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Formulation and Evaluation of Mouth Dissolving Tablet of Almotriptan Malate

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ABSTRACT

Mouth dissolving tablet disintegrates and dissolves rapidly in the saliva, within a few seconds without the need of drinking water or chewing. A mouth dissolving tablet usually dissolves in the oral cavity within 15 seconds to 3 minutes. Almotriptan malate is an anti migraine drug with bitter taste and shows hepatic metabolism. In the present work, Mouth dissolving tablets of almotriptan malate were prepared by direct compression method using sodium starch glycolate and croscarmellose sodium as superdisintegrant with a view to enhance patient compliance and to avoid gastric dysmotility which is common with migraine drugs and for fast action of drug. The prepared batches of tablets were evaluated for hardness, friability, drug content uniformity, wetting time, water-absorption ratio and in-vitro dispersion time. Short-term stability studies on the promising formulation indicated that there are no significant changes in drug content and disintegration time.

Keywords: Almotriptan malate, Superdisintegrant, Sodium starch glycolate, Crosscarmellose sodium, Taste masking.

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INTRODUCTION

Despite of tremendous innovations in drug delivery, the oral route remains the preferred route for administration of therapeutic agents because of accurate dosage, low cost therapy, self-medication, non-invasive method and ease of administration leading to high level of patient compliance. The oral cavity is an attractive site for the administration of drugs because of ease of administration^[1].

Mouth dissolving tablets disintegrates and dissolves rapidly in the saliva, within a few seconds without the need of drinking water or chewing. A mouth dissolving tablet usually dissolves in the oral cavity within 15 seconds to 3 minutes. Most of the MDTs include certain super disintegrates and taste masking agents.

Recently, the European Pharmacopoeia adopted the term fast dissolving tablet for a tablet that disperses or disintegrates within a minute or second in the mouth before swallowing^[2].

Mouth dissolving tablets have a rapid dissolution and fast absorption which provide rapid onset of action. It provides good stability, accurate dosing, easy of manufacturing. Mouth dissolving tablets are made by a direct compression method using super Disintegrate as an important component.

MATERIALS AND METHOD

Materials

Almotriptan malate was obtained as a gift sample from MSN laboratories PVT. Ltd. (Hyderabad). Croscarmellose sodium was obtained as a gift sample from Maple biotech (Pune). Sodium starch glycolate purchased from Yarrow chem products (Mumbai). Microcrystalline Cellulose, Mannitol, Magnesium Stearate, Talc, Methanol, saccharin sodium and vanillin were purchased from Lobachem Pvt. Ltd. Potassium Dihydrogen Phosphate, Sodium hydroxide and Hydrochloric acid were purchased from Lobachem and Merck Pvt Ltd.

METHODS

Drug Characterization

Melting point determination

Capillary tube was taken and one end was sealed by heating. Capillary tube was filled with drug powder upto 2-3mm high. The capillary tube was putted inside melting point apparatus and temperature was increased slowly. The temperature was noted when the drug gets starts melting and again noted when drugs completely melted.

UV spectroscopy

About 25mg of pure almotriptan malate was weighed accurately and transferred to 250ml standard volumetric flask. It was dissolved in methanol then made up to the volume with the same methanol. This solution was sonicated for 10 min and it was further diluted with same solvent to

give a stock solution containing 100µg/ml of almotriptan malate. Baseline correction was performed using methanol and sample was scanned between the range of 200-400 nm and wavelength of maximum absorbance (λ max) was noted [3].

Calibration curve

Accurately weighed 25mg of Atorvastatin Malate was transferred into a 250ml volumetric flask & dissolved in methanol. Then sonicated for 10 minute and the volume was made up with methanol to obtain a 100µg/ml stock solution of Almotriptan Malate.

Solubility studies

Solubility of almotriptan malate and was determined in various mediums. A definite amount of almotriptan malate was dissolved in same amount of various mediums at room temperature. Further dilution was prepared and samples were examined on UV spectrophotometer [4].

Table 1: Solubility data of Almotriptan malate in different mediums:

S.no.	Solvent	Solubility (mg/ml) Mean±SD
1	Phosphate buffer pH 6.8	38.41±0.094
2	Distilled water	52.28± 0.11
3	0.1N HCL	5.42±0.042

FORMULATION OF TABLETS

Taste masking of drug

First mannitol was melted in a porcelain dish at 120°C on a hot plate. The drug Almotriptan malate was added and mixed properly, then immediately cooled in an ice bath. The solid dispersion was stored for 24 h then passed through 60# [5].

