

**Review Article****Novel study in fast dissolving drug delivery system: a review**

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ABSTRACT

Novel drug delivery systems are becoming increasingly sophisticated as pharmaceutical scientists acquire a better understanding of the physicochemical and bio-chemical parameters pertinent to their performance. Despite tremendous advancements in drug delivery, the oral route remains the perfect route for the administration. 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. Some tablets are designed to dissolve in saliva remarkably fast, within a few seconds, and are true fast-dissolving tablets. Others contain agents to enhance the rate of tablet disintegration in the oral cavity, and are more appropriately termed fast-disintegrating tablets, as they may take up to a minute to completely disintegrate.

Introduction

Patient compliance is one of the most important aspects in the pharmacy practice. Now days, pharmacy companies are coming up with development of new drug delivery systems to ensure the delivery of the drugs to the patients efficiently and with fewer side effects. Solid dosage forms are popular because of ease of administration, accurate dosage, self-medication, pain avoidance and most importantly the patient compliance. 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 [1-3]. 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 [4]. 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.[6,7] When such tablets are placed in oral cavity, saliva quickly penetrates into the pores to cause rapid tablet disintegration [8,9,10]. 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 superdisintegrates 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

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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 [13-18].

Fast dissolving drug delivery system [19]

- A fast dissolving tablet can be defined as a solid dosage form that can disintegrates into smaller granules which slowly dissolve in the mouth. The disintegration time for fast dissolving tablet varies from a few seconds to more than a minute depending on the formulation and the size of the tablet.
- A fast disintegrating or dissolving system or tablet can be defined as a solid dosage form that can disintegrate or dissolve within 30 seconds, in the oral cavity resulting in a solution or suspension without administration of water.
- The fast disintegrating tablets are synonymous with fast dissolving tablets; melt in mouth tablets, rapid melts, Porous tablets, Orodispersible, quick dissolving or rapidly disintegrating tablets.

Advantages of FDTS [20,21]

- 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 esophagus.
- 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.

FDT can be administer to the patients who cannot swallow tablets/cap such as the elderly, stroke victims, bedridden patients& patients who refuse to swallow such as pediatric, geriatric & psychiatric patients. Rapid drug therapy is possible. Certain studies concluded increased bioavailability/proved rapid absorption of drugs through pre-gastric absorption of drugs from mouth, pharynx & esophagus as saliva passes down. Some advantages of the recent oral fast dissolving drug delivery system are depicted in the figure-1 given below:

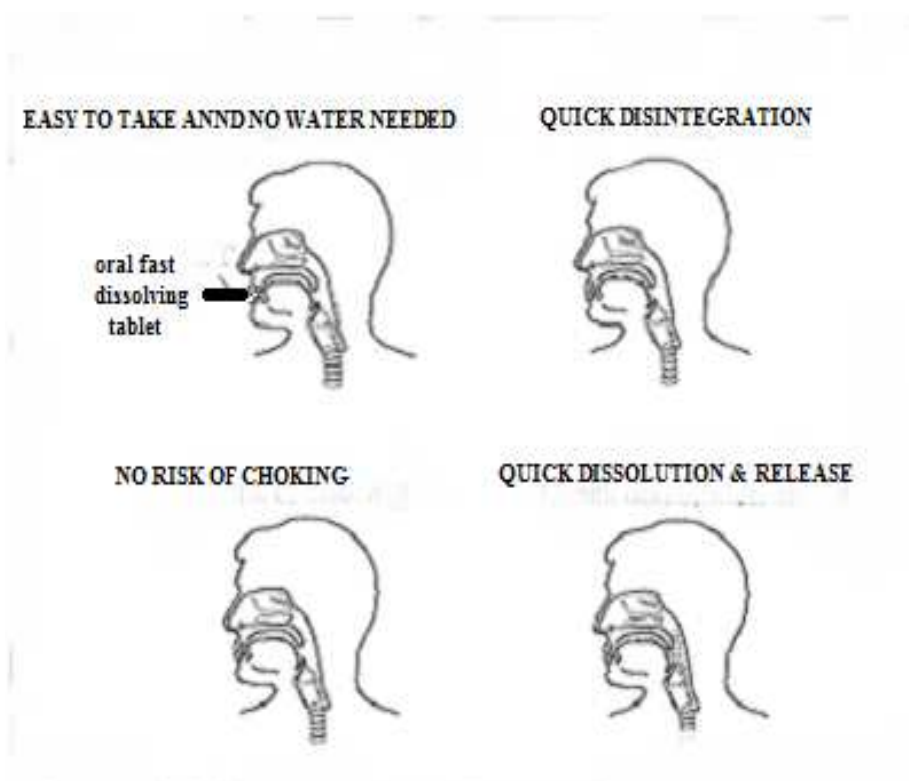


Figure 1: Advantages of Oral Fast Dissolving Tablets

Limitations of FDTS [22,23]

- 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.
- 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.
- Drugs difficult to formulate into FDT with relatively larger doses.
- Drugs with short half-life and frequent dosing and those who require controlled or sustained release are unsuitable candidates of FDTs.
- Drugs with relatively large doses are difficult to formulate into FDTs.

