ejpmr, 2021,8(11), 299-303

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

ORAL FAST DISINTEGRATING TABLET: AN OVERVIEW

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Article Received on 16/09/2021 **Article Revised on 06/10/2021** **Article Accepted on 26/10/2021**

ABSTRACT

In the present scientific scenario the drug delivery technology has become highly competitive and rapidly evolving with ever increasing demand. Fast dissolving tablet (FDT) is one such type of an innovative and unique drug delivery system which is swiftly gaining much attention in the research field of rapid dissolving technology. Most of the drug products available in the market are for oral drug administration.[1] Oral route is preferred due to easy of administration, versatility, patient compliance and accurate dosing. However, oral administration is not suitable for people with dysphasia, a condition that results in a difficulty in swallowing. Also, for many geriatric paediatric patients, oral administration might not be a preferred route.[2] In this regards, oral disintegrating tablets (ODT) provide a useful alternative. When ODT comes in contact with saliva, this tablets disintegrate instantaneously (within 30 sec) resulting in the release of drug. Furthermore, since it under goes pre-gastric absorption, it bypasses first pass metabolism, which can be beneficial for drugs with significant hepatic metabolism.

KEYWORDS: Oral disintegrating tablets, Dysphasia, Swallowing problems, Orodispersible tablets, Oral films.

INTRODUCTION

Oral disintegrating tablets are solid single unit dosage forms that are placed on tongue, allowed to disperse or dissolve in saliva without the need of water, frequently releasing of the drug for quick onset of action. Oral disintegrating tablets are well accepted by wide range of population especially as pediatric and geriatric patients who have difficulty in swallowing of conventional dosage forms. Some drugs are absorbed from mouth, pharynx and esophagus as saliva passes down to stomach. The bioavailability of such drug will be increase due to first pass metabolism.[3]

Consumer satisfaction is the buzzword of the current millennium, and movement to achieve it has already begun in the pharmaceutical industry. An inability or un willingness to swallow solid oral dosage forms such as tablets and poor taste of medicine are some of the important reasons for consumer dissatisfaction.[4]

Recent developments in technology have presented viable alternatives for the patients who may have difficulty in swallowing tablets or liquids. Traditional tablets and capsules administered with an 8-oz. glass of water may be inconvenient or impractical for some patients. For example a very elderly patient may not be able to swallow a daily dose of tablets. An eight year old child with allergies could use a more convenient dosage form of antihistamine syrup. A schizophrenic patient in the institution setting can hide a conventional tablet under his or her tongue to avoid his/ her daily dose of atypical antipsychotic. A middle-aged women undergoing radiation therapy for breast cancer may be too nauseous to swallow her H_2-blocker[2].[5]

To overcome these drawbacks, Orally disintegrating tablets (ODT) or Fast Dissolving Tablets (FDT) has emerged as alternative oral dosage forms. These are novel types of tablets that disintegrate/dissolve/ disperse in saliva within few seconds. According to European Pharmacopoeia, the orally dispersible tablet should disperse/disintegrate in less than three minutes. The basic approach used in development of FDT is the use of super disintegrants like Crospovidone (Polyplasdone XL-10), Sodium starch glycolate (Primo gel, Explotab) and Pregelatinized starch (Starch-1500) etc., which provide instantaneous disintegration of tablet after putting on tongue, thereby releasing the drug in saliva. The bioavailability of some drugs may be increased due to absorption of drugs in oral cavity and also due to pre gastric absorption of saliva containing dispersed drugs that pass down into the stomach. Moreover, the amount of drug that is subjected to first pass metabolism is reduced as compared to standard tablets.[6]

Over the past three decades, ODT have gained much attention as a preferred alternative to conventional oral dosage forms such as tablets and capsules. ODT is a solid dosage form that disintegrates and dissolves in the mouth (either on or beneath the tongue or in the buccal

cavity) without water within 60 seconds or less. The US Food and Drug Administration Center for Drug Evaluation and Research (CDER) defines in the Orange Book an ODT as "A solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue. The European Pharmacopoeia however defines a similar term, that is fast dissolving tablet is a tablet that can be placed in the mouth where it disperses rapidly before swallowing.[7]

Orally Disintegrating Tablets

The centre for drug evaluation and Research defines orally disintegrating tablets as a dosage form –"A solid dosage form which disintegrates rapidly within a matter of seconds when placed under the tongue". The disintegrating time for orally disintegrating tablet varies from seconds to minutes, depends upon the size of tablet and formulation. European pharmacopeia defined orally disintegrating tablets as-"Uncovered tablet which disperse before ingestion in the buccal cavity". Different technological techniques such as freeze drying or moulding or direct compression etc are used to prepare the formulation of this type in the pharmaceutical market.[8]

Desired Characteristics of ODTS

1. Bioavailability
2. Rapid drug therapy intervention is possible.
3. Sufficient mechanical strength
4. Allow high drug loading.
5. Rapid onset of therapeutic action
6. Good compatibility with development technology.
7. Leaves no residue in mouth after oral administration
8. Stability
9. Conventional packaging and processing equipments allows the manufacturing of tablets at low cost.
10. Be compatible with taste masking and other excipients.

