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A REVIEW ON ORODISPERSIBLE TABLET

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ABSTRACT: 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 oral formulation. They are also solid unit dosage forms, which disintegrate in the mouth within a minute in the presence of saliva due to super disintegrants in the formulation. Thus this type of drug delivery helps a proper peroral 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 of preparation is the compression method. Other special methods are molding, melt granulation, phase-transition process, sublimation, freeze-drying, spray-drying, and effervescent method. 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.

Keywords: Disintegration, manufacturing processes, orodispersible tablets, superdisintegrants

1. INTRODUCTION

Oro-Dispersible Tablet: Oral delivery is current standard in the pharmaceutical industry wherever it is regarded as the safest, most suitable and most economical method of drug delivery. The oral cavity is an attractive site for the administration of drugs because of ease of administration. Oro-dispersible drug delivery system are Novel Drug Delivery techniques that make the tablets disintegrate in the mouth without chewing and water, and immediate

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release and enhanced bioavailability, with better patient compliance. Recently, the European Pharmacopeia adopted the term orodispersible tablet for a tablet that disperses or disintegrates within a minute or second in the mouth before swallowing. United States Food and Drug Administration (FDA) defined Oro-dispersible tablet as "a solid dosage form containing medicinal substances or active ingredient which disintegrate or dissolve rapidly within seconds when placed upon the tongue.[1]

Oro-dispersible tablets have a quick dissolution and rapid absorption which provide rapid onset of action. Moreover, drug candidates that undergo pregastric absorption when formulated as ODTs may oral bioavailability of drug is enhanced by avoiding the hepatic first pass metabolism. It provides good stability, accurate dosing, easy of manufacturing Oro-dispersible tablets are made by a direct compression method using super Disintegrate as an important component.[2]

Ideal properties of orodispersible tablets:

• Not require water to swallow and should dissolve or disintegrate in the mouth within a few seconds

• High drug loading

• Be compatible with taste masking and other excipients

• Have a pleasing mouth feel

• Leave minimal or no residue in the mouth after oral administration

• Exhibit low sensitivity towards environmental conditions such as humidity and temperature

Advantages of orodispersible tablets:

• Administration to patients who cannot swallow, like the elderly, stroke victims and bedridden patients; patients who should not swallow, like renal failure patients; and patients who refuse to swallow, such as pediatrics, geriatric and psychiatric patients

•Patient's compliance for disabled bedridden patients and for traveling and busy people, who do not have ready access to water

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Good mouth feel property helps to change the basic view of medication as "bitter pill," particularly for pediatric patients due to improved taste of bitter drugs

• The 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

• Pregastric absorption can result in improved bioavailability, reduceddose and improved clinical performance by reducing side effects

Disadvantage of orodispersible tablets :

•Orodispersible is hygroscopic in nature so must be keep in dry place

• Sometime it possesses mouth feeling

• ODT requires special packaging for properly stabilization and safety of stable product

• Dose uniformity is a technical challenge

1.1 Various methods of preparation of orodispersible tablets : There are several methods for the preparation of orodispersible tablets but the prepared products vary in their properties depending on the method of preparation. The properties in which they vary are mechanical strength of the tablets, swallow ability, bioavailability, drug dissolution in saliva, stability, and to some extent taste. Various process of manufacturing of orodispersible tablets are molding, compaction, spray-drying, freeze-drying, and some special methods are melt granulation, phase transition, and sublimation.[3]

Molding methods : Tablets formed by molding process are highly porous in structure, resulting in high rate of disintegration and dissolution. This process includes moistening, dissolving, or dispersing the drugs with a solvent then molding the moist mixture into tablets by applying lower pressure in compression molding, but always lower than the conventional tablet compression. The powder mixture may be sieved prior to the preparation in order to increase the dissolution.

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Molded tablets have low mechanical strength, which results in erosion and breakage during handling.[4]

Compaction methods : Conventional methods for the preparation of tablets such as dry granulation, wet granulation, and direct compression are also exist for the preparation of orodispersible tablets. Some important super disintegrants, which are used during preparation of orodispersible tablets, are crosspovidone, crosscarmellose sodium, sodium alginate, acrylic acid derivatives. Baclofen orodispersible tablets were prepared by direct compression method using crosspovidone and sodium starch glycolate as super disintegrants.Even orodispersible tablets of Carbamazepine were prepared by this method having microcrystalline cellulose and crosspovidone (2%-10%).In all the cases it has been found that preparation by compression method along with addition of super disintegrants in correct concentration obey all the properties of orodispersible tablets.[5]

