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A Review on Orally Disintegrating Tablets:Innovations and Advances

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ABSTRACT

The Rapid growing area for the last few decades in the pharmaceutical industry, are the Oral Disintegrating Tablets. They effortlessly dissolve or disintegrate in saliva within 60 seconds. Here, disintegration plays a critical role, disintegrants or superdisintegrants in the dosage forms are included for advancement of solid orals. The Excipients used in the formulation of ODT's allow quick release of the drug, with faster dissolution. The innovations in the platform of formulating ODTs are aimed at both increasing the performance of the dosage form by decreasing the disintegration time and increasing the patient compliance. These achievements require constant promotion of formulation variables as well as techniques in the production of dosage forms. An attempt is made by this article to divulge the strategies which are used by inventors for improving the performance and acceptability of ODTs.

Keywords: Zydis Technology, Orasolv Technology, Super Disintegrants, Fast Dissolving.

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INTRODUCTION

The prevailing tablet seems to be more popular because of its easy portability and comparatively low cost of manufacturing, but it has poor patient compliance in case of pediatrics and geriatrics patients, in response to this Oral Disintegrating tablets were developed as an alternative to tablet, capsules & syrups. These ODT's comes under the category of Mouth Dissolving Drug delivery Systems (MDDs). A variety of MDDs like mouth dissolving tablets (MDTs) and mouth dissolving film (MDFs) were made marketable. MDFs evolved over the past few years in market in the form of breath strips which are novel and widely accepted by customers. The goal of the present review was to study the practicability of fast dissolving drug delivery systems. Upon consuming, these tablets disintegrate in saliva present in mouth without additional water for easy delivery of APIs [1]. Fast disintegrating tablets (FDTs) have received ever increasing demand during the last decade and the field has become a rapidly growing area in the pharmaceutical industry because of such tablets readily dissolve or disintegrate in the saliva generally less than 60 seconds. Controlled drug delivery systems are starting their stride in today's pharmaceutical market, but the solid orals especially tablets are most common and friendly approach with better patient compliance as on date[2-7]. These conventional tablets are intended to be swallowed whole and desired to disintegrate, release the medicaments for dissolution and providing therapeutic efficacy rapidly in the gastrointestinal tract. As disintegration plays a crucial role, so for development of solid orals, formulators are fascinating towards selection of proper disintegrants / superdisintegrants in dosage systems. Disintegrants are substances or mixture of substances added to the drug formulations, which assist dispersion or breakup of tablets and contents of capsules into smaller particles for dissolution. Superdisintegrants are those substances, which improves disintegration compared to disintegrants. The disintegration of dosage forms depends on various physical factors of disintegrants/superdisintegrants [8, 9]

They are:

1. Hardness of the tablets.
2. Nature of Drug substances
3. Compatibility with other excipients
4. Proportion of disintegrants used
5. Percentage of disintegrants present in the formulation.
6. Presence of surfactants.
7. Mixing and types of addition.

Superdisintegrants should possess the following characteristics:

1. Good flow properties
2. Non-toxic and Inert
3. Poor water solubility with good hydration capacity
4. Good compressibility
5. Poor gel formation
6. Requirement of least quantity.

Advantages of Orally Disintegrating Tablets [10, 11]

ODT formulations are easily swallowable and have good stability, easy production process, smaller packing size and better patient compliance. Their palatability is the added advantage of these dosage form compared to the other conventional dosage forms. Since the Oral Disintegrating Tablets are designed to disperse or dissolve at once when they contact saliva, it is not necessary to chew the tablet or drink water to swallow the entire tablet. Advantages like comfort and increase in patient compliance can be gained with application of orally disintegrating tablets to the aged, paralyzed patients as well as to the pediatric, geriatric and psychiatrically dysphagic patients.

Most of the patients experience difficulty in swallowing tablets and hard gelatinous capsules, as a result of which, they fail to take their medicine as prescribed. It is reported that swallowing difficulty (dysphasia) that can be observed due to neoplasia, neuromuscular and metabolic disorders, infectious diseases, iatrogenic causes, anatomic abnormalities, autoimmune disorders and reasons such as stress/anxiety has been observed widespread throughout the entire age groups and that 35% of the overall population has been affected.

