World Journal of Pharmaceutical Sciences
ISSN (Print): 2321-3310; ISSN (Online): 2321-3086
Published by Atom and Cell Publishers
Available online at: http://www.wjpsonline.org/
Review Article

A review on fast dissolving tablets (FDTs)

Chhote Lal Singh, Neeraj Rajput*, MunishGarg Monga

R. V. Northland Institute, Chithera, Dadri, GautamBudh Nagar, Uttar Pradesh, India-203207

Received: 27-09-2014 / Revised: 15-10-2014 / Accepted: 21-10-2014

ABSTRACT

The oral route is the most acceptable routes among the various routes for different age group of the patients because it is regarded as safest, most convenient and economical route. Therefore, recently researcher and pharmaceutical companies developed the fast dissolving tablet (FDT) by modifying the physiochemical parameter of drugs to their need with improved patient compliance and convenience. FDTs are solid dosages forms which dissolve rapidly in saliva without chewing and additional water. USFDA define FDTs to be the solid oral preparation that disintegrate rapidly in the oral cavity with an in-vitro disintegration time of 30 seconds or less. FDTs improved patient compliance and also overcome the disadvantages of conventional dosage form especially dysphagia (difficulty in swallowing) in pediatric and geriatric patients. Over the last decade FDTs have grown steadily in demand and importance as a convenient, potentially safer alternative to conventional tablets and capsules. The growing importance for this is due to the potential advantages offered by this technology for various kinds of patients suffering from different diseases and disabilities. This review includes ideal properties, characteristics, challenges in formulation, suitability of drug candidates, various technologies developed for FDT, patented technologies, evaluation methods and various marketed products.

Keywords: Fast dissolving tablets (FDT), Superdisintegrants, Bioavailability, Evaluation

INTRODUCTION

Drug delivery system (DDS) makes a significant contribution to global pharmaceutical sales through market segmentation and moving rapidly [1]. Oral administration is the most popular route for systemic effects due to its ease of ingestion accurate dosage, self-medication, pain avoidance and most important patient compliance.The most popular dosage forms are conventional tablets and hard gelatin capsules. One important drawback of such dosage forms is Dysphagia (Difficulty in swallowing) for many patients almost 50% of the population is affected by such problem. [2] In the elderly population dysphagia is either a part of the aging process or a consequence of a disease, such an advanced Alzheimer's disease, stroke or cancer. The magnitude of the problem is significant because oral abnormalities were seen in 63% and pharyngeal dysfunction was seen in 25% of 56 subjects with a mean age of 83 years [3].Injections 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 increase research in biopharmaceuticals so far has generate predominantly chemical entities with low molecular weight [4]. Drinking water plays important role for swallowing of oral dosage forms. In some cases such as motion sickness, sudden episodes of allergic attacks or coughing and unavailability of water, swallowing conventional tablets may be difficult [5]. To solve these problems, fast disintegration tablets have started which gaining popularity and acceptance as new drug delivery systems aim for providing the safety of a drug molecule because they are easy to administer and lead to better patient compliance [6]. Fast disintegrating tablets are also known as "Fast-dissolving", "Mouth-dissolving", "Rapid-dissolve", "Quick-disintegration", "Orally-disintegrating", "Rapimelt", "Fast-melt", "Orodispersible", "Melt-in-mouth", "Quick-dissolving", "Porous tablets" and "Effervescent drug absorption system". [7] During the past decade, the FDT technology makes tablets dissolve or disintegrate in the mouth without additional water intake, has drawn a greater deal of attention. The tablets disintegrate into smaller granules or melt in the mouth from a hard solid structure to a gel like structure, allowing by patients. The disintegration time for those tablets varies from a fewseconds to more than a minute. [8] Table

***Corresponding Author Address: Neeraj Rajput,** R. V. Northland Institute, Dadri, Greater Noida, GautamBuddh Nagar, Uttar Pradesh-203 207, India; E-mail: neeraj.rajput37@gmail.com and chhotelal007@gmail.com*

1.describessome examples of commercially available product on the market. It also lists the information of the drugs, technology, marketing company and company that developed the technology.

