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# ORAL DISINTEGRATING TABLETS(ODTS): A REVIEW

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**ABSTRACT**
Recently ODT terminology has been approved by United States Pharmacopoeia, British Pharmacopoeia, and Centre for Drug Evaluation and Research (CDER). US FDA defined ODT tablets as "A solid dosage form containing medicinal substances which disintegrates rapidly usually within a matter of seconds, when placed upon the tongue. The newest generation of ODTs can produce more robust, versatile tablets that overcome some of the limitations of earlier ODTs. The performance of ODTs depends on the manufacturing technology and the most necessary property of such a dosage form is the ability of rapidly disintegrating and dispersing or dissolving in the saliva, thereby obviating the need for water intake. Disintegrates are substances or mixture of substances added the drug to the formulation that facilitates the breakup or disintegration of tablets or capsule content into smaller particles that dissolve more rapidly than in the absence of disintegrates. Examples of superdisintegrants are croscarmellose, crosspovidone, sodium starch glycolate which represent example of cross linked cellulose.

**KEYWORDS:** Orally disintegrating tablets, super disintegrates, Drug delivery systems.

## INTRODUCTION

Drug delivery systems (DDS) are a strategic tool for expanding markets/indications, extending product life cycles and generating opportunities. DDS has made a significant contribution to global pharmaceutical sales through market segmentation, and are moving rapidly. Orally disintegrating tablets (ODT) are oral solid dosage forms that disintegrate in the oral cavity in easy swallow residue. Orally disintegrating tablets are also known as "Mouth dissolving tablets", "Orodispersible tablets", "Melt- in-mouth Fast dissolving drug delivery, Rapimelts tablets, Porous tablets, Quick dissolving tablets"[2] etc.

Recently ODT terminology has been approved by United States Pharmacopoeia, British Pharmacopoeia, and Centre for Drug Evaluation and Research (CDER). US FDA defined ODT tablets as "A solid dosage form containing medicinal substances which disintegrates rapidly usually within a matter of seconds, when placed upon the tongue". European pharmacopoeia also adopted the term Orally disintegrating tablet as a tablet that is to be placed in the mouth where it disperses, rapidly before swallowing despite various terminologies used. Recently, ODT have started gaining popularity and acceptance as new drug delivery systems, because they are easy to administer and lead to better patient compliance especially in elderly and children. In order to allow fast dissolving tablets to dissolve in the mouth, they are made of either very porous or soft molded matrices or compressed into tablets with very low compression force, which makes the tablets friable and/or brittle, which are difficult to handle, often requiring specialized peel-off blister packaging.[3-6]

Along with the rapid market growth of ODT products, the technologies, too, have advanced considerably over the years. The newest generation of ODTs can produce more robust, versatile tablets that overcome some of the limitations of earlier ODTs. Companies such as Eurand can produce pleasant tasting tablets, overcoming the common problem of poor drug taste compromising the benefits of an ODT. In addition, some companies is developing controlled release ODTs, significantly broadening the applications of this dosage form. A key reason that companies choose an ODT over other delivery technologies is that it is a relatively easy 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.[7]

**Table. 1: Some of the common applications of ODTs.**

| MEDICATION TYPE | INDICATIONS |
|---|---|
| **Fast acting** | Pain, fever, migraine, diarrhoea, heart burn, anxiety, insomnia |
| **Compliance-critical** | Parkinson's disease, Alzheimer's disease, Psychosis, Schizophrenia, Hypertension, Cholesterol, Transplantation |
| **Paediatric** | Cough, cold, allergy, pain, fever |

**Ideal properties for ODTs[8-10]**

The performance of ODTs depends on the manufacturing technology and the most necessary property of such a dosage form is the ability of rapidly disintegrating and dispersing or dissolving in the saliva, thereby obviating the need for water intake. ODTs should depict some ideal characteristics to distinguish them from traditional conventional dosage forms. Important desirable characteristics of these dosage forms.

- Convenient and easy to administer as does not require water for oral administration for swallowing purpose, but it should dissolve or disintegrate in the mouth usually within few seconds.
- Allow high drug loading.
- Provide pleasant feeling in the mouth.
- Be compatible with taste masking and other excipients.
- Leave negligible or no residue in the mouth after oral administration.
- Have sufficient strength to withstand the rigors of the manufacturing process and post-manufacturing handling.
- Insensitive to environmental conditions such as humidity and temperature.
- Adaptable and amenable to conventional processing and packaging equipments at nominal expense.

