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FAST DISSOLVING DRUG DELIVERY SYSTEM - A REVIEW

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ABSTRACT

The new generation of Fast dissolving drug delivery system (FDDS) technologies brings valuable benefits to patients, life cycles and profits. Over recent years advancement in Fast dissolving drug delivery is widely expected to change the landscape of pharmaceutical industries for the foreseeable future. Fast dissolving drug delivery have become a significant priority worldwide. It may be possible to achieve rapid absorption of drugs and increased bioavailability, reduced toxicity, rapid onset of theuraptic action, improved delivery of poorly water-soluble drugs and also it is regarded as the most economical and safest method of drug delivery. This article includes requirement for fast dissolving drug delivery system, their advantages, disadvantages, formulation, various technologies, evaluation method, various marketed products and applications.

KEYWORDS

Fast dissolving drug delivery system, Superdisintegrants, Oral route and Methods.

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INTRODUCTION

Consumer satisfaction is the buzzword of the current millennium, and moment to achieve it has already begun in the pharmaceutical industry. An inability or un willingness to swallow solid oral dosage forms such as tablets and poor taste of medicine are some of the important reasons for consumer dissatisfaction[1]. Recent developments in technology have presented viable alternatives for the patients who may have difficulty in swallowing tablets or liquids. Traditional tablets and capsules administered with an 8-oz. glass of water may be inconvenient or impractical for some

patients. For example a very elderly patient may not be able to swallow a daily dose of tablets. An eight year old child with allergies could use a more convenient dosage form of antihistamine syrup. A schizophrenic patient in the institution setting can hide a conventional tablet under his or her tongue to avoid his/ her daily dose of atypical antipsychotic. A middle-aged women undergoing radiation therapy for breast cancer may be too nauseous to swallow her H_2-blocker[2].

To overcome these drawbacks, Fast Dissolving Tablets (FDT) or orally disintegrating tablets (ODT) has emerged as alternative oral dosage forms. These are novel types of tablets that disintegrate/dissolve/ disperse in saliva within few seconds. According to European Pharmacopoeia, the orally dispersible tablet should disperse/disintegrate in less than three minutes. The basic approach used in development of FDT is the use of super disintegrants like Crospovidone (Polyplasdone XL-10), Sodium starch glycolate (Primo gel, Explotab) and Pregelatinized starch (Starch-1500) etc. which provide instantaneous disintegration of tablet after putting on tongue, thereby releasing the drug in saliva. The bioavailability of some drugs may be increased due to absorption of drugs in oral cavity and also due to pre gastric 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[3].

Over the past three decades, FDT have gained much attention as a preferred alternative to conventional oral dosage forms such as tablets and capsules. FDT is a solid dosage form that disintegrates and dissolves in the mouth (either on or beneath the tongue or in the buccal cavity) without water within 60 seconds or less[4]. The US Food and Drug Administration Center for Drug Evaluation and Research (CDER) defines in the Orange Book an FDT as "A solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue. The European Pharmacopoeia however defines a similar term, that is fast dissolving tablet is a tablet that can be placed in the mouth where it disperses rapidly before swallowing[5].

These tablets are distinguished from conventional sublingual tablets, lozenges, and buccal tablets which require more than a minute to dissolve in the mouth. In the literature, FDT are also called orally disintegrating, orodisperse, mouth-dissolving, quick-dissolve, fast-melt, and rapid-disintegrating tablets and freeze-dried wafers. FDTs release drug in the mouth for absorption through local oro mucosal tissues and through pregastric (e.g., oral cavity, pharynx, and esophagus), gastric (i.e., stomach), and postgastric (e.g., small and large intestines) segments of the gastrointestinal tract (GIT). Conventional oral dosage forms refers to tablets and capsules that must be swallowed with water for dissolution, release, and absorption of the drug in the stomach and GIT distal sites.

Recent market studies indicate that more than half of the patient population prefers FDTs to other dosage forms and most consumers would ask their doctors for FDTs (70%), purchase FDTs (70%), or prefer FDTs to regular tablets or liquids (>80%). These responses may, in part, be attributed to know FDT advantages such as ease of administration, ease of swallowing, pleasant taste, and the availability of several flavors. FDTs also offer clinical advantages such as improved safety and in some cases, improved efficacy and other broader indications[6]. FDT products have been developed for numerous indications ranging from migraines (for which a rapid onset of action is important) to mental illness (for which patient compliance is important for treating chronic indications such as depression and schizophrenia.

Dozens of FDT products have been launched worldwide over the past decades. All through these products have the Common characteristic of quick disintegration and dissolution when placed in the mouth in the presence of saliva, their physical attributes vary. For example, several techniques for making compressed tablets (e.g., Dura Solv, CIMA Labs, Eden Prairie, MN; Ora Solv, CIMA Labs; and WOWTAB, Yamanouchi, Norman, OK) that are easy to handle and can be packaged in blister packs or bottles. In contrast, some lyophilization manufacturing processes (e.g., Zydis, Cardinal Health, and Dublin, OH) produce fragile freeze-dried tablets and compressed multi particle tablets that can be packaged only in unit-dose blisters because of their high friability.

The administration of FDTs may not inherently result in a faster therapeutic onset, but it can circumvent problems such as difficulty in swallowing traditional solid oral dosage forms, particularly by paediatric and geriatric patients. Since FDTS dissolve quickly, they cannot provide controlled or sustained release, except those that contain slow-dissolving, microparticulate-coated drugs, which quickly disperse and are swallowed[5]. Fast dissolve tablets are in demand now-days because of their ability to release the medicament in fraction of minutes. There are particularly useful for treatment of conditions like hypertension and arthritic pain for obvious reasons[7].

