

Orodispersible tablets: A new trend in drug delivery

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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.

Key words: Disintegration, manufacturing processes, orodispersible tablets, superdisintegrants

INTRODUCTION

Drug delivery through oral route is the most common and preferred route of drug administration both for solid and liquid dosage forms. However, solid dosage forms are popular because of the ease of administration, accurate dosage, self-medication, pain avoidance, and most importantly the patient compliance.^[1] Tablets and capsules are the most popular solid dosage forms. However, many people face difficulty in swallowing tablets and hard gelatin capsules. This difficulty in swallowing is called dysphasia.^[2] It has been found that this problem has been encountered in all groups of patient, but especially with pediatric and geriatric populations. Thus, these conventional dosage forms result in high incidence of noncompliance and ineffective therapy with respect to swallowing specially in the case of pediatric, geriatric, or any mentally retarded persons. Orodispersible tablets are also called as orally disintegrating tablets, mouth-dissolving tablets, rapid-dissolving tablets, fast-disintegrating tablets, fast-dissolving tablets. 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.^[3] 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 swallowing. It offers several advantages with respect to its stability, administration without water, accurate dosing, easy manufacturing, small packaging size, and handling.^[4-7] 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.^[8] Since the absorption is taking place directly from the mouth, so, bioavailability of the drug increases.^[9] 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 its numerous advantages.

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, swallowability, bioavailability, drug dissolution in saliva, stability, and to some extent taste.^[4] 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.

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.^[10] Molded tablets have low mechanical strength, which results in erosion and breakage during handling.

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.^[11,12] Baclofen orodispersible tablets were prepared by direct compression method using crosspovidone and sodium starch glycolate as super disintegrants.^[13] Even orodispersible tablets of Carbamazepine were prepared by this method having microcrystalline cellulose and crosspovidone (2%-10%).^[14] 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.^[13,14]

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.^[15,16]

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.^[5]

SOME SPECIAL METHODS OF PREPARATION

Melt granulation

It is a unique method for the preparation of orodispersible tablets by incorporating superpolystate.^[17] 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 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 croscarmellose sodium.

Phase transition process

Kuno *et al.*^[18] 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.

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.^[19]

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, croscopovidone, 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.^[20,21]

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.^[22] 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.^[4] In masking the bitter taste of metronidazole, Mohire *et al.*,^[22] 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 *Glycyrrhiza 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*.^[2] 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.^[22] Encapsulation or coating of drugs is another method where the bad taste can be masked.^[23,24]

EVALUATION OF ORODISPERSIBLE TABLETS

Hardness/crushing strength

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

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.^[13]

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.^[4,13] The wetting 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.^[25] 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:

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

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.^[4] 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.

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.^[4] A tablet is placed in each of the six tubes of the apparatus, and one disc is added to each tube.^[13] 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.^[26] Even Narazaki *et al.* carried out the disintegration test with rotary-shaft method. The apparatus consisted of stainless steel wire gauze on which orodispersible tablets were placed and slightly immersed in medium. Here, the rotary shaft is used to provide rotation and mechanical stress.^[27]

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. Swamy *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 $37 \pm 0.5^\circ\text{C}$ as a dissolution medium.^[20,27] 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.

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. 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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