Experimental design

Mouth dissolving tablet of almotriptan malate was prepared using croscarmellose sodium and sodium starch glycolate as super disintegrants. Tablets were prepared by direct compression method. Nine batches were prepared by using the 5, 7.5, and 10% of super disintegrant. The weight of the tablet was constant to 100 mg. solid dispersion of drug and mannitol 37.5mg, equivalent to 6.25 mg of Almotriptan malate was taken for further tablet development.

Table 2 Composition of Mouth Dissolving Tablets

S.No.	Name of ingredient	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)	F7 (mg)	F8 (mg)	F9 (mg)
1	Drug+mannitol	37.5	37.5	37.5	37.5	37.5	37.5	37.5	37.5	37.5
2	Crosscarmellose sodium	5	7.5	10	5	7.5	10	5	7.5	10
3	Sodium starch glycolate	5	5	5	7.5	7.5	7.5	10	10	10
4	Microcrystalline cellulose	44	41.5	39	41.5	39	36.5	39	36.5	34
5	Saccharin sodium	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
6	Talc	2	2	2	2	2	2	2	2	2

7	Mg. stearate	2	2	2	2	2	2	2	2	2
8	vanillin	2	2	2	2	2	2	2	2	2
9	Total weight	100	100	100	100	100	100	100	100	100

Preparation of Tablets

Mouth dissolving tablet of almotriptan malate were prepared by direct compression method. Weighed all the ingredients accurately according to the formula. All the ingredients were mixed step by step with drug: mannitol complex and triturated for 15 minute and passed through sieve no. #60. Subsequently talc magnesium stearate and again mixed ^[6]. The powder was compressed by multi station tablet punching machine (Aidmach Pvt. Ltd.) with 6mm flat punch, B-tooling and corresponding dies.

EVALUATION OF TABLETS

Weight variation

The twenty tablets were selected randomly from every formulation and their average weight was determined. All Tablets were weighed individually and compared with average weight. If more than two tablets deviate from the range, retest 20 tablets and not more than 2 tablets should deviate from 40 tablets.

Thickness

Thickness of tablet was determined by using vernier calliper (Mitutoya, Model CD-6 CS, Japan).

Hardness

The hardness of the tablet was determined using Monsanto hardness tester apparatus (Sheetal Scientific Industries, Mumbai, India). Placed the tablet on the lower plunger and zero reading was taken from Monsanto tester scale. The range of Monsanto hardness tester is “0 to 20” kg. The knob was moved forward until the tablet breaks and the force required for breaking the tablet was noted. Three tablets from each formulation batch were tested randomly and the average reading noted.

Friability

Twenty tablets were weighed and placed in a Roche friabilator (Electrolab, India). Twenty reweighed tablets were rotated at 25 rpm for 4 min. The tablets were then dedusted and reweighed and the percentage of weight loss was calculated. The percentage friability of the tablets was measured as per the following formula,

$$\text{Percentage friability} = \frac{\text{Initial Weight} - \text{Final weight}}{\text{Initial Weight}} \times 100$$

Wetting time

Five tissue papers of 10 cm diameter were placed in a petridish with a 10 cm in diameter. Ten milliliters of water containing Eosin, a water-soluble dye, is added to petridish. A tablet was placed

carefully on the surface of the tissue paper. The time required to reach the water upper surface of the tablet was noted as a wetting time. The results are tabulated in table no.5.

Water absorption ratio

A piece of tissue paper folded twice was placed in a small petridish containing 10 ml of water. A tablet was put on the tissue paper and the time required for the water to diffuse from the wetted absorbent paper throughout the entire tablet was then recorded using a stopwatch.

The wetted tablets were the reweighed. The water absorption ratio and R was determined using following equation

$$R = 100 \times \frac{W_a - W_b}{W_b} \times 100$$

Where,

W_a = Weight of the tablet after absorption of water

W_b = Weight of the tablet before absorption of water

Disintegration Time

One tablet was introduced into each tube and disc was added to each tube. The assembly was introduced in the beaker containing phosphate buffer pH6.8. The apparatus operated until the tablet completely disintegrate. The time was noted down until the tablets completely disintegrate. The assembly was removed.

