International Journal of Pharmaceutics & Drug Research
ISSN: 2347-6346
Available online at http://ijpdr.com

Original Research Article

FORMULATION AND EVALUATION OF BUCCAL MUCOADHESIVE TABLETS OF RIZATRIPTAN

Brij Kishor* Jogendra Singh, Muraree Lal, Sapna Avinash Kondalkar, Deepak Tripathi, Avinash K Kondalkar
Sun Institute of Pharmaceutical Education & Research (SIPER), Lahar

***Correspondence Info:**
Brij Kishor
Sun Institute of Pharmaceutical Education & Research (SIPER), Lahar
Email: brijkishor@gmail.com

***Article History:**

Received: 19/05/2023
Revised: 11/06/2023
Accepted: 08/06/2023

ABSTRACT

Migraine, defined as headache occurring on 15 days per month for more than 3 months with migraine symptoms on 8 days per month is a debilitating ailment affecting 0.5% to 5% of the general population. So, The ideal properties of medications related to migraine is the dosage form must be fast dissolving and avoid first pass metabolism Mucoadhesive buccal films provide several distinct advantages, including their small thickness, ease of administration, direct systemic absorption followed by a prolonged effect, and both local and systemic effects. The goal of this study was to create and test a Rizatriptan mucoadhesive for an anti-migraine effect. The mucoadhesive tablets were evaluated for a series of parameters such as hardness, thickness, weight variation, friability, drug content, in vitro swelling study, in mucoadhesive strength, and in-vitro drug release study. Results showed that maximum drug content of 99.85±0.23 is present in F5 formulation. The thickness & hardness for F5 was seen to be 3.14±0.07mm & 4.3±0.2 kg/cm^2. The weigh variation &friability for F5 was noted to be 249±4mg & 0.825±0.047% respectively. At 12 hrs maximum swelling index of 106.65 is observed in F5 again. The *In vitro* drug release study of buccal tablet suggest that % Cumulative Drug Release for F5 was seen 99.78% which is highest among all formulations. When the regression coefficient values of were compared, it was observed that 'r2' values of Korsmeyer-Peppas was maximum i.e. 0.967. In conclusion these Rizatriptan mucoadhesive tablets appear promise as a controlled drug delivery strategy, which can lead to improved bioavailability and therapeutic efficacy.

Keywords: Migraine, Headache, Buccal drug delivery, Mucoadhesive tablet, Rizatriptan, Bioavailability, Controlled drug release

INTRODUCTION:

Migraine is a common chronic headache illness characterised by repeated attacks lasting 4-72 hours, having a pulsing quality, being moderate to severe in severity, being increased by normal physical activity, and being associated with nausea, vomiting, photophobia, or phonophobia. It has been dubbed the "seventh disabler" because to its significant impact on patient quality of life (QOL).It is the most common cause of headache in children and adolescents. The study of migraine in the paediatric population is crucial due to the stress it places on children and their families, as well as the diagnostic and therapeutic challenges posed by diverse phenotypes and probable differential diagnoses.

The ideal properties of medications related to migraine is the dosage form must be fast dissolving and avoid first pass metabolism (Haan *et al*., 2004; Natoli *et al*., 2010).

Buccal drug delivery, as an alternative to oral drug administration, is gaining popularity due to numerous advantages such as good accessibility, epithelial robustness, easy removal of dosage form in case of need, relatively low enzymatic activity, preventing drug degradation in the gastrointestinal tract, and avoiding hepatic first-pass metabolism. Buccal medication administration dosage forms include buccal pills, buccal patches, sticky gels, and so on. An ideal buccal medication delivery device should have high bioadhesive characteristics in order to remain in the oral cavity for the desired duration (Verma *et al*., 2011).

The oral mucosa has several features that make it an appealing site for drug administration, but it also presents significant problems to researchers, prompting them to investigate novel delivery ways to address these challenges. Mucoadhesive buccal films provide several distinct advantages, including their small thickness, ease of administration, direct systemic absorption followed by a prolonged effect, and both local and systemic effects (Ahuja *et al.*, 1997).

Because of the versatility of the manufacturing processes, mucoadhesive film release can be oriented either towards the buccal mucosa or towards the oral cavity; in the latter case, it can provide controlled release of the drug via GI tract administration or absorption in blood via mucosa.

