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OVERVIEW OF APPROACHES IN DEVELOPMENT OF FAST DISSOLVING TABLETS

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ABSTRACT

Fast dissolving tablet is considered to allow administration of an oral solid dose form in the absence of water or fluid intake. Such tablets once placed on the tongue it readily dissolve or disintegrate in the saliva without chewing or water within less than 60 seconds. Fast- or mouth dissolving tablets 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. This review includes requirements for fast disintegrating tablets, salient features, advantages, limitations, challenges in formulation, various technologies developed for fast disintegrating tablets. These are novel types of tablets that disintegrate/dissolve/disperse in saliva within few seconds. Fast dissolving tablets (FDTs) have received ever-increasing demand during the last decade, and the field has become a rapidly growing area in the pharmaceutical industry. This article also reviews the Need, advantages, challenges, limitations, mechanism of superdisintegrants, various formulation technologies (conventional and patented), marketed product of Fast dissolving tablets safest, most convenient and most economical method of drug delivery products.

INTRODUCTION

Oral routes of drug administration have wide acceptance up to 50-60% of total dosage forms.Solid dosage forms are popular because of ease of administration, accurate dosage, selfmedication,pain avoidance and most importantly the patient compliance. The most popular solid dosage forms are being tablets and capsules; one important drawback of this dosage forms for some patients, is the difficulty to swallow. Drinking water plays an important role in the swallowing of ordispersible tablets are not only indicated for people who have swallowing difficulties, but also are ideal for active people4. Fast dissolving tablets are also called as mouth-dissolving tablets, melt-in mouthtablets,Orodispersible tablets, rapimelts, porous tablets, quick dissolving etc. Fast dissolving tablets are those when put on tongue disintegrate instantaneously releasing the drug which dissolve or disperses in the saliva5. The faster the drug into solution, quicker the absorption and onset of clinical effect. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablets dosage form. The advantage of mouth dissolving dosage forms are increasingly being recognized in both, industry and academics7. Their growing importance was underlined recently when European pharmacopoeia adopted the term " Orodispersible tablet" as a tablet that to be placed in the mouth where it disperses rapidly before swallowing.According to European pharmacopoeia, the ODT should disperse/disintegrate in less than three minutes. .

A Rapid disintegrating drug delivery system is the novel concept of drug delivery system which was developed to overcome the basic drawbacks of conventional tablets.[1,2] On the basis of recent developments dispersible tablets can be distinguished in two forms: one which directly disintegrates or dissolves in the mouth without a need of drinking water and second which requires addition of water to form dispersion within seconds of time, and easy to taken by the patient. In both the cases, bioavailability of drug is significantly greater due to instant dispersion and solubility than those observed from conventional dosage form.[3] Paracetamol (4'-hydroxyacetanilide, N-acetyl p- aminophenol, acetaminophen, PAR) is a widely used over-the-counter analgesic and antipyretic drug without any gastric irritation and ulcerative effects.[4,5,6,7] Paracetamol is white crystalline powder having bitter in taste.[7] According to Biopharmaceutical Classification system , Paracetamol is a class IV, a low soluble and low permeable drug.[8,9] A drug with poor aqueous solubility will typically exhibit dissolution rate limited absorption, and a drug with poor membrane permeability will typically exhibit permeation

