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Original Article

Formulation and characterization of mouth dissolving mucoadhesive buccal film of Zolmitriptan

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ABSTRACT: Fast dissolving buccal film drug delivery system is an alternative to tablets, capsules, and syrups for pediatric and geriatric patients who experience in difficulties of swallowing traditional oral solid dosage forms. It improves the efficacy of API by dissolving within minute in oral cavity after the contact with less saliva as compared to fast dissolving tablets, without chewing and no need of water for administration. Oral films provide better drug utilization by avoiding the first pass metabolism, enhance drug bioavailability. Fast dissolving buccal films of zolmitriptan were prepared by solvent casting method using Polymers (E4, E10, E15) in different ratio as film forming agent, PEG 400 as plasticizer, Tween 80 as permeation enhancer, glycerin as surfactant.

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INTRODUCTION

Buccal delivery of drug, as an alternative to the oral route of drug administration, is a subject of growing interest because of its numerous advantages such as good accessibility, robustness of epithelium, facile removal of dosage form in case of need, relatively low enzymatic activity, prevent drug degradation in gastrointestinal tract and avoid hepatic first-pass metabolism. There are various dosage forms for buccal drug delivery like buccal tablets, buccal patch, adhesive gels etc.

A suitable buccal drug delivery system should possess good bioadhesive properties, so that it can be retained in the oral cavity for desired duration. Bioadhesive polymers have been used extensively for use in buccal drug delivery systems like polyacrylic acid, polycyanoacrylate, various grades of Hydroxypropyl methyl cellulose, etc. The development of newer excipients for potential use as mucoadhesive polymers continues to be of interest.

In addition, it should release the drug in a unidirectional way towards the mucosa, in controlled and predictable manner, to elicit the required therapeutic response. This unidirectional drug release can be achieved by using bilayer devices using polymers like Ethyl cellulose, carbopol, magnesium separate, polycarbophil, etc. [1].

Zolmitriptan is 5-HT1receptor agonist used in the treatment of migraine. Migraine is a mysterious disorder characterised by pulsating headache, usually restricted to one side, which comes in attacks lasting 4-48 hours and is often associated with nausea, vomiting, sensitivity to light and sound, vertigo, loose motion and other symptoms [2].

The half-life of the Zolmitriptan is 2.5 to 3 hrs and it undergoes hepatic metabolism, the absolute oral bioavailability is about 40-50%. Bioavailability of drug in film dosage form is greater than the convectional dosage form [3].

Among the various transmucosal routes, buccal mucosa has excellent accessibility, an expanse of smooth muscle and relatively immobile mucosa, hence suitable for administration of retentive dosage form. Direct access to the systemic circulation through the internal jugular vein bypasses drugs from the hepatic first pass metabolism leading to high bioavailability [4]. It had been a great challenge to the pharmaceutical sciences in order to enhance localised drug delivery or to deliver 'difficult' molecules (proteins and oligo-nucleotides) into the systemic circulation. Mucoadhesive systems remain in close contact with the absorption tissue, the mucous membrane releasing the drug at the action site leading to increase in bioavailability [5].

Figure 1: Mucoadhesive film

Hence, zolmitriptan is a suitable drug for buccal dosage forms and may provide a better therapeutic profile than oral route. In the present investigation, Hydroxy propyl methyl cellulose (HPMC) is one the polymers which is having good mucoadhesive property so therefore various formulations were developed by using release rate controlling and gel forming polymers like HPMC E4M, HPMC E10M, HPMC E15M, Sodium phosphate monobasic dehydrate, Glycerin, Polyethylene 200 & 400, tween 60 and tween 80 was used as plasticizer and permeation enhancer respectively. The prepared patches were evaluated for various parameters related to delivery.

In the proposed research work, we have prepared buccal patches with the aim to achieve: Greater therapeutic efficacy, avoidance of gastrointestinal disturbances and improve the bioavailability of zolmitriptan by avoiding hepatic metabolism, and improve patient compliances.

MATERIAL AND METHODS

Material: Zolmitriptan was obtained as gift sample from Ross & Robinz Bio Tech in Solan, Himachal Pradesh. HPMC E4M, HPMCE10M, HPMC E15M were purchased from Colorcon, Mumbai. Sodium phosphate monobasic dehydrate were obtained as gift sample from Rankem, India and Glycerin Rohit Pharma, Lucknow, respectively. Polyethlene glycol 200 were purchased from Thomas Baker chemical Pvt. New Delhi. Polyethylene glycol 400 and tween 80 are obtained from S.D. Fine chemical limited, Bangalore.