Spray-drying method : Here, orodispersible tablets are made up of hydrolyzed or unhydrolyzed gelatin as supporting agent for matrix, mannitol as bulk agent, and sodium starch glycolate or croscarmellose sodium as disintegrating agent. Sometimes in order to improve the disintegration and dissolution, citric acid and sodium bicarbonate are used. Finally, the formulation is spray-dried in a spray drier. Orodispersible tablets prepared through this method are disintegrated in less than 20s.[6]

Freeze-drying method : This is a very popular process for the preparation of orodispersible tablets. Tablets prepared by this process have low mechanical strength, poor stability at higher temperature and humidity, but glossy amorphous structure resulting in highly porous, lightweight product. There are various patents on this particular technology.[7]

1.2 SOME SPECIAL METHODS OF PREPARATION :

Melt granulation : It is a unique method for the preparation of orodispersible tablets by incorporating superpolystate.Superpolystates are hydrophilic waxy binders with a melting point 33-37°C and Hydrophilic –Lipophilic Balance value is 9. They play a dual role as a binder that

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increases the physical resistance of the tablets and also as a disintegrants, which help the tablet to melt in the mouth, and solubilize rapidly leaving no residue in the mouth. Superpolystates were introduced in the formulation of orodispersible tablets by melt-granulation method. Here, granules are formed by the molten form of this material. Crystallized paracetamol was used as a model drug along with mannitol and crosscarmellose sodium.[8]

Phase transition process : Kuno *et al*. investigated this process by compressing powder containing two sugars alcohols. One with high and another with low melting point, and they are heated at a temperature between their melting point and then compressed finally in order to get the tablets. Example of sugar alcohols are erythriol (m.p. 122°C), xylitol (m.p. 93-95°C), trehalose (97°C), and mannitol (166°C). After heating, tablet hardness was increased due to an increase in interparticle bonds or the bonding surface area in tablets induced by phase transition of lower melting point sugar alcohol.[9]

Sublimation : In this process, subliming material 'camphor' is used. It was sublimed in vacuum at 80°C for 30 min after preparation of tablets. Here, also tablets prepared are porous in nature. In conventional types, sometimes rapid disintegration does not occur. Therefore, in order to improve porosity, volatile substance camphor is added in the preparation, which gets sublimed from the formed tablet.[10]

Effervescent method : Orodispersible tablets are also prepared by effervescent method by mixing sodium bicarbonate and tartaric acid of concentration 12% (w/w) along with super disintegrants like pregelatinized starch, sodium starch glycolate, crospovidone, and croscarmellose. First, sodium bicarbonate and tartaric acid were preheated at a temperature of 80°C to remove absorbed/residual moisture and thoroughly mixed in the motor. Finally, the blends are compressed in the punch.[11]

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1.3 Approaches for taste masking : There are various drugs which do not taste good. Since orodispersible tablets dissolve in mouth, so proper taste-masking is very much essential, especially in the case of bitter taste drugs, e.g., metronidazole. Various approaches have been explored in order to mask the bitter or any other bad taste of the drugs which include addition of sweeteners and flavors or encapsulating the unpleasant drugs into the microparticles or by the adjustment of pH. In masking the bitter taste of metronidazole, Mohire *et al*, used three approaches as addition of sweetener like sodium saccharin, formation of complex and finally by numbness of the tongue. A complex was prepared by triturating drug and *Glycerrhiza glabra* extract in a ratio of 1:3 in the presence of a solvent, and numbness of tongue is carried out by adding eugenol to the drug and disintegrating mixture. They found good results in the case of the complex formation of drug with *G. glabra*. However, the most popular and general approach is the addition of sweeteners and flavors. Highly water soluble and quickly dissolvable sugar-based excipients are mannitol, aspartame, and citric acid. Flavors are mint, orange, peppermint, and strawberry. Encapsulation or coating of drugs is another method where the bad taste can be masked.[12]

2. EVALUATION OF ORODISPERSIBLE TABLETS :

Hardness/crushing strength : The hardness of the tablet is measured by using conventional hardness testers like Monsanto hardness tester. The limit is toward the lower range in order to help early disintegration in mouth.[13]

Friability : It is a difficult job to maintain the percentage of friability within the limit, since all the methods of preparation of orodispersible tablets have a tendency to increase the percentage of friability. In all aspect, the range is within limit of 0.1%-0.9%. Roche friabilator is used in conventional form in order to measure friability of the tablets.[14]