Rizatriptan is indicated for the acute treatment of diagnosed migraine with or without aura. Rizatriptan is not indicated for the prophylactic therapy of migraine nor the treatment of cluster headache. In Canada, rizatriptan is approved in adults.In the US, the oral tablet formulations are used in patients six years of age and older and the oral film formation is approved for patients 12 years of age and older weighing 40 kg or more (Wellington and Plosker, 2002). The goal of this study was to create and test a Rizatriptan mucoadhesive table that would initially show quick release and afterwards prolonged release of the drug, thereby satisfying the need for an anti-migraine effect. This was accomplished through the use of several mucoadhesive polymers and medication release modifiers.

MATERIALS AND METHODS

Chemicals

HPMC K-4Carbopol, Na Alginate, Magnesium stearate, Talc, Lactose were obtained from Loba chemicals Pvt Ltd Mumbai. Ethanol, Methanol & Distilled water were obtained from Merk India. All chemicals & reagents used were of laboratory grade.

Preparation of Rizatriptan buccal tablet

Direct compression was taken after to manufacture the buccal tablets of Rizatriptan (Nafee *et al.*, 2004 Kesavan *et al.*, 2010).

Evaluation of tablets

All the tablets were evaluated for following various parameters which includes;

General Appearance

Five tablets from various batches were randomly selected and organoleptic properties such as color, odor, taste, shape, were evaluated. Appearance was judged visually.

Thickness and diameter

Thickness and diameter of tablets were determined using Vernier caliper. Five tablets from each batch were used, and an average value was calculated (Bookya *et al.*, 2018).

Drug content

Twenty tablets were taken and amount of drug present in each tablet was determined. The tablets were crushed in a mortar and the powder equivalent to 10mg of drug was transferred to 10ml standard flask. The powder was dissolved in 5 ml of phosphate buffer pH 6.8 and made up to volume with of phosphate buffer pH 6.8. The sample was mixed thoroughly and filtered through a 0.45µ membrane filter. The filtered solution was diluted suitably and for drug content by UV spectrophotometer using of phosphate buffer pH 6.8 as blank.

Hardness

For each formulation the hardness of five tablets was resolved utilizing the Monsanto hardness tester (Cadmach).

Friability

The friability of sample of 10 tablets was estimated utilizing a Friability tester (Electro Lab). Ten tablets were weighed, rotated at 25 rpm for 4 minutes. Tablets were reweighed after removal of fines (dedusted) and the percentage of weight loss was calculated (Chaudhari S, Harsulkar, 2012).

Uniformity of weight

Twenty tablets were randomly selected from each batch individually weighed, the average weight and standard deviation of 20 tablets was calculated.

Swelling Index

Swelling study of individual polymers and combinations was carried out using eight-stage USP type 1 Dissolution Test Apparatus (Lab India, DS 8000) at 50 rpm, and phosphate buffer pH 6.8 was used as medium, and the temperature was maintained at 37 ± 0.5°C. Weight of individual tablet was taken prior to the swelling study (W_1). The tablet was kept in a basket. The weight of tablet was taken at time interval of 2, 4, 8, 12 hours (W_2). Percent hydration (swelling index) was calculated using the following formula:

Swelling index = $(W_2 - W_1) \times 100/W_2$,

Where W_1 is the initial weight of tablet and W_2 is the weight of hydrated tablet

Dissolution rate studies

In vitro drug release of the sample was done using USP-type II dissolution apparatus (Paddle type). The dissolution medium, 900 ml phosphate buffer pH 6.8 was set into the dissolution flask maintaining the temperature of 37 ± 0.5^0C and rpm of 75. One Rizatriptan tablet was set in every container of dissolution apparatus. The mechanical assembly was permitted to keep running for 12 hours. Sample measuring 5 ml were pulled back after each 1 hour up to 2 hours using 10ml pipette.

The new disintegration medium (37^0C) was supplanted each time with a similar amount of the sample and takes the absorbance using spectroscopy.