A major claim of these FDDTs is increased bioavailability compared to traditional tablets. Because of dispersion in saliva while still in oral cavity, there can be pre-gastric absorption from some formulation in those case where the drug dissolve quickly. Buccal, pharyngeal, and gastric regions are all areas of absorption of many formulations. Any pregastric absorption avoids first pass metabolism and can be a great advantage in drug that undergo a great deal of hepatic metabolism. [9]

BIOPHARMACEUTICAL CONSIDERATION [2, 4, 13]: When new drug delivery system put on, it is most important that to consider Biopharmaceutical factor like metabolism and excretion.

Pharmacokinetic: Study has done on absorption, distribution, metabolism and excretion in the consideration. Drug attains therapeutic level when it completely absorbed and therefore elicits pharmacological effect, so both rate and extend of absorption is important. In conventional dosage form, there is delay in disintegration and therefore dissolution while FDT is rapidly disintegrates in oral cavity and dissolution is fast. When FDTs is disintegrating in mouth then absorption 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. Many factors like tissue permeability, perfusion rate, binding of drug to tissue, disease state, drug interaction etc depends on drug distribution. 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 (Vd) of lipid soluble drugs.Intensity of action and duration 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.
- Concomitant illnesses are often present in elderly, which is also taken into consideration, while multiple drug therapy prescribed.
- Altered response to drug therapy-elderly show diminished bronchodilator effect of theophylline shows increased sensitivity to barbiturates.
- Immunity is less and taken into consideration while administered antibiotics.

  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.

DESIRED CRITERIA FOR FDTs [10, 11]

Fast Dissolving Tablet should-

- Require no water for oral administration but it should dissolve or disintegrate in the mouth within few seconds.
- Have a pleasing mouth feel.
- Leave minimal or no residue in the mouth after oraladministration.
- Rapid dissolution and absorption of drug, which mayproduce rapid onset of action.
- Exhibit low sensitivity to environment condition such as humidity and temperature.
- Allow the manufacture of tablets using conventional processing and packaging equipment at low cost.
- Ability to provide advantages of liquid medication inthe form of solid preparation.
- Some drugs are absorbed from the mouth, pharynxand esophagus as the saliva passes down into thestomach, and in such cases bioavailability of drugs is increased.

THE NEED FOR DEVELOPMENT OF FAST DISINTEGRATING TABLETS [2, 4, 15]

Fast disintegrate tablets are developed due topatient'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.

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 suffering from hand tremors and dysphasia condition.

- Central nervous system and internal muscles of pediatric patients are not developed completely so they are unable to swallow easily.
- Patients who travel 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.
- Bedridden patients, mentally challenged patients and psychiatric patients.

Effectiveness factor: Dispersion in saliva in oral cavity causes pre-gastric absorption of drug which dissolves. Buccal, pharyngeal and gastric regions are all areas of absorption for man drugs. Any pre-gastric absorption avoids first pass hepatic metabolism which increase the bioavailability. Furthermore, safety profiles may be improved for drugs that produce significant amounts of toxic metabolite 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.

CHALLENGES IN FORMULATION OF FAST DISINTEGRATING TABLETS (FDTS)

Taste masking: As most drugs are not pleasant, the fast disintegrating drugs usually contain the medicament in a taste-masked form. The rapid disintegrating drugs 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. [12]

Amount of drug: 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. [13]

Mechanical strength and disintegration time: ODTs are formulated to obtain disintegration time usually less than a minute. While doing so, maintaining a good mechanical strength is a prime challenge. Many ODTs are fragile and there are many chances that such fragile tablet will break during packing, transport or handling by the patients. Tablets based on technologies like Zydis need special type of packaging. [14]

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. [15]

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. [16]

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. [17]

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. [18, 19]

LIMITATION OF FDTS [20]

- Drug with relatively large dose are difficult to formulate into FDT e.g. antibiotics like ciprofloxacin with adult dose tablet containing about 500mg at the drug.
- Patients who concurrently take anticholinergic medications may not be the best candidates for FDT. Similarly patients with Sjogren's syndromes or dryness of the mouth due to decreased saliva production may not be good candidates for these tablet formulation.