Advantages of ODTS

1. It can be administered to the patient who cannot swallow conventional dosage form such as bedridden patients, elderly and patient effected by renal failure and thus improves patient compliance.
2. It is suitable for bedridden, disabled, traveller and busy persons who does not contain water every time.
3. Good mouth feel property helps to mask the bitterness of medicines.
4. Rapid drug therapy intervention.
5. It provides rapid absorption of drugs and increased availability.[8]

Significance of ODTs

ODTs offer dual advantages of solid dosage forms and liquid dosage forms along with special features which include:

- **Accurate dosing:** Being unit solid dosage forms, provide luxury of accurate dosing, easy portability and manufacturing, good physical and chemical stability and an ideal alternative for paediatric and geriatric patients.
- **Enhanced bioavailability:** Bioavailability of drugs is enhanced due to absorption from mouth, pharynx and oesophagus.
- **Rapid action:** Fast onset of therapeutic action as tablet gets disintegrated rapidly along with quick dissolution and absorption in oral cavity.
- **Patient compliance:** No need of water to swallow the dosage form. Hence, it is convenient for patients who are traveling and do not have immediate access to water.
- **Ease of administration:** Convenient to administer specially for geriatric, paediatric, mentally disabled and bed ridden patients who have difficulty in swallowing.
- **Obstruction free:** No risk of suffocation in airways due to physical obstruction when swallowed, thus providing improved safety and compliance.
- **Enhanced palatability:** Good mouth feel, especially for paediatric patients as taste masking technique is used to avoid the bitter taste of drug.
- **Simple packaging:** No specific packaging required. It can be packaged in push through blisters.
- **Business avenue:** Provide new business opportunities in the form of product differentiation, line extension, uniqueness and life cycle management.
- **Cost effective:** Conventional processing and packaging equipments allow the manufacturing of tablets at low cost.

Ideal characteristics of ODTs

ODTs should depict some ideal characteristics to distinguish them from traditional conventional dosage forms. Important desirable characteristics of these dosage forms include:

- No water requirement for swallowing purpose but it should dissolve or disintegrate in the mouth usually within fraction of seconds.
- Provide pleasant feeling in the mouth.
- Be compatible with taste masking.
- Be portable without fragility concern.
- Leave negligible or no residue in the mouth after oral administration.
- Exhibit low sensitivity to altered environmental conditions such as humidity and temperature.
- Allow high drug loading.
- Adaptable and amenable to conventional processing and packaging equipment at nominal expense.

Various approaches employed in manufacture of ODTs

There are number of techniques generally employed in the formulation of orally disintegrating dosage forms. These techniques have their own advantages as well as disadvantages and are described below:

i) Direct compression

Direct compression is one of the popular techniques for preparation of these dosage forms. The advantages of this method include easy implementation, use of conventional equipments along with commonly available excipients, limited number of processing steps and cost effectiveness.

Disintegration and solubilization of directly compressed tablets depend on single or combined action of disintegrants, water-soluble excipients and effervescent agents. The basic principle involved in development of these dosage forms using this technique is addition of super disintegrants in optimum concentrations so as to achieve rapid disintegration along with pleasant mouth feel. It is considered as the best method to prepare orally disintegrating dosage forms since the prepared tablets offer higher disintegration due to absence of binder and low moisture contents. This approach is also considered as disintegrant addition technology. Bi *et al* and Watanabe *et al* developed fast-dissolving tablets using microcrystalline cellulose and low substituted hydroxy propyl cellulose as disintegrating agents in the range of 8:2-9:1. Shu *et al* also prepared rapid oral disintegrating tablets by direct compression using co-ground mixture of D-mannitol and Crospovidone.[9]

ii) Freeze Drying

A process in which water is sublimated from the product after freezing. Lyophilization is a pharmaceutical technology, which allows drying of heat sensitive drugs and biological at low temperature under conditions that allow removal of water by sublimation. Lyophilization results in preparations, which are highly porous, with a very high specific surface area, which dissolve rapidly and show improved absorption and bioavailability.

iii) Moulding

In this method, molded tablets are prepared by using water-soluble ingredients so that the tablets dissolve completely and rapidly. The powder blend is moistened with a hydro-alcoholic solvent and is molded into tablets under pressure lower than that used in conventional tablet compression. The solvent is then removed by air-drying. Molded tablets are very less compact than compressed tablets. These possess porous structure that enhances dissolution.

iv) Spray-Drying

Spray drying can produce highly porous and fine powder that dissolve rapidly. The formulations are incorporated by hydrolyzed and non-hydrolyzed gelatins as supporting agents, mannitol as bulking agent, sodium starch glycolate or croscarmellose sodium as disintegrating agent and an acidic material (e.g. citric acid) and / or alkali material (e.g. Sodium bicarbonate) to enhance disintegration and dissolution. Tablet compressed from the spray dried powder disintegrated within 20 seconds when immersed in an aqueous medium.

v) 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 tetraamine. 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 40ºC to 60ºC. The disintegration time in the oral cavity was found to be about 25s.

vi) 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.

