IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Research Article
January 2021 Vol.:20, Issue:2

Formulation and Characterization of Mouth Dissolving Tablets of Almotriptan Malate

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ISSN 2349-7203
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Submitted: 10 December 2020
Revised: 30 December 2020
Accepted: 20 January 2021

Keywords: MDT, Almotriptan malate, superdisintegrant, β-cyclodextrin

ABSTRACT

The objective of the work was to design mouth dissolving tablets of a drug meant for the management of the acute headache phase of migraine attacks. Tablets containing a complex of almotriptan malate with β-cyclodextrin were prepared by direct compression. After optimization of drug and β-CD ratio, the formula of MDT was developed by experimental designing and different formulations were prepared by direct compression method with the help of different superdisintegrants (Crospovidone (CP), Sodium starch glycolate (SSG), and Croscarmellose sodium (CCS)) in different concentration (1%, 3%, and 5%) and optimized based on *in-vitro* disintegration time, drug content, and drug release profile. Then the optimized batch M9 was further formulated and evaluated for pre and post-compression parameters. Stability study was performed according to ICH guidelines and the stability study was conducted at 40 °C ± 2°C/75% ± 5% relative humidity as per guidelines. Thus, after performing a stability study it was concluded that the formulated MDTs were stable as there were no appreciable changes in the critical parameters of formulation i.e. disintegration time, drug content, and drug release.

INTRODUCTION:

Mouth dissolving drug delivery system (MDDDS) is a new generation of formulations that combine the advantages of both liquid and conventional tablet formulations, and at the same time, offer added advantages over both the traditional dosage forms. They provide the convenience of a tablet formulation and also allow the ease of swallowing provided by a liquid formulation. MDDDS offers the luxury of much more accurate dosing than the primary alternative, oral liquids. This segment of the formulation is specially designed for dysphagic, geriatric, pediatric, bed-ridden, traveling, and psychotic patients who are unable to swallow or refuse to swallow conventional oral formulations. As they dissolve/disintegrate very fast when placed in the mouth, MDDDS are the most convenient dosage forms for dysphagic, pediatric and geriatric patients with swallowing problems. They do not require water for administration, this is a good alternative for travelers and bedridden patients. They simply vanish when placed in the mouth, so cannot be hidden in the mouth by psychotic patients. These products not only increase the patient's compliance but also fetch large revenues to manufacturers due to line extension of the existing formulation.

In the recent past, several new advanced technologies have been introduced for the formulation of mouth dissolving tablets (MDTs) with very interesting features, like extremely low disintegration time, exceptional taste-masking ability, pleasant mouthfeel, and sugar-free tablets for diabetic patients. The technologies utilized for the fabrication of MDDDS include lyophilization, molding, direct compression, cotton candy process, spray drying, sublimation, mass extrusion, nanonization and quick dissolve film formation. These techniques are based on the principles of increasing porosity and/or addition of super disintegrants and water-soluble excipients in the tablets. The formulations prepared from these techniques differ from each other based on the factors like mechanical strength of the final product, drug and dosage form stability, mouthfeel, taste, rate of dissolution of the formulation in saliva, rate of absorption from saliva, and overall drug bioavailability(Shukla et al., 2009 a).

MDT products have been developed for numerous indications ranging from migraines (for which rapid onset of action is important) to mental illness (for which patient compliance is important for treating chronic indications such as depression and schizophrenia).

MATERIALS AND METHODS:

The materials used for the preparation of mouth dissolving tablets were Almotriptan malate (Torrent Pharmaceutical Pvt limited, Ahmedabad), Beta–Cyclodextrin (Loba Chemical), Croscarmellose Sodium (Fisher scientific), Crospovidone (Finar scientific), and Sodium Starch Glycolate (Finar scientific). The instruments used for the preparation of mouth dissolving tablets were UV /Visible Spectrophotometer (Systronics, Ahmedabad), FTIR (Bucker, Germany), Dissolution Apparatus (EI laboratory, H.P), Rotatory evaporator (Perfit India Pvt. Ltd), Optical Microscope (Lyzer, Haryana), Micro-Centrifugation (REMI laboratory Mumbai), pH Meter (EI laboratory, H.P), Brookfield viscometer.

(PRO-II extra model, Brookfield viscometer, USA), Multi-station tablet machine (Khera Made, Delhi), Disintegration Apparatus (EI Laboratory, India), and Stability Chamber (Jyoti Instrument, Gwalior, India).