Ideal properties of FDTS [24-26]

- Not require water or other liquid to swallow.

- Easily dissolve or disintegrate in saliva within a few seconds.
- Have a pleasing taste.
- Leave negligible or no residue in the mouth when administered.
- Be portable and easy to transport.
- Be able to be manufactured in a simple conventional manner within low cost.
- Be less sensitive to environmental conditions like temperature, humidity etc.

Challenges for development of FDTS [27-37]

- **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.
- **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.

- **Aqueous solubility:** Water-soluble drugs pose various formulate ion challenges because they form eutectic mixtures, which result in freezing-point depression and the format ion of a glassy solid that may collapse upon drying because of loss of supporting structure during the sublimate ion 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.
- **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.
- **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.
- **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.
- **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 flavors and cooling agents like menthol improve the mouth feel.
- **Sensitivity to environmental conditions:** FDTs should exhibit low sensitivity to environment conditions such as humidity and temperature as most of the materials used in FDTs are meant to dissolve in minimum quantity of water.
- **Cost:** The technology used for FDTs should be acceptable in terms of cost of the final product. Methods like Zydis and Orasolv that require special technologies and specific packaging increase the cost to a remarkable extent.
- **Tablet strength, Friability and porosity:** In order to allow fast disintegrating tablets to disintegrate in the mouth, they are made of either very porous or soft-molded matrices or compressed into tablets with very low compression force, which makes the tablets friable and/or brittle, which are difficult to handle, often requiring specialized peel-off blister packaging.

Drug selection criteria [38]

The drug selection criteria for fast dissolving tablets include:

- Partially non- ionized at the oral cavities Ph.
- Ability to permeate the oral mucosa.
- Small to moderate molecular weight.
- Have the ability to diffuse and partition into the epithelium of the upper GIT.
- Good stability in water and saliva.
- Drugs which have lower bioavailability are good candidates for FDT.
- Short half-life and frequent dosing drugs are unsuitable for FDT.
- Very bitter taste and odor drugs are unsuitable for ODT. Patients who concurrently take ant cholinergic medications may not be the best candidates for these drugs.
- Drugs having ability to diffuse and partition into the epithelium of the upper GIT ($\log P > 1$, or preferable > 2); and those able to permeate oral mucosal tissue are considered ideal for FDT formulations.
- Drugs which require controlled or sustained release are unsuitable candidates of fast dissolving oral dosage forms.

Criteria for excipients [39-41]

The ideal characteristics of excipients for oral dispersible tablets include:

- 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.

Various approaches for FDTS [42]

The fast-dissolving property of the tablet is attributable to a quick ingress of water into the tablet matrix resulting in its rapid disintegration. Hence, the basic approaches to developing fast dissolving tablets include maximizing the porous structure of the tablet matrix, incorporating the appropriate disintegrating agent, and using highly water-soluble excipients in the formulation.

Need for development of FDTS [43]

The need for development of FDTS includes following factors:

- **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:
 - ✓ Patients who are unwilling to take solid preparation due to fear of choking.
 - ✓ An eight-year old with allergies who desires a more convenient dosage form than antihistamine syrup.
 - ✓ Pediatric and geriatric patients who have difficulty in swallowing or chewing solid dosage forms.
 - ✓ A middle-aged woman undergoing radiation therapy for breast cancer may be too nauseous to swallow her H₂- blocker.
 - ✓ A patient with persistent nausea, who may be journey, or has little or no access water
 - ✓ A schizophrenic patient in an institutional setting who may try to hide a conventional tablet under his or her tongue to avoid their daily dose of an atypical antipsychotic.
 - ✓ Very elderly patients who may not be able to swallow a daily dose of antidepressant.
- **Effectiveness factor:** Increased bioavailability and faster onset of action are a 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 all areas of absorption for many drugs. Any pregastric absorption avoids first pass metabolism and can be a great advantage in drugs that undergo a great deal of 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 pregastric 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, value-added product line extension, and extend patent protection, while offering its patient population a more convenient dosage form. This leads to increased revenue, while also targeting underserved and undertreated patient populations. Marketers build a better brand and company image when they offer a unique easier-to-take form that satisfies the need of an underserved.

Formulation aspects in developing FDTS [44]

Orally disintegrating tablets are formulated by utilizing several processes, which differ in their methodologies and the FDTS formed vary in various properties such as:

1. Mechanical strength of tablets
2. Taste and mouth feel
3. Swallow ability
4. Drug dissolution in saliva
5. Bioavailability
6. Stability

Composition of FDTS [45]

Fast dissolving film is a thin film with an area of 2-8 cm² containing an active ingredient:

Table No.1: Various ingredients of FDTS

S. No.	Types of ingredients	Percentage in formulation
1.	Active pharmaceutical agent	1-25%
2.	Water soluble film forming polymer	40-50%
3.	Plasticizer	0-20%
4.	Sweetening agent	3-6%
5.	Saliva stimulating agent	2-6%
6.	Colors and Flavors	0-10%

Mechanisms of tablet disintegration [46- 48]

- By capillary action (Wicking)
 - By swelling
 - Because of heat of wetting
 - Due to release of gases
 - By enzymatic action
 - Due to disintegrating particle/particle repulsive forces
 - Due to deformation.
- **By capillary action (Wicking):** Disintegration by capillary action is always the first step. When we put the

tablet 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.

