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Review of Orodispersible Tablet and Manufacturing Technologies

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ABSTRACT:

An increased need for more patient-compliant dose formulations has emerged in recent years. Due to its versatility, safety, high patient compliance, simplicity of swallowing, and ability to prevent discomfort, the oral route has long been the preferred method for administering drugs. Patients who have dysphagia, particularly those who are elderly or young, have challenges. Patients who are institutionalised, have mental retardation, or who are travelling without access to water all confront difficulties. Orodispersible tablets are solid unit dose forms that dissolve or break down quickly in the mouth without the use of water. The difficulties listed above are mostly solved by ODT technology. This article reviews the available literature on ODT, including its formulation, assessment, difficulties, production processes, and patented technologies.

Keywords: Oral disintegrating tablets, ODT preparation, Evaluation, Orodispersible technologies

INTRODUCTION:

The oral route has always been the most effective method for administering medicinal medicines. In comparison to all other administrative routes, it is the most favoured, wanted, and often utilised path. Additionally, oral medicine is frequently acknowledged as the initial strategy for pursuing the development of novel pharmacological entities[1]. The tablet is one of the most often used dosage forms since it is simple to process, convenient, precise in dosing, patient-compliant, and stable. Dysphagia, a condition that can affect people of all ages, is particularly problematic for children and the elderly, as well as individuals who are institutionalised and who experience nausea, vomiting, and motion sickness[2]. Due to its many benefits and high patient compliance compared to many other routes, the oral route is currently the recommended method of administration for the majority of therapeutic drugs used to elicit systemic effects.

The majority of currently available medication delivery devices are tablets and hard gelatin capsules. However, numerous patient populations, including the elderly, kids, and patients who are delayed intellectually, recalcitrant, queasy, or on restricted liquid intake/diets, have trouble swallowing these dose forms. Similar effects occur to those who are on the go or have limited access to water[3,4,5]. Pharmaceutical chemists have created a unique oral dose form called as Orodispersible Tablets (ODTs) to address these medical demands. ODTs dissolve quickly in saliva, often in a couple of seconds, without drink any water. Drug bioavailability, start of clinical impact, and drug solubility and absorption may be much higher than those seen with traditional dose forms.[6,7,8.] According to Joseph Juran, there are two definitions of quality: the first is that a product's features must satisfy the needs of its clients, and the second is that a product must be devoid of flaws.

Both of Joseph Juran's definitions have a significant effect on product costs.[9] Using a risk-based strategy, or Quality by Design (QbD), the International Conference on Harmonisation (ICH) produced the Q8 R2 guideline for pharmaceutical development.[10] Since January 2013, the Food and Drug Administration has mandated that generic manufacturers include the QbD paradigm in their Module 3 Quality 3.2.P.2 Pharmaceutical Development in their Abbreviated New Drug.

Ideal properties of ODT's: [12]

- require no water for oral delivery and quickly dissolve, scatter, or disintegrate in the mouth.
- Feel delightful in the mouth.
- Possess a palatable taste-masking quality.
- Be tougher and less supple.
- After administration, leave little to no residue in the mouth. show little susceptibility to environmental factors like humidity and temperature.
- Permit the production of tablets using standard processing and packaging machinery.

Advantages and Disadvantages: [13,14,15]

Advantages:

1. Increased patient comfort and compliance.
2. No need for water or other liquids.
3. The taste of bitter and nasty medications is covered up.
4. Simplicity of administration for mentally ill, uncooperative, and impaired individuals.
5. After consumption, leaves little to no residue in the mouth.
6. Delicious taste that has been sweetened and has a satisfying tongue feel.
7. Heavily drugged.
8. Enhancements to bioavailability
9. Flexible and appropriate for production using current methods.
10. Affordable; less expensive to produce, package, and distribute than the present commercially available drugs.
11. ODT technology is adaptable and may be utilised to create improved veterinary medications, prescription medications, over-the-counter medications, and line extensions.
12. The new, innovative technology enables the integration of microencapsulated medicines for improved bioavailability and instant release.

Disadvantages:

1. Because they are hygroscopic by nature, rapid-melt tablets must be kept in a cold, dry environment.
2. In order to effectively stabilise and safeguard the stable ODT's, special packaging is needed.
3. If improperly prepared, it might leave a bad taste and disturbing sensation in the mouth.
4. Because the mechanical strength of these tablets is quite low, handling them requires caution.

Challenges

Mechanical Strength and Disintegration Time

Since orodispersible tablets are highly breakable and have a high likelihood of breaking during packing and transportation, maintaining sufficient hardness is necessary for ODT's to have reduced disintegration time [16].

Taste masking

to prevent the bitter taste from being detected in the mouth since the patient's compliance and acceptance of a medication are negatively impacted when a bitter tablet dissolves in the oral cavity [16].