rate limited absorption.[10] Therefore, 'Formulation scientist' focuses on two areas for improving the oral bioavailability of drugs include: (i) enhancement of solubility and dissolution rate of poorly water-soluble drugs and (ii) enhancement of permeability of poorly permeable drugs.[11] There are various technology available for the enhancement of solubility as well as dissolution profile of active in which the Hydrotropy methods,[12] solid dispersion method,[13] use of carrier as co solvent, uses of surfactants, superdisintegrants, and polymers are some commonly used approaches for enhancement of aqueous solubility of formulations have been reported in literature.[14,15,16,17] Recent advances in Novel Drug Delivery System (NDDS) molecule by formulating a convenient dosage form for administration and to achieve better patient compliance. To develop a chemical entity, a lot of money, hard work and time are required. So focus is rather being laid on the development of new drug delivery systems for already existing drugs, with enhanced efficacy and bioavailability, thus reducing the dose and dosing frequency to minimize the side effects. [1] Recently aims to enhance safety and efficacy of already used drug the European Pharmacopoeia adopted the term orodispersible tablet as a tablet to be placed in the mouth where it disperses rapidly before 11, Explotab).Polyvinylpyrrolidone. The conventional dosage forms (tablet and capsule) have wide acceptance up to 50-60% of total dosage forms.Tablet is still most popular conventional dosage forms existing today because of ease of self administration ,compact in nature, easy to manufacture and it can be deliver in accurate dose. One important drawback of solid dosage forms is the difficulty in swallowing (dysphagia) or chewing in some patients particularly pediatric and geriatric patients. The problem of swallowing is common phenomenon in geriatric patient due to fear of choking, hand tremors, dysphasia and in young individuals due to underdeveloped muscular and nervous systems and in schizophrenic patients which leads to poor patient compliance1. Difficulties in swallowing of tablet and capsule are also occur when water is not available, in diarrhea, coughing during the common cold, allergic condition and bronchial infection2. Approximately one-third of the population (mainly pediatric and geriatric) has swallowing difficulties, resulting in poor compliance with oral tablet drug therapy which leads to reduced overall therapy effectiveness. For conventional dosage forms are pioneer of drug administration systems. The most widely used and accepted is the oral route of drug administrations. The oral dosage forms are widely used for ease of self-administration and low cost as compared to other dosage forms [1]. It is however associated with some drawbacks such as dysphagia (difficulty in swallowing), low bioavailability and delayed onset of action. In order to overcome these issues researchers have long explored the "oral cavity" to harness its

drawback to enhance the drug's permeability as well as bioavailability. The "oral cavity" has a good permeability because of mucosal lining being relatively less keratinized in the buccal mucosa [2]. Drug absorbed via "oral cavity" directly enters into systemic circulation by a jugular vein ensuring, a rapid onset of action, avoidance of first pass metabolism, and drug degradation in gastric region and enzymatic hydrolysis in intestine [3]. Keeping in mind the advantages of the "oral cavity", an Oral Dispersible Tablet, commonly known as the Fast Dissolving Tablets are a widely accepted formulations. 1 quickly without requiring water, or chewing, providing best alternative for the patient suffering from difficulty in swallowing (Gedamand Ghuge, 2010). Fast disintegrating tablets have an edge over conventional dosage form because of greater bioavailability. Mouth dissolving dosage forms are increasingly being recognized in both industry and academia (Khurana and Bedi, 2009). Uniqueness and majority of orally administered dosage form especially fast dissolving drug delivery systems have started gaining popularity and acceptance because of rapid disintegration, dissolution, self-administration that without water or chewing (Sharma and Yadav, 2010). Recent advances in technology and novel drug delivery systems (NDDS) have presented viable dosage alternatives for patients who have difficulty in swallowing tablets or capsules and further, the aim to enhance safety and efficacy of drug molecule by formulating a convenient dosage form for administration and to achieve better patient compliance; one such approach is fast dissolving tablets (Liberman and Karnig, 1987; Lohitnavy *et al*., 2003). Higher incidences of gastrointestinal complications are associated with conventional dosage forms, when administered through oral route.

ADVANTAGES OF FDT

- Improved patient Ease of Administration to the patient who cannot swallow then consequently compliance.
- No water needed. Which is useful for patients who are traveling and do not have immediate access to water.
- Rapid dissolution, absorption of the drug and hereafter increase bioavailability Pregastric absorption of drug be able to increase oral bioavailability of drug, and as result of reduces dose administration.
- The risk of blocking or suffocation during oral administration of conventional formulation due to physical obstruction is avoided, thus providing improved safety.
- Good chemical stability as conventional oral solid dosage form.] Suitability of administration and accurate dosing as compared to liquid formulation.

- Suitability for geriatric and pediatric patients, who experience difficulties inswallowing 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 un-cooperative, or are on reduced liquid intake plans or are nauseated.
- Beneficial in cases such as motion sickness, suede episodes of allergic attack or coughing, where an ultra rapid on set of action required.
- An increased bioavailability, particularly in cases of insoluble and hydrophobic drugs, due to rapid disintegration and dissolution of these tablets.
- 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 feel property of Mouth dissolving drug delivery system helps to change the basic view of medication drugs.
- Convenience of administration and accurate dosing as compared to liquid formulations.
- Benefit of liquid medication in the form of solid preparation.
- More rapid drug absorption from the pre-gastric area i.e. mouth, pharynx and esophagus which may produce rapid onset of action.
- Pre-gastric absorption can result in improved bioavailability, reduced dose and improved clinical performance by reducing side effects.
- New business opportunities: product differentiation, line extension and life-cycle management, exclusivity of product promotion and patent-life extension (Kuchekar et al., 2003 and Bradoo., 2001).
- Have adequate strength to withstand the rigidities of the manufacturing process and post manufacturing handling. Beneficial then liquid formulation in terms of administration as well as transportation.