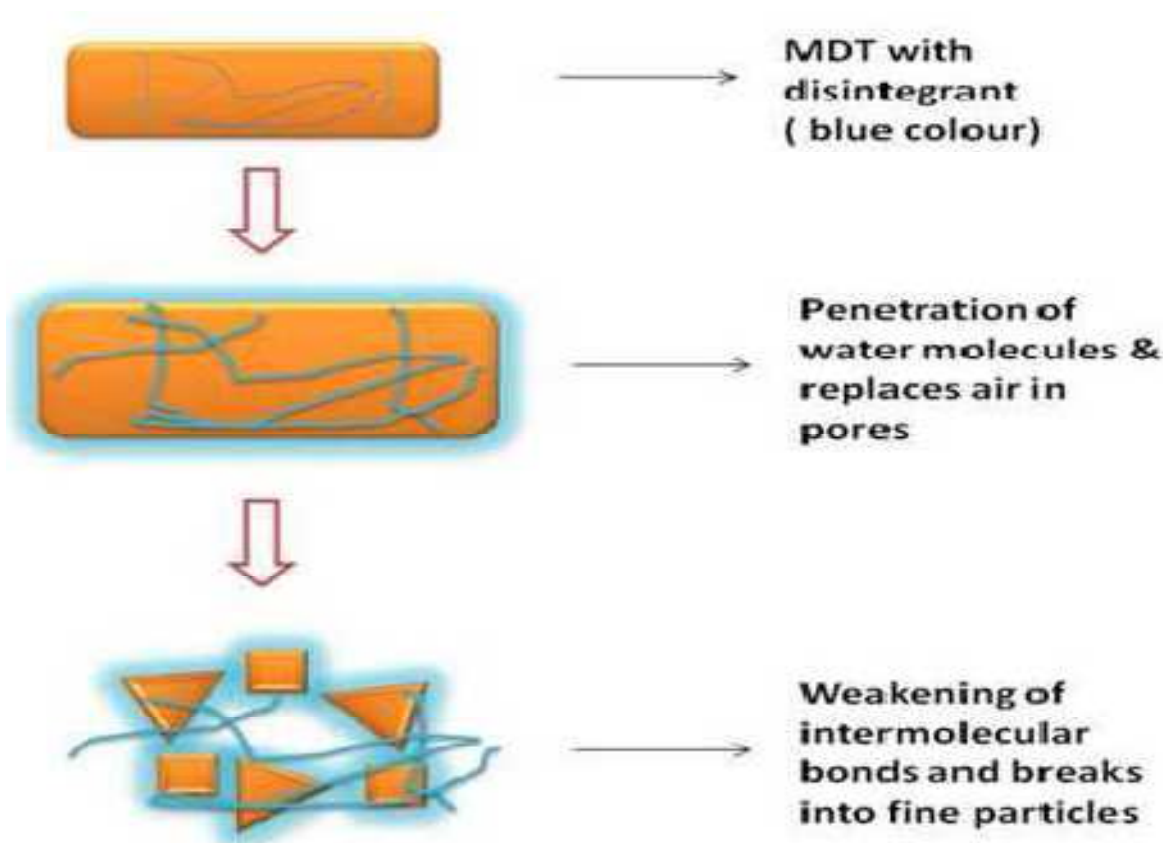


Figure 2: Wicking Mechanism of FDTs

- **By swelling:** Perhaps the most widely accepted general mechanism of action for tablet disintegration is swelling. 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 slow down.
- **Because of heat of wetting (air expansion):** When disintegrates with exothermic properties gets wetted, localized stress is generated due to capillary air expansion, which helps in disintegration of tablet.
- **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 in to two separate fraction of formulation.
- **By enzymatic reaction:** Here, enzymes present in the body 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 burst or the accelerated absorption of water leading to an enormous increase in the volume of granules to promote disintegration.
- **Due to disintegrating particle/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 non-swelling 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.
- **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 aqueous media or water. Occasionally, the swelling capacity of starch was improved when granules were extensively deformed during compression.

