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REVIEW ARTICLE

FAST DISINTEGRATING TABLETS: A NEW ERA IN NOVEL DRUG DELIVERY SYSTEM AND NEW MARKET OPPORTUNITIES

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ABSTRACT

Fast disintegrating tablets (FDTs) have received ever-increasing demand during the last decade and the field has become a rapidly growing area in the pharmaceutical industry. Fast disintegrating tablets (FDTs) are those solid dosage forms when put on tongue, disintegrate or dissolve instantaneously, releasing the drug, within a few seconds without the need of water. Fast disintegrating tablets (FDTs) aim for designing dosage forms, convenient to be manufactured and administered, free of side effects, offering immediate release and enhanced bioavailability, to achieve better patient compliance. Fast disintegrating tablets have been formulated for pediatric, geriatric, and bedridden patients and for active patients who are busy and traveling and may not have access to water. Such formulations provide an opportunity for product life extension in the many elderly persons which have difficulty in taking conventional oral dosage form (viz., solutions, suspensions, tablets, and capsules) because of hand tremors and dysphagia. The current article is focused on ideal requirements, need for development of FDTs, challenges in formulation, suitability of drug candidates, superdisintegrants employed, various technologies developed for FDTs, patented technologies like Wowtab, Durasolv, Orasolv, Flashtab, Zydis, Frosta technology, Sheaform, Ceaform technology, Nanocrystal technology which have gained importance in international market, evaluation methods and various marketed products.

Keywords: Fast disintegrating tablets (FDTs), Superdisintegrants, Enhanced bioavailability, Patient's compliance, Patented technology, Evaluation.

1. INTRODUCTION

Drug delivery system is an efficient tool for enhancing market, extending product life cycles and creating opportunities. Drug delivery system (DDS) makes a significant contribution to global pharmaceutical sales through market segmentation, and is moving rapidly [1]. Despite of tremendous innovations in drug delivery, the oral route remains the preferred route for administration of therapeutic agents because of accurate dosage, low cost therapy, self medication, non invasive method and ease of administration leading to high level of patient compliance [2].The most popular dosage forms are being conventional tablets and hard gelatin capsules. One important drawback of such dosage forms is 'Dysphagia' or difficulty in swallowing for many patients; almost 50% of the population is affected by such problem. Hence they do not comply with prescription, which results in high incidence of non-compliance and ineffective therapy [3]. Recently, fast disintegrating drug delivery systems have started gaining popularity and acceptance as new drug delivery systems, because they are easy to administer and lead to better patient compliance [4]. In some cases such as motion sickness, sudden episodes of allergic attacks or coughing and unavailability of water, swallowing conventional tablets may be difficult. Particularly the difficulty is experienced by pediatric and geriatric patients. To overcome such problems, fast disintegrating tablets or orally disintegrating tablets have emerged as an alternative dosage form [5].Recent advances in novel drug delivery systems (NDDS) aim for enhancing the safety of a drug molecule while maintaining its therapeutic efficacy so as to achieve better patient compliance. Pharmaceutical technologists have put in their best efforts to develop a fast dissolving/ disintegrating drug delivery system (FDDTs) [6].The Center for Drug Evaluation and Research(CDER), US FDA defined Fast-dissolving/disintegrating tablets (FDDTs) are "A solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue". Recently European Pharmacopoeia also adopted the term "Oro Dispersible Tablet" defined as ''uncovered tablet for buccal cavity, where it disperses before ingestion" [7]. Fast disintegrating tablets (FDT) are also known as 'fast dissolving', 'mouth dissolving', 'rapid-dissolve', 'quick disintegrating', 'orally disintegrating', 'rapimelt', 'fast melts', 'orodispersible', 'melt-in-mouth', 'quick dissolving', 'porous tablets', 'EFVDAS' or 'Effervescent Drug Absorption System' [8]. Fast disintegrating tablets are those when put on tongue disintegrate instantaneously releasing the drug which dissolve or disperses in the saliva. When Faster the drug into solution, quicker the absorption and onset of clinical effect. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablets dosage form. The advantage of mouth dissolving dosage forms are increasingly being recognized in both, industry and academics. The basic approach in development of FDT is the use of superdisintegrants like cross linked carboxymethyl cellulose (croscarmellose), sodium starch glycolate (primogel, explotab), cross linked polyvinylpyrollidone (crospovidone) etc, which provide instantaneous disintegration of tablet after putting on tongue, their by release the drug in saliva. The bioavailability of some drugs may be increased due to absorption of drug 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 tablet [9]. The target populations for

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these new fast-dissolving/disintegrating dosage forms have generally been pediatric, geriatric, and bedridden or developmentally disabled patients. Patients with persistent nausea, who are traveling, or who have little or no access to water are also good candidates for FDDTs [10]. Pharmaceutical marketing is another reason for the increase in available orally /disintegrating products. 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 undertreated patient populations [11].

1.1. Biopharmaceutical Consideration [12]

When new drug delivery system put on, it is must that to consider Biopharmaceutical factor like metabolism and excretion.

Pharmacokinetics:

Study has done on absorption, distribution, metabolism and excretion in this consideration. Drug attains therapeutic level after absorption and therefore elicits pharmacological effect, so both rate and extend of absorption is important. There is delay in disintegration and therefore dissolution in conventional dosage form while FDTs is rapidly disintegrates in oral cavity and dissolution is rapid. Due to disintegration of FDTs in mouth absorption in started from mouth, pharynx and esophagus. Some factors like age, GI pH, and blood flow through GI are taken into consideration, because elders may be considered as separate unique Medicare population. There are many factors on which drug distribution depends like tissue permeability, perfusion rate, binding of drug to tissue, disease state, drug interaction etc. In geriatric patients, decrease in body mass and total body water result in decreased volume of distribution of water-soluble drugs and increased volume of distribution (V_d) of lipid soluble drugs. Duration and intensity of action depends upon rate of drug removal from the body or site of action i.e. biotransformation. Decrease in liver volume, regional blood flow to liver reduces the biotransformation of drug through oxidation, reduction and hydrolysis. Excretion by renal clearance is slowed, thus half-life of renal excreted drugs increase.

Pharmacodynamics:

Drug receptor interaction impaired in elderly as well as in young adult due to undue development of organ.