Table 1: Various formulations of buccal tablets of Rizatriptan

Excipients (mg)	F1	F2	F3	F4	F5	F6
Rizatriptan	10	10	10	10	10	10
HPMC K-4	25	50	75	25	50	75
Carbopol	-	-	-	25	50	75
Na Alginate	25	25	25	25	25	25
Magnesium stearate	10	10	10	10	10	10
Talc	10	10	10	10	10	10
Lactose	170	145	120	145	95	45
Total Weight	250	250	250	250	250	250

Table 2: Result of pre-compression properties of Rizatriptan

F. Code	Bulk density(gm/ml)	Tapped density(gm/ml)	Compressibility index	Hausner ratio
F1	0.332	0.445	25.393	1.340
F2	0.325	0.436	25.459	1.342
F3	0.336	0.442	23.982	1.315
F4	0.342	0.453	24.503	1.325
F5	0.327	0.436	25.000	1.333
F6	0.335	0.447	25.056	1.334

Table 3: Results of post compression properties of Rizatriptan buccal tablets

Formulation code	Thickness (mm)	Hardness (kg/cm2) n=3	Weight variation (mg) n=3	Friability (%) n=3	Drug content (%) n=3
F1	3.12±0.09	4.5±0.2	250±5	0.754±0.015	98.85±0.23
F2	3.15±0.10	4.7±0.3	255±4	0.658±0.023	98.78±0.21
F3	3.16±0.08	4.6±0.3	248±5	0.821±0.041	99.12±0.25
F4	3.11±0.09	4.5±0.4	250±2	0.756±0.036	98.65±0.14
F5	3.14±0.07	4.3±0.2	249±4	0.825±0.047	99.85±0.23
F6	3.12±0.08	4.2±0.04	251±3	0.814±0.031	98.62±0.17

Table 4: Results of Swelling Index of Rizatriptan buccal tablets

Formulation Code	% Swelling Index			
	2 hrs.	4 hrs.	8hrs.	12hrs.
F1	23.65	48.85	68.85	75.56
F2	29.95	49.98	70.12	79.98
F3	30.25	50.23	73.32	83.12
F4	29.95	52.32	74.45	81.12
F5	36.65	62.23	82.26	106.65
F6	30.25	58.89	78.84	95.56

Table 5: *In-vitro* drug release study of buccal tablets

Time	% Cumulative Drug Release					
(hr)	F1	F2	F3	F4	F5	F6
0.5	43.25	39.98	36.65	32.25	23.32	21.12
1	55.65	53.32	45.65	42.23	35.65	26.65
1.5	65.65	63.32	58.98	51.56	46.52	38.89
2	83.32	78.85	76.65	68.98	55.42	46.65
3	98.85	88.65	84.45	78.85	65.44	58.98
4		99.12	96.65	86.65	73.32	65.56
6			99.12	96.65	86.65	69.98
8				99.05	93.32	73.32
12					99.78	88.98

Table 6: *In-vitro* drug release data for optimized formulation F5

Time (h)	Square Root of Time(h)$^{1/2}$	Log Time	Cumulative*% Drug Release	Log Cumulative % Drug Release	Cumulative % Drug Remaining	Log Cumulative % Drug Remaining
0.5	0.707	-0.301	23.32	1.368	76.68	1.885
1	1	0	35.65	1.552	64.35	1.809
1.5	1.225	0.176	46.52	1.668	53.48	1.728
2	1.414	0.301	55.42	1.744	44.58	1.649
3	1.732	0.477	65.44	1.816	34.56	1.539
4	2	0.602	73.32	1.865	26.68	1.426
6	2.449	0.778	86.65	1.938	13.35	1.125
8	2.828	0.903	93.32	1.970	6.68	0.825
12	3.464	1.079	99.78	1.999	0.22	-0.658

Table 7: Regression analysis data of Rizatriptan buccal tablets

Batch	Zero Order	First Order	Higuchi	Korsmeyer-Peppas
	r^2	r^2	r^2	r^2
F4	0.834	0.934	0.949	0.967

RESULTS AND DISCUSSION

The pre-compression properties of Rizatriptan was first performed for all the six formulations. The bulk density varied from 0.325 to 0.342 gm/ml. The range of tapped density for all six formulations determined to be 0.436 to 0.453 gm/ml. The Compressibility index extends from 23.982 to 25.549. The Hausner ratio varied from 1.325 to 1.342. The result of of post compression properties revealed that maximum drug content of 99.85±0.23 is present in F5 formulation. The thickness & hardness for F5 was seen to be 3.14±0.07mm & 4.3±0.2 kg/cm^2. The weigh variation &friability for F5 was noted to be 249±4mg & 0.825±0.047% respectively.

