Review Article

Orally Disintegration Tablets – Patient Friendly Tablets

Amar Issa[1]*, Oussama Mansour[2], Tamim Hammad[3]
[1*]Department of Pharmaceutics, Faculty of Pharmacy, Al Andalus University, Tartous, Syria.
[2]Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Al Andalus University, Tartous, Syria.
[3]Department of Pharmaceutics, Faculty of Pharmacy, Tishreen University, Latakia, Syria.
***Corresponding author's E-mail:** mansouroussama@yahoo.fr

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ABSTRACT

It is a worldwide known fact that patient compliance is one of the most crucial key factors in recovery and healing. Occasionally, hard-to-swallow tablets are one of the barriers against patient compliance. Hence, pharmaceutical industry has spawned many trials to create and develop new dosage forms for known drugs in order to make them much easier to be taken so that patients positively enjoy the experience. However, one of the most important dosage forms which gained a considerable attention of researchers and pharmaceutical industrialists over the last decades is Orally Disintegrating Tablets (ODTs) which disintegrate in mouth rapidly, usually within a matter of seconds, when placed upon the tongue without the need for water. Thus, they are very integral in terms of getting over the challenge of patient compliance that facing the pharmaceutical industry nowadays. Additionally, they could be a cost-effective dosage form. All in all, ODTs are indeed a very valuable product not only for patients but also for pharmaceutical companies. The purpose of the study is to shed light on ODTs as a very valuable product not only for patients, but also for pharmaceutical companies. On the other hand, it aims to review the development and the significant growth in their formulation, excipients and preparation techniques. Besides, it shows ODTs characteristics, properties of drug candidates and the promising outlook of this dosage form.

Keywords: Orally Disintegrating Tablets, ODTs, Direct compression, Freeze drying

INTRODUCTION

Hectic life style and the industrial revolution nowadays have drawn the attention of both academia and researchers in pharmaceutics to the importance of introducing patients a significantly improved experience with dosage forms.[1-4] On one hand, tablets are definitely the most attractive option for researchers for so many reasons. First, specificity in dose. Second, good patients compliance compared to other dosage forms like injection solutions and suppositories. Third, good physical and chemical stability and finally the ability to mask the bitter taste of some drugs.[5-6] On the other hand, there is no doubt that taking tablets is not always easy especially by pediatric and geriatric patients and by some other categories such as travelling patients who suffer from inaccessibility to water and patients who are not cooperative like epilepsy patients and depressed patients who try to take their drugs without drawing others' attention. Therefore, advancements in pharmaceutical sciences and industries have resulted in producing a new dosage form called orally disintegrating Tablets (ODTs) to cater the needs of such patients.[3,7-12]

ODTs are solid dosage forms which disintegrate in mouth rapidly, usually within a matter of seconds when placed upon the tongue and the resulting suspension is swallowed without the need for water, making this dosage form a convenient, potentially more effective alternative to conventional solid dosage forms in terms of obviating the challenge of patient compliance. In addition to that, ODTs are able to release the active ingredients rapidly, giving the fast effect that is needed for some cases like allergy, pain, and anxiety. Besides, drug candidates which undergo pre-gastric absorption when formulated as ODTs may show increased oral bioavailability.[10-14]

Moreover, ODTs offer many advantages for pharmaceutical companies. First of all, ODTs have a great brand value because they enable companies to tap into new patient populations due to their convenience and ease of use. Another key reason that companies choose an ODT over other delivery technologies is that it is a relatively easy, cost effective and often less risky delivery option to develop. Since the route of administration remains the same, ODTs that are formulated as bioequivalent line extensions or generic versions of an existing oral dosage form have minimal clinical requirements to gain approval.[15]

Also, ODTs enable the creation of branded, differentiated line extensions and extend the patent life and market exclusivity for drugs that no longer have patent protection. Consequently, a new dosage form allows a manufacturer to protect market share and thereby increase revenues.[15]

As a whole, features of ODTs make them introduce lots of benefits for both patients and manufacturers.