- Decreased ability of the body to respond baro reflexive stimuli, cardiac output, and orthostatic hypotension may see in taking antihypertensive like prazosin.
- Decreased sensitivity of the CVS to β-adrenergic agonist and antagonist. Immunity is less and taken into consideration while administered antibiotics.
- Altered response to drug therapy-elderly show diminished bronchodilator effect of theophylline shows increased sensitivity to barbiturates.
- Concomitant illnesses are often present in elderly, which is also taken into consideration, while multiple drug therapy prescribed.

Research workers have clinically evaluated drug combination for various classes' cardiovascular agents, diuretics, anti-hypertensive in geriatrics. The combination choice depends on disease state of the patient.

1.2. Requirements of fast disintegrating tablets [13]

The tablets should

- Not require water to swallow and should dissolve or disintegrate in the mouth within a few seconds.
- Allow high drug loading.
- Be compatible with taste masking and other excipients.
- Have a pleasing mouth feel.
- Leave minimal or no residue in the mouth after oral administration.
- Have sufficient strength to withstand the rigors of the manufacturing process and post manufacturing handling.
- Exhibit low sensitivity to environmental conditions such as humidity and temperature.
- Be adaptable and amenable to existing processing and packaging machinery.
- Allow the manufacture of tablets using conventional processing and packaging equipments at low cost.

1.3. Advantages of fast disintegrating tablets [14-17]

FDTs offer dual advantages of solid dosage forms and liquid dosage forms along with special features which include:

- **Accurate dosing*:*** 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.
- **Enhanced bioavailability:** Bioavailability of drugs is enhanced due to absorption from mouth, pharynx and esophagus.
- **Rapid action:** Fast onset of therapeutic action as tablet gets disintegrated rapidly along with quick dissolution and absorption in oral cavity.
- **Patient compliance:** No need of water to swallow the dosage form. Hence, it is convenient for patients who are traveling and do not have immediate access to water.
- **Ease of administration:** Convenient to administer specially for geriatric, pediatric, mentally disabled and bed ridden patients who have difficulty in swallowing.
- **Obstruction free:** No risk of suffocation in airways due to physical obstruction when swallowed, thus providing improved safety and compliance.
- **Enhanced palatability:** Good mouth feel, especially for pediatric patients as taste masking technique is used to avoid the bitter taste of drug.
- **Simple packaging:** No specific packaging required. It can be packaged in push through blisters.
- **Business avenue:** Provide new business opportunities in the form of product differentiation, line extension, uniqueness and life cycle management.
- **Cost effective:** Conventional processing and packaging equipments allow the manufacturing of tablets at low cost.

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2. THE NEED FOR DEVELOPMENT OF FAST DISINTEGRATING TABLETS [18]

The need for non-invasive delivery systems persists due to patient's poor acceptance and compliance with existing delivery regimes, limited market size for drug companies and drug uses, coupled with high cost of disease management.

2.1. Patient factors

Fast disintegrating dosage forms are particularly suitable for patients, who for one reason or the other; find it inconvenient to swallow traditional tablets and capsules with an 8-oz glass of water. These include the following:

- Geriatric patients mainly suffering from conditions like hand tremors and dysphasia.
- Pediatric patients who are unable to swallow easily because their central nervous system and internal muscles are not developed completely.
- Traveling patients suffering from motion sickness and diarrhea that do not have easy access to water.
- Patients with persistent nausea for a long period of time are unable to swallow. Especially cancer patients after taking their chemotherapy are too nauseous to swallow the H2 blockers, which are prescribed in order to avoid gastric ulceration.
- Mentally challenged patients, bedridden patients and psychiatric patients.

2.2. Effectiveness factor

Increased bioavailability and faster onset of action are a major claim of these formulations. Dispersion in saliva in oral cavity causes pre-gastric absorption from some formulations in those cases where drug dissolves quickly. Buccal, pharyngeal and gastric regions are all areas of absorption for many drugs. Any pre-gastric absorption avoids first pass metabolism and can be a great advantage in drugs that undergo hepatic metabolism. Furthermore, safety profiles may be improved for drugs that produce significant amounts of toxic metabolites mediated by first-pass liver metabolism and gastric metabolism, and for drugs that have a substantial fraction of absorption in the oral cavity and pre-gastric segments of GIT.

2.3. 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.

3. CHALLENGES IN FORMULATION OF FAST DISINTEGRATING TABLETS (FDTS)

3.1. 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 [19].

3.2. 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 [17,20].

3.3. Aqueous solubility:

Water-soluble drugs pose various formulation challenges because they form eutectic mixtures, which result in freezing-point depression and the formation of a glassy solid that may collapse upon drying because of loss of supporting structure during the sublimation process. Such collapse sometimes can be prevented by using various matrix-forming excipients such as mannitol than can induce crystallinity and hence, impart rigidity to the amorphous composite [21, 22].

3.4. Hygroscopicity:

Several orally disintegrating dosage forms are hygroscopic and cannot maintain physical integrity under normal conditions of temperature and humidity. Hence, they need protection from humidity which calls for specialized product packaging [23].

3.5. 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 [24].

3.6. 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 [25].

3.7. Mouth feel:

FDTs should not disintegrate into larger particles in the oral cavity. The particles generated after disintegration of the FDTs should be as small as possible. Moreover addition of flavours and cooling agents like menthol improve the mouth feel [19].

3.8. 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 [19].

4. DRUG CANDIDATES SUITABLE FOR FAST DISINTEGRATING TABLETS (FDTS) [26]

Several factors must be considered while selecting an appropriate drug candidate for development of orally fast disintegrating dosage forms.

- Drugs which require controlled or sustained release are unsuitable candidates of fast dissolving oral dosage forms.
- Drugs which are very bitter or otherwise unacceptable taste because taste masking cannot be achieved.
- Patients with Sjogren's syndrome or dryness of the mouth due to decreased saliva production may not be good candidates for FDT formulations.
- Drugs with a short half-life and frequent dosing.
- Patients who concurrently take anticholinergic medications may not be the best candidates for these drugs.
- The drugs which have significantly different pharmacokinetic profiles compared with the same dose administered in a conventional dosage form. E.g. selegiline, apomorphine, buspirone etc.
- The drugs that produce a significant amount 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 segments of the pre-gastric GIT.
- 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.

