). The Fast Dissolving tablets (FDTs) are also known as Orodispersible tablets, Orally Disintegrating tablets, Mouth Dissolving tablets, Porous tablets, Fast Disintegrating tablets, Quick Disintegrating tablets, Rapid Dissolving tablets, Quick Melt tablets and Rapid Melt tablets.

However, of all the above terms **United States Pharmacopoeia (USP)** approved these dosage forms as ODTs. United States Food and Drug Administration (FDA) defined ODTs as "A solid dosage form containing medicinal substances or active ingredients which disintegrates rapidly within a few seconds when placed up on tongue". The benefits of these dosage forms were highlighted by the adoption of the term, "Orodispersible Tablet", by the **European Pharmacopoeia** by which it completely described about a tablet that can be placed in the oral cavity where it dispersed fully by rapid rate before the process of swallowing.

Mouth dissolving tablets are formulated mainly by two techniques first use of super disintegrants like crosscarmellose sodium, sodium starch glycolate and crosspovidone. Another method is maximizing pore structure of the tablets by freeze drying and vacuum-drying. It results in the quick dissolution and rapid absorption by which it shows rapid onset of action. Then the drug candidates undergo pre-gastric absorption when formulated as RDTs and may show increased oral bioavailability. It mainly provide good stability, accurate dosing, easy manufacturing.¹⁻⁴

Hence, it has become important in the era of pharmaceutical industries to develop such dosage forms that not only involve ease administration of the tablet but also provide good bioavailability for the patients.

Criteria for Fast dissolving Drug Delivery System⁵⁻⁶:

- No Requirement of water for oral administration, yet dissolve / disperse/ disintegrate in mouth in the matter of seconds.
- Having a pleasing mouth feel.
- Have an acceptable taste masking property.
- Harder and less friable by nature.
- Leave minimal or no residue in the mouth after administration.
- Exhibit low sensitivity to the environmental conditions (temperature and humidity).
- Allow the manufacturing of tablet using conventional processing and packaging equipments⁴.

ADVANTAGES OF FDTS⁸⁻⁹

- 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.
- 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 lifecycle management, and exclusivity of product promotion.

Requirements of fast dissolving tablets¹⁰⁻¹³

Patient factors

Fast dissolving dosage forms are suitable for those patients (particularly pediatric and geriatric patients) who are not able to swallow traditional tablets and capsules with an 8-oz glass of water. These include the following:

- Patients who have difficulty in swallowing or chewing solid dosage forms.
- Patients in compliance due to fear of choking.
- Very elderly patients of depression who may not be able to swallow the solid dosage forms
- An eight-year-old patient with allergies desires a more convenient dosage form than antihistamine syrup.
- A middle-aged patient undergoing radiation therapy for breast cancer may be too nauseous to swallow her H₂-blocker.
- A schizophrenic patient who may try to hide a conventional tablet under his or her tongue to avoid their daily dose of an atypical antipsychotic.
- A patient with persistent nausea, who may be a journey, or has little or no access to water.

Effectiveness factor

Increased bioavailability and faster onset of action are the major claim of these formulations. Dispersion in saliva- in oral cavity causes pregastric absorption from some formulations in those cases where drug dissolves quickly. Buccal, pharyngeal and gastric regions are the 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.

Manufacturing and marketing factors

As a drug nears the end of its patent life, it is common for pharmaceutical manufacturers to develop a given drug entity in a new and improved dosage form. A new dosage form allows a manufacturer to extend market exclusivity, unique product differentiation and extend patent protection. For examples, Eisai Inc. launched Aricept FDT, a line extension of donepezil for Alzheimer's disease, in Japan in 2004 and in the U. S. in 2005 in response to a generic challenge filed in the U. S. by Ranbaxy.