FDA Definition and Requirements for ODTs

FDA has defined ODTs as a solid dosage form containing medicinal substances which disintegrates rapidly, usually within a matter of seconds, when placed upon the

tongue.[13,14] Occasionally, It is worth pointing out that the US FDA ODT guideline suggests 30 seconds (*in vitro*) as the preferred disintegration time whereas the disintegration time that recommended by European pharmacopoeia is less than 3 minutes.[13,16]

On the other hand, the term of Orally Disintegrating tablets (ODTs) for this dosage form was coined by USA Pharmacopoeia (USP).[17] Meanwhile, it was called Orodispersible tablets by European Pharmacopoeia.[15] According to FDA Guidance, products labeled as ODTs should match the primary characteristics for this dosage form such as:[13,14]

Patient compliance: ODTs should have a pleasant taste and a pleasant mouth feel. Therefore, tablet should left minimal or no residue in the mouth after swallowing.

Tablet size

Weight of the tablet should not exceed 500 mg.

Disintegration time

Tablets should not take longer than 30 seconds to disintegrate.

Ease of Administration

ODTs should require no water for oral administration. Occasionally, this parameter can be affected by many factors like tablet size and drug solubility.

In addition to that, the tablets should be durable enough to withstand the handling required to package them in either bottles or blister packs. Ironically, it is not surprising that increasing the mechanical strength will delay the disintegration time.

So, a good compromise between these two parameters is always essential**.** However, ODTs generally should show low sensitivity to environment conditions such as humidity and temperature since most of the materials used in ODTs are meant to dissolve in minimum quantity of water.[2,11-13,15]

ODT Drug Candidates

Several factors must be considered when selecting drug candidates for delivery as ODT dosage owing to the effect of some properties of many drugs on the tablet properties and thus the ODTs performance.

For instance, the solubility, crystal morphology, particle size, hygroscopicity, compressibility, and bulk density of a drug can significantly affect the final tablet's characteristics, such as tablet mechanical strength and disintegration time.[18]

By the way, clinical needs play integral role in selecting drugs for ODTs. Consequently, the highest percentage of the ODT world market is in three therapeutic categories: central nervous system, gastrointestinal, and oncology.[15]

In general, drugs with the greatest potential for success with ODTs are treatments for GERD, pain, schizophrenia and other CNS diseases, Parkinson's disease, migraine, nausea and sleep aids.[19]

ODTs Preparation Techniques

Along with the rapid market growth of ODT products which reached the peak of 20% each year from 2003 on, the technologies, too, have advanced considerably over the years.[15] Occasionally, many techniques have been reported for the formulation of ODTs.[20-23]

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

Freeze-Drying or Lyophilization[5,20-22,24]

Freeze drying is a pharmaceutical process in which water is sublimed from the product after it is frozen. It is used to dry extremely heat-sensitive materials.

In this process the initial liquid solution or suspension is frozen, the pressure above the frozen state is reduced and the water removed by sublimation. Hence, there are three states of matter involved: liquid to solid, then solid to vapor.

Figure 1 represents the phase diagram for the water system which clarifies the process of freeze drying. However, the diagram consists of three separate areas, each representing a single phase of water, either solid, liquid or vapor. Two phases can coexist along a line under the conditions of temperature and pressure defined by any point on the line. The point O is the one unique point where all three phases can coexist, and is known as the triple point. Its coordinates are a pressure of 610 Pa and a temperature of 0.0075°C.

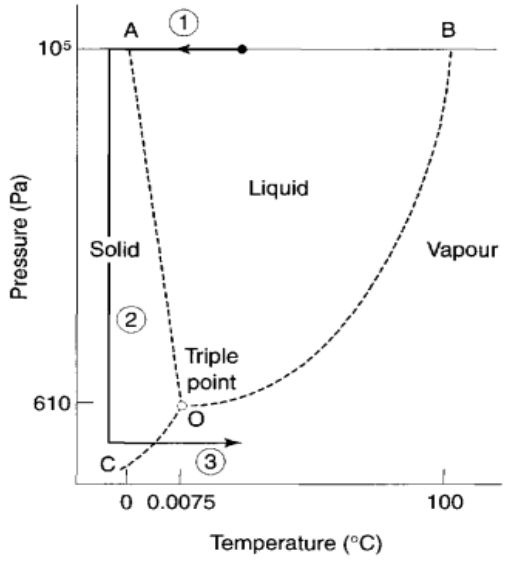

Figure1: The phase diagram for water.

