Review Article

Oral Disintegrating Tablets: A Review

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ABSTRACT

In the design of dosage forms, comforts of drug administration and patient conformity have considerable prominence. Recent and rising technologies can manufacture robust, versatile tablets with extraordinary taste masking and controlled release. Orally disintegrating tablets (ODTs) are solid dosage forms that disintegrate in the mouth in less than 60 s, and are thus swallowed without the need for water. Rapid disintegration of tablet cause quick dissolution and thus fast onset of action. ODTs are suitable dosage form for special populations like pediatrics, geriatrics, psychotic, dysphagic, bedridden patients, unconscious patients, young patients with under developed muscular and nervous system, patients with hand tremors problems and frequent traveller patients. It provides good stability, accurate dosing, easy manufacturing, decreased packaging size; self-administration is possible during the journey, as water is not required. ODTs are an economical method of drug delivery. ODTs are very important drug delivery system in cases where drug absorbed from buccal cavity. Various scientific techniques including spray drying, sublimation, freeze drying, molding, direct compression etc. have been employed for the development of ODTs. Today, ODTs are more widely available as over the counter products for the treatment of numerous diseases. The aim of this article is to review the advantages, limitations, formulation challenges, manufacturing techniques, patented technologies, marketed formulations and evaluation tests of ODTs.

Keywords: Marketed formulation, ODTs, patent, tablet, technology

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INTRODUCTION

Oral administration of drugs is preferred due to its ease of swallowing, distress avoidance, versatility and most significantly, patient compliance. The large number of patients find it difficult to swallow tablets and capsules, and do not take their medicines as prescribed. It is estimated that 50 % of the population affected by this problem, which finally results in a higher chance of noncompliance and ineffective therapy. For these reasons, tablets that can disintegrate in the oral cavity, have attracted enormous attention [1]. Solid dosage forms as oral tablets have the most considerable place among the entire pharmaceutical formulations [2].

Taste-masking is a crucial step in the formulation of an acceptable fast dissolving/disintegrating tablet (FDDT). Traditional tablet formulations generally do not solve the issues related to taste masking, because it is supposed that the dosage form will not disintegrate until it passes through the oral cavity. To eliminate the bitterness, the tablet can be prepared by adding flavors and sweetening agent or by sugar coating on the tablets. Many FDDT technologies combine unique types of taste masking as well [3-5].

ODTs technology, which makes tablets dissolve or disintegrate in the oral cavity without any additional water intake, has drawn a great deal of attention. ODTs are a solid dosage form that provides the rapid disintegration or dissolution of solid to present as suspension or solution form even when placed in the mouth under limited bio-fluid [6, 7]. Orally disintegrating tablets are known by various names such as orodispersible tablets, quick disintegrating tablets, fast disintegrating tablets, fast or rapid dissolving tablets, porous tablets, mouth dissolving tablets and rapimelts. The excipients used in ODT technology are

usually hydrophilic in nature and can be selected on the basis of drug's physicochemical properties like hydrophilicity or hydrophobicity. If the active pharmaceutical ingredient is hydrophobic in nature, then dosage form is called disintegrating tablet whereas, if it is hydrophilic, then the dosage form is called fast dissolving tablet [8-10].

The ODT formulation defined by the Food and Drug Administration (FDA) as "a solid dosage form containing medicinal substances which disintegrates rapidly, usually within a matter of seconds when placed upon the tongue". U.S. Food and Drug Administration approved Zydis, ODT formulation of Claritin (loratadine) in December 1996. It was followed by a Zydis ODT formulation of Klonopin (clonazepam) in December 1997, and a Zydis ODT formulation of Maxalt (rizatriptan) in June 1998. Further a number of drugs have been approved by regulatory authorities for ODT formulations [11]. The aim of this article is to review the advantages, limitations, formulation challenges, manufacturing techniques, patented technologies, marketed formulations and evaluation tests of ODTs.

Advantages of ODTs

The advantages of ODTs include [12-17]:

- No need of water to swallow the tablet.
- Compatible with taste masking and have a pleasing mouth feel.
- Can be easily administered to paediatric, elderly and mentally disabled patients.
- No residue in the oral cavity after administration.
- Manufacturing of the tablets can be done using conventional processing and packaging equipments at minimum cost.
- Allow high drug loading.
- Accurate dose can be given as compared to liquids.
- Dissolution and absorption of the drug is fast, offering a rapid onset of action.
- Advantageous over liquid medication in terms of administration as well as transportation.
- Some amount of drugs is absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach, thus reducing first pass metabolism, which offers improved bioavailability and thus reduced dose and side effects.
- No risk of suffocation due to physical obstruction when swallowed, thus offering improved safety.
- ODTs are suitable for sustained and controlled release actives.
- Unit packaging.

