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Review Article

CONCEPTS AND SALIENT FEATURES OF ORODISPERSIBLE DRUG DELIVERY SYSTEMS – A REVIEW

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Abstract: The development of pharmaceutical technology in past years has presented the development of alternative dosage forms for the patients who have difficulty in swallowing tablets. Fast disintergrating drug delivery system (FDDDS), are the system which disintergrates and releases the active ingredient quickly without the need of water. Among the FDDDSs, the fast disintergrating tablets (FDT) is the more acceptable form of drug delivery system because of its convenience of self-administration and compactness. The oral route remains the perfect route for the administration of therapeutic agents because of the low cost therapy and ease of administration, which leads to high patient compliance.FDT are tablets, when placed on toungue,disintergrates instantaneously, releasing the drug, which disperses or dissolve in the saliva.FDT have been formulated for pediatric, geriatric, and bedridden patients and for active patients who are busy and traveling and may not have access to water. Fast dissolving tablets are also known as orodispersible, quickdissolve, fast melt, fast dissolve, fast disintegrate, rapid-dissolve, rapid melts or orally dissolve tablets.European pharmacopoeia recently adopted the term "Oro-dispersible tablet" as a tablet to be placed in mouth where it disappears rapidly before swallowing. According to European Pharmacopoeia also, the FDT are the tablets which disintegrate in less than three minutes.This article focuses on classification of Fast Disintergrating Drug Delivery System, the advantages and limitation of Fast Dissolving Tablets.

Keywords: Fast Dissolving Tablets, Salient Features,Challenges, Benefits, Limitations.

INTRODUCTION

Oral route is the most preferred route for the delivery of the drugs till date as it bears various advantages over the other route of drug administration, but oral drug delivery systems still need some advancements to be made because of their some drawbacks related to particular class of patients which includes geriatric, paediatrics and dysphasic patients associated with many medical conditions as they have difficulty in swallowing or chewing solid dosage forms. Many paediatric and geriatric patients are unwilling to take solid preparations due to fear of choking. Even with fast dissolving tablets there is a fear of choking due to its tablet type appearance[1.]

One study showed that 26% of 1576 patients experienced difficulty in swallowing tablets,(dysphagia). The most common complaint was tablet size, followed by surface form and taste. The problem of swallowing tablets was more evident in geriatric and paediatric patients, bedridden patients as well as travelling patients who may not have ready access to water. For example, a very elderly patient may not be able to swallow a daily dose ofantidepressant. An eight year- old with allergies could use a more convenient dosage formthan antihistamine syrup. A Schizophrenic patient in the institutional setting can hide aconventional tablet under his or her tongue to avoid their daily dose of atypicalantipsychotic. A middle aged woman undergoing radiation therapy for breast cancer may be too nauseous to swallow her H_2-blocker.

Fast-dissolving/disintegrating tablets (FDDTs) are a perfect fit for all of these patients[2].Drinking water plays an important role in the swallowing of oral dosage forms. Often times people experience inconvenience in swallowing conventional dosage forms such as tablet when water is not available, in the case of the motion sickness (kinetosis) and sudden episodes of coughing during the common cold,allergic condition and bronchitis. For these reason, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention[1,3].

Fast-dissolving drug-delivery systems came into existence in the late 1970's as an alternative to tablets, capsules and syrups for paediatrics and geriatric patients who experience difficulties in swallowing traditional oral solid-dosage forms. These systems consist of the solid dosage forms that disintegrate and dissolve quickly in the oral cavity without the administration of water. This is an innovative tablet technology where the dosage form containing active pharmaceutical ingredients disintegrates rapidly, usually in a matter of seconds, without the need for water, providing optimal convenience to the patient[1].

Fast disintegrating drug delivery systems are broadly classified into three categories[4].