Size of tablet:

The size of the tablet, which is difficult to accomplish, is what determines how well it can be administered [17].

Amount of drug:

The weight of the pill should not exceed 500 mg, which is difficult to formulate when creating an ODT [18].

Hygroscopicity:

Because hygroscopic ODT cannot retain their physical integrity in normal temperature and humidity settings, they must be protected from humidity using specific product packaging [18].

Mouth feel:

ODT should not disintegrate into larger particles; instead, the particles should be tiny and have a pleasing mouth feel [16].

Good packaging design:

In the beginning, packaging design has to be improved to protect ODTs from the environment and moisture [17].

Ingredients Used for Preparation of ODT's: [19,20,21]

Superdisintegrants

By adding superdisintegrants, the rate of disintegration and dissolution is accelerated. They are effective at low concentrations and more efficient at dissolving.

Examples: Crosspovidone, Microcrystalline Cellulose, Sodium Starch Glycolate, and CMC.

Lubricants

Lubricants lessen friction when pills are being compacted and ejected.

Examples: Magnesium stearate and Talc.

Binders

The chosen binders must generate quick release of active substances and have the necessary melting and binding properties. By carefully choosing binders, tablets' stability and integrity are preserved.

Examples: PVP, polyvinyl alcohol, and hydroxypropyl methyl cellulose.

Emulsifying agents

are used to stabilise immiscible mixtures and improve bioavailability in pharmaceutical products. ODTs are more soluble because the interfacial tension is lower.

Examples: For instance, sodium dodecyl sulphate.

Colour

Adding colour will improve the dosage form's look.

Examples: are Redironoxide, Sunset Yellow, and Amaranth 3.

Flavours

Adding tastes helps to mask the bitterness and unpleasant taste, which increases acceptance and patient compliance.

Examples: Citrus oil, vanilla, clove, and peppermint oil.

Bulking agents

The use of bulking agents will enhance the drug's textural properties and speed its oral breakdown.

Examples: Mannitol and starch hydrolysate.

Technologies used to manufacture Orodispersible tablets:

Conventional Technologies

1. Freeze Drying
2. Tablet Moulding
3. Direct Compression
4. Spray Drying.
5. Sublimation.

Freeze drying: [22]

In the process of making ODTs, a porous material is created during the freeze-drying process. A frozen suspension or medicinal solution containing additives that form structures is subjected to the process of lyophilization, which involves the removal of solvents. A glossy amorphous structure is imparted by the freeze-drying of the medicinal active substance and additives, creating a very porous and light product.

When the finished tablet is put on the tongue, the dissolution and disintegration are expedited, and the freeze-dried tablet dissolves instantly to release the active ingredient. The lyophilization process is the subject of several patents.

Moulding: [22]

In the moulding procedure, the drug is moistened, dissolved, or dispersed with a solvent before being compressed into tablets at a lower pressure than usual (lower pressure compression moulding) and having the solvent evaporated from the drug solution or suspension (no vacuum lyophilization), as appropriate.

This method produces tablets that are air dried. Considering that less compression force is utilised while making moulded tablets than when making regular tablets, this results in a highly porous structure that accelerates the product's breakdown and dissolve rate. The powdered mixture should be sieved through a very fine screen or

mesh 22 to further enhance the solubility. Comparatively, speaking, the lyophilisation method is more difficult to scale up for industrial manufacture of tablets than the moulding method.

Direct compression: [23]

It is the simplest method of creating tablets. Direct compression uses standard machinery, readily available excipients, and a constrained number of processing stages. The ultimate weight of the pill can safely exceed that of most production techniques, and even huge dosages can be accommodated. Thanks to the availability of better tablets, particularly tablet disintegrants and sugar-based excipients, this approach may now be used to fast-dissolving tablets.

Spray drying: [24]

In this method yields highly porous and fine powders. The formulation used sodium starch glycolate/croscarmellose as a disintegrant agent, hydrolyzed and unhydrolyzed gelatin as a medium supportive agent, mannitol as a bulking agent, and both.This technology is used to provide quick dissolving (20 sec), however it has a high production cost, takes a long time to make, and results in tablets with very little mechanical strength.

Sublimation: [25]

This method is based on adding readily volatilized solid substances, such as camphor, ammonium bicarbonate, naphthalene, urea, and urethane, to other excipients in the tablet mixture before compressing the mixture into tablets. When the volatile ingredient is eliminated by sublimation, a porous structure is subsequently created, lengthening the disintegration period.

EVALUATION PARAMETERS Of ODT's:

The pharmacopoeia-required evaluation criteria for tablets, coupled with a few unique tests, are to be carried out.

