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Fast dissolving tablet: A review on revolution of novel drug delivery system and new market opportunities

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Abstract

Oral delivery is currently the gold standard in the pharmaceutical industry where it is regarded as the safest, most convenient and most economical method of drug delivery having the highest patient compliance. The tablet is the most widely utilized oral dose format. A novel tablet concept which offers ease of oral administration and benefits of increased patient compliance is the fast dissolving/disintegrating tablet (FDDT). This tablet format is designed to allow administration of an oral solid dose form in the absence of water or fluid intake. Such tablets readily dissolve or disintegrate in the saliva generally within <60 seconds. The oral drug delivery market was estimated to be worth \$35bn in 2006 & forecast to reach \$52bn by 2010 with a CAGR of 10%. Of this, the FDDT, taste masked & micro emulsion formulation segments constitute a 22% share with an expected CAGR of 17% to 2010. There is a clear opportunity for new enhanced oral products arising within this market segment. Formulation advances using a conventional tableting process have led to the development of mechanically robust tablets which readily dissolve/disintegrate within <50 seconds and can be formulated in a range of sizes from 10 -15mm. The tablets produced are stable, and can withstand shipment in conventional tablet containers without loss of integrity. Pre-clinical canine studies with a range of formulations have demonstrated palatability and ease of administration. A number of FDDT products for human and veterinary administration are currently under development and the delivery of water soluble as well as lipophilic drug compounds. Fast- or mouth dissolving 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.

Introduction

The concept of Fast dissolving Drug Delivery System emerged from the desire to provide patient with more conventional means of taking their medication. It is difficult for many patients to

swallow tablets and hard gelatin capsules. Hence they do not comply with prescription, which results in high incidence of non-compliance and ineffective therapy¹. In some cases such as motion sickness, sudden episodes of allergic attacks or coughing and unavailability of water, swallowing conventional tablets may be difficult². Particularly the difficulty is experienced by pediatric and geriatric patients. Such problems can be resolved by means of Fast Dissolving Tablet. When put on tongue, this tablet disintegrates instantaneously, releasing the drug, which dissolves or disperses in the saliva. 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 tablet dosage form. Approximately one-third of the population, primarily the geriatric and pediatric populations, has swallowing difficulties, resulting in poor compliance with oral tablet drug therapy which leads to reduced overall therapy effectiveness. A new tablet dosage format, the fastdissolving tablet has been developed which offers the combined advantages of ease of dosing and convenience of dosing in the absence of water or fluid. These tablets are designed to dissolve or disintegrate rapidly in the saliva generally within <60 seconds (range of 5-50seconds). Due to the constraints of the current FDDT technologies as highlighted above, there is an unmet need for improved manufacturing processes for fastdissolving tablets that are mechanically strong, allowing ease of handling and packaging and with production costs similar to that of conventional tablets. Fast dissolving tablet (FDT) is a new dosage form which can be disintegrated inside the mouth within a minute. A comprehensive review of current technologies in making fast dissolving tablet was conducted. Two approaches in making fast dissolving tablet were proposed and tested. A large number of materials were surveyed to find candidates for formulating fast dissolving tablets. Mannose was chosen as the best candidate for further investigation. The mechanisms of fast dissolution of mannose tablets were studied. It was found that the dissolution rate of the material in the tablets determined the disintegration kinetics of the tablets. The strength of mannose tablets was improved by the moisture treatment process. Strong liquid bridges at the surfaces of mannose particles were formed during the humidity treatment, and those liquid bridges resulted in solid bridges that subsequently strengthened the tablets. An optimized pore size distribution inside the mannose tablet was necessary for the particles to merge, yet maintain interconnected pores for fast absorption of water into the tablet. Poly (acrylic acid) superporous hydrogel (SPH) particles showed a high swelling property in various aqueous solutions, and had a very good compressibility and compactability. Poly (acrylic acid) SPH particles were used as a super-disintegrant in tablet formulation. The effect of SPH particles on disintegration time and hardness of fast dissolving tablet were compared to common super disintegrants such as sodium starch glycolate and carboxymethylcellulose sodium. The particle size of SPH had a great effect on the disintegration time of FDTs. A fractional factorial experiment with 19 runs was conducted to evaluate the effects of ketoprofen, SPH, filler and tableting pressure on disintegration time and tensile strength of FDTs. The addition of SPH significantly decreased the disintegration time of FDTs, but had a negative impact on tensile strength. The results indicate that PAA SPH is a promising super-disintegrant for making FDTs.