5. DRUGS TO BE PROMISING IN CORPORATE IN FAST DISINTEGRATING TABLETS (FDTS) [27, 28]

Table 1: List of Drug to be incorporate in FDTs

Drug Category	Examples
Analgesics and Anti-inflammatory Agents:	Aloxiprin, Auranofin, Azapropazone, Benorylate, Diflunisal, Etodolac, Fenbufen, Fenoprofen , Calcim, Flurbiprofen, Ibuprofen, Indomethacin, Ketoprofen, Meclofenamic Acid, Mefenamic Acid, Nabumetone, Naproxen, Oxaprozin, Oxyphenbutazone, Phenylbutazone, Piroxicam, Sulindac.
Anthelmintics:	Albendazole, Bephenium Hydroxynaphthoate, Cambendazole, Dichlorophen, Iverrnectin, Mebendazole, Oxarnniquine, Oxfendazole, Oxantel Embonate, Praziquantel, Pyrantel Embonate, Thiabendazole.
Anti-Arrhythmic Agents:	Amiodarone, Disopyramide, Flecainide Acetate, Quinidine Sulphate.
Anti-bacterial Agents:	Benethamine Penicillin, Cinoxacin, Ciprofloxacin, Clarithromycin, Clofazimine, Cloxacillin, Demeclocycline,Doxycycline, Erythromycin, Ethionamide, Imipenem, NalidixicAcid, Nitrofurantoin, Rifampicin, Spiramycin, Sulphabenzamide, Sulphadoxine, Sulphamerazine, Sulphacetamide, Sulphadiazine, Sulphafurazole, Sulphamethoxazole, Sulphapyridine, Tetracycline, Trimethoprim.
Anti-coagulants:	Dicoumarol, Dipyridamole, Nicoumalone, Phenindione.
Anti-Depressants:	Amoxapine, Ciclazindol, Maprotiline, Mianserin, Nortriptyline, Trazodone, Trimipramine Maleate, Acetohexamide, Chlorpropamide, Glibenclamide, Gliclazide, Glipizide, Tolazamide, Tolbutamide.
Anti-Epileptics:	Beclamide, Carbamazepine, Clonazepam, Ethotoin, Methoin, Methsuximide, Methylphenobarbitone, Oxcarbazepine, Paramethadione, Phenacemide, Phenobarbitone, Phenytoin, Phensuximide, Primidone, Sulthiame, Valproic Acid.
Anti-Fungal Agents:	Amphotericin, Butoconazole Nitrate, Clotrimazole, Econazole Nitrate, Fluconazole, Fiucytosine, Griseofulvin, Itraconazole, Ketoconazole, Miconazole, Natamycin,Nystatin, Sulconazole Nitrate, Terbinafine, Terconazole, Tioconazole, Undecenoic Acid.
Anti-Hypertensive Agents:	Amlodipine, Carvedilol, Benidipine, Dilitazem, Diazoxide, Felodipine, Indoramin, Isradipine, Nifedipine, Nimodipine, Phenoxybenzamine, Prazosin, Reserpine.
Anti-Malarials:	Amodiaquine, Chloroquine, Chlorproguanil, Halofantrine, Mefloquine, Proguanil, Pyrimethamine, Quinine Sulphate.
Anti-Migraine Agents:	Dihydroergotamine Mesyiate, Ergotamine Tartrate, Methysergide Maleate, Pizotifen Maleate, Sumatriptan Succinate.
Anti-Muscarinic Agents:	Atropine, Benzhexol, Biperiden, Ethopropazine, Hyoscine Butyl Bromide, Hyoscyarnine, Mepenzolate Bromide, Orphenadrine, Oxyphencylcimine, Tropicamide.
Anti-Neoplastic Agents & Immunosuppressants:	Aminoglutethimide, Amsacrine, Azathiopnne, Busulphan, Chlorambucil, Cyclosporin, Dacarbazine, Estramustine, Etoposide, Lomustine, Melphalan, Mercaptopurine, Methotrexate, Mitomycin, Mitotane, Mitozantrone, Procarbazine, Tamoxifen Citrate, Testolactone.
Anxiolytic, Sedatives, Hypnotics and Neuroleptics:	Alprazolam, Amyiobarbitone, Barbitone, Bentazeparn, Bromazepam, Bromperidol, Brotizoiam, Butobarbitone, Carbromal, Chlordiazepoxide, Chlormethiazole, Chlorpromazine, Clobazam, Clotiazepam, Clozapine, Diazepam, Droperidol, Ethinamate, Flunanisone, Flunitrazepam, Fluopromazine, Flupenuiixol Decanoate, Fluphenazine Decanoate, Flurazepam, Haloperidol, Lorazepam, Lormetazepam, Medazepam, Meprobamate, Methaqualone, Midazolam, Nitrazepam, Oxazepam, Pentobarbitone, Perphenazine Pimozide, Prochlorperazine, Suipiride, Temazepam, Thioridazine, Triazolam, Zopiclone.
Anti-Parkinsonian Agents:	Bromocriptine Mesylate, Lysuride Maleate.
Anti-Gout Agents:	Allopurinol, Probenecid, Sulphinpyrazone.
Anti- Protozoal Agents:	Benznidazole, Clioquinol, Decoquinate, Diiodohydroxyquinoline, Diloxanide Furoate, Dinitolmide, Furzolidone, Metronidazole, Nimorazole, Nitrofurazone, Omidazole, Tinidazole.
Anti-Thyroid Agents:	Carbimazole, Propylthiouracil.
β-Blockers:	Acebutolol, Alprenolol, Atenolol, Labetalol, Metoptolol, Oxprenolol, Propranolol.
Cardiac Inotropic Agents:	Amrinone, Digitoxin, Digoxin, Enoximone, Lanatoside C, Medigoxin.
Corticosteroids:	Beclomethasone, Betamethasone, Budesonide, Cortisone Acetate, Desoxymethasone, Dexamethasone, Fludrocortisone Acetate, Flunisolide, Flucortolone, Fluticasone Propionatu, Hydrocortisone, Methylprednisolone, Prednisolone, Prednisone, Triamcinolone.
Diuretics:	Acetazolarnide, Amiloride, Bendrofluazide, Bumetanide, Chlorothiazide, Chlorthalidone, Ethacrynic Acid, Frusemide, Metolazone, Spironolactone, Triamterene
Gastro-Intestinal Agents:	Bisacodyi, Cimetidine, Cisapride, Diphenoxylate, Domperidone, Famotidine, Loperamide, Mesalazine, Nizatidine, Omeprazole, Ondansetron, Ranitidine, Sulphasaiazine.

