

Review Article

An overview on recent trends of fast dissolving drug delivery system

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ARTICLE INFO

Received 14 Dec 2015

Revised 20 Jun 2016

Accepted 12 Jul 2016

Keywords:

- Fast dissolving tablets
- Superdisintegrants
- Oral disintegrating tablets
- Direct compression

ABSTRACT

Oral drug delivery remains the preferred route of drug delivery. 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. Novel technologies with improved performance, patient compliance, and enhanced quality have emerged in the recent past. FDTs have received ever-increasing demand during the last decade, and the field has become a rapidly growing area in the pharmaceutical industry. As a drug entity nears the end of its patent life, it is common for pharmaceutical manufacturers to develop a given drug entity in a new and improved dosage form. Fast or mouth dissolving tablets have been formulated for paediatric, geriatric, and bedridden patients and for active patients who are busy and travelling and may not have access to water, which is a major benefit over conventional dosage form. This article reviews the selection, advantages, disadvantages, mechanism of superdisintegrants, formulation technologies (conventional and patented), and marketed product of fast dissolving tablets. The review also covers the evaluation parameters including pre-compression and post compression parameters FDTs.

1. INTRODUCTION

Drug delivery systems (DDS) are a strategic tool for expanding markets/indications, extending product life cycles and generating opportunities. The oral route of drug administration is the most important method for administering drugs for systemic effects [1]. Except in certain cases the parenteral route is not routinely used for self administration, e.g. insulin. The topical route of administration has only recently been employed to deliver drugs to the body for systemic effects. The parenteral route of administration is important in treating medical emergencies in which the subject is comatose or cannot swallow. Nevertheless it is probable that at least 90% of all drugs used to provide systemic effects are administered by the oral route [2]. The tablet is the most widely used dosage form existing today because of its convenience in terms of self-administration, compactness and ease in manufacturing. But many patients find difficulty in swallowing tablets and hard gelatin capsules; consequently fail to take medication as prescribed which results in high incidence of non-compliance and ineffective therapy [3]. The problem of

choking is common phenomenon in geriatric patients due to fear of choking, hand tremors, dysphasia. Fast dissolving drug delivery system (FDDS) was introduced in late 1970 as the alternative to conventional tablet, capsule and syrups especially for the geriatric and paediatric patients suffering from the dysphasia problem. MDTs offer several advantages over other dosage forms like effervescent tablets, dry syrups and chewing gums/tablets, which are commonly used to enhance patient's compliance [4]. Administering effervescent tablets/granules and dry syrups involve unavoidable preparation that include the intake of water. Elderly patients cannot chew large pieces of tablets or gums and sometimes experience the bitter or unpleasant taste of the drug in the dosage form if the taste masking coat ruptures during mastication [5]. There is an important role of drinking water in the swallowing of oral dosage forms but some time people experiences an inconvenience in swallowing. The problems can be resolved by means of Mouth Dissolving Tablets (MDTs), when water is not available as during journey, also in case of the motion sickness (kinetosis) and sudden episodes of coughing during the common cold, allergic condition and bronchitis [6].

Definition

The Centre for Drug Evaluation and Research (CDER), US FDA defined Oral Disintegrating Tablets (ODT) as “*A solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue.*” A fast dissolving tablet can be defined as a solid dosage form that can disintegrate into smaller granules which slowly dissolve in the mouth. The disintegration time for fast dissolving tablet varies from a few seconds to more than a minute depending on the formulation and the size of the tablet. A fast disintegrating or dissolving system or tablet can be defined as a solid dosage form that can disintegrate or dissolve within 30 seconds, in the oral cavity resulting in a solution or suspension without administration of water [7].

The fast disintegrating tablets are synonymous with fast dissolving tablets; melt in mouth tablets, rapimelts, porous tablets, orodispersible, quick dissolving or rapidly disintegrating tablets. Their growing importance was underlined recently when European pharmacopoeia adopted the term “Orodispersible tablet” as a tablet that to be placed in the mouth where it disperses rapidly, before swallowing significance of this drug delivery system includes administration without water, accuracy dosage, easy portability, alternative to liquid dosage forms ideal for pediatrics and geriatric patients and rapid onset of action [8].