Preparation of Tablets Containing Complex of Almotriptan malate with β-CD

Tablet containing 50 mg of Almotriptan malate was prepared by direct compression method. Drug β-cyclodextrin complex equivalent to 50 mg and all the excipients except the lubricant were passed through a #20 mesh screen. The drug blend was prepared by mixing them manually in a polyethylene bag for10–12 min. The lubricant was added to this blend and mixed properly again for 2 min. All formulations were prepared according to the experimental design; varying concentrations of the disintegration-promoting agent (1, 3, and 5%), as shown in Table No. Powdered lubricated blend was compressed into a tablet by compression machine **(**Lachman et al., 1991; Late et al., 2009).

Evaluation of Optimized Tablets

Hardness test: Hardness is the force required to break a tablet in a diametric compression test. It was measured using a Monsanto tablet hardness tester. It is expressed in kg/cm^2. A significant strength of mouth dissolve tablet is difficult to achieve due to the specialized processes and ingredients used in the manufacturing. The limit of crushing strength for a mouth dissolve tablet is usually kept in a lower range to facilitate early disintegration in the mouth **(**Lachman et al., 1991**)**.

Friability test: Friability test is performed to determine the effect of friction and shocks, which may often cause the tablet to chip, cap or break. Hardness is not an absolute indicator

of strength, therefore another measure of a tablet's strength, Friability, is often measured. Friability of the tablet is determined using Roche 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 a height of 6 inches in each revolution. A pre-weighed sample of tablets was placed in the friabilator and was subjected to 100 revolutions. Tablets were reweighed after 100 revolutions. The friability (F) is given by the formula **(**Lachman et al., 1991**).**

$$F = \frac{W_{initial} - W_{final}}{W_{initial}} X100$$

Weight variation test: The weight variation test was done by weighing 20 tablets individually, calculating the average weight, and comparing the individual tablet weight to the average weight (Lachman et al., 1991).

Dispersion time test: MDT was added to 10 ml of PBS (pH=6.8) at 37± 2ºC. The time required for complete dispersion of a tablet was measured. This test was performed for 3 tablets and the average time taken for dispersion with standard deviation was recorded (Venkatlaxmi et al., 2009).

***In-vitro* drug release after dispersion**

To 10 ml of phosphate buffer solution, pH 6.8 one tablet was put and time required for complete dispersion was noted. Immediately after complete dispersion of the tablet, 1ml of the solution was withdrawn; suitably diluted, and filtered, then the amount of drug released after the dispersion of a tablet was checked UV spectrophotometrically at 272.0 nm (Venkatlaxmi et al., 2009).

Wetting time test: A piece of tissue paper folded twice was placed in a small Petri dish containing 6 ml of distilled water. A tablet was placed on the paper, and the time required for complete wetting was measured (Madgulkar et al., 2009).

Disintegration time test: The disintegration time was defined as the time necessary for the MDT to completely disintegrate until no solid residue remains. The time required for the disintegration of six MDTs, placed in each tube of disintegration test apparatus, was measured at 37 ± 2ºC using distilled water. A total of six tablets were tested for each

concentration, and the values reported are mean ± standard deviation **(**Lachman et al., 1991; Chandrasekhar et al., 2008).

Drug content uniformity test: Tablets were powdered and the blend equivalent to 50 mg of drug was weighed and dissolved in PBS pH 6.8. The solution was then filtered and diluted suitably. The drug content was then analyzed spectrophotometrically at 272 nm. The test was performed in triplicate (Lachman et al., 1991; Madgulkar et al., 2009).

***In-Vitro* dissolution study:** *In-vitro* dissolution study was performed in 900 ml phosphate buffer pH 6.8 using USP type II (paddle) apparatus at 50 rpm for 10 minutes (37 ± 0.5°C). Aliquots of the dissolution medium (1 ml) were withdrawn at specific time intervals (2, 4, 6, 8, and 10 min.) and replaced immediately with an equal volume of fresh medium. The samples were filtered and diluted with a suitable amount of phosphate buffer pH 6.8 and analyzed for drug content by measuring the absorbance at 272 nm. Drug concentration was calculated from the standard calibration curve and expressed as % cumulative drug dissolved (Lachman et al., 1991; Madgulkar et al., 2009).

