



MOUTH DISSOLVING TABLET

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ABSTRACT

Oral route is considered as one of the most convenient route for administration of various pharmaceutical dosage forms like, tablet, capsule, syrup, suspension and emulsion. Fast Dissolving Drug Delivery systems have developed various fast disintegrating preparations like mouth dissolving film, MDT. Oral thin film are new dosage form that are prepared from hydrophilic polymer which are when placed in mouth, buccal cavity disintegrate rapidly. Mouth dissolving film is superior as compare to mouth dissolving tablet as the cost of production is low. Geriatric and pediatric patients are facing difficulty in swallowing of tablet and capsule, the oral film can bypass it, along with that it has other advantages like self-administrable, fast dissolving, rapid absorption that make it versatile dosage form. The aim of this article is to review the ideal properties, significance, characteristics, limitation, choice of drug candidates, challenges in formulation, approaches for preparation of MDTs, Patented technologies on MDTs, Suitable drug candidates for MDTs, Marketed product of MDTs, and Evaluation tests of MDTs.

KEYWORDS: Mouth Dissolving tablets (MDT, s), preformulation studies, patented technology, evaluation

INTRODUCTION

Advances in drug delivery have presented alternate optimized dosage form for paediatric, bedridden, nauseous and uncompliant patients. Traditional dosage forms like tablets and capsules have to be administered with 250 ml of water that is to be considered impractical and incompatible for most of the patients. To overcome these types of problems fast dissolving drug system is introduced that dissolves and disintegrates in the oral cavity without the need of water and chewing. According to European Pharmacopoeia, the dispersion/disintegration time should be less than three minutes. Super disintegrates like cross linked carboxymethylcellulose, cross povidone, sodium starch glycol ate and polyvinyl lpyrrolidone are used as a common approach for the formulation of fMDT, which provides immediate disintegration of tablet after placing upon tongue by releasing drug on saliva. Another approach used in development of MDT is to maximizing pore structure of tablets. Different types of techniques have been used for the formulation of mouth dissolving tablets are freeze drying, sublimation technology, tablet molding, spray drying, direct compression etc have been tried by researchers to maximize the pore structure of the tablet matrix.

IDEAL PEROPERTIES OF MDT

- Not require water or other liquid to swallow
- Easily dissolve or disintegrate in saliva within a few seconds.
- Have a pleasing taste.
- Leave negligible or no residue in the mouth when administered.
- Be portable and easy to transport.
- Be able to be manufactured in a simple conventional manner within low cost.
- Be less sensitive to environmental conditions like temperature, humidity.

ADVANTAGES OF MDT

- 1) Easy administration for patients who have difficulty in swallowing the tablets.
- 2) Best dosage form for paediatric, elderly and mentally disabled patients who refuse the tablet.
- 3) There is no requirement of water for administration of tablet.
- 4) Dissolution and absorption rate is high.
- 5) Dosage form provides rapid or immediate onset of action.
- 6) Does not leave any residue or metabolite in mouth after the ingestion of tablet.
- 7) Lesser chances of first pass metabolism hence improving stability of the dosage form.
- 8) Can be administered anywhere anytime when there is need for tablet during travelling, walking.

CONVENTIONAL TECHNOLOGIES MDT's

1. Freeze drying/Lyophilisation
2. Molding
3. Sublimation
4. Spray Drying
5. Direct Compression
6. Mass Extrusion
7. Nanonization
8. Cotton Candy Process
9. Fast Dissolving Films

1) Freeze drying/Lyophilization

It is one of the first generation techniques for preparing MDT, in which sublimation of water takes place from the product after freezing. The formulations show enhanced dissolution characteristics due to the appearance of glossy amorphous structure to bulking agents and sometimes to drug. The ideal drug characteristics for this process are relative water insolubility with fine particle size and good aqueous stability in suspensions. Primary problems associated with water-soluble drugs are formation of eutectic mixture, because of freezing point depression and formation of glassy solid on freezing, which might collapse on sublimation. The addition of mannitol or crystal forming materials induces crystallinity and imparts rigidity to amorphous material. The advantage of using freeze-drying process is that pharmaceutical substances can be processed at non-elevated temperature, thereby eliminating adverse thermal effects.

2) Molding Moulding:

Tablets prepared by this method are solid required smaller particles in the matrix. It can dissolve totally to form solid solution or dissolve partially in molten carrier. It is of 3 types:

- Compression moulding
- Heat moulding
- No vacuum lyophilisation

3) Sublimation

This process involves addition of some inert volatile substances like urea, urethane, naphthalene, camphor, etc. to other excipients and the compression of blend into tablet. Removal of volatile material by sublimation creates pores in tablet structure, due to which tablet dissolves when comes in contact with saliva. Additionally several solvents like cyclohexane, benzene etc. Can also be used as pore forming agents. Mouth dissolving tablets with highly porous structure and good mechanical strength have been developed by this method.

4) Sprays-Drying

Spray-drying for the production of MDTs. The formulations contained hydrolysed and non-hydrolysed gelatine as a supporting agent for the matrix, mannitol as a bulking agent and sodium starch glycolate or croscarmellose as a disintegrant. By adding an acid (e.g., citric acid) or an alkali (e.g., sodium bicarbonate) disintegration and dissolution were further enhanced. The porous powder was obtained by spray drying the above suspension which was compressed into tablets. Tablets manufactured by this method shows disintegration time < 20 sec in an aqueous medium.

