REVIEW ARTICLE

Orodispersible Tablets: A Review on Recent Trends in Drug Delivery

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ABSTRACT

The creation of dosage forms that are easy to manufacture and administer, with rapid release and enhanced bioavailability, was a recent achievement in new drug delivery systems. To get the required result, the drugs should be delivered to the site of action at a speed and concentration that maximizes therapeutic benefit while minimizing adverse effects. The most well-known and favored course of medication organization is through the oral route. Several orodispersible medication formulations have recently been brought to the market. The use of oral lyophilizers and orodispersible granules or films has expanded the therapeutic options. The pediatric and geriatric populations may benefit from advantages such as simplicity of administration and convenience of usage. This study focuses on orodispersible tablets, a novel method in drug delivery systems increasingly emphasized in the formulation industry. Due to super disintegrants in the formulation, an orally disintegrating tablet dissolves in the mouth within a minute in the presence of saliva and without the need to drink extra water. This study focused on the technologies that are now accessible and the progress that has been achieved in the field of orodispersible tablet manufacturing. Apart from traditional formulation processes, this review delves into the details of certain novel technologies such as freeze-drying, direct compression, tablet molding, sublimation, and fast dissolving films, as well as their benefits and drawbacks. Several scientists have created orodispersible tablets using patented technologies such as Zydis, wow tab, flash tab, Oroquick, and Orosolv technology. They are subjected to hardness, friability, wetting time, moisture absorption, Disintegration, dissolution tests, and all other solid dosage forms.

Keywords: Bioavailability, Disintegration, Orodispersible tablets, Patented technologies.

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INTRODUCTION

The medicine should be given to its action at a rate and concentration that maximizes therapeutic efficacy while minimizing adverse effects to achieve the desired result. To create an acceptable dosage form, a complete investigation of the physicochemical principles that determine a given drug formulation should be performed.[1]

The oral route of medicine administration is the most common and recommended way of drug delivery for both solid and liquid dosage forms. Orodispersible tablets (ODT) are solid single-unit dosage forms put in the mouth, allowed to disperse/dissolve in saliva, and then taken without water.[2]

Difficulty swallowing (dysphasia) is frequent in all age groups, particularly the elderly, and can also be noticed while taking traditional pills and capsules. This condition is linked to various severe disorders, including stroke, Parkinson's disease, AIDS, and other neurological diseases such as cerebral palsy. ODT is simple to administer because no water is necessary for ingesting the pills, making it appropriate for elderly, pediatric, and travelling patients.[3]

ODTs have been researched for their potential to increase the bioavailability of poorly water-soluble drugs by modifying the drug's dissolving profile, in addition to improving patient compliance. Nonetheless, because of ODT's rapid Disintegration, the active substance comes into contact with taste receptors, and the need for a pleasing flavor becomes a critical part of patient palatability. As a result, masking the taste of unpleasant active chemicals is a significant barrier to overcome to manufacture ODT products properly. In summary, oral administration of bitter active compounds via ODT formulations should result in greater patient compliance, improved palatability, and a favorable therapeutic outcome.[4]

Commercially marketed ODT is manufactured using various methods, such as lyophilization, molding, freeze-drying, sublimation, rapid dissolving films, and direct compression. The lyophilization and molding methods generate ODT that disintegrates in approximately 30 seconds despite having minimal physical resistance and great friability. On the other hand, tablets produced by direct compression are less brittle but disintegrate more slowly.[5]

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Recently, a novel preparation method for orodispersible tablets, such as the WOW tab technology, flash tab technique, Zydus, and orosoly methods, were created as patent technology for ODT. The current research highlights the manufacture, characteristics, and benefits; medicines integrated into ODT; and evaluations of the orally disintegrating tablet. [6]

CHALLENGES

Mechanical Strength and Disintegration Time

ODTs must have a shorter disintegration period in the oral cavity because they are composed of porous or soft-molded matrices or crushed with a low compression force, making the tablets brittle and challenging to handle. Only a few techniques, such as Wowtab and CIMA laboratories, can create sufficiently rigid and robust tablets to be packed in multi-dose bottles. [7]

Taste Masking and Mouth Feel

As most pharmaceuticals are unpleasant to taste, therefore, drug taste masking is essential for patient compliance and acceptability, which is impacted when a bitter drug tablet dissolves in the oral cavity. Covering the taste of bitter-tasting drugs selected for ODT is challenging for formulation researchers. Larger particles should not disintegrate from ODT; instead, tiny particles with a pleasant tongue feel should disintegrate.[8]