Method: Fast dissolving buccal films are preferably formulated using the solvent casting method, whereby the water soluble ingredients are dissolved to form a clear viscous solution and the drug along with other excipients is dissolved in suitable solvent then both the solutions are mixed and stirred and finally casted in to the Petri plate and dried.

Table 5: Formulation Chart

Formulation	Drug (mg)	HPMC E4 (mg)	HPMC E10 (mg)	HPMC E15 (mg)	Glycerin (ml)	Tween 80 (ml)	PEG 400 (ml)	Buffer	Water
F1	150	150	-	-	0.3	-	0.4	q.s.	q.s.
F2	150	-	150	-	0.3	-	0.4	q.s.	q.s.
F3	150	-	-	150	0.3	-	0.4	q.s.	q.s.
F4	150	75	-	75	0.3	-	0.4	q.s.	q.s.
F5	150	-	75	75	0.3	-	0.4	q.s.	q.s.
F6	150	150	-	-	0.3	0.7	0.4	q.s.	q.s.
F7	150	-	150	-	0.3	0.7	0.4	q.s.	q.s.
F8	150	-	-	150	0.3	0.7	0.4	q.s.	q.s.
F9	150	75	-	75	0.3	0.7	0.4	q.s.	q.s.
F10	150	-	75	75	0.3	0.7	0.4	q.s.	q.s.

Figure 2: Mucoadhesive buccal film

Evaluation of Mucoadhesive buccal film:

Weight variation: For evaluation of patch weight, three patches of every formulation is selected randomly and individual weight of each 1x1cm patch was taken on digital balance. The average weight was calculated [6-9].

Film thickness: Thickness of the film is measured by using screw gauge with a least count of 0.01 mm at different places on the film. The thickness of the film was measured at three different places and the average of thickness is measured [10-13].

Surface pH: For determination of surface pH three patches of each formulation is allowed in contact with 1ml of distilled water. The surface pH was noted by bringing a combined glass electrode or pH paper near the surface of patches and allowing equilibrate for 1 min. A mean of three reading is recorded [14-17].

Folding endurance: Folding endurance of the film is determined by repeatedly folding one film at the same place till it broke, which was considered satisfactory to reveal good films properties. The number of times of films could be folded at the same place without breaking gave the value of the folding endurance. This test was done on randomly selected three films from each formulation [18-21].

Drug content uniformity: This parameter was determined by dissolving film of 1 × 1cm diameter containing drug in 50 ml simulated salivary fluid with occasional shaking. Filtration was carried out to remove insoluble residue, 1 ml of the filtrate was diluted to 10 ml with simulated salivary fluid (pH 6.8). The absorbance was measured at specified nm using an UV spectrophotometer. The experiments were carried out in triplicate for the films of all formulations [22-26].

Tensile Strength: Tensile strength of the buccal patches was determined by using modified analytical balance strength machine. The sensitivity of the machine is one gram. It consists of 2 load cell grips. The lower one is fixed and upper one is movable. The test patch of specific size is fixed between these cell grips and force was gradually applied, till the patch breaks. The tensile strength of the patch was taken directly from the dial reading [27].

Percentage moisture content: The buccal patches was weighed accurately and kept in desiccators containing anhydrous calcium chloride. After three days, the patches were taken out and weighed. The moisture content (%) was determined by the formula [28-31];

$$\% \text{ Moisture content} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

***In vitro* dissolution test**: The *in vitro* dissolution study is carried out in stimulated saliva solution pH 6.8 phosphate buffer using USP paddle (Type II) apparatus at 37±0.5°C. Samples are withdrawn at regular time interval and analyzed by UV-Visible spectrophotometer. In-vitro drug dissolution was performed using USP paddle apparatus. The studies were carried out at 37°C with stirring speed of 50 rpm in 900 mL of pH 6.8 phosphate buffer dissolution medium. 5 ml of samples were withdrawn at predetermined time intervals of 1,2,3,4,5,6 minutes and replaced with the same volume of buffer. The samples were collected and the absorbance was determined at 223 nm UV-visible spectrophotometer [32-36].