DRUGS TO BE PROMISING IN CORPORATE IN FAST DISINTEGRATING TABLETS (FDTS) ARE GIVEN IN TABLE 2

EXCIPIENTS USED IN FDT's PREPARATION

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

SUPER DISINTEGRANTS [21, 22]

In present's day, demand for faster disintegrating formulation is increased. So, pharmacist needs to formulate disintegrants i.e. Superdisintegrants which are effective at low concentration and have greater disintegrating efficiency and they are more effective intragranularly. This superdisintegrants

act by swelling and due to swelling pressure exerted in the outer direction or radial direction, it causes tablet to burst or the accelerated absorption of water leading to an enormous increase in the volume of granules to promote disintegration.(Table 3)

FACTORS TO BE CONSIDERED FOR SELECTION OF SUPERDISINTEGRANTS [23]

Disintegration- The disintegrants must quickly wick saliva into the tablet to generate the volume expansion and hydrostatic pressure necessary to provide rapid disintegration in the mouth.

Compatibility-It is desirable to have ODT with acceptable hardness and less friability at a given compression force to produce robust tablets that avoid the need to use specialized packaging while maximizing production speed.

Mouth feel- Large particles can result in a gritty feeling in mouth. Thus, small particles are preferred. If the tablet forms a gel-like consistency on contact with water, however, it produces a gummy texture that many consumers find objectionable.

Flow- In typical tablet formulation, superdisintegrants are used at 2-5 wt % of the tablet formulation. With ODT formulation, disintegrants level can be significantly higher.

Bulking materials**[24]:** Bulking materials are significant in the formulation of fast-melting tablets. The material contributes functions of a diluent, filler and cost reducer. Bulking agents improve the textural characteristics that in turn enhance the disintegration in the mouth, besides; adding bulk also reduces the concentration of the active in the composition. The recommended bulking agents for this delivery system should be more sugar-based such as mannitol, polydextrose, lactitol, DCL (direct compressible lactose) and starch hydrolystate for higher aqueous solubility and good sensory perception. Bulking agents are added in the range of 10 percent to about 90 percent by weight of the final composition.

Lubricants**[25]:** Lubricants, though not essential excipients, can further assistin making these tablets more palatable after they disintegratein the mouth. Lubricants remove grittiness and assist in thedrug transport mechanism from the mouth down into thestomach.

Emulsifying Agents **[5, 25]:** Emulsifying agents are important excipients for formulating fast-melting tablets they aid in rapid disintegration and drug release without chewing, swallowing or drinking water. In addition, incorporating emulsifying agents is useful in stabilizing the immiscible blends and enhancing bioavailability. A wide range of emulsifiers is recommended for fast tablet formulation, including alkyl sulphates, propylene glycol esters, lecithin, sucrose esters and others. These agents can be incorporated in the range of 0.05 percent to about 15 percent by weight of the final composition.

Taste masking **[26, 27, 28]:** The materials for taste-masking purpose have often been classified depending upon the basic taste. Flavouring and perfuming agents can be obtained from either natural or synthetic sources. Natural products include fruit juices, aromatic oils such as peppermint and lemon oils, herbs, spices, and distilled fractions of these. They are available as concentrated extracts, alcoholic or aqueous solutions, syrups, or spirit. Apart from these conventional materials, many compositions have been found to show effective taste-masking abilities with improved flavour such as alkaline earth oxide, alkaline earth hydroxide, or an alkaline hydroxide. Another composition includes phosphorylated amino acid such as phosphotyrosine, phosphoserine, and phosphothreonine and mixtures thereof. Anethole effectively masked bitter taste as well as the aftertaste of zinc, which is used in treating the common cold. Clove oil and calcium carbonate, which has been found to be particularly useful to mask the unpalatable active in formulations which are intended to be chewed or dissolve in mouth prior to ingestion in solution.