Many patients find in difficult to swallow tablets and hard gelatin capsules and thus do not comply with prescription, which results in high incidence of non-compliance and ineffective therapy[2]. The aim of novel drug delivery system (NDDS) is to enhance safety and efficacy of drug molecule by formulating a convenient dosage form for administration and to achieve better patient compliance; one such approach is "fast dissolving tablets"[8-11]. Fast dissolving tablets are gaining importance as a potential drug delivery system. This dosage form dissolves and disintegrates in the oral cavity within minutes without need of water or chewing. This formulation is useful in administration of drug in pediatric, geriatric patients and also in patients suffering from chemotherapy induced nausea and vomitting[12].

Most of the marketed fast dissolving tablets consists of non-steroidal anti-inflammatory drugs e.g. Rofecoxib, Ketoprofen and anti-hypertensive drugs e.g. Atenolol, Metoprolol, anti-emetic drugs e.g. Ondansetron, Granisetron. Disintegrants can help to facilitable drug dissolution and subsequently improvement in bioavailability. Though starch is a good disintegrant it has some problems e.g. high levels required in formulation lack of compressibility which weakens the tablet structure[12]. Therefore, the need of development of a new disintegrant arises which eliminates all disadvantages that starch has. A number of disintegrants, known super disintegrants like sodium starch glycolate (Explotab), crospovidone (Polyplasdone XL), pregelatinized starch(Starch 1500) markedly improve tablet disintegrantion by swelling and or capillary action, cause tablet to break into fragments[13]. The efficiency of these super disintegrants in any fast dissolving dosage forms depend on its selection, concentrations methods of incorporation and steps used for preparation[12].

Fast dissolving drug delivery is rapidly gaining acceptance as an important new drug delivery technology[14, 15]. Not all fast dissolving technologies actually dissolve; some use different disintegrants[16,9] and / or effervescent agents that cause the dosage form to disintegrate rapidly in the patients mouth within a minute and can be gulped easily without the need of water. Thus, it offers increase patients compliance and convenience. Patient convenience and compliance oriented research has resulted in bringing out many safer and newer drug delivery systems. Fast dissolving tablet is one such example with increased consumer choice, for the reason of rapid disintegration or dissolution self-administration even without water or chewing [17-19].

FAST DISSOLVING TABLETS

Definition

United States food and Drug Administration (FDA) defined Fast dissolving tablet (FDT) as "A solid dosage form containing medical substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue[20], prepared by direct compression method. "The disintegration time for FDTs generally ranges from several seconds to about a minute.

These are also known as melt-in-mouth tablets, repimelts, porous tablets, oro-dispersible, quick dissolving or rapid disintegrating tablets.

Advantages of fast dissolving drug delivery system[21]

1. Ease of administration to patients who refuse to swallow a tablet, such as paediatric and geriatric patients, mentally ill, disabled and uncooperative.
2. Convenience of administration and accurate dosing as compared to liquids.
3. No need of water to swallow the dosage from, which is highly convenient feature for patients who are traveling and do not have immediate access to water.
4. Good mouth feels property of FDTs helps to change the basic view of medication as "Bitter pill", particularly for paediatric patients.

5. Ability to prove advantages than solid dosage form.
6. Rapid dissolution of drug and absorption, which may produce rapid onset of action.
7. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach; in such cases bioavailability of drugs in increased.
8. Pregastric absorption can result in improved bioavailability and as a result of reduced dosage, improved clinical performance through a reduction of unwanted effects (Figure No.1).

Characteristics of fast dissolving drug delivery systems[23]

a. Ease of administration

FDT are easy to administer and handle hence, leads to better patient compliance. Usually, elderly people experience difficulty in swallowing the conventional dosage forms (Tablets and capsules) because of tremors of extremities and dysphagia. Fast dissolving delivery systems may offer a solution for these problems.

b. Taste of the medicament

Orodispersible delivery systems usually contain the medicament in taste-masked form. These delivery systems dissolve or disintegrate in patient's mouth, thus releasing the active ingredients which come in contact with the taste buds and hence, taste masking of the drugs becomes critical to patient compliance.

c. Mouth feel

Mouth feel is critical, and patients should receive a product that feels pleasant. Any large particles from the disintegrating tablet that are insoluble or slowly soluble in saliva would lead to an unpleasant gritty feeling. This can be overcome by keeping the majority of the particles below the detectable size limit. In some cases, certain flavors can imbibe an improved mouth feel perception, resulting in a product that is perceived as being less gritty, even if the only change is the flavor. Effervescence can be added to aid disintegration and improve mouth feel by reducing the "dryness" of a products (Table No.1).

Ingredients commonly used in Fast Dissolving Tablets (Table No.2)

Super disintegrants[24]

Use of disintegrants is the basic approach in development of FDTs. Disintegrants play a major role in the disintegration and dissolution of FDT. It is essential to choose a suitable disintegrant, in an optimum concentration so as to ensure quick disintegration and high dissolution rates.

Super disintegrants provide quick disintegration due to combined effect of swelling and water absorption by the formulation. Due to swelling of superdisintegrants, the wetted surface of the carrier increases, this promotes the wettability and dispersibility of the system, thus enhancing the disintegration and dissolution. The optimum concentration of the superdisintegrant can be selected according to critical concentration of disintegrant. Below this concentration, the tablet disintegration time is inversely proportional to the concentration of the superdisintegrant, whereas if concentration of superdisintegrant is above critical concentration, the disintegration time remains almost constant or even increases.

Sodium starch glycolate, Ac-di-sol (croscarmellose sodium), crospovidone, microcrystalline cellulose, pregelatinized starch are some of examples of super disintegrants.

Sugar based excipients[25]

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. So taste masking is necessary in most of the cases. Sorbitol, mannitol, xylitol, dextrose, fructose etc. are mainly used. Aqueous solubility and sweetness impart a pleasing mouth feel and good taste masking. But not all sugar-based materials have fast dissolution rate and good compressibility or compactability. However technologies are developed to make use of the sugar based excipients in the design of fast dissolving tablets other ingredients commonly used are water soluble diluents, lubricants, plasticizers, binders, colors are flavors.