At 12 hrs maximum swelling index of 106.65 is observed in F5 again. The swelling profiles show the incorporation of water into the tablet matrix, resulting in an increase in weight. It has been found that the swelling condition of the polymer (in the formulation) is critical for its bioadhesive behaviour. Adhesion occurs quickly after swelling begins, but the link created between the mucosal layer and the polymer is weak. The degree of hydration increases the adhesion until over-hydration causes an abrupt decline in adhesive strength due to disentanglement at the polymer/tissue interface.

In vitro drug release tests for F1 through F6 formulations were carried out usingn dissolution media and detecting drug concentration UV spectrophotometrically nm. The experiments lasted 12 hours.

The *In vitro* drug release study of buccal tablet suggest that % Cumulative Drug Release for F5 was seen 99.78% which is highest among all formulations. When the regression coefficient values of were compared, it was observed that ‘r2’ values of Korsmeyer-Peppas was maximum i.e. 0.967 hence indicating drug release from formulations was found to follow Korsmeyer-Peppas kinetics.

CONCLUSION

We discovered that the medicine Rizatriptan and polymers utilised in the study were compatible with each other. The created formulations were found to have certain similarities in their general look, thickness, weight variation, and ability to endure friability. However, they differed in terms of hardness, in vitro swelling, and in vitro drug dissolution.

Analysing the findings revealed that Formulation F5, which contains high quantities of polymers (HPMC K4), performs better and has the necessary degree of hardness, long residence period, and greatest drug release profile. Korsmeyer's Peppas plot revealed that diffusion was the specific mechanism of drug release.

DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

REFERENCES

- Haan, J., Hollander, J. & Ferrari, M.D. (2007) Migraine in the elderly: A review. *Cephalalgia*, 27, 97–106
- Natoli, J.L., Manack, A., Dean, B., Butler, Q., Turkel, C.C., Stovner, L. & Lipton, R.B. (2010) Global prevalence of chronic migraine: A systematic review. *Cephalalgia*, 30, 599–609

- Verma, S., Kaul, M., Rawat, A. & Saini, S. (2011) An overview on buccal drug delivery system. *International Journal of Pharmaceutical Sciences and Research*, 2, 1303.
- Ahuja, A., Khar, R.K. & Ali, J. (1997) Mucoadhesive drug delivery systems. *Drug Development and Industrial Pharmacy*, 23, 489–515
- Wellington, K. & Plosker, G.L. (2002) Rizatriptan: An update of its use in the management of migraine. *Drugs*, 62, 1539–1574
- Nafee, N.A., Ismail, F.A., Boraie, N.A. & Mortada, L.M. (2004) Mucoadhesive delivery systems. I. Evaluation of mucoadhesive polymers for buccal tablet formulation. *Drug Development and Industrial Pharmacy*, 30, 985–993
- Kesavan, K., Nath, G. & Pandit, J.K. (2010) Sodium alginate based mucoadhesive system for gatifloxacin and its in vitro antibacterial activity. *Scientia Pharmaceutica*, 78, 941–957
- Madgulkar, A., Kadam, S. & Pokharkar, V. (2009) Development of buccal adhesive tablet with prolonged antifungal activity: Optimization and ex vivo deposition studies. *Indian Journal of Pharmaceutical Sciences*, 71, 290–294
- Padmaja, B., Satla, S.R. & Raparla, R. (2018) Formulation development and evaluation of candesartan buccal tablets. *International Journal of Pharmaceutical Sciences and Research*, 9, 3827–3832.
- Chaudhari, S. & Harsulkar, A. Design and in-vitro evaluation of mucoadhesive buccal tablets of carvedilol. *International Journal of Pharmacy and Technology*. Res (2012), 4, 1827–1833.
- Wagner, J.G. (1969) Interpretation of percent dissolved-time plots derived from in vitro testing of conventional tablets and capsules. *Journal of Pharmaceutical Sciences*, 58, 1253–1257
- Gibaldi, M. & Feldman, S. (1967) Establishment of sink conditions in dissolution rate determinations: Theoretical considerations and application to non disintegrating dosage forms. *Journal of Pharmaceutical Sciences*, 56, 1238–1242
- Higuchi, T. (1963) Mechanism of sustained-action medication: Theoretical analysis of rate of release of solid drugs dispersed in solid matrices. *Journal of Pharmaceutical Sciences*, 52, 1145–1149