Limitations of ODTs

It includes [18-20]:

- The tablets commonly have insufficient mechanical strength. Hence, conscientious handling is necessary.
- The tablets may leave an unpalatable taste and grittiness in the oral cavity if not formulated properly.
- Drugs which have large doses, can cause problems to formulate them into ODTs.
- Patients who simultaneously take anti-cholinergic drugs are not suitable candidates for ODTs.

Difficulties with existing oral dosage form [21-24]:

- The patient may suffer from tremors, therefore they may face difficulties to take a powder and liquid medication. In dysphasia, physical barriers and adherence to the esophagus may cause gastrointestinal ulceration.
- Ingestion of solid dosage forms like tablets and capsules can give rise to difficulties for young adults by causing hindrance in the development of muscular and nervous system.
- Liquid medicaments such as suspensions and emulsions are packed in multi-dose container: therefore content uniformity in each dose may not be maintained.
- Buccal and sublingual formulation may cause irritation of oral mucosa.

Challenges in the formulation of ODTs [25-27]:

- Mechanical strength and disintegration time: Disintegration time will extend if the mechanical strength is more, so a good cooperation between these two parameters is always necessary.
- Taste masking: Efficient taste masking of the bitter drugs must be done so that the taste of the drug is not felt in the oral cavity.
- Mouth feel: The particles produced after disintegration of the ODT should be very

small. ODT should not leave any residue in the mouth after oral administration. Addition of flavors and cooling agents like menthol enhance the mouth feel.

- Sensitivity to environmental conditions: ODTs should have low sensitivity to environmental conditions such as humidity and temperature.
- Cost: The technology adopted for an ODT should be acceptable in terms of cost of the final product.

The fast dissolving property of the ODTs requires rapid absorption of water into the tablet matrix, thus requires some standard approaches such as maximizing the porous structure of the tablet, incorporation of appropriate disintegrating agent and the use of water-soluble excipients in the formulation. Excipients used in ODTs contain at least one superdisintegrant, a diluent, a lubricant, a permeabilizing agent, sweeteners and flavourings. Type, examples and concentration of various excipients are presented in (**Table 1**).

Table 1: Type, examples and range in use (% in weight) of various excipients used in ODTs [28-31]:

Type of the excipients	Examples	w/w (%)
Superdisintegrants	Croscarmellose sodium, crospovidone, sodium starch glycolate, microcrystalline cellulose, carboxy methyl cellulose, modified corn starch, polacrilin potassium etc.	1-15 %
Binder	Polyvinylpyrolidone, polyvinyl alcohol, hydroxy propyl methylcellulose etc.	5-10 %
Antistatic agent	Sodium laury lsulfate, sodium dodecyl sulfate, polyoxyethylene sorbitan fatty acid esters, polyoxyethylene stearates etc.	0-10 %
Diluents	Magnesium carbonate, calcium sulphate, magnesium trisilicate etc.	0-85 %

APPROACHES FOR PREPARATION OF ODTs

Various preparation techniques have been developed on the basis of different principles, thus present different properties of ODTs by means of mechanical strength, stability, mouth feel, taste, swallowability, dissolution profile and bioavailability. Some of those technologies are patented. Basic pharmaceutical processes to manufacture ODTs are explained as follows:

Spray drying

Spray drying methods are used to a great extent in pharmaceutical and biochemical procedures. Spray drying provides a rapid and economically efficient way to eliminate solvents and produces highly porous and fine powders. The formulations are compounded by hydrolyzed and non hydrolyzed gelatins as supporting agents, mannitol as bulking agent, croscarmellose sodium or sodium starch glycolate as disintegrating agent. An acidic material (e.g., citric acid) or alkali material (e.g., sodium bicarbonate) is used to improve disintegration and dissolution behaviour. Tablets prepared by the compression of spray dried powder, when immersed in an aqueous medium, showed a disintegration time of 20 s [32-34].

