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REVIEW ARTICLE ON ORAL DISINTEGRATION TABLETS

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ABSTRACT

The desire of improved palatability in orally administered products has prompted the development of numerous formulations with improved performance and acceptability. Orally disintegrating tablets are an emerging trend in novel drug delivery system and have received ever-increasing demand during the last few decades. The field has become a rapidly growing area in the pharmaceutical industry and gaining popularity due to ease of administration and better patient compliance especially for geriatric and pediatric patients. ODTs are solid unit dosage forms, which disintegrates or dissolves rapidly in the mouth without chewing and water. This type of property in dosage form can be attained by addition of different excipients, from which disintegrated is the key adjuvant. In recent years, several newer agents have been developed known as superdisintegrants. Diverse categories of superdisintegrants such as synthetic, semi-synthetic, natural and co processed blends etc. have been employed to develop effectual mouth dissolving tablets and to overcome the limitations of conventional tablet dosage forms. The objective of the present article is to highlight the various kinds of superdisintegrants along with their role in tablet disintegration and drug release, which are being used in the formulation to provide the safer, effective drug delivery with patient compliance. This review focuses on various synthetic superdisintegrants, natural superdisintegrants from different plant sources, co-processed excipients blend and their efficiency.

KEYWORDS: Orally disintegrating tablet, superdisintegrants, excipients, formulation, dissolution.

INTRODUCTION

The most important drug delivery route is undoubtedly the oral route. Drug delivery companies are focusing on solid oral drug delivery systems that offer greater patient compliance and effective dosages.[1] Tablet is the most popular among all dosage forms existing today because of its convenience of self administration, compactness and easy manufacturing. Many patients find it difficult to swallow tablets and hard gelatin capsules The difficulty is experienced in particular by pediatric and geriatric patients, but it also applies to people who are ill in bed and to those active working patients who are busy or traveling, especially those who have no access to water[2] and flavor, ease of administration and swallowing, need for quick action in some indications can be counted as main reasons for increasing indent for the ODTs.[3]

Orally disintegrating tablets are also called as oral dispersible tablets, quick disintegrating tablets, mouth dissolving tablets, fast dissolving tablets, fast disintegrating tablets, rapid dissolving tablets. Currently, a wide spectrum of innovative, directly compressible co-processed excipients is available to meet these criteria for an ODT.[4] The manufacturers of these excipients continue to invest in technologies to meet the challenges stemming from solubility and/or delivery of APIs in nearly all areas of therapeutic developments. These therapeutic areas can include analgesics (non-steroidal and opioids), antimigraine, antianginal, antiemetics, tranquillizers, antipsychotics, antihistaminics, antispasmodics, antitussives, glucocorticoids, hypnotics/ sedatives, and vasodilators among others. Those technologies give formulators the opportunity to design and develop the ODTs more cost-effectively.[5]

Recent market studies indicate that most of the patient population prefers ODTs to other dosage forms and would ask their doctors for ODTs (70%), purchase ODTs (70%), or prefer ODTs to regular tablets or liquids (>80%). United States Food and Drug Administration (FDA) defined ODT as “A solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue.” The disintegration time for ODTs generally ranges from several seconds to about a minute.[6] On analyzing the behavior of disintegration time in the oral cavity as well as wetting time by surface free energy we came to know, that for a faster wetting a molecule should have high polar component of surface free energy and the agents which meet these special requirements are called as superdisintegrants.[7] The ease of availability of these

agents and the simplicity in the direct compression process suggest that their use would be a more profitable alternative in the preparation of ODT than the sophisticated and patented techniques.

Merits of Orally Disintegrating Tablets

- Convenience of administration and accurate dose as compared to liquids. No need of water to swallow the dosage form.
- Convenient for administration to traveling patients and busy people who do not have accesses to water.
- Good mouth feel property helps to change the perception of medication as bitter pill particularly in pediatric patients.
- Ease of administration to patients who refuse to swallow a tablet, such as pediatric, geriatric, mentally ill, disabled and uncooperative patients.
- Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach; in such cases bioavailability of drugs is increased.
- Rapid drug therapy intervention.
- Ability to provide advantages of liquid medication in the form of solid preparation.
- Rapid dissolution of drug and absorption, which may produce rapid onset of action
- Insensitive to environmental conditions such as humidity and temperature.

Formulation Processes for Making Fast-Dissolving Tablets[7-15]

Various processes can be used to develop orally disintegrating tablets with different methodologies and the ODTs formed vary in various properties such as,

1. Mechanical strength of tablets
2. Taste and mouth feel
3. Swallow ability
4. Drug dissolution in saliva
5. Bioavailability
6. Stability

Several processes employed in formulating ODTs include freeze-drying, direct compression, cotton candy process, molding, spray drying, sublimation, mass extrusion, nanonization, compaction and fast dissolving films. Direct compression represents the simplest and most cost effective tablet manufacturing technique. This technique can now be applied to

preparation of ODT because of the availability of improved excipients especially superdisintegrants and sugar based excipients. Recently new materials termed as "superdisintegrants" have been developed to improve the disintegration processes.[16]

Superdisintegrants: These are also called as super-absorbing materials. Disintegrating agents are substances routinely included in the tablet formulations to aid in the break-up of the compacted mass into the primary particles to facilitate the dissolution or release of the active ingredients when it is put into a fluid environment. They endorse moisture penetration and dispersion of the tablet matrix. The major function of disintegrants is to oppose the efficiency of the tablet binder and physical forces that act under compression to structure the tablet.