Mechanism of action of superdisintegrants

(Figure No.2 and 3)[1, 22]

By capillary action

Disintegration by capillary action is always the first step. When the tablet is placed into suitable aqueous medium, the medium penetrates into the tablet and replaces the air adsorbed on the particles, which weakens the intermolecular bond and breaks the tablet

into fine particles. Water uptake by tablet depends upon hydrophilicity of the drug/excipient and on tableting conditions. For these types of disintegrants, maintenance of porous structure and low interfacial tension towards aqueous fluid is necessary which helps in disintegration by creating a hydrophilic network around the drug particles.

By swelling

Perhaps the most widely accepted general mechanism of action for tablet disintegration is swelling the tablets with high porosity, show poor disintegration due to lack of adequate swelling force. On the other hand, sufficient swelling force is exerted in the tablet with low porosity. It is worthwhile to note that if the packing fraction is very high, fluid is unable to penetrate in the tablet and disintegration is again slows down (Figure No.3).

By air expansion

When disintegrants with exothermic properties gets wetted, localized stress is generated due to capillary air expansion, which helps in disintegration of tablet. This explanation, however, is limited to only a few types of disintegrants and cannot describe the action of most modern disintegration agents.

Due to release of gases

Carbon dioxide released within tablets on wetting due to interaction between bicarbonate and carbonate with citric acid or tartaric acid. The tablet disintegrates due to generation of pressure within the tablet. This effervescent mixture is used when pharmacist needs to formulate very rapidly dissolving tablets or fast disintegrating tablet. As these disintegrants are highly sensitive to small changes in humidity level and temperature, strict control of environment is required during manufacturing of the tablets. The effervescent blend is either added immediately prior to compression or can be added onto two separate fraction of formulation[22].

By enzymatic reaction

Enzymes presents in the body also act as disintegrants. These enzymes destroy the binding action of binder and helps in disintegration. Actually due to swelling, pressure exerted in the outer direction or radial direction, it causes tablet to accelerate absorption of water leading to an enormous increase in the volume of granules to promote disintegration[26].

Due to particle repulsive forces

Another mechanism of disintegration attempts to explain the swelling of tablet made with non-swellable disintegrants. Guyot-Hermann has proposed a particle repulsion theory based on the observation that nonswelling particle also cause disintegration of tablets. The electric repulsive forces between particles are the mechanism of disintegration and water is required for it. Researchers found that repulsion is secondary to wicking[9] (Figure No.4).

Due to deformation

Hess had proved that during tablet compression, disintegrated particles get deformed and these deformed particles get into their normal structure when they come in contact with water. Occasionally, the swelling capacity of starch was improved when granules were extensively deformed during compression. This increase in size of the deformed particles produces a breakup of the tablet. This may be a mechanism of starch as a superdisintegrant (Figure No.4).

Criteria for Fast dissolving Drug Delivery System

An ideal FDT should possess the following properties[26, 27]

1. Not require water to swallow, but it should dissolve or disintegrate in the mouth in matter of seconds
2. Have a pleasing mouth feel
3. Have an acceptable taste masking property
4. Be harder and less friable
5. Leave minimal or no residue in mouth after administration
6. Exhibit low sensitivity to environmental conditions (temperature and humidity)
7. Allow the manufacture of tablet by using conventional processing and packaging equipments

Following conventional techniques are used for preparation of fast dissolving drug delivery system[28]

Disintegrant Addition

Disintegrant addition technique is one of the popular techniques for formulating Fast-dissolving tablets because of its easy implementation and cost effectiveness. The basic principle involved in formulating Fast-dissolving tablets by disintegrant addition technique is addition of super disintegrants in optimum concentration so as to achieve rapid disintegration along with the good mouth feel.

Freeze Drying

A process in which water is sublimated from the product after freezing. Lyophilization 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. Lyophilization results in preparations, which are highly porous, with a very high specific surface area, which dissolve rapidly and show improved absorption and bioavailability.

Moulding

In this method, molded tablets are prepared by using water-soluble ingredients so that the tablets dissolve completely and rapidly. The powder blend is moistened with a hydro-alcoholic solvent and is molded into tablets under pressure lower than that used in conventional tablet compression. The solvent is then removed by air-drying. Molded tablets are very less compact than compressed tablets. These possess porous structure that enhances dissolution.

Sublimation

The slow dissolution of the compressed tablet containing even highly water soluble ingredients may be due to the low porosity of the tablets. Inert solid ingredients that volatilize readily (e.g. urea, ammonium carbonate, ammonium bicarbonate, hexa methelene tetramine, camphor etc.) were added to the other tablet ingredients and the mixture is compressed into tablets. The volatile materials were then removed via sublimation, which generates porous structures. Additionally, several solvents (e.g. cyclohexane, benzene) can be also used as pore forming agents (Figure No.5).

Spray-Drying

Spray drying can produce highly porous and fine powder that dissolve rapidly. The formulations are incorporated by hydrolyzed and non-hydrolyzed gelatins as supporting agents, mannitol as bulking agent, sodium starch glycolate or croscarmellose sodium as disintegrating agent and an acidic material (e.g. citric acid) and / or alkali material (e.g. Sodium bicarbonate) to enhance disintegration and dissolution. Tablet compressed from the spray dried powder disintegrated within 20 seconds when immersed in an aqueous medium.

Mass- Extrusion

- Particles swell to precompression size and break up the matrix.
- Water is drawn into the pores and particles repel each other due to the resulting electrical force.

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 cut into even segments by using heated blade and to form tablets. The dried cylinder can also be subjected to coat the granules of bitter tasting drugs and thereby masking their bitter taste.

Direct Compression[29]

It is the easiest way to manufacture tablets. Conventional equipment, commonly available excipients and a limited number of processing steps are involved in direct compression. Also high doses can be accommodated and final weight of tablet can more easily be controlled than that of other production methods. Directly compressed tablet's disintegration and solubilization depends on single or combined action of disintegrants, water soluble excipients and effervescent agent. Disintegrant efficacy is strongly affected by tablet size and hardness, large and hard tablets have disintegration time more than that usually required. As consequences, products with optimal disintegration property often have medium to small size and/or high friability and low hardness. Breakage of tablet edges during handling and tablet rupture during the opening of blister alveolus, all results from insufficient physical strength.

