

Review Article



Orodispersible Tablets: A New Trend in Drug Delivery

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ABSTRACT

The oral route is the most popular and favoured method of drug administration. Orodispersible tablets are becoming more common among novel oral drug delivery systems because they increase patient compliance and provide some additional benefits over other oral formulations. They are also strong unit dosage types that, in the presence of saliva, disintegrate in the mouth within a minute due to super disintegrants in the formulation. As a result, this method of drug delivery aids in proper peroral administration of paediatric and geriatric patients who have difficulty swallowing. Various scientists have used various methods to create orodispersible tablets. The compression process is, however, the most popular method of preparation. Molding, melt granulation, phase-transition technique, sublimation, freeze-drying, spray-drying, and the effervescent method are some of the other unique processes. The flavour of these tablets is significant since they dissolve immediately in the mouth. To mask the drug's acidic flavour, a variety of techniques have been used. In this area, a number of scientists have looked at a variety of drugs. They are tested in the fields of stiffness, friability, wetting time, moisture absorption, disintegration test, and dissolution test, much as any other solid dosage types.

Keywords: Disintegration, manufacturing processes, orodispersible tablets, superdisintegrants.

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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 compliance¹.

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 dysphasia². Thus, these conventional dosage forms result in high incidence of noncompliance and ineffective therapy with respect to swallowing. Orodispersible tablets are novel drug delivery systems capable of overcoming the disadvantages of conventional tablets³.

Orodispersible tablets may be defined as uncoated tablets intended to be placed in the mouth where they disperse readily within 3 min before swallowing⁴. 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 swallowing⁵.

Orodispersible tablets are also called as orally disintegrating tablets, mouth-dissolving tablets, rapid dissolving tablets, fast-disintegrating tablets, fast-dissolving tablets⁴.

Advantages of Orodispersible Tablets:

It offers several advantages with respect to:

- ✓ Its stability
- ✓ Administration without water
- ✓ Accurate dosing
- ✓ Easy manufacturing
- ✓ Small packaging size and handling⁶⁻⁹.
- ✓ Its ease of administration in the population especially for pediatric, geriatric, or any mentally retarded persons.
- ✓ Due to the presence of super disintegrants, it gets dissolved quickly, resulting in rapid absorption of drug which in turn provides rapid onset of action¹⁰
- ✓ 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 metabolism¹¹.
- ✓ Reduce risk of suffocation¹².



- ✓ Medication as “bitter pill” has changed by excellent mouth feel property produced by use of flavors and sweeteners in ODTs¹¹.

Excipients Used in the Formulation of Orodispersible Tablets¹³:

- Diluents: For Example: Lactose, Spray dried lactose, MCC, Mannitol, Sorbitol, Dibasic calcium phosphate
- Binders: For Example: Gelatin, glucose, lactose, MC, EC, HPMC, starch, Povidone, Sodium alginate, CMC, Acacia.
- Superdisintegrants: For Example: Croscarmellose sodium, Crospovidone, SSG, starch.
- Lubricants: For Example: Insoluble- Steric acid, Magnesium stearate, Talc, Paraffin, Soluble- SLS, Sodium benzoate, PEG.
- Glidants: For Example: Colloidal Silicon dioxide, Corn starch, Talc etc.
- Anti adherents: For Example: talc
- Sweetners: For Example: Sucrose, Sucralose, Saccharin, Aspartame, etc.
- Flavours: For Example: Peppermint, Vanilla, Orange, Banana, Cinnamon, Mango
- Colours: For Example: Sunset yellow

VARIOUS TECHNIQUES USED IN PREPARATION OF ORODISPERSIBLE TABLETS

Various technologies used in the manufacture of orodispersible tablets consist are:

- Direct compression
- Sublimation
- Freeze-drying or lyophilization
- Tablet Molding
- Spray drying
- Cotton candy process
- Mass extrusion
- Phase transition
- Nanonization
- Fast dissolving films

Direct compression

In this method, the excipients or the formulation ingredients are basically mixed and then compressed into tablets¹⁴.

This technique is mainly preferred because of the availability of improved excipients especially superdisintegrants and sugar based excipients¹⁵.

Sublimation

In this technique, highly volatile substances like camphor, urea and urethane are added to the blend before compression. When highly volatile substances are compressed, they can be easily removed by sublimation. This improves the dissolution rate as the end product is a porous structure due to the evaporation of the volatile substances^{16, 17}.