**Advantages of orally disintegrating tablets**

- Improved compliance/added convenience
- Ease administration for patients who are mentally ill, disabled and uncooperative
- No water needed
- Can be designed to leave minimal or no residue in mouth after administration and also to provide a pleasant mouth feel.
- No chewing needed , Better taste obtained by taste masking
- Improved stability, low sensitivity to environmental condition
- Suitable for controlled/sustained release actives
- Allows high drug loading.
- Ability to provide advantages of liquid medication in the form of solid preparation.
- Adaptable and amenable to existing processing and packaging high speed machinery.

**Table 2: Some ODT technological patents.**

| ODT Technologies | Technological basis | Patent owners |
|---|---|---|
| Zydis | Lyophilisation | R.P.Scherer Inc. |
| Quicksolv | Lyophilisation | Janseen Pharmaceutica |
| Flashtab | Multiparticulate compressed tablets | Prographarm |
| Lyoc | Lyophilisation | Cephalon Corporation |
| Orasolv | Compressed tablets | Cima Labs Inc. |
| Durasolv | Compressed tablets | Cima Labs Inc. |
| Wowtab | Compressed molded tablets | Yamanouchi Pharma Technologies, Inc. |
| Flashdose | Cotton candy process | Fuisz Technologies, Ltd. |
| AdvaTab | Microencapsulation | Eurand |
| Multiflash | Multi-unit tablet | Prographarm |
| EFVDAS | Effervescent system | Elan Corporation |

**Techniques for preparing Orally disintegrating Tablets**

**A. Freeze drying[11-12]**

A process in which water is sublimated from the product after freezing. Lyophilisation is a pharmaceutical technology which allows drying of heat sensitive drugs and biologicals at low temperature under conditions that allow removal of water by sublimation. Lyophilisation results in preparations, which are highly porous, with a very high specific surface area, and which dissolve rapidly and show improved absorption and bioavailability. Jaccard and Leyder used lyophilisation to create an oral pharmaceutical preparation that not only dissolves rapidly but also improved the bioavailability of several drugs such as Spironolactone and Trolendomycin. Corveleyn and Remon studied various formulation and process parameters by using hydrochlorothiazide as a model drug on the basis of which US Patent 6,010,719 was granted. Tablets prepared by lyophilisation, are fragile and possess low mechanical strength, which make them difficult to

handle and they also exhibit poor stability on storage under stressed conditions.

**B. Molding**[13-14]

Tablet produced by molding are solid dispersion. Molded tablets disintegrate more rapidly and offer improved taste because the dispersion matrix is generally made from water soluble sugars. The active ingredient in most cases is absorbed through the mucosal lining of the mouth. The manufacturing process of molding tablets involves moistening the powder blend with a hydro-alcoholic solvent followed by pressing into mold plates to form a wetted mass (compressing molding). The solvent is then removed by air drying. Thus the process is similar to what is used in the manufacture of tablet triturates. Such tablets are less compact than compressed tablets and possess a porous structure that hastens dissolution.

Molded forms are also prepared using a heat molding process that involves setting the molten mass that contains a dispersed drug. The heat molding process uses an agar solution as a binder and a blister packaging well as a mold to manufacture a tablet. The process involves preparing a suspension that contains a drug, agar, and sugar (e.g., mannitol or lactose), pouring the suspension into the blister packaging well, solidifying the agar solution at room temperature to form a jelly, and drying at • $300^0$ C under vacuum. Another process used is called no vacuum lyophilisation, which involves the evaporation of a solvent from a drug solution or suspension at standard pressure. Evaporated a frozen mixture containing a gum (e.g., acacia, carrageenan, guar, tragacanth, or xantham), a carbohydrate (e.g., dextrose, lactose, maltose, mannitol, or maltodextrin), and a solvent in a tablet shaped mould. Molded tablets typically do not possess great mechanical strength. Erosion and breakage of the molded tablet often occur during handling and opening of blister packs.

**C. Spray drying**[15-16]

Spray drying is a process by which highly porous, fine powders can be produced. Spray-dryers are invariably used in the pharmaceutical industry to produce highly porous powders. Applying this process to the production of fast dissolving tablets. The formulations that were produced contained hydrolyzed and unhydrolyzed gelatin as a support agent for the matrix, mannitol as a bulking agent, and sodium starch glycolate or croscarmellose as a disintegrant. Disintegration and dissolution was further enhanced by adding an acid (e.g., citric acid) or an alkali (e.g., sodium bicarbonate). The formulation was spray dried to yield a porous powder. Tablets manufactured from this powder disintegrated in less than 20 second in an aqueous medium.