Patented Technologies for Fast Disintegrating Tablets[30]

Each technology has a different mechanism, and each fast-dissolving/disintegrating dosage form varies regarding the following:

- Mechanical strength of final product
- Drug and dosage form stability
- Mouth feel
- Taste
- Rate of dissolution of drug formulation in saliva
- Swallow ability
- Rate of absorption from the saliva solution and
- Overall bioavailability.

Zydis Technology

Zydis, the best known of the fast-dissolving /disintegrating tablet preparations was the first marketed new technology tablet. The tablet dissolves in the mouth within seconds after placement on the tongue. A Zydis tablet is produced by lyophilizing or freeze-drying the drug in a matrix usually consisting of gelatin. The product is very lightweight and fragile, and must be dispensed in a special blister pack. Patients should be advised not to push the tablets through the foil film, but instead peel the film back to release the tablet. The Zydis product is made to dissolve on the tongue in 2 to 3 seconds. The Zydis formulation is also self-preserving because the final water concentration in the freeze-dried product is too low to allow for microbial growth[1].

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 packed into conventional packaging system like blisters. Durasolv is an appropriate technology for products requiring low amounts of active ingredients[2].

Orasolv Technology

Orasolv Technology has been developed by CIMA labs. In this system active medicament is taste masked. It also contains effervescent disintegrating agent. Tablets are made by direct compression technique at low compression force in order to minimize oral dissolution time. Conventional blenders and tablet machine is used to produce the tablets. The tablets produced are soft and friable and packaged in specially designed pack and place system[3].

Flash Dose Technology

Flash dose technology has been patented by Fuisz. Nurofen meltlet, a new form of ibuprofen as melt-in-mouth tablets, prepared using flash dose technology is the first commercial product launched by Biovail Corporation. Flash dose tablets consist of self-binding shear form matrix termed as "floss". Shear form matrices are prepared by flash heat process[24].

Wowtab Technology

Wowtab Technology is patented by Yamanouchi Pharmaceutical Co. WOW means "Without Water ". In this process, combination of low mouldability saccharides and high mouldability saccharides are used to obtain a rapidly melting strong tablet. The active ingredient is mixed with a low mouldability saccharide and granulated with a high mouldability saccharide and compressed into tablet[25].

Oraquick Technology[31]

The OraQuick fast-dissolving/disintegrating tablet formulation utilizes a patented taste masking technology. KV Pharmaceutical claims its microsphere technology, known as Micro Mask, has superior mouth feel over taste-masking alternatives[32]. The taste masking process does not utilize solvents of any kind, and therefore leads to faster and more efficient production. Also, lower heat of production than alternative fast-dissolving/disintegrating technologies makes OraQuick appropriate for heat-sensitive drugs. KV Pharmaceutical also claims that the matrix that surrounds and protects the drug powder in microencapsulated particles is more pliable, meaning tablets can be compressed to achieve significant mechanical strength without disrupting taste masking. OraQuick claims quick dissolution in a matter of seconds, with good taste-masking. There are no products using the OraQuick technology currently on the market, but KV Pharmaceutical has products in development such as analgesics, scheduled drugs, cough and cold, psychotropics, and anti-infectives.

Quick - Dis Technology[33]

Lavipharm Laboratories Inc. (Lavipharm) has invented an ideal intraoral fast-dissolving drug delivery system, which satisfies the unmet needs of the market. The novel intraoral drug delivery system, trademarked Quick-Dis™, is Lavipharm's proprietary patented technology and is a thin, flexible, and quick-dissolving film. The film is placed on the top or the floor of the tongue. It is retained at the site of application and rapidly releases the active agent for local and/or systemic absorption. The Quick-Dis™ drug delivery system can be provided in various packaging configurations, ranging from unit-dose pouches to multiple-dose blister packages.

The typical disintegration time, which is defined as the time at which the film begins to break when brought into contact with water, is only 5 to 10 seconds for the Quick-Dis™ film with a thickness of 2 mm. The

dissolving time, which is defined as the time at which not less than 80% of the tested film is dissolved in aqueous media, is around 30 seconds for Quick Dis™ film with a thickness of 2 mm. The typical release profile of an active ingredient exhibited by a Quick-Dis™ drug delivery system is 50% released within 30 seconds and 95% within 1 minute.

Nanocrystal Technology[34]

For fast dissolving tablets, Elan's proprietary NanoCrystal 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 NanoCrystal technology. NanoCrystal 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.

NanoCrystal™ Fast dissolving technology provides for:

- Pharmacokinetic benefits of orally administered nanoparticles (<2 microns) in the form of a rapidly disintegrating tablet matrix.
- Product differentiation based upon a combination of proprietary and patent-protected technology elements.
- Cost-effective manufacturing processes that utilize conventional, scalable unit operations.
- Exceptional durability, enabling use of conventional packaging equipment and formats (i.e., bottles and/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.

NanoCrystal colloidal dispersions of drug substance are combined with water-soluble GRAS (Generally Regarded as Safe) ingredients, filled into blisters, and lyophilized. The resultant wafers are remarkably robust, yet dissolve in very small quantities of water in seconds. This approach is especially attractive when working with highly potent or hazardous materials because it avoids manufacturing operations (e.g., granulation, blending, and tableting) that generate large quantities of aerosolized powder and present much higher risk of exposure. The freeze-drying approach also enables small quantities of drug to be converted into ODT dosage forms because manufacturing losses are negligible.