Sublimation

Compressed tablet which contains highly water-soluble components can show slow dissolution behaviour, due to the low porosity of the tablets that reduces water penetration into the matrix. By conventional methods, volatile materials are compressed into tablets, these volatile materials can be removed by sublimation, which results in extremely porous structures. The volatile materials which can be used are ammonium carbonate, urea, ammonium bicarbonate, camphor and hexa methylene tetramine. In a few cases, thymol, menthol, camphor, an organic acid such as adipic acid and fatty acid such as arachidic acid, myristic acid, capric acid, and palmitic acid were used as the volatile materials and the sublimation temperature ranged from 40 ^{0}C to 60 ^{0}C. The disintegration time in the oral cavity was found to be about 25 s [35, 36].

Freeze drying

Lyophilization process involves removal of solvents from a frozen drug solution or a suspension containing structure-forming excipients. The tablets formed by this process are usually very light and have highly porous structures that allow, rapid dissolution or disintegration. Lyophilization is done at very low temperature to eliminate the adverse thermal effects that may alter drug stability during processing. The freeze dried dosage form have relatively few stability concerns during its shelf life. The drying process may give rise to the glassy amorphous structure of excipients and drug substance [37, 38].

Molding

Molded tablets are made up of water-soluble ingredients. The powder mixture is sprinkled with a solvent (usually water or ethanol). The mixture is molded into tablets under pressure. Applied pressure should be lower than those used in conventional tablet compression. This process is also known as compression molding. Air drying can be used to remove the solvent. Due to lower pressure; a highly porous structure is created, that enhances the dissolution. The powder blend should be passed through a very fine screen, to improve the dissolution rate. Molded tablets disintegrate more rapidly and provide improved taste because of their highly water-soluble, sugar components. However, molded tablets generally do not have high mechanical strength. The chances of breakage of the molded tablets during tablet handling and opening of blister pockets, is very high. If the hardness enhancing agents are used in the formulation, decrease in disintegration rate is observed. Mechanical strength and good disintegration of the tablets can be improved by using non-conventional equipment and by using multistep processes [39, 40].

Mass extrusion

The mass extrusion technology involves softening the active blend using the solvent mixture of water soluble polyethylene glycol and methanol. Expulsion of softened mass through the extruder or syringe is carried out, to get a cylinder of the product which is then cut into even segments using a heated blade to form tablets [40, 41].

Direct compression

Direct compression is the easiest and cost-effective tablet manufacturing process. This method can be applied to manufacture ODT by selecting appropriate combinations of excipients, which can provide fast disintegration and optimum physical resistance. Sugar-based excipients are widely used as bulking agents because of their aqueous solubility, sweetness, pleasing mouth feel, and good taste masking. Tablets obtained by conventional compression method are less friable, but disintegrate more slowly. The compression method, with or without wet granulation, is a convenient and cost effective way to prepare tablets with sufficient structural integrity [42, 43].

PATENTED TECHNOLOGIES FOR PREPARATION OF ODTs

Various recent patents in the field of ODTs are briefly listed in (**Table 2**).

Table 2: Various recent patents in ODT field

Title	Patent Number	Publication Year
Fast disintegrating tablet	EP1058538B2	2012
Disintegrating particle	EP2465539A1	2012
Fast dissolving solid	EP2493457A1	2012
Rapidly disintegrating tablet	US20120028949	2012
Quick dissolve compositions and tablets based thereon	US20120082729	2012
Orodispersible tablets	US20120077888	2012
Taste-masked orally disintegrating tablets of memantine hydrochloride	EP2583669A1	2013
Orally disintegrating tablet	EP2591774A1	2013
Mozavaptan formulations	EP2609909A1	2013
Coated effervescent tablet	EP2595609A1	2013
Orally disintegrating composition comprising mirtazapine	T0418/09	2013
Fast release solid oral compositions of entecavir	WO2013072937A2	2013

Many patented technologies are available for preparing mouth dissolving tablets. Some commercially useful technologies are:

Zydis (R.P. Scherer, Inc.)

Zydis is the first mouth dissolving dosage tablet within the market. Tablets are prepared by distinctive freeze drying technology. The active drug is incorporated into an exceedingly soluble matrix, that is then reworked into blister pockets and freeze dried to get rid of water by sublimation. Zydis matrix is created from a variety of ingredients so as to get completely different objectives. Polymers like albumin, dextran or alginates are used to impart strength throughout handling. These form a shiny and amorphous structure. Mannitol or sorbitol is added to impart crystallinity, elegance and hardness. Numerous gums are used to forestall sedimentation of distributed drug particles. Water is employed as a medium to make sure the formation of a porous dosage form. Collapse protectants like glycerin is also used to forestall shrinkage, throughout freeze drying and long run storage. If necessary, suspending agents, preservatives and hydrogen ion concentration adjusting agents are also used. Zydis formulations are packed in blister packs to safeguard the formulation from environmental wetness. A secondary wetness proof foil punch is usually needed as this formulation type is incredibly wetness sensitive [44-47].

