A Review on: Mouth Dissolving Tablet And Natural Super Disintegrants

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Abstract- *Drug delivery technology has become extremely competitive and rapidly changing in today's scientific environment. Oral administration is currently the best dosage form in the pharmaceutical industry, where it is recognized as the safest, most convenient, most cost-effective mode of drug administration with the highest patient compliance. Fast dissolving tablets (FDTs) have seen a surge in popularity over the last decade, and the field has become a hotbed of innovation in the pharmaceutical industry. MDTs are tablets that dissolve quickly in saliva without the need for water and can be taken after being placed in the mouth. The demand for MDT (Mouth Dissolving Tablet) is particularly high in geriatric, pediatric, and patients with swallowing difficulties. Traditional dosage forms such as tablets and capsules are increasingly experiencing issues such as dysphagia, resulting in a high rate of non-compliance and rendering therapy ineffective. To avoid the drawbacks associated with traditional dosage forms, mouth dissolving tablets with good hardness, dose homogeneity, and ease of administration have been developed, and they are now the preferred dosage form for pediatrics, geriatrics, and travelling patients. This review discusses the different aspects of formulation, including benefits, drawbacks, use of natural super disintegrants in MDT, and numerous MDT evaluation parameters.*

Keywords- Orodispersible tablet (ODTs), Fast dissolving tablet, Orally disintegrating tablet, Quick dissolving tablet, Natural super disintegrants.

I. INTRODUCTION

In the treatment of any condition, an optimum dosage form is one that achieves the desired therapeutics concentration of drug in plasma and maintains it constant for the entire duration of medication therapy. This is achievable by administration of conventional dosage form in a particular dose and at a particular frequency. Thus, drug may be administered by variety of routes in a variety of dosage forms[1].

Drugs are more frequently taken by oral route. Although a few drugs administered orally are intended to be dissolved in the mouth, the majority of drugs administered orally are swallowed. Compared with alternate routes, the oral route of drug administration is the most popular and has been successfully used for conventional delivery of drug. It is considered most natural, uncomplicated, convenient, safe administration of drugs, great flexibility in dosage form design, ease of production and low cost[2].

Oral route has widely accepted up to 50-60% of total dosage forms of drug administration. Solid dosage forms are popular because they are simple to administer, provide correct dosage, allow patients to self-medicate, reduce discomfort, and most significantly, ensure patient compliance. Tablets and capsules are the most common solid dosage forms. The inability to ingest these dose forms is a big disadvantage. Because of its convenience of self-administration, compactness, and ease of manufacture, the tablet is the most common of all dosage forms available today; however, hand tremors, dysphasia in case of geriatric patients, the underdeveloped muscular and nervous systems in young individuals and in case of uncooperative patients, the problem of swallowing is common condition which leads to poor patient compliance[1].

Dysphagia or difficulty in swallowing is observed to affect nearly 30-35% of general population. This condition is also associated with number of medical conditions such as Stroke, Parkinson's disease, and neurological disorders such as cerebral palsy. Elder patients will have difficulties in taking conventional dosage forms (Solutions, Suspensions, Tablets, Capsules) because of hand tremors, and dysphagia[3].

Because of underdeveloped muscular and neurological systems, young people sometimes have difficulty swallowing. Mentally ill, handicapped, and uncooperative patients are among those who may have difficulty swallowing solid dose forms. In some situations, such as motion sickness, abrupt episodes of allergy attack or coughing, or a lack of water, swallowing tablets becomes difficult, and as a result, patients are unable to take medicines as prescribed, resulting in noncompliance and inefficient treatment.

To overcome these medical needs and problems pharmaceutical companies takes effort to develop a novel type of dosage form for oral administration. The tablet that

disintegrates and dissolves quickly in saliva without the use of water is known as a fast dispersible tablet. In most cases, the MDT tablet dissolves in the oral cavity in a matter of seconds to minutes. The faster the medicine dissolves in solution, the faster it is absorbed and begins to work. Some medications are absorbed through the mouth, pharynx, and esophagus as saliva flows down into the stomach, resulting in much higher bioavailability than that seen with traditional tablet dosage forms. These tablets are helpful not only for persons who have difficulty swallowing, but also for healthy people[3,4].