Characteristics of Fast Dissolving Delivery System

Easy administration

FDDs are easy to administer and handle hence, leads to better patient compliance. Generally, geriatrics experience trouble in consuming the conventional dosage forms (tablets, capsules, solutions and suspensions) because of extreme tremors and dysphasia. Fast Dissolving Delivery Systems may offer a best solution for these problems. [12]

Taste of the medicament

MDDs generally contain the medicament in taste masked form. Taste-masking is of crucial importance in the formulation of an appropriate FDDT. Conventional tablet formulations usually do not address the issue of taste masking, because it is pretended that the dosage form will not dissolve until it passes the oral cavity. Most of the oral suspensions, syrups, and chewable tablets

simply contain flavors, sugars and other sweeteners to overwhelm or complement the bitter taste of the drug[13]. Current methods of taste masking in fast dissolving/disintegrating tablets include sweeteners and flavors; however, these are not a sufficient means for taste-masking many bitter drugs.

Hygroscopicity

Many fast dissolving dosage forms are hygroscopic and cannot be able to maintain its integrity under normal condition. Special type packaging is to be done. [14]

Friability

Fast dissolving tablets are made of both very porous and soft moulded matrices to dissolve, disintegrate rapidly or compressed into tablets with very low compressional force, which makes the tablets friable and/or brittle which are difficult to handle, often requiring specialized peel-off blister packaging.[12]

Mouth feel

Mouth feel is critical, and patients should receive a product that feels pleasant. Any large particles from the Disintegrating tablet that are insoluble or slowly soluble in saliva would lead to an unpleasant gritty feeling. This can be overcome by keeping the majority of the particles below the detectable size limit. In some cases, certain flavors can imbibe an improved mouth feel perception, resulting in a product that is perceived as being less gritty, even if the only change is the flavor.[15]

Formulation Aspects of ODTs [11]

The ingredients that are used in the formulation of ODTs should quickly release the drug, resulting in rapid dissolution. This comprises both the Active pharmaceutical ingredient and the Additives.

A. **Selection of drug candidate:** Several factors may be considered while selecting an appropriate drug candidate for development of orally disintegrating tablets. The ultimate characteristics of a drug for dissolution in mouth and pregastric absorption from fast dissolving tablets include,

1. Good solubility in water and saliva
2. Free from bitter taste
3. Partially unionized at oral cavity pH
4. Dose lowers than 20mg
5. Ability to permeate oral mucosal tissue
6. Small to moderate molecular weight

There are no particular limitations as long as it is a substance which is used as an active pharmaceutical ingredient. Researchers have formulated ODT for various categories of drugs used for therapy in which rapid peak plasma concentration is required to achieve the desired pharmacological response. They include neuroleptics, cardiovascular agents, analgesics, anti-allergic, anti-epileptics, anxiolytics, sedatives, hypnotics, diuretics, anti-parkinsonism agents, anti-bacterial agents and drugs used for erectile dysfunction. In contrast, the following characteristics may render unsuitable for delivery as an orally disintegrating tablet:

1) Short half life and frequent dosing.
2) Very bitter or otherwise unacceptable taste because taste masking cannot be successfully achieved.
3) Require controlled or sustained release.

B. Selection of excipients: The excipients role is crucial in the formulation of fast-dissolving tablets. The excipients temperature should be preferably around 30–35^{0}C for rapid dissolving properties. The excipients mainly used in ODT formulation are at least one disintegrate, a diluents, a lubricant, and optionally a swelling agent, sweeteners, and flavoring agents etc. Ideal bulk excipients for orally disintegrating dosage forms should have the following properties:

- Faster disintegration and dissolution without leaving any residue.
- Taste masking
- Enables sufficient drug loading and remains relatively unaffected by changes in humidity or temperature.

Method of incorporation of disintegrants:

The imbibition of superdisintegrants in the dosage forms are mainly of 3 types

a. **Intragranular or during granulation**: Superdisintegrants and other excipients are blend together and then granulation is proceeded.