Histamine H,-Receptor Antagonists:	Acrivastine, Astemizole, Cinnarizine, Cyclizine, Cyproheptadine, Dimenhydrinate, Flunarizine, Loratadine, Meclozine, Oxatomide, Terfenadine, Triprolidine.
Lipid Regulating Agents:	Bezafibrate, Clofibrate,Fenofibrate, Gemfibrozil, Probucol.
Nitrates and Other Anti-Anginal Agents:	Amyl Nitrate, Glyceryl Trinitrate, Isosorbide Dinitrate, Isosorbide Mononitrate, Pentaerythritol Tetranitrate.
Nutritional Agents:	Betacarotene, Vitamin A, Vitamin B 2 ,Vitamin D, Vitamin E, Vitamin K.
Opioid Analgesics:	Codeine, Dextropropyoxyphene, Diamorphine, Dihydrocodeine, Meptazinol, Methadone, Morphine, Nalbuphine, Pentazocine.
Local Anaesthetics:	Lidocaine
Neuro -Muscular Agents:	Pyridostigmine.
Proteins, Peptides and Recombinant Drugs:	Insulin (Hexameric/Dimeric/Monomeric Forms), Glucagon, Growth Hormone (Somatotropin), Polypeptides or their Derivatives, (Preferably with a molecular weight from 1000 to 300,000), Calcitonins and synthetic modifications there of, Enkephalins, Interferons (Especially Alpha-2 Interferon for treatment of common colds).
Sex Hormones:	Clomiphene Citrate, Danazol, Ethinyloestradiol, Medroxyprogesterone Acetate, Mestranol, Methyltestosterone, Norethisterone, Norgestrel, Oestradiol, Conjugated Oestrogens, Progesterone, Stanozolol, Stiboestrol, Testosterone, Tibolone.
Stimulants:	Amphetamine, Dexamphetamine, Dexfenfluramine, Fenfluramine, Mhazindol, Pemoline.

6. EXCIPIENTS COMMONLY USED FOR FDTs PREPARATION

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

Table 2: Name and weight percentage of various excipients

Name of the excipients	Percentage used
Superdisintegrants	1-15 %
Binder	5-10 %
Antistatic agent	0-10 %
Diluents	0-85 %

6.1. Superdisintegrants:

In recent years, several newer agents have been developed known as "Superdisintegrants". A "Superdisintegrants" is an excipient, which is added to tablet or capsule blend to aid in the breakup of the compacted mass, when put into a fluid environment. This is especially important for immediate release product where rapid release of the product is required [29]. These newer substances are more effective at lower concentrations with greater disintegrating efficiency and mechanical strength. The use of superdisintegrants is the basic approach in the development of fast disintegrating tablets (FDTs). Superdisintegrants plays a major role in the dissolution and disintegration of the tablets. It is essential to choose an optimum concentration of superdisintegrants so as to ensure rapid disintegration and high dissolution rates of tablets [30]. Superdisintegrants provide rapid 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 [31-33]. The optimum concentration of the superdisintegrant can be selected according to the critical concentration of the disintegrant. Below this concentration, the tablet disintegration time is inversely proportional to the concentration of the superdisintegrant, where as above this concentration the disintegration time remains almost constant or even increases [34].

Common superdisintegrants used in formulation are croscarmellose sodium (Vivasol, Ac-Di-Sol), crospovidone (Polyplasdone), carmellose (NS-300), carmellose calcium (ECG-505), sodium starch glycolate (SSG) etc. Recently few ion exchange resins (e.g. Indion 414) are found to have superdisintegrant property and are widely used in pharmaceutical industry.

Table 3: List of super disintegrants [9]

Superdisintegrants	Example	Mechanism Of Action	Special comment
Crosscarmellose® Ac-Di-Sol® Nymce ZSX® Primellose® Solutab® Vivasol® L-HPC	Crosslinked cellulose	-Swells 4-8 folds in < 10 seconds. -Swelling and Wicking both.	-Swells in two dimensions. -Direct compression or granulation -Starch free
Crosspovidone Crosspovidon M® Kollidon® Polyplasdone®	Crosslinked PVP	-Swells very little And returns to original size after compression but act by capillary action	-Water insoluble and spongy in nature so get porous tablet
Sodium starch glycolate Explotab® Primogel®	Crosslinked starch	-Swells 7-12 folds in < 30 seconds	-Swells in three dimensions and high level serve as sustain release matrix
Alginic acid NF Satialgine®	Crosslinked alginic acid	-Rapid swelling in aqueous medium or wicking action	-Promote disintegration in both dry or wet granulation
Soy polysaccharides Emcosoy®	Natural super disintegrant	-	-Does not contain any starch or sugar. Used in nutritional products.
Calcium silicate		-Wicking Action	Highly porous, Optimum concentration is b/w 20-40%

Mechanism of action of superdisintegrants [35]

The tablet breaks to primary particles by one or more of the mechanisms listed below: -

(a) Porosity and capillary action (Wicking)

Capillary action **(figure 1)** is always the first step in tablet disintegration. Suitable aqueous medium into which tablet is placed, penetrates into the tablet and replaces the air adsorbed on the particles there by weakens the intermolecular bond and breaks the tablet into fine particles. Water uptake by tablet depends upon hydrophilicity of the drug /excipients 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.

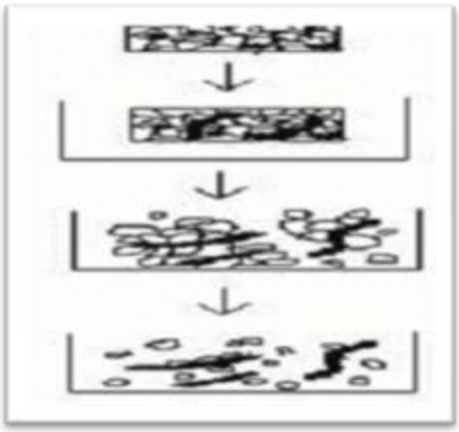

Figure 1: Porosity and capillary action (Wicking) [9, 35, 47] (*Disintegrant pull water into the pores and reduces the physical bonding forces between the particles)*

(b) Swelling

The general mechanism of action for tablet disintegration is swelling **(Figure 2).**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 to penetrate in the tablet and disintegration is again slows down.