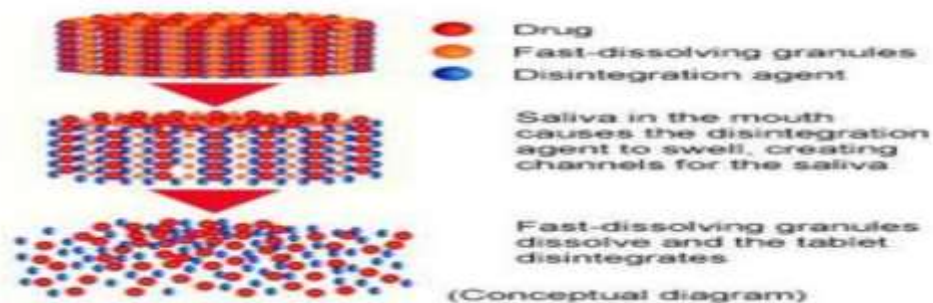


Fig 1 Conceptual diagram of FDTs

Conventional Techniques Used in the Preparation of Fast Dissolving Drug Delivery System¹⁴⁻¹⁷

1. Freeze Drying or Lyophilization:

Removal of solvent from a frozen suspension or solution of drug with structure-forming additives is known as lyophilization. It is a pharmaceutical technology where the drying of heat sensitive drugs and biological at low temperature under conditions that allow removal of water by sublimation. Figure 1 shows first of all; the material is frozen to bring it below its eutectic point. Then primary drying is carried out to reduce the moisture to around 4% w/w of dry product. Finally, secondary drying is done to reduce the bound moisture to the required volume. Due to lyophilization, bulking agent and sometimes drug acquire glossy amorphous structure and thus dissolution is enhanced

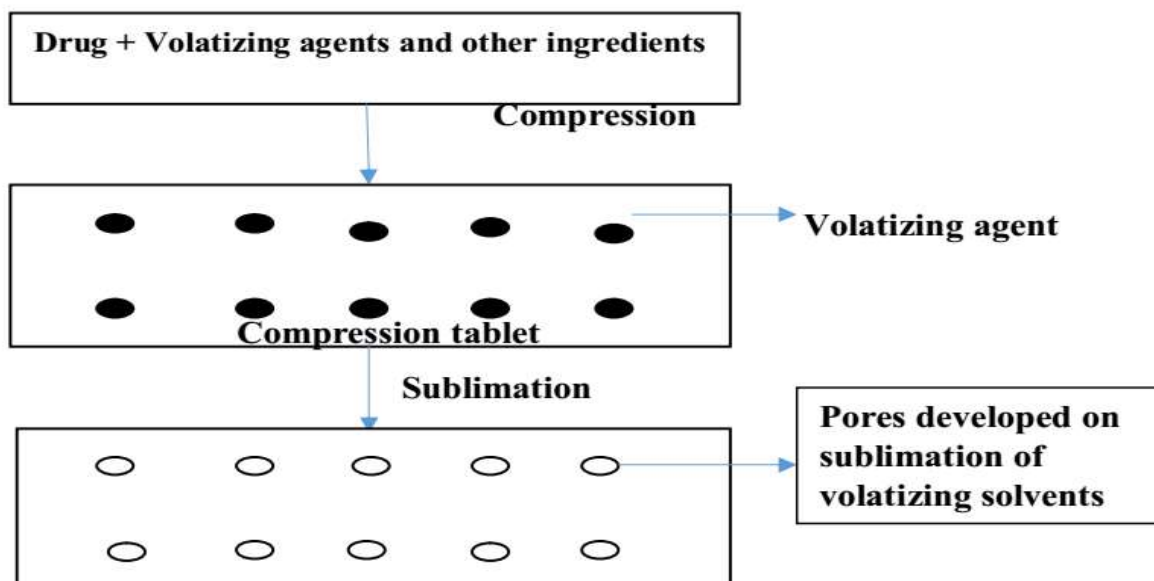
2. Spray Drying:

It is a process where highly porous fine powders are produced. The composition of a spray drying process contains a bulking agent such as mannitol and lactose, a disintegrating agent such as sodium starch glycollate and crosscarmellose sodium, an acidic ingredient such as citric acid, which when compressed shows faster disintegration and also enhanced dissolution.

3. Sublimation:

This process involves addition of some inert volatile substances like urea, urethane, naphthalene, ammonium carbonate, benzoic acid, phthalic anhydride, camphor, etc. to other excipients and the compression of blend into tablet. The volatile material is then removed which thus creates some pores in the structure of the tablet, due to which the tablets get easily dissolved when they come in contact with the saliva. Solvents such as cyclohexane, benzene, etc. can also be used as pore forming agents in the structure of the tablets. Fast dissolving tablets with highly porous structure and good mechanical strength could be developed by this method.

Fig 2 sublimation process



4. 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 re-crystallized 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 MDTs.