Size of Tablet

Their size determines the degree of ease with which tablets are administered. It has been stated that the most superficial size of tablet to swallow is 7–8 mm, whereas the most accessible size to handle is one bigger than 8 mm. As a result, producing a pill size that is easy to take and maintain is difficult.[9]

Amount of Drug

The amount of drugs that can be integrated into each unit dosage limits the applicability of ODT technology. The mass of the tablets should not exceed 500 mg, which is difficult to achieve when developing an ODT.[10]

Hygroscopicity

Hygroscopic ODT does not maintain physical integrity at standard temperature and humidity settings; thus, they are shielded from humidity by a specific product container.[10]

Good Packaging Design

At the outset, package design should be enhanced to prevent ODTs from the environment and humidity.[11]

Advantages of Formulating Orodispersible Tablets

The benefits of Orodispersible tablets include the ease with which it may be given to individuals who have trouble swallowing, such as the elderly, stroke patients, and children. ODTs provide most of the characteristics of solid dosage forms, including good stability, consistent dosing, ease of manufacture, small container size, and ease of handling by patients. ODTs benefit from liquid formulations, like the ease of administration and minimal danger of asphyxia due to a dosage form's physical blockage. Since people travelling have limited access to water, this promotes compliance among chronic patients.[12]

Drugs with a pleasant mouth taste may help reinforce psychological beliefs about medicine. The administration is simple for both young and elderly individuals. Drug absorption from the pre-gastric regions of the GIT is faster and more efficient, enhancing bioavailability and effectiveness. Since only a few components are required, the cost is kept to a minimum; dispense dissolved or dispersed medication in the solid dosage form.[13,14]

Disadvantages of Orodispersible Tablets

The mechanical strength of the tablets is generally insufficient. As a result, it needs special packaging and handling process. Another drawback is that ODT may leave an unpleasant taste and grittiness on the tongue if not correctly prepared. Difficulties generating massive dosages (usually greater than 500 mg) and substantial taste masking of bitter-tasting actives.[15,16]

PREPARATION TECHNIQUES FOR ORODISPERSIBLE TABLETS

Water needs to enter the tablet structure quickly to produce fast Disintegration and immediate tablet dissolution. This is achieved by including a suitable disintegration agent or highly water-soluble super disintegrants in the tablet formulation. There are two approaches for preparing orodispersible tablets: Conventional techniques and Patented techniques.[17]

CONVENTIONAL TECHNIQUES

Freeze-drying or Lyophilization

The process of eliminating the solvent from a frozen suspension or solution that contains medicine and other excipients is known as lyophilization. The drug is dissolved or distributed in an aqueous carrier solution. The mixture is pumped into the prefabricated blister pack wells. Liquid nitrogen is used to freeze the medication solution included in the blister packets. They are then placed in refrigerators to finish the freeze-drying process. Finally, the blisters are packed and sent to their destinations.[18]

Tablets that have undergone lyophilization are very porous, dissolve quickly, and have enhanced absorption and bioavailability. Humidity and higher temperatures will affect the lyophilized product of ODT. When put on the tongue, a lyophilized tablet will quickly dissolve. Compared to regular tablet pressing, freeze-drying is a more costly manufacturing method.[19]

Tablet Molding

This method is implemented for drug molecules dissolved in water or ethanol. The components are molded into tablets at a reduced pressure than traditional tablet compression force. By drying or evaporating, the solvent is eliminated. Molded Tablets have a porous structure, resulting in a rapid rate of disintegration.[20]

Direct Compression

Orodispersible tablets can be made using traditional tablet preparation processes, e.g., dry Granulation, wet Granulation, and direct compression. By limiting the number of processing stages, conventional compression apparatus with primary ingredients is employed. Rapidly disintegrating tablets are made using microcrystalline cellulose as well as low substituted hydroxypropyl cellulose as a polymer.[21]

Rapid Disintegration can also be enhanced by applying co2 effervescent substance to the tablet, which effectively masks the taste of pharmaceutical ingredients. According to specific reports, high concentrations of super disintegrants have been used to provide good oral dispersibility with a pleasant feeling. Direct compression is cost-effective had many of the same advantages as traditional tablet manufacturing. It can sometimes include many disintegrants and hence have a lower tablet hardness than conventional tableting methods.[22]