Table 1: List of Common Disintegrants and Superdisintegrants

S.No	Excipient	Category	Conc	Stability Criteria
1	Alginic acid	Disintegrant	1-5%	Hydrolyzes slowly at room temperature
2	Colloidal Silicon Dioxide	Disintegrant	5-10%	Hydroscopic , but do not liquefy upon absorption of water
3	Cross-povidone	Superdisintegrant	2-5%	As hygroscopic in nature, stored in an air-tight container, in a cool and dry place.
4	Methyl cellulose	Disintegrant	2-10%	Slightly hygroscopic, but stable
5	Micro-crystalline cellulose	Superdisintegrant	5-15%	Stable at dry and air tight condition
6	Starch	Superdisintegrant	5-15%	Stable at dry and air tight condition

b. **Extragranular or prior to compression:** In this process, the superdisintegrants are mixed with prepared granules before compression.
c. **Incorporation of superdisintegrants at intra and extra granulation steps:** In this process part of superdisintegrants are added to intragranular and a part to extragranules. This method usually produces better results and more complete disintegration than type '**a'** and type **'b'**

Mechanism of Superdisintegrants

Swelling

Feasibly the most widely accepted mechanism of action for tablet disintegration is swelling. Tablets with high porosity show poor disintegration due to lack of adequate swelling force. To achieve good disintegration low porosity tablets with adequate swelling force are to be made. It is advantageous to note that if the packing fraction is very high, fluid is unable to imbibe into the tablet and disintegration lowers.

Wicking

Disintegration by wicking or capillary action is always the debut. When we place the tablet into suitable fluid, the fluid penetrates into the tablet and replaces the air adsorbed on the particles, which weakens the intermolecular bond and breaks the tablet in to fine particles. Water uptake by tablet depends upon hydrophilicity of the particle 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 particle[17]**.**

Due to disintegrating particle/particle repulsive forces

Another mechanism of disintegration attempts to explain the swelling of tablet made with 'non-swellable' Disintegrants. Guyot-Hermann has proposed a particle repulsion theory based on the observation that non-swelling particle also cause disintegration of tablets. The electric repulsive forces between particles are the mechanism of disintegration and water is required for it. Researchers found that repulsion is secondary to wicking.[17]

Due to deformation

During tablet compression, disintegrant particles get deformed and these deformed particles become normal when they come in contact with aqueous fluids. Infrequently, 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.

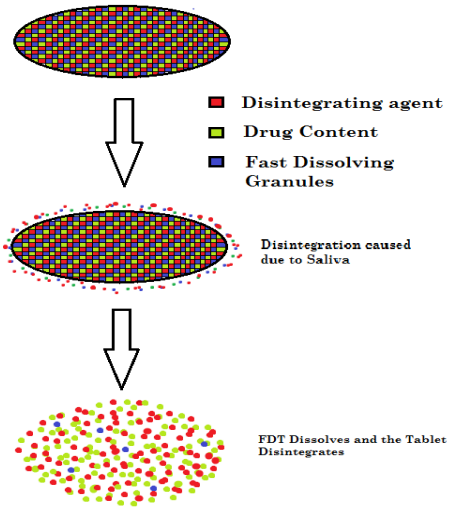

Figure 1 : Mechanism of Superdisintegrant

APPROACHES FOR FAST DISSOLVING DELIVERY SYSTEM

The fast-dissolving property of the tablet is attributable to a quick ingress of water into the tablet matrix resulting in its rapid disintegration.

Conventional Technologies for Fast Dissolving Tablets

I) Freeze drying or Lyophilization

The tablets prepared by this technique are very porous in nature and disintegrate rapidly when comes in contact with saliva. In this process, water is sublimated from the product after freezing the material. It is further frozen to bring it below its eutectic point. Primary drying is then carried out to reduce the moisture to around 4% w/w of dry product. Finally, to achieve the required volume, secondary drying is done. This also reduces the bound moisture. The major disadvantages of this technique are high cost of equipment and processing, and packaging issues[18].

II) Moulding

Tablets prepared by this technique are solid dispersions. The drug can exist as discrete particles or micro particles in the matrix. It can dissolve to form a solid solution or dissolve partially and remaining, if any, stays undissolved and dispersed in the matrix. Disintegration time, drug dissolution rate and mouth feel depends on the type of dispersion[18].