The lines on the phase diagram represent the inter phase equilibrium lines, which show:

1. The boiling points of water points which represent the transition of liquid water to vapor by reduction of the external pressure above the water or by increasing temperature. (BO in Figure 1).
2. The melting points of ice which represent the transition of ice to liquid water on reduction of the external pressure above it or by increasing temperature. (AO in Figure 1).
3. Line (CO in Figure 1) that consists of points which represent the conversion of solid ice into vapor without passing through the liquid phase. This status can occur if solid ice is maintained at a pressure below the triple point while heating.

Tablets formulated by this technique usually have porous structure and large specific surface area which give rapid dissolution and consequently, increase absorption and bioavailability.

Following diagram (Figure 2) summarizes the stages of ODTs preparation process by freeze drying method:

1. The mixture is prepared by weighing the active ingredient and dispersing or solving it in an aqueous solution for the polymer or the carrier.
2. The mixture is poured in a blister pack.
3. The liquid material is frozen by liquid Nitrogen.
4. The frozen solvent is sublimed in order to obtain a high porous product.
5. Eventually, since the freeze drying process is completed, the product is packed by an Aluminum blister.

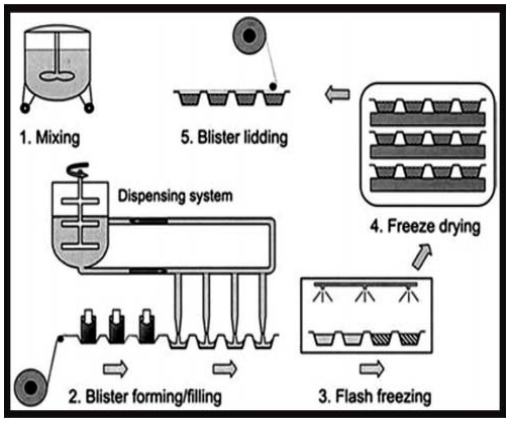

Figure 2: The stages of ODTs preparation process by freeze drying method.

However, Table (1) demonstrates some examples for used excipients in preparing ODTs by freeze drying.

On the other hand, there are some disadvantages of preparing ODTs by freeze drying like high cost, long time and insufficient mechanical strength due to the fragility of tablets which makes the conventional packaging unsuitable and increases the sensitivity to temperature and humidity.

Table 1: Used Excipients in preparing ODTs by freeze drying.

Excipient	Usage	Example
Polymer	Bulking agent/ increase mechanical strength	Gelatin, Dextrin
Saccharides	Increase hardness and patient compliance	Mannitol, Sorbitol
Suspending agent	Insure a good dispersing in the aqueous solvent.	Acacia gum
Preservatives	Prevent the growth of microorganisms	Parabens
Buffers	Prevent the changes in pH	Phosphate buffer
Flavoring agent	Increases patient compliance	
water	Forms the porous units	

Tablet Molding

Preparation process of ODTs by molding can be divided into two major methods: solvent method, and heat molding.

Solvent method

Solvent method is used to prepare ODTs by using water-soluble disintegrating agents which provide a rapid dissolution. Occasionally, the powder mixture is moistened with a solvent (usually ethanol or water), and then the mixture is molded into tablets under pressures lower than those used in conventional tablet compression. Thus, this process is also known as compression molding. Finally, the solvent is removed by air-drying. Rapid dissolution of molded tablets can be explained by the higher porous structure than conventional tablets owing to the fact that molded tablets are usually compressed at a lower pressure than conventional tablets.[2,18,21]

Heat molding

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 (under a low pressure of 0.03-0.06 bar). However, molded tablets typically do not have great mechanical strength. Yet, it can be enhanced by using of binder agents.[2,18,21]

Sublimation

There is no doubt that low porous structure is the main cause of the slow dissolution of conventional tablets even if they contain highly soluble ingredients. Hence, sublimation was a good phenomenon to be used in the preparation of ODTs. Figure 3 simplifies steps of ODTs preparation by sublimation which include adding Inactive volatile solid excipients like urea, ammonium carbonate, camphor etc. to the other ingredients, and compressing

the mixture into tablet. Eventually, removal of volatile ingredients by sublimation generates a porous structure.[2,21]