RESULTS AND DISCUSSION:

Based on results revealed from optimization by employing experimental design, the M9 which contains 5% of crospovidone was found to be superior based on drug content, disintegration time, and *in-vitro* drug release.

Then the optimized batch M9 was further formulated and evaluated for pre and post-compression parameters.

The pre-compression test was performed on the following crucial factors like bulk density, tapped density, angle of repose, Hausner's ratio, and Carr's index, the results were found to be 0.42 ± 0.04 g/cm^3, 0.50 ± 0.05g/cm^3, 29·05 ± 0.19º, 15.97 ± 0.40% and 1.18 ± 0.05 respectively. Based on pre-compression parameters, it was found that the powder blend was possessed good flow properties and can be successfully compressed into tablets.

After the pre-compression test, the powder blend was compressed into tablets and it was evaluated based on post-compression analysis for various factors which include hardness, friability, weight variation, dispersion time, *in-vitro* drug release after dispersion, wetting time, disintegration time, drug content, and drug release.

Hardness was measured using Monsanto tablet hardness tester and it was found to be 3.4 ± 0.52 Kg/cm^{2}which showed that the tablet could maintain its physical integrity up to the ultimate user.

Friability was determined using Roche friabilator and it was found to be 0.77 ± 0.06 % which indicates that the tablet possesses sufficient mechanical strength that can resist the shock and abrasion and maintain its physical integrity.

Weight variation was determined using twenty tablets and it was found to be 2.5 % indicate content uniformity and showed that there was minimal variation in weight of the prepared tablets.

Dispersion time was found to be below 30 seconds indicates that the tablets can rapidly release the drug which can be available for dissolution.

In-Vitro drug release after dispersion was found to be 67.5 ± 2.21 % indicates that tablet immediately releases more than 60 % of the total drug present in approx. 1 minute. Based on the above study, tablet can be classified as an immediate release dosage form.

The wetting time of the tablet was found to be approx. 20 seconds which showed that the tablet rapidly absorbs the media and prepares itself for fast disintegration.

Disintegration time test revealed that tablet was disintegrated in approx. 25 seconds which showed that the tablet possesses an optimum concentration of superdisintegrant in it which allows rapid absorption of media and subsequent swelling and rapid disintegration of the tablet. Based on the above study prepared tablets can be classified as MDT.

The drug content of the formulation was determined and the tablet showed drug content 98.33 ± 0.67 % indicating the content uniformity and homogeneity in preparation.

An *in-vitro* drug release study was also performed. MDTs are designed to disintegrate and dissolve within few minutes along with the complete release of the drug for fast onset of action. The *in-vitro* drug release study revealed that the tablet was able to release approx. 85 % in 2 minutes and followed approx. 96 % release of drug in 8 to 10 minutes. Based on this study prepared tablets can be classified as MDT which can be able to release the drug rapidly.

Table No. 1: Ingredients used in the formulation of MDTs

Sr. No.	Ingredients	Status	Acceptable limits of ingredients
1.	Sodium starch glycolate (SSG)	Superdisintegrant	1-8 % w/w
2.	Croscarmellose sodium (CCS)	Superdisintegrant	0.5-5 % w/w
3.	Crospovidone (CP)	Superdisintegrant	1-5 % w/w
4.	Microcrystalline cellulose (MCC)	Directly compressible filler and disintegrant	5-15 % w/w (as disintegrant)
5.	Talc	Lubricant	0.25-10 % w/w
6.	Aerosil	Glidant	0.1-0.5 % w/w
7.	Mannitol	Sweetening agent and Diluent Direct compressible filler	10-90 % w/w

Table No. 2: Hardness of MDT

Sr. No.	Formulation batch No.	Hardness (Kg/cm^2)
1.	M9	3.4 ± 0.52

(±SD) (n=3)

Table No. 3: Friability (%) of MDT

Sr. No.	Formulation Batch No.	Friability (%)
1.	M9	0.77 ±0.06

(±SD) (n=3)

Table No. 4: Weight variation test

Sr. No.	Formulation Batch No.	Weight Variation
1.	M9	2.5%

Table No. 5: Dispersion time test

Sr. No.	Formulation Batch No.	Dispersion Time (second)
1.	M9	28.13±1.02

(±SD) (n=3)

Table No. 6: *In-vitro* drug release after dispersion

Sr. No.	Formulation Batch No.	% drug release
1.	M9	67.5±2.21

(±SD) (n=3)