II.a) Different moulding techniques can be used to prepare mouth-dissolving tablets:

Compression moulding:

The powder mixture previously wetted with a solvent like ethanol/water is compressed into

mould plates to form a wetted mass.

Heat moulding

A molten matrix in which drug is dissolved or dispersed can be directly moulded into Orodispersable Tablets.

No vacuum lyophilization

This process involves evaporation of solvent from a drug solution or suspension at a standard pressure. Moulded tablets possess porous structure, which facilitates rapid disintegration and easy dissolution and also offer improved taste due to water-soluble sugars present in dispersion matrix. But moulded tablets lack good mechanical strength and can undergo breakage or erosion during handling and opening of blister packs. However, adding sucrose, acacia or polyvinyl pyrrolidone can increase mechanical strength[18].

III) Spray drying

This method can produce high porous and fine powders that dissolve faster. The formulations are incorporated with supporting agents like hydrolyzed and non hydrolyzed gelatins, mannitol as bulking agent, sodium starch glycolate or crosscarmellose sodium as superdisintegrants and an acidic/ or alkali material to enhance disintegration and dissolution. Tablet compressed from the spray dried powder disintegrated within 20 seconds when placed in an aqueous fluid[18,19].

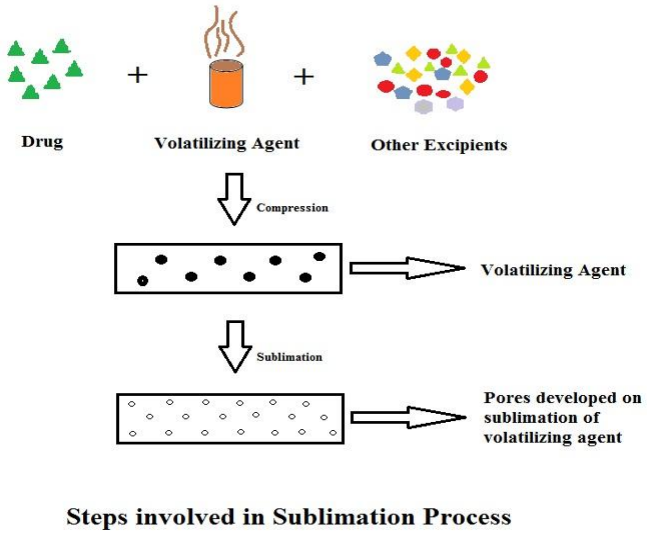

Figure 2: Steps involved in sublimation process

IV) Sublimation

The slow dissolution of the compressed tablet containing even highly water-soluble ingredients is due to the low porosity of the tablets. Inert solid ingredients that volatilize readily (e.g. urea, ammonium carbonate, ammonium bicarbonate, hexamethylene tetramine, camphor etc.) were

added to the other tablet ingredients and the mixture is compressed into tablets. The volatile materials were then removed via sublimation, which generates porous structures. Additionally, several solvents (e.g. cyclohexane, benzene) can be also used as pore forming agents.[19-23]

V) Direct compression

Direct compression is the simplest and economic tablet manufacturing technique. This technique can now be applied to preparation of ODT because of the availability of advanced excipients especially superdisintegrants and sugar based excipients.[24]

V.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. [24]

V.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, maltilol, maltose, mannitol, sorbitol, starch hydrolysate, polydextrose and xylitol, which display high aqueous solubility and sweetness, and hence impart taste masking property and a pleasing mouth feel.

VI) Mass extrusion

This technology involves softening of 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 tablets.[25]

VII) Cotton Candy Process

This process is so named as it utilizes a unique spinning mechanism to produce thread-like crystalline structure, which mimic cotton candy. Cotton candy process involves formation of matrix of polysaccharides or saccharides by simultaneous action of flash melting and spinning. The matrix formed is partially recrystallized to have improved flow properties and compressibility. This candy floss matrix is then milled and blended with active ingredients and excipients and subsequently compressed to ODT. This process can accommodate larger drug doses and offers improved mechanical strength. However, high-process temperature limits the use of this process[25]

Challenges in formulation of ODTS

As ODTs are different from conventional tablets, they need to overcome several challenges to maintain its unique properties.