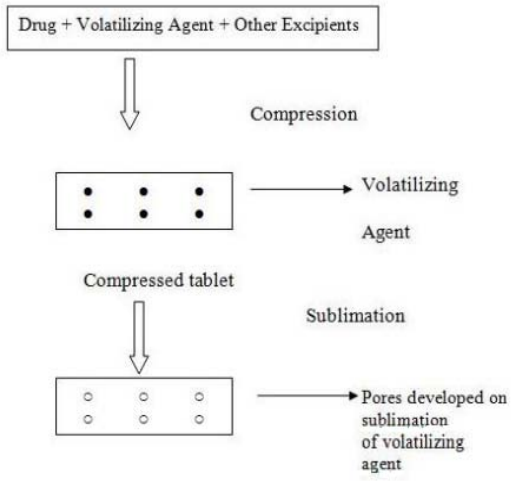

Figure 3: Preparation of ODTs by sublimation

Mass Extrusion

Mass extrusion technology can be summarized by softening the active blend using a solvent mixture of water soluble polyethylene glycol with methanol and expulsion of softened mass through the extruder or syringe to obtain cylinder of the product into even segments employing heated blade to form tablets.[2,18,21]

Spray Drying

This technology depends on using spray dried powders in the formulation of ODTs. The spray drier provides a large surface area for heat and mass transfer by atomizing the liquid to small droplets. These are sprayed into a stream of hot air, so that each droplet dries to an individual solid particle. There are many forms of spray drier and Figure 4 shows a typical design.[5]

However, spray dried powders do not only have large surface area, but also a porous structure which may enhance dissolution. Additionally, spray dried powders are free-flowing with almost spherical particles, and is especially convenient for tablets as it has excellent flow and compaction properties.[2,18,21]

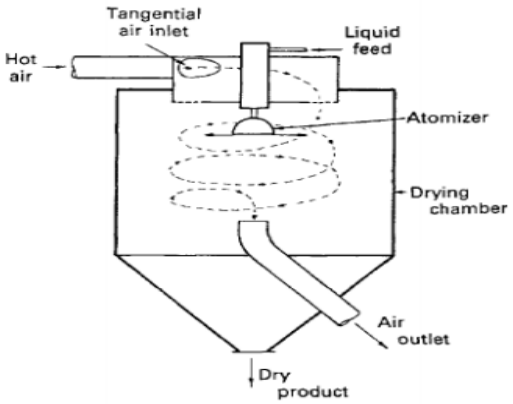

Figure 4: A typical spray drier

Direct Compression

Direct compression is the easiest and fastest method to prepare ODTs for so many reasons such as the ability to do it by conventional equipment, available excipients and easy steps. Occasionally, other used methods to prepare ODTs like freeze drying and spray drying require longer processing time and a higher cost for equipment. Besides, although ODTs which prepared by these technologies disintegrate instantly when places upon the tongue, yet, they are typically fragile and can break during handling or when blister packets are opened. Yet, ODTs which are prepared by direct compression have a good mechanical strength.

Disintegration of ODTs which prepared by direct compression relies on single or combined action of disintegrants (superdisintegrants such as Crospovidon), water-soluble excipients and effervescent agents.[21,25,26-29]

However, many researches have been carried out in order to prepare ODTs of different PAIs in different methods. For example, Anupama K. have worked on preparing ODTs for Oxcarbazepine by direct compression using different diluents like Mannitol, Di-calcium phosphate and different disintegrants such as Crospovidon and Sodium Croscarmillose. However, formulations which are prepared by Mannitol and Crospovidon had the least disintegration time (30 ± 5 sec)[27]. In addition to that, Suinita A have formulated ODTs for Rizatriptan Benzoate using different diluents as Lactose, Mannitol and Microcrystalline Cellulose and different disintegrants like Crospovidon, Sodium Croscarmillose and Sodium Starch Glycolate. Occasionally, the disintegration time for formulated tablets was in the range of 20 sec and 90 sec. Yet, Crospovidon has given ODTs with the least disintegration time.[29]