The orally disintegrating tablets are also called as mouth dissolving tablets, orodispersible tablets, quick disintegrating tablets, fast disintegrating tablets, porous tablets, rapimelts. United States Pharmacopoeia (USP) approved these dosage forms as ODTs. Recently, European Pharmacopoeia has used the term "orodispersible tablet" for tablets that disperse readily and within three minutes before swallowing.

Orally Disintegrating (OD) Tablet technology has been approved by United States Pharmacopoeia (USP), Centre for Drug Evaluation and Research (CDER). United States Food and Drug Administration (FDA) defined ODT as "A solid dosage form containing medicinal substances or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue". The disintegration time for ODTs generally ranges from several seconds to about a minute[5].

Benefits of mouth dissolving tablet[1,4,5,6]:

- Easy to administration to the patients who cannot swallow, such as the elderly stroke patients, bed ridden patients, patients with renal failure and who deny to swallow such as pediatric, geriatric and psychiatric patients.
- Fast dissolution and absorption of the drug, which shows quick onset of action.
- High bioavailability/fast absorption through pre-gastric absorption of drugs from the mouth, pharynx and esophagus as saliva passes down.
- Convenient to administer and patient complaint for disabled, bedridden patients, for travelers and busy people who do not always have available water.
- Good mouth feel property helps particularly in children.
- The risk of chocking of suffocation while oral administration of formulation due to physical obstruction is avoided, thus providing improved safety.
- Novel business opportunity like product differentiation, product promotion, patent extension and life cycle management.

Drawbacks of mouth dissolving tablet:

- The tablets usually have insufficient mechanical strength. Hence, careful and proper handling is required.
- Extra packaging care is required.

Requirements of mouth dissolving tablet:

An ideal mouth dissolving tablet should:

- Require no water for oral administration, disperse in the mouth within few seconds,
- Have a pleasant mouth feeling,
- Have an acceptable taste masking property,
- Have good mechanical strength and less friable,
- Leave minimal or no residue in mouth after administration,
- Exhibit low sensitivity to environmental conditions,
- Allow the manufacture of the tablet using conventional processing and packing equipment,
- Less dose required,
- Ability to permeate oral mucosal tissue.

Salient features of mouth dissolving tablet[5,6]:

- Easy to administration to patient who deny to swallow tablets, such as pediatric, geriatric and psychiatric patients.
- No need of water to swallow the tablet, which is highly convenient feature for patients who are travelling and do not have immediate availability of water.
- Fast dissolution and absorption of drug, which will produce quick onset of action.
- Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach, in such scenario bioavailability of drugs is improved.
- Pre-gastric absorption can result in improved bioavailability and as a result of reduced dosage, improve clinical performance through a reduction of unwanted effects.
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Super disintegrants:

Selection of disintegrants is the basic step in development of MDTs. The disintegration and dissolution of

MDT is aided by disintegrants. To achieve speedy disintegration and high dissolution rates, it is important to select the right disintegrant in the right concentration. Because of the combined impact of swelling and water absorption by the formulation, super disintegrants promote fast disintegration. The wetted surface of the carrier increases as super disintegrants swell, promoting the system's wettability and dispersibility, and thereby boosting disintegration and dissolution. The ideal super disintegrant concentration can be chosen based on the disintegrant's critical concentration.The tablet disintegration time is inversely proportional to the super disintegrant concentration below this concentration, however when the super disintegrant concentration is above critical concentration, the disintegration time remains nearly constant or even increases.[7]

Disintegrants play a critical part in the disintegration and dissolve of direct compression mouth dissolving tablets. The right type of disintegrant and the right amount of disintegrant are crucial for a high disintegration rate. Other formulation ingredients, such as water-soluble excipients or effervescent agents, can help in dissolution and disintegration.

