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Review

A REVIEW ARTICLE: MOUTH DISSOLVING TABLETS

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Abstract:

Due to better accessibility and tolerability for patients, mouth dissolving tablet is the most essential and recommended way of drug delivery. One more difficulty can be solved by administering the new drug with the mouth dissolving tablet formulation so that the drug quickly dissolves and breaks in the mouth in fewer minute due to the effect of super disintegrating agents that maximize the pore structure of the formulation. Whenever, the medicines that interact with saliva exclude the need for water and discharge the medicine quickly. This article focused on standard selection of drug, features, technologies developed for the mouth dissolving tablets, and assessment methods. The major role played by the super disintegrant and inactive substances for enhancing the bioavailability of drug and improves the drug release in the oral cavities.

Keywords: *Mouth dissolving tablet, Rapid disintegration, Superdisintegrant, Improved bioavailability*

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INTRODUCTION

In spite of important innovations in drug delivery, the oral path is still the greatest standard approach to administer therapeutic agents because of its exact dosage, inexpensive therapy, self-medicated, non-invasive (in the cavity) manner, and comfort administration, which all give to great patient comfort [1].

This particular formulation segment is intended specifically for patients who are dysphasic, elderly, young, bedridden, or psychotic and who either cannot or will not swallow traditional oral formulations. MDTS are the most convenient dose forms for dysphasic, pediatric, and elderly patients with swallowing issues since they dissolve/disintegrate quickly when placed in the mouth. They are an excellent substitute for bedridden patients and travellers because they don't require water for administration. Psychotic patients are unable to conceal them in their mouths since they immediately disappear when placed there. Because the current formulation's line has been extended, these medications not only improve patient compliance but also generate significant profits for the makers [2–3].

The Food and Drug Administration (FDA) classifies all mouth dissolving tablets that have been permitted as orally disintegrating tablets. A tablet which melts in the mouth in fewer minutes before swallowing is bring up as an orodispersible tablet by the European Pharmacopeia. Patients can easily swallow such a tablet since it breakdowns into minute particles or melts in the mouth from solid to a gel-like configuration. Good MDTs take anywhere from a few seconds to around a minute to disintegrate [4-5]. MDT is defined as "A dosage form comprising an active substance or active drug which splits quickly, generally within fewer second, when located upon the tongue" by the US Food and Drug Administration [6].

MOUTH DISSOLVING PHENOMENON

For the production of oral dispersible tablets, additional care is paid to superdisintegrants. The quick dissolution and breakdown ensure by the process of absorption and swelling of water inside tablets. The carrier's surface wets by the swelling mechanism of superdisintegrants, which enhance breakdown of tablets and rises dissolution. The

performance of super dispersants affects by the thickness of matrix and swelling ability of dissolved liquid. Because of high swelling capability and compactness, matrix shows high degradation [7].

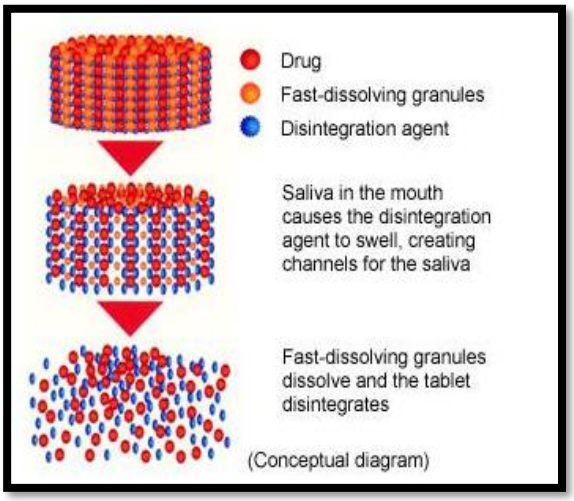

Figure 1: Mechanism of mouth dissolving

PRROPERTIES OF MOUTH DISSOLVING TABLET [8]

1. Allow heavy drugs to be loaded.
2. For swallowing, water does not necessary, but it should be dissolve in fewer seconds.
3. Accept flavor masking.
4. Be tougher and less hard.
5. After oral administration, residue should not present in the mouth.
6. Little sensitivity to environmental surroundings (temperature and humidity).
7. It should be cost saving.
8. Pleasurable in the mouth.

ADVANTAGES OF MOUTH DISSOLVING TABLET [9]

1. Improved Compliance / Greater Comfort
2. No water needed
3. Chewing is not necessary
4. Better taste
5. Better stability
6. Suitable for both controlled and immediate release agents
7. Appropriate and Easygoing to current process and packing machine
8. Enables high drug loading.
9. The ability to deliver the benefits of liquid medications in a solid dosage form.
10. It has cost saving property.