Freeze-drying or lyophilization

It is a process in which solvent is removed from a frozen drug solution or a suspension containing structure forming excipients. Freeze drying process normally consists of three steps: a) Material is frozen to bring it below the eutectic point, b) Primary drying to reduce the moisture around 4% w/w of dry product and c) Secondary drying to reduce the bound moisture up to required final volume. The resulting tablets are usually very light and have highly porous structures that allow rapid dissolution or disintegration. This process may result in a glassy amorphous structure of excipients as well as the drug substance leading to the enhanced dissolution rate^{16, 18-20}.

Tablet Molding

Molding process includes moistening, dissolving or dispersing the drug with a solvent then molding the moist mixture into tablets (compression molding with lower pressure than conventional tablet compression), evaporating the solvent from drug solution, or suspension at ambient pressure, respectively²¹.

The molded tablets formed by compression molding are air-dried. As the compression force employed is lower than conventional tablets, the molded tablet results in highly porous structure, which increases the disintegration and dissolution rate of the product. However, to further improve dissolution rate of the product powder mixture should be sieved through very fine screen. As molding process is employed usually with soluble ingredients (saccharides), which offers improved mouth feel and disintegration of tablets. However, molded tablets have low mechanical strength, which results in erosion and breakage during handling²².

Spray drying

Spray drying is one of the oldest forms of drying and one of the few technologies available for the conversion of a liquid, slurry, or low-viscosity paste to a dry solid (free-flowing powder). The spray-drying process is carried out in three fundamental stages. The first stage is atomization of a liquid feed into fine droplets. In the second stage, spray droplets mix with a heated gas stream and the dried particles are produced by the evaporation of the liquid from the droplets. The final stage involves the separation of the dried powder from the gas stream and collection of

these powders in a chamber. The components included supporting agents like non hydrolyzed and hydrolyzed gelatin, a bulking agent like mannitol and a volatilizing agent^{16, 23}.

Cotton candy process

This process is so named as it utilizes an inimitable spinning mechanism to produce floss like crystalline structure, which mimics cotton candy. In this process matrix of polysaccharides are formed by simultaneous action of flash melting and spinning. This candy floss matrix is then milled and blended with active ingredients and excipients after recrystallization and subsequently compressed to orodispersible tablet²⁴.

Mass Extrusion

In this technique, a blend of active drug and other ingredients is softened using solvent mixture of water soluble polyethylene glycol, using methanol and then softened mass is extruded through the extruder or syringe to get a cylinder of product, which is finally cut into even segments with the help of heated blades to get tablets²⁵.

Phase transition

In this method mixture of the low and high melting point sugar alcohols, as well as a phase transition in the manufacturing method, is main for the creating ODTs without any difference in the apparatus. The mixture is heating at about 93 °C for 15 min. After heating, the medium pore size of the tablets was increased and tablet hardness was also improved. The increase of the tablet hardness with heating and the storage did not depend on the crystal state of the lower melting point of the sugar alcohol²⁶.

Nanonization

The ionization process contains a reduction in the particle size of the drug to nano-size by milling technique. The drugs are stabilized against agglomeration surface absorption on selected stabilizers. This process is suitable for poorly water-soluble drugs²⁷.

Fast dissolving films

It contains a nonaqueous solution having water-soluble film-forming polymers (pullulan, carboxymethyl cellulose, hydroxypropyl methylcellulose, hydroxyethylcellulose, hydroxypropyl cellulose polyvinyl pyrrolidone, polyvinyl alcohol or sodium alginate.), a drug and another taste-masking agent which are used to develop a film as the solvent evaporates. In the case of bitter-tasting drugs resin adsorbate or coated microparticles of a drug can be used in a film. Characteristics: These are thin films of 2×2 inches dimensions; dissolve fast within 5 seconds²⁴.

PREFORMULATION STUDIES²⁸⁻³²

Angle of Repose

Angle of repose was determined by using funnel method. The accurately weighed blend was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of blend. The drug (as solid dispersion)-excipients blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation:

$$\tan \theta = h/r$$

Where, h= height of the pile of the blend r= radius of the pile of the blend.

