IJPSR (2012), Vol. 3, Issue 09 (Review Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 01 May, 2012; received in revised form 09 June, 2012; accepted 15 August, 2012

MOUTH DISSOLVING TABLETS: AN OVERVIEW

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Keywords:
Mouth dissolving tablets,
Patient's compliance

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ABSTRACT

The gold standard in pharmaceutical industry is the oral delivery because it is the easiest, safest, economical and convenient method for the drug delivery. Mouth dissolving tablets have becomes the most demanding application during last decades and in the pharmaceutical industry this field has become a rapidly area. Mouth dissolving tablets during insertion in the mouth should have to dissolve or disintegrate in the mouth within 15sec to 3 minutes without the help or need of any drinking agent like water. These mouth dissolving tablets can be given anytime, anywhere to anyone who needs this without the presence of water and these will show the effective action in few minutes.

INTRODUCTION: For administration of drugs, oral route is considered the most widely used route[1]. In this method the main limitation of commonly used oral drug delivery such as tablets and capsules is swallowing difficulty (dysphasia) mostly in case of pediatric and geriatric patients feel most incompliance to take the tablets and capsules. To make the patients convenient for the administration of these dosage forms plays a vital in design and formulation of dosage forms.

To overcome this problem and to make the oral route more convenient for patients a new drug delivery method is evolved known as mouth dissolving drug delivery system, orodispersible or mouth-melt etc. These MDTs should dissolve or disintegrate in the mouth within few seconds without the need of water, chewing with the help of saliva present in the mouth.

For mouth dissolving tablet formulation the main criteria is to eliminate the bitterness of the tablet by adding sweetening agent or by sugar coating on the tablets.

To increase the tablet disintegration, super-disintegrants are added in it, which are very helpful to increase the bioavailability of tablet and to increase the disintegration property of tablet in saliva. Disintegrants are mainly added in the tablets by three methods. These methods are extra- granular, intra-granular and partially extra- granular and intra-granular method. Time for MDT disintegration is normally assumed to be less than 1 min.

The patients can feel the normal disintegration time of MDT from 5-30sec. MDT's are mainly prepared by various methods like direct compression, wet granulation, solid dispersion and tablet molding etc. Direct compression method is the most widely used and easiest or cost effective method for MDT as compared to other methods.

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IJPSR: ICV- 4.57

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MDT's are mainly used in some serious conditions like:

- Motion sickness [2]
- Parkinsonism
- Pediatric and geriatric patients
- Unconsciousness
- Mentally disabled patients
- Absence of water

MDT**:** These are the tablets which dissolve or disintegrate quickly in the saliva to show their action within few seconds without the help if water. A mouth dissolving tablet mainly dissolves in the mouth within 15sec-3mins.Mostly the MDT's superdisintegrants and taste masking agents.

Ideal Characteristics of MDT:

A MDT should have following properties:

- A MDT should be dissolve or disintegrate in the mouth within few seconds.
- It should not require any liquid or water to show its action.
- It should not leave any residue in the mouth after the administration of the tablet.
- It should be cost effective.
- It should be less effective by environmental conditions like humidity, temperature etc.

MDT Advantages:

- Easy for administration to patients which cannot swallow he tablets like pediatric and geriatric, unconscious and mentally disabled patients [3]**.**
- Does not require water to take the tablet during travelling.
- Quick disintegration and dissolution of drug tablet to produce rapid action.
- Bioavailability of drug can be increased by avoiding the passage of the drug from pharynx and esophagus.
- It has good mouth feel property that helps to take the medicine easily than the bitter pills in pediatric patients.
- There is no risk of suffocation and chocking during MDT uptake.
- It is helpful in some cases like motion sickness, during coughing etc.
- These MDT's are stable for longer duration of time, till it is consumed.

Criteria for drug selection:

The main criteria's for a drug to be selected are as follows:

- It should not have bitter taste.
- The dose should be less than 20mg.
- Moderate molecular weight should be small.
- Should be of good solubility in water and saliva.
- Should have extensive First pass metabolism.
- Should have oral tissue permeability.