These materials are not planned to absorb significant amounts of water or aqueous fluids, but planned to swell very fast. These are used as a structural weakener for the disintegrable solid dosage forms. They are physically dispersed within the matrix of the dosage form and will expand when the dosage form is exposed to the wet environment.[17]

These substances are more effective at lower concentrations with greater disintegrating efficiency and mechanical strength.[18,19] These are generally used at a low level in the solid dosage form, typically 1 - 10 % by weight relative to the total weight of the dosage unit.[20] Their particles are generally small and porous, which allow for rapid tablet disintegration in the mouth without an objectionable mouth-feel from either large particles or gelling.

The particles are also compressible which improves tablet hardness and its friability.[21] These are effective and provide improved compressibility, compatibility and have no negative impact on the mechanical strength of formulations containing highdose drugs.

Generally, one gram of superdisintegrant absorbs 1040 g of water or aqueous medium. After absorption, swelling pressure and isotropic swelling of the superdisintegrants particles create stress concentrated areas where a gradient of mechanical properties will exist due to which whole structure will integration.

Challenges in Formulating ODTS

Palatability[21]

As most drugs are unpalatable, orally disintegrating drug delivery systems usually contain the medicament in a taste-masked form. Delivery systems disintegrate or dissolve in patient's

oral cavity, thus releasing the active ingredients which come in contact with the taste buds; hence, taste-masking of the drugs becomes critical to patient compliance. General taste masking techonologics taste masking with lipophilic vehicle ,miscellaneous masking agents etc.

Mechanical strength[22]

These ODTs are made of either very porous and soft-molded matrices or compressed into tablets with very low compression force, which makes the tablets friable and/or brittle, difficult to handle, and often requiring specialized peel-off blister packing that may add to the cost. Only few technologies can produce tablets that are sufficiently hard and durable to allow them to be packaged in multidose bottles, such as Wowtab by Yamanouchi-Shaklee, and Durasolv by CIMA labs.

Hygroscopicity

Several orally disintegrating dosage forms are hygroscopic and cannot maintain physical integrity under normal conditions of temperature and humidity. Hence, they need protection from humidity which calls for specialized product 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 lower than 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.

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. This collapse can be prevented by using various matrix-forming excipients like mannitol. This mannitol can induce crystalline 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.

Short half life

ODTs are immediately releasing dosage forms and the absorption of maximum amount of dose takes place in the pre-gastric region. these have short half life.

Cost of the tablet

These are easily fragile, these products require special unit dose packaging which may add to the cost of the dosage form.

ODT Evaluation of Special Concern[22-24]

Crushing strength and friability can be assessed as stated in pharmacopoeias. But some tests are of special concern and these include the following.

Wetting time

Wetting time of dosage form is related to the contact angle. It needs to be assessed to give an insight into the disintegration properties of the tablets; a lower wetting time implies a quicker disintegration of the tablet. For this purpose, a tablet is placed on a piece of tissue paper folded twice and kept in a small Petri dish (ID = 6.5 cm) containing 6 ml of water, and the time for complete wetting is measured.

Disintegration test

The time for disintegration of ODTs is generally less than one minute and actual disintegration time that patient can experience ranges from 5-30 seconds. The standard procedure of performing disintegration test for these dosage forms has several limitations and they are not suitable for the measurement of very short disintegration times. The method needs to be modified for ODTs as disintegration is required without water; thus the test should mimic disintegration in salivary contents. A modified dissolution apparatus is applied to an ODT with a disintegration time that is too fast to distinguish differences between tablets when the compendia method is used. A basket sinker containing the tablets is placed just below the water surface in a container with 900mL of water at 37 0C, and a paddle rotating at 100 rpm is used. The disintegration time is determined when the tablet has completely disintegrated and passed through the screen of the sinker 40. Various scientists41 have

developed new in vitro methods that allow an accurate determination of disintegration test. The disintegration test is performed using a texture analyzer instrument.

Dissolution test

The development of dissolution methods for ODTs is comparable to the approach taken for conventional tablets, and is practically identical. Dissolution conditions for drugs listed in a pharmacopoeia monograph, is a good place to start with scouting runs for a bioequivalent ODT. Other media such as 0.1M Hcl and buffer (pH 4.5 and 6.8) should be evaluated for ODT much in the same way as their ordinary tablet counterparts. It has been suggested that USP 2 paddle apparatus is the most suitable and common choice for orally disintegrating tablets, with a paddle speed of 50 rpm commonly used.

CONCLUSION

Orally disintegrating tablets have better patient acceptance and compliance and may offer improved biopharmaceutical properties, improved efficacy, and better safety compared with conventional oral dosage forms. Prescription ODT products initially were developed to overcome the difficulty in swallowing conventional tablets among pediatric, geriatric, and psychiatric patients with dysphagia. Today, ODTs are more widely available as OTC products for the treatment of allergies, cold, and flu symptoms. The target population has expanded to those who want convenient dosing anywhere, anytime, without water. The potential for such dosage forms is promising because of the availability of new technologies combined with strong market acceptance and patient demand. By paying close attention to advances in technologies, pharmaceutical companies can take advantage of ODTs for product line extensions or for first-to-market products. With continued development of new pharmaceutical excipients, one can expect the emergence of more novel technologies for ODTs in the days to come.

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