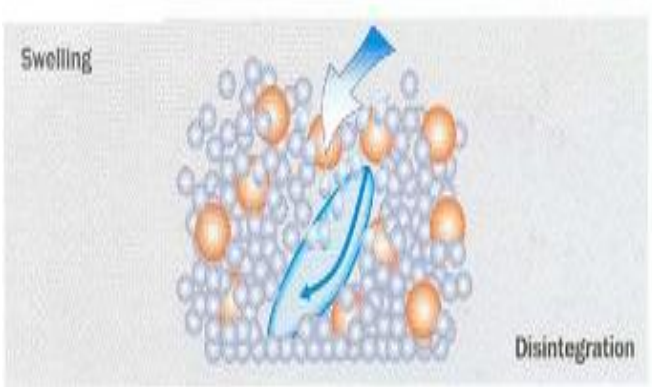

Figure 2: Swelling [47] *(Particles swell and break up the matrix form within; swelling sets up; localized stress spread through out the matrix)*

(c) Due to disintegrating particle/particle repulsive forces

Another mechanism of disintegrating attempts to explain the swelling of tablet made with 'non swellable' disintegrants. Guyot-Hermann has proposed a particle repulsion theory **(figure 3)** 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.

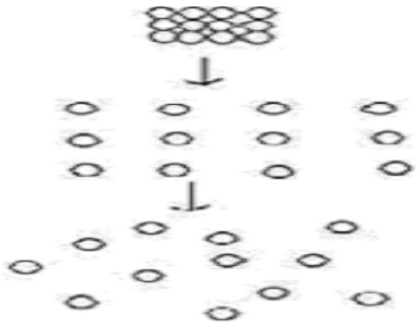

Figure 3: Repulsion Theory [9, 35] (Water is drawn into the pores and particles repel

each other due to the resulting electrical force)

(d) Due to deformation :(Elastic recovery)

Most materials, which undergo a plastic deformation during compression, try to return to their initial shape as soon as possible (stored potential energy). In the tablet matrix, there is no means to recover the former shape. But as soon as water penetrates into the tablet matrix and the forces, which keep the particles together, are diminished, those particles have the ability to expand back.

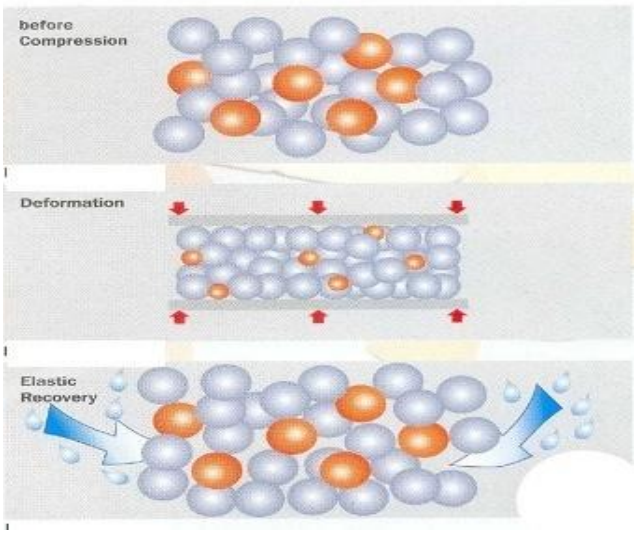

Figure 4: Elastic recovery [47]

In **figure 4** elastic particles are shown before compression (red). After compression, these particles are plastically deformed. After penetration of water into the tablet, these particles return back to their initial shape.

(e) Due to release of gases

Carbon dioxide released with in tablets on wetting due to interaction between bicarbonate and carbonate with citric acid or tartaric acid. The tablet disintegrates due to

generation of pressure with in 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 two separate fraction of formulation.

(f) 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.

(g) Because of heat of wetting (air expansion)

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

6.2 Binders:

The choice of a binder is critical in a fast- dissolving formulation for achieving the desired sensory and melting characteristics, and for the faster release of active ingredient. Binders can either be liquid, semi solid, solid or mixtures of varying molecular weights such as polyethylene glycol. Main role of Binders is to keep the composition of these fast-melting tablets together during the compression stage. Binders commonly used are cellulosic polymers, povidones, polyvinyl alcohols, and acrylic polymers. Among the cellulosic polymers it will be advantageous to select ethylcellulose, hydroxypropylcellulose (HPC), and hydroxypropylmethylcellulose (HPMC), alone or in admixtures, and the most commonly acrylic polymer used are the ammonio-methacrylate copolymer (Eudragit. RL and RS), polyacrylate (Eudragit NE), and polymethacrylate (Eudragit E). The temperature of the excipient should be preferably around 30–35°C for faster melting properties. Further, its incorporation imparts smooth texture and disintegration characteristics to the system.

6.3. Antistatic agent and diluents

The most common antistatic agents used are colloidal silica (Aerosil), precipitated silica (Sylod.FP244), micronized or non- micronized talc, maltodextrins, beta.-cyclodextrins, etc. Magnesium stearate, stearic acid, sodium stearylfumarate, micronized polyoxyethylene glycol (micronized Macrogol 6000), leucine, sodium benzoate are used as lubricant. An additional thickening agent, generating a stabilized suspension, is added to avoid settling of the particles and moreover provide a pleasant mouth feeling. Commonly used Diluents are most commonly selected from cellulose derivatives and preferably microcrystalline cellulose, starches, lactose, polyols and preferably mannitol. [36]

7. VARIOUS TECHNIQUES FOR "FDTs" PREPARATION: Many techniques are used for the preparation of fast disintegrating tablets which are shown in table 4.[16, 21, 30, 37, 38]

Table 4: Different techniques with method and characteristics of prepared fast disintegrating tablets