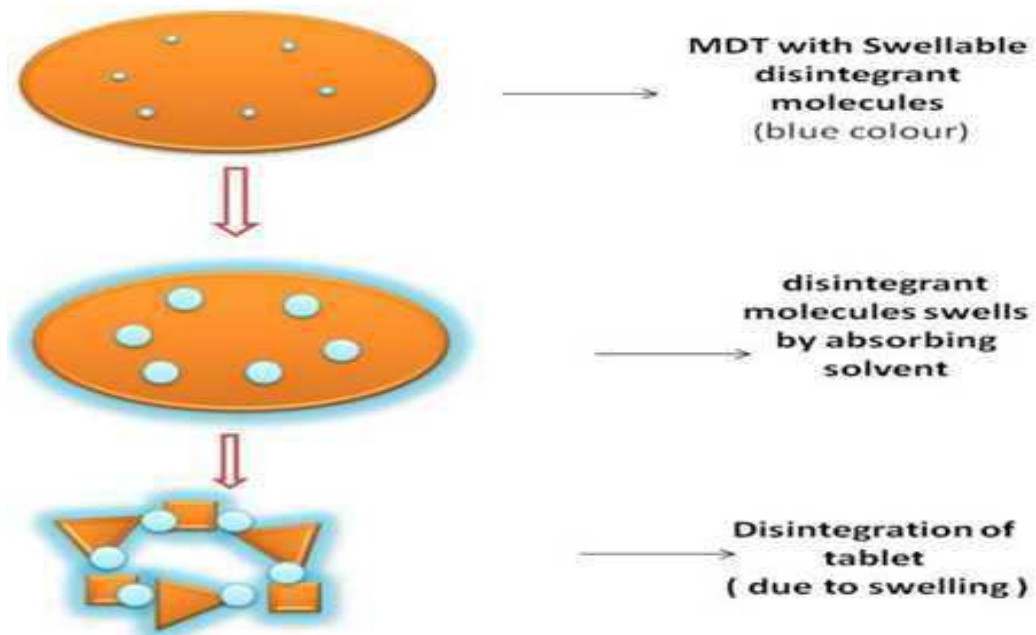


Figure 3: Swelling mechanism of FDTs

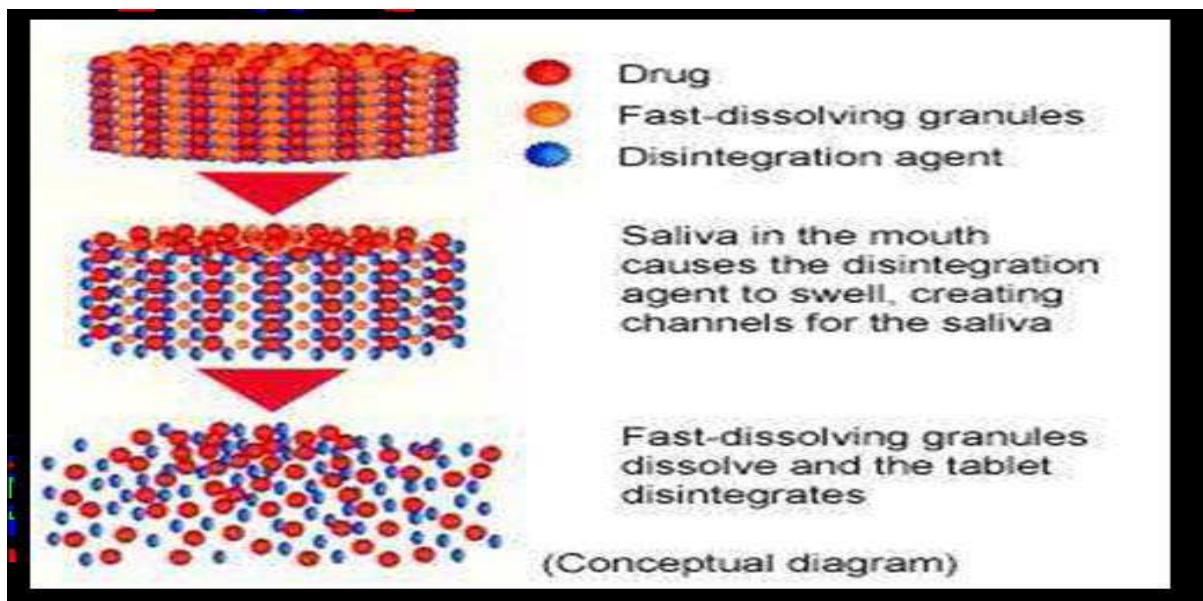


Figure 4: Conceptual mechanism of FDT Disintegration (By release of gases)

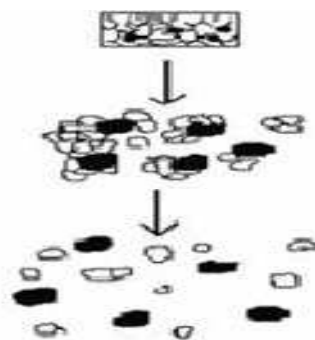


Figure 5: Disintegration of FDTs by Deformation

Various techniques for preparation of FDTs[49, 50]

Techniques for the preparation of FDTs include:

A) Non Patented Technology:

Various non-patented technologies include:

Freeze-Drying or Lyophilization: Freeze drying is the process in which water is sublimed from the product after it is frozen. This technique creates an amorphous porous structure that can dissolve rapidly. A typical procedure involved in the manufacturing of ODT using this technique is mentioned here. The active drug is dissolved or dispersed in an aqueous solution of a carrier/polymer. The mixture is done by weight and poured in the walls of the preformed blister packs. The trays holding the blister pack sare passed through liquid nitrogen freezing tunnel to freeze the drug solution or dispersion. Then the frozen blister packs are placed in refrigerated cabinets to continue the freeze-drying. After freeze-drying the aluminum foil backing is applied on a blister-sealing machine. Finally the blisters are packaged and shipped. The freeze-drying technique has demonstrated improved absorption and increase in bioavailability.

