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REVIEW ARTICLE

A review on recent advances of oral mouth dissolving tablet

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ABSTRACT

Mouth dissolving tablets are disintegrating and dissolve rapidly in mouth cavity without need of water. Many tablets are design to dissolve in mouth fast in few second and other true fast dissolving tablets. Oral mouth dissolving tablets are developed with the aim of sufficient ingredient not more hardness and fast disintegration without water. Tablets are frequently widely acceptable solid dosage form for being compact offering uniform dose and painless drug delivery system. Oral mouth dissolving tablets dissolve in saliva within few second when administered orally. Such tablets can be used anywhere and anytime without water and thus these are suitable for pediatric, geriatric and mentally disabled patient.

Key words: Mouth dissolving tablets, Conventional techniques, Rapid disintegration, direct compression.

INTRODUCTION:

Oral mouth dissolving tablets are great advantage for the patient who can not administered or swallow the tablet easily. The patient who can swallow the tablet easily and suffer difficulty in swallowing is known as Dysphagia. This condition is common in all age group epically in elder patient [1]. This problem can be overcome by using oral mouth dissolving tablets. Oral drug delivery system is an important route drug delivery system. A variety of bioadhessive mucosal dosage form have been developed such as gels, ointment, adhesive tablets and recently use of polymeric film for oral delivery also called as mouth dissolving film. Oral mouth dissolving tablets are disintegrate or dissolve in buccal cavity without need of water or without chewing. Fast dissolving drug delivery system are must include the substance mask the taste of adhesive ingredient. Mouth dissolving of tablet results in quick dissolution and rapid absorption which provide rapid onset of action [2,3].

IDEAL CHARECTERSTICS OF MOUTH DISSOLVING TABLETS:

A mouth dissolving tablet should be

- Not affected by environ mental condition like temperature, humidity etc. [4,5] .
- It shoul be easily portable and transported.
- It should be able to produce in a simple manner within low cost.
- It should not create any toxic effect and no residue when put in mouth.
- It can be easily disintegrate of dissolve in oral cavity without use of water [6] .

MERIT OF MDT:

- It can be easily used by children, older, elderly and mentally person [7].
- It can be accurate dosing as compared to liquid dosage form .
- Benifical in cases such as motion sickness.
- Easily disintegrate or dissolve in oral cavity without use of water .
- Good mouth feel property helps to change the perception of medication as bitter pill particularly in pediatric patients.

DEMERIT OF MDT:

- Tablet may leave unpleasant taste in the oral cavity if it is not manufactured properly.
- Tablet have usually insufficient mechanical strength hence carefully handling is required.
- The tablets may leave unpleasant taste and/or grittiness in mouth if not formulated properly.
- Patients have to stop eating, chewing, smoking, and possibly talking during drug therapy to keep the drug in sublingually [8,9].
- From formulation point of view, MDTs is hygroscopic in nature and therefore needed to be placed in dry place and it also requires special packaging for properly stabilization and safety of stable product [10,11].

CRITERIA OF MDT:

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- Drug must dissolve or disintegrate quickly typically over 10-30 min period for effective absorption.
- Allowing the medicament to be rapidly absorbed.
- Should not be bitter tested
- Dose should be less than 20 mg.
- Should have small to moderate molecular weight.
- Should have good stability in water and saliva.
- Should be partially non ionized at oral cavities

PREFORMULATION STUDY OF DRUGS:

- Particle size: Should be less than 5 micrometer.
- Porosity: Should be high for better absorption.
- Density: Should be low.
- Hardness: Should be low.
- Friability: Should be less than 1%
- Drug Solubility: Aqueous solubility in various pH media is one of the most important properties of drug substance. These properties significantly affect the drug absorption and bioavailability.
- Disintegration time: The time for disintegration should be less than one min.

TASTE MASKING AGENTS IN MDTs FORMULATION:

Along with fast disintegration the taste masking is also very important for the formulation of MDT, to achieve patient‟s compliance. Two approaches commonly utilised for taste masking; firstly by reducing solubility of the drug in the pH of saliva, secondly by altering the affinity and nature of drug which will interact with the taste receptor . Number of natural and artificial taste masking agents has been evolved in the formulation of oro-dispersible tablet formulation. Mostly sweetening agent Aspartame (Quarrechin, France) is used as sweetening agent.