Mechanism of super disintegrants:

Disintegrants usually work in following ways:

1. **Wicking**: Water transport into the tablet.
2. **Swelling**: Particles absorb water and expand, like a dry sponge, pushing against the interior of a tablet or capsule causing it to fall apart or discharge its contents.
3. **Elastic recovery**: Stored potential energy is released from disintegrant particles after contact with a fluid environment.
4. **Repulsion**: Electrostatic forces separate the particles

Various types of synthetic super disintegrants used are as follows:

- Crosspovidone
- Microcrystalline cellulose
- Sodium starch glycollate
- Sodium carboxy methyl cellulose
- Croscarmellose sodium
- Calcium carboxy methyl cellulose
- Modified corn starch
- Kyron

Natural super disintegrants[8]:

Natural materials have advantages over synthetic materials because they are chemically inert, non-toxic, less expensive, biodegradable, and widely available. To improve the solubility of poorly water-soluble drugs, reduce disintegration time, and provide nutritional supplementation, natural polymers such as locust bean gum, banana powder, mango peel pectin, Mangifera indica gum, and Hibiscus rosa-sinenses mucilage are used as binders, diluents, and super disintegrants. Natural polymers are nontoxic, biodegradable, eco-friendly, free of negative effects, renewable, and provide nutritional support. Natural polymers have been shown in research to be safer and more effective than synthetic polymers.

Natural polymers are beneficial because of their established biocompatibility and safety. Because of their cost-effectiveness and regulatory approval, natural gums are among the most common hydrophilic polymers. Polymers are commonly used in floating drug delivery systems to focus medication distribution to a specific area of the gastrointestinal tract, such as the stomach. Furthermore, these polymers are nontoxic and chemically modifiable, as well as capable of gel formation.

All the polymers mentioned in table no. 1 are approved by US Food and Drug Administration (FDA). Natural polymers, such as chitosan, guar gum, Locust, and bean gum, are GRAS (Generally Recognized as Safe) according to the FDA's Code of Federal Regulations (CFR 21).

Table no. 1: FDA Approved natural polymers used in fast dissolving tablets[8]

Sr. no.	Natural polymer	Marketed drug	Disintegration time	Concentration used
1	Chitin and chitosan	Cinnarizine	60 sec	3% w/w
2	Guar gum	Glipizide	30 sec	1% w/w
3	Gum karaya	Amlodipine, Granisetron hydrochloride	17.10 sec	4% w/w
4	Agar and treated agar	Theophylline	20 sec	1-2% w/w
5	Fenugreek seed mucilage	Metformin hydrochloride	15.6 sec	4% w/w

6	Soy polysaccharide	Lornoxicam	12 sec	8% w/w
7	Gellan gum	Metronidazole	155 sec	4% w/w
8	Mango peel pectin	Aceclofenac	11.59 sec	0.1–4% w/w
9	Lepidium sativum mucilage	Nimesulide	17 sec	5–15% w/w
10	Plantago ovata seed mucilage	Granisetron HCl	17.10 sec	5% w/w
11	Aegle marmelos gum	Aceclofenac	8–18 min	6% w/w
12	Locust bean gum	Nimesulide	13 sec	10% w/w
13	Lepidium sativum	Nimesulide	17 sec	10% w/w
14	Mangifera indica gum	Metformin HCL, paracetamol	3–8 min	6% w/w
15	Hibiscus rosa-sinensis mucilage	Aceclofenac	20 sec	6% w/w
16	Dehydrated banana powder	Ondansetron HCl/propranolol, gabapentin	15–36 sec	6% w/w

Benefits of natural polymers:[8]

The various benefits of natural polymers include the following:

- They are biodegradable since they are naturally occurring and produced by all living organisms.
- All of these plant components are essentially sugar polysaccharides that are biocompatible and non-toxic.
- They are less expensive to use as natural resources. When compared to synthetic materials, the cost of production is lower. Agriculture is important to India and many other developing countries, and large sums of money are invested in agriculture.
- Natural chemicals derived from various plant sources are widely used in the pharmaceutical sector and gathered in enormous numbers due to the simple manufacturing techniques involved.
- The government of India and other homogeneous developing countries promotes the production of plants as pharmaceutical excipients, and it also provides facilities for bulk production of gum and mucilage, which have a wide range of applications in industries.
- Natural materials have a lower risk of side effects and undesirable effects than synthetic materials.