METHODOLOGY TECHNIQUES FOR PREPARING FAST DISSOLVING TABLETS

Freeze Drying/ Lyophilization**[29]:** A process, in which water is sublimated from the product after freezing, is called freeze drying. Freeze-dried forms offer more rapid dissolution than other available solid products. The lyophilisation process imparts glossy amorphous structure to the bulking agent and sometimes to the drug, thereby enhancing the dissolution characteristics of the formulation.

Molding**[30, 31]:** Molding process includes moistening, dissolving, or dispersing the drug with a solvent then molding the moist mixture into tablets (compression molding with lower pressure than conventional tablet compression), evaporating the solvent from drug solution, or suspension at ambient pressure (no vacuum lyophilization), respectively. The molded tablets formed by compression molding are air dried. As the

compression force employed is lower than conventional tablets, the molded tablet results in highly porous structure, which increases the disintegration and dissolution rate of the product. However, to further improve dissolution rate of the product powder mixture should be sieved through very fine screen. As molding process is employ usually with soluble ingredients (saccharides) which offers improved mouth feel and disintegration of tablets. However, molded tablets have low mechanical strength, which result in erosion and breaking during handling.

***Spray drying*[32, 33]:** Spray drying is a process by which highly porous, fine powders can be produced. Spray-dryers are invariably used in the pharmaceutical industry to produce highly porous powders. Allen *et al.* have reported applying this process to the production of fast dissolving tablets.25-28 Spray Drying can be used to prepare rapidly dissolving tablet. This technique is based upon a particulate support matrix that is prepared by spray drying and aqueous composition containing support matrix and other components to form a highly porous & fine powder. This is then mixed with active ingredient & compressed into tablet. The fast dissolving tablet prepared from spray drying technique disintegrated within 20 seconds.

***Sublimation* [34]:** The basic principle involved in preparing fast dissolving tablets by sublimation technique is addition of a volatile salt to the tableting components, mixing the components to obtain a substantially homogeneous mixture & volatizing a volatile salt. The removal of volatile salts creates pores in the tablet, which help in achieving rapid disintegration when the tablet comes in contact with saliva. Camphor, Naphthalene, Urea, ammonium bicarbonate, etc, can be used to prepare porous tablets of good mechanical strength. Koizumi *et al.* used mannitol as diluent and camphor as a volatile material to prepare porous compressed tablets. The tablets were subjected to vacuum at 800C for 30 min to eliminate the camphor and thus form the pores in the tablet. Makino et.al utilized water as a pore forming material in order to prepare porous tablets with excellent mechanical strength and dissolution character.

***Mass-Extrusion* [35]:** 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. The dried cylinder can also be used to coat granules of bitter tasting drugs and thereby masking their bitter taste.

***Direct Compression Method* [36]:** In this method, tablets are compressed directly from the mixture of the drug and excipients without any preliminary treatment. The mixture to be compressed must have adequate flow properties and cohere under pressure thus making pre-treatment as wet granulation unnecessary. Few drugs can be directly compressed into tablets of acceptable quality. A type of disintegrant and its proportion are of prime importance. The other factors to be considered are particle size distribution, contact angle, pore size distribution, tablet hardness and water absorption capacity. All these factors determine the disintegration. The disintegrant addition technology is cost effective and easy to implement at industrial level. Cousin et al, using carboxymethyl cellulose as disintegrating agent and one swelling agent consisting of modified starch or microcrystalline cellulose formulated rapidly disintegrable multi particular tablets. The tablets disintegrate in the mouth in less than 60 seconds. Gas Evolving disintegrants have been used to formulate fast dissolving tablets.

EVALUATION PARAMETER OF FAST DISSOLVING TABLET

***Tablet hardness*[37]:** 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. Ten tablets are taken from each batch for testing of hardness by Pfizer tablet tester.

***Uniformity of weight*[38]:** This test is done by sampling and weighing 20 tablets at random and average weight is calculated. Not more than two of the individual weights deviate from the average weight by more than the percentage and none deviate by more than twice the percentage.

***Friability test*[39]:** Friability test is tested by using Roche friabilator. The weight of 10 tablets are noted initially (W_1) and placed in the friabilator for 4min/100rpm. The tablets are reweighted and note as (W_2). The difference in the weight is noted and express as percentage.