Spray Drying

Hydrated and non-hydrolyzed gelatins as supporting agents, mannitol as a bulking agent, and sodium starch glycolate/ croscarmellose as a disintegrant. A disintegration/dissolution agent such as citric acid and sodium bicarbonate can improve disintegration/dissolution. This technology is used to obtain quick dissolving (20 sec). However, it comes at a high cost and takes a long time to make, and it generates tablets with a meagre mechanical strength as well.[23]

Sublimation

Subliming substances such as urea, camphor, ammonium bicarbonate, and hexamethylenetetramine are added to the other tablet component. Reduced pressure and temperature sublimate the volatile ingredient in a vacuum, leaving the tablets porous after production. When it comes to conventional kinds, fast Disintegration is not always the case. Dissolution-enhancing porous structure employing volatile solvents, such as cyclohexane or benzene.[24]

Fast Dissolving Films

It consists of a non-aqueous solution comprising water-soluble film-forming polymers (pullulan, carboxymethyl cellulose, polyvinyl alcohol, or sodium alginate), a drug, and many other flavors masking ingredients, all of which are often used form a film after the solvent evaporates. Resin adsorbate or coated tiny particles of a medicine can be used in a film for bitter-tasting pharmaceuticals. These are thin films with a diameter of 22 inches that dissolve quickly in 5 seconds and leave a pleasant aftertaste.[25]

Melt Granulation

Using a thermally conductive binder, Abdelbery *et al.* present a new method for making ODT that involves agglomerating pharmaceutical powders. There are high-speed, high-shear mixers that operate at temperatures exceeding the melting point of the binder. A hydrophilic waxy binder super polystrate makes ODTs with appropriate mechanical strength. This binder enhances the hardness of the ODT solubilizes rapidly and dissolves in the oral mucosa without leaving any trace.[12]

Effervescent Method

Effervescent orodispersible tablets are made by combining sodium bicarbonate with tartaric disintegrants such as sodium starch glycolate, cross povidone, and croscarmellose. To eliminate absorbed/residual moisture, sodium bicarbonate and tartaric acid were warmed at 80°C and well combined in the motor. The mixtures are finally crushed in the punch.[26]

IMPORTANT PATENTED ODTS TECHNOLOGIES

Zydis Technology

Zydis is a one-of-a-kind freeze-dried tablet that has the pharmaceutical physically trapped or dissolved inside a matrix of quickly dissolving carrier material. When patients put zydis pills in their mouths, the freeze-dried structure rapidly disintegrates, and they do not need water to consume them. The zydis matrix comprises a mix of components that collaborate to achieve various objectives. Polymers such as gelatin, dextran, or alginates add strength and resilience during handling. These combine to produce a glossy amorphous structure that adds stability. Zydis pharmaceuticals are wrapped in blister packs to preserve the formula from environmental dampness.[27]

Orosolv Technology

Traditional blenders and tablet machines are utilized, but a low compression force is used to speed up the tablet's oral Disintegration. Because Orasolv tablets are more brittle than traditional dose forms, CIMA, the company that makes them, devised a specific handling and packaging approach to compensate.[28]

Flash Tab Technology

This Technology tablet has an active component in the form of microcrystals. Traditional methods such as coacervation, microencapsulation, and extrusion spheronization can create drugs in micro granules. Tablets are made utilizing a shear form matrix that comprises fibrous polysaccharides that are compressed to produce thin sugar fibres that dissolve quickly when exposed to saliva. The tablets generated by this process are soft, brittle, humidity sensitive, and have a large surface area for dissolving, allowing them to dissolve in a matter of a few seconds.[29]

Wowtab Technology

Yamanochi Pharmaceutical Company has patented this technique, and WOW stands for "Without water." Two distinct types of saccharides are used in the preparation of the WOW tab, such as saccharides with high moldability and hardness (maltose, mannitol, and sorbitol), are mixed with limited moldability saccharides (lactose, glucose, mannitol, xylitol) and compressed to produce a tablet formulation with appropriate hardness and quick-dissolving rate. WOW, tab composition is more environmentally stable due to its considerable hardness. An excellent flavour masking ingredient is utilized in this technology to generate a good tongue feel

using proprietary smooth melt action. The Wow tab product melts in less than 15 seconds.[30]