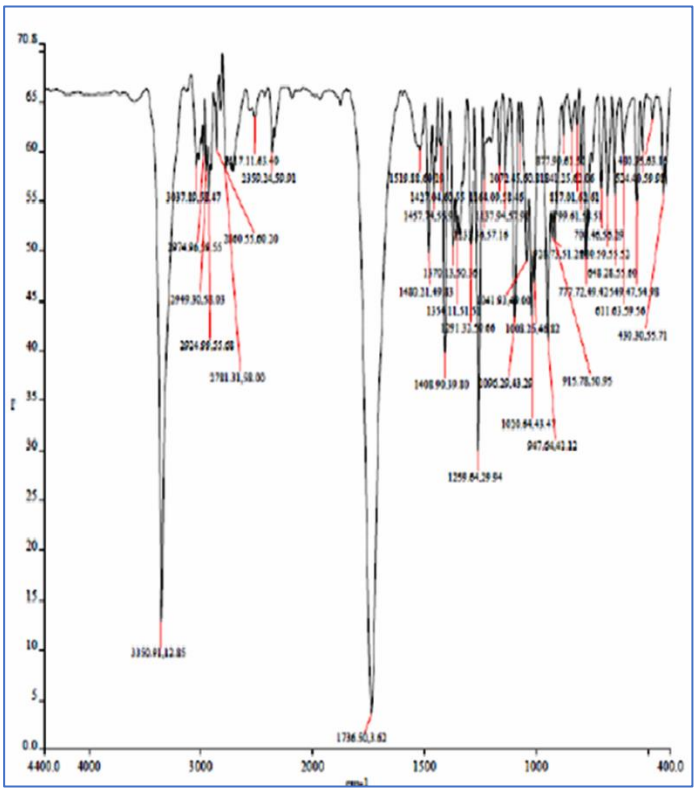

Figure 3: FTIR Spectra of Pure Drug

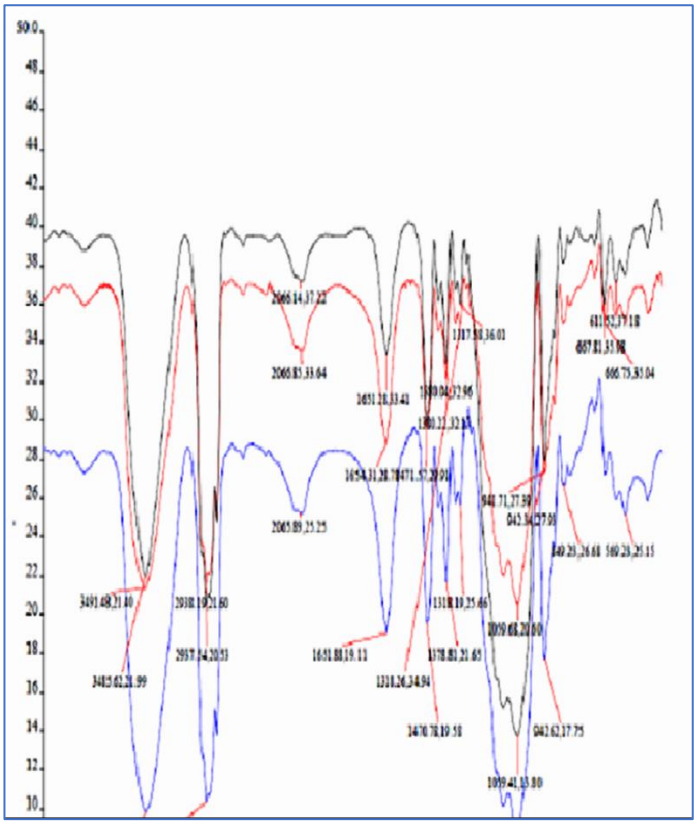

Figure 4: FTIR Spectra of Polymer HPMC E4, HPMC E10, HPMC E15

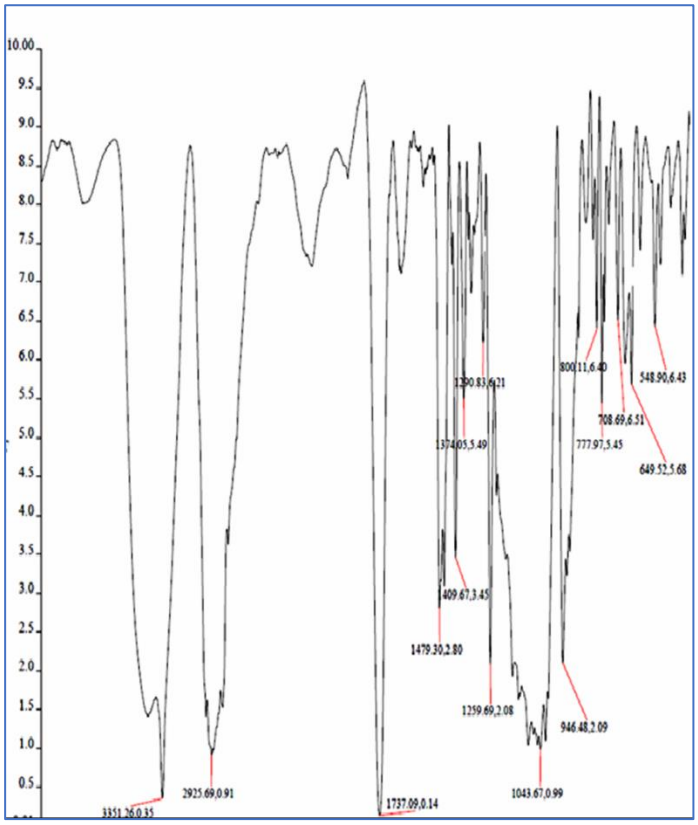

Figure 5: FTIR Spectra of Drug with Polymer HPMC E4, HPMC E10, HPMC E15

Evaluation results of fast dissolving film:

Table 10: Evaluation Data of Formulation F1, F2...F10

Formulation	Drug content (%)	Wt. variation (mg)	Surface pH	Folding endurance (No. of folds/mm^2)	Disintegration time (sec.)	Tensile strength (n/m^2)	Thickness (mm)	% Moisture content
F1	99	05.71±0.24	6.78±0.02	4.60±0.51	42±0.002	141.2	0.08±0.01	6.8
F2	98.5	06.16±0.03	6.63±0.02	4.30±0.51	54±0.001	142.4	0.05±0.00	3.17
F3	99.3	18.78±0.65	6.70±0.01	4.60±0.51	56±0.002	135.8	0.20±0.02	3.57
F4	95.32	14.62±0.51	6.85±0.01	4.30±0.51	95±0.002	145.1	0.10±0.03	1.40