Percentage friability= (initial weight-final weight/initial weight) ×100

***Water absorption ratio*[9]:** A piece of tissue paper folded twice is place in small petri-dish containing 6 ml water. A tablet is put on the tissue paper and allowed to completely wet. The wetted tablet is

then weighed. Water absorption ratio R is determined by using following equation.

$R= 100* W_a- W_b/ W_a$

In-Vitro Disintegration **[40]:** The test is carry out on 6 tablets using tablet disintegration tester and distilled water at $37^0C±2^0C$ is use as a disintegration media and the time in second taken for completedisintegration of the tablet with no palable mass remaining in the apparatus is measure in second.

In-Vitro Dissolution **[41]:** In vitro dissolution studies of fast dissolving tablets are performed by using apparatus as specified at 50 rpm and Sorenson's buffer (900 ml) is use as dissolution medium at $37^0C±0.5^0C$. Sample of dissolution medium is withdrawn at a specific time interval and filter. Adsorption of filtered solution is checked by UV spectroscopy and drug content is determined from standard calibration curve.

CONCLUSION

FDTs concept evolved to overcome some of the problems that existed in conventional solid dosage form i.e. difficulty in swallowing of tablet in pediatric and geriatric patients who constitute a large proportion of world's population. FDT may lead to improve efficacy, bioavailability, rapid onset of action, better patient compliance due to its quick absorption from mouth to GIT as the saliva passes. Fast dissolving tablet acts like solid dosage form when outside the body and solution when administered. In future FDT may be most acceptable and prescribed dosage form due to its quick action (within minute). Their characteristic advantages such as administration without water, anywhere, anytime lead to their increased patient compliance in today's scenario of hectic life. Considering the many benefits of FDTs, a number of formulations are prepared in FDT forms by most of the pharmaceutical companies. FDTs need to be formulated for pediatric, geriatric, psychotic patients for those patients who are busy in travelling; patients who are may not have access to water. The technologies depicted in this article demonstrate how recent advances in formulation development and processing technologies meet the efforts to achieve more sophisticated drug delivery system. Because of increased patient demand, popularity of these dosage forms will surely expand in future.

ACKNOWLEDGEMENTS

The authors would like to grateful of the authorities of R.V. Northland Institute, Dadri, G. B. Nagar, India for providing required facilities.

Tablet 1 Examples of fast dissolving tablets currently available on the market

Drugproduct	Activeingredient	Indication	Marketing company	Technology	Technology Company
Alavert	Loratadine	Allergy	Wyeth	OraSolv/DuraSolv	Cima Lab
Aricept	Donepezil	Alzheimers	Eisai		
Benadryl Fast	Diphenhydramine pseudoephedrine	Allergy, cold, sinus	Johnson & Johnson	WOWTAB	Astellaspharma
Claritin RediTabs	Loratadine	Allergy	Schering-Plough	Zydis	Cardinal Health
PrevacidSoluTab	Lansoprazole	Duodenal ulcer	TAP		
RemeronSolTab	Mirtazapine	Depression	Organon	Durasolv	Cima Lab
Maxalt-MLD	Rizatriptan benzoate	Migrane	Merck	Zydis	Cardinal Health
Zofran ODT	Ondansetron	Nausea	GlaxoSmithKline	Zydis	Cardinal Health

Zomig ZMT	Zolmitriptan	Migrane	AstraZeneca	OraSolv/DuraSolv	Cima Lab
ZyprexaZydis	Olanzapine	Schizophrenia	Eli Lilly	Zydis	Cardinal Health

Table 2: 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, BepheniumHydroxynaphthoate, Cambendazole, Dichlorophen, Iverrnectin, Mebendazole, Oxarnniquine, Oxfendazole, OxantelEmbonate, Praziquantel, PyrantelEmbonate, 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:	DihydroergotamineMesyiate, 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, FlupenuiixolDecanoate, FluphenazineDecanoate, Flurazepam, Haloperidol, Lorazepam, Lormetazepam, Medazepam, Meprobamate, Methaqualone, Midazolam, Nitrazepam, Oxazepam, Pentobarbitone, PerphenazinePimozide, Prochlorperazine, Suipiride, Temazepam, Thioridazine, Triazolam, Zopiclone.
Anti-Parkinsonian Agents:	BromocriptineMesylate, Lysuride Maleate.
Anti-Gout Agents:	Allopurinol, Probenecid, Sulphinpyrazone.
Anti- Protozoal Agents:	Benznidazole, Clioquinol, Decoquinate, Diiodohydroxyquinoline, DiloxanideFuroate, 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, GlycerylTrinitrate, IsosorbideDinitrate, IsosorbideMononitrate, PentaerythritolTetranitrate.
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