2. SALIENT FEATURES OF FAST DISSOLVING DRUG DELIVERY SYSTEM

- Ease of administration to patients who refuse to swallow a tablet, such as paediatric and geriatric patients and, psychiatric patients.
- Convenience of administration and accurate dosing as compared to liquids.
- No need of water to swallow the dosage form, which is highly convenient feature for patients who are travelling and do not have immediate access to water.
- Good mouth feels properly of MDDS helps to change the basic view of medication as “bitter pill”, particularly for paediatric patients.
- Rapid dissolution of drug and absorption which may produce rapid, onset of action.
- Some drugs are absorbed from the mouth pharynx and oesophagus as the saliva passes down into the stomach, in such cases bioavailability of drugs is increased.
- Ability to provide advantages of liquid medication in the form of solid preparation.
- Pre-gastric absorption can result in improved bioavailability and as a result of reduced dosage, improved clinical performance through a reduction of unwanted effects [9].

3. ADVANTAGES OF FDT

- Administration to the patients who cannot swallow, such as the elderly, stroke victims, bedridden patients, patients

affected by renal failure and patients who refuse to swallow such as paediatric, geriatric and psychiatric patients.

- Rapid drug therapy intervention.
- Achieve increased bioavailability/rapid absorption through pre-gastric absorption of drugs from mouth, pharynx and oesophagus as saliva passes down.
- Convenient for administration and patient compliant for disabled, bedridden patients and for travellers and busy people, who do not always have access to water.
- Good mouth feel property helps to change the perception of medication as bitter pill particularly in paediatric patients.
- The risk of choking or suffocation during oral administration of conventional formulations due to physical obstruction is avoided, thus providing improved safety.
- New business opportunity like product differentiation, product promotion, patent [10].

4. DISADVANTAGES OF IMMEDIATE DRUG RELEASE TABLET

MDTs usually have inadequate mechanical strength. Hence, vigilant handling is required during formulation process.

- The tablets may leave disagreeable taste and/or grittiness in mouth if not formulated appropriately.
- Drugs with larger doses are difficult to formulate into MDTs e.g. Rifampin (600 mg), ethambutol (1000 mg) etc.
- Proteinaceous drugs should be avoided, if co-administration of enzyme inhibitors such as aprotinin, bestatin, puromycin and bile salts are required for the inhibition of proteolytic enzymes present in saliva.
- Patients who concomitantly take anticholinergic medication may not be the best candidates for MDTs and patients like Sjogren’s syndrome or dryness of the mouth due to decrease saliva production may not be good candidates for these tablet formulation.
- Some drugs resist compression, due to their amorphous nature or low-density and Bioavailability problems.
- Chance of GI irritation caused by locally high concentrations medicament.
- Difficulty in swallowing tablets in a small proportion of people and so size and shape become important considerations.
- Slow onset of action as compared to parenteral and solutions [11, 12].

5. SELECTION OF THE FDTs DRUG CANDIDATES

Several factors must be considered when selecting drug candidates for delivery as FDT dosage forms:

- 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.
- Patients who concurrently take anticholinergic medications may not be the best candidates for these drugs.
- Patients with Sjogren's syndrome or dryness of the mouth due to decreased saliva production may not be good candidates for FDT formulations.
- Drugs which are having short half-life and needs frequent dosing, which are very bitter or either having unacceptable taste whose taste masking cannot be achieved or which require controlled or sustained release are inappropriate for FDT formulation [13].

6. DRUGS USED IN FAST DISSOLVING DRUG DELIVERY SYSTEM

Example of some drug candidates best for FDT:

- **Analgesic and anti-inflammatory Agents**—Ibuprofen, Proxicam, Mefenamic Acid.
- **Anti-bacterial Agent**-Erythromycin, Tetracycline, Doxycycline, Rifampicin
- **Anti-fungal Agents** - Griseofulvin, Miconazole
- **Anti-Malarial** - Chlorquine, Amodiaquine
- **Anti-Gout Agent**- Allopurinol, Probenecid
- **Anti-Hypertensive** - Amlodipine, Nefidipine
- **Anti-Coagulants** - Glipizide, Tolbutamide
- **Anti-Protozoal Agents** - Benznidazole, Tinidazole
- **Anti-Thyroid agent** - Carbimazole
- **Cardiac Inotropic Agent** - Digitoxin, Digoxis
- **Gastro-Intestinal Agents** - Omeprazole, Ranitidine, Fomatidine etc.
- **Nutritional Agents** -Vitamin A, Vitamin B, Vitamin D, etc.
- **Oral Vaccine** - Influenza, Hepatitis, Polio, Tuberculosis, etc. [14].