Dissolution Study

In vitro release of almotriptan malate from tablets was monitored by using 900 ml of simulated intestinal fluid, SIF (USP phosphate buffer solution, pH 6.8) at 37±0.5⁰C and 50 rpm using programmable dissolution tester [Paddle type, model TDT-08L, Electrolab, (USP), India]. 5 ml Aliquots were withdrawn at five minutes time intervals and were replenished immediately with the same volume of fresh buffer medium. Aliquots, following suitable dilutions, were assayed spectrophotometrically (UV- 1700, Shimadzu, Japan) at 227 nm.

RESULTS AND DISCUSSION

Mouth dissolving drug delivery is rapidly gaining acceptance as an important drug delivery technology. In such drug delivery, different dosage forms disintegrate rapidly in the patient's mouth within a minute and can be gulped easily without need of water. This rapid disintegration can be achieved by use of high levels of disintegrate and/or effervescent agents along with water soluble diluents. Hence, it offers increased patient compliance and convenience. Mouth dissolving tablet of almotriptan malate was formulated. Total nine batches were prepared for orodispersible formulation. All the formulations were subjected to evaluation, Tablet weight varied from 97 to 103 mg, and thickness 2.4 to 2.9 mm. All the tablets exhibited friability values between 0.6 to 0.8

all tablets disintegrated in less than 1 minute. The drug released at the time interval of 30 minutes was found to be upto 97.2% of batch F8.

Table 3 Evaluation of Flow properties of powder (Drug excipient mixture)

Formulation	Bulk density (gm/ml) Mean±SD	Tapped density(gm/ml) Mean±SD	Carr's index (%) Mean±SD	Angle of repose (o) Mean±SD	Hausner' ratio Mean±SD
F1	0.360±0.003	0.422±0.001	14.67±0.498	21.26±0.115	1.16±0.005
F2	0.421±0.001	0.487±0.002	13.43±0.416	23.23±0.986	1.15±0.005
F3	0.372±0.000	0.428±0.002	13.62±0.057	22.50±0.449	1.14±0.005
F4	0.400±0.005	0.464±0.001	14.32±0.871	21.95±0.682	1.15±0.005
F5	0.385±0.001	0.445±0.001	13.40±0.440	23.46±0.611	1.15±0.005
F6	0.419±0.001	0.481±0.002	12.90±0.624	25.31±0.695	1.14±0.005
F7	0.408±0.001	0.470±0.001	13.21±0.173	21.74±0.773	1.14±0.005
F8	0.428±0.004	0.492±0.002	12.88±0.453	23.03±0.950	1.14±0.005
F9	0.457±0.001	0.496±0.003	12.22±0.305	25.33±0.577	1.13±0.005

Table 4 Determination of physicochemical properties of Mouth dissolving tablet

Formulation	Weight variation(mg) Mean±SD	Hardness (Kg/cm2) Mean±SD	Thickness (mm) Mean±SD	Friability (%) Mean±SD
F1	102.67±1.92	4.3±0.14	2.5±0.045	0.81
F2	101.85±2.14	4.1±0.31	2.7±0.069	0.79
F3	99.56±6.45	3.9±0.25	2.8±0.057	0.82
F4	103.15±3.21	3.7±0.19	2.9±0.038	0.77
F5	98.25±5.12	3.8±0.34	2.4±0.027	0.69
F6	98.45±4.65	3.3±0.22	2.7±0.021	0.72
F7	101.41±3.79	3.0±0.27	2.6±0.032	0.76
F8	100.34±2.16	3.1±0.21	2.5±0.058	0.61
F9	97.82±6.12	2.8±0.32	2.6±0.062	0.86

Table 5: Other Evaluation parameters

Formulations	Disintegration Time (sec) Mean±SD	Drug Content (%) Mean±SD	Wetting time (sec) Mean±SD	Water absorption Ratio (%) Mean±SD
F1	32.35±0.284	94.6±1.227	39.58±0.656	23.64±3.65
F2	33.52±0.462	95.46±0.659	41.52±0.559	25.45±2.95
F3	31.19±0.266	95.85±0.857	38.12±0.235	26.19±4.26
F4	28.51±0.307	96.12±0.622	40.45±0.345	29.35±3.86
F5	30.30±0.435	96.64±0.526	38.28±0.612	30.54±2.68
F6	28.40±0.255	97.18±0.451	36.57±0.456	32.56±1.85
F7	29.45±0.412	98.56±0.957	32.65±0.359	36.45±3.43
F8	27.10±0.231	98.91±0.352	30.43±0.235	37.35±2.62
F9	28.52±0.354	98.12±0.564	31.26±0.653	41.65±1.25