Table 1: Taste masking agents (Flavors and sweeteners)

Sr. No.	Name
1.	Sodium phenolate
2.	Sod. Bicarbonate, citric acid, orange/ cream flavor
3.	Sod. Bicarbonate, citric acid, lemon flavor
4.	Sod. Citrate dehydrate, sod. Saccharine , refined sugar
5.	Sodium bicarbonate, citric acid, cherry flavor
6.	Starch, lactose and mannitol

Table 2: Taste masking agents (lipophilic vehicles)

Sr. No.	Name
1.	Hydrogenated oil and HPMC
2	Molten stearyl stearate
3.	Magnesium aluminium silicate and soyabean lecithin
4.	Glyceryl monostearate and AMCE
5.	Hydrogenated oil and surfactants

TECHNOLOGY USED IN MANUFACTURING OF MDTs:

- Conventional method
- Patented technology

CONVENTIONAL METHOD:

- Lyophilisation or freeze-drying
- Spray drying
- Sublimation
- Molding
- Direct compression
- Nanonization
- Mass extrusion
- Disintegrates addition

Lyophilisation or freeze-drying:
Freeze drying (lyophilization) is a drying process applicable to the manufacture of certain pharmaceuticals and biological that are thermolabile or otherwise unstable in aqueous solution for prolonged storage periods, but that are stabe in dry state. Most commonly, it would be frozen by a mechanical refrigerator device, often the refrigerated shelves in the freeze-drying chamber, at a temperature of -50˚c or lower [12] . The disadvantages of this technique is that it is time consuming and expensive.

Spray drying:
From formulation point of view, MDTs is hygroscopic in nature and therefore needed to be placed in dry place and it also requires special packaging for properly stabilization and safety of stable product. Spray drying is a method of producing a dry powder from a liquid or slurry by rapidly drying with a hot gas. The formulation thet were produced contained hydrolysed and unhydrolysed gelatine as a support agent for the matrix, mannitol as a bulking agent and sodium starch glycolate or crosscarmellose as a disintegrant. The formulation was spray dried to yield a porous powder. Tablets manufactured from this powder disintegrated in less than 20 second in an aquous medium [13].

Sublimation:
Sublimation technology involves the incorporation of volatile inert solid compounds in the formulation and then compressed together to form tablets. The tablets formed are then subjected to sublimation which causes the inert substances to volatilize readily which left a porous tablet structure. This tablet when placed in the mouth readily dissolves in the saliva. The substances used are camphor, naphthalene, ammonium bicarbonate, ammonium carbonate, benzoic acid, hexamethylene tetramine, urea and urethane. Koizumi et al. applied the sublimation technique to prepare highly porous compressed tablets that were rapidly soluble in saliva [14].

Molding:
Water-soluble ingredients so that the tablets dissolve completely and rapidly. The powder blend is moistened with a hydro-alcoholic solvent and is molded into tablets under pressure lower than that used in conventional tablet compression. The solvent is then removed by air-drying. Molded tablets are very less compact than compressed tablets. These possess porous structure that enhances dissolution.

Direct Compression:
Direct compression is easiest way to manufactured tablets. Low manufacturing cost, conventional equipments and limited number of processing steps led this technique to be a preferable one. However disintegration and dissolution of directly compressed tablets depend on single or combined effect of disintegrant, water soluble excipients and effervescing agents. It is essential to choose a suitable and an optimum concentration of disintegrant to ensure quick disintegration and dissolution. Superdisintegrants are newer substances which are more effective at lower concentrations with greater disintegrating efficiency and mechanical strength. Effective Superdisintegrants provide improved compressibility, compatibility and have no negative impact on the mechanical strength of formulations containing high dose drugs. Directly compressed tablet's disintegration and solubilization depends on single or combined action of disintegrants, water soluble excipients and effervescent agent.

Nanonization:
It involves reduction in the particle size of drug to nanosize by milling the drug using a proprietary wet-milling technique. The nanocrystals of the drug are stabilized against agglomeration by surface adsorption on selected stabilizers, which are then incorporated into MDTs. This technique is especially soluble drugs. Other advantages of this technology include fast disintegration/dissolution of nanopartides leading to increased absorption and hence higher bioavailability and reduction in dose, cost effective manufacturing process, conventional packaging due to exceptional durability and wide range of doses (up to 200 mg of drug per unit).

Mass extrusion:
In this technique, a blend of active drug andother ingredients is softened using solvent mixture of water soluble polyethylene glycol, using methanol and then the 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 tablets. The dried cylinder can be used to coat the granules of bitter tasting drugs and thereby masking their bitter taste.

Disintegrates addition:
Disintegrate addition technique is one popular techniques for formulating Fast-dissolving tablets because of its easy implementation and cost-effectiveness. The basic principle involved in formulating Fast-dissolving tablets by disintegrates addition technique is addition of superdisintegrants in optimum concentration so as to achieve mouth dissolving along with the good mouth feel.

PATENTED TECHNOLOGY

- Flash dose technology
- Wowtab technology
- Orasolv technology
- Durasolv technology
- Zydis technology
- Flashtab technology

Flash dose technology:

This technology is based on the prepration of sugar based matrix known as floss, which is made from a combination of excipients either alone or in combination of drugs. Two plateform fuisz technologies called sheaform and ceaform are currently being utilized in the prepration of wide range of oral fast desolving products. Fuisz has patented flash dose technology. Nurofen melted, a new from of ibuprofen ass melt in mouth tablets prepared using flash dose technology is the first commercial product launched by Biovailcoporation. Sheaform matreices are prepared by flash heat process[15].