II. FORMULATION ASPECTS IN DEVELOPING MDT[5]:

Orally disintegrating tablets are formulated by utilizing several processes and properties such as:

- Mechanical strength of tablets
- Taste and mouth feel
- Swallowability
- Drug dissolution in saliva
- Bioavailability
- Stability

The simplest way of producing orodispersible tablets is by direct compression. The primary benefit of direct compression is that it has a lower manufacturing cost. It is made with standard equipment, readily available excipients, and simply a few manufacturing procedures. The disintegrants used play a significant role in the disintegration and breakdown of directly compressed fast disintegrating tablets. For a good disintegration rate, selecting the right type of disintegrant and the right amount of disintegrant is critical. Other formulation ingredients, such as water-soluble excipients or effervescent agents, can improve dissolution or disintegration qualities even further.

The various processes employed in formulating MDTs:[9,10]

1. **Freeze drying or lyophilization:** Freeze drying is a method of removing water from a product after it has been frozen. Freeze-dried dosage forms dissolve more quickly than other solid dosage forms. The lyophilization procedure gives the bulking agent and, in certain cases, the drug a glossy amorphous structure, which improves the formulation's dissolving characteristics.

2. **Molding:** Tablets prepared by molding are solid dispersions. Whether and to what extent the drug dissolves in the molten carrier determines the physical form of the medication in the tablet. The

drug might be disseminated in the matrix as discrete particles or microparticles. It can either dissolve completely in the molten carrier to create a solid solution or partially dissolve in the molten carrier with the remaining particles remaining undissolved and scattered in the matrix. The type of dispersion or dissolution will affect the disintegration time, drug dissolution rate, and mouth feel.

3. **Cotton candy process:** This method uses a special spinning mechanism to create a floss-like crystalline structure, similar to cotton candy. The simultaneous action of flash melting and spinning results in the creation of a matrix of polysaccharides or saccharides in the cotton candy process. To increase flow characteristics and compressibility, the matrix is partially recrystallized. After milling and blending with active ingredients and excipients, the candy flos matrix is compressed to ODT.

4. **Spray drying:** Spray drying is a technique for creating extremely porous, fine powders. When compressed into tablets, the composition contains a bulking agent (mannitol and lactose), a disintegrant (sodium starch glycolate and croscarmellose sodium), an acidic ingredient (citric acid), and/or alkaline ingredients (sodium bicarbonate), all of which show rapid disintegration and enhanced dissolution when compressed into tablets.

5. **Mass extrusion:** This technology entails softening the active blend with the solvent, mixing water-soluble polyethylene glycol with methanol, and extruding the softened mass through an extruder or syringe to produce a cylinder of the product, which is then cut into even segments with a heated blade to produce tablets.

6. **Sublimation:** This procedure involves adding a sublime salt to the tableting ingredients, compressing the mixture, and then sublimating the salt out. Tablets are made with the active substance, a diluent, a sublime salt (camphor/ammonium bicarbonate), a binder, and various excipients combined together. The tablets disintegrate in 10-20 seconds and have enough mechanical strength.

7. **Sugar based excipient:** Sorbitol, mannitol, dextrose, xylitol, fructose, maltose and polydextrose have been used as bulking agents. Because of their high aqueous solubility and sweetness, which impart a pleasing mouth feel and good taste masking, nearly all formulations for rapidly dissolving tablets contain sugar-based materials.

8. **Direct compression:** It is the simplest method of producing tablets. Direct compression uses standard equipment, widely available excipients, and a small number of processing stages. Disintegration and solubilization of directly compressed tablets is dependent on the action of disintegrants, water soluble excipients, and effervescent agents individually or in combination. Tablet size and hardness have a significant impact on disintegrant efficacy. Disintegration time for large and hard tablets is longer than is generally necessary. As a consequence, products with optimal disintegration properties often have medium to small size and /or high friability and low hardness.

III. EVALUATION OF MOUTH DISSOLVING TABLET:[12,13,14]

MDT formulations need to be evaluated for the evaluation parameters such as Bulk density, tapped density, Carr's index, Hausner's ratio, and Angle of repose were evaluated for the powder mix before the formulation. Tablet appearance, thickness, hardness, friability, weight variation, drug content etc. were evaluated after the formulation.

1. **General Appearance:** General appearance of the tablet can be evaluated by visual observation of the prepared tablets such as tablet size, shape, color, existence or absence of an odor, taste, surface texture, physical flaws, and consistency and readability of any identifying marking, as are the tablet's overall look, visual identity, and overall "elegance".