**D. Sublimation**

The key to rapid disintegration for mouth dissolving tablets is the presence of a porous structure in the tablet matrix. Conventional compressed tablets that contain highly water soluble ingredients often fall to dissolve rapidly because of low porosity of the matrix. Hence, to generate porous matrix, volatile ingredients are used that are later subjected to a process of sublimation. Solid ingredients that displayed high volatility (e.g., ammonium bicarbonate, ammonium carbonate, benzoic acid, camphor, hexamethonium tetramine, naphthalene, phthalic anhydride, urea, and urethane) were compressed along with other excipients into a tablet. The volatile material was then removed by sublimation, leaving behind a porous matrix. Solvents such as cyclohexane and benzene were also suggested for the generation of porosity in the matrix.

Sublimation technology to manufacture tablets that rapidly dissolve in saliva. Mannitol is used as a matrix former, and camphor was used as a sublimating agent. The tablets dissolved in 10-20 seconds and displayed satisfactory handling properties. Makino et al.27 reported a method using water as pore forming material. A mixture of drug and a carbohydrate (e.g. erythritol, glucose, sucrose, xylitol). The water was then removed, yielding highly porous tablets with satisfactory mechanical strength and a high dissolution rate.

**E. Direct compression**

It is the easiest way to manufacture tablets. Conventional equipment, commonly available excipients and a limited number of processing steps are involved in direct compression. Also high doses can be accommodated and final weight of tablet can easily exceed that of other production methods. This technique can now be applied to fast dissolving tablets because of the availability of improved tablet excipients, especially tablet disintegrants and sugar-based excipients. Addition of disintegrants in fast dissolving tablets, leads to quick disintegration of tablets and hence improves dissolution. In many fast dissolving tablet technologies based on direct compression, the disintegrants principally affect the rate of disintegration and hence the dissolution.

The introduction superdisintegrants and a better understanding of their properties have increased the popularity of this technology. Tablet disintegration time can be optimized by concentrating the disintegrants. Below critical concentration, tablet disintegration time is inversely proportional to disintegrants concentration. Above the critical concentration level, however, disintegration time remains approximately constant or even increases. 1, 6, 21 Microcrystalline cellulose, cross linked carboxymethyl cellulose sodium, cross linked polyvinyl pyrrolidone and partially substituted hydroxypropyl cellulose, though water insoluble, absorb water and swell due to capillary action and are considered as effective disintegrants in the preparation of fast dissolving tablets. Bi *et al.* and Watanbe *et al.* used microcrystalline cellulose (MCC) and low substituted hydroxypropyl cellulose (HPC) to manufacture rapidly disintegrating tablets.

The ratios of MCC to HPC varied from 8:2 to 9:1. Ito and Sugihan investigated applying agar powder as a disintegrants because the powder absorbs water and swells considerably without forming a gel at physiological temperatures. Fast disintegration of tablets can also be achieved by incorporating effervescent disintegrating agents, which generates carbon dioxide. This phenomenon also resulted in partial taste masking of unacceptable taste of the drug. The major drawback of effervescent excipients is their hygroscopicity (i.e., the ability to absorb atmospheric moisture). Hence, their manufacture requires control of humidity conditions and protection of the final product. This is reflected by the overall cost of the product. Another approach to fast dissolving tablets by direct compression is the use of sugar-based excipients (e.g., dextrose, fructose, isomalt, maltitok, maltose, mannitol, sorbitol, starch hydrolyze, polydextrose, and xylitol), which display high aqueous solubility and sweetness, and hence, impart taste masking and a pleasing mouth feel.

**F. Mass Extrusion[17]**

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

**Table 3: Some of the marketed preparations of ODTs.**

| Trade name | Active drug | Manufacturer |
|---|---|---|
| Zontec MD | Cetrizine | Zosat pharma India |
| Zofer MD | Odansetron | Sun pharma |
| Vomidon MD | Domperidon | Olcare lab |
| Valus | Valdecoxib | Glen mark |
| Ugesic | Piroxicam | Mayer organic Ltd. |
| Torrox MT | Rofecoxib | Torrent pharma |
| Romilast | Moontelukast | Ranbaxy Labs Ltd. |
| Rofixx MD | Rofecoxib | Cipla Ltd. |

**Patented technology for the orally disintegrating tablets**

Each technology has a different mechanism, and each fast dissolving/ disintegrating dosage form varies regarding the following.