5) Direct compression

It is simplest tablet manufacturing technique. In this all the weighed quantities are mixed thoroughly in mortar and pestle then compressed directly in suitable punch machine. The tablets formed from this technique have following benefits:

- Accommodation of high dose and final weight of tablet can exceed that of other method.
- Processing steps involved in this are limited.
- Cost effective

6) Mass - Extrusion

This technology involves softening of the active blend using the solvent mixture of water soluble polyethylene glycol and methanol. This softened mass is extruded through the extruder or syringe and a cylindrical shaped extrude is obtained which are finally cut into even segments using heated blade to form tablets. Granules of bitter drugs can be coated using this method to mask their taste.

7) Canonization

A recently developed Nano melt technology involves reduction in the particle size of drug to Nano size by wet-milling technique. Surface adsorption of the Nano crystals of the drug is done on selected stabilizers for stabilizing them against agglomeration, which are then incorporated into MDTs. This technique is mainly advantageous for poor water soluble drugs and also for a wide range of doses (up to 200 mg of drug per unit).

PATENTED METHOD

Zaydis technology:

Zaydis is considered to first mouth dissolving dosage form in which water-soluble matrix is used to incorporate active drug which then transformed to blister pockets from which frozen water molecules get removed by process of sublimation and then addition of gums may carried out to prevent disperse drug sedimentation.

Oriol technology:

It is said to be the first lab mouth dissolve formulation in which taste masking of active drug is carried out and an effervescent agent may also be used. But there is one limitation of this technology that tablets formed are very soft and fragile.

Durnacol technology:

In this technology for the formulation of tablets fillers, drug, lubricants are required.

Wow tab technology:

Wow means without water, no water is required. For this carbohydrates of high and low mould ability are used for the preparation of granules.

Flash dose technology:

In this masking of bitter drug is carried out by using combination of two technologies- shear form and deform technology. In this sugar based matrix is called floss.

Nanocrystal technology:

MDTs formed by this novel approach is by decreasing particle size, decrease in particle size result in larger surface area which helps in the dissolution of tablets.

PREFORMULATION STUDIES OF MDT, s

Reformulation study relates to pharmaceutical and analytical investigation carried out proceeding and supporting formulation development efforts of the dosage form of the drug substance.

1. Bulk Density (Db):

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weight powder (passed through standard sieve # 20) into a measuring cylinder and initial weight was noted. This initial volume is called the bulk volume. From this the bulk density is calculated according to the formula mentioned below. It is expressed in g/ml and is given by

$$D_b = M / L_b$$

Where, M is the mass of powder

L_b is the bulk volume of the powder.

2. Tapped Density (Dt):

It is the ratio of total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder for 750 times and the tapped volume was noted if the difference between these two volumes is less than 2%. If it is more than 2%, tapping is continued for 1250 times and tapped volume was noted. Tapping was continued until the difference between successive volumes is less than 2% (in a bulk density apparatus). It is expressed in g/ml and is given by

$$D_T = M / V_T \text{ Where,}$$

M is the mass of powder

V_T is the tapped volume of the powder.

3. Angle of Repose (q):

The friction forces in a loose powder can be measured by the angle of repose (q). It is an indicative of the flow properties of the powder. It is defined as maximum angle possible between the surface of the pile of powder and the horizontal plane $\tan(q) = h/r$

$$q = \tan^{-1}(h/r)$$

Where, q is the angle of repose.

H is the height in cms

R is the radius in cms.

Table no 1: Angle of Repose as an indication of powder flow properties

Sr. No	Angle of Repose	Type of Flow
1.	< 20	Excellent
2.	20 -30	Good
3.	30-34	Passable
4.	>34	Very poor

5. Carr's index (or) % compressibility:

It indicates powder flow properties. It is expressed in percentage and is give

$$Dt - Db$$

$$I = \frac{Dt - Db}{Dt} \times 100$$

Where, Dt is the tapped density of the powder and Db is the bulk density of the powder.

Table 2: Relationship between % compressibility and flow ability

% Compressibility	Flow ability
5-12	Excellent
12-16	Good
18-21	Fair passable
23-35	Poor
33-38	Very poor
<40	Very very poor

EVALUATION OF MOUTH DISSOLVING TABLETS

1) Weight variation:

20 tablets were selected randomly from the lot and weighted individually to check for weight variation. Weight variation specification as per I.P. is shown in Table 3.

Table Weight 3: Variation Specification as per IP

Average Weight of Tablet	% Deviation
80 mg or less	±10
More than 80 mg but less than 250 mg	±7.5
250 mg or more	±5

2) Friability (F):

Friability of the tablet determined using Roche friabilator or Electro lab friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at I height of 6 inches in each revolution. Prewighted sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. Tablets were dusted using a soft muslin cloth and reweighed. The friability (F) is given by the formula.

$$W_{\text{initial}} - W_{\text{final}}$$

$$F = \frac{W_{\text{initial}} - W_{\text{final}}}{W_{\text{initial}}} \times 100$$

W initial

Disintegration:

Disintegration time is determined by placing 6 ml of phosphate buffer (pH 6.8), inside the vessel in such way that 2 ml of the media is below the sieve and 4 ml above the sieve. Tablets placed on the sieve and the whole assembly is to put on a shaker. The time in which all the particles pass through the sieve is taken as a disintegration time of the tablet. Six tablets are chosen randomly from the composite samples and average value is determined.

CONCLUSION

The development of mouth dissolving also provides an opportunity for a line of extension in market. MDT has been most preferable for patients having difficulty to swallow, motion sickness and allergic conditions. So, it can be concluded that mouth dissolving tablets are better option to control risk of disease because such tablets would release the drug immediately when placed upon tongue. They also offer several biopharmaceutical advantages such as improved efficiency over conventional dosage forms like they require smaller amount of active ingredient to be effective, improve absorption profiles and offer better drug bioavailability than regular tablets and capsules.

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