On the other hand, Rajitha K have formulated and compared Buspiron ODTs prepared by different methods like direct compression and freeze drying. As a consequent, they have succeed in attaining ODTs with a disintegration time of 35 sec and 30 sec by direct compression and freeze drying, respectively.[30] Meanwhile, Karsono have formulated ODTs for Ibuprofen by freeze drying technique using water soluble matrix consisting gelatin 5% and mannitol in different ratios. The results had shown that ODTs used higher amount of gelatin 5% showed faster disintegration time.[22]

Additionally, Issa A have carried out a comparative study of different formulations of Chlorpheniramine maleate ODTs which are prepared by direct compression technology using different diluents such as Lactose, Mannitol and Glucose and different super disintegrants like Kollidon-cl® (Crospovidon), Microcrystalline Cellulose and Sodium Starch Glycolate. The comparative study of prepared formulations have shown that the lowest disintegration time (17 ± 2.5 sec) was found in the formulation which contains glucose as a diluent and kollidon-CL® as a disintegrant. However, this result was explained by the high solubility of glucose compared to

the other two diluents. On the other hand, this might be due to high porosity of Kollidon-CL which is a cross-linked synthetic polymer. Hence, water can get throw the pores rapidly exhibiting high capillary activity. That can accelerate tablet swelling and disintegration with little tendency to form gels. Additionally, as Kollidon-CL is non-ionic compound, the disintegration is independent of the acidity of gastrointestinal tract.[31]

Marketed Branded Excipients for Preparing ODTs by Direct Compression

There is no doubt that pharmaceutical and commercial features which ODTs have, especially which are prepared by direct compression method are the main reasons for the increasing demand for ODTs day by day. Besides, development in the manufacturing processes of Oral dosage forms and ODTs including changing the process of tablet preparation by wet granulation to direct compression requires the development of added excipients in order to achieve formulations with desired end effects. Eventually, Pharmaceutical companies have competed to create and market suitable excipients for preparing ODTs by direct compression in order to alternate many excipients by a single appropriate one.[2,5,18]

However, the most successful marketed excipients around the world to prepare ODTs by direct compression are Coprocessed blends of excipients, modified Mannitol, modified sugars and modified resins.

Coprocessed Blends of Excipients

Ludiflash®

Ludiflash® is composed of the following.[32,33]

1. 90 % Mannitol: (Fast-dissolving filler with a mildly sweet taste).
2. 5 % Kollidon® CL-SF (Crospovidone): Highly effective disintegrant which makes tablets disintegrate with very little liquid and offers a pleasantly smooth and creamy mouthfeel.
3. 5 % Kollicoat® SR 30 D (Polyvinyl acetate): (Hydrophobic binder for enhanced disintegration).

Ludiflash® is designed by BASF and it is the one of the novel excipients for Fast dissolving drug delivery which disintegrate rapidly within seconds with soft, creamy consistency.

It is specially designed for direct compression on standard high speed tablet machine for hard tablet with very low friability. Ludiflash® have good flowability, and low hygroscopicity and gives highly porous tablets which disintegrate quickly releasing the active pharmaceutical ingredients rapidly.

Pharmabust®

Pharmabust® is a mixture of highly compatible spray dried excipients. It is mainly composed of Mannitol and other excipients which allow rapid disintegration. Pharmabust® is smooth and creamy and helps to mask taste and grittiness the actives.[2,15,18]

F_Melt®

It is a mixture of spray dried excipients which contains of carbohydrates, disintegrants and some inorganic components. This system is suitable for direct compression manufacturing of fast-dissolving oral tablets containing Active Pharmaceutical Ingredients (APIs) and lubricants. F-Melt® exhibits excellent tabletting properties and facilitates rapid water-penetration for a fast disintegration time within 30 seconds. It has advantages of highly flowability, with less sticking or capping.[2,15,18]

Modified chitosan with silicon dioxide

This is the new excipients based on co precipitation of chitosan and silica. Occasionally, Chitosan is a polysaccharide which composed of copolymer for Glucosamine and N-Acetyl Glucosamine. The physical interaction between chitosan and silica create an insoluble, hydrophilic highly absorbent material, resulting in superiority in water uptake, water saturation for gelling formation. It is superdisintegrant with improved flow and compaction properties. It acts as both superdisintegrant and filler.[2,15,18]

