ORALLY DISINTEGRATING TABLETS: A SHORT REVIEW

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ABSTRACT

The oral route is widely accepted and common method of drug delivery. Nowadays, with the rising the patient compliance and ease of drug administration, especially for pediatrics, new dosage forms are being introduced. When the ODT (oral disintegrating tablets) are placed on the tongue, with the help of saliva they disintegrate and then they are absorbed into the bloodstream from the oromucosal cavity without the need for water. These dosage forms have some advantages over the conventional oral dosage forms due to the fact that,amongst all other advantages, they bypass hepatic metabolism, which means that more of the drug is absorbed into the systemic circulation, leading to higher bioavailability and higher therapeutic efficacy. Novel techniques have been investigated to formulate ODT's in order to achieve desired tablet characteristics to improve API compatibility and patient acceptance with this oral dosage form.

Keywords: Oral dosage forms, oral disintegrating tablet, hepatic metabolism, novel techniques.

INTRODUCTION

Orally disintegrating tablet (ODT) is a dosage form that contains active ingredients and disintegrates without extra water when placed into oral cavity rapidly (Bi et al., 1996).

There are some variations related to the definition of the ODT's in different pharmacopoeias and FDA. According to FDA; ODT's are solid dosage forms that disintegrate in a few seconds after they are placed on the tongue (Davtyan and Voronkina, 2016).

The active ingredient is released, dissolved, or dispersed in the saliva in the oral cavity, and then after swallowing, it can be absorbed to blood circulation. ODTs are distinguished from classic sublingual tablets, which take more than few minutes to dissolve in oral cavity (Hu et al., 2013). To formulate a convenient oral dosage form for oral administration, we have to put into consideration swallowing difficulties, especially for geriatrics and pediatrics, leading to low patient observance (Handa et al., 2016). To solve the swallowing problem, ODT's have been developed. These rapidly disintegrate tablets in the oral cavity, after that are swallowed easily without extra water that is a significant advantage over classic type oral dosage forms (Desai et al., 2016)

In recent years, some new ODT technologies allow high drug loading and they provide an acceptable taste of the formulation after oral administration (Hooda, 2012). ODT's have been evaluated for their potency in developing bioavailability especially for drugs which have solubility problem by improving the dissolution profile of the formulation (Sharma et al., 2015).

Orodispersible tablets, quick disintegrating tablets, mouth dissolving tablets, fast disintegrating tablets, rapid dissolving tablets, and fast dissolving tablets are names used to describe orally disintegrating tablets (Desai et al., 2016).

Advantages of ODT's

1. Increased bioavailability and faster onset of action: Oromucosal absorption leads to pre gastric absorption, especially for formulations where the active ingredient dissolves rapidly. Any pre gastric absorption avoids hepatic metabolism and this has a great edge over drugs that get metabolized fairly (Hannan et al., 2016).

2. Gastric and buccal regions are absorption areas for a lot of active ingredients. The buccal area has high amount blood circulation, but its permeability property is not high as the sublingual area. Drugs are quickly absorbed into the circulatory system under the oral mucosa. (Bhati and Nagrajan, 2012).

3. Enhanced safety drug profile that produce high quantity of toxic metabolites mediated by first pass hepatic metabolism, and for active ingredients that have important parts of absorption in oral cavity and gastrointestinal system (Sharma, 2013).

4. Increased patient compliance in ODT's due to:

• Removal of pain related with injection and convenience of administration compared to parenteral formulations.

• Ease of administration to patients having difficulty in swallowing (Klancke, 2003).

• Convenience where water is not available (Sharma et al., 2015).

5. Useful for pediatric and geriatric patients (Sharma, 2013).

6. It provides fast drug delivery because there is the large surface area contact with the oral cavity.

7. Enables high drug loading (Abdelbary et al., 2005).

Limitations in ODT's

1. One of the crucial disadvantages of ODT's is related to the mechanical strength of the tablets: ODT's have a porous and soft molded matrix and are compressed in a tablet form with low compression, which creates a friable and brittle tablet that is difficult to handle (Sotoyama et al., 2017).

2. Bitter drugs are not easy to formulate as ODT's. Therefore, taste masking materials should be used before formulating this kind of drugs (Baber, 1994).

3. Several ODT formulations may be hygroscopic and in this case, they cannot protect their physical integrity from humidity. Hence, they require specialized packaging (Sharma, 2013).

4. Decreasing the amount of saliva which can occur as a result of taking drug formulations like some antidepressants, can directly affect the bioavailability of the ODT formulations in a negative way (Mathew, 2015).

5. Dosage form stability (Abdelbary et al., 2005).

Target population for ODT's

Oral disintegrating tablets are more suitable for child and elderly patients who cannot swallow conventional solid dosage forms. Some examples of target population for Orodispersible tablets include:

• Patients who are non-compliant due to fear of choking (Pseudodysphagia).

• Infants and children.

• Patients undergoing radiation therapy who may be too nauseous to swallow (Sotoyama et al., 2017).

Technologies used for ODT formulations

The technologies used in preparation of ODT'S can be mainly categorized into two groups. These are: Conventional technologies and patented technologies. The latter is composed of more methods from the former. (Rao and Venkatachalam, 2010)

Conventional Technologies

1. Lyophilization: Lyophilization is a process that allows the drying of heat-sensitive active ingredient under low temperature by the application of vacuum to remove water by sublimation. Active ingredients are dissolved in an aqueous solution, transferred to preformed blisters and subjected to flush to freeze out with nitrogen, then placed in a refrigerator to complete the process (Davtyan and Voronkina, 2016).