Orasolv (Cima Labs, Inc.)

The OraSolv technology, unlike Zydis, disperses in saliva with the assistance of almost undetectable effervescence. The tablet matrix breaks up within one minute, and the coated drug powder remains left behind. Coating of the drug powder and effervescence are measures of taste masking in OraSolv [48]. This technology produces tablets by the low compression process. It uses an effervescent disintegrant pair that releases gas upon contact with water. The widely used disintegration pairs usually include an acid source such as tartaric acid, malic acid, fumaric acid, citric acid, adipic acid, and succinic acid, and a carbonate source like sodium carbonate, sodium bicarbonate, potassium carbonate, potassium bicarbonate. Fizzing sensation is provided by the carbon dioxide produced in the reaction. Effervescent agents are used in concentrations of 20-25 % of the total weight of the tablet. Currently, six marketed products are available, which are based on this technology; four Triaminic Softchew formulations, and each of Tempra Firs Tabs and Remeron Sol Tab [49-51].

Durasolv (Cima Labs, Inc.)

As a second generation technology, the DuraSolv technology was developed by Cima labs. Stronger tablets are produced, that can be packed in blisters or bottles. The key ingredients in these formulations are non-direct compression fillers and lubricants. The particle size of the non-direct compression filler is preferably between 20-65 μm, while for direct compressible fillers at least 85 % of the particles are over 100 μm in size. These non-direct compression fillers, such as mannitol, dextrose, sorbitol, sucrose and lactose have the advantage of quick dissolution and avoids some of the sandy or gritty texture usually present in direct compressible versions of the sugar. The amount of non direct compression filler is generally about 60-95 % of the total weight of the tablet. The tablets have low friability, which is about 2 % or less, when tested according to USP. The disintegration time is less than 60 s. DuraSolv technology is not compatible with larger doses of active pharmaceutical ingredients, due to the reason that formulation is subjected to high pressure on compaction. Unlike OraSolv, the structural integrity of any taste masking agent may be compromised with high drug doses. DuraSolv is currently available in two products: NuLev and Zomig ZMT [52, 53].

Orodis technology

Orodis is compressed technology, have a fast disintegration time (15 to 30 s). This technology produces very hard tablets, which are easy to handle. Tablets can be packed in push-through blisters. Materials used in this technology meet USP and EP standards [54].

Melt Ease technology

This technology is developed by nutrition formulators. Tablet dissolution can be achieved within 5 s (average 400 mg tablet). This technology provides the best mechanism available, to ensure compliance. Sales can be increased in two important

markets (children and the elderly), for many nutritional supplements at a very marginal development cost [55].

Quick Dis technology

Lavipharm laboratories have invented an ideal intraoral fast-dissolving drug delivery system, trademarked Quick-Dis. It is a thin, flexible, and quick-dissolving film. The film is placed on the top or the floor of the tongue. The Quick-Dis drug delivery system can be made available in various packaging configurations, such as unit-dose pouches and multiple-dose blister packages. The typical disintegration time of 2 mm Quick-Dis film is only 5-10 s. The dissolving time, which is defined as the time at which not less than 80 % of the tested film is dissolved in aqueous media, is around 30 s, for Quick Dis film with a thickness of 2 mm. The distinctive release profile of an active ingredient exhibited by a Quick-Dis drug delivery system is 50 % released within 30 s and 95 % within 1 min [56, 57].

Wowtab (Yamanouchi Pharma Technologies)

This technology employs a combination of low and high moldability saccharides to manufacture fast dissolving tablets using traditional granulation and tableting technique. According to the patent, the saccharides can be divided into two groups: high and low moldability saccharides. Low moldability saccharides produce tablets with hardness between 0-2 kg, when 150 mg of such a saccharide compresses under pressure of 10-15 kg/cm2 using a die, 8 mm in diameter. Commonly used low moldability saccharides are glucose, lactose, mannnitol, xylitol and sucrose. High moldability saccharides produce tablets with hardness above 2 kg when prepared under identical conditions. High moldability saccharides are sorbitol, maltose, maltitol and oligosaccharides [58, 59].