Tablet Molding: Molding process is of two type's i.e. solvent method and heat method. Solvent method involves moistening the powder blend with a hydro alcoholic solvent followed by compression at low pressures in molded plates to form a wetted mass (compression molding). 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. The heat molding 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. Binding agents, which increase the mechanical strength of the tablets, need to be incorporated. Taste masking is an added problem to this technology.

Spray Drying: In this technique, gelatin can be used as a supporting agent and as a matrix, mannitol as a bulking agent and sodium starch glycolate or cross carmellose or cross

povidone are used as superdisintegrants. Tablets manufactured from the spray-dried powder have been reported to disintegrate in less than 20 seconds in aqueous medium. This spray-dried powder, which compressed into tablets showed rapid disintegration and enhanced dissolution.

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

Direct compression: 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. Addition of disintegrants in fast dissolving tablets, leads to quick disintegration of tablets and hence improves dissolution. In many fast dissolving tablet technologies based on direct compression, the disintegrants principally affect the rate of disintegration and hence the dissolution. The introduction superdisintegrants and a better understanding of their properties have increased the popularity of this technology. Tablet disintegration time can be optimized by concentrating the disintegrants. Below critical concentration, tablet disintegration time is inversely proportional to disintegrants concentration.⁶ Melt Granulation¹¹ In this process, FDTs can be prepared by incorporating a hydrophilic waxy binder (superpolystate) like PEG-6-stearate. Super polystate is a waxy material with melting point of 33-37°C and a hydrophilic- lipophilic balance. 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 FDTs by melt granulation method where granules are formed by the molten form of this material.

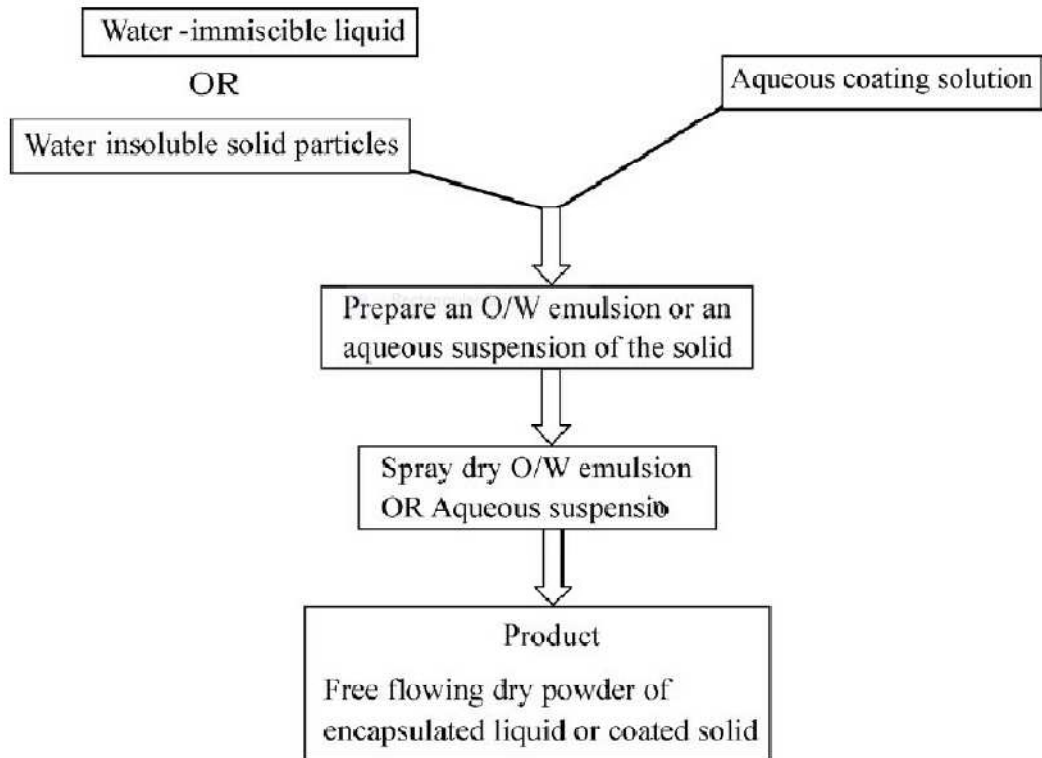


Figure 6: Flowchart for coating liquid and solid particles using spray-dry process

