

ORODISPERSIBLE TABLET: A Patient Friendly Dosage Form (a Review)

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Background: The most common and preferred route of drug administration is through the oral route. Orodispersible tablets are gaining importance among novel oral drug delivery system as they have improved patient compliance and have some additional advantages compared to other formulation. They are also solid unit dosage forms, which disintegrate in the mouth within a minute in the presence of saliva due to superdisintegrants in the formulation. Thus this type of drug delivery helps a proper per oral administration in pediatric and geriatric population where swallowing is a matter of trouble. Various scientists have prepared orodispersible tablets by following various methods. However, the most common method is the direct compression method. Other special methods are Freeze Drying, Tablet Molding, Sublimation, Spray Drying, Mass extrusion, Phase transition process, etc. Since these tablets dissolve directly in the mouth, so, their taste is also an important factor. Various approaches have been taken in order to mask the bitter taste of the drug. A number of scientists have explored several drugs in this field. Like all other solid dosage forms, they are also evaluated in the field of hardness, friability, wetting time, moisture uptake, disintegration test and dissolution test.

Key words: Disintegration; Manufacturing process; Orodispersible tablets; Superdisintegrants.

INTRODUCTION

Now a day's, there has been an enhanced demand for more patient-friendly and compliant dosage forms. As a result, the demand for developing new technologies has been increasing annually. For most therapeutic agents used to produce systemic effects, the oral route still represents the preferred way of administration, owing to its several advantages and high patient compliance compared to many other routes. Tablet is the most popular among all dosage forms existing today because of its convenience of self administration.¹

Advances in novel drug delivery (NDDS) aim to enhance safety and efficacy of drug molecule by formulating a convenient dosage form for ease of administration and to achieve better patient compliance. Dysphagia is the common problem encountered in all age groups in concern to conventional solid dosage forms like tablets and capsules. Especially, many elderly persons face difficulties in administering conventional oral dosage forms because of hand tremors and dysphagia. Swallowing problem is common in children because of their underdeveloped muscular and nervous systems. In some cases such as motion

sickness, sudden episodes of allergic attack or coughing, and an unavailability of water, swallowing conventional tablets may be difficult. To fulfill these medical needs, formulators have devoted considerable efforts for developing a novel type of dosage form for oral administration known as orodispersible tablet (ODT).² This is an innovative technology where the dosage form containing active pharmaceutical ingredients disintegrates rapidly in saliva usually in a matter of seconds without the need for water, providing optimal convenience to the patient and are thus quite suitable for children, elderly and mentally disabled patients.³

Orodispersible tablets are also called as orally disintegrating tablets, quick disintegrating tablets, mouth dissolving tablets, fast disintegrating tablets, fast dissolving tablets, rapid dissolving tablets, porous tablets, and rapimelts.² Recently, European pharmacopoeia has used the term orodispersible tablets. This may be defined as uncoated tablets intended to be placed in the mouth where they disperse readily within 3 min before swallowing. United States Pharmacopoeia has also approved these dosage forms as orodispersible tablets. Thus, orodispersible tablets are solid unit dosage forms like conventional tablets, but are composed of super disintegrants, which help them to dissolve the tablets within a minute in the mouth in the presence of saliva without any difficulty of swallowing⁴. It offers several advantages with respect to its stability, administration without water, accurate

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dosing, easy manufacturing, small packaging size, and handling. Its ease of administration in the population especially for pediatric, geriatric, or any mentally retarded persons makes it a very popular dosage form. Due to the presence of super disintegrants, it gets dissolved quickly, resulting in rapid absorption of drug which in turn provides rapid onset of action. Since the absorption is taking place directly from the mouth, so, bioavailability of the drug increases. Drugs present in orodispersible tablets are also not suffering from first pass metabolism. This type of drug delivery is becoming popular day by day due to numerous advantages.⁵