7. EXCIPIENTS USED IN THE FORMULATION OF FDT

Excipients balance the properties of the actives in fast-melting tablets. This demands a thorough understanding of the chemistry of these excipients to prevent interaction with the actives. Determining the cost of these ingredients is another issue that needs to be addressed by formulators. The role of excipients is important in the formulation of fast-melting tablets. These inactive food-grade ingredients, when incorporated in the formulation,

impart the desired organoleptic properties and product efficacy. Excipients are general and can be used for a broad range of activities, except some activities that require masking agents [15].

7.1. Bulking agents

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. Mannitol in particular has high 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 [15, 16].

7.2. Binders

Main role of Binders is to keep the composition of these FDT together during the compression stage. Binders are used to impart smooth texture and disintegration characteristics to the system. Commonly used binders are cellulosic polymers such as ethylcellulose, hydroxypropylcellulose (HPC), and hydroxypropylmethylcellulose (HPMC), alone or in admixtures, povidones, polyvinyl alcohols, and acrylic polymers. The most commonly acrylic polymers are used as ammonio-methacrylate copolymer (Eudragit. RL and RS), polyacrylate (Eudragit. NE), and polymethacrylate (Eudragit. E). The right selection of a binder or combination of binders is essential to maintain the integrity and stability of the tablet. Binders can either be liquid, semi solid, solid or mixtures of varying molecular weights such as polyethylene glycol. 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 [15].

7.3. Emulsifying Agents

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 sulfates, 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 [15, 16].

7.4. Disintegrants

Disintegrants expand and dissolve when wet causing the tablet to break apart in the digestive tract, releasing the active ingredients for absorption. Disintegrant types include:

- Water uptake facilitators
- Tablet rupture promoters

They ensure that when the tablet is in contact with water, it

rapidly breaks down into smaller fragments, thereby facilitating dissolution. Examples of disintegrants include: cross linked polyvinyl pyrrolidone, sodium starch glycolate, cross linked sodium carboxymethyl cellulose (crosscarmellose) [15].

Mechanism of Superdisintegrants

There are four major mechanisms for tablets disintegration as follows :

(i) Swelling: Perhaps the most widely accepted general mechanism of action for tablet disintegration is swelling. Tablets with high porosity show poor disintegration due to lack of adequate swelling force. On the other hand, sufficient swelling force is exerted in the tablet with low porosity. It is worthwhile to note that if the packing fraction is very high, fluid is unable to penetrate in the tablet and disintegration is again slows down [16].

(ii) Porosity and capillary action (Wicking): Disintegration by capillary action is always the first step. When we put the tablet into suitable aqueous medium, the medium penetrates into the tablet and replaces the air adsorbed on the particles, which weakens the intermolecular bond and breaks the tablet into fine particles. Water uptake by tablet depends upon hydrophilicity of the drug/excipient and on tableting conditions. For these types of disintegrants maintenance of porous structure and low interfacial tension towards aqueous fluid is necessary which helps in disintegration by creating a hydrophilic network around the drug particles [16].

(iii) Due to disintegrating particle/particle repulsive forces: Another mechanism of disintegration attempts to explain the swelling of tablet made with ‘non-swellaible’ disintegrants. Guyot-Hermann has proposed a particle repulsion theory based on the observation that non-swelling particle also cause disintegration of tablets. The electric repulsive forces between particles are the mechanism of disintegration and water is required for it. Researchers found that repulsion is secondary to wicking [16].