Table 3: List of super disintegrants

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%

REFERENCE

1. Kashyap S, Sharma V, Singh L, Fast disintegrating tablet: A boon to pediatric and geriatric, Imperial Journal of Pharmaceutics & Cosmetology 2011; 1(1): 1-11
2. Sharma Deepak, Kumar Dinesh, Singh Mankaran, Singh Gurmeet, Rathore M.S,Fast disintegrating tablets: a new era in novel drug delivery system and new market opportunities; Journal of Drug Delivery & Therapeutics; 2012; 2(3): 74-86
3. Nilausen D.O, Zuiker R.G.J.A, Gerven J. The Perception and pharmacokinetic of a 20-mg Dose of escitalopramorodispersible Tablet in a relative bioavailability study in healthy men, Clinical Therapeutic 2011; 1492-1501
4. Panigrahi R, Behera S. A review on fast dissolving tablet. Webmedcentral quality and patient safety 2010; 1(9): WMC00809.
5. Tiwari N, A review on: formulation and evaluation of fast dissolving tablet, ijarpb 2013; 3(1): 60-69
6. Slowson M, Slowson S, What to do when patients cannot swallow their medications, Pharma Times 1985; 51 : 90-96
7. Sreenivas SA, Dandagi PM, Gadad AP, Godbole AM, Hiremath AP, Mastiholimath VS, Bhagvati ST, Orodispersible tablet: New- fanged drug delivery system–A review, Indian Journal of Pharmaceutical Education & Research, 2005; 39 (4) :177-181
8. Jeong SH, Takaishi Y, Fu Y, Park K, Material properties for making fast dissolving tablets by a compression method, J. Mater. Chem 2008; 18 : 3527-3535
9. Kumar P, Pasupathi A, Chandira M, Bhowmik D, Chirajib, Jayakar B, Formulation and evaluation of fast dissolving tablets of rupatadinefumarate Der Pharmacia Letter 2009 ; 1(2): 151-163
10. Modi A and Tayade P. Enhancement of dissolution profile by solid dispersion (kneading) technique. AAPS Pharm. Sci. Tech 2006; 7(3): 68-75
11. Khan T, Nazim S, Shaikh S, Shaikh A, Khairnar A, Ahmed A, An approach for rapid disintegrating tablet: A Review, International Journal of Pharmaceutical Research & Development 2011; 3(3) :170 - 183
12. Reddy LH, Ghosh BR, Fast dissolving drug delivery systems: A review of the literature, Indian Journal of Pharmaceutical Sciences 2002; 64(4) : 331-336
13. Ghosh TK, Chatterjee DJ, Pfister WR, Quick dissolving oral dosage forms: scientific and regulatory considerations from a clinical pharmacology and biopharmaceutical perspective. In: Ghosh TK and Pfister WR (Eds). drug delivery to the oral cavity: molecules to market. NY, USA: CRC Press 2005 :337-356
14. Deshpanday K.B, Ganesh N.S,Orodispersible Tablets: An overview of formulation and technology,International Journal of Pharma and Bio Sciences 2011: 726-735