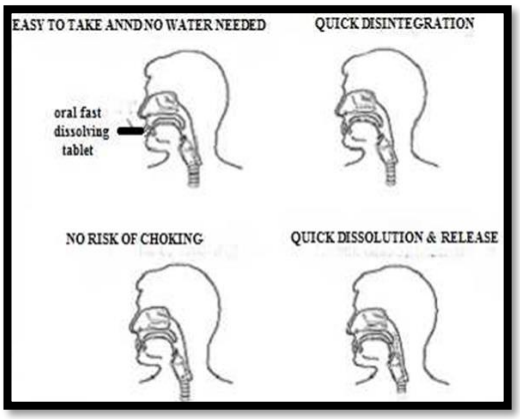

Figure 2: Administration of mouth dissolving tablet

DISADVANTAGES OF MOUTH DISSOLVING TABLETS [5, 10-12]

1. The tablets might leave disagreeable mouth feel, so it should make carefully.
2. Patients cannot administer anticholinergic drug with mouth dissolving tablet simultaneously who concurrently. Likewise, who have the problem of mouth dryness they are not good subjects for mouth dissolving tablet.
3. Higher dose of drug shows unsuitability to dissolve in the mouth.
4. Inadequate mechanical power. Hence, handling is necessary.

DRUG SELECTION CRITERIA [13–16]

A medication that meets the following requirements is excellent for in vitro dissolution from the mouth dissolving tablet:

- Fewer dose >20 mg.
- Partition capability and drawn-out into the upper GIT epithelium.
- Excellent stability in saliva and water.
- Capacity to enter the mucosal tissue of the mouth.
- Modest to small molecular weight.

❖ Unfitting drug properties for Mouth dissolving tablets:

- Needed sustained or regulated release.
- Frequent dose and brief half-life.
- It is impossible to perform taste masking for extremely harsh or undesirable tastes.

SUPERDISINTEGRANTS SELECTION

Rate of disintegration depends upon superdisintegrants, but they can change the friability, mouth feel and hardness when amount is in excess. The following desirable factors should be taken for formulation and pick the right superdisintegrants, which will Yield fast disintegration when the tablet make interaction with saliva in the mouth.

- To produce fewer friable tablets, it should be compact.
- Provide patients with a comfortable mouth feel. Therefore, it is better to have smaller particle sizes to ensure patient compliance.
- Possess a smooth flow, as this enhances the whole blend's flow properties.

MECHANISM OF SUPERDISINTEGRANTS

- **Swelling:** The most widely accepted mechanism of action for tablet disintegration is swelling, the diffusion of water diffusion is important method of disintegration. When the particles reach to proper medium, so they get swell and generating a swelling force which can causes the matrix to breakdown. If the swelling force is enough so tablet do not breaks fast. So it is vital to recall that, if the pressing portion is really great, fluid cannot enter inside tablet and breaking reverse [17–19].
- **Surface tension and porosity (wicking):** The porosity of tablet produces channels for soaking the fluid into the tablets. The particle of the tablet weakens and it reduces the intermolecular force of tablet while placing in the fluid medium. The absorption of water into the tablet is calculated by the hydrophilicity of the drug or inactive substances. The 'non-swellable' disintegrants caused the development of the tablet [20].
- **Deformation;** When fluid and disintegrated particles get interacted, they return to the unique arrangement because tablet compression caused by deformation. The distorted particle size rises under pressure, the ability of the starch to develop is get improved and results in the breakdown of tablet.

EXCIPIENTS FOR FORMULATION OF MOUTH DISSOLVING TABLETS

- **Binders:** HPMC, PVA, Polyvinylpyrrolidine.
- **Superdisintegrants:** Microcrystalline cellulose, Crospovidone, Sodium carboxy methyl cellulose, Croscarmellose, Calcium carboxy methyl cellulose.
- **Lubricants:** Mag. Stearate, Stearic acid, Polyethylene glycol, Colloidal silicon dioxide, Liquid paraffin.
- **Flavors:** Flavoring aromatic oil, clove oil, cooling flavor, anise oil, thyme oil, peppermint oil, eucalyptus oil.

- **Filers:** Calcium carbonate, Calcium sulfate, Magnesium carbonate, Mannitol, Calcium phosphate, calcium sulfate, aluminum hydroxide, sorbitol, xylitol.
- **Surface active agents:** SLS, spans, Sodium dodecyl sulfate, tweens.
- **Sweeteners:** Sugars derivatives, Aspartame.