5. Mass Extrusion:

In this technique, a blend of active drug and other ingredients is softened using solvent mixture of water soluble polyethylene glycol, using methanol and then the softened mass is extruded through the extruder or syringe to get a cylinder of product, which is finally cut into even segments with the help of heated blades to get tablets.

6. Tablet Moulding:

In this process water soluble ingredients are used, so that tablet disintegrates and dissolve rapidly. Process of tablet moulding can be categorized into three types:-

- a. **Solvent method:** - Here the powder blend is moistened with a hydro alcoholic solvent followed by compression at low pressures in moulded plates to form a wetted mass (compression moulding). The solvent is then removed by air-drying. The tablets manufactured in this manner are less compact than compressed tablets and possess a porous structure that hastens dissolution.
- b. **Heat method:-** The heat moulding process involves preparation of a suspension that contains a drug, agar and sugar (e.g. mannitol or lactose) and pouring the suspension in the blister packaging wells, solidifying the agar at the room temperature to form a jelly and drying at 30°C under vacuum.
- c. **No vacuum lyophilisation:** - This process involves evaporation of solvent from a drug solution or suspension at a standard pressure.

7. Phase Transition Process:-

Tablets were produced by compressing a powder containing two sugar alcohols with high and low melting points and subsequent heating at a temperature between their melting points. Before heating process, the tablets do not have sufficient hardness because of low compatibility. The tablet hardness was increased after heating process, due to the increase of inter particle bonds or the bonding surface area in tablets induced by phase transition of lower melting point sugar alcohol.

8. Melt Granulation:

It is prepared by incorporating a hydrophilic waxy binder (super polystate) PEG-6-stearate. Super polystate is a waxy material with an m.pt. of 333°C and a hydrophilic- lipophilic balance of 9. It not only acts as a binder and increases the physical resistance of tablets, but also helps in the disintegration of tablets as it melts in the mouth and solubilizes rapidly leaving no residue. Super polystate was incorporated in the formulation of MDTs by melt granulation method where granules are formed by the molten form of this material.

9. **Direct compression methods:-** It is an easy way to formulate MDTs since limited number of processing steps are followed, involves low manufacturing cost and also accommodate high dose the final weight of tablet can easily exceed that of other production method.
10. **Effervescent Agents:** - Interaction between bicarbonate and carbonate with citric acid or tartaric acid causes disintegration of the tablet where carbon dioxide is released due to this interaction on wetting. The tablet disintegrates due to generation of pressure within the tablet. The effervescent blend is either added immediately prior to compression or can be added in to two separate fraction of formulation.

Formulation Excipients Used In FDTs ¹⁹⁻²²

All the excipients used in FDTs must be water soluble. Excipients used in the preparation of the conventional dosage forms are used. Some of the commonly used excipients are:-

- a. **Superdisintegrants:** - These are the agents which are added to the tablet formulation to enhance the breakup of the compacted mass when it is put into aqueous environment. Examples: Crosspovidone, crosscarmellose, sodium starch glycolate, gellan gum, xanthan gum, calcium silicate. Super disintegrants provide quick disintegration due to combined effect of swelling and water absorption by the formulation. Due to swelling of super disintegrants, the wetted surface of the carrier increases, this promotes the wettability and dispensability of the system, thus enhancing the disintegration and dissolution. It is essential to choose a suitable disintegrate, in an optimum concentration so as to ensure quick disintegration and high dissolution rate.

Table 1 List of superdisintegrants

S N	Super disintegrants	Nature	Mechanism of Action	Brand Names
1.	Crosscarmellose	Modified cellulose or Cross linked Cellulose	Wicking due to fibrous structure swelling with minimal gelling	Ac-Di-Sol Nymce 25 X Nymcel
2.	Crosspovidone	Cross linked PVP	Water wicking, swelling and possibly some deformation recovery	Kollidon Polyplasdone
3.	Aliginic acid NF	Cross linked Aliginic acid	Wicking action	Satialgine
4.	Sodium starch glycolate	Modified starch	Rapid and extensive swelling with minimal showing gelling	Explotab Primogel
5.	Sodium Alginate	Sodium salt of Alginic acid	Swelling	-
6.	Soy Polysaccharides	Natural disintegrant	-	EMCOSOY
7.	Calcium silicate	-	Wicking Action	-
8.	Ion exchange resin	Resins	-	Amberlite (IPR 88)