(iv) Due to deformation: During tablet compression, disintegrated particles get deformed and these deformed particles get into their normal structure when they come in contact with aqueous media or water. Occasionally, the swelling capacity of starch was improved when granules were extensively deformed during compression. This increase in size of the deformed particles produces a breakup of the tablet. This may be a mechanism of starch and has only recently begun to be studied [16].

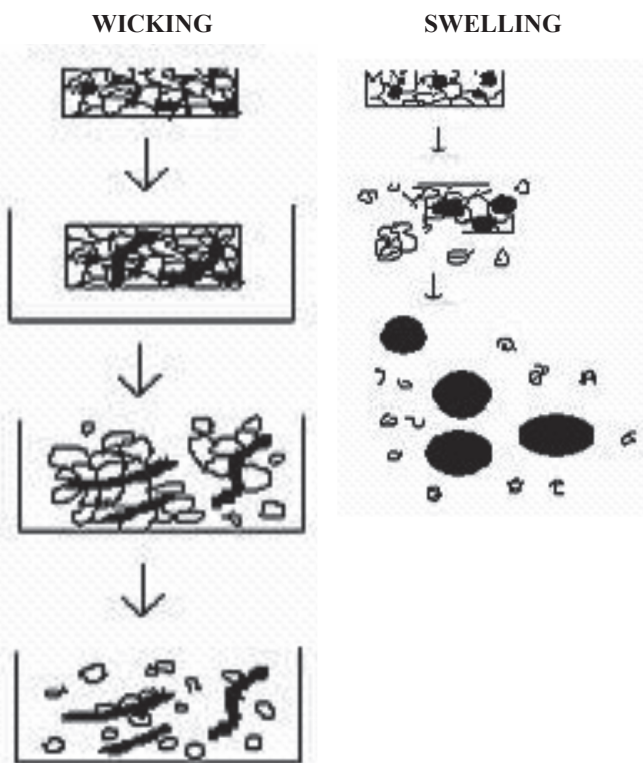


Fig. 1: Water is pulled by disintegrant and reduce the physical bonding force between particles
Fig. 2: Particles swell and break-up the matrix form within

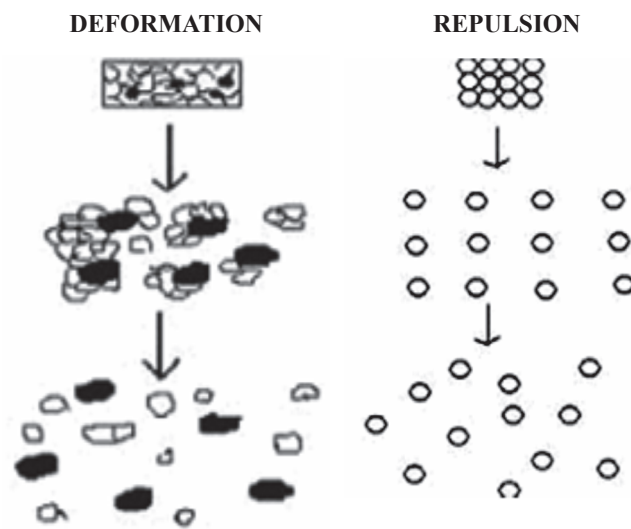


Fig. 3: Particles swell to pre-compression size and break up matrix
Fig. 4: Water is drawn into pores and particles repel each other because of resulting electrical force

7.5. Lubricants

Lubricants prevent ingredients from clumping together and from sticking to the tablet punches or capsule filling machine. Lubricants also ensure that tablet formation and ejection can occur with low friction between the solid and die wall. Common minerals like talc or silica, and fats, e.g. vegetable stearin, magnesium stearate or stearic acid are the most frequently used lubricants in tablets or hard gelatine capsules. They remove grittiness and assist in the drug transport mechanism from the mouth down into the stomach [17].

7.6. Glidants

Glidants are used to promote powder flow by reducing interparticle friction and cohesion. These are used in combination with lubricants as they have no ability to reduce die wall friction. Examples include colloidal silicon dioxide, talc, and etc [17].