Wetting time : Wetting time is the indication of the inner structure of the tablets and to the hydrophilicity of the excipients. Thus, wetting time of a dosage form is related with the contact angle. The lower the wetting time the quicker is the disintegration of the tablets. The wetting

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time can be measured by using five circular tissue papers of 10 cm in diameter, which are placed in a petridish of 10 cm diameter Ten millilitres of water-soluble dye like eosin solution is added to the 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 the wetting time. For measuring water-absorption ratio, the weight of the tablet before keeping in the petridish is noted (W_b).The wetted tablet from the petridish is taken and reweighted (W_a). The water-absorption ratio, R can be determined according to the following equation:[15]

$R = 100\ (W_a - W_b)/W_b$.

Moisture-uptake studies : It is an important study in the case of orodispersible tablets. This study is carried out in order to assess the stability of the tablets. Ten tablets were kept in the desiccators over calcium chloride at 37°C for 24 h. The tablets were then weighted and exposed to 75% relative humidity, at room temperature for 2 weeks.Required humidity was achieved by keeping saturated sodium chloride solution at the bottom of the desiccators for 3 days. One tablet as control (without super disintegrant) was kept to assess the moisture uptake due to other excipients. Tablets are weighed and the percentage increase in weight is recorded.[16]

Disintegration test : The *in-vitro* disintegration time was determined by disintegration test apparatus. The time for disintegration of orodispersible tablets is generally <1 min and actual disintegration time that patient can experience ranges from 5 to 30 s. A tablet is placed in each of the six tubes of the apparatus, and one disc is added to each tube. The standard procedure of performing disintegration test for these dosage forms has several limitations. It is expected that disintegration test for orodispersible tablets should mimic disintegration in mouth within salivary contents. Sunada *et al*. performed disintegration test by using modified United States Pharmacopoeia Apparatus II by taking 900 ml of medium maintaining 37°C with r/min 100. It was carried out by taking a 1 l cylindrical vessel. Orodispersible tablets were placed in basket sinker in the middle of the vessel with a distance of 6-8.5 cm. Even Narazaki *et al*. carried out the disintegration test with rotary-shaft method. The apparatus consisted of stainless steel wire

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gauze on which orodispersible tablets were placed and slightly immersed in medium. Here, the rotary shaft is used to provide rotation and mechanical stress.[17]

Dissolution test : It is an important test as the drug-release profile can be obtained by performing this test. Both the USP dissolution test apparatus can be used. Dissolution of orodispersible tablets is very fast. Therefore, USP 2 Paddle-type apparatus at 50-100 r/min is used for dissolution testing. Swammy *et al*. carried out *in vitro* dissolution study of pheniramine maleate orodispersible tablets in type II apparatus with r/min 550 using 900 ml phosphate buffer of pH 6.8 at 37 ± 0.5°C as a dissolution medium.USP type I basket apparatus have certain application in the case of orodispersible tablets, but tablet fragments or disintegrated tablet masses may become trapped on the inside top of the basket at the spindle. An erroneous-dissolution profile is obtained, where little or no effective stirring occurs. Thus, type II is more preferred due to reproducible-dissolution profile.[18]

3. Future prospective for orodispersible tablets :

Future challenges for many ODT manufacturers include reducing costs by finding ways to manufacture with conventional equipment, using versatile packaging, improving mechanical strength and taste-masking capabilities. ODTs may be suitable for the oral delivery of drugs such as protein and peptide-based therapeutics that have limited bioavailability when administered by conventional tablets because these products usually degrade rapidly in the stomach. Furthermore, there is a scopeto develop controlled release ODTs prepared using different drug carriers

4. CONCLUSIONS: 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 improved patient compliance, convenience, bioavailability, and rapid onset of action. However, common people are not much aware of this delivery system. Therefore, pharmacists are responsible to spread the knowledge regarding this system. It is the duty of the pharmacist to counsel the patients regarding its use, advantages, storage and maintenance. This dosage form should be handled carefully since they do not have sufficient mechanical strength.

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Patients who suffer from dryness of mouth should not be prescribed orodispersible tablets, since minimum volume of saliva is necessary for it to disintegrate/dissolution. This dosage form is very much suitable for children having no primary teeth and for geriatric patients who have lost their teeth permanently. Thus, in near future, it is expected that this delivery system will get much importance as that of conventional delivery.

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