Wowtab technology:

Wowtab Technology is patented by "Yamanouchi Pharmaceutical Co. " WOW means "Without Water ". In this process, combination of low mouldability saccharides and high mouldability saccharides is used to obtain a rapidly melting strong tablet. The active ingredient is mixed with a low mouldability saccharide and granulated with a high mouldability saccharide and compressed into tablet.

Orasolv technology:

In this system active medicament is taste masked. It also contains effervescent disintegrating agent. Tablets are made by direct compression technique at low compression force in order to minimize oral dissolution time. Conventional blenders and tablet machine is used to prepare the tablets.

Durasolv technology:

Durasolv has much higher mechanical strength due to the use of higher compaction pressures during tableting. The tablets made by this technology consist of a drug, fillers and a lubricant. Tablets are prepared by using conventional tableting equipment and have good rigidity. Durasolv is so durable that it can be packaged in either traditional blister packaging or vials.

Zydis technology:

This technology involves softening the active blend using the solvent mixture of water soluble polyethylene glycol, using methanol and expulsion of softened mass through the extruder or syringe to get a cylinder of the product into even segments using heated blade to form tablets. The dried cylinder can also be used to coat granules of bitter tasting drugs and thereby masking their bitter taste.

Flashtab technology:

This is patented by Ethypharm France. This technology includes granulation of excipients by wet or dry granulation method followed by compression into tablets. Excipients used in this technology are two types. Disintegrating agents include reticulated polyvinylpyrrolidine or carboxymethyl cellulose. Swelling agents include carboxymethylcellulose, starch, modified starch, microcrystalline cellulose, carboxy methylated starch, etc. These tablets have satisfactory physical resistance[16].

CHALLENGES IN MDTs:

- Rapid disintegration
- Taste and mouth feel character
- Good package design
- Ease of administration
- Sensitivity to environmental condition
- Cost
- Amount of drug
- Aquous solubility
- Size of tablet

EVALUATION OF MOUTH DISSOLVING TABLETS:

- Hardness
- Friability
- Thickness
- Uniformity of weight
- Wetting time
- Water absorption ratio
- In-vitro disintegration time
- Dissolution time

Hardness:

The limit of hardness of MDT is usually kept in lower range to facilitate early disintegration in mouth. The hardness of MDTS may be measured using hardness tester (Monsanto Hardness tester). It is expressed in kg or pound [17].

Friability:

Friability is the loss of weight of tablet in the container due to removal of fine particles from the surface. Friability test is carried out to access the ability of the tablet to withstand abrasion in packaging, handling and transport. Roche friabilator is employed for finding the friability of the tablets. Weigh the tablets which have average weight more than 6.5gm from each batch and place in Roche friabilator that will rotate at 25 rpm for 4 minutes. Dedust the all tablets and weigh again. The

percentage of friability can be calculated using the formula.

Thickness:
Thickness of tablet can be measured by using digital vernier callipers[18].

Uniformity of weight:
Weight variation test is done as per standard procedure. Ten tablets from each formulation are weighed using an electronic balance and the average weigh are calculated.

Wetting time:
Five circular tissue papers of 10 cm diameter are placed in a petridish with a 10 cm diameter. Ten millimeters of water-containing Eosin, a water-soluble dye, is added to petridish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as a wetting time.

Water absorption ratio:
A piece of tissue paper folded twice was placed in a small Petri dish containing 6 ml of water. A tablet was put on the paper & the time required for complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio (R), was determined using following equation,
R = 10 (Wa /Wb)
Where- Wb is weight of tablet before water absorption & Wa is weight of tablet after water absorption.

In-vitro disintegration time:
Disintegration times for sublingual tablets are determined using USP tablet disintegration apparatus with phosphate buffer of pH 6.8 or 0.1 n HCl as medium. The volume of medium is 900 ml and temp is 37± 2 °C. The time in seconds is taken for complete disintegration of the tablets with no palatable mass remaining in the apparatus is measured.

In-vitro dissolution time:
In-vitro dissolution study is performed by using USP Type II Apparatus (Paddle type) at 50 rpm. The amount of drug dissolved is determined by suitable analytical technique.

CONCLUSION:
The oral route is most popular route for the administration of therapeutic agents by mouth dissolving film because of the low cost of therapy and ease of administration which lead to increase in patient compliance. Mouth dissolving tablet can be considered as the best possible dosage form to be administered if the taste and dissolution pattern of the drug candidate can be improved. They combine the greater stability of a solid dosage form and the good applicability of a liquid. Mouth dissolving oral films has several advantages over the conventional dosage forms. So they are of great importance during the emergency cases such as allergic reactions and asthmatics attacks whenever immediate onset of action is desired. And more importantly, mouth dissolving films are travel friendly dosage forms where water may not be carried by person or patient. And hence, mouth dissolving film becomes unique, elegant, selective and needful dosage form.

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