Table No. 7: Wetting time of MDT

Sr. No.	Formulation Batch No.	Wetting Time (second)
1.	M9	20.18 ±2.0

(±SD) (n=3)

Table No. 8: Disintegration time of MDT

Sr. No.	Formulation Batch No.	Disintegration Time (second)
1.	M9	25.37 ± 1.77

(±SD) (n=3)

Table No. 9: Drug content uniformity test

Sr. No.	Formulation Batch No.	% Drug content
1	M9	98.33 ±0.67

(±SD) (n=3)

Table No. 10: Dissolution profile of MDT

Sr. No.	Time (min.)	% cumulative drug release of optimized batch (M9)
1.	0	0
2.	2	85.09 ± 2.20
3.	4	88.41 ± 1.72
4.	6	90.04± 0.92
5.	8	92.95 ± 1.34
6.	10	96.50 ± 1.87

(±SD) (n=3)

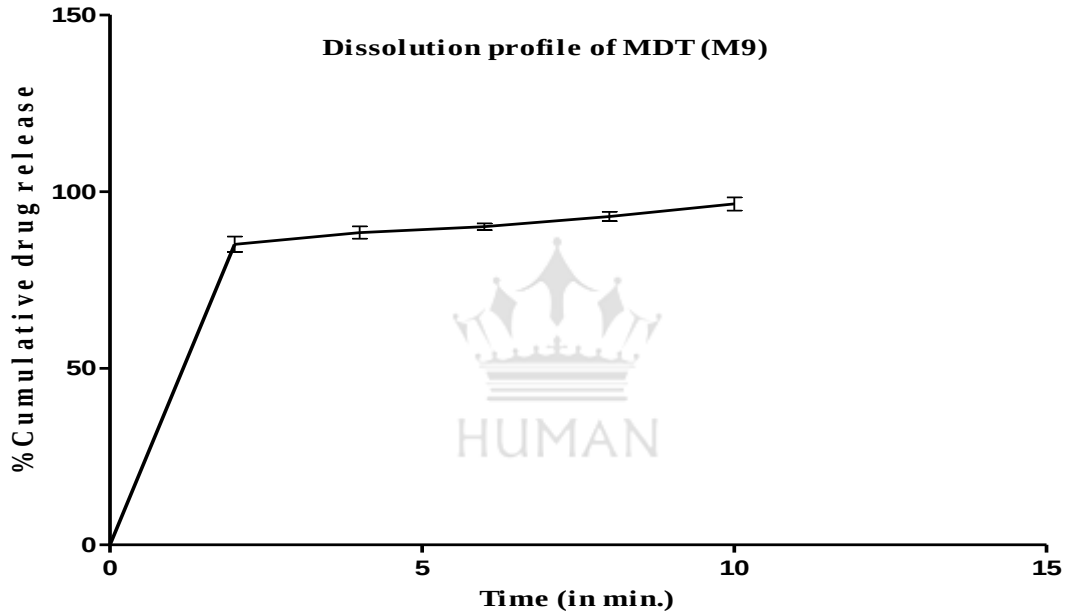

Figure No. 1: Dissolution profile of MDT (M9)

Acknowledgments:

The authors are grateful to Sri Satya Sai Institute of Pharmaceutical Sciences, Ram Krishna Dharmarth Foundation University, Bhopal for providing the research facilities.

REFERENCES:

1. Ansel HC, Popovich NG, Allen LV. Pharmaceutical Dosage Form and Drug Delivery. seventh ed., Lippincott Williams and Wilkins; 2002:196-225.
2. Aulton ME. Pharmaceutics the Science of Dosage form Design. second ed., Churchill Livingstone; 2002:113-120.
3. Bhowmik D, Krishnakanth CB. Fastdissolving tablet: an overview. J Chemi Pharm Res. 2009; 1(1): 163-177.