2. Addition of Disintegrant: This method involves the addition of a material which has superdisintegrant property like microcrystalline cellulose derivatives and crosscarmellose sodium to the ODT formulations to obtain fast disintegration.

3. Molding: A Hydroalcoholic solvent and a water soluble material are used for this technique. Then, this mixture molded into tablets under low pressure than used in conventional tablet compression. (Davtyan and Voronkina, 2016).

4. Sublimation: Easily evaporated solid ingredients like camphor are used in the ODT formulations and the mixture is compressed into tablets. Then, a volatile material is evaporated from the formulation by sublimation method in order to obtain ODT formulation.

5. Spray-Drying: Spray-drying technique is achieved by utilizing gelatins as supporting agents, mannitol as a bulking agent, crosscarmellose as disintegrating agents and acidic and alkali materials to increase the deformation of ODT formulations (Manivannan, 2009).

6. Cotton candy process: This method includes the polysaccharides matrix of melting suddenly. Then, this candy matrix is blended with an active material and other formulation ingredients to ODT formulation.

7. Melt granulation: Hydrophilic waxy binder is used in this method. PEG-6-stearate is commonly used as a binder. But PEG-6-stearate is not used as a binder to increase physical strength of the formulation but it also used as a disintegrant in the ODT formulation (Mishra et.al, 2006).

Patented Technologies

Diverse techniques have been developed for ODT formulations. Finished ODT formulations are evaluated according to theirs different parameters like mechanical resistance, stability, and bioavailability. (Nagar et al., 2011).

Some examples of patented technologies are:

1. ZYDIS®:

Process involved: Lyophilization

Patent owner: R.P.Scherer Inc

Advantages: Easy dissolution, increased bioavailability on ODT.

Disadvantages: Costly technique, and stability problem at high temperature.

Brand name drugs: Loratidine (Claritin Reditab®) (Baber, 1994).

2. ORASOLV®:

Process involved: Tablet compression.

Patent owner: Cima Labs Inc.

Advantages: Taste masking is twofold and rapid dissolution on ODT.

Disadvantage: Low mechanical strength.

Brand name drugs: Paracetamol (Tempra Quicklets®), Zolmitriptan(Zolmig Repimelt®) (Bi et al., 1999).

3. DURASOLV®:

Process involved: Molding

Patent owner: Cima Labs Inc.

Advantages: Higher mechanical resistance.

Disadvantage: Cannot be used for active ingredient with low potency.

Brand name drugs: Hyoscyamine Sulfate (NuLev®), Zolmitriptan (Zolmig ZMT®) (Hannan et.al, 2016)

4. FLASHTAB®:

Process involved: Lyophilization

Patent owner: Ethypharm.

Advantage: Only conventional tableting technology.

Brand name drugs: Ibuprofen (Nurofen, Flashtab®) (Sastry et al., 2000).

5. ORAQUICK®:

Process involved: Micro-mask taste masking.

Patent owner: KV Pharm. Co., Inc.

Advantage: Easy production and appropriate for heat-sensitive APIs.

Brand name drugs: Hyoscyamine Sulfate® ODT (Velmurugan and Vinushitha, 2010).

6. FLASHDOSE®:

Process involved: Cotton candy method.

Patent owner: Fuisz Technology.

Advantage: High surface area on ODT.

Disadvantage: It needs high temperature for melting the matrix.

Brand name drugs: Tramadol HCl (Relivia Flash dose®) (Mishra et.al, 2006).

Quality controls of ODT's

The quality control tests which are conducted over ODT's are almost identical with conventional tablets, including: Weight variation, hardness, friability test, in-vitro, in-vivo disintegration tests, uniformity of dispersion are performed for the purpose of ensuring uniformity in the weight of tablets in a batch. The hardness of a tablet indicates its resistance Kg value of the applied force for breaking the tablet is determined of the ODT tablet (Thyssen et al., 2007).

As distinct from conventional tablets, according to FDA, in-vitro and in-vivo disintegration time of ODT's should be less than 30 second (Kraemer et al., 2012).

Differences in quality control of ODT's what should be highlighted are wetting time and taste sensation/mouth feel.

The determination of wetting time of tablets can be performed easily. For this aim, tissue papers are put in a Petri-dish containing 0.2% w/v solution. Then, sample tablet is placed on the

surface of the paper.The time needed for the tablet to develop a blue color on the upper surface is noted as the wetting time (Zhang and Carlin, 2010).

Mouth feel is an important parameter for ODT's as patients may sometimes reject tablets with an unpleasant mouth feel. The sample tablet is applied on the tongue in order to evaluate of its mouth feel. Then, healthy volunteers evaluate the tablet taste with using different score values like 0 = good, 1 = tasteless, 2 = slightly bitter, 3 = bitter, and 4 = awful. (Bhati and Nagrajan, 2012).

CONCLUSION

As a conclusion; when we compare the ODT's with conventional oral dosage forms, we can say that they have important advantages like higher bioavailability and patient compliance. Nevertheless, ODT's have some disadvantages like limited tablet weight, short disintegration time, high cost, and packaging problems. Orally disintegrating tablets may be evaluated as a first option for pediatric and geriatric patients who have swallowing problem.

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