7.7. Flavours and Sweeteners

Flavours and taste-masking agents make the products more palatable and pleasing for patients. The addition of these ingredients assists in overcoming bitterness and undesirable tastes of some active ingredients. Both natural and synthetic flavours can be used to improve the organoleptic characteristic of fast-melting tablets. Formulators can choose from a wide range of sweeteners including sugar, dextrose and fructose, as well as non-nutritive sweeteners such as aspartame, sodium saccharin, sugar alcohols and sucralose. The addition of sweeteners contributes a pleasant taste as well as bulk to the composition [18].

8. CONVENTIONAL TECHNOLOGIES FOR PREPARATION OF FDTs

8.1. Freeze Drying or Lyophilization

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 characteristic of the formulation. The entire freeze drying process is done at non elevated temperature to eliminate adverse thermal effects that may affect drug stability. 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 and their limited ability to accommodate adequate concentration of drugs [19].

8.2. Direct Compression

Easiest way to manufacture tablets is direct compression. Low manufacturing cost, conventional equipments and limited number of processing steps led this technique to be a preferable one. However disintegration and dissolution of directly compressed tablets depend on single or combined effect of disintegrant, water soluble excipients and effervescent agents. It is essential to choose a suitable and an optimum concentration of disintegrant to ensure quick disintegration and dissolution. Superdisintegrants are newer substances which are more effective at lower concentrations with greater disintegrating efficiency and mechanical strength. On contact with water the superdisintegrants swell, hydrate, change volume or form and produce a disruptive change in the tablet. Effective superdisintegrants provide improved compressibility, compatibility and have no negative impact on the mechanical strength of formulations containing high dose drugs. The type of disintegrants and its proportion are of prime importance. Also factors to be considered are particle size distribution, contact angle, pore size distribution and water absorption capacity. Studies revealed that the water insoluble superdisintegrants like sodium starch glycolate and Croscarmellose sodium show better disintegration property than the slightly water soluble agents like Crospovidone, since they do not have a tendency to swell. Superdisintegrants that tend to swell show slight retardation of the

disintegration property due to formation of viscous barrier. There is no particular upper limit regarding the amount of superdisintegrant as long as the mechanical properties of the tablet are compatible with its intended use. The superdisintegrant may be used alone or in combination with other superdisintegrants [20].



8.3. Sublimation Methods

The low porosity of compressed tablets may reduce water penetration into the tablet matrix resulting in slow disintegration or dissolution because these processes only occur at the surface. However, when volatile solids are compressed into tablets using a conventional method, they can be removed by sublimation to produce highly porous structures (Fig. 5). Typical materials used for this purpose include camphor, menthol, thymol, urea, ammonium carbonate, and ammonium bicarbonate for example; camphor can be incorporated into FDTs and then sublimated in a vacuum oven resulting in highly porous tablets with a porosity of up to 40%. The sublimation method is useful for making highly porous tablets, but vacuum treatment is a time consuming and costly process. Use of other materials, which could be sublimed under more general conditions (e.g., room temperature and/or normal pressure), would be of greater utility [20].

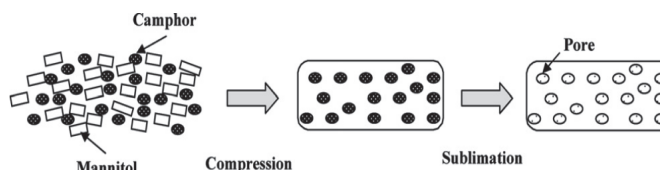


Fig. 5: Schematic view of the preparation of a porous tablet using sublimation of camphor

8.4. 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 and 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 [21].

8.5. 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. The dried cylinder can also be used to coat granules of bitter tasting drugs and thereby masking their bitter taste [22].

8.6. Moulding

In this method, moulded tablets are prepared by using water-soluble ingredients so that the tablets dissolve completely and rapidly. The powder blend is moistened with a hydro-alcoholic solvent and is moulded into tablets under pressure lower than that used in conventional tablet compression. The solvent is then removed by air-drying. Molded tablets are very less compact than compressed tablets. These possess porous structure that enhances dissolution [22].