Advantages of fast dissolving tablets

1. Improved patient compliance
2. Rapid onset of action and may offer an improved bioavailability.
3. Patient having difficulty in swallowing tablet can easily administer this type of dosage form
4. Useful for pediatric, geriatric and psychiatric patients

5. Suitable during traveling where water is may not be available
6. Gives accurate dosing as compared to liquids
7. Good chemical stability.
8. Free of need of measuring, an essential drawback in liquids.

Techniques used formulation of fast dissolving tablets

Many techniques have been reported for the formulation of Fast dissolving tablets or Orodispersible tablets.

1. Freeze drying / lyophilization
2. Tablet Moulding
3. Spray drying
4. Sublimation
5. Direct compression
6. Mass extrusion

Freeze-Drying or Lyophilization:

Freeze drying is the process in which water is sublimed from the product after it is frozen. This technique creates an amorphous porous structure that can dissolve rapidly. A typical procedure involved in the manufacturing of ODT using this technique is mentioned here. The active drug is dissolved or dispersed in an aqueous solution of a carrier/polymer. The mixture is done by weight and poured in the walls of the preformed blister packs. The trays holding the blister packs are passed through liquid nitrogen freezing tunnel to freeze the drug solution or dispersion. Then the frozen blister packs are placed in refrigerated cabinets to continue the freeze-drying. After freeze-drying the aluminum foil backing is applied on a blister-sealing machine. Finally the blisters are packaged and shipped. The freeze-drying technique has demonstrated improved absorption and increase in bioavailability. The major disadvantages of lyophilization technique are that it is expensive and time consuming; fragility makes conventional packaging unsuitable for these products and poor stability under stressed conditions.

Tablet Molding:

Molding process is of two types i.e. solvent method and heat method. Solvent method involves moistening the powder blend with a hydro alcoholic solvent followed by compression at low pressures in molded plates to form a wetted mass (compression molding). The solvent is then removed by air-drying. The tablets manufactured in this manner are less compact than compressed tablets and possess a porous structure that hastens dissolution. The heat molding process involves preparation of a suspension that contains a drug, agar and sugar (e.g. mannitol or lactose) and pouring the suspension in the blister packaging wells, solidifying the agar at the room temperature to form a jelly and drying at 30°C under vacuum. The mechanical strength of molded tablets is a matter of great concern. Binding agents, which increase the mechanical strength of the tablets, need to be incorporated. Taste masking is an added problem to this technology.

The taste masked drug particles were prepared by spray congealing a molten mixture of hydrogenated cottonseed oil, sodium carbonate, lecithin, polyethylene glycol and an active

ingredient into a lactose based tablet triturate form. Compared to the lyophilization technique, tablets produced by the molding technique are easier to scale up for industrial manufacture.

Spray drying :

In this technique, gelatin can be used as a supporting agent and as a matrix, mannitol as a bulking agent and sodium starch glycolate or croscarmellose or crospovidone are used as superdisintegrants. Tablets manufactured from the spray-dried powder have been reported to disintegrate in less than 20 seconds in aqueous medium. The formulation contained bulking agent like mannitol and lactose, a superdisintegrant like sodium starch glycolate & croscarmellose sodium and acidic ingredient (citric acid) and/or alkaline ingredients (e.g. sodium bicarbonate). This spray-dried powder, which compressed into tablets showed rapid disintegration and enhanced dissolution.