Future Advantages of FDT

Orodispersable tablets can offer several biopharmaceutical advantages such as improved efficiency over conventional dosage forms. For example, they require smaller amounts of active ingredient to be effective, improve absorption profiles, and offer better drug bioavailability than regular tablets and capsules. In addition, FDTs may be suitable for the oral delivery of drugs such as protein and peptide-based therapeutics that have limited bioavailability when administered by conventional tablets. These products usually degrade rapidly in the stomach. Because drugs delivered in FDTs may be absorbed in the pregastric sites of highly permeable buccal and mucosal tissues of the oral cavity, they may be suitable for delivering relatively low-molecular weight and highly permeable drugs[28-32].

Future possibilities for improvements in FDTs and drug delivery are bright, but the technology is still relatively new. Several drug delivery technologies that can be leveraged on improving drug therapy from MDTs have yet to be fully realized[3].

Table No.1: Various therapeutic areas in which the Fast dissolving dosage forms are available[24]

S.No	Target population	Therapeutic areas
1	Paediatric	Antibiotics Anti-asthmatics Cough/cold/Allergy Anti-epileptics Analgesics/Antipyretics Antidepressants
2	Adult and Elderly	Parkinson's Antimigraine Alzheimer's Anti-emetics Cancer Diabetes AIDS Gastric Relief Psychotherapeutics Cardiovascular Cough/ Cold/ Allergy Analgesics/ NSAIDS

Table No.2: Popular Disintegrants used in Tablet

S.No	Disintegrants	Mechanism	Concentration % w/w
1	Starch	Disintegrate forms pathways throughout the tablet matrix that enable water to draw into the structure by capillary action, thus leading to disruption of tablet.	5-20
2	Pregelatinized starch	Responsible for increased dissolution rate from this tablet is rapid disintegration due to superior swelling capacity.	5-15
3	Sodium Starch Glycolate (Explotab and Primogel)	Involves rapid absorption of water leading to an enormous increase in volume of granules result in rapid and uniform disintegration.	1-3
4	Cross-linked polyvinyl Pyrrolidone (Cross Povidone, CrosspovidonM, Kollidon, Polyplasdone)	The capillary activity of cross povidone for water is responsible for its tablet disintegration property.	0.5-5
5	Cellulose (Ac-Di-Sol, Nymce ZSX, Primellose Solutab)	They show their ability to swell on contact with water results in rapid tablet disintegration.	1-3
6	Microcrystalline Cellulose (Avicel)	Allowing water to enter the tablet matrix by means of capillary pores, which break the hydrogen bonding between adjacent bundles of cellulose microcrystals and exhibit very good disintegrant property.	10-20
7	Alginates (Alginic Acid, Satialgine)	High affinity for water absorption and high sorption capacity make it an excellent disintegrant.	1-5

8	Soy polysaccharides (Emcosoy)	Natural super disintegrant, Rapid swelling in aqueous medium or wicking action. Does not contain any starch or sugar. Used in nutritional products.	5-15
9	Gums (Guar Gums, Gum Karaya, Agar, Gellan Gum)	As disintegrants because of their tendency to swell in water	3-8
10	Chitin and Chitosan	Moisture sorption and water uptake was found the major mechanism of disintegration while dissolution related to swelling capacity	1-5
11	Smecta	Their layered leaves like structure consist of aluminium and octahydral layers sandwiched between two tetrahydral silica layers. It has a large specific area and high affinity for water makes it good disintegrant.	5-15
12	Isapghula Husk	Plantago ovata seeds husk has high swellability and gives uniform and rapid disintegration.	5-15
13	Polacrillin Potassium	It swells up at very fast rate upon contact with water or gastro intestinal fluid and act as an effective tablet disintegrant.	10-20
14	Ion Exchange Resins Ambrelite IPR 88, Indion, Doshion	Resins have ability to swell in the presence of water, showed disintegration of tablet.	0.5-5
15	Gas–Evolving disintegrants (Citic Acid, Tatric Acid, Sodium Bi Carbonate)	These react in contact with water to liberate carbon dioxide that disrupts the tablet.	>10%

Table No.3: Some of Promising Drug Candidates for Fast Dissolving Tablets[27]

S.No	Category	Examples
1	Antibacterial agents	Ciprofloxacin, tetracycline, erythromycin, rifampicin, penicillin, doxycyclin, nalidixic acid, trimethoprim, sulphacetamide, sulphadiazine etc.
2	Anthelmintics	Albendazole, mebendazole, thiabendazole, livermectin, praziquantel, pyrantel embonate, dichlorophen etc.
3	Antidepressants	Trimipramine maleate, nortriptyline HCl, trazodone HCl, amoxapine, mianserin HCl etc.
4	Antidiabetics	Glibenclamide, glipizide, tolbutamide, tolazamide, gliclazide, chlorpropamide etc.
5	Analgesics/anti-inflammatory agents	Diclofenac sodium, ibuprofen, ketoprofen, mefenamic acid, naproxen, oxyphenbutazone, indomethacin, piroxicam, phenylbutazone etc.
6	Antihypertensives:	Amlodipine, carvedilol, diltiazem, felodipine, minoxidil, nifedipine, prazosin HCl, nimodipine, terazosin HCl etc.
7	Antiarrhythmics	Disopyramide, quinidine sulphate, amiodarone HCl, etc.
8	Antihistamines	Acrivastine, cetrizine, cinnarizine, loratadine, fexofenadine, triprolidine etc.
9	Anxiolytics, sedatives hypnotics and neuroleptics	Alprazolam, diazepam, clozapine, amylobarbitone, lorazepam, haloperidol, nitrazepam, midazolam, phenobarbitone, thioridazine, oxazepam etc.
10	Diuretics	Acetazolamide, clorthiazide, amiloride, furosemide, spironolactone, bumetanide, ethacrynic acid etc.
11	Gastro-intestinal agents	Cimetidine, ranitidine HCl, famotidine, domperidone, omeprazole, ondansetron HCl, granisetron HCl etc.
12	Corticosteroids	Betamethasone, beclomethasone, hydrocortisone, prednisone, prednisolone, methyl prednisolone.
13	Antiprotozoal agents	Metronidazole, tinidazole, omidazole, benznidazole.