METHOD OF PREPARATION OF MOUTH DISSOLVING TABLETS

DIRECT COMPRESSION

The simplest and cost-effective tablet formulation technique is direct compression. Due to the accessibility of enhanced excipients, superdispersants and sugar-based excipients it is mostly usable technique [21]. Limited quantity of drugs can be pushed directly into regular featured tablets. The technology of dispersion additive is cost-saving and easy to applicable on an industrial level. [22] The compressible mixture have appropriate flow properties and must form under pressure so that swelling processing as wet granulation is extreme.

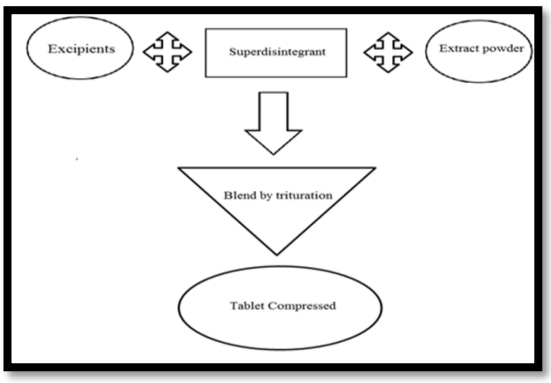

Figure 3: Direct compression method

Freeze drying: While placing in the mouth, saliva helps to pass easily and lyophilized mass to dissolve, it can be converted into tablets with a remarkably permeable open matrix net. Drug is grouped with a freeze-dried matrix and water-soluble matrix to form a quickly dissolve part in the mouth. The optimal pharmacological properties of freeze-dried formulations have chemical stability, little dose, tiny particle size and flavourlessness. The process of preparation is relatively luxurious and time-taking [23].

Spray drying: In the technique of spray drying, a formulation include gelatin used as a supporting agent and matrix, lactose, cross-povidone, sodium starch glycolate, and croscarmellose are used as super-dissolving agents and mannitol as a filler. Spray-dried method leads to dissolve tablet fast and diffuse it well. The degradation time is less than 25 seconds [24].

Sublimation: Volatile components are added to the arrangement for forming porous matrix, which are to subjected to method termed as sublimation. Greatly volatile components can also be pressed with alternatives tablet excipients like ammonium carbonate, ammonium bicarbonate, camphor, benzoic acid, urea, and ester anhydride. With the process of sublimation volatile material is removed, and leaving frequently the polymer matrix [25].

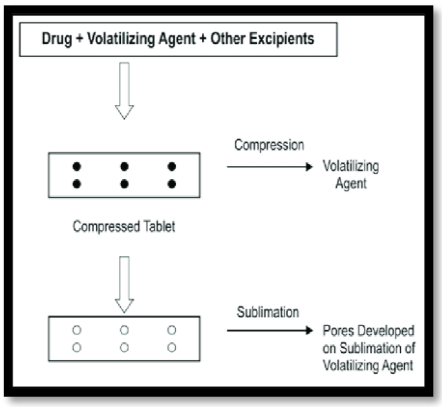

Figure 4: Sublimation process

Mass Extrusion: The method comprises softening the mixture with a solvent mixture of water-soluble and methanol and polyethylene glycol eliminating the resulting weaker paste through an injector to form a cylinder of product into constant parts using a heated blade to form tablets. [26-27]

Phase transition: The tablet is prepared in two stages. Mouth dissolving tablet was prepared by reduction of a powder comprising xylitol and erythritol and then heating nearly 20 min at 93C [28]. The average pore size of the tablet improved after heating and the hardness of tablet also enhanced. During heating the increase of tablet hardness and storage was independent of the lesser melting point crystal-like state of the sugar alcohol [29].

MANUFACTURING PROCESS OF MOUTH DISSOLVING TABLET [30]

- The microcrystalline cellulose, lactose and active drug were mixed and4 no. sieve were used.
- Hydroxypropylmethylcellulose dissolve in purified water and binder was prepared.
- For mixing, high speed mixer is used.
- Granule pulp was dried in air at 440 to 550C for 6 to 10 min and sieved in no. 10 seive.
- Dry granules were sieved.
- Microcrystalinecellulose, mag. Stearate and dry granules were mixed in dry blender.
- Granules were compressed into tablet and tablet coat the tablet in coating pan.