Sublimation:

To generate a porous matrix, volatile ingredients are incorporated in the formulation that is later subjected to a process of sublimation. Highly volatile ingredients like ammonium bicarbonate, ammonium carbonate, benzoic acid, camphor, naphthalene, urea, urethane and phthalic anhydride may be compressed along with other excipients into a tablet. This volatile material is then removed by sublimation leaving behind a highly porous matrix. Tablets manufactured by this technique have reported to usually disintegrate in 10-20 sec. Even solvents like cyclohexane; benzene can be used as pore forming agents.

Direct Compression

Direct compression represents the simplest and most cost effective tablet manufacturing technique. This technique can now be applied to preparation of ODT because of the availability of improved excipients especially superdisintegrants and sugar based excipients.

(a) Superdisintegrants:

In many orally disintegrating tablet technologies based on direct compression, the addition of superdisintegrants principally affects the rate of disintegration and hence the dissolution. The presence of other formulation ingredients such as water-soluble excipients and effervescent agents further hastens the process of disintegration.

(b) Sugar Based Excipients:

This is another approach to manufacture ODT by direct compression. The use of sugar based excipients especially bulking agents like dextrose, fructose, isomalt, lactilol, maltitol, maltose, mannitol, sorbitol, starch hydrolysate, polydextrose and xylitol, which display high aqueous solubility and sweetness, and hence impart taste masking property and a pleasing mouthfeel. Mizumoto et al have classified sugar-based excipients into two types on the basis of molding and dissolution rate.

Type 1 saccharides (lactose and mannitol) exhibit low mouldability but high dissolution rate.

Type 2 saccharides (maltose and maltitol) exhibit high mouldability and low dissolution rate.

Mass-Extrusion

This technology involves softening the active blend using the solvent mixture of water-soluble polyethylene glycol and methanol and subsequent expulsion of softened mass through the extruder or syringe to get a cylinder of the product into even segments using heated blade to form tablet. The dried cylinder can also be used to coat granules for bitter drugs and thereby achieve taste masking.

Important Patented Technologies for Fast Dissolving Tablets***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 material designed to achieve a number of objectives. To impart strength and resilience 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 while various gums are used to prevent sedimentation of dispersed drug particles in the manufacturing process. Collapse protectants such as glycine 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.

2. Durasolv Technology :

Durasolv is the patented technology of CIMA labs. The tablets made by this technology consist of drug, filler and a lubricant. Tablets are prepared by using conventional tableting equipment and have good rigidity.

These can be packaged into conventional packaging system like blisters. Durasolv is an appropriate technology for product requiring low amounts of active ingredients.

3. Orasolv Technology :

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

4. Flash Dose Technology :

Flash dose technology has been patented by fuisz. Nurofen meltlet, a new form of ibuprofen as melt in mouth tablets prepared using flash dose technology is the first commercial product launched by biovail corporation. Flash dose tablets consist of self-binding shear form matrix termed as “floss”. Shear form matrices are prepared by flash heat processing.

5. Wow tab Technology :

Wow tab technology is patented by Yamanouchi Pharmaceutical Co. WOW means “Without Water”. In this process, combination of low mouldability saccharides and high mouldability

saccharides is used to obtain a rapidly melting strong tablet. The active ingredient is mixed with a low mouldability saccharide (eg. lactose, glucose, and mannitol) and granulated with a high mouldability saccharide (eg. Maltose, oligosaccharides) and compressed into table

6. Flash tab Technology :

Prographarm laboratories have patented the Flash tab technology. Tablet prepared by this system consists of an active ingredient in the form of micro crystals. Drug micro granules may be prepared by using the conventional techniques like coacervation, micro encapsulation and extrusion spheronisation. All the processing, utilized conventional tableting technology.