A. Fast Disintegration: ODTs need to disintegrate in mouth as soon as possible in small amount of saliva of the patient.

B. Taste of Active ingredients: A pleasant taste inside the mouth becomes crucial for patient acceptance. If a product taste bad, the consumer could prefer swallowable tablets and care less about convenience of carrying ODT. If a product taste great then patient may prefer ODT over conventional Tablet. Unless the drug is tasteless or does not have an undesirable taste, taste masking techniques should be used. An ideal taste masking technology should provide drugs without grittiness and with good mouth feel.

C. Drug Properties: ODT technology should be versatile enough to accommodate unique properties of drugs such as solubility, crystal morphology, particle size, hygroscopicity, compressibility and bulk density of drug. These drug properties can significantly affect the final tablet's characteristics such as tablet strength and disintegration.

D. Tablet Strength and Porosity: Strength of a tablet is related to compressional pressure, and porosity is inversely related to compression pressure. There should be proper balance of these two properties in tablets to get the quality ODT. Low compression pressure causes ODTs to be soft, friable, and unsuitable for packaging in conventional blisters or bottles. A strategy to increase tablet mechanical strength without sacrificing tablet porosity or requiring special packaging to handle fragile tablets should be provided.

E. Moisture Sensitivity: Theoretically ODTs should have low sensitivity to moisture. But practically, it is very challenging as many high water soluble excipients are used in formulation to enhance fast dissolving properties as well to create good mouth feel. These highly water soluble excipients are susceptible to moisture, some will even deliquesce at high humidity. A good packaging should be provided to ODTs to protect from various environmental conditions.

Patented Technologies for Fast Dissolving Delivery System [26,27,30]

Currently, four fast-dissolving/disintegrating technologies have reached the U.S. market

1) Zydis technology (R.P. Scherer, Inc.),
2) WOWTAB technology(Yamanouchi Pharma Technologies Inc.),
3) OraSolv (Cima Labs, Inc.)
4) DuraSolv (Cima Labs, Inc.).

Table 2 : Patented Technologies for Fast Dissolving Delivery System

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, MaisonsAlfort, 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

Others Patented Technologies of FDDS[26,27,30]

1. FlashDose (Fuisz Technologies, Ltd.)
2. Flashtab (Prographarm Group)
3. OraQuick (KV PharmaceuticalCo., Inc.)
4. Quick –Dis Technology (Lavipharm Laboratories Inc.)
5. Ziplets/Advatab, (Passanocon Barnago, Italy)
6. Lyoc technology (PHARMALYCO)
7. Pharmaburst technology (SPI Pharma, NewCastle)
8. Frosta technology (Akina)
9. Nanocrystal Technology (Elan, King of Prussia)
10. Quicksolv (Janssen Pharmaceuticals).

Currently, four fast-dissolving/disintegrating technologies have reached the U.S. market

Zydis Technology

Zydis technology is patented by By Cardinal formerly R. P. Scherer. Zydis, the best known of the fast-dissolving/disintegrating tablet was the first marketed new technology tablet. The tablet gets dissolved in the mouth within seconds when placed on tongue. Lyophilizing or freeze-drying the drug in a matrix is used to produce the tablet by this technology. Special blister type packing is used because the tablet is very fragile and light weight. Patients should be advised to peel the film back to release the tablet but not to push the tablets through the foil film as it may break the tablet. The Zydis tablet is made to dissolve on the tongue in 2 to 3 seconds. In addition, to mask the bitter tasting drug it utilizes microencapsulation with specialized polymers or complexation with ion exchange resins. The combination of lyophilization and taste masking

creates a product that is both attracting to the eye and also to the senses of taste and touch. [31]