DISADVANTAGES OF FDT

- 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 formulate properly.

CHALLENGES IN FORMULATING FDT

Palatability

As most drugs are unpalatable, orally disintegrating drug delivery systems usually contain the medicament in a taste-masked form. FDT disintegrate or dissolve in patient's oral cavity, thus releasing API comes in contact with taste buds, so taste-masking become a critical to patient compliance.

Mechanical strength

Order to allow FDTs to disintegrate in oral cavity, they are either vary porous or compressed into tablets with very low compression force, which makes tablets friable, difficult to handle and requiring specialized packing. These tablets have very poor mechanical strength.

Hygroscopicity

Several fast dissolving dosage forms are hygroscopic in nature and not able to maintain physical integrity under normal conditions of temperature and humidity. So, require special packaging.

Amount of drug

The application of technologies used for ODTs is limited by the amount of drug that can be incorporated into each unit dose. For lyophilized dosage forms, the drug dose must be lowerthan 400 mg for insoluble drugs and less than 60 mg for soluble drugs. This parameter is particularly challenging when formulating a fast-dissolving oral films or wafers.

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.

Size of tablet

The degree of ease when taking a tablet depends on its size. It has been reported that the easiest size of tablet to swallow is 7-8 mm while the easiest size to handle was one larger than 8 mm. Therefore, the tablet size that is both easy to take and easy to handle is difficult to achieve.

ADVANCED TECHNOLOGIES

Quick –Dis technology

Lavipharm Laboratories Inc. (Lavipharm) has invented an ideal intraoral fast-dissolving drug delivery system, which satisfies the unmet needs of the market. The novel intraoral drug delivery system, trademarked Quick-Dis™, is Lavipharm's proprietary patented technology and is a thin, flexible, and quick-dissolving film. The film is placed on the top or the floor of the tongue. It is retained at the site of application and rapidly releases the active agent for local and/or systemic absorption. The Quick-Dis™ drug delivery system can be provided in various packaging configurations, ranging from unit-dose pouches to multiple-dose blister packages. The typical disintegration time, which is defined as the time at which the film begins to break when brought into contact with water, is only 5 to 10 seconds for the Quick-Dis™ film with a thickness of 2 mm. 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 seconds for Quick Dis™ film with a thickness of 2 mm. The typical release profile of an active ingredient exhibited by a Quick-Dis™ drug delivery system is 50% released within 30 seconds and 95% within 1 minute. (Dobetti., 2001 and Rish., 2004).

Nanocrystal technology

For fast dissolving tablets, Elan's proprietary Nanocrystal technology can enable formulation and improve compound activity and final product characteristics. Decreasing particle size increases the surface area, which leads to an increase in dissolution rate. This can be accomplished predictably and efficiently using Nanocrystal technology. Nanocrystal particles are small particles of drug substance, typically less than 1000 nanometers (nm) in diameter, which are produced by milling the drug substance using a proprietary wet milling technique. (Kaushik et al., 2004).

CONCLUSION

It can be concluded that, 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. This feature makes this formulation a highly recommendable choice for geriatric and pediatric patients. FDT in the near future is expected to grow at a great and rapid pace, owing to the advancement in the scientific research of new excipients, resulting in a future-ready, combative arena of pharmaceutical drug delivery systems.

The popularity of FDTs has increased tremendously over the last decade. FDT need to be formulated for pediatric, geriatric, bedridden, psychotic patients, for those patients who are busy in traveling, patients who are may not have access to water. Such products provide opportunity for the product line extension in the market place and extension of patent term of innovator. The clinical studies show FDTs can improve patient compliance, provide a rapid onset time of action, and increase bioavailability. Considering the many benefits of FDTs, it is only a matter of time until a majority of oral formulations are prepared in FDT forms.

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