Table-1 List of commercially Available Fast dissolving tablets

Trade Name	Active Drug	Manufacturer
Felden fast melt	Piroxicam	Pfiser Inc., NY, USA
Claritin redi Tab	Loratidine	Schering plough Corp., USA
Maxalt MLT	Rizatriptan	Merck and Co., NJ, USA
Zyprexa	Olanzapine	Eli Lilly, Indianapolis, USA
Pepcid RPD	Famotidine	Merck and Co., NJ, USA
Zofran ODT	Ondansetron	Glaxo Wellcome, Middlesex, UK
Zoming-ZMT	Zolmitriptan	AstraZeneca, Wilmington, USA
Zeplar TM	Selegiline	Amarin Corp., London, UK
Tempra Quiclets	Acetaminophen	Bristol Myers Squibb, NY, USA
Febrectol	Paracetamol	Prographarm, Chateaufort, France
Nimulid MDT	Nimesulide	Panacea Biotech, New delhi, India
Torrox MT	Rofecoxib	Torrent pharmaceuticals, India
Olanex instab	Olanzapine	Ranbaxy lab. Ltd. New-delhi, India
Romilast	Montelukast	Ranbaxy lab. Ltd. New-delhi, India
Benadryl Fastmelt	Diphenhydramine and pseudoephedrine	Warner Lambert, NY, USA

Role of community pharmacist counseling of patients

The Pharmaceutical Care is an important health care intervention which is mandatory for quality use of medicine. The Patients are supposed to get all the practical information regarding the drugs they are prescribed by doctors. The community pharmacist is the globally accepted professional to cater the pharmaceutical care to the patients at the time of dispensing the medicine itself. Pharmacists are in the ideal position to become familiar with the different technologies, and educate their patients on what to expect upon taking their first dose. The majority of patients receiving FDDT preparations have little understanding of this new dosage form. Patients may be surprised when tablets begin to dissolve in the mouth. They might expect a faster onset of therapeutic action. Clarification from the pharmacist can avoid any confusion or misunderstanding. As with all dosage form technologies, some patient populations are better served by their use than others. Patients who concurrently take anticholinergic medications may not be the best candidates for these drugs. Similarly, patients with Sjögren's syndrome or dryness

of the mouth due to decreased saliva production may not be good candidates for these tablet formulations. Although no water is needed to allow the drug to disperse quickly and efficiently, most technologies utilize the body's own salivation. Decreased volume of saliva may slow the rate of dissolution/disintegration and decrease the bioavailability of the product. Although chewable tablets have been on the market for some time, they are not the same as the new FDDTs. Patients for whom chewing is difficult or painful can use these new tablets easily. FDDTs can be used easily in children who have lost their primary teeth, but do not have full use of their permanent teeth. Patients may mistake fast-dissolving/disintegrating for effervescent tablets. Pharmacists may wish to stress the difference between the use of quick-dissolving and effervescent tablets. Keeping in view of the advantages of the delivery system, rapidly disintegrating dosage forms have been successfully commercialized, and because of increased patient demand, these dosage forms are expected to become more popular. The current needs of the industry are improved solubility/stability, biological half-life and bioavailability enhancement of poorly absorbed drugs. Key issues facing the biopharma industry are to improve safety (decreasing gastrointestinal side effects), improve efficacy for organ targeting, and improved compliance via sustained release or easy to swallow dosage forms.

Drugs to be promising in corporate in fast dissolving tablets

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

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, Ivermectin, Mebendazole, Oxamniquine, 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, Nalidixic Acid, 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-Gout Agents:

Allopurinol, Probenecid, Sulphinpyrazone.

Anti-Hypertensive Agents:

Amlodipine, Carvedilol, Benidipine, Darodipine, Dilitazem, Diazoxide, Felodipine, Guanabenz Acetate, Indoramin, Isradipine, Minoxidii, Nicardipine, Nifedipine, Nimodipine, Phenoxybenzamine, Prazosin, Reserpine, Terazosin.

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, Hyoscyamine, Mepenzolate Bromide, Orphenadrine, Oxyphencylmine, Tropicamide.