S.No.	Techniques	Method and characteristics of prepared FDTs
1	**Disintegrant addition**	The basic principle involved in formulating Fast disintegrating tablets by disintegrates addition technique is addition of superdisintegrants in optimum concentration so as to achieve mouth dissolving along with the good mouth feel. Sodium starch glycolate, crospovidone and crosscarmellose are some of the popular superdisintegrants. **Characteristics:** Similar to conventional tablets with higher % of disintegrants, lower hardness and higher % of friability.
2	**Freeze Drying or Lyophilization**	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. The drug is dissolved or dispersed in an aqueous solution of a carrier. The mixture is poured into the wells of the preformed blister packs. The trays holding the blister packs are passed through liquid nitrogen freezing tunnel to freeze the drug solution. Then the frozen blister packs are placed in refrigerated cabinets to continue the freeze-drying. **Characteristics:** The preparations are highly porous, have high specific surface area, dissolve rapidly and ultimately show improved absorption and bioavailability.
3	**Tablet Molding**	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 hydroalcoholic solvent and is molded into tablets under pressure lower than that used in conventional tablet compression. The solvent is then removed by air drying. **Characteristics:** Molded tablets are very less compact than compressed tablets. These possess porous structure that enhances dissolution.
4	**Sublimation**	Inert solid ingredients that volatilize rapidly like urea, camphor ammonium carbonate, ammonium bicarbonate, hexamethylenetetramine) 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 structure. **Characteristics:** Porous structure that enhances dissolution by using volatile material or solvent e.g. cyclohexane, benzene etc.
5	**Spray-Drying**	The formulations are incorporated by hydrolyzed and non hydrolyzed gelatins as supporting agents, mannitol as bulking agent, sodium starch glycolate or crosscarmellose sodium as disintegrating and an acidic material (e.g. citric acid) and or alkali material (e.g. sodium bicarbonate) to enhance disintegration and dissolution.

		Characteristics: Prepared tablet disintegrates within 20 seconds when immersed in an aqueous medium.
6.	**Direct Compression**	Direct compression method is the easiest way to manufacture tablets. Conventional equipment, commonly available excipients and a limited number of processing steps are involved in direct compression. **Characteristics:** It is most cost effective tablet manufacturing technique.
7	**Mass-Extrusion**	This technology involves softening the active blend using the solvent mixture of water soluble polyethylene glycol, using methanol and expulsion of softened mass through the extruder or syringe to get a cylinder of the product into even segments using heated blade to form tablets. **Characteristics:** The dried product can be used to coat granules of bitter tasting drugs and thereby masking their bitter taste.
8.	**Cotton candy process**	Involves the formation of matrix of polysaccharides by simultaneous action of flash melting and spinning. This candy floss matrix is then milled and blended with active ingredients and excipients after re-crystallization and subsequently compressed to FDTs. **Characteristics:** It can accommodate high doses of drug and offers improved mechanical strength
9	**Nanonization**	Involves size reduction of drug to nanosize by milling the drug using a proprietary wet-milling technique. The nanocrystals of the drug are stabilized against agglomeration by surface adsorption on selected stabilizers, which are then incorporated into FDTs. **Characteristics:** It is used for poorly water soluble drugs. It leads to higher bioavailability and reduction in dose, cost effective manufacturing process, conventional packaging due to exceptional durability and wide range of doses (up to 200 mg of drug per unit).
10	**Compaction** **a)Melt granulation** b) **Phase-transition process**	Prepared by incorporating a hydrophilic waxy binder (super polystate) PEG-6-stearate. Super polystate not only acts as binder and increase physical resistance of tablet but also helps the disintegration of tablet. **Characteristics:** It melts in the mouth and solubilizes rapidly leaving no residue. Prepared by compressing a powder containing two sugar alcohols with high and low melting points and subsequent heating at a temperature between their melting points. The tablet hardness was increased after heating process due to increase of inter particle bond induced by phase transition of lower melting point sugar alcohol. **Characteristics:** The compatibility increased and so sufficient hardness gained by the formulation.
11	**Fast Dissolving Films**	A non-aqueous solution is prepared containing water soluble film forming polymer (pullulan, carboxymethylcellulose, hydroxypropyl methylcellulose, hydroxyl ethyl cellulose, hydroxyl propylcellulose, polyvinyl pyrrolidone, polyvinyl alcohol or sodium alginate, etc.), drug and other taste masking ingredients are used to form a film after evaporation of solvent. In case of a bitter drug, resin adsorbate or coated micro particles of the drug can be incorporated into the film. **Characteristics:** The thin films size less than 2X2 inches, dissolution in 5 sec, instant drug delivery and flavored after taste

8. IMPORTANT PATENTED TECHNOLOGIES FOR FAST DISINTEGRATING TABLETS

8.1. Zydis technology: Zydis formulation is a unique freeze dried tablet in which drug is physically entrapped or dissolved within the matrix of fast-dissolving carrier material**.** 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 materials designed to achieve a number of objectives. To impart strength during handling, polymers such as gelatin, dextran or alginates are incorporated. These form a glossy amorphous structure, which imparts strength. To obtain crystallinity, elegance and hardness, saccharides such as mannitol or sorbitol are incorporated. Water is used in the manufacturing process to ensure production of porous units to achieve rapid disintegration. Various gums are used to prevent sedimentation of dispersed drug particles in the manufacturing process. Collapse protectants suchas glycines prevent the shrinkage of zydis units during freeze drying process or long term storage. Zydis products are packed in blister packs to protect the formulation from moisture in the environment.[39, 40]

8.2. Orasolv technology: Orasolv technology has been developed by "CIMA" labs. This technology involves taste masking of active drug. Effervescent disintegrating agent is also used. Conventional blenders and tablet equipments are used for preparation of tablets. Less force of compaction is used for manufacturing to obtain soft and quickly disintegrating tablets. There is a limitation of this technology that soft and fragile tablets are formed, therefore needed to be packed in specially designed pick and place package system.

8.3. Durasolv technology: DuraSolv is Cima's second-generation fast-dissolving/ disintegrating tablet formulation. This is one of the suitable technologies to prepare products requiring low amounts of active drug. This technology uses drug, fillers and a lubricant to prepare the tablet. Conventional tableting equipment is used to prepare the tablet. Due to higher force of compaction used, tablets prepared are rigid. Dosage form can be packaged into conventional packaging system like blisters.[41]

8.4. Wowtab technology: Wowtab Technology is patented by Yamanouchi Pharmaceutical Co. WOW means "Without Water ".The active ingredients may constitute upto 50% w/w of the tablet. In this technique, saccharides of both low and high mouldability are used to prepare the granules. Mouldability is the capacity of a compound to be compressed. Highly mouldable substance has high compressibility and thus shows slow dissolution. The combination of high and low mouldability is used to

produce tablets of adequate hardness. Active ingredients are mixed with low mouldability saccharides and then granulated with high mouldabiity saccharides and then compressed into tablet. The Wowtab product dissolves quickly in 15 s or less. Wowtab product can be packed in both into conventional bottle and blister packs. [42]