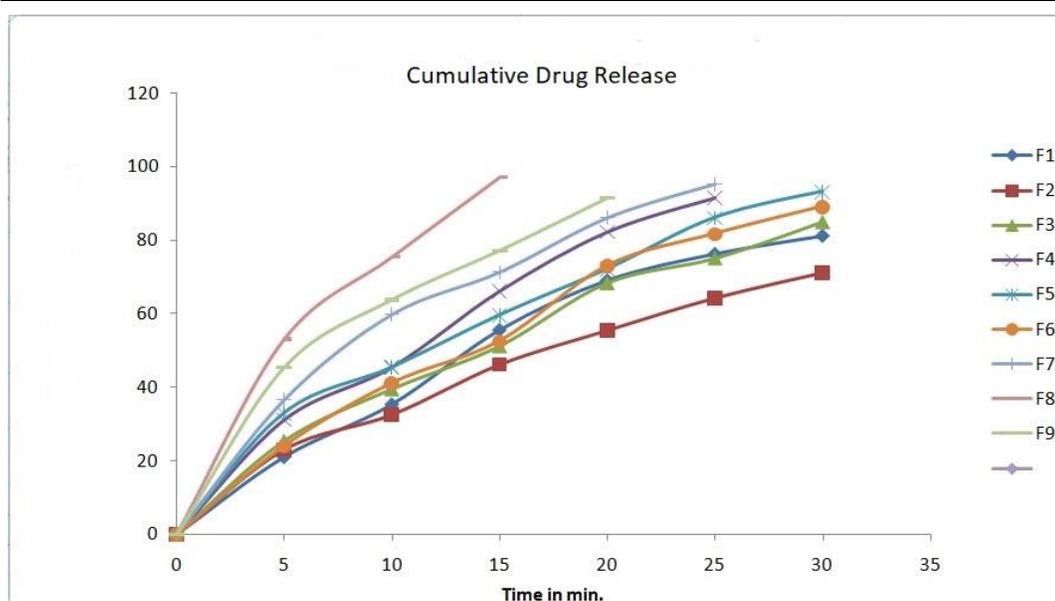
Table 6 *In vitro* drug release study

Time in (min)	% Cumulative drug Release (Mean±SD)								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
5	21.1±0.23	23.1±0.12	25.5±0.26	31.2±0.41	33.1±1.20	34.1±0.89	39.6±0.86	53.2±0.38	45.5±0.45
10	35.4±	32.6±	39.6±	45.5±	45.5±	48.2±	59.8±	75.5	63.9±

	0.35	0.26	0.34	0.39	0.95	0.62	0.93	±0.32	0.62
15	55.6±	46.2±	51.3±	66.2±	59.7±	62.6±	71.3±	97.2	77.3±
	0.21	0.15	0.62	0.23	0.85	0.66	1.12	±0.12	0.74
20	69.1±	55.5±	68.5±	82.3±	72.2±	73.1±	86.1±		91.6±
	0.12	0.29	0.21	0.39	1.31	0.76	0.86		0.83
25	76.3±	64.3±	75.2±	91.6±	86.2±	81.8±	95.3±		
	0.32	0.13	0.36	0.29	1.41	0.87	0.95		
30	81.2±	71.2±	85.1±		93.3±	89.2±			
	0.11	0.25	0.65		0.93	0.79			

Table 7 Stability studies

Time	Color	Disintegration in (sec)			%Drug release		
		2-8°C	Room temp.	40±2°C	2-8°C	Room temp.	40±2°C
Initial day	White	27.10	27.10	27.10	97.2	97.2	97.2
15 days	White	27.19	27.15	27.17	97.12	97.14	97.11
30 days	White	27.26	27.20	27.25	97.05	97.08	97.02

Figure 1: *In vitro* drug release of mouth dissolving tablet

CONCLUSION

The present study was carried out to prove that Mouth dissolving tablet of Almotriptan malate can be formulated. The tablets formulated for rapid onset of action for treatment of acute migraine.

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