8.7. Cotton Candy Process

This process is so named as it utilizes an inimitable spinning mechanism to produce floss like crystalline structure, which mimics cotton candy. This technique involves formation of matrix of polysaccharides or saccharides by simultaneous action of flash melting and spinning. The matrix formed is partially recrystallized to have better flow properties and compressibility. This matrix is milled and blended with active ingredients as well as excipients and subsequently compressed to ODTs. This process can accommodate high doses of drug and offers improved mechanical strength. However, high process temperature limits the use of this process [23].

8.8. Phase Transition

Kuno *et al.*, proposed a novel method to prepare ODTs with sufficient hardness by involving the phase transition of sugar alcohol. In this technique, ODTs are produced by compressing and subsequently heating tablets that contain two sugar alcohols, one with high and other with a low melting point. Heating process enhances the bonding among particles leading to sufficient hardness of tablets which was otherwise lacking owing to low/little compatibility [23].

9. PATENTED TECHNOLOGY

Some of the important patented technologies for preparation of FDTs [24] and the list of patented technologies and their products are given in Table 1.

The various technologies were developed for the formulation of ODTs and patented. These are:

9.1 Zydis Technology

Zydis was the first marketed technology developed by R.P. Scherer, Inc. for formation of new generation tablets. Zydis tablet is produced by lyophilizing or freeze-drying the drug in a matrix usually consisting of gelatin. The product is very light weight and fragile, which is dispensed in a special blister-packing. The preparation is also self-preserving because due to freeze drying, there is very little amount of water left in the drug for the attack of the microorganisms. The disintegration time of the tablets made by Zydis technology is few seconds [25].

9.2. Flash Dose Technology

Fuisz has patented Flash dose technology. Nurofen meltlet, a new form of ibuprofen as melt-in-mouth tablets, prepared using flash dose technology is the first commercial product launched by Bioavail Corporation. Flash dose tablets consist of self-binding shear form matrix termed as “floss.” Shear form matrices are prepared by flash heat processing [25].

9.3. Ora Quick Technology

KV Pharmaceutical Co. Inc. OraQuick utilizes its own patented taste masking technology i.e. MicroMask®. In MicroMask® technology, taste-masking process is done by incorporating drug into matrix microsphere. In this technique, tablet is prepared

Table 1. List of patented technologies based branded products

Patented technology	Basis of technology	Technology developed by company	Active ingredient	(Brand names)
Zydis	Lyophilization R.	R.P. Scherer	Loratidine	Claritin reditab and dimetapp quick dissolve
Orasolv	Direct compression	Cima Labs, Inc.	Paracetamol Zolmitriptan	(Temptra quicklets), (Zolmig repimelt),
Durasolv	Direct compression	Cima Labs, Inc.	Hyoscyamine sulfate Zolmitriptan	(NuLev) (Zolmig ZMT)
Wowtab	Direct compression	Yamanouchi Pharma Tech. Inc.	Famotidine	(Gaster D)
Flashdose	Cotton candy process	Fuisz Technology Ltd.	Tramadol HCl	(Relivia flash dose)
Flashtab	Direct compression	Ethypharm	Ibuprofen	(Nurofen Flash Tab)
Quicksolv	Lyophilization	Janssen pharmaceuticals	Cisapride monohydrate Risperidone	Propulsid quicksolv risperdal MTab
Lyoc	Lyophilization	Farmalyoc	Phloroglucinol Hydrate	Spasfon Lyoc
Oraquick	Micromask taste masking	K.V. Pharm. Co., Inc.	Hyoscyamine sulfate ODT	Hyoscyamine sulfate ODT
Ziplets	Direct compression	Eurand International	Ibuprofen (Cibalgina due fast)	(Cibalgina due fast)

by dissolving the sugar (sucrose, mannitol, sorbitol, xylose, dextrose, fructose, or mannose) and protein (albumin or gelatin) in a suitable solvent such as water, ethanol, isopropyl alcohol and ethanol-water mixture. The solution of matrix is then spray dried, yielding highly porous granules. In addition, utilization of lower heat of production is advantageous for heat-sensitive drugs. Granules formed then mixed with drug and other excipients and compressed at low compression force. KV pharmaceuticals claimed that matrix formed protects and surrounds the drug powder in microencapsulated particles is more reliable during this step [26].