8.5. Flashtab technology: The Flashtab technology is yet another fast dissolving/disintegrating tablet formulation. Prographarm laboratories have patented the Flashtab technology. It utilizes most of the same excipients as in conventional compressed tablets. A disintegrating agent and a swelling agent are used in combination with coated drug particles in this formulation to produce a tablet that disintegrates in the mouth in less than one minute. [43]

8.6. 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. [44,45,46]

8.7. Flash Dose technology: Flash dose technology has been patented by Fuisz. Nurofen meltlet, a new form of Ibuprofen as melt-in-mouth tablets. Flash dose tablets consist of self binding shear form matrix termed as "floss". Shear form matrices are prepared by flash heat processing. [47]

8.8. Frosta technology: Akina patents this technology. It utilizes the concept of formulating plastic granules and compressing them 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 mixing the porous plastic material with water penetration enhancer followed by granulating with binder. The tablets obtained have excellent hardness and rapid disintegration time ranging from 15 to 30 sec depending on size of tablet.[10]

8.9. Sheaform Technology: The technology is based on the preparation of floss that is also known as 'Shearform Matrix', which is produced by subjecting a feed stock containing a sugar carrrier by flash heat processing. In this process, the sugar is simultaneously subjected to centrifugal force and to a temperature gradient, which raises the temperature of the mass to create an internal, flow condition, which permits part of it to move with respect of the mass. The floss so produced is amorphous in nature so it is further chopped and recrystallised by various techniques to provide aciform flow properties and this facilitate blending the recrystallised matrix is then blended with other tablet excipients and an active ingredient. The resulting mixture is compressed into tablet.[48]

8.10. Ceform Technology: In ceform technology microspheres containing active ingredient are prepared. The essence of ceform microsphere manufacturing process involves placing a dry powder, containing substantially pure drug material or a special blend of drug materials plus other pharmaceutical compounds, and excipients into a precision engineered and rapidly spinning machine. The centrifugal force of the rotating head of the ceform machine throws the dry drug blend at high speed through small heated openings. The microspheres are then blended and/or compressed into the pre-selected oral delivery dosage format. The ability to simultaneously process both drug and excipient generates a unique microenvironment in which materials can be incorporated into the microsphere that can alter the characteristics of the drug substance.[48]

8.11. Pharmaburst technology: Pharmaburst™ is a "Quick Dissolve" delivery system patented by SPI Pharma. Pharmaburst is a co-processed excipient system with specific excipients, which allows rapid disintegration and low adhesion to punch faces mouldablilty saccharine are used to obtain rapid melting strong tablet. The active ingredient mixes with low mouldablilty saccharides.[49]

8.12. Lyoc tech: This is patented technology of Laboratories L. Lafon, Maisons Alfort, France .It utilizes a freeze drying process but differ from Zydis in that the product is frozen on the freeze dryer shelves. To prevent inhomogeneity by sedimentation during this process, these formulations require a large proportion of undissolved inert filler (mannitol), to increase the viscosity of the inprocess suspension. The high proportion of filler reduces the potential porosity of the dried dosage form and results in denser tablets with disintegration rates that are comparable with the loosely compressed fast melt formulations.[49]

8.13 OraQuick-: KV Pharmaceutical claims its microsphere technology, known as MicroMask, has superior mouth feel over taste-masking alternatives. The taste masking process does not utilize solvents of any kind, and therefore leads to faster and more efficient production. Also, lower heat of production than alternative fast-dissolving/disintegrating technologies makes OraQuick appropriate for heat-sensitive drugs. KV Pharmaceutical also claims that the matrix that surrounds and protects the drug powder in microencapsulated particles is more pliable, meaning tablets can be compressed to achieve significant mechanical strength without disrupting taste masking. OraQuick claims quick dissolution in a matter of seconds, with good taste-masking. There are no products using the OraQuick technology currently on the market, but KV Pharmaceutical has products in development such as analgesics, scheduled drugs, cough and cold, psychotropics, and anti-infectives.[49]

8.14. Quick-Dis Technology: 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,

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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. [49]

8.15. 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 formulation was a disintegrating agent. It provides rapid swelling and/or good wetting capability to the tablets and thereby a quick disintegration. The disintegrating agents include starch or modified starches, microcrystalline cellulose, alginic acid, cross-linked sodium carboxymethyl cellulose, and cyclodextrin polymers. A combination of two or more disintegrating agents produced better disintegration results. [50, 51]

8.16. Nanocrystal technology: For fast disintegrating 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 & patent-protected technology elements.
- Cost-effective manufacturing processes that utilize conventional, scalable unit operations.
- Exceptional durability, enabling use of conventional packaging equipment & formats (bottles &/or blisters).
- Wide range of doses (up to 200mg of API per unit).
- Use of conventional, compendial inactive components.
- Employment of non-moisture sensitive in-actives.

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 FDT dosage forms because manufacturing losses are negligible. [52, 53]

List of Patented technologies based branded Products: The list of patented technologies and their brand products are given in table 5. [26]

Table 5: For patented technology and their brand products

S. N.	Technology	Process involved	Patent owner	Drugs Used (Brand name)
1	Zydis	Lyophilization	R.P.Scherer Inc.	Loratidine (Claritin Reditab and Dimetapp Quick Dissolve)
2	Quicksolv	Lyophilization	Jansen Pharmaceutical	Cisapride monohydrate (Propulsid Quicksolv), Risperidone (Risperdal M-tab)
3	Flashtab	Lyophilization	Ethypharm	Ibuprofen (Nurofen Flashtab)
4	Lyoc	Multiparticulate Compressed tablets	Farmlyoc	Phloroglucinol Hydrate (Spasfon Lyoc)
5	Orasolv	Compressed Tablets	Cima Labs Inc.	Paracetamol (Tempra Quicklets), Zolmitriptan (Zolmig Repimelt)
6	Durasolv	Molding	Cima Labs Inc.	Hyoscyamine Sulfate (NuLev), Zolmitriptan (ZMT)
7	Rapitab	Compressed Tablets	Schwarz Pharma	-
8.	Wow tab	Compressed Molded Tablets	Yamanouchi Pharma Technologies, Inc.	Famotidine (Gaster D)
9	Fast melt	Molding	Élan Corp.	-
10	Ziplets	Molding	Eurand	Ibuprofen (Cibalgina Due Fast)
11	Flashdose	Cotton candy process	Fuisz Technology Ltd	Tramadol HCl (Relivia Flash dose)
12	Oraquick	Micromask taste Masking	KV Pharm. Co., Inc.	Hyoscyamine Sulfate ODT
13	Advatab	Microcaps & diffuscap CR Technology	Eurand International	AdvaTab cetrizine, AdvaTab Paracetamol