Advantage of ODTs

It can be easily administered to pediatric, elderly and mentally disabled patients, accurate dosing as compared to liquids, Dissolution and absorption of drug is fast, offering rapid onset of action, bioavailability of drugs is increased as some drugs are absorbed from mouth, pharynx and esophagus through saliva, advantageous over liquid medication in terms of administration as well as transportation, cost effective, high drug loading is possible, have acceptable taste and pleasant mouth feeling, no residue in the mouth after oral administration, free of risk of suffocation due to physical obstruction when swallowed, thus offering improved safety, avoid first pass metabolism.³

Disadvantages of Fast Dissolving Tablets

Hygroscopic in nature, low amount of drug can be incorporated in each dose, some time it possesses mouth feeling, highly fragile sometimes, ODT requires special packaging for properly stabilization & safety of stable product, eating and drinking may become restricted.⁶

Need to Formulate ODTs

The need for non - invasive drug delivery systems continues due to patient's poor acceptance and compliance with existing delivery regimes, limited market size for drug companies and drug uses coupled with high cost of disease management. ODT is one such dosage form which is useful for Geriatric patients mainly suffering from conditions like hand tremors and dysphagia.⁷

Challenges in Formulating ODTs

Mechanical strength and disintegration time

ODTs are formulated to obtain disintegration time usually less than a minute. While doing so, maintaining a good mechanical strength is a prime challenge. Many ODTs are fragile and there are many chances that such fragile tablet will break during packing, transport or handling by the patients.⁸

Taste masking

Many drugs are bitter in taste. A tablet of bitter drug dissolving/ disintegration in mouth 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.⁴

Mouth feel

ODTs should not disintegrate into larger particles in the oral cavity. The particles generated after disintegration of the ODTs should be as small as possible. ODTs should leave minimal or no residue in mouth after oral administration. Moreover addition of flavours and cooling agents like menthol improve the mouth feel.⁹

Sensitivity to environmental conditions

ODTs generally should exhibit low sensitivity to environment conditions such as humidity and temperature as most of the materials used in ODTs are meant to dissolve in minimum quantity of water.⁶

Cost

The technology used for ODTs should be acceptable in terms of cost of the final product.¹⁰

Evaluation of ODTs

Tablet thickness

Tablet thickness is an important characteristic in reproducing appearance and also in counting by using filling equipment. Some filling equipment utilizes the uniform thickness of the tablets as a counting mechanism. Thickness was recorded using vernier caliper.¹¹

Weight variation

A number of 20 tablets were selected randomly from the lot and weighed individually to check for weight variation.¹

Friability

Friability Attempts for decreasing the disintegration time increase the friability of ODTs than the conventional tablets. Dosage forms like Zydis are very fragile. Friability is a measure of mechanical strength of the tablet. If a tablet has more friability it may not remain intact during packaging, transport or handling. Roche friabilator is used to determine the friability by following procedure. Pre weighed tablets are placed in the friabilator. Friabilator consist of a plastic chamber that revolves at 25 rpm, dropping those tablets at a distance of 6 inches with each revolution. The tablets are rotated in the friabilator for at least 4 minutes.⁴ At the end of test tablets are dusted and reweighed; the loss in the weight of tablet is the measure of friability and is expressed in percentage as:

% Friability = $1 - (\text{loss in weight} / \text{Initial weight}) \times 100$

Hardness (crushing strength)

Tablet hardness is measured with hardness testers like Monsanto. A tablet is placed in the hardness tester and load required to crush the tablet is measured. The hardness of ODTs is generally kept lower than conventional tablets as increased hardness delays the disintegration of the tablet. The force is measured in kg and the hardness of about 3-5 kg/cm² is considered to be satisfactory for uncoated tablets⁴.

Water absorption ratio

A small piece of tissue paper folded twice is placed in a small petridish containing 6 ml of water. Put a tablet on the paper and the time required for complete wetting is measured. The wetted tablet is then reweighed. Water absorption ratio, R is determined by using following formula:

$$R = 100 \times \frac{W_a - W_b}{W_b}$$

Where, W_b is the weight of tablet before water absorption and W_a is the weight of tablet after water absorption.