9.4. Durasolv Technology

Durasolv is the patented technology of CIMA labs. The tablets made by this technology consist of a drug, fillers and a lubricant. Tablets are prepared by using conventional tableting equipment and have good rigidity. Durasolv is an appropriate technology for products requiring low amounts of active ingredients [26].

9.5. Wowtab Technology

WOWTAB technology employs a combination of low and high-moldability saccharides to produce fast-dissolving tablets using conventional granulation and tableting techniques. According to the patent, saccharides were divided into two groups: those with high mold ability and those with low mold ability. Low mold ability saccharides produce tablets with hardness between 0 and 2 kg, when 150 mg of such a saccharide is compressed under pressure of 10–50 kg/cm² using a die 8 mm in diameter. The typical low mold ability saccharides include lactose, mannitol, glucose, sucrose, and xylitol. High-mold ability saccharides produce tablets with hardness above 2 kg when prepared under the identical conditions. The typical high mold ability saccharides are maltose, mannitol, sorbitol, and oligosaccharides. When tablets are made by compressing a saccharide having low mold ability or high mold ability alone, the desired properties of adequate hardness and quick disintegration in the mouth cannot be achieved simultaneously. Moreover, if saccharides having low mold ability and high mold ability are mixed (physical mixture) before tableting, quick disintegration and dissolution in the mouth cannot be obtained. As clearly indicated in the patents, there is no single saccharide that can make tablets having both high strength and fast disintegration properties. For this reason, a saccharide having low mold ability was granulated with a saccharide having high mold ability as a binder. The low-mold ability saccharides were used as the main component. The tablets show an adequate hardness and fast disintegration and dissolution when put in the mouth [27].

9.6. Nanocrystal Technology

For fast dissolving tablets, Elan's proprietary Nanocrystal technology can enable formulation and improve compound activity and final product characteristics. Decreasing particle size increases the surface area, which leads to an increase in dissolution rate. This can be accomplished predictably and efficiently using Nanocrystal technology. Nanocrystal particles are small particles

of drug substance, typically less than 1000 nanometers (nm) in diameter, which are produced by milling the drug substance using a proprietary wet milling technique [28].

9.7. Pharmabust Technology

SPI Pharma, New castle, patents this technology. It utilizes the co-processed excipients to develop ODT, which dissolves within 30-40 seconds. This technology involves dry blending of drug, flavour, and lubricant followed by compression into tablets. Tablets obtained have sufficient strength so they can be packed in blister packs and bottles [28].

9.8. Dispersible Tablet Technology

Lek (Kovacic *et al.*, 1991) in Yugoslavia was issued patents for dispersible tablets of dihydroergotoxine (Milovac *et al.*, 1991) 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 acid. 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 [29].

9.9. Frosta Technology

Akina patents this technology. It utilizes the concept of formulating plastic granules and coprocessing at low pressure to produce strong tablets with high porosity. The process involves usually mixing the porous plastic material with water penetration enhancer and followed by granulating with binder. The tablets obtained have excellent hardness and rapid disintegration time ranging from 15 to 30s depending on size of tablet [29].

10. FUTURE PERSPECTIVE

With continued innovations in pharmaceutical excipients, one can expect the emergence of more novel technologies for FDTs in the days to come. These innovations may involve modifying formulation composition and processing to achieve new performance end-points or the merger of new technological advances with traditional pharmaceutical processing techniques for the production of novel fast dissolving dosage forms. It is reasonable to expect that future trends in innovations of drug delivery systems will continue to bring together different technological disciplines to create novel technologies.

11. CONCLUSION

The introduction of fast dissolving drug delivery system has

encountered the delivery of conventional dosage form. Due to the increasing demand of novel drug delivery, the fast dissolving drug delivery system has become one of the mile stone in the novel drug delivery system. The FDTs have potential advantages over conventional dosage forms, with their improved patient compliance, convenience, bioavailability and rapid onset of action had drawn the attention of many manufactures over a decade. Due to the constraints of the current FDDT technologies as highlighted above, there is an unmet need for improved manufacturing processes for fast dissolving tablets that are mechanically strong, allowing ease of handling and packaging and with production costs similar to that of conventional tablet.

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