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Formulation And Evaluation of Esomeprazole Buccal Patches

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ABSTRACT

The buccal route has a relatively robust mucosa, has the advantage of allowing excellent accessibility, and reasonable patient compliance. Within the oral mucosal cavity, the buccal region offers attractive route of administration for local or systemic drug delivery. The mucosa has a rich blood supply, and it is relatively permeable. Recently interest has been focused on the delivery of drug to or via mucous membrane by the use of mucoadhesive material, several mucoadhesive formulations are available under development and drug delivery via buccal mucosa is gaining importance of a novel route of drug administration. The purpose of this study was to develop and optimize formulations of mucoadhesive patches of Esomeprazole. The patches were prepared by the solvent casting method using Chitosan as basic polymer and HPMC and Eudragit L 100.

KEY WORDS: Buccal Patches, Esomeprazole, solvent casting Method, FTIR studies, In vitro drug release studies.

INTRODUCTION

Buccal patches are highly flexible and thus much more readily tolerated by the patient than tablets. Buccal patches also ensure more accurate dosing of the drugs as compared to gels and ointments in oral cavity.[1] The oral drug delivery is the most preferred route by majority of the patients amongst the various available roués of drug delivery.[2] Oral transmucosal drug delivery can be achieved through 1 of the 3 types of oral mucosa: sublingual, gingival, and buccal. Absorption of therapeutic agents from the oral cavity provides a direct entry for such agents into the systemic circulation, thereby avoiding first-pass hepatic metabolism and gastrointestinal degradation.[3] However, the buccal route of drug delivery has received the most attention because of its unique advantages over the other oral transmucosal routes.[4] An ideal patch should be flexible, elastic, and soft yet strong enough to withstand breakages due to stress from activities in the mouth. Moreover, it must also possess good mucoadhesive strength so that it is retained in the mouth for the desired duration. To prevent discomfort, swelling of the patch should not be too extensive.[5] Recently developed mucoadhesive buccal delivery systems such as adhesive tablet, films, patches, disks, strips, ointment, gel, and creams. Tablets, films and patches appear to be the most preferred formulations.[6] Esomeprazole magnesium trihydrate is a proton pump inhibitor and is approved by FDA for the treatment of symptomatic gastroesophageal reflux disease, treatment and maintenance of erosive esophagitis. The bioavailability of Esomeprazole magnesium trihydrate is 48% and plasma elimination half-life is 1-1.5 h.[7]

MATERIALS

Esomeprazole was obtained from Aurbindho labs, HYD. HPMC and Eudragit were procured from Synpharma Research Labs, Hyderabad, and other chemicals the reagents used were of analytical grade.

METHODOLOGY

Compatibility studies of drug and polymers[8]

In the formulation of Esomeprazole patch formation, API and Excipient may interact as they are in close communication with each other, which could lead to the instability of drug. FT-IR spectroscopy was employed to

ascertain the compatibility between Esomeprazole and the selected polymers. The pure drug and drug with excipients were scanned separately.

Formulation design:

Table-1: Formulation Design of Esomeprazole buccal Patches

S. No	F.Code	Ingredients (mg)				
		Drug (mg)	HPMC k100M	Eudragit	PEG	DMSO
1	F1	100	100	-	1ml	0.1ml
2	F2	100	200	-	1ml	0.1ml
3	F3	100	-	100	1ml	0.1ml
4	F4	100	-	200	1ml	0.1ml

Preparation method:[9]

Solvent casting method

Esomeprazole buccal patches were formulated by the solvent casting evaporation technique. The drug Esomeprazole was diffuse in methanol. Polymers HPMC K100M, eudragit were taken in a boiling tube, to this add Esomeprazole drug which was previously dissolved in suitable solvent. Sufficient care was taken to prevent the creation of lumps. PEG was taken as a plasticizer and Dimethyl sulfoxide as permeation enhancer and added to the mixture and mixed well. It was set aside for 2 hours to exclude any entrapped air and was then transferred into a previously cleaned petri plate (40cm^2), drying of patches was carried out in vacuum oven at room temperature. Dried patches were packed in aluminium foil and stored in a desiccator for further evaluation.

Characterization of Buccal formulation [10,11,12]

Physicochemical evaluation

Physical appearance:

All the formulated Esomeprazole films were observed for color, clarity, flexibility, and smoothness.

Folding endurance:

Buccal patches folding endurance was estimated by frequently double over at the same place till it broke. The number of times the film could be folded at the same place without breaking is the folding endurance. This was restated on all the films for three times and the mean values plus standard deviation was calculated.

Thickness of the film:

The thickness of each film was measured by using screw gauze. Buccal patches thickness was estimated at various sites on each patch and the average thickness of the Buccal patch was capture as the thickness of the patch.

Weight uniformity:

The formulated Buccal patches are to be dried at 60^{0}C for 6 hours before trial. A identify the area of 4.52 cm^2 of film is to be cut in different parts of the patch and weigh in digital balance. The average weight and standard deviation values are to be calculated from the individual weights.

Drug content:

The formulated Buccal patch was assayed for drug content in each case. Three patches from each formulation were assayed for content of drug. Each formulation was casted in triplicate and one patch from each was taken and assayed for content of drug.

The Buccal films (4.52 cm^2) were added to conical flask containing 100 ml of phosphate buffer pH 7.4 contain 0.5% SLS. This was then stirred with magnetic bead at 400 rpm for 2 hrs. The contents were filtered, and the filtrate was analysed spectrophotometrically. Similarly, a blank was prepared from Buccal films without drug.

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Moisture absorption studies:

The buccal patches were weighed exactly and placed in a desiccator containing aluminium chloride to maintain 79.50% RH. After 3 days, the films were taken out and weighed. The percentage of moisture uptake was calculated using the following formula.

$$\text{Perentage moisture uptake} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

Moisture loss studies:

Three patches were weighed separately and kept in a desiccator contains calcium chloride at 37^0C for 24 hours. Then the last weight was noted when there was no further change in the weight of the patch. The percentage of moisture loss was calculated using the following formula.

$$\text{Percentage moisture loss} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Final weight}} \times 100$$

***In vitro* release study:**[13]

The release rate of the drug was determined by using Franz diffusion cell apparatus temperature maintained at 37± 0.5 ^{0}C and stirred at a rate of 200 rpm. Sink conditions was maintained all over the study. The vessel containing 10ml of phosphate buffer pH 6.8 phosphate buffer solution. Aliquots of 1ml of samples were withdrawn at various time meanwhile and then analyzed using a UV Spectrophotometer.

% release rate of drug was determined using the following formula.

$$\text{Perentage drug release} = \frac{\text{Da}}{\text{Dt}} \times 100$$

Where, Dt = Total amount of the drug in the film

Da = The amount of drug released

Stability studies:[14]

Optimized medicated buccal films were subjected to short term stability testing. The Buccal films were sealed in aluminium foils and kept in a humidity chamber maintained at 40 ± 2 ^{0}C and 75 ± 5% RH for 3 months as per ICH guidelines.

RESULTS AND DISCUSSION

Compatibility studies of drug and polymers:

All these peaks have appeared in formulation and physical mixture, indicating no chemical interaction between Esomeprazole and polymer. It also confirmed that the stability of drug during microencapsulation process.