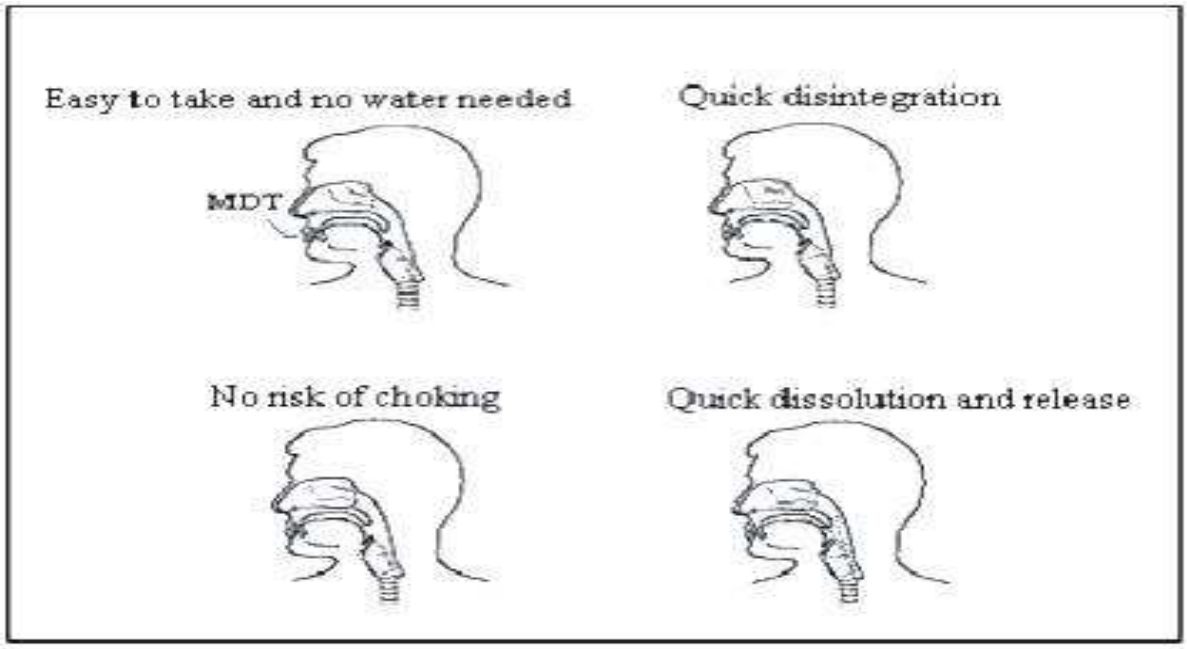
Table No.4: Comparison of Fast Dissolving Techniques

S.No	ZYDIS (R.P. SCHERER, INC)		
	Novelty	**Handling/Storage**	**Drug release/bioavailability**
1	First to market	Do not push tablet through foil	Dissolves in 2 -10s
2	Freeze Dried	Do not use dosage form from damaged package Sensitive to degradation at humidities > 65%	May allow for pre-gastric absorption leading to enhanced bioavailability
ORASOLV (CIMA LABS, INC)			
1	Unique taste masking	Packaged in patented oil packs	Disintegrates in 5 - 45s depending upon the size of the tablet
2	Lightly compressed		No significant change in drug bioavailability
DURASOLV (CIMA LABS, INC)			
1	Similar to Orasolv, but with better mechanical strength	Packaged in foil or bottles	Disintegrates in 5 - 45s depending upon the size of the tablet
		Package in bottles	No significant change in drug bioavailability
WOWTAB (YAMANOUCHI PHARMA TECHNOLOGIES, INC)			
1	Compressed dosage form	Avoid exposure to moisture or humidity	Disintegrates in 5 - 45s depending upon the size of the tablet
2	Proprietary taste masking	Avoid exposure to moisture or humidity Require specialized Packaging	No significant change in drug bioavailability
FLASHDOSE (FUISZ TECHNOLOGIES, LTD)			

1	Unique spinning mech[m] producing floss-like crystalline structure as cotton candy	Avoid exposure to moisture and humidity	Dissolves within 1 min Enhanced bioavailability
FLASHTAB (PROGRAPHARM GROUP)			
1	Compressed dosage form containing Drug as microcrystals	—	Dissolves within 1 min

Table No.5: Marketed Fast Disintegrating Tablets[1, 24]

S.No	Name of the Product	Active Ingredients	Company
1	Feldene Fast, Melt	Piroxicam	Pfizer, USA
2	Claritin Reditabs	Loratidine	Schering Plough Corp, USA
3	Mazalit MTL	Rizatritan	Merckasnd Co. USA
4	Zyprexia	Olanzapine	Eli Lilly, USA
5	Nimulid-MD	Nimesulide	Panacea Biotech, India
6	Pepcid RPD	Famotidine	Merck and Co., USA
7	ZopranODT	Ondansetron	Glaxo Wellcome, UK
8	Zooming – ZMT	Zolmitriptan	Astrazeneca, USA
9	Zeplar TM	Selegilline	Amarin Corp, UK
10	Torrox MT	Rofecoxib	Torrent Pharmaceutical, India
11	Romilast	Montelukast	Ranbaxy Labs Ltd. India
12	Mosid-MT	Mosapride citrate	Torrent Pharmaceutical, India