Uniformity of dispersion

Keep the Two tablets in 100ml water and stir gently for 2 minutes. The dispersion is passed through 22 meshes. The tablets will consider passing the test if no residue remained on the screen.⁸

Wetting time

Five circular tissue papers of 10 cm diameter are placed in a petridish with a 10 cm diameter. Ten millimeters of water containing Eosin, a water-soluble dye, is added to petridish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as a wetting time.¹

Disintegration time

According to the European pharmacopoeia the fast disintegrating or ODTs should disintegrate within 3 minutes without leaving any residue on the screen. However it is difficult to assess the disintegration rate even in small amounts of water. Further the conventional test employs a volume of 900 ml of distilled water compared to the volume of saliva in humans, which is limited to a few ml. Thus the disintegration rate obtained from conventional test does not appear to reflect the actual disintegration rate in human mouth. To overcome these problems, several new methods have been proposed.⁹ One of these methods uses a Charge Couple Device (CCD) camera or texture analyzer to evaluate the disintegration time of tablets. In another method, a modified DT apparatus is used. Here a wire basket of 3cm height

and 2 cm diameter and mesh size of #10 is placed above a beaker containing 900 ml of simulated saliva. The basket is so positioned in the liquid that it contains only 6 ml of the liquid. The assembly is supported with a heater to maintain temperature at 37°C and a magnetic stirrer. DT is noted at 25 rpm. One of the simplest methods is to take 6ml of simulated saliva in a measuring cylinder and place the tablet in it. The liquid is neither shaken nor stirred and DT is noted.⁸

In vivo disintegration time

In vivo disintegration time is determined using a panel of healthy human volunteers. The DT noted by the volunteers by placing the tablet in mouth.¹²

Taste/ Mouth sensation

Mouth-feel is critical, and patients should receive a product that feels pleasant. One tablet from each batch is tested for the sensation by placing the tablet on the tongue. The healthy human volunteers are used for evaluation of mouth feel. Taste evaluation is done by a panel of 5 members using time intensity method. Sample equivalent to 40 mg i.e. dose of drug is put in mouth for 10 seconds and record taste instantly and then after 10 seconds, 1, 2, 4 and 6 minutes. Volunteer's opinion for the taste is rated by giving different score values i.e. 0 = good, 1 = tasteless, 2 = slightly bitter, 3 = bitter, 4 = awful.¹³

Dissolution test

The dissolution method for oral disintegrating tablets is the same as that of conventional tablets. USP 2 paddle apparatus is most suitable and common choice for dissolution test of oral disintegrating tablets, where the paddle speed is 50 rpm is used. The USP 1 (basket) apparatus may have certain application for such tablets but is used less frequently due to specific physical properties of tablets.

Future Prospects

These dosage forms may be suitable for the oral delivery of drugs such as protein and peptide-based therapeutics that has limited bioavailability when administered by conventional tablets. These products usually degrade rapidly in the stomach. Should next generation drugs are predominantly protein or peptide based, tablets may no longer be the dominant format for dosing such moieties. Injections generally are not favored for use by patients unless facilitated by sophisticated auto-injectors¹³. Inhalation is one good alternative system to deliver these drugs, but the increased research into biopharmaceuticals so far has generated predominantly chemical entities with low molecular weights.

The developments of enhanced oral protein delivery technology by ODTs which may release

these drugs in the oral cavity are very promising for the delivery of high molecular weight protein and peptide.¹⁴

CONCLUSION

Orodispersible tablets have potential advantages over conventional solid dosage form. This drug delivery is one of the great inventions of all the novel drug-delivery systems. They have better patient acceptance and compliance and may offer improved biopharmaceutical properties, improved efficacy, rapid onset of action 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.

Conflicts of interests: Nil

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