Anti-Neoplastic Agents and Immunosuppressants:

Aminoglutethimide, Amsacrine, Azathiopne, Busulphan, Chlorambucil, Cyclosporin, Dacarbazine, Estramustine, Etoposide, Lomustine, Melphalan, Mercaptopurine, Methotrexate, Mitomycin, Mitotane, Mitozantrone, Procarbazine, Tamoxifen Citrate, Testolactone.

Anti Protozoal Agents:

Benznidazole, Clioquinol, Decoquinol, Diiodohydroxyquinoline, Diloxanide Furoate, Dinitolmide, Furzolidone, Metronidazole, Nimorazole, Nitrofurazone, Omidazole, Tinidazole.

Anti-Thyroid Agents:

Carbimazole, Propylthiouracil.

Anxiolytic, Sedatives, Hypnotics and Neuroleptics:

Alprazolam, Amyobarbitone, Barbitone, Bentazepam, Bromazepam, Bromperidol, Brotizoiam, Butobarbitone, Carbromal, Chlordiazepoxide, Chlormethiazole, Chlorpromazine, Clobazam, Clotiazepam, Clozapine, Diazepam, Droperidol, Ethinamate, Flunarisone, Flunitrazepam,

Fluopromazine, Flupenuixol Decanoate, Fluphenazine Decanoate, Flurazepam, Haloperidol, Lorazepam, Lormetazepam, Medazepam, Meprobamate, Methaqualone, Midazolam, Nitrazepam, Oxazepam, Pentobarbitone, Perphenazine Pimozide, Prochlorperazine, Suiipride, Temazepam, Thioridazine, Triazolam, Zopiclone.

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:

Acetazolamide, Amiloride, Bendrofluazide, Bumetanide, Chlorothiazide, Chlorthalidone, Ethacrynic Acid, Frusemide, Metolazone, Spironolactone, Triamterene.

Anti-Parkinsonian Agents:

Bromocriptine Mesylate, Lysuride Maleate.

Gastro-Intestinal Agents:

Bisacodyl, Cimetidine, Cisapride, Diphenoxylate, , Domperidone, Famotidine, Loperamide, Mesalazine, Nizatidine, Omeprazole, Ondansetron, Ranitidine, Sulphasaiazine.

Histamine H₁-Receptor Antagonists:

Acrivastine, Astemizole, Cinnarizine, Cyclizine, Cyproheptadine, Dimenhydrinate, Flunarizine, Loratadine, Meclozine, Oxatomide, Terfenadine, Triprolidine.

Lipid Regulating Agents:

Bezafibrate, Clofibrate, Fenofibrate, Gemfibrozil, Probucol.

Local Anaesthetics:

Lidocaine

Neuro -Muscular Agents:

Pyridostigmine.

Nitrates and Other Anti-Anginal Agents:

Amyl Nitrate, Glyceryl Trinitrate, Isosorbide Dinitrate, Isosorbide Mononitrate, Pentaerythritol Tetranitrate.

Nutritional Agents:

Betacarotene, Vitamin A, Vitamin B₂, Vitamin D, Vitamin E, Vitamin K.

Opioid Analgesics:

Codeine, Dextropropoxyphene, Diamorphine, Dihydrocodeine, Meptazinol, Methadone, Morphine, Nalbuphine, Pentazocine.

Oral Vaccines:

Vaccines designed to prevent or reduce the symptoms of diseases of which the following is a representative

Influenza, Tuberculosis, Meningitis, Hepatitis, Whooping Cough, Polio, Tetanus, Diphtheria, Malaria, Cholera, Herpes, Typhoid, HIV, Aids, Measles, Lyme Disease, Travellers Diarrhea, Hepatitis A, B And C, Otitis Media, Dengue Fever, Rabies, Parainfluenza, Rubella, Yellow Fever, Dysentery, Legionnaires Disease, Toxoplasmosis, Q-Fever, Haemorrhagic Fever, Argentina Haemorrhagic Fever, Caries, Chagas Disease, Urinary Tract Infection Caused By E.Coli, Pneumococcal Disease, Mumps, File://H:\Gits Mdt\Fast Dissolving Tablet The Future Of Compaction And Chikungunya.