Conventional techniques for Mouth Dissolving Tablets:

There are many conventional techniques for the formulation of MDT's. These are as follows [4]:

- Freeze drying/Lyophilization
- Spray drying
- Sublimation
- Direct compression
- Mass extrusion
- Tablet molding

Freeze drying/Lyophilization: Freeze drying is one of the best techniques for the preparation of mouth dissolving tablet water is sublimed from the product when it is frozen. In this technique an amorphous porous structure is created that can be dissolved rapidly. For the manufacturing of mouth dissolving tablet, the typical procedure is mentioned here. In an aqueous solution of a carrier/polymer the active drug is dissolved or dispersed. By weight the mixture is done and in the preformed blister packs walls, it is poured.

The blister packs are placed in the trays and these trays are passed through the freezing tunnel of liquid nitrogen so that the drug solution or dispersion becomes frozen. To continue the freeze drying the frozen blister packs are placed in the refrigerator. When the freeze drying is complete, then on the blister sealing machine the aluminum foil packing is applied. At the end the blisters are packaged. Freeze drying method has showed improvement in absorption and the bioavailability is increased. The main disadvantage of this technique is its higher cost and more time consumption. The conventional packaging becomes unsuitable due to fragility.

Spray drying: In spray drying technique gelatin is used as a matrix and as a supporting agent Crosscarmellose sodium, sodium starch glycolate and crosspovidone are used as the superdisintegrants. Mannitol is used as a bulking agent. From spray dried powder the prepared tablets have been reported to disintegrate in an aqueous medium less than 20seconds.The formulation contained lactose and mannitol as a bulking agent, crosscarmellose sodium and sodium starch glycolate as superdisintegrants and citric acid as an acidic ingredient. Finally this spray dried powder was compressed into tablets and these tablets showed quick disintegration property and the dissolution rate was also enhanced.

Sublimation: The presence of porous structure in the tablet matrix is the key for rapid disintegration of MDT [5, 6]. Due to low porosity of the matrix, the tablet made from conventional compressed method that contain high amount of water soluble ingredients often dissolve quickly. Volatile ingredients are used to create the porous matrix, which further subjected to sublimation process.

The solid ingredients which are inert in nature with high volatility (e.g. ammonium carbonate, ammonium bicarbonate, camphor, benzoic acid, urea, urethane, naphthalene) have been used for this sublimation process. The other solvents like benzene and cyclohexane were also used to generate the porosity in the matrix.

Direct compression: This is the quickest and the easiest method to manufacture the tablets. In this method we use conventional equipments, excipients that are available commonly and the steps are limited in direct compression. In this method high doses can be prepared. Due to improved tablet excipients like disintegrants and some sugar based excipients, this technology is now used for mouth dissolving tablets. In MDT the presence of disintegrants leads to rapid disintegration and also improves the dissolution.

Tablets prepared by direct compression mainly affect the dissolution and disintegration process of the tablet. By different concentration of disintegrants tablet disintegration time can be optimized. The tablet disintegrants concentration is inversely proportional to tablet disintegration time. However, tablet disintegration time remains approximately constant or even increases above critical concentration. By incorporating effervescent disintegrating agents, mouth dissolving tablets can also be achieved, which will generate the carbon dioxide. Hence, the use of sugar based excipients (e.g. fructose, dextrose, isomalt, maltose, sorbitol, starch) is another approach to prepare the mouth dissolving tablets by direct compression.

Mass extrusion: In this mixture the active blend can be made soften by 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 blades to form tablets. To coat the granules of bitter tasting drugs and to mask the bitter taste the dried cylinder can be used.

Tablet molding: By using water soluble ingredients molded tablets are prepared, so that they can dissolve completely and rapidly. With the help of hydro-alcoholic solvent the powder blend is moistened and under lower pressure than that of used in conventional

tablet compression is molded into tablet. With the help of air drying the solvent is removed. Molded tablets are very less compact than of compressed tablets. These tablets enhance dissolution due to presence of porous structure in it.

Patented technologies for MDT's: The main patented technologies for mouth dissolving tablets are as follows [7]:

Zydis technology: Zydis was the first marketed technology which was developed by R.P. Scherer. Inc., for new generation tablet formation. By freeze drying the drug in a matrix, consisting of gelatin the Zydis tablet was produced. The product is dispensed in a special blister packing because it is very light weight and fragile. Due to freeze drying, there is very little amount of water left in a drug for the attack of microorganism, so this preparation is self preserving. The tablets made by Zydis technology have very few seconds disintegration time.