Flashdose (Fuisz Technologies, Ltd)

Fuisz technologies have three fast dissolution, oral drug delivery systems. Earlier generations of fast dissolving tablets like Soft Chew and EZ Chew, requires some chewing. However, these paved the way for Fuisz's development. Granular excipients are compressed to form tablets, and this technology uses the same excipients as do conventional compressed tablets. Excipients used in this technology can be divided into two sections of components: disintegrating agents, like carboxymethylcellulose or polyvinylpyrrolidone; and swelling agents such as starch, carboxymethylated starch, microcrystalline cellulose, modified starch, and directly compressible sugars [60, 61].

Flashtab (Ethypharm)

This technology produces tablets by compression of granular excipients. Combination of Shearform and Ceform technologies is used, to mask the bitter taste of the drug. Floss, a sugar based matrix, which is made up of a mixture of excipients (crystalline sugars) alone or in combination with drugs, is used to form tablets. Nurofen meltlet (containing ibuprofen), as a mouth-dissolving tablet is prepared by this technology. The product was launched by Biovail corporation [45, 62].

OraQuick (KV Pharmaceuticals)

KV pharmaceutical claims its MicroMask microsphere technology, has superior mouth feel over other taste masking options. The taste masking process does not require any solvent and therefore production is faster and more efficient. OraQuick is suitable to process heat sensitive drugs. KV pharmaceuticals also claim that the matrix, protects the drug powder in a microencapsulated particles is more pliable, this means that the tablets can be compressed to achieve remarkable mechanical strength without disrupting taste masking. [63-66].

NanoCrystal (Elan)

For ODT, Elan's proprietary NanoCrystal technology can enable formulation and improve compound activity and final product properties. On decreasing the particle size, surface area will increase, this leads to an increase in dissolution rate. This technology provides the following benefits: pharmacokinetics benefits of orally administered nanoparticles, in the form of rapidly disintegrating tablet matrix, extraordinary strength, empower the use of traditional packaging equipment and formats (i.e., bottles or blisters) and a wide range of doses (up to 200 mg of active pharmaceutical ingredient per unit) [67-69].

Dispersible tablet technology

Tablets of dihydroergotoxine and

cimetidine, which were claimed to disintegrate in less than 1 min when comes in contact with water at room temperature, were prepared. In the free base form, dihydroergotoxine is poorly soluble in water. Improvements in dissolution rate of dihydroergotoxine methanesulphonate were observed with dispersible tablets containing 0.8-10 %, preferably about 4 % by weight, of an organic acids. Disintegrating agents, in the cimetidine formulation, provides rapid swelling and good wetting capability to the tablets. Commonly used disintegrating agents include starch or modified starches, alginic acid, cross-linked sodium carboxymethyl cellulose, microcrystalline cellulose, and cyclodextrin polymers [70, 71].

AdvaTab technology

AdvaTab technology is developed by Eurand pharmaceuticals. It produces ODT tablets based on a proprietary tablet composition, designed and patented by Kyowa Hakko Kogyo (Tokyo, Japan), in which the lubrication is applied onto each tablet by utilizing a spray during the manufacturing process. Conventional tablets are produced using an internal lubrication system, which disperses lubricant inside and on the exterior surface of the tablets. AdvaTab is produced by using 10-30 times less hydrophobic lubricant and these tablets can be 30-40 % stronger than conventional tablets. Very hard and durable tablets are produced by this technology. The hardness of the tablet does not inhibit the entry of liquid, upon contact with saliva [72, 73].

Pharmaburst technology

Pharmaburst technology (SPI Pharma, New Castle, Delaware) uses off -the-shelf coprocessed excipients to create an ODT that, depending on the type of active ingredient and loading (up to 700 mg), dissolves within 30-40 s. The amount of pharmaburst required in a formulation depends on the active pharmaceutical ingredient in the tablet. It is mandatory to perform initial studies on a formulation by modulating the concentration of pharmaburst from 50-80 %, depending on the required mouth feel and disintegration time. The manufacturing process involves a dry blend of a drug, flavor, and lubricants that are compressed into tablets on a tablet press with stock tooling [74].