- Mechanical strength of final product;
- Drug and dosage form stability;
- Mouth feel;
- Taste;
- Rate of dissolution of drug formulation in saliva;
- Swallow ability;
- Rate of absorption from the saliva solution; and
- Overall bioavailabili

**ZYDIS TECHNOLOGY[18-19]**

Zydis, the best known of the fast-dissolving/ Disintegrating tablet preparations, and was the first marketed new technology tablet. The tablet dissolves in the mouth within seconds after placement on the tongue. Zydis tablet is produced by lyophilizing or freeze-drying the drug in a matrix usually consisting of gelatin. The product is very lightweight and fragile, and must be dispensed in a special blister pack. Patients should be advised not to push the tablets through the foil film, but instead peel the film back to release the tablet. The Zydis formulation is also self-preserving because the final water concentration in the freeze-dried product is too low to allow for microbial growth. A major claim of the Zydis product is increased bioavailability compared to traditional tablets. Because of its dispersion and dissolution in saliva while still in the oral cavity, there can be a substantial amount of pre-gastric absorption from this formulation. Buccal, pharyngeal and gastric regions are all areas of absorption of the Zydis formulation. Any pre-gastric absorption avoids first-pass metabolism and can be an advantage in drugs that undergo a great deal of hepatic metabolism. However, if the amount of swallowed drug varies, there is the potential for inconsistent bioavailability. While the claimed increase in bioavailability is debatable, it is clear that the major advantage of the Zydis formulation is convenience. The amount of drug that could be incorporated should generally be less than 60 mg for soluble drugs. The particle size of the insoluble drugs should be less than 50mm and not more than 200mm to prevent sedimentation during processing. There are some disadvantages to the Zydis technology. The process of freeze-drying is a relatively expensive manufacturing process. As mentioned earlier, the Zydis formulation is very lightweight and fragile, and therefore should not be stored in backpacks or the bottom of purses. Finally, the Zydis formulation has poor stability at higher temperatures and humidity. It readily absorbs water, and is very sensitive to degradation at humidity greater than 65%.

**ORASOLV TECHNOLOGY[20]**

The OraSolv technology, unlike Zydis, 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 twofold. The unpleasant flavor of a drug is not merely counter-acted by sweeteners or flavors, both coating the drug powder and effervescence are means of taste

masking in OraSolv. This technology is frequently used to develop over the counter (OTC) formulations. The major disadvantage of the OraSolv formulations is its mechanical strength. The OraSolv tablet has the appearance of a traditional compressed tablet. However, the OraSolv tablets are only lightly compressed, yielding a weaker and more brittle tablet in comparison with conventional tablets. For that reason, Cima developed a special handling and packaging system for OraSolv. An advantage that goes along with the low degree of compaction of OraSolv is that the particle coating used for taste masking is not compromised by fracture during processing. Lyophilisation and high degrees of compression, as utilized in OraSolv's primary competitors, may disrupt such a taste masking approach. The OraSolv technology is utilized in six marketed products. These formulations can accommodate single or multiple active ingredients and tablets containing more than 1.0 g of drug have been developed. Their disintegration time is less than 30s.

**DUROSOLV 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 tablets are prepared by using conventional tableting equipment and have good rigidity (friability less than 2%). The DuraSolv product is thus produced in a faster and more cost-effective manner. DuraSolv is so durable that it can be packaged in traditional blister packaging, pouches or vials.[17] 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. Unlike OraSolv, the structural integrity of any taste masking may be compromised with high drug doses. 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.

**FLASH DOSE TECHNOLOGY**

Fuisz Technologies has three oral drug delivery systems that are related to fast dissolution. The first two generations of quick dissolving tablets, Soft Chew and EZ Chew, require some chewing. However, these paved the way for Fuisz's most recent development, Flash Dose. The Flash Dose technology utilizes a unique spinning mechanism to produce 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 quickly once placed onto the tongue. Flash dose tablets consist of self-binding shear form matrix termed as "floss". Shear-form matrices are prepared by flash heat processing and are of two types.

- Single floss or Unif loss, consisting of a carrier, and two or more sugar alcohols, of which one is xylitol.
- Dual floss consists of a first shear form carrier material (termed "base floss", contains a carrier and at least one sugar alcohol generally sorbitol), and a second shear form binder matrix ("binder floss", contains a carrier and xylitol).

Interestingly, by changing the temperature and other conditions during production, the characteristics of the product can be altered greatly. Instead of a floss-like material, small spheres of saccharides can be produced to carry the drug. The process of making microspheres has been patented by Fuisz, and is known as CEFORM and serves as an alternative method of taste masking.

**CONCLUSION**

Fast dissolving drug system (OFDDS) is one such novel approach to increase consumer acceptance by virtue of rapid disintegration,self-administration without water or chewing. Orally disintegrating tablets (ODT) are solid unit dosage forms like conventional tablets, but are composed of superdisintegrants, which help them to disintegrate the tablet rapidly in saliva without the need to take it with water.

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