Durasolv technology: This is the CIMA labs patented technology [4]. The tablet consists of drug fillers and a lubricant made by this technology. In this method the tablets are prepared by using conventional tabletting equipment and have good rigidity property.

Orasolv technology: This technology was also prepared by CIMA labs [8]. To minimize the oral disintegration and dissolution time, these are prepared by direct compression at low compression force. Orasolv is a slightly effervescent tablet example because it can dissolve rapidly in mouth. In it the active ingredients are dispersed in saliva due to the action of effervescent agent and also taste masked. The low mechanical strength is the major limitation of this technology. The tablets prepared by this method need to be packaged in a specially designed pack because these are very soft and fragile in nature.

Wow tab technology: This technology follows the combination of low and high mouldability saccharides to prepare mouth dissolving tablets by using conventional tablet technique and granulation process [9]. According to patent, the low mouldability saccharides are lactose, mannitol, sucrose and glucose etc, whereas the high mouldability saccharides include maltitol, maltose, oligosaccharides and sorbitol etc.

When tablets are prepared by compressing both low and high mouldability saccharides, only then the desired properties of hardness and quick disintegration in mouth can be achieved.

Cotton candy technology: This technology is patented by Fuisz [10]. This technology produces floss like crystalline structure due to their unique spinning mechanism. The active drug in a tablet can be incorporated by crystalline sugar. The final product prepared by this technology has a very high surface area for dissolution. It disperses and dissolves quickly, when placed on tongue.

Oraquick technology: The patented taste masking technology is utilizes by the mouth dissolving tablet formulation. K V Pharmaceutical company, claims that its taste masking technology i.e. microsphere technology has superior mouth feel over taste masking alternatives. Any kind of solvents are not utilized by taste masking process. Therefore it leads to superior and fast efficient production. Without disrupting taste masking the tablets of significant mechanical strength are obtained by after compression. Only K V Pharmaceutical has their products in the market in different classes of drugs like cough and cold, analgesic, psychotics and anti-infective in developmental stage.

Flashtab technology: The Flashtab technology has patented by Prographarm laboratories [11]. In this technology, the tablet which consists an active ingredient in the form of microcrystals are prepared, having rapidly disintegrating property. By using the conventional techniques like microencapsulation, coacervation and simple pan coating drug microgranules can be prepared. The active ingredients of the microgranules or microcrystal's are compressed into tablets by addition of granulated mixture of excipients prepared by wet or dry granulation method. The tablets prepared by this technology have less than one minute disintegrating time and good mechanical strength.

Evaluation of blend: The evaluation of prepared blend was carried out by the following methods [12]:

- Angle of repose
- Bulk density

- Tapped density
- Carr's compressibility index
- Hausner's ratio

Angle of repose: This was measured by using funnel method. The amount of blend was taken in a funnel and height was adjusted in a way in which the apex of heap just touches the tip of funnel. The drug excipients blend was allowed to flow freely on to the surface. The diameter of the cone of powder was measured and by using following equation angle of repose was calculated.

$$\tan \theta = h/r$$

Where h= height of the powder; r = radius of powder

Bulk density: This was determined by pouring an accurately weighed quantity of blend into a graduated cylinder and then the volume and weight was measured.

Bulk density = weight of powder/ volume of packing

Tapped density: This was determined by known amount of mass of drug excipients blend in a graduated cylinder. The cylinder was allowed to fall on a hard surface under its own weight from 10 cm height at 2 sec intervals. The tapping was continued until no further change in volume was noted.

TBD = weight of powder / volume of tapped packing

Where, TBD = tapped bulk density

Carr's compressibility index: It was determined by following method;

Carr's compressibility index (%) = TBD – BD x 100

Where, TBD = tapped bulk density; BD = bulk density

Hausner's ratio: It can be calculated as;

Hausner's ratio = TBD / BD

Where, TBD = tapped bulk density; BD = bulk density

Evaluation of MDT's: There are several methods for the evaluation of MDT. Some of them are as follows [13, 14];

Hardness and Friability: Hardness of tablets was measured by using Monsanto hardness tester or by Pfizer hardness tester with ten tablets and then their standard deviation was also calculated.