Frosta technology

Highly plastic granules are compressed at low pressure to produce strong tablets with high porosity. The highly plastic granules comprise three types of components: a poriferous and plastic material, a water penetration enhancer, and a binder. Tablets can be made by mixing porous, plastic material with a water penetration enhancer at certain ratios. The porous and plastic materials can make close contacts to increase the chances of bonding by compression. During granulation, the binder secures the porous material and water penetration enhancer. If the binder is in the liquid or semi-solid state, it should not destroy the porous structure of the porous materials. Aqueous binder solutions with very low water activity can be used to achieve this [75, 76].

Ceform technology

In the ceform microsphere manufacturing process, dry powder containing pure drug material or a blend of drug materials and excipients is placed into a precision engineered and rapidly spinning machine. The centrifugal force exerted by the revolving head of the machine throws the dry drug blend at high speed through small heated openings. The microspheres are then blended and compressed into tablets. The ability to simultaneously process both drug and excipient generates a specific microenvironment, this microenvironment can be used to incorporate the materials into the microsphere, that can alter the characteristics of the drug substance [77].

Lyo (Pharmalyoc)

This technique involves preparation of oil in water emulsion, which can be placed directly into blister cavities, followed by freeze-drying. Non-homogeneity during freeze-drying is avoided by incorporating inert filler to increase the viscosity. A high proportion of filler reduces porosity of tablets due to which disintegration is lowered [78-82].

MARKETED FORMULATIONS

Large numbers of commercial products of different active drugs are available in the market [83]. Some of them are listed in (**Table 3**).

Table 3: Marketed formulations of ODTs

Trade Name	Active Drug	Manufacturer
Felden fast melt	Piroxicam	Pfizer Inc., NY, USA
Ugesic	Piroxicam	Mayer organic Ltd.
Esulide MD	Nimesulide	Doff Biotech
Kazoldil MD	Nimesulide	Kaizen Drugs
Mosid MD	Mosapride	Torrent Pharma
Valus	Valdecoxib	Glenmark
Vomidon MD	Domperidone	Olcare lab
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
Zofer MD	Ondansetron	Sun Pharma
Ondem MD	Ondansetron	Alkem Pharma
Zoming-ZMT	Zolmitriptan	AstraZenecea, USA
Zeplar TM	Selegilline	Amarin Corp. London
Tempra Quiclets	Acetaminophen	Bristol Myers Squibb. USA
Febrectol	Paracetamol	Prographarm. France
Nimulid MDT	Nimesulide	Panacea Biotech. India
Torrox MT	Rofecoxib	Torrent Pharmaceuticals, India
Rofixx md	Rofecoxib	Cipla ltd. Mumbai ,India
Olanex Instab	Olanzapine	Ranbaxy Lab. Ltd, India
Romilast	Monteleukast	Ranbaxy Lab. Ltd, India
Zontec MD	Cetrizine	Zosta Pharma India
Lonazep MD	Olnazepine	Sun Pharma
Nime MD	Nimesulide	Maiden Pharma
Imodium lingual	Imodium	R.P. Scherer Corp., U.S.A
Pepcidin Rapitab	Pepcid	Merck & Co., U.S.A
Cibalginadue Fast	Ibuprofen	Novartis Consumer Health
Nurofen Flashtab	Ibuprofen	Boot healthcare
Hyoscyamine sulphate ODT	Hyoscyamine sulfate	Ethex Corporation
Risperdal M Tab	Risperidone	Janssen
Imocdium Instant Melts	Lopermide HCl	Janssen
Propulsid Quick Sol	Cisapride monohydrate	Janssen
Alavert	Loratadine	Wyeth Consumer Healthcare
NuLev	Hyoscyamine sulfate	Schwarz Pharma
Kemstro	Baclofen	Schwarz Pharma
Nasea OD	Ramosetoron HCl	Yamanouchi
Gaster D	Famotidine	Yamanouchi
Fluoxetine ODT	Fluoxetine	Biovail
Zolpidem ODT	Zolpidem tartrate	Biovail
Excedrin Quick Tabs	Acetaminophen	Bristol-Myers Squibb
Abilify Discmelt	Aripiprazole	Otsuka America
Aricept ODT	Donepezil	Eisai Co.
FazaClo	Clozapine	Azur Pharma
Relivia Flash dose	Tramadol HCl	Fuisz Technology, Ltd
Domray MD	Domperidone	Ray Remedies

EVALUATION OF ODTS

Precompression characterization of tablet

Prior to compression, the powder blends should be evaluated for their bulk and tapped density and from these values compressibility index and Hausner's ratio should be calculated, while the flow properties of powder blends should be assessed from the angle of repose [84].