Table 3: Patented Products of Zydis technology

Patented Technology	Products	Name of the Company	Composition
Zydis	Claritin, Reditab	R. P. Scherer / Schering Plough, Kenilworth, USA.	Micronized loratidine (10mg), citric acid, mannitol, gelatin, mint flavor
	Feldene Melt	Pfizer Inc, NY, USA	Piroxicam (10 or 20 mg), mannitol, gelatin, aspartame, citric anhydrous
	Maxalt-MLT	R.P.Scherer / Merck & Co., NY, USA.	Rizatriptan (5 or 10 mg), mannitol, gelatin, aspartame, peppermint flavor
	Pepcid RPD	Merck & CO., NY, USA.	Famotidine (20 or 40 mg), mannitol, gelatin,aspartame
	Zyprexa Zydis	R.P.Scherer/Eli Lilly, Indianapolis, USA	Olanzapine (5, 10, 15 or 20 mg), mannitol, gelatin, aspartame, methyl paraben sodium, propyl paraben sodium
	Zofran ODT	R.P.Scherer/GlaxoWellcome, Middlesex, UK.	Ondansetron (4 or 8 mg), mannitol, gelatin, aspartame, methyl paraben sodium, propyl paraben sodium, strawberry flavor

Wowtab Technology

Wowtab technology is patented by Yamanouchi Pharmaceutical Co. The WOW in Wowtab symbolizes the tablet is to be given "With Out Water". The Wowtab technology utilizes sugar and sugar-like (e.g., mannitol) excipients. This process uses a combination of low mouldability saccharides (rapid dissolution) and high mouldability saccharide(good binding property).The two different types of saccharides are combined to form a tablet formulation with adequate hardness and fast dissolution rate. The active ingredient is mixed with low mouldability saccharides and granulated with high mouldability saccharides and compressed into tablet. Due to its significant hardness, the Wowtab formulation is a bit more stable to the environment than the Zydis or OraSolv.[27, 30]

Orasolv Technology

OraSolv was Cima's first fast-dissolving/disintegrating dosage form. Unlike Zydis, the tablet disperses in the saliva with the aid of almost imperceptible effervescence. The OraSolv technology is best described as a fast-disintegrating tablet. The tablet matrix dissolves in less than one minute, leaving coated drug powder. The taste masking associated with the OraSolv formulation is two-fold. In this technology, coating the drug powder and effervescence are means of taste masking in OraSolv. This technology is frequently used to develop over-the-counter formulations. The major disadvantage of the OraSolv formulations is its mechanical strength because the Orasolv tablets are only lightly compressed. [26]

Table 4 : Patented products of Orasolv

Patented Technology	Products	Name of the Company	Composition
Orasolv	Remeron Soltab	CIMA / Organon, GlaxoWellcome, Middlesex, UK.	Mirtazepine (15,30 or 45 mg), mannitol, aspartame, citric acid, crosspovidone, Avicel, NaHCO3, HPMC, magnesium stearatepovidone, PMA, starch, sucrose, orange flavor
	Tempra First Tabs	CIMA / Mead Johnson, Bristol Myers Squibb, NY, USA.	Acetaminophen (80 or 160 mg),mannitol (currently available in Canada)

DuraSolv Technology

DuraSolv is Cima's second-generation fast-dissolving/disintegrating tablet formulation. Produced in a fashion similar to OraSolv, DuraSolv has much higher mechanical strength than its predecessor due to the use of higher compaction pressures during tableting. DuraSolv is so durable that it can be packaged in either traditional blister packaging or vials. DuraSolv tablets are prepared by using conventional tableting equipment and have good rigidity(friability less than that 2%). The DuraSolv product is thus produced in a faster and more cost-effective manner. One disadvantage of DuraSolv is that the technology is not compatible with larger doses of active ingredients, because the formulation is subjected to such high pressures on compaction. The drug powder coating in DuraSolv may become fractured during compaction, exposing the bitter-tasting drug to a patient's taste buds. Therefore, the DuraSolv technology is best suited for formulations including relatively small doses of active compound.[27]

Table 5 : Patented products of Durasolv[28,29]

Patented Technology	Products	Name of the Company	Composition
Durasolv	Nulev	CIMA/Schwarz Pharma.	Hyoscyaminesulphate (0.125mg), aspartame, colloidal silicon dioxide, crospovidone, mint flavor, magnesium stearate, mannitol, Avicel
	ZOMIG-ZMT®	Glenmark Generics Ltd	Zolmitriptan (2.5mg), mannitol USP, microcrystalline cellulose NF, crospovidone NF, aspartame NF, sodium bicarbonate USP, citric acid anhydrous USP, colloidal silicon dioxide NF, magnesium stearate NF and orange flavor