9. Marketed products: The commercialized products of FDTs which are available in market are given in table 6.[26]

Table 6: Marketed products

Brand/ Trade name	Active Drug	Manufacturer Company
Benadryl Fastmelt	Diphenhydramine	Pfizer
Benadryl Fast melt	Diphenhydramine	Warner Lambert
Cibalginadue FAST	Ibuprofen	Novartis Consumer Health
Domray MD	Domperidone	Ray Remedies
Dolib MD	Rofecoxib	Panacea
Feldene melt	Piroxicam	Pfizer
Febrectol	Paracetamol	Prographarm
Imodium Instant melts	Loperamide Hcl	Janssen
Kemstro	Baclofen	Schwarz Pharma
Klonopin Wafers	Clonaxepam	Roche
Maxalt-MLT	Rizatriptan Benzoate	Merck
Mosid MT	Mosapride	Torrent
Nulev	Hyoscyamine sulfate	Schwarz Pharma
Nimulid MD	Nimusulide	Panacea
Orthoref MD	Rofecoxib	Biochem
Olanex Instab	Olanzepine	Ranbaxy
Pepcid ODT	Famotidine	Merck
Rofaday MT	Rofecoxib	Lupin
Torrox MT	Rofecoxib	Torrent
Valus	Valdecoxib	Glenmark
Zotacet MD	Cetrizine Hcl	Zota Pharma
Zyprexa	Olanzapine	Eli lilly
Zofran ODT	Ondansetron	GSK
Zomig ZMT and Rapimelt	Zolmitriptan	Astra Zeneca
Claritin redi Tab	Loratidine	Schering plough Corp., USA
Olanex instab	Olanzapine	Ranbaxy lab. Ltd. New-Delhi, India
Romilast	Montelukast	Ranbaxy lab. Ltd. New-Delhi, India

10 EVALUATION OF FAST DISINTEGRATING TABLETS: Tablets from all the formulation were subjected to following quality control test.[54, 55]

10.1. General Appearance: The general appearance of a tablet, its visual identity and over all "elegance" is essential for consumer acceptance and tablet's size, shape, colour, presence or absence of an odour, taste, surface texture, physical flaws and consistency and legibility of any identifying marking.

10.2. Size and Shape: The size and shape of the tablet can be dimensionally described, monitored and controlled.

10.3. Tablet thickness: Tablet thickness is an important characteristic in reproducing appearance and also in counting by using filling equipment. Some filling equipment utilizes the uniform thickness of the tablets as a counting mechanism. Ten tablets were taken and their thickness was recorded using micrometer.

10.4. Weight variation: 20 tablets were selected randomly from the lot and weighted individually to check for weight variation. Weight variation specification as per I.P. is shown in following table 7.

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

10.5. 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.

10.6. Friability (F): Friability of the tablet determined using Roche friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at height of 6 inches in each revolution. Pre -weighted sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. The friability (F) is given by the formula.

$$F = \frac{W_{int.} - W_{fin}}{W_{int.}}$$

Where, W_{int} - Weight of tablets before friability.

W_{fin} - Weight of tablets after friability.

10.7. Wetting Time: Wetting time of dosage form is related to the contact angle. It needs to be assessed to give an insight into the disintegration properties of the tablets; a lower wetting time implies a quicker disintegration of the tablet. For this purpose, a tablet is placed on a piece of tissue paper folded twice and kept in a small Petri dish (ID = 6.5 cm) containing 6 ml of water, and the time for complete wetting is measured.

10.8. Water absorption Ratio: A piece of tissue paper folded twice was placed in a small Petridish containing 6 ml of water. A tablet was put on the paper & the time required for complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio, R, was determined using following equation,

$$R = 10 (w_a/w_b)$$

Where, w_a is weight of tablet before water absorption &

w_b is weight of tablet after water absorption.

10.9. In vitro dispersion time: In vitro dispersion time was measured by dropping a tablet in a beaker containing 50 ml of Sorenson's buffer pH 6.8. Three tablets from each formulation were randomly selected and in vitro dispersion time was performed.

10.10. In vitro Dissolution test: The development of dissolution methods for FDTs is comparable to 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 FDT. Other media such as 0.1 M HCl and buffer (pH 4.5 and 6.8) should be evaluated for FDT much in the same way as their ordinary tablet counterparts. It has been suggested that USP 2 paddle apparatus is the most suitable and common choice for orally disintegrating tablets, with a paddle speed of 50 rpm commonly used.

10.11. Stability testing of drug (temperature dependent stability studies): The fast disintegrating tablets are packed in suitable packaging and stored under the following conditions for a period as prescribed by ICH guidelines for accelerated studies.

(1) 40 ± 1 °C

(2) 50 ± 1°c

(3) 37 ±1 ° C and RH 75% ± 5%

The tablets were withdrawn after a period of 15 days and analyzed for physical characterization (Visual defects, Hardness, Friability, Disintegrations and Dissolution etc.) and drug content. The data obtained is fitted into first order equations to determine the kinetics of degradation. Accelerated stability data are plotting according Arrhenius equation to determine the shelf life at 25°C.

10.12. Packaging: Packing is one of the important aspects in manufacturing FDT. The products obtained by various technologies vary in some of the parameters especially in mechanical strength to a good extent. The products obtained by lyophilization process including various technologies such has Zydis, Lyoc, Quicksolv, and Nanocrystal 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, Ziplets, etc. technologies have sufficient mechanical strength to withstand transport and handling shock so they are generally packed in push through blisters or in bottles.[12]

CONCLUSION: FDTs is a growing technology, offering considerable benefits for lifecycle management, development timelines, patient convenience and market share. By paying close attention to advances in technologies, pharmaceutical companies can take advantage of FDTs for product line extensions or for first-to-market products. With continued development of new pharmaceutical excipients, one can expect the emergence of more novel technologies for FDTs in the days to come. The successful marketed FDTs have good taste and rapid release properties. With rapid acceptance of FDTs by patients and pharmaceutical companies, the market for this dosage form is promising, and the product pipeline continues to grow rapidly. The clinical studies show FDTs can improve patient compliance, provide a rapid onset time of action, and increase bioavailability. Considering the many benefits of FDTs, it is only a matter of time until a majority of oral formulations are prepared in FDT forms.

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