Modified Mannitols

Mannitol is a widely used excipient in orally disintegrating dosage forms as a sweetener and it gives good mouth feel. Therefore, Mannitols are modified nowadays in order to make them multifunctional so they can perform functions of more than one excipient.[2,15,18]

Orocell®

Orocell® is a spheronised mannitol compound with different uses as a binder, filler and carrier in immediate release oral disintegrating tablet (ODT) preparations. In addition to that, it is worth to pointing out that Orocell® has exceptional features such as excellent flow, out-standing disintegration performance, good taste with cooling sensation.

However, Orocell® is divided into two types according to its particle size: Orocell 200® (<315µm) and Orocell 400® (<500µm)[2,15,18].

Mannogem EZ®

Mannogem EZ® is a spray dried mannitol with a sweetening power about a half as much as sucrose. Occasionally, Mannogem EZ® is especially designed for direct compression tablets. Therefore, it is known for it is free flowing, excellent compressibility. Moreover, Mannogem EZ® is a nonhygroscopic and it disintegrates rapidly leaving a good mouth feel which make it suitable for orally disintegrating dosage forms.[2,15,18]

Pearlitol SD®

Pearlitol SD® is a granulated Mannitol. It occurs as odorless, slightly sweet tasting (its sweetening power is nearly 40% as much as sucrose), crystalline powder.

However, Pearlitol SD® is nonhygroscopic and has good physical and chemical stability. On the other hand, it has a good flowability and compressibility and it can be used in different process like wet granulation, direct compression and freeze drying.

According to its particle size, Pearlitol SD® has two types: Pearlitol 100 SD® (100µm), Pearlitol 200 SD® (200µm).[2,15,18]

Modified Sugars

Advantose 100®

Advantose 100® is a combination of fine and coarse spray-dried particles of maltose. Consequently, it has good flowing and compressing properties. Furthermore, it has lower density and better solubility than lactose. Hence, its disintegration is not only good by itself, but also can improve disintegration of other excipients.[2,15,18]

Glanel Q®

Glanel Q® is a multifunctional excipient. It occurs as white, odorless, water soluble, crystalline substance derived from sucrose.

By the way, Glanel Q® has very low hygroscopic nature, good chemical stability and excellent compressing properties as good flowability, homogeneity of the mixture and thus content uniformity. Glanel Q® can act as binder and filler. Therefore, there is no need to use low compressed binders.[2,15,18]

Glucidex IT®

Glucidex® it is micro granulated maltodixtrin which enables almost instantaneous dispersal and dissolution in water. Its free-flowing properties make it ideal as a diluent for directly compressed tablets especially for vitamins and supplement tablets.[2,15,18]

Modified Resins

Polacrilin Potassium (Amberlite IPR88®)

Polacrilin Potassium is the potassium salt of a cross linked metacrylic acid with divinyl benzene. However, it is weakly acidic cation exchange resin.

It is used effectively at 1-2% of solid dosage forms as a disintegration due to its extremely large swelling capacity in aqueous solutions. Besides, and it is also useful in taste masking.[2,15,18]

Many researchers have tried to use many marketed excipients in order to prepare ODTs. For instance, a study has been carried out by Baker.

In order to formulate ODTs for Sumatriptan by direct compression method using Polacrilin Potassium. As a consequent, the disintegration time for prepared ODTs was 45 sec.[33]

Besides, Sandra Kruz prepared ODTs for Respiredone by direct compression method using Ludiflash® and the disintegration time was 27 sec.[34] Eventually, Ashutosh Mohapatra formulated ODTs for Metformin using Pearlitol SD® and the attained disintegration time was 85 sec.[34]

Patented Technologies

No one can deny that high profits and product features and distinctions which pharmaceutical companies can gain by ODTs is a vital reason for the rapid growth of ODTs market.[5]

Consequently, pharmaceutical companies compete to maintain market share and maximize commercial returns by developing ODTs preparation technologies and creating many new developed patented methods such as Zydis®, Orasolv®, Durasolv®, Shearform®, Ceform®, Flashdose®, Flashtab®, Wowtab®.