1. Orally disintegrating films and wafers
2. Fast disintegrating capsules
3. Fast disintegrating tablets

1. Orally disintegrating films and wafers

Orally fast-dissolving film is new drug delivery system for the oral delivery of the drugs. It was developed on the basis of technology of the transdermal patch. The delivery system consists of a very thin oral strip, which is simply placed on the patient's tongue or any oral mucosal tissue, instantly wet by saliva the film rapidly hydrates and adheres onto the site of application. It then rapidly disintegrates and dissolves to release the medication for oromucosal and intragastric absorption. Technology Catalysts forecasts the market for drug products in oral thin film formulations was valued of $500 million in 2007 and could reach $2 billion in 2012. Based on upward global growth trends of the past decade, the fast dissolving dosage market could produce revenues of $13 billion by 2015[1,4].

Special features of mouth dissolving films [1]

- Thin elegant film
- Available in various size and shapes
- Unobstructive
- Excellentmucoadhesion
- Fast disintegration
- Rapid release

2. Fast disintegrating capsules

Fast disintegrating capsules for administration in the oral cavity are prepared either by perforation or by vacuum-drying of conventional capsules. When compared to other fast disintegrating dosage forms such as lyophilized sponges or tablets, capsules have various advantages. Particularly, higher drug-loading capacity and absence of compression during manufacture are of importance. A US patent was granted in September 2004 for the development of fast disintegrating capsules using foam burst technology. In this technology, gas is blown into the film during development, resulting in a film with a honeycombed structure. The voids in the film may be empty, gas-filled or filled with other materials. The light honeycombed structure results in capsules that dissolve rapidly in the oral cavity[4.]

3. Fast disintegrating tablets

Some tablets are designed to dissolve in saliva remarkably fast, within a few seconds, and are true fast-dissolving tablets. Others contain agents to enhance the rate of tablet disintegration in the oral cavity, and are more appropriately termed fast-disintegrating tablets. Fast disintegrating tablets are the most common dosage form in fast disintegrating drug delivery system. The dosage form begins to disintegrate immediately after coming into contact with saliva, with complete disintegration normally occurring within 30–50 s after administration. The solution containing the active ingredients is swallowed, and the active ingredients are then absorbed through the gastrointestinal epithelium to reach the target and produce the desired effect. Researchers have formulated FDT for various categories of drugs, which are used for therapy in which rapid peak plasma concentration is required to achieve desired pharmacological response. These include neuroleptics, cardiovascular agents, analgesics, anti-allergic and drugs for erectile dysfunction. These are novel types of tablets that dissolve/ disintegrate/ disperse in saliva within few seconds without water. According to European pharmacopoeia, these orodispersible Tablets (ODTs) should dissolve/disintegrate in less than three minutes.The benefits of ODTs is to improve patient's compliance, rapid onset of action, increased bioavailability and good stability which make these tablets popular as a dosage form of choice in the current market[4,5,6,7.]

Orodispersible tablets are also called as mouth dissolving tablets, fast disintegrating tablets, orally disintegrating tablets, quick disintegrating tablets, fast dissolving tablets, rapid dissolving tablets, porous tablets, quick melt tablets and rapid melt tablets ,effervescent drug absorption system, (EFVDAS)[6,8,9].US Food and Drug Administration Center for Drug Evaluationand Research (CDER) defines, in the "Orange Book," an ODT as "a solid dosage form containing medicinal substances, which disintegrates rapidly, usuallywithin a matter of seconds, when placed upon the tongue." European Pharmacopoeia described ODTs as "uncoated tablets intended to be placed in the mouth where they disperse rapidly before being

Swallowed" and as tablets which should disintegrate within 3 minutes[8].Fast disintegrating tablets, (FDT) are characterized by high porosity, low density, and low hardness. The US FDA has specifically defined two main criteria to be fulfilled by the FDTs in its publication 'Guidance for Industry: Orally disintegrating tablets':

1. Orally disintegrating tablets should have an in vitro disintegration time of approximately 30 sec or less.
2. The weight of orally disintegrating tablet should not exceed 500 mg, although the combined influence of tablet weight, size, and component solubility all factors into the acceptability of an orally disintegrating tablet for both patients and regulators.