- b. **Sugar Based Excipients:** - Sugar based excipients are used for taste masking and as bulking agents. Most of the drugs are having unpleasant or bitter taste. And the basic requirement for designing FDTs is that the drug should not have disagreeable taste. Sorbitol, mannitol, xylitol, dextrose, fructose, etc. are mainly used. Aqueous solubility and sweetness impart a pleasing mouth feel and good taste masking.
- c. **Taste masking agents:** - These are the agents which are used to mask the bitter taste of the drugs. Example: Hydroxy propyl methyl cellulose, magnesium aluminium silicate, glyceryl monostearate, eudragit, microcrystalline cellulose, cyclodextrin, amberlite. Other than these flavoring and sweetening agents are also used as taste masking agents.

- d. **Flavouring agents:** - Flavoring agents are the substances which makes the product more palatable and pleasing feel for patients. These agents help in reducing the bitterness and obnoxious odour of drug substances. Examples: vanilla, citrus oils, fruit essences.
- e. **Emulsifying Agents:** - 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-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.

PATENTED TECHNOLOGIES ²⁴⁻²⁵

1. **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.
Orosolv 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 paksolv, 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.
2. **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.
3. **Wowtab Technology:** Yamauchi 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.
4. **Flashtab Technology (Ethypharm 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.
5. **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. 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.
6. **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).
7. **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.
 8. **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.
 9. **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.
 10. **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.
 11. **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.
 12. **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.
 13. **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
 14. **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.

EVALUATION

PREFORMULATION STUDIES FAST DISSOLVING TABLET

1. **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:-

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

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

Where θ = Angle of repose.

2. **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

V_b is the bulk volume of the powder.

3. 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

V_t is the tapped volume of the powder.

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

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

Where **Dt** is the tapped density of the powder

Db is the bulk density of the powder.

Table: 2

S.N.	% Compressibility	Flow Ability
1	5-10	Excellent
2	12-16	Good
3	18-21	Fair Passable
4	23-25	Poor
5	33-38	Very Poor
6	<40	Very Very Poor

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

$$= \frac{\bar{n}t}{\bar{n}d} \text{ Where, } \bar{n}t = \text{tapped density}$$

$$\bar{n}d = \text{bulk density.}$$

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.

S.N.	Average Weight of Tablet	% Deviation
1	80 mg or less	± 10
2	80 mg to 250 mg	± 7.5
3	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.

Uniformity of Weight: 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.

S.N.	Average Weight of Tablet	Maximum% Difference allowed
1	130 mg or less	10
2	130-324 mg	7.5
3	More than 324	5

Accelerated Stability Study: 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 = $75\% \pm 5\%$.

(ii) 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.

(iii) 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.

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:-

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

Wetting Time: 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.

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

Where l is the length of penetration, r is the capillary radius, θ is the surface tension, h is the liquid viscosity, t is the time, and θ 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.

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.

Disintegration Time: The test was carried out on 6 tablets using the apparatus specified in I.P.1996 distilled water at 37°C ± 2°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.

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.

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.

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.

Marketed Preparations

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®	Cisapride	Gastrointestinal prokinetic Agent	Janssen
Quicksovl®	Monohydrate		
Tempra Quicksovl®	Acetaminophen	Analgesic	Bristol-Mters squibb
Remeron® Soltab®	Mirtazapine	Anti-dipression	Organon Inc.
Triaminic® Softchews®	Various combination	Pediatric cold cough, Allergy	Novartis consumer Health
Zomig-ZMT® and Rapimelt®	Zolmitriptan	Anti-migraine	AstraZeneca Alavert®
DuraSolv® Alavert®	Loratadine	AstraZeneca 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

Now days there are wide range of products available commercially in market, which are produced by the same technologies as employed in the manufacturing of fast dissolving tablets. Still there is broad area for research on this technology. Some of the major challenges like formulating a drug of bitter taste and moisture absorbing nature create problems for formulation scientist. When the dose of drug is large, it creates problem of enhanced disintegration time. The two points to be considered in case of FDTs are shortening the disintegration time and at the same time keeping other parameters problems may be solved by using taste masking and super-disintegrating agents without significant increasing the weight and volume of final dosage forms. There is also a scope to develop better packaging system to formulate FDTs more stable during handling, in mind like friability, taste and mouth feel and tablet strength within the accepted range.

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