However, the capability of each technology varies in terms of manufacturing process and tablets characteristics.

Occasionally, Table (2) simplifies some examples for patented technologies and summarizes their advantages and disadvantages.[5,9-11,21,25]

On the other hand, Table 3 represents some examples of the most successful ODT products like Lilly's ODT zyprexaZydis which grew 22% to more than $400 million in sales world-wide.[2,5,21]

Today's ODTs Technologies

It is widely known that the first generation of ODT technologies has certain limitations like lacking the ability to effectively masking poor tasting APIs.

Additionally, many are very friable which make them hard to package conventionally and posing stability problems during storage.

Moreover most earlier technologies are limited to immediate release applications. As a result, the new generation of ODTs technologies overcomes many of these problems.

For instance, Eurand's AdvaTab® ODT technology incorporates taste-masked drug substances to produce ODTs with excellent physical robustness, mouth feel and disintegration properties by combining AdvaTab® with Eurand's Microcaps® coacervation (microencapsulation) technology that ensure highly effective taste-masking performance.

On the other hand, the AdvaTab® technology can also be used in combination with specialized functional polymers and coating processes to create ODTs with sustained, modified, and customized release profiles, and combinations of release profiles in a single dose.

For example, it can be combined with Diffucaps® which involves the preparation of a drug core that is then coated with one or more layers of functional polymers by fluid bed coating process, permitting the development of ODT formulations with sustained-release profiles over one to 12 hours.[5,35]

Table 2: Examples for patented technologies to prepare ODTs.

Patented Technology	Employed Technology	Company	Basic excipients	Advantages	Disadvantages
Zydis®	Freeze drying	Catalent	Polymers. Saccharids. Water. Suspending agents.	Rapid oral disintegration (2-3 sec.) Low sensitivity to microbial growth	Fragility. High sensitivity to temperature and humidity. Expensive process.
Orasolv®	Direct Compression	CIMA	Effervescent agents.	Unique taste masking	Fragility.
Durasolv®	Direct Compression	CIMA	Effervescent agents.	Better rigidity than ODTs produced by Orasolv®. Appropriate for low amounts of active ingredient.	Inappropriate for doses larger than 500mg.
Shearform®	Unique spinning mechanism (flash heat processing) to produce a floss-like crystalline structure, like cotton candy	Fuisz	Saccharide carrier.	Rapid dissolution	Low mechanical strength.
ceform®	Direct compression	Fuisz	Microspheric excipients.	Rapid dissolution. Good stability. Unique taste masking.	
Flashdose®	Ceform® + Shearform®	Fuisz	Microencapsulated saccharides.	Unique taste masking Rapid dissolution	Fragililty High sensitivity to moisture.
Wowtab®	compression WOW(without water)	Yammano ushi	Combination of low-mouldability and high-mouldabiity saccharides.	• Adequate dissolution rate and hardness.	

Table 3: Examples of marketed ODT Products

Technology	Marketing Company	Indication	Active ingredient	Product
OraSolv/DuraSolv	Wyeth	Allergy	Loratadine	Alavert
WOWTAB	Johnson and Johnson	Allergy, cold, sinus	Diphenhydramine pseudoephedrine	Benadryl Fast
Zydis	Schering-Plough	Allergy	Loratadine	Claritin RediTabs
Zydis	Eli Lilly	Schizophrenia	Olanzapine	ZyprexaZydis
Durasolv	Organon	Depression	Mirtazapine	RemeronSolTab
Zydis	Merck	Migrane	Rizatriptan benzoate	Maxalt-MLD
Zydis	GlaxoSmithKline	Nausea	Ondansetron	Zofran ODT
OraSolv/DuraSolv	AstraZeneca	Migrane	Zolmitriptan	Zomig ZMT

CONCLUSION

All in all, ODTs are one of the most promising pharmaceutical dosage forms which offer considerable benefits for lifecycle management, development timelines, patient convenience and market share. Besides, it is worth mentioning that pharmaceutical companies have promising opportunity to create ideal technologies and develop novel excipients in order to produce patient-friendly tablets.

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