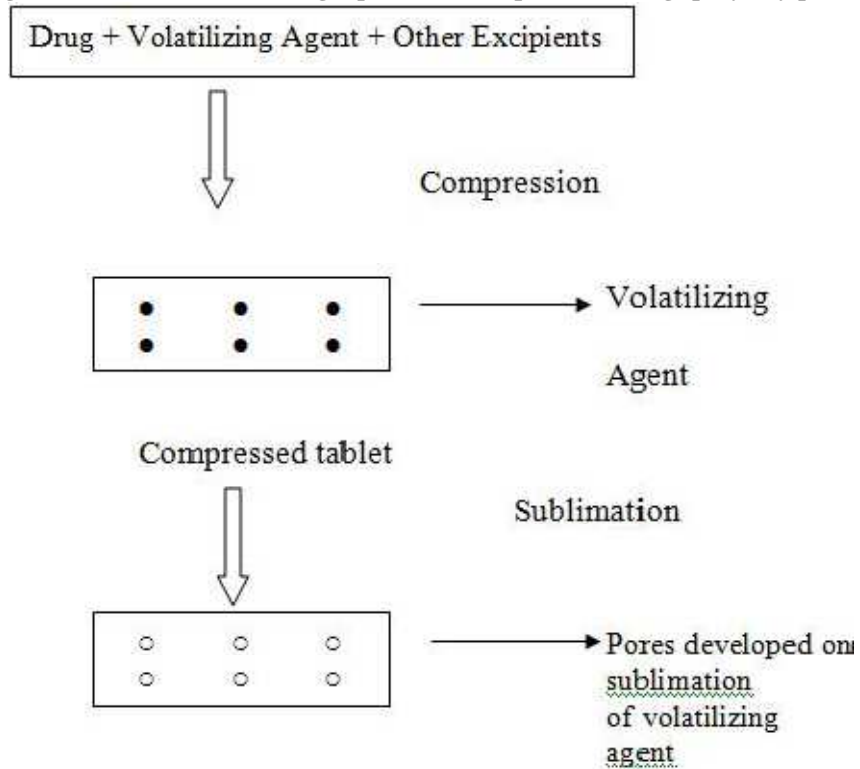


Figure 7: Schematic Diagram of Sublimation Technique for Preparation of FDTS

B) Patented Technology:

Following table shows the various patented technologies:

Table No.2: Patented Technologies

SNo.	Technique	Key Attributes	Methods	Company Names
1.	Zydis®	Freeze-drying on-blister packing	Lyophilization	<u>R.P.Scherer, Inc.</u>
2.	Durasolv	Direct compression using water-	Direct Compression	CimaLabs, Inc.
3.	Orasolv	low compression force and an effervescent couple as a water-soluble disintegrating agent	Direct Compression	CimaLabs, Inc.
4.	Flashdose		Cotton Candy Process	Fuisz Technology Ltd.
5.	WOWTAB®	High- and low-moldability	Direct Compression	Yamanouchi Pharma
6.	Flashtab	Granulation of excipients by wet or dry granulation	Direct Compression	Ethypharm France
7.	Pharmaburst	Direct Compression Of Powder Mixture	Lyophilization	KV Pharma. Co. Inc.
8.	Advatab	Direct Compression using External Lubrication System	Micro caps And Diffuscap CR Technology	Eurand International
9.	Lyoc	Freeze Drying	Lyophilization	Farmalyoc Laboratories
10.	Advantol™	Directly Compressible Excipients System	Direct compression	SPI Pharma

Evaluation of FDTs [51, 52]**A) FOR GRANULES**

Evaluation parameters for granules are as follows:

1. Angle of Repose
2. Porosity
3. Compressibility
4. Bulk Density
5. Tapped Density
6. Carr's Index
7. Hausner's Ratio

B) FOR TABLETS

Evaluation parameters for tablets are as follows:

1. Hardness
2. Weight Variation
3. Accelerated Stability Study
4. Wetting Time
5. Friability
6. Dissolution Test
7. Thickness Variation
8. Disintegration Test
9. Packaging

Future prospects [53, 54]

There are several biopharmaceutical advantages such as improved efficiency over conventional dosage forms for Fast disintegrating tablets. 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. There are still many aspects to improve in the FDT formulations. The disintegration times of most FDTs on the market are acceptable i.e., less than 60 seconds but certainly there is a room for improvement. Because the disintegration time is related to other formulation variables, a balance has to be maintained between shortening the disintegration time and other tablet properties. The tablet hardness, friability, and stability can be further improved to such a level that multi-tablet packaging in conventional bottles becomes a norm. There may be no magic solution to this, but more effective use of existing taste masking technologies is expected to alleviate the problems associated with taste masking. The future of FDTs lies in the development of FDTs with controlled release properties. Despite advances in the FDT technologies, formulation of hydrophobic drugs is still a challenge, especially when the amount of drug is high. The low dose drugs, such as Loratadine with 10 mg dose, pose little problem, but as the dose increases, the formulation sacrifices its fast disintegrating property. A new technology is being developed to incorporate higher doses of hydrophobic drugs without affecting the fast disintegrating property too severely. If one FDT can deliver drugs with short half-lives for 12-24 hours, it would be a quantum improvement in the FDT technology. The added convenience and compliance of such formulations would be enormous. In addition, the ability to formulate drugs in large doses will bring another important technological advance. In general, the FDT formulations require large amounts of excipients, and having large doses of drug will only make the final formulation too big to handle. An FDT formulation that would require fewer excipients than the drug itself would be a breakthrough. While the problems to be solved are not easy, the history suggests that it is just a matter of time before they are solved. The safety and efficacy

profile of drugs in orodispersible tablet is same like their conventional tablet dosage form. Based on conventional techniques, new techniques are developed like Zydis, Wow

Tab, Flash tab technology and many more, which leads to getting a patent and new mark.