Others Patented Technologies of FDDS

Flash Dose Technology

Fuisz Technologies has three oral FDDs. The first two generations of fast dissolving tablets

require some chewing are Soft Chew and EZ Chew. However, this begun the way for Fuisz's the most recent development, Flash Dose. The Flash Dose technology utilizes a unique spinning mechanism to produce a floss-like crystalline structure, much like cotton candy. This crystalline sugar can then incorporate the active drug and be compressed into a tablet. This procedure has been patented by Fuisz and is known as Shear form. The final product has a very high surface area for dissolution. It disperses and dissolves rapidly once placed onto the tongue. Interestingly the characteristics of the product can be altered greatly by changing the temperature and other conditions during production process.[2-7]

Flashtab Technology

Prographarm laboratories have patented the Flashtab technology[22]. In his technology active ingredient is placed in the form of microcrystals. Drug microgranules may be prepared by using the conventional techniques like coacervation, extrusion-spheronization, simple pan coating methods and microencapsulation. The microcrystals of the active ingredient are added to the granulated mixture of excipients prepared by wet or dry granulation, and subjected to compression to produce tablets. All the processing utilized the conventional tableting technology, and the tablets produced are reported to have good mechanical strength and disintegration time less than 60 seconds.[30]

Oraquick Technology

The OraQuick fast-dissolving/disintegrating tablet formulation utilizes a patented taste masking technology. KV Pharmaceutical claims its microsphere technology, known as MicroMask, has superior mouth feel over taste masking alternatives[34]. The taste masking process does not utilize solvents of any kind, and therefore leads to faster and more efficient production. Also, lower heat of production than alternative fast dissolving/disintegrating technologies makes OraQuick appropriate for heat-sensitive drugs. KV Pharmaceutical also claims that the matrix that surrounds and protects the drug powder in microencapsulated particles is more pliable, meaning tablets can be compressed to achieve significant mechanical strength without disrupting taste masking.

Quick –Dis Technology

LAVIPHARM LABORATORIES INC, has invented an ideal intraoral fast-dissolving drug delivery system, which satisfies the unmet needs of the market. Lavipharm's proprietary patented technology trademarked Quick-Dis™, is a thin, flexible, and quick-dissolving film. The film is placed on the top or the base of the tongue. It is retained at the site of application and rapidly releases the active agent for local and/or systemic absorption. The Quick-Dis™ drug delivery

system can be provided in various packaging configurations, ranging from unit-dose pouches to multiple-dose blister packages.[30]

Ziplets/Advatab

Ziplets/Advatab technology is patented by PASSANO CON BARNAGO, Italy. It utilizes water-insoluble ingredient combined with one or more effective disintegrants to produce ODT. This technology produces a tablet with improved mechanical strength and optimal disintegration time at low compression force. The main advantage of this technology is it can handle high drug loading and coated drug particles and does not require special packaging, so they can be packed in push through blisters or bottles.[32]

Lyoc

Lyoc technology is patented by PHARMALYCO. Oil in water emulsion is prepared and placed directly into blister cavities followed by freeze-drying. Non-homogeneity during freeze-drying is avoided by incorporating inert filler to increase the viscosity finally the sedimentation. High proportion of filler reduces porosity of tablets due to which disintegration is lowered. [32]

Pharmaburst technology

This technology is patented by SPI Pharma, New Castle. It utilizes the co-processed excipients to develop ODT, which dissolves within 30-40 Seconds. This technology involves dry blending of drug, flavor, and lubricant followed by compression into tablets. Tablets produced by this technology have sufficient strength so they can be packed in blister type packaging and bottles. [32]

Frosta technology

AKINA patents this technology. It utilizes the concept of formulating plastic granules and compressing them at low pressure to produce strong tablets with high porosity. Plastic granules composed of porous and plastic material, water penetration enhancer, and binder. The tablets obtained have excellent hardness and rapid disintegration time ranging from 15 to 30 sec depending on size of tablet.