The FDA guidance defines the upper limits of the orally disintegrating tablet category, but it does not supersede or replace the original regulatory definition mentioned. In other words, disintegration within a matter of seconds remains the target for an orally disintegrating tablet[4].

The basic approach used in development of Mouth Dissolving Tablets, (MDT) is the use of superdisintegrants like Cross linked carboxymethyl cellulose (Croscar-meliose), Sodium starch glycolate (Primogel, Explotab). Polyvinylpyrrolidone(Polyplasdone) 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 subject to first pass metabolism is reduced as compared to standard tablets. Another approach used in developing MD tablets is maximizing pore structure of the tablets[7].

Different types of technologies have been employed for the formulation of mouth dissolving tablets viz freeze-drying, Tablet Molding, Direct Compression Method, spray drying

and sublimation Technology etc. have been tried by researchers to maximize the pore structure of tablet matrix[10].

Criteria for Fast dissolving DrugDelivery System: [2, 3, 5, 10, 11, 12]

The tablets should

- Not require water to swallow, but it should dissolve or disintegrate in the mouth in matter of seconds.
- Be compatible with taste masking.
- Be portable without fragility concern.
- Have a pleasant mouth feel.
- Leave minimum or no residue in the mouth after oral administration.
- Exhibit low sensitive to environmental condition as temperature and humidity.
- Allow the manufacture of tablet using conventional processing and packaging equipments.

Salient Features of Fast Dissolving Drug Delivery System: [2, 3, 5]

- Ease of Administration to the patient who cannot swallow, such as the elderly stroke victims, bedridden patients, patient affected by renal failure and patient who refuse to swallow such as paediatric, geriatric & psychiatric patients.
- No need of water to swallow the dosage form, which is highly convenient feature for patients who are traveling and do not have immediate access to water.
- Rapid dissolution and absorption of the drug, which will produce quick onset of action.
- Some drugs are absorbed from the mouth, pharynx and oesophagus as the saliva passes down into the stomach. In such cases bioavailability of drug is increased.
- Pre-gastric absorption can result in improved bioavailability and as a result of reduced dosage; improve clinical performance through a reduction of unwanted effects.
- Good mouth feel property helps to change the perception of medication as bitter pill particularly in paediatric patient.
- The risk of chocking or suffocation during oral administration of conventional formulation due to physical obstruction is avoided, thus providing improved safety.
- New business opportunity like product differentiation, product promotion, patent extensions and life cycle management.
- Beneficial in cases such as motion sickness, sudden episodes of allergic attack or coughing, where an ultra-rapid onset of action required.
- Stability for longer duration of time, since the drug remains in solid dosage form till it is consumed. So, it combines advantage of solid dosage form in terms of stability and liquid dosage form in terms of bioavailability.
- Good mouth feels properly of MDDS helps to change the basic view of medication as "bitter pill", particularly for paediatric patients.
- Allow high drug loading
- Cost effective.

Benefits of fast dissolving tablets: [2, 3,4,5,7,10,11,12]

- Administered without water, anywhere, any time.
- Suitability for geriatric and pediatric patients, who experience difficulties in swallowing and for the other groups that may experience problems using conventional oral dosage form, due to being mentally ill, the developmentally disable and the patients who are uncooperative, or are on reduced liquid intake plans or are nauseated.
- An increased bioavailability, particularly in cases of insoluble and hydrophobic drugs, due to rapid disintegration and dissolution of the tablets.
- Convenience of administration and accurate dosing as compared to liquid Formulations.
- Ability to provide advantages of liquid medication in the form of solid preparation.
- Improved patient compliance

Limitations of Mouth Dissolving Tablets [2,3,5,10,12]