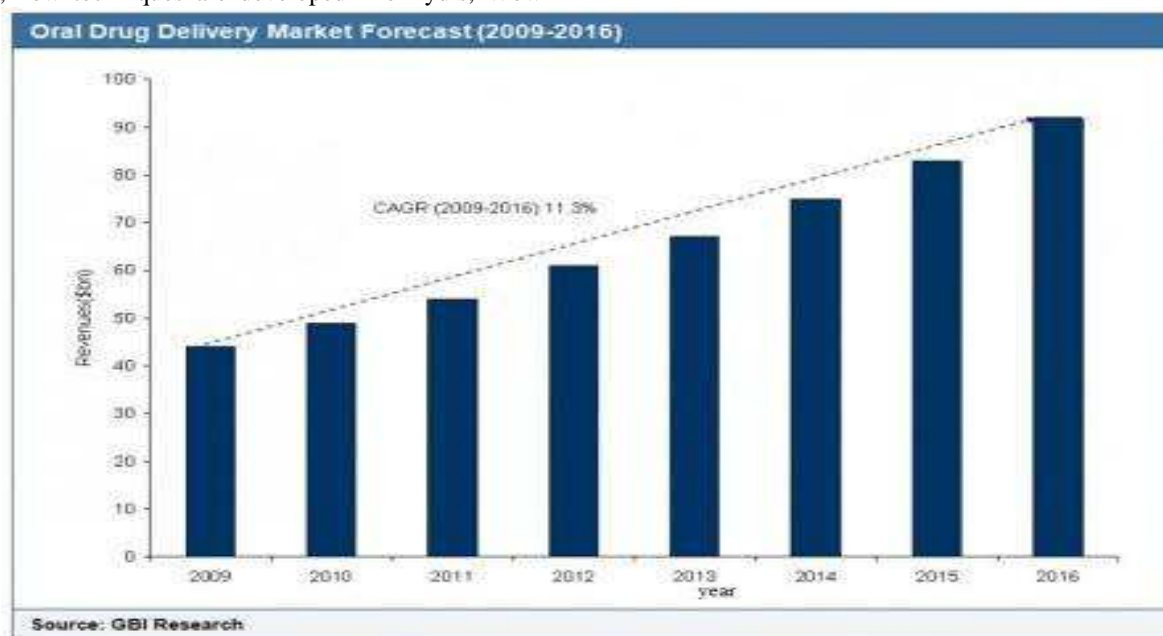


Figure 8: Oral Drug delivery system market forecast (2009-2016)

Drugs to be promising incorporated in FDTS [55, 56]

There are no particular limitations as long as it is a substance which is used as a pharmaceutical active ingredient:

Table No.3: Drugs included in FDTS

S.No.	Types Of Drug	Examples
1.	Analgesics and Anti-inflammatory Agents	Aloxiprin, Auranofin, Azapropazone, Benorylate, Diflunisal, Etodolac, Fenbufen, FenoprofenCalcim, Flurbiprofen, Naproxen, Ibuprofen, Indomethacin, Ketoprofen, Meclofenamic Acid, Mefenamic Acid, Nabumetone, Sulindac, Oxaprozin, Oxyphenbutazone, Phenylbutazone, Piroxicam.
2.	Anthelmintics	Albendazole, BepheniumHydroxynaphthoate, Cambendazole, Dichlorophen, Ivermectin, Mebendazole, Oxarnniquine, Oxfendazole, OxantelEmbonate, Praziquantel, PyrantelEmbonate, Thiabendazole.
3.	Anti-Arrhythmic Agents	Amiodarone, Disopyramide, Flecainide Acetate, Quinidine Sulphate.
4.	Anti-bacterial Agents	Benethamine Penicillin, Cinoxacin, Ciprofloxacin, Clarithromycin, Clofazimine, Cloxacillin, Demeclocycline, Doxycycline, Erythromycin, Ethionamide, Imipenem, Nalidixic Acid, Nitrofurantoin, Rifampicin, Spiramycin, Sulphabenzamide, Sulphadoxine, Sulphamerazine, Sulphacetamide, Sulphadiazine, Sulphafurazole, Sulphamethoxazole.