4. Deshmukh KR, Patel V,VermaS,Pandey AK. A review on mouth dissolving tablet techniques.IJRAP.2011; 2(1):66-74.
5. Indian Pharmacopoeia Volume 1. Indian Pharmacopoeia Commission. 2007:134-135,143,244.
6. KhemariyaP**,**Vaidya VD, Jadon RS, Mishra S, Shukla A. Preparation and evaluation of mouth dissolving tablets of meloxicam.Int J Drug Deliv.2010; 2:76-80.
7. Konapure SA, Chaudhari PS, Oswal RJ, Kshirsagar SS, Mouth dissolving tablets: An innovative technology, Int J App Bio Pharm Tech.2011; 2(1):496-503.
8. LachmanL,LiebermanHA,Kanig JL. The Theory and Practice of Industrial Pharmacy.Third ed., Varghese Publishing HouseBombay; 1991:171, 182-184, 296-330.
9. Madgulkar AR, Bhalekar MR, Padalkar RR. Formulation design and optimization of novel taste masked mouth-dissolvingtablets of tramadol having adequate mechanical strength. AAPS PharmSciTech.2009; 10(2):574-581.
10. Martin A,Physical pharmacy.Fourthed., Lippincott Williams and Wilkins: 212-237.
11. Pandey S,kumar B, Gupta A. A review on pharmaceutical application of cyclodextrins. IJPT.2010; 2(3): 281-319.
12. Patel AR and Vavia PR. Preparation and evaluation of taste masked famotidine formulation using drug/β-cyclodextrin/polymer ternary complexationapproach.AAPSPharmSciTech. 2008; 9(2):544-550.
13. Rao NG, Patel T, Gandhi S. Development and evaluation of carbamazepine fast dissolving tablets prepared with complex by direct compression technique. Asian J Pharm.2009:97-103.
14. Ratnaparkhi P, Mohanta GP, Upadhyay L. Review on: fast dissolving tablet. J Pharm Res. 2009, 2(1):5-11.
15. RaymondRC, Sheskar PJ, Rowe RC. Handbook of Pharmaceutical Excipients. ; Fifthed, Pharmaceutical Press London; 2006:132-134,212-220, 701-703.
16. Patel.H.A, Patel.J.K, Patel.K.N and Patel.R.R; "studies on formulation and in vitro evaluation of fast dissolving tablets of domperidone", Indian J Pharm Sci, Jan-April 2010; 2(1):470-476.
17. Bradoo.R; "Fast Dissolving Drug Delivery Systems", JAMA India, 2001; 4 (10), 27-31.
18. Kuchekar B. S, Badhan.C., and Mahajan, H. S; "Mouth dissolving tablets: A novel drug delivery system", Pharma Times, 2003, 35:7-9.
19. Bhardwaj.V, Shukla.V, Goyal.N, Salim.M.D and Sharma.P.K; "Formulation and evaluation of fast disintegrating sublingual tablets of amlodipine besylate using different superdisintegrants", Int J Pharmacy Pharm Sci, 2010; 2(3): 89-93.
20. The Merck index; "Encyclopedia of chemicals, drugs and biologicals", Merck research laboratory, 2006; 14th edition, 40.
21. Burton, W.N., Landy, S.H., Downs, K.E., Runken, M.C. The impact of migraine and the effect of migraine treatment on workplace productivity in the United States and suggestions for future research. Mayo Clin. Proc. 2009, 84 (5); 436–445.
22. Singh S, and Shah D. Development and Characterization of Mouth Dissolving Tablet of Zolmitriptan. Asian Pacific Journal of Tropical Disease. 2012, 2; S457-S464
23. http://www.drugs.com/ppa/almotriptan-malate.html
24. SharmaV, Choprahimanshu. Role of taste and taste masking of bitter drugs in pha-maceutical industries- an overview. Int J Pharm pharm Sci. 2010; 2(4):14-18.
25. Shukla D, Chakraborty S, Singh S, Mishra B. Mouth dissolving tablets I: an overview of evaluation techniques.Sci Pharm. 2009 a; 77:309–326.
26. Shukla D, Chakraborty S, Singh S, Mishra B. Mouth dissolving tablets II: an overview of evaluation techniques.Sci Pharm. 2009 b; 77:327–341.
27. Siddiqui N, Garg G, Sharma P. Fast dissolving tablets: preparation, characterization and evaluation: an overview. Int J Pharm Sci Rev Res. 2010; 4(2):87-94.
28. Singh R, Bharti N, Madan J, Hiremath SN. Characterization of cyclodextrin inclusion complexes – a review. J Pharm Sci Tech. 2010; 2 (3):171-183.
29. Sweetman SC, Martindale: The Complete Drug Reference. Thirty sixthed, Pharmaceutical Press; 2009: 94-95.