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 Thereof, Enkephalins, Interferons (Especially Alpha-2 Inter Feron 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.

There are no particular limitations on the amount of these drugs to be mixed as long as it is the usual effective treatment amount. It should be around 50 weight/weight % or below of the entire tablet, and is preferably 20 weight/weight % or below.

Optimal disintegration properties often have medium to small size and /or high friability and low hardness. Breakage of tablet edges during handling and tablet rupture during the opening of blister alveolus, all result from insufficient physical resistance.

Fast-dissolving delivery system for both pediatric and geriatric populations

Advances in technology continue to break the barriers of conventional encapsulation methods. Today, active ingredients can be delivered with a level of convenience, performance and bioavailability never before seen in the marketplace. And, as our scientific understanding of the prevention and management of diseases continues to grow, companies find themselves in ever-greater competition—investing millions of dollars to develop novel ways of delivering nutrients orally to patients. Such companies are constantly focusing on delivery systems that offer greater patient compliance, effective dosages and minimal chances of side effects. Fast-dissolving

tablets or rapid-melt tablets are one such innovation; it is one of the fastest-growing segments in the pharmaceutical market, as evidenced by an estimated \$28 billion in 2002 sales. This novel type of delivery system offers convenience for treatment-resistant populations who have difficulty swallowing oral dosage forms. The demand for these formulations has gone up significantly for children and older populations. They are particularly convenient for pediatrics and geriatric segments of the population because they rapidly disintegrate in the mouth without the need for chewing or drinking water. The disintegration times of these tablets depend largely on the size of the dosage form and hardness parameters. Fast-melting formulations even offer advantages for drug-compliant patients who take other orally administered pills, such as chewable, suspensions and effervescent tablets. When placed in the mouth, these tablets disintegrate in a few seconds, resulting in quick absorption of the actives through the buccal and oesophageal mucous, thus offering faster bioavailability of active ingredients with minimal side effects. Fast-melting tablets can also serve as carriers for a wide range of nutritional and dietary supplements including calcium, caffeine, antioxidants and folic acid. A novel, fast-dissolving delivery system that releases active ingredients in seconds is one of the fastest-growing segments of the supplements marketplace. Fast-dissolving tablet technologies are important for patients who have difficulty taking conventional oral dosage forms as well as for pharmaceutical firms seeking line extensions in the marketplace. This article describes existing fast-dissolving technologies and discusses several techniques used to formulate such tablets, namely tablet molding, freeze-drying, spray-drying, sublimation, disintegrant addition, and the use of sugar-based excipients. As a result of increased life expectancy, the elderly constitute a large portion of the worldwide population today. These people eventually will experience deterioration of their physiological and physical abilities. Many elderly persons will have difficulties in taking conventional oral dosage forms (*viz.*, solutions, suspensions, tablets, and capsules) because of hand tremors and dysphasia. Swallowing problems also are common in young individuals because of their underdeveloped muscular and nervous systems. Other groups that may experience problems using conventional oral dosage forms include the mentally ill, the developmentally disabled, and patients who are uncooperative, on reduced liquid-intake plans, or are nauseated. In some cases such as motion sickness, sudden episodes of allergic attack or coughing, and an unavailability of water, swallowing conventional tablets may be difficult. To fulfill these medical needs, formulators have devoted considerable effort to developing a novel type of tablet dosage form for oral administration, one that disintegrates and dissolves rapidly in saliva without the need for drinking water. The development of a fast-dissolving tablet also provides an opportunity for a line extension in the marketplace, A wide range of drugs (*e.g.*, neuroleptics, cardiovascular drugs, analgesics, antihistamines, and drugs for erectile dysfunction) can be considered candidates for this dosage form.