Bulk Density (Db)

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weighed powder (passed through standard sieve # 20) into a measuring cylinder and initial weight was noted. This initial volume is called the bulk volume. From this the bulk density is calculated according to the formula mentioned below. It is expressed in g/ml and is given by

$$D_b = \frac{\text{Mass of the powder (M)}}{\text{Bulk volume of the powder (V}_b\text{)}}$$

Tapped Density (Dt)

It is the ratio of total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder for 750 times and the tapped volume was noted if the difference between these two volumes is less than 2%. If it is more than 2%, tapping is continued for 1250 times and tapped volume was noted. Tapping was continued until the difference between successive volumes is less than 2 % (in a bulk density apparatus).

$$D_t = \frac{\text{Mass of the powder (M)}}{\text{Tapped volume of the powder (V}_d\text{)}}$$

Carr's Index (Or) % Compressibility

Compressibility index (CI) was determined by measuring the initial volume (V₀) and final volume (V) after hundred tapings of a sample in a measuring cylinder. CI was calculated using equation

$$\text{Compressibility Index (CI)} = \frac{V_0 - V}{V} \times 100$$

EVALUATION OF ORODISPERSIBLE TABLETS³³⁻³⁶

General Appearance

The general appearance of tablets includes size, shape, colour, odour, taste, surface texture.

Size, Shape, Thickness and Diameter

Size and shape of the tablet can be dimensionally described, monitored and controlled. Ten tablets should be taken and their thickness was measured by Vernier calipers.

Uniformity of Weight

Randomly 20 tablets should be selected and to be weighed individually and together in a single pan balance. The average weight should be noted with the standard deviation. United States Pharmacopoeia (USP- 29) limit for weight variation in case of tablets is as follows: for weight 130mg or less, $\pm 10\%$, for 130 mg through 324 mg, $\pm 7.5\%$ and more than 324 mg, $\pm 5\%$ [37].

$$\% \text{ Weight Variation} = \frac{\text{Individual weight} - \text{Average weight}}{\text{Average weight}} \times 100$$

Friability

Friability of the tablet determined using Roche friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at a height of 6 inches in each revolution. Pre-weighed sample of tablets were placed in the friabilator and were subjected to the 100 revolutions³⁸. Tablets were dusted using a soft muslin cloth and reweighed. The friability (F) is given by the formula

$$F = \frac{\text{Initial weight} - \text{Final weight}}{\text{Final weight}}$$

Compressed tablets should not lose more than 1% of their initial weight.

Hardness of Tablet

Hardness of tablet is defined as the force applied across the diameter of the tablet in the order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. The hardness of prepared tablets can be determined for 10 tablets of each batch by using Monsanto or Pfizer tablet hardness tester.

Wetting Time

Five circular tissue papers of 10 cm diameter should be placed in a petri dish with a 10 cm diameter. Add ten ml of water containing water soluble dye (eosin) is to be added to the Petri dish. A tablet should be carefully placed on the surface of tissue paper. The time required for water to reach the upper surface of the tablet is to be noted as the wetting time. Three trials for each batch and standard deviation should be determined³⁹.

$$di/dt = rY\cos\theta/(4\eta l)$$

Where l = length of penetration

r = capillary radii

γ = surface tension

η = liquid viscosity

t = time

θ = contact angle

The pore sizes become smaller and wetting time increases with an increase in compression force or a decrease in porosity. A linear relationship exists between wetting time and disintegration time. Thus wetting is the important step in disintegration process.

Water Absorption Ratio

The weight of the tablet should be noted before keeping in the petri dish (W_b). The fully wetted tablet should be taken from the petri dish and reweighed (W_a). The water absorption ratio R can be determined according to the following formula

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

Disintegration Time

Disintegration time is very important for FDTs which is desired to be less than 60 seconds. This rapid disintegration assists swallowing of the tablet and also plays a role in drug absorption in buccal cavity, thus promoting bioavailability. In vitro disintegration time can be determined using disintegration test apparatus without disks. The test should be carried on six tablets using distilled water at $37^\circ \pm 2^\circ$ as disintegration media. Time is noted in seconds for complete disintegration of the tablet with no palpable mass remaining in the apparatus. The test should be carried in triplicate⁴⁰.

In vitro Dissolution studies

The development of dissolution methods for FDTs commensurate with 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 investigation for a bioequivalent FDT. Other media such as 0.1N HCl and buffers (pH - 4.5 and 6.8) should be evaluated for FDT much in the same way as conventional tablets.

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