Angle of repose

The frictional forces in loose powder or granules can be measured by the angle of repose. This is the angle between the surface of a pile of powder or granules and the horizontal plane. It is determined by the

funnel method. Pour the blend through a funnel, that can be raised vertically to a maximum cone height (h). The radius of the heap (r) should be measured. The angle of repose is calculated by following formula:

$$\tan \Theta = \frac{h}{r}$$

Bulk density and tapped density

An accurately weighed amount of powder should be introduced in 100 ml measuring cylinder. Note the initial volume, then the cylinder should be tapped 100 times on a plane hard surface and tapped volume of packing should be recorded [85]. Bulk density (BD) and tapped density (TD) should be calculated using following formula:

$$BD = \frac{\text{weight of powder}}{\text{volume of packing}}$$

$$TD = \frac{\text{weight of powder}}{\text{tapped volume of packing}}$$

BD = weight of powder/ volume of packing

TD = weight of powder/tapped volume of packing

Carr's index (Compressibility)

Compressibility index of powder can be determined by following formula [86]:

$$\text{Carr's index (\%)} = \frac{(\text{Tapped density} - \text{Bulk density}) \times 100}{\text{Tapped density}}$$

Hausner's ratio

Hausner's ratio is an index of ease of powder flow. It is calculated by the following formula:

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

Postcompression characterization of tablets

Weight variation test

Individually weigh 20 tablets, which are selected at random and calculate the average weight.

Tablet hardness

Monsanto hardness tester can be used to determine the crushing strength.

Tablet Friability

Weigh twenty tablets of formulation and subject them to abrasion by employing a Roche friabilator at 25 rpm for 4 min. Weigh the tablets and compare with their initial weights to obtain percentage friability.

$$\text{\% Friability} = \frac{(W1 - W2) \times 100}{W1}$$

Where W1 = Weight of tablets before test (initial weight)

W2 = Weight of tablets after test (final weight)

Thickness

The diameter and punch size of tablets depends on the die and punches selected for making the tablets. The thickness of tablet is measured by screw gauge. Tablet thickness should be controlled within a ± 5 % variation of a standard value. In addition, the thickness must be controlled to facilitate packaging. The thickness in millimeters (mm) should be measured individually for ten preweighed tablets using screw gauge. The average thickness and standard deviation should be reported [87].

***In vitro* disintegration time**

For this test, six tablets are employed in water at 37 ^{0}C using a tablet disintegration tester. The time required for disintegrating the tablets and passing completely through the sieve is recorded.

***In vitro* dissolution study**

The release rate of drug from ODTs is determined using USP dissolution testing apparatus 2 (paddle method). The dissolution test is performed using 900 ml of 0.1 N HCl at 37±0.5 ^{0}C at 100 rpm.

Wetting time

Use a piece of tissue paper (10.75×12 mm), fold it twice and place it in a culture dish (d= 6.5 cm) containing 6 ml of water. Put a tablet on the paper and record the time required for complete wetting.

***In vitro* dispersion time**

Put the tablets in 10 ml of phosphate buffer solution (pH 7.4) at 37±0.5 °C. Measure the time required for complete dispersion of tablets [88].

Water absorption ratio (R)

Note the weight of the tablet prior to placement in the petri dish (Wb) utilizing a digital weighing balance. Note the weight of the tablets after wetting (Wa). Water absorption ratio, R, can be determined according to the following equation:

$$R = 100 \times \frac{Wa - Wb}{Wb}$$

where Wb and Wa are tablet weights before and after water absorption, respectively [89].

CONCLUSION

All the available ODTs technologies work on the primary concept, to maximize the porous structure of the tablet matrix to achieve speedy tablet disintegration in the buccal cavity along with good taste-masking properties and satisfactory mechanical strength. Future challenges for many ODT manufacturers include reducing costs by finding ways to manufacture with conventional equipment, varieties in packaging, enhanced mechanical strength and taste-masking potential. Hence, demand by patients and the accessibility of various technologies have increased the acceptance of oral disintegrating tablets, which in turn prolongs the patent life of a drug. The techniques and technologies described in this article represent how recent developments in formulation and processing technologies make the efforts to achieve mouth dissolving tablets. One can consider the emergence of more novel technologies for ODTs in the coming days. Thus ODTs will have tremendous scope as a delivery system for most of the drugs in the near future.

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