Table-3 Fast dissolving tablets currently available in market

Product	Manufactured By/For	Active ingredient	Category	Indication	Intended Age Group
Abilify Discmelt	Otsuka America/Bristol-Myers Squibb	aripiprazole	Atypical antipsychotics	Schizophrenia, Bipolar disorder, adjunct therapy for Major Depressive Disorder	13 years+ for Schizophrenia, 10 years+ for Bipolar disorder, adults for MDD

Alavert Quick Dissolving Tablets	Wyeth	Loratadine	Anti-histamines	Allergy	6 years+
Allegra ODT	Sanofi Aventis	Fexofenadine	Anti-histamines	Allergic rhinitis, Urticaria	6-11 years
Aricept ODT	Eisai Co.	Donepezil	Acetylcholinesterase inhibitors ^[2]	Alzheimer's disease	adults
Benadryl FastMelt	Pfizer	Diphenhydramine	Anti-histamines	Allergy	6 years+
Calpol Fast Melts	McNeil Healthcare UK	Paracetamol	Analgesics	Pain	6 years+
Clarinox RediTabs	Schering-Plough	Desloratadine	Anti-histamines	Allergy	6 years+
Claritin RediTabs	Schering-Plough	Loratadine	Anti-histamines	Allergy	6 years+
Clonazepam ODT	Par Pharmaceutical	Clonazepam	Benzodiazepines	Anxiety, Panic Disorder, Seizure Disorders	infants+
FazaClo	AzurPharma	Clozapine	Antipsychotics	treatment-resistant Schizophrenia	adults
Jr. Tylenol Meltaways	McNeil Consumer Healthcare	acetaminophen	Analgesics, Anti-pyretics	Pain, Fever	6 years+
Klonopin Wafers ^[25]	Roche	clonazepam	Benzodiazepines	Panic Disorder, Seizure Disorders	infants+ for seizure disorders, adults for Panic Disorder
Loratadine Redidose	Ranbaxy	loratadine	Antihistamines	Allergy	6 years+
Maxalt-MLT	Merck & Co.	Rizatriptan	Triptans/Serotonin agonists	acute Migraine	18 years+
Mirtazapine ODT	Teva Pharmaceuticals	Mirtazapine	Antidepressants	Major Depressive Disorder	adults
Nurofen Meltlets	Reckitt Benckiser	Ibuprofen	NSAIDs	Pain, Fever, Inflammation	12 years+
Ondansetron ODT	Teva Pharmaceuticals	Ondansetron	Antiemetics	Nausea, Vomiting	4 years+
Orapred ODT	Sciele Pharma	Prednisolone	Corticosteroids	Asthma, severe Allergy, Hemolytic anaemia, Stevens-Johnson syndrome, certain types of Tuberculosis; acute treatment of arthritis, bursitis, COPD, Leukemia,	adults and children weighing over 44lbs/20.1kg

				Lupus, Multiple sclerosis, Ulcerative colitis	
Parcopa	Schwarz Pharma	Carbidopa/levodopa	DDC inhibitors [carbidopa]	Parkinson's disease	adults
Prevacid SoluTab	Takeda Pharmaceuticals	Lansoprazole	Proton pump inhibitors	Gastro-esophageal Reflux Disease (GERD), Ulcers	1 year+
Remeron SolTab	Schering-Plough	Mirtazapine	Antidepressants	Major Depressive Disorder	adults
Risperdal M-Tab	Janssen	Risperidone	Atypical antipsychotics	Schizophrenia, Bipolar disorder, Irritability associated with Autistic disorder	13 years+ for Schizophrenia, 10 years+ for Bipolar disorder, 5 years+ for Autism
UNISOM SleepMelts	Chattem	Diphenhydramine	Anticholinergic	Nighttime Sleep Aid	Adults and children 12 years+
Zelapar	Valeant Pharmaceuticals Int'l	Selegiline	Monoamine oxidase inhibitors (MAOIs) ^[10]	adjunct therapy in Parkinson's disease	adults
Zofran ODT	GlaxoSmithKline	Ondansetron	Antiemetics	Nausea, Vomiting	4 years+
Zomig-ZMT	AstraZeneca	Zolmitriptan	Triptans/Serotonin agonists	Migraine	adults
Zyprexa Zydis	Eli Lilly and Company	Olanzapine	Atypical antipsychotics	Bipolar disorder, Schizophrenia	adults