Angle of Repose: [26]

The powder blend's angle of repose was calculated using the fixed funnel method. A funnel was filled with the exact calculated amount of powder mixture. The funnel's height was maintained such that the pinnacle of the powder heap was barely touched by the top of the funnel. There was no surface resistance as the powder was allowed to pass through the funnel. Using the following equation, the powder cone's diameter, height, and angle of repose were all measured:

Tan = h/r where h and r are the height and radius of the powder cone, respectively.

Bulk density and tapped density: [27]

Each formula's 5g of powder were added to a 25 ml measuring cylinder. To break up any possible agglomerates, it was first gently shaken. The initial volume was recorded, then the cylinder was allowed to drop from a height of 2.5 cm to a hard surface at intervals of 2 seconds. The tapping was kept up until the loudness remained steady.

LBD (loose bulk density) and TBD (tapped bulk density)

Were calculated using the formulas:

LBD = weight of the powder/ volume of packing.

TBD = weight of the powder/ tapped volume of the packing.

Compressibility Index and Hausner's ratio: [27]

The following formulas was used to calculate the granule compressibility index and Hausner's ratio.

Carr's index = [(TBD – LBD) x 100] / TBD.

Hausner's ratio = Tapped density / Bulk density.

Post-compression Parameters

The formulated tablets were evaluated for the following parameters,

Tablet hardness: [28]

Hardness is a very important factor that prevents tablet fracture during shipping, handling, and storage. In order to promote early disintegration in the mouth, the crushing intensity limit for ODT is often maintained at a lower range. The Monsanto hardness tester was used to gauge the tablet's hardness, which was stated in units of kg/cm2.

Tablet thickness: [28]

Some of the tablets that had been developed were randomly selected, and their thickness was measured by putting them in between the Vernier calliper's two arms. Each measurement was taken five times on average.

Weight variation: [29]

Twenty tablets were randomly chosen from each formulation and each tablet was weighed using a digital balance. To calculate the weight variance, the individual weights were recorded and compared to the average weight of the pills.

Friabilty: [30]

Since all the elements involved in the production of ODT's are to blame for the increase in friability value, the formed tablets should be well within the bound ranges (0.1 - 0.9%). Twenty pills were chosen at random, weighed, and then put in a plastic chamber Roche friabilator attached to a motor rotating at a speed of 25 rpm for four minutes. The pills were reweighed, and the percentage loss was determined using,

Friability = [(Initial weight – Final weight) / (Initial weight)] x 100

In-vitro disintegration time: [31]

ODT's typically take around one minute to dissolve, whereas patient experiences take between five and thirty seconds. Using the tablet disintegration instrument, the disintegration times of all formulations were calculated. Six pills were inserted one by one in each tube of the disintegration test equipment. The medium was kept at a constant temperature of 37° C, and the duration of the tablet's complete breakdown was recorded. The ODT disintegration test should replicate salivary breakdown in the mouth.

Wetting time and absorption ratio (R): [29]

Another important metric that must be examined in order to understand the tablet's disintegration characteristics is the ODT wetting time. Using a tissue paper that had been folded twice, a petri dish with an internal diameter of 5 cm and 6 ml of water was used. It was carefully topped with the ODT pill. Wetting time is the length of time it takes for the water to thoroughly wet the tablet's upper surface.

The equation was then used to determine the water absorption ratio,

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

Where,

W_a and W_b are weights of the tablet before and after water absorption.

Dissolution test: [32]

The process used to create dissolve procedures for ODT's is comparable to and substantially equal to that used for conventional tablets. The USP 1 and 2 dissolution equipment are utilised. Although, USP 1 has many uses, it frequently results in ineffective stirring and inconsistent dissolving profiles because tablet fragments and other brokendown materials get caught on the interior of the basket at the spindle. The best and most popular option for ODT's is USP 2, which has a paddle and a speed of 50 rpm. ODT typically dissolves under USP monograph conditions relatively quickly, therefore profiles can be obtained utilising slower rates of ODT.

CONCLUSION:

Since a substantial section of the world's population comprises of elderly and paediatric patients, the development of fast-dissolving tablets has made it possible to administer medications without experiencing any issues. Anti-allergic, analgesic, and mental health medications are the main uses of this technique. One of the key issues that was addressed with the creation of this innovative medicine delivery method was dysphagia. ODT's are a cutting-edge drug delivery technology that differs from traditional drug delivery in a number of ways, including better patient compliance, increased bioavailability, and a quicker beginning of effect.

ODT's can be delivered without water since they dissolve and scatter in saliva.

The fundamental idea behind ODT technology is to maximise the tablet matrix's porosity structure in order to accomplish quick disintegration in the oral cavity as well as to give superior tongue feel, taste-masking capabilities for bitter medications, and strong mechanical strength.

In order to provide better results, newer, more affordable technology and enhanced quality goods, further research is desperately needed in this promising sector.

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