Oroquick Technology

The OraQuick fast-dissolving/disintegrating tablet formulation uses a unique flavour masking technique. Microsphere technology, known as MicroMask, offers a better mouthfeel than other taste-masking options. The flavor masking method does not use any solvents, resulting in quicker and more effective production. Also, because OraQuick produces less heat than other fast-dissolving/disintegrating technologies, it is suitable for heat-sensitive drugs. Because the matrix surrounding and protecting the pharmaceutical powder in microencapsulated particles is more flexible, tablets may be compressed to produce substantial mechanical strength without interfering with flavour masking.[28]

OraQuick claims rapid dissolving in seconds and superior flavour masking. There are presently no drugs on the market that use the OraQuick technology, but K.V. Pharmaceutical is working on analgesics, scheduled medications, cough and cold, psychotropics, and anti-infectives.[31]

Evaluation of ODTs

Hardness

The tablet is broken by applying force across the width of the tablet. The hardness of 10 tablets from each formulation is measured using a Pfizer hardness tester. The tablet is put on a hardness tester to determine the force necessary to break it. To aid rapid breakdown in the mouth, the mechanical strength of ODTs is limited to the lowest range.[32]

Friability

Because all preparing orodispersible tablets tend to raise the percentage of friability, maintaining the ratio of friability within the limit might be challenging. The Roche Friabilator, which is used to measure tablet friability and is reported as a percentage, is used to estimate hardness also. The range is 0.1–0.9% in all aspects. Initially, ten pills were weighed, placed in a friabilator, and spun at 25 rpm for 4 minutes before being reweighed. The acceptability value was computed using the pharmacopoeia employed to measure friability, the loss in tablet weight due to abrasion.[33]

Wetting Time

The shorter the wetting time, the faster the pills dissolve. To determine the wetting time, five circular tissue sheets with a diameter of 10 cm are placed in a Petri dish. Ten millilitres of water-soluble dye, such as eosin solution, are placed in the Petri plate. On the tissue paper's surface, a tablet is softly placed. The wetting time is the length of time it takes for water to reach the tablet's top surface. To establish the water-absorption ratio, the weight of the tablets before they are placed in the Petri dish is recorded (Wb). The wetted tablet from the Petri dish is begun taking and reweighted (Wa). The water-absorption ratio, R, can be calculated using the equation below:[34]

$$R = 100\ (Wa - Wb)/Wb.$$

Disintegration Test

The disintegration test device was used to determine the in-vitro disintegration time. The disintegration duration of ODTs is the essential feature since they must break down in a minimal amount of saliva in a brief period, typically 1 minute. The real disintegration time that patients might experience ranges from 5 to 30 seconds. One tablet is placed into each of the apparatus's six tubes. The conventional technique for performing disintegration tests has numerous drawbacks for these dosage formulations. Researchers began to look for alternative tests because there was no ODT-specific disintegration test. According to assumptions, the disintegration test for orodispersible tablets is intended to imitate the Disintegration in the mouth within salivary contents.[35]

Dissolution Test

Since orodispersible tablets dissolve quickly, the FDA advises using apparatus two at a speed of 25–75 rpm to assess drug dissolution of ODTs. In contrast, apparatus one will be used at a rate of 50 rpm/min. Selecting media to portray in vivo media is one of the most challenging tasks. Studies have suggested various mediums to simulate dissolving in the oral cavity. The usage of Simulated Saliva (S.S.) is one of the mediums utilized for this.[36,37]

Moisture-uptake Studies

In this investigation, the tablets' stability is evaluated. Ten tablets were kept in desiccators over calcium chloride at 37°C for 24 hours. For two weeks, weighted tablets were subjected to 75% relative humidity at room temperature. Desiccators were filled with a saturated sodium chloride solution for three days to produce the required moisture. One tablet was retained as a control (without super disintegrant) to measure the moisture absorption due to the formulation's other excipients. The % increase in weight of the tablets is observed.[34]

CONCLUSIONS

Orodispersible tablets are one of the most promising novel drug-delivery techniques. ODTs can be more effective than traditional solid dose forms. When delivered, a fast-dissolving tablet behaves as a solid dose form when outside the body and as a solution when within the body. As a result, patient compliance, convenience, bioavailability, and time to action have all improved.

Because of its lack of mechanical strength, this dosage form should be handled with caution. Many more types of drugs might be produced using ODT in the future.

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