Friability of 20 tablets was measured by using Roche friabilator at 25 rpm for 4 minutes. The percentage friability of tablets was measured by the following method;

Percentage friability = Initial weight – Final weight x 100 / Initial weight

Uniformity of weight: The tablets were taken and weighed individually on weighing balance [15]. The average weight was calculated from these weights.

Wetting time: It was measured by using a piece of tissue paper (12cm x 10.75cm) folded twice and placed in Petri dish (ID 9 cm) containing 6 ml phosphate buffer pH 6.8 equal to the saliva pH [16]. After that the wetting time was noted.

Drug content: Ten tablets were powdered and the blend equivalent to active dose was weighed and dissolved in suitable quantity of pH 6.8 solution [17, 18]. The solution was filtered and analyzed on UV-Spectrophotometer.

***In vitro* Dissolution study:** Dissolution studies for the development of MDT and standard formulations were monitored [19, 20, 21, 22]. These experiments were performed in a dissolution media having 900ml phosphate buffer (pH 6.8) at 37°C ± 1°C, with the 50 rpm stirring speed. Samples were withdrawn at proper interval 0.5min, 1min, 2min……5min. and proper sink condition was maintained. The samples were analyzed by UV-Spectrophotometer.

***In vitro* Disintegration time:** It was measured by dropping the tablet in 10ml measuring cylinder containing 6ml of phosphate buffer or simulated salivary fluid (pH 6.8) [23]. Time taken for complete disintegration was measured.

Marketed formulation of MDT's: The following table shows some commercially marketed mouth dissolving tablets [3];

MARKETED FORMULATION OF MDT'S

Trade name	Active drug	Manufacturer
Felden fast melt	Piroxicam	Pfizer Inc., NY, USA
Claritin redi Tab	Loratidine	Schering plough Corp., USA
Maxalt MLT	Rizatriptan	Merck and Co., NJ, USA
Zyprexia	Olanzapine	Eli lilly, Indianapolis, USA
Pepcid RPD	Famotidine	Merck and Co., NJ, USA
Zofran ODT	Ondansetron	Glaxo Wellcome, Middlesex, UK
Zoming-ZMT	Zolmitriptan	AstraZeneca,Wilmington, USA
Zeplar TM	Selegilline	Amarin Corp., London, UK
Tempra Quiclets	Acetaminophen	Bristol myers Squibb, NY, USA
Febrectol	Paracetamol	Prographarm,Chateauneuf, France
Nimulid MDT	Nimesulide	Panacea Biotech, New Delhi , India
Torrox MT	Rofecoxib	Torrent pharmaceuticals , India
Olanex instab	Olanzapine	Ranbaxy lab. Ltd. New-Delhi, India
Romilast	Montelukast	Ranbaxy lab. Ltd. New-delhi, India
Stemetil MD	Prochlorperazine maleate	Abbott Pvt. Ltd. Baddi, Solan HP.

CONCLUSION: The technologies described in this article demonstrate, how recent advances in the formulation development and processing technologies meet the efforts to achieve more sophisticated drug delivery system. Mouth dissolving tablets need to be formulated for pediatric, geriatric, psychotic patients, bedridden and for those who are busy in travelling and may not have to assess to water. The drugs delivered in MDT'^{S} may be absorbed in the pregastric sites of highly permeable buccal and mucosal tissues of the oral cavity and they may be suitable of low molecular weight and highly permeable drugs.

REFERENCES:

1. Kumar VD, Sharma I, and Sharma V: A comprehensive review on fast dissolving tablet technology, Journal of Applied Pharmaceutical Sciences 2011; 05(01):50-58.
2. Kaur T, Gill B, Kumar S, Gupta GD: Mouth Dissolving Tablets: A Novel Approach to Drug Delivery. International Journal of Current Pharmaceutical Research 2011; 03(1):1-7.
3. Arya A**,** Chandra A: Fast drug delivery system: A review. Scholars Research Library 2010; 02(02):350-361.
4. Ghosh T, Ghosh A, Prasad D: A review on new generation orodispersible tablets and its future prospective. International Journal of Pharmacy and Pharmaceutical Sciences 2011; 03(01):1-7.
5. Deshpande KB, Ganesh NS: Orodispersible tablets: An overview of formulation and technology. International Journal of Pharma and Bio sciences 2011; 02(01):726-734.
6. Nand P, Vashist N, Anand A, Drabu S: Mouth dissolving tablets: A novel drug delivery system. International Journal of Applied Biology and Pharmaceutical Technology 2010; 01(03): XX.
7. Bhowmik D, Chiranjib B, Krishnakanth, Pankaj, Chandria RM:Fast dissolving tablets: An overview. Journal of Chemical and Pharmaceutical Research 2009; 01(01):163-177.
8. Fu Y, Yang S, Jeong HS, Kimura S, and Park K: Orally fast disintegrating tablets: Developments, Technologies, Taste-Masking and Clinical Studies. Critical reviews ^{TM} in therapeutic drug carrier systems 2004; 21(6):433-475.
9. Manivannan R: Oral disintegrating tablets: A future compaction. International Journal of Pharmaceutical Research and Development 2009; 01(10):1-10.
10. Pawar PB, Mansuk AG, Ramteke KH, Sharma YP, Patil SN: Mouth dissolving tablet: A review. International Journal of Herbal Drug Research 2011; 01(02):22-29.
11. Reddy LH, Ghosh B, Rajneesh: Fast dissolving drug delivery systems: A review of the literature. Indian Journal of Pharmaceutical Sciences 2002; 64(4):331-336.
12. Panigrahi R, Behera S: A review on Fast dissolving tablets. Web med Central Quality and Patient Safety 2010; 1(09):1-15.
13. Chacko AJ, Jose S, Babu N, Lucille, Michelle M: Design and development of orodispersible tablets of Promethazine Theoclate using co-processed superdisintegrants and subliming materials. International Journal of Innovative Pharmaceutical Research 2010; 01(02):53-56.
14. Kumar R, Patil MB, Patil SR, Paschapur MS: Development and characterization of mouth-in-tablets of Haloperidol by sublimation technique. International Journal of Pharmacy and Pharmaceutical Sciences 2009;01(01):65-73.
15. Jain CP, Naruka PS: Formulation and Evaluation of fast dissolving tablets of Valsartan. International Journal of Pharmacy and Pharmaceutical Sciences 2009; 01(01):219-226.
16. Kulkarni SV, Kumar RP, Basavaraj, Someshwara RB, Ramesh B, Kumar AP:Efect of superdisintegrants on formulation of taste masked disintegrating Lisinopril tablets. International Journal of current Pharmaceutical Research 2011; 03(01):11-14.
17. Narmada GY, Mohini K, Prakash RB, Gowrinath DXP, Kumar KS: Formulation, Evaluation and Optimization of fast dissolving tablets containing Amlodipine Besylate by sublimation method. ARS Pharmaceutica 2009; 50(03):129-144.
18. Hindustan AA, Anuradha CM, Chitta SK, Kishore KRB, Jagadeesh KD: Novel approach in formulation and evaluation of mouth dissolving tablets of Ondansetron Hydrochloride**.** International Journal of Applied Biology and Pharmaceutical Technology 2010; 01(02):582-588.
19. Deshpande RD, Gowda DV, Vasanti S, Mahammed N, Maramwar DN: Design and evaluation of mouth dissolving tablets of Ebastine by sublimation technique**.** Scholars Research Library 2011; 03(04):193-199.

20. Venkatesh DN, Sankar S, Meyyanathan SN, Elango K: Design and development of Prochlorperazine maleate sustained release tablets: Influence of hydrophilic polymers on the release rate and *In vitro* evaluation. International Journal of Pharmaceutical Sciences and Nanotechnology 2010; 03(02):965-977.
21. Kohle SR, Choudhari PD, More DM: Development and evaluation of melt-in-mouth tablets by sublimation techniques. Internationa; Journal of Pharmaceutical Studies and Research 2011; 02(01):65-76.
22. Gudas GK, Manasa B, Rajesham VV, Kumar SK, Kumari JP: Formulation and Evaluation fast dissolving tablets of Chlorpromazine HCL. Journal of Pharmaceutical Science and Technology 2010; 02(01):99-102.
23. Metker V, Kumar A, Pathak N, Padhee K, Sahoo S: Formulation and evaluation of orodispersible tablets of Lornoxicam. International Journal of Drug Development and Research 2011; 03(01):281-285.

How to cite this article:
Chawla G and Jain N: Mouth Dissolving Tablets: An Overview. *Int J Pharm Res Sci*. 3(9); 2919-2925.