2. **Size and Shape:** The size and shape of the tablet can be dimensionally described, monitored and controlled.

3. **Tablet thickness:** Tablet thickness is an important characteristic in reproducing appearance and also in counting by using filling equipment. Some filling equipment utilizes the uniform thickness of the tablets as a counting mechanism. Ten tablets are taken and their thickness will be measured using vernier caliper or micrometer in mm.

4. **Tablet hardness:** 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. Hardness of the tablet of each formulation was determined using Monsanto Hardness tester.

5. **Weight variation:** The average weight was obtained after a total of twenty tablets were selected randomly. After that, individual tablets were weighed and their weights were compared to an average weight.

6. **Friability:** Friability of the tablets was calculated by using Roche Friability apparatus. The apparatus uses a plastic chamber that revolves at 25 rpm, dropping the tablets from a height of 6 inches with each rotation to subject a number of tablets to the combined effect of abrasions and shock. The friability apparatus was filled with pre-weighed sample tablets and rotated for 100 revolutions. The tablets were re-weighed after being dusted.

7. **Content uniformity test:** A quantity of powder equivalent 10mg of drug was placed to a 25ml volumetric flask and 15ml water was added. By gently shaking the stoppered flask for 15 minutes, the drug is extracted in water. The liquid is then filtered after the volume is adjusted to the mark with distilled water. After proper dilution, the absorbance was measured to estimate the drug content. The standard calibration curve plotted to calculate the drug content. The average of three determinations was used to calculate the mean percent drug content.

8. **Disintegration test:**The tablets were placed in each tube of the disintegration test apparatus, and the tablet rack was positioned in a 1-liter beaker containing 900 ml of distilled water, where the time of disintegration was recorded. The disintegration of the formulations was tested at room temperature to distinguish between them.

9. **In vitro dispersion time:** Tablet was added to 10ml of dissolution medium solution at 37±0.5°C. Time required for complete dispersion of a tablet was measured.

10. **Wetting time and Water absorption ratio:** In a small Petri dish (internal diameter 5cm) containing 6ml of water, a piece of tissue paper folded twice was placed. A tablet was placed on the paper and the time required for complete wetting of the tablet was measured, the wetted tablet was then weighed.

Water absorption ratio 'R' was determined using following equation:

$$R = 100 \times Wb - Wa / Wa$$

Where, Wa is weight of tablet before water absorption and Wb is weight of tablet after water absorption.

11. **Dissolution study:** A dissolution equipment was used to test the in vitro dissolution of mouth dissolving tablets. 900mL of appropriate dissolution media was used as the dissolving medium. The temperature of the dissolving media was maintained at 37±0.5°C throughout the experiment. One tablet was used in each test. Samples of dissolving medium (5ml) were extracted with a syringe fitted with a pre-filter at predefined intervals and analyzed for drug release by measuring absorbance. The volume removed was replaced with a new quantity of dissolving medium at each time interval. The percentage of medication released cumulatively was calculated and plotted against time.

12. **Stability testing:** The tablet was packed in an amber-colored bottle with aluminium foil laminated on the upper portion of the bottle, and the packed formulations were kept in ICH-certified stability chambers. For 3 months, the temperature was kept at 40°C and the relative humidity was kept at 75% (zone III according to ICH guidelines). The tablets were examined for changes in appearance, drug content, and in vitro drug release tests before and after one month, as per the procedure.

IV. CONCLUSION

When compared to traditional oral dosage forms, orally disintegrating tablets have higher patient acceptance and offer improved biopharmaceutical characteristics, efficacy, and safety. These tablets are currently receiving more industry acceptability, with an emphasis on pediatrics, geriatrics, and people of all ages. To achieve patient compliance, recent trends in patient-oriented dosage forms have emerged. A variety of formulation-related issues contribute to a high level of non-compliance, necessitating the creation of a patient-centred drug delivery system. Natural polymers, which are used as a binder, super disintegrant and diluent, increased the drug release rate from the tablet while reducing the dissolving and disintegration time. As a result, natural super disintegrants promote faster drug breakdown and greater bioavailability, resulting in more effective therapy and better patient

compliance. Thus, natural super disintegrants can be used as effective disintegrants in tablet formulations.

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