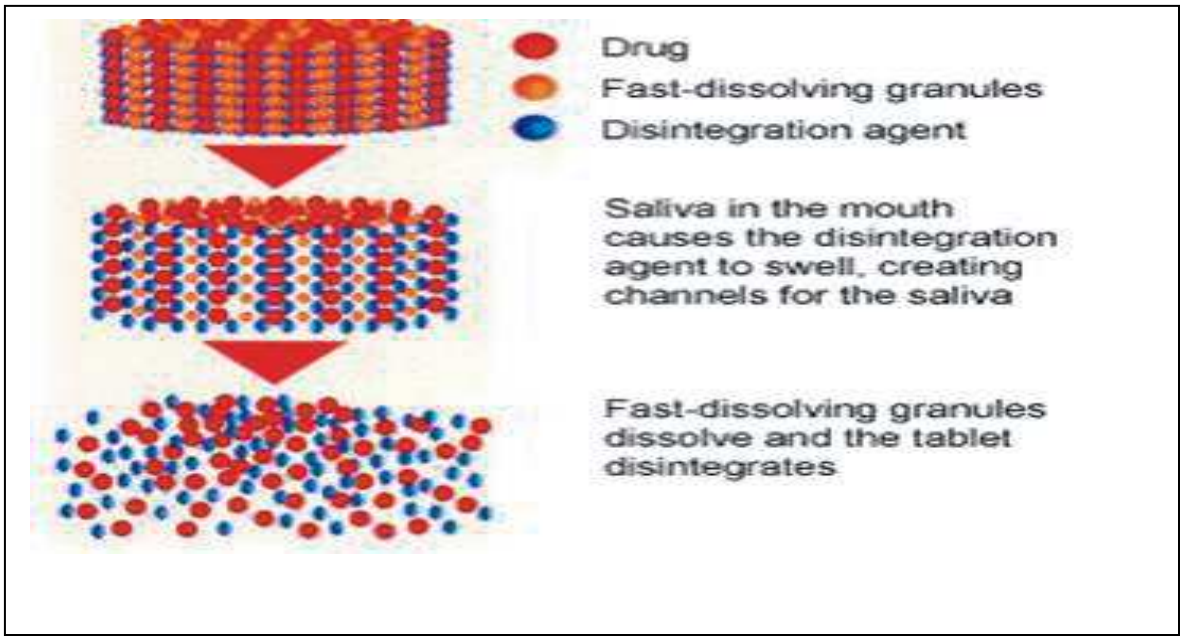


Figure No.2: Mechanism of action of superdisintegrants[1]

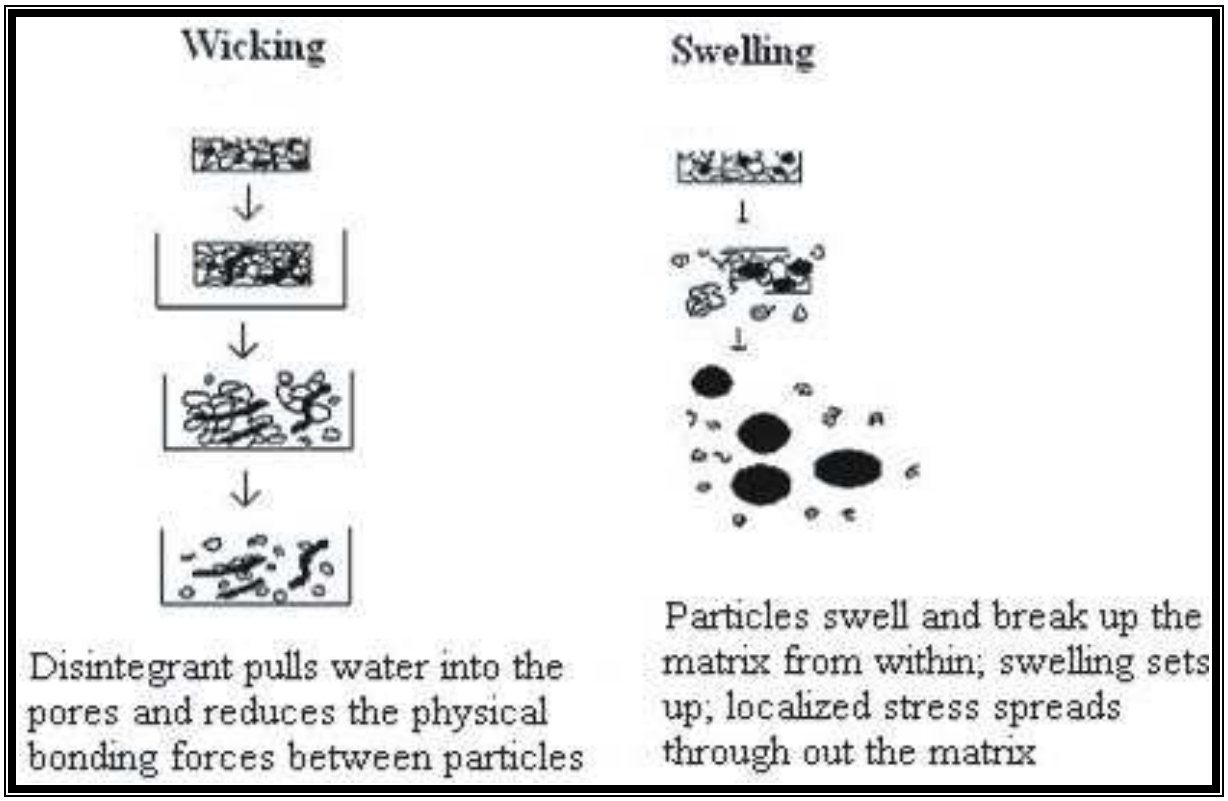


Figure No.3: Disintegration of Tablet by wicking and swelling[22]