F5	97.42	15.43±0.81	6.66±0.02	5.60±0.51	90±0.002	146.6	0.16±0.03	2.30
F6	89.43	06.5±0.20	6.53±0.01	4.30±0.51	100±0.002	150.3	0.19±0.02	3.46
F7	82.20	06.08±0.21	6.84±0.02	4.60±0.51	105±0.003	154.9	0.07±0.01	5.23
F8	97.77	19.48±0.48	6.56±0.01	4.30±0.51	108±0.002	148.9	0.17±0.02	2.78
F9	78.56	19.60±0.55	6.82±0.02	5.30±0.51	114±0.002	140.5	0.22±0.02	1.17
F10	90.51	18.60±0.42	6.84±0.02	5.60±0.60	108±0.003	140.8	0.11±0.01	2.55

Table 11: Drug Release Profile

Formulation/ Time	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
0	0	0	0	0	0	0	0	0	0	0
1	48.92	52.33	52.28	49.50	51.41	51.19	51.13	52.52	48.88	51.42
2	65.77	68.12	67.30	64.80	60.31	67.08	66.21	68.02	67.16	60.32
3	75.65	72.90	78.78	68.82	67.05	76.01	77.29	77.19	71.06	67.04
4	80.72	87.60	89.02	77.74	78.81	87.12	89.27	88.41	78.15	78.56
5	93.84	97.13	97.51	88.51	85.51	94.13	99.51	99.96	91.22	85.62
6	97.12	99.87	98.11	93.81	94.24	97.94	99.073	97.81	94.87	96.82