- The tablets usually have insufficient mechanical strength. Hence, careful handling
- Is required.
- The tablets may leave unpleasant taste and/or grittiness in mouth if not formulated
- properly
- Fast dissolving tablet is hygroscopic in nature so must be keep in dry place.
- Drugs with larger doses are difficult to formulate into Fast Dissolving Tablets e.g. rifampin (600 mg), ethambutol (1000mg) etc.
- Patients who concurrently take anticholinergic medications may not be the best candidates for FDTs and patients with Sjogren's syndrome or dryness of mouth due to decreased saliva production may not be the good candidates for these tablet formulations.
- FDTs require special packaging for proper stabilization and safety of stable product

CHALLENGES IN FORMULATING FAST DISSOLVING TABLETS [6, 10]

1) **Mechanical strength and disintegration time:** Many FDTs are fragile and there are many chances that such fragile tablet will break during packing, transport or handling by the patients.So, maintaining a good mechanical strength is very important while formulating FDT.Tablets based on technologies like Zydis need special type of packaging. It is very natural that increasing the mechanical strength will delay the disintegration time. So a good compromise between these two parameters is always essential.
2) **Taste masking:** Many drugs are bitter in taste. A tablet which is bitter will seriously affect patient compliance and acceptance for the dosage form. So effective taste masking of the bitter drugs must be done so that the taste of the drug is not felt in the oral cavity.
3) **Hygroscopicity:** Many orally disintegrating dosage forms are hygroscopic. They cannot uphold physical integrity under normal conditions of temperature and humidity Henceforth, they need protection from humidity which demands a specialized product packaging.

4) **Mouth feel:** The particles generated after disintegration of the FDTs should be as small as possible and it should leave minimal or no residue in mouth after oral administration. Moreover addition of flavours and cooling agents like menthol can improve the mouth feel.
5) **Amount of drug:** The application of FDT technologies used for FDTs is limited by the amount of drug that can be incorporated into each unit dose. For lyophilized dosage forms, the drug dose must be less than 400 mg for insoluble drugs and lower than 60 mg for soluble drugs. This parameter is especially challenging during formulating a fast-dissolving oral films or wafers.
6) **Cost:** The technology used for FDTs should be acceptable in terms of cost of the final product. Cost for methods like Zydisand Orasolv that require special technologies and specific packaging is really high.
7) **Size of tablet:** The degree of ease when taking tablets depends on its sizeIt has been reported that the easiest size of tablet to swallow is 7-8 mm while the easiest size to handle was larger than 8 mm. Therefore, the tablet size that is both easy to take and easy to handle is difficult to achieve.
8) **Aqueous Solubility:** Water-soluble drugs pose various formulation challenges because they form eutectic mixtures, which result in freezing-point depression and the formation of a glassy solid that may collapse upon drying because of loss of supporting structure during the sublimation process. Such collapse sometimes can be prevented by using various matrix-forming excipients such as mannitol than can induce crystallinity and hence, impart rigidity to the amorphous composite.

CONCLUSION

The FDTs have potential advantages over conventional dosage forms, with their improved patient compliance, convenience, bioavailability and rapid onset of action had drawn the attention of many manufactures over a decade. FDTs formulations obtained by some. of these technologies have sufficient mechanical strength quick disintegration/dissolution in the mouth without water. However, common people are not much aware of this delivery system. Therefore, pharmacists are responsible to spread the knowledge regarding this system. This dosage form should be handled carefully since they do not have sufficient mechanical strength. Patients who suffer from dryness of mouth should not be prescribed with FDTs, since minimum volume of saliva is necessary for it to disintegrate/dissolution These FDTs can be used easily in children who have lost their primary teeth and in geriatric patients who have lost their teeth permanently. They remain solid during storage, which aid in stability of dosage forms and transform into liquid form within few seconds after its administration. As they have significant advantages as both solid and liquid dosage forms, FDTs may be developed for most of the available drugs in near future. Fast dissolving tablets can offer several biopharmaceutical advantages such as improved efficiency over conventional dosage forms. For example, they require smaller amounts of active ingredient to be effective, improve absorption profiles, and offer better drug bioavailability than regular tablets and capsules[2, 6].

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