15. Hirani J.J, Rathod D.A, Vadalia K.R, Orally disintegrating tablets: A Review: Tropical Journal of Pharmaceutical Research, April 2009; 8 (2): 161-172
16. Sugihara M, Hidaka M, Saitou A, Discriminatory features of dosage form and package, Japanese Journal of Hospital Pharmacy 1986; 12 : 322-328
17. Bhandari S, Mittapalli RK, Gannu R, Rao YM, Orodispersible tablet: An overview, Asian Journal of Pharmaceutics 2008 : 2-10
18. Seager H. Drug-delivery products and Zydis Fast dissolving dosage form. J Pharm Pharmacol, 1998; 50: 375-382
19. Lies MC, Atherton AD, Copping NM. Freeze-dried dosage forms and methods for preparing same. US Patent 5,188,825 : 1993
20. Reddy Brahma D.R. et.al. Rapimelt: A Review. JPBMS 2011: 6(10)
21. Sharma S. New generation of tablet: fast dissolving tablet. latest reviews.Pharmainfo.Net 2008 : 6(1)
22. Kumaresan C. Orally disintegrating tablet - mouth dissolving, sweet taste and target release profile. Pharmaceutical review 2008 : 6
23. Deshmukh VN. Mouth Dissolving drug delivery system: A review. International Journal of Pharm Tech Research 2012; 4(1) : 412-421
24. Garg A, Gupta M.M. mouth dissolving tablets: A review. Journal of Drug Delivery & Therapeutics; 2013 ; 3(2) : 207-214
25. Chowdary K.P.R, Shankar K.R, Suchitra B. Recent research on orodispersible tablets – a review. Int. Res J Pharm. App Sci 2014; 4(1):64-73
26. Johnson JR, Wang LH, Gordon MS, Chowhan ZT. Effect of formulation solubility and hygroscopicity on disintegrating efficiency in tablets prepared by wet granulation. Journal of Pharmaceutical Sciences 1991; 80:469–71
27. Catania JS, Johnson AD. U. S. Patent 5633006 : 1997
28. Nelson SL. U.S. Patent 5766622 :1998
29. Gohel M, Patel M, Amin A, Agrawal R, Dave R,Bariya N. Formulation design and optimization of mouth dissolve tablets of Nimesulide using vacuum drying technique. AAPS Pharm Sci Tech 2004; 5(3):36-40
30. Van Scoik KG. Solid Pharmaceutical dosage in tablet triturates form and method of producing the same. US Patent 5,082,667
31. Meyers GL, Battist GE, Fuisz RC. Process and apparatus for making rapidly dissolving dosage units and product Therefore. PCT Patent WC 95/34293-A1 :1995
32. Allen, LV (1998), "Rapidly dissolving dosage form", US Patent 5,776 : 491
33. Allen, LV (2000), "Method for producing a rapidly dissolving dosage form", US Patent 6,066 :337
34. Agrawal V.A, Rajurkar R.M, Thonte S.S, Ingale R.G. Fast disintegrating tablet as a new drug delivary system: a review.Pharmacophore2011, Vol. 2 (1): 1-8
35. Verma A.K,Sachan A.K. a review on fast dissolving tablet as an efficient technique for oral drug delivery. Journal of Chemical and Pharmaceutical Sciences. 2013; 29-34
36. Jain D, Mishra A. A Review - Formulation and development of orodispersible tablet.Www.pharmaerudition.org May 2014; 4(1): 21-38
37. Saroha k and Kumar G, Paul Y. Formulation and evaluation of fast dissolving tablet of Amoxicillin Trihydrate using synthetic superdisintegrants. Int J Pharm Bio Sci 2013 : 254-262
38. Rane D. R, Gulve H. N, Patil V. V, Thakare V. M, Patil V. R. Formulation and evaluation of fast dissolving tablet of albendazole. International Current Pharmaceutical Journal 2012; 1(10): 311-316
39. Bhupathi S.K, Jithendra R, Bandaru and Bhupathi V. V. Design and evaluation of fast dissolving tablet of TerbutalineSulphate. Research Journal of Pharmaceutical, Biological and Chemical 2012: 138-153
40. Shrivastava M, Chourasiya D, Soni S, Patidar D, Jatav R. Formulation and *in-vitro* evaluation of mouth dissolving tablets of phenytoin sodium using different disintegrating agent. IJNDDT 2012 :249-255
41. Chander H, Kumar S, Bhatt B. Formulation and evaluation of fast dissolving tablet of Ramipril.Pelagia Research Library 2011; 2 (6): 153-160