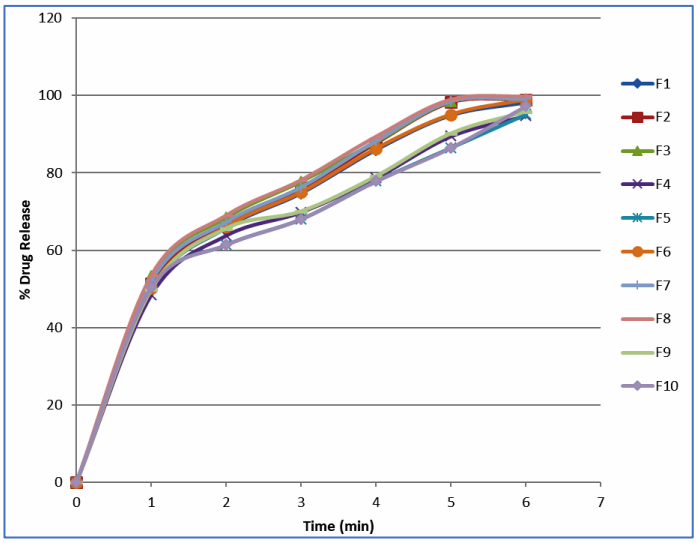

Figure 6: Dissolution Profile

RESULTS AND DISCUSSION: NOT GIVEN AT ALL

CONCLUSION

The mucoadhesive buccal film of zolmitriptan was successfully prepared by Solvent casting method. A combination of polymer HPMC E4M, HPMC E15M and HPMC E10M of shows good mucoadhesive strength and in-vitro drug release. The preparation of mucoadhesive buccal film of zolmitriptan shows increase in the bioavailability thus avoiding the hepatic first pass effect. The patients get advantages of the mucoadhesive buccal film for the treatment of migraine as marketed preparation shows erratic drug absorption

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REFERENCES

1. Darekar *et al*., Formulation and Evaluation of Bilayer Buccal Tablet of Sumatriptan Succinate. *International Journal of Pharmacy and Pharmaceutical Sciences*, 2014; 06: 469-475.
2. Satpathy Pragati Ranjan *et al*., Development and Validation of RP-HPLC method for the assay of Zolmitriptan. *International Journal of Pharma Sciences*, 2011; 3: 197-200.
3. Ms. Mital S. Panchal, Mr. Hiren Patel, Mrs. Aarti Bagada, Dr. K. R. Vadalia, Formulation and Evaluation of Mouth Dissolving Film of Ropinirole Hydrochloride by Using Pullulan Polymers. *Int J of Phar Res & Allied Sci*, 2012; 1(3): 60-72.
4. Padole *et al*., Buccal Tablets of Lisinopril by Direct Compression Method for Buccal Drug Delivery. *International Research Journal of Pharmaceuticals*, 2012;02: 30-38.
5. Borgaonkar *et al*., Formulation and in-vitro Evaluation of Buccal Tablets of Loratadine for Effective Treatment of Allergy. *International Journal of Research in Pharmacy and Chemistry*, 2011;01: 551-559.
6. Kaur Navpreet *et al*., Design, Development and Evaluation of Mucoadhesive Patches of Losartan for Buccal Delivery. *European Journal of Pharmaceutical and Medical Research*, 2014; 1: 105-126.
7. Mahanthesha M.K, *et al*., Design and Evaluation of Timolol Maleate Buccal Patches Using Tween as Permeation Enhancer. *International Journal of Universal Pharmacy and Bio Sciences*, 2013; 2(3): 2319-8141.
8. Komaragiri Sasi Deepthi, *et al*., Formulation and Characterization of Atenolol Fast Dissolving Films. *Indian Journal of Pharmaceutical Science & Research*, 2012; 2 (2): 58-62.
9. Bhattacharjee Sayan, *et al*., Design, Development and Evaluation of Mucoadhesive Film for Water Insoluble Drug Using Different Plasticizers. *International Journal of Pharmacy and Pharmaceutical Sciences*, 2014; 6 (3): 107-110.
10. Surve G.D *et al*., Review on Mouth Dissolving Film Technology. *International Journal for Pharmaceutical Research Scholars*, 2014; 3: 635-645.
11. Abdelzaher Mona M, *et al*., Formulation and evaluation of simvastatin buccal film. *Journal of Applied Pharmaceutical Science*, 2015; 5: 070-077.
12. Mukesh *et al*., Formulation and Evaluation of Mouth Dissolving Film of Amlodipine Besylate. European Journal of Biomedical and Pharmaceutical sciences, 2014;1: 60-79.
13. Hardik *et al*., Formulation Development and Evaluation of Fast Dissolving Film of Cyproheptadine Hcl. *Pharma Science Monitor*, 2015; 6 (2):222-247.
14. Raghavendra Rao N.G. and Suryakar V.B., Formulation and Evaluation of Montelukast Sodium Mucoadhesive Buccal Patch for Chronic Asthma attacks. *International Journal of Pharma and Bio Sciences*, 2010; 1.
15. Gorle Ashish *et al*. Development and evaluation of buccal film containing antihypertensive agent. *The Pharma Innovation Journal*, 2015; 4:53-60.
16. Govindasamy Parthasarathy *et al*., Chitosan Based Unidirectional Release Buccal Patches of Carbamazepine: Formulation Development and *In Vitro*, Ex Vivo Characterization. Research and Reviews: *Journal of Pharmacy and Pharmaceutical Sciences*, 2013; 2: 47-58.
17. Rani B. Samyuktha, Formulation and *In- Vitro* Characterization of Venlafaxine Hcl Mucoadhesive Buccal Patches. *International Journal of Inventions in Pharmaceutical Sciences*, 2013; 1 (1):15-21.
18. Raghavendra Rao N.G. and Munde M.R., Formulation and *in-vitro* Evaluation of MucoadhesiveBuccal Films of Zolmitriptan. *Journal of Pharmacy Research*, 2011; 4:2682-2685.
19. Bhura Nikunj *et al*., A Review on Fast Dissolving Film. *International Journal of Pharmaceutical Research and Bio-Sciences*, 2012; 1: 66-89.