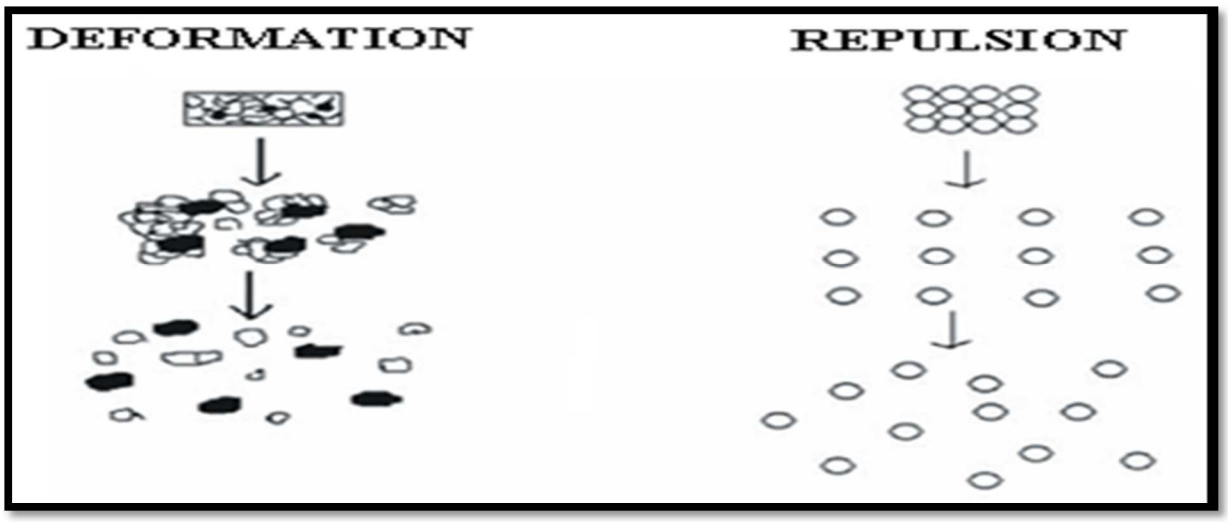


Figure No.4: Disintegration by Deformation and repulsion[1]

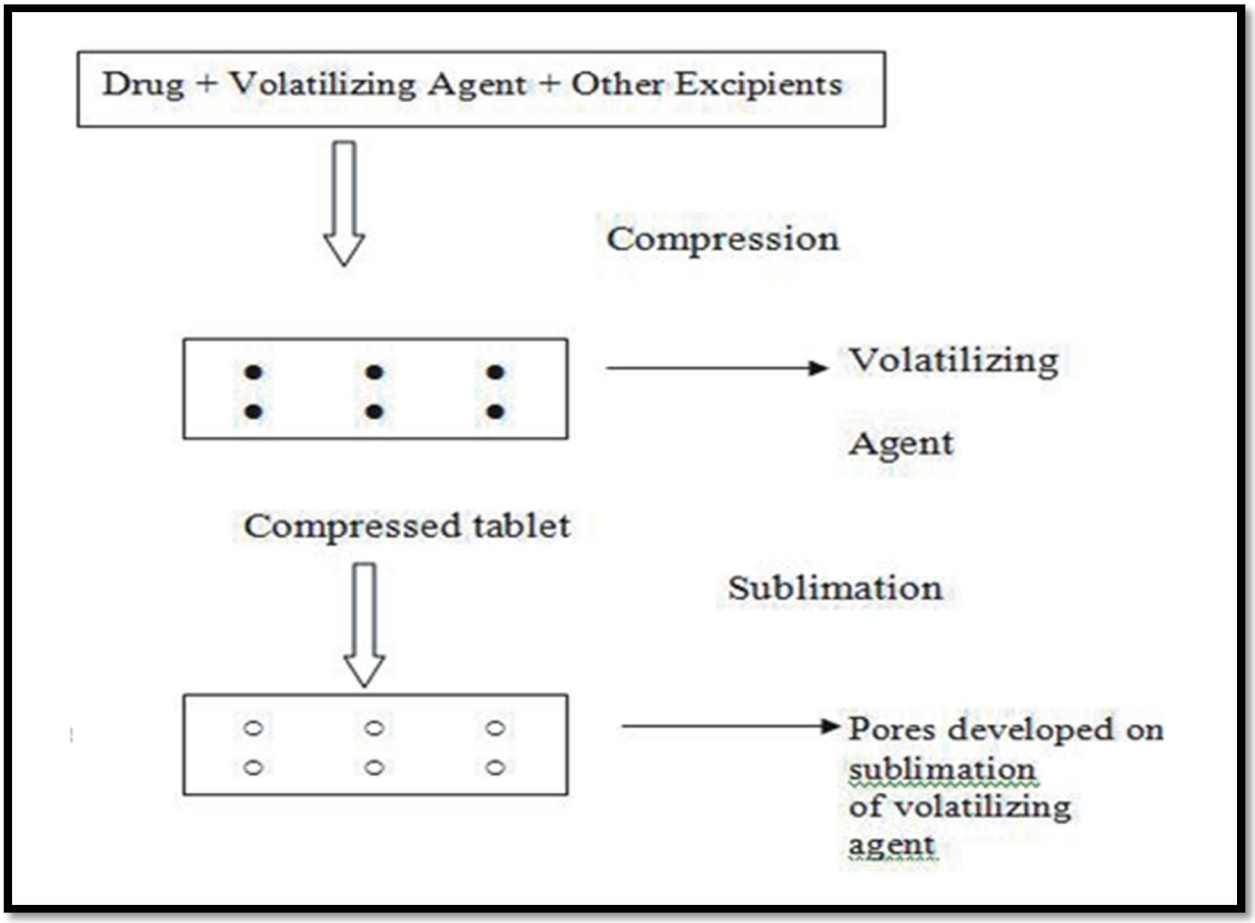


Figure No.5: Sublimation technique for preparation of FDTs

CONCLUS ION

The study of formulating orally disintegrating dosage forms is aims at increasing the patient compliance and decreasing the disintegration time. It also aims of masking the objectionable taste of active ingredients. As compared to other complicated processes such as freeze drying etc. The formulation of orally disintegrating dosage form is easy and overall cost of manufacturing is low. The potential of orally disintegrating dosage form to disintegrate in the oral cavity within seconds, fast onset of action, increasing patient compliance and taste masking of active ingredient makes it an attractive drug delivery form. However, an addition of active ingredient in dosage form like orally disintegrating tablets, orally disintegrating films, oral wafers, buccal patches and chewing gums are excepted to provide a highly acceptable means of delivering drug to geriatric and pediatric patients. So the upcoming years a oral drug delivery becomes a much popular in the field of pharmaceutical drug delivery.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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