Formulation Development of ODTs

Selection of active pharmaceutical ingredient is one of the most important parameters to formulate ODTs. It should be dissolved in the oral cavity and absorbed. Also it shouldn't have bitter taste. It is better if it is in low dose, small to moderate molecular weight, good solubility in water and/or saliva, non-ionized property in pH 5.5-7.4 and ability to be absorbed via oral mucosa.

Excipient selection is important for disintegrating the tablet immediately and also important for masking bitter taste. Main excipient groups are diluents; disintegrants that have different disintegrate mechanisms, flavours, and taste masking agents, sweeteners, binders, lyoprotectans, glidants and lubricants. To accomplish the challenges, specific excipients can be used in different ranges.

Also selection of manufacturing method is as important as selection of Excipients. Because different technologies have various advantages and disadvantages. Some of those methods are patented. Those patented technologies are WOWTAB®, ORASOLV®, DURASOLV® EFVDAS®, FLASHTAB® (main approach is conventional tablet processes with modifications), ZYDIS®, LYOC®, QUICKSOLV® (main approach is freeze drying method) and FLASHDOSE® (main approach is floss formation). In Table 1, some marketed ODTs and their manufacturing technologies, and major advantages were give.

Active ingredients	Local Brand Name	Category	Manufacturing technology	Technological basis	Advantages of technology
Loratadine	Claritin	Antihistaminic	Zydis*	Lyophilization	Very fast disintegration
Mirtazapine	Remeron	Antidepressant	Orasolv*	Compresses tablets	Effervescent disintegration
Olanzapine	Zyprexa	Antipsychotic; serotonin-Dopamine antagonist	Zydis*	Lyophilization	Very fast disintegration
Ondansetron	Zofran ODT	Nootropic; Antiemetic; Serotonin Receptor Antagonist	Zydis*	lyophilization	Very fast disintegration
Risperidone	Risperdal	Antipsychotic; Dopamine Receptor Antagonist; Serotonin-Dopamine Antagonist	Zydis*	Lyophilization	Very fast disintegration
Rizatriptan	Maxalt	Antimigraine; Serotonin Receptor Agonist	Zydis*	Lyophilization	Very fast disintegration
Tramadol	Ultram	Analgesic(Non-narcotic)	Flash Dose*	Cotton Candy Process	Effectively taste masking
Zolmitriptan	Zoming	Antimigraine; Serotonin Receptor agonist	Durasolv*	Compressed tablets	Easy to formulate low dose of active ingredient and higher mechanical strength than Orasolv
Zolpidem	Ambien	Sedative/Hypnotic	Flash Dose*	Cotton Candy Process	Effectively taste mask

Additionally recent innovator system called 'SeDeM-ODT' can be mentioned as an accessorily to the selection of excipients, that can be used in direct compression manufacturing method. 'SeDeM-ODT' is new and based on the earlier SeDeM expert systems that provide to predict compliance of powder blend to produce immediate release tablets by direct compression. One of major advantages of this expert system is that it avoids application of unnecessary inactive ingredients.

As established in previous reviews, direct compression is the most preferred manufacturing method to produce ODTs. By using 'SeDeM-ODT' expert system, many excipients can be evaluated. The 'SeDeM-ODT' expert system has 12 parameters (bulk density, tapped density, inter-particle porosity, Carr index, cohesion index, Hausner ratio, angle of repose, powder flow, loss on drying, hygroscopicity, particle size, homogeneity index) which classified into 5 factors (dimensions, compressibility, flowability/powder flow, lubricity /stability, lubricity/dosage) to determine the index of good compression (IGC). That complies to analyse the suitability of 43 excipients for direct compression manufacturing method.

Some tests are being conducted to prove the quality of ODTs. But the most critical tests are disintegration and dissolution tests to prove *in-vitro* equivalence of the formulation. There are some compendial and non-compendial methods for disintegration test and there are different limitations for those tests. Frequently disintegration tests are being conducted to USP current edition. Dissolution tests are usually being conducted at pH 1.2 and pH 6.8 to simulate oral and Pregastric absorption. But sometimes different mediu0ms can be chosen up to APIs p^{Ka}.[10]

CONCLUSION

Fast Dissolving tablets are considered to be contemporary dosage forms. These dosage forms and their route of administration results in better efficacy, rapid onset of action, enhanced bioavailability, and improved patient compliance. There are many marketed product of this category which have been introduced in the recent past. Some of the recent product in the Indian and global market are listed in table. The primary attractive factor of MDT is quick disintegration in oral cavity without the aid of water, along with sufficient mechanical strength. This feature makes this formulation a highly recommendable choice for geriatric and paediatric patients. FDT in the near future is expected to grow at a great and rapid pace, owing to the advancement in the scientific research and discovery of new excipients, resulting in a future-ready, combative arena of pharmaceutical drug delivery systems.

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