MARKETED FORMULATIONS OF MOUTH DISSOLVING TABLETS

Drug	Category	Company	Brand name
Piroxicam	Anti arthritis	Pfizer Inc., NY, USA	Feldene Melt
Loratidine	Anti-histaminic	Ranbaxy	Loratadine, Redidose
Famotidine	H_2 receptor blocker	Merck and Co., NJ, USA	Pepcid
Paracetamol	NSAIDs	Prographarm, Chateauneuf, France	Panadol,Tylenol
Nimesulide	NSAIDs	Panacea Biotech, New delhi , India	NisureMD
Olanzapine	Antipsychotic	Eli Lilly	Zyprexa Zydis
Montelukast	Anti asthmatic	Ranbaxy Lab. Ltd. Newdelhi,India	Romilast
Cisapride monohydrate	Anti-emetic	Jannsen	Propulsid
Ibuprofen	NSAIDs	Eurand International	Zyprexa
Promethazine	Antihistamine	Aventis	Phenergan
Cefixime	Antibiotic	Lupin	Suprax
Glipizide	Anti-diabetic	Pfizer	Glucotrol
Valsartan	Anti-hypertensive	Abbott	Humira

Table 1: Marketed formulation of MDTs

EVALUATION PARAMETERS

Thickness: Measuring the thickness of tablet is modest. It is measured by the instrument termed Vernier Calipers. 5 tablets were taken and measure the thickness.

Weight variation test: The individual weight and average weight of randomly selected 20 tablets were calculated. The abnormality of each individual tablet was calculated and compared with the standard values set in the pharmacopoeia [31].

The percentage difference of each tablet is calculated by the given formula %.

Weight variation % = Tablet individual weight – Average weight of 20 tablets /Average weight of 20 tablets × 100

Hardness: Monsanto hardness tester and Pfizer hardness tester takes part for measuring the hardness of tablet. The breaking force is a function of calculating the hardness (kg/cm2). The standard and resultant value should be match [32].

Water absorption ratio: It is a similar procedure to set the watering time. After complete wetting, initial and final weight of the tablet were determined and ratio of water absorption was considered using the formula:

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

Where, R- water absorption ratio, Wa (weights of tablet after wetting) and Wb (weight of water before wetting).

Disintegration time: The 6 tablets were randomly selected and test the time of disintegration of the tablets. The average time is compared with the standard.

Wetting time: The most important parameters of orodispersible tablets are wetting and water absoption ratio. In a small Petri dish water-soluble dye solution were placed and kept the filter paper on petridish. The tablet kept on the paper and the time need for wetting of the tablet was calculated. Tissue paper should be twice folded and positioned in a small size culture dish which has 6 ml of water [33-34].

Uniformity of dispersion: Two tablets were randomly selected and mixed for two minutes in 100 ml of water. 22 mesh size is used to pass the dispersion. The residual remained on the screen, if tablet passed the test.

Friability: The extent of tablet breakage should be measured under physical stress conditions like transportation, packaging. Friability was assessed using a Roche fibrilator. 6 tablets were taken and determined friability 25 rpm for 4 minutes. The percentage of weight loss is [35].

Weight loss % = before weight of tablet− after weight of tablets /Weight of total tablets × 100

FUTURE PROSPECTS

With numerous pharmaceutical benefits such as enhanced effectiveness compared with conventional preparations of mouth dissolving tablets. For example, they need lesser extent of active ingredient which will be effective, progress absorption profiles and offer healthier bioavailability of drug than conservative tablets and capsules. Mouth dissolving tablet formulations continue to have many areas for improvement. Most mouth dissolving tablets on the market have reasonable decay times like fewer minutes, but absolute progress will be enhanced. Although the progress in mouth dissolving tablets procedures, the preparation of hydrophobic drugs is quite a challenge, specifically when the higher amount of drug is there. A new technique establishes to increase higher amount of doses of hydrophobic drugs devoid of major outcome on the dissolution properties of oral. The foremost improvement in mouth dissolving tablet technology is to deliver the particular dose of drug with half-life 12 to 24 hours. Such formulations would be enormous, suitable and reliable. Mouth dissolving tablet formulations necessitate great amounts of excipients and more drug doses and make preparation easy to handle [36].

CONCLUSION

In the present age of medication, mouth dissolving tablets are mostly favored dosage form as related to conventional oral dosage form like tablet and capsules. This article mainly covers a wide variety of methods for formulating mouth dissolving tablets, and their merits, demerits, and quality standards. Article gave outcome that mouth dissolving tablet might helpful for the pediatric, geriatric and dysphasic patients and enhance the drug bioavailability. With seeing the difficulty in the population regarding swallowing, so they preferred mouth dissolving tablet for overall therapy effectiveness. Mouth dissolving tablet s are designed that they dissolve/ disintegrate in saliva within less than 60 seconds.

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