Table 3. Some Patented technologies

Formulation	Key attributes	Company
Zydis®	Freeze-drying on blister packing	RP Scherer (Cardinal)
Lyoc	Freeze-drying on the shelves of freeze dryer	Laboratories L. Lafon, Maisons Alfort, France
Flashtab	Granulation of excipients by wet or dry granulation method and followed by compressing into tablets	Ethypharm France.
OraSolv	low compression force and an effervescent couple as a water-soluble disintegrating agent	Cima Labs Inc.
DuraSolv	Direct compression using water-soluble excipients	Cima Labs Inc.
WOWTAB®	High- and low-moldability saccharides	Yamanouchi Pharma
Pharmabrust	Direct compression of powder mixture	SPI Pharma

Advantol™ 200	Directly compressible excipient system	SPI Pharma
Advatab®	Direct compression using external lubrication system	Eurand

Table-4 Marketed Fast Dissolving Tablets in India

Name of the Product	Active Ingredients
Imodium Lingual	Imodium
Pepcidin Rapitab	Quick releasing antiulcer preparation of pepcid
Mosid – MT	Mouth melt tablet of Mosapride citrate.
Calritin Reditabs	Immediate Dissolving formulation of Claritin
Nimulid – MD	Nimesulide
Zyrof Meltab	Rofecoxib
Claritin Reditab	micronized loratadine
Feldene Melt	piroxicam (10 or 20 mg),
Maxalt-MLT	rizatriptan (5 or 10 mg), peppermint flavour
Pepcid RPD	famotidine (20 or 40 mg),
Zyprexa Zydis	olanzapine (5, 10, 15 or 20 mg),
Zofran ODT	ondansetron (4 or 8 mg), strawberry flavor
Remeron Soltab	mirtazepine (15, 30, or 45 mg), orange flavor

Conclusion

The fundamental principle used in the development of the fast-dissolving tablet is to maximize its pore structure. Researchers have evaluated spray dried materials and plastic materials for development of such tablets. Vacuum-drying and freeze-drying techniques have been tried by researchers to maximize the pore structure of tablet matrix. Freeze drying is cumbersome and yields a fragile and hygroscopic product. Therefore, a vacuum-drying technique was adopted in the present investigation after addition of a subliming agent to increase porosity of the tablets. It is likely that a porous hydrophilic matrix will easily pick up the disintegrating medium and break quickly. The tablet is the most widely used dosage form because of its convenience in terms of

self-administration, compactness, and ease in manufacturing. The basic approach followed by all the currently available technologies engaged in the formulation of Fast dissolving tablets is to maximize the porous structure of the tablet matrix and incorporate super disintegrating agents in optimum concentration so as to achieve rapid disintegration and instantaneous dissolution of the tablet along with good taste masking properties and excellent mechanical strength. The availability of the various technologies and manifold advantages of Fast dissolving tablets will surely increase its popularity in the near future. However, geriatric and pediatric patients experience difficulty in swallowing conventional tablets, which leads to poor patient compliance. To overcome this weakness, scientists have developed innovative drug delivery systems known as fast dissolving tablets. Their characteristic advantages such as administration without water, anywhere, anytime lead to their suitability to geriatric and pediatric patients. They are also suitable for the mentally ill, the bedridden and patients who do not have easy access to water. The benefits, in terms of patient compliance, rapid onset of action, increased bioavailability, and good stability make these tablets popular as a dosage form of choice in the current market.

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