				Sulphapyridine, Tetracycline, Trimethoprim.
5.	Anti-coagulants			Dicoumarol, Dipyridamole, Nicoumalone, Phenindione.
6.	Anti-Depressants			Amoxapine, Ciclazindol, Maprotiline, Mianserin, Nortriptyline, Trazodone, Trimipramine Maleate., Acetohexamide, Chlorpropamide, Glibenclamide, Gliclazide, Glipizide, Tolazamide, Tolbutamide.
7.	Anti -Epileptics			Beclamide, Carbamazepine, Clonazepam, Ethotoin, Methoin, Methsuximide, Phensuximide, Methylphenobarbitone, Oxcarbazepine, Paramethadione, Phenacemide, Phenobarbitone, Phenytoin, Primidone, Sulthiame, Valproic Acid
8.	Anti-Fungal			Amphotericin, Butoconazole Nitrate, Clotrimazole, Econazole Nitrate, Fluconazole, Fiucytosine, Griseofulvin, Itraconazole, Ketoconazole, Miconazole, Natamycin, Nystatin, Sulconazole Nitrate, Terbinafine, Terconazole, Tioconazole, Undecenoic Acid
9.	Anti -Gout Agents			Allopurinol, Probenecid, Sulphinpyrazone
10.	Anti -Hypertensive Agents			Amlodipine, Carvedilol, Benidipine, Darodipine, Dilitazem, Diazoxide, Felodipine, Guanabenz Acetate, Indoramin, Isradipine, Minoxidii, Nicardipine, Nifedipine, Nimodipine, Phenoxybenzamine, Prazosin, Reserpine, Terazosin
11.	Anti-Malarials			Amodiaquine, Chloroquine, Chlorproguanil, Halofantrine, Mefloquine, Proguanil, Pyrimethamine, Quinine Sulphate
12.	Anti -Migraine Agents			DihydroergotamineMesyiate, Ergotamine Tartrate, Methysergide Maleate, Pizotifen Maleate, Sumatriptan Succinate.
13.	Anti -Muscarinic Agents			Atropine, Benzhexol, Biperiden, Ethopropazine, Hyoscine Butyl Bromide, Hyoscyamine, Mepenzolate Bromide, Tropicamide, Orphenadrine, Oxyphencylmine
14.	Anti-Neoplastic Agents and Immunosuppressants			Aminoglutethimide, Amsacrine, Azathiopne, Busulphan, Chlorambucil, Cyclosporin, Dacarbazine, Estramustine, Etoposide, Lomustine, Melphalan, Mercaptopurine, Methotrexate, Mitomycin, Mitotane, Mitozantrone, Procarbazine, Tamoxifen Citrate, Testolactone
15.	Anti Protozoal Agents			Benznidazole, Clioquinol, Decoquinat, Diiodohydroxyquinoline, DiloxanideFuroate, Dinitolmide, Furzolidone, Metronidazole, Nimorazole, Nitrofurazone, Omidazole, Tinidazole
16.	Anti -Thyroid Agents			Carbimazole, Propylthiouracil. Anxiolytic, Sedatives, Hypnotics and Neuroleptics: Alprazolam, Amyiobarbitone, Barbitone, Bentazepam, Bromazepam, Bromperidol, Brotizoiam, Butobarbitone, Carbromal, Chlordiazepoxide, Chlormethiazole,

		Chlorpromazine, Clobazam, Clotiazepam, Clozapine, Diazepam, Droperidol, Ethinamate, Flunansone, Flunitrazepam, Fluopromazine, FlupenuixolDecanoate, FluphenazineDecanoate, Flurazepam, Haloperidol, Lorazepam, Lormetazepam, Medazepam, Meprobamate, Methaqualone, Midazolam, Nitrazepam, Oxazepam, Pentobarbitone, PerphenazinePimozide, Prochlorperazine, Suipiride
17.	Anxiolytics, Sedatives, Hypnotics and Neuroleptics	Alprazolam, Barbitone, Clobazam, Clozapine, Diazepam
18.	Cardiac Ionotropic Agents	Digitoxin
19.	Gastro-Intestinal Agents	Omeprazole, Ranitidine
20.	Nutritional Agents	Vitamin A, B & D
21.	Oral Vaccine	Hepatitis, Polio & Influenza

Conclusion

Fast disintegrating tablets have better patient acceptance and offer improved biopharmaceutical properties, improved efficacy and better safety as compared with conventional oral dosage forms. By using new manufacturing technologies, many drugs can be formulated in the form of fast disintegrating tablets to provide the advantages of liquid medication in the form of solid preparation. FDT need to be formulated for pediatric, geriatric, bedridden, psychotic patients, for those patients who are busy in travelling, patients. As a drug entity 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. Fast dissolving/disintegrating tablet formulations are similar to many sustained release formulations that are now commonly available. An extension of market exclusivity, which can be

provided by a fast- dissolving/disintegrating dosage form, leads to increased revenue, while also targeting underserved and under-treated patient populations. Although the cost to manufacture these specialized dosage forms exceeds that of traditional tablets, this additional cost is not being passed on to the consumer. Due to the constraints of the current FDDT technologies as highlighted above, there is an unmet need for improved manufacturing processes for fast dissolving tablets that are mechanically strong, allowing ease of handling and packaging and with production costs similar to that of conventional tablets. To fulfill these medical needs, formulators have devoted considerable effort to developing a novel type of tablet dosage form for oral administration, one that disintegrates and dissolves rapidly in saliva without the need for drinking water.

Conflict of interest statement

We declare that we have no conflict of interest.

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