Nanocrystal Technology

This is patented by Elan, King of Prussia. Nanocrystal technology includes lyophilization of colloidal dispersions of drug substance and water-soluble ingredients filled in to blister pockets. This method avoids manufacturing process such as granulation, blending, and tableting, which is more advantageous for highly potent and hazardous. [32]

Quick solv

This technology is patented by Janssen Pharmaceuticals. It utilizes two solvents in formulation a matrix, which disintegrates instantly. Methodology includes dissolving matrix components in

water using an excess of alcohol (solvent extraction). Thus the product formed has uniform porosity and adequate strength for handling.[17,32]

Table 6 : Drug Suitable for Fast Dissolving Drug Delivery System

Category	Drug
NSAIDs	Ketoprofen, Piroxicam, Paracetomol,Rofecoxib.
Anti-ulcer	Famotidine, Lansoprazole
Anti-histaminic	Loratadine, Diphenhydramine, Meclizine
Hypnotics and sedatives	Zolpidem, Clonazepam, Atenolol
Antipsychotics	Olanzepine, Risperidone, Pirenzepine
Antiparkinsonism	Selegiline, RamosetoronHCl, Ondansetron, Baclofen
Antiemetic	Sumatriptan, Rizatriptan benzoate, Zolmitriptan
Antimigrane	Mitraxepine, Fluoxetine
Antidepressant	Baclofen, Hydrochlorthiazide, Tramodol HCL
Miscellaneous	Propyphenazone, Spiranolactone, Phloroglucinol.

Table 7: Commercially available Fast Dissolving Tablets in India[19]

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
Zyprexia	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	Selegilline	Amarin Corp., London, UK
Tempra Quiclets	Acetaminophen	Bristol myers Squibb, NY, USA
Febrectol	Paracetamol	Prographarm, Chateauneuf, 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

Current & Future Developments

The innovations in the platform of developing ODTs are designed at both increasing the performance of the dosage form by decreasing the disintegration time and increasing the patient acceptance by masking the disagreeable taste of the active ingredients. These achievements require constant upgradation of formulation variables as well as technologies involved in the production of dosage forms. This article attempted to unveil the strategies that have been used by inventors for improving the performance and acceptability of ODTs. The use of superdisintegrants for achieving these aims is not new. However, with the improvement design of new techniques, it has become possible to develop ODTs with reduced content of

superdisintegrants and with better mouth feel. Further, incorporation of active ingredients in dosage forms such as fast dissolving films, chewing gums and micro particles are expected to provide a highly acceptable means of delivery drugs to especially, pediatric and geriatric patients. The use of techniques like freeze drying, direct compression and effervescence are highly suitable for formulating stable and acceptable dosage forms of vitamins, enzymes and thermolabile drugs. The development of Durasolv and Orasolv technologies are worth mentioning in this regard. Similarly, considerable research towards producing modified microcrystalline cellulose or starch in order to engineer them suitable for direct compression has significantly reduced the product development time for optimizing ODT formulation. The application of nanotechnology to formulation is expected to further enhance the acceptance and performance of these dosage forms. However, not much work seems to have been done in this particular specialized area. Nevertheless, judicious use of excipients and technology can be expected to make the task of formulating an acceptable and effective ODT easier than before.

CONCLUSION

Fast dissolving drug delivery system has better patient compliance, improved efficacy and better safety compared with conventional oral dosage forms. Today, fast disintegrating tablets are more widely available as OTC products for the treatment of allergies, cold and flu symptoms. The future potential for these products is promising because of the availability of new technologies combined with strong market acceptance and patient demand. Future possibilities for improvements in Rapid disintegrating and drug delivery are bright, but the technology is still relatively new. The research is still continuing. More products need to be commercialized to use this technology properly. Mouth dissolving films are intended for the application in the oral cavity and they are innovative and promising dosage form especially for use in pediatrics and geriatrics. Mouth dissolving films have several advantages over conventional dosage forms and fast dissolving tablets. Fast dissolving tablets have gained considerable attention as a preferred alternative to conventional tablets and capsules due to better patient compliance. This review discusses the method of preparation, properties, advantages, mechanisms, drugs to be incorporated in the fast dissolving drug delivery system and evaluation of the mouth dissolving tablet are emphasized.

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