20. Jacob Liji *et al*., Design, Development and Evaluation of Muccoadhesive Patches of Nifedipine for Buccal Delivery. *Asian Journal of Pharmaceutical Science & Technology*, 2012; 2 (1):13-22.
21. Bansal Sumedha *et al*., Formulation and Evaluation of Fast Dissolving Film of An Antihypertensive Drug. *International Journal of Pharmaceutical, Chemical and Biological Sciences*, 2013;3(4): 1097-1108.
22. Mahajan Apoorva, Formulation & Evaluation of Fast Dissolving Buccal films of Sertraline. *International Journal of Drug Development & Research*, 2012; 4 (1): 220-226.
23. Puratchikody Ayarivan *et al*., Development and characterization of Eudragit based mucoadhesive buccal patches of salbutamol sulfate. *Saudi Pharmaceutical Journal*, 2011; 19: 207–214.
24. Deore VA. *et al*., Development and Statistical Optimization of Mucoadhesive Buccal patches of Indomethacin: *In-vitro* and Ex-vivo evaluation. *International Journal of Advances in Pharmacy, Biology and Chemistry*, 2013; 2: 405-422.
25. Senthil A. *et al*., Formulation and Evaluation of Venlafaxine Hydrochloride Buccal Patch. *International Research Journal of Pharmacy*, 2012; 3 (3):282-286.
26. Swapnil. Patil *et al*., Fast Dissolving Oral Films: An Innovative Drug Delivery System. *International Journal of Research and Reviews in Pharmacy and Applied science*, 2013; 2: 482-496.
27. Sarathchandran C. *et al*, Formulation and Evaluation of Fumarate Buccal Patches by Using Selected Polymers. *International Journal of Pharmaceutical, Chemical and Biological Sciences*, 2013; 3: 854-860.
28. Chauhan Nitesh S, *et al*, Formulation and Evaluation of Fast Dissolving Oral Film of Dicyclomine as potential route of Buccal Delivery. *International Journal of Drug Development & Research*, 2012; 4:410.
29. Sravanthi R.R *et al*., Mucoadhesive Buccal Films: An Innovative Drug Delivery System", *International Journal of PharmTech Research*, 2014; 6(5): 1665-1678.
30. Panda B.P. *et al*., Development of Innovative Orally Fast Disintegrating Film Dosage Forms: A Review. *International Journal of Pharmaceutical Science and Nanotechnology*, 2012; 5 (2):1666-1674.
31. Bhimavarapu Rama devi *et al*., Development and In-vitroEvaluation of Mucoadhesive Buccal Patches of Sertraline HCL. *American Journal of Advanced Drug Delivery*, 2013; 1:313-322.
32. Chinnala *et al*., Formulation and Evaluation of Mouth Dissolving Films Containing Tizanidine Hydrochloride. *International Journal of Pharma Research and Health Sciences*, 2015; 3 (2):621-635.
33. Magdy I. Mohamed *et al*. Development of a Novel Ketorolac Tromethamine Sublingual Film. *Journal of American Science*, 2015; 11 (7): 27-37.
34. Desu Prasanna *et al*., Formulation and Evaluation of Mouth Dissolving Films of Zolmitriptan. *International Research Journal of Pharmacy*, 2012; 3 (5):373-376.
35. Radha Madhavi B *et al*., Buccal Film Drug Delivery System-An Innovative and Emerging Technology. *Molecular Pharmaceutics & Organic Process Research*, 2013; 1(3):1-6.
36. Sridhar Iswarya *et al*., Formulation and Characterization of Buccal Patches of Ondansetron Hydrochloride. *International Journal of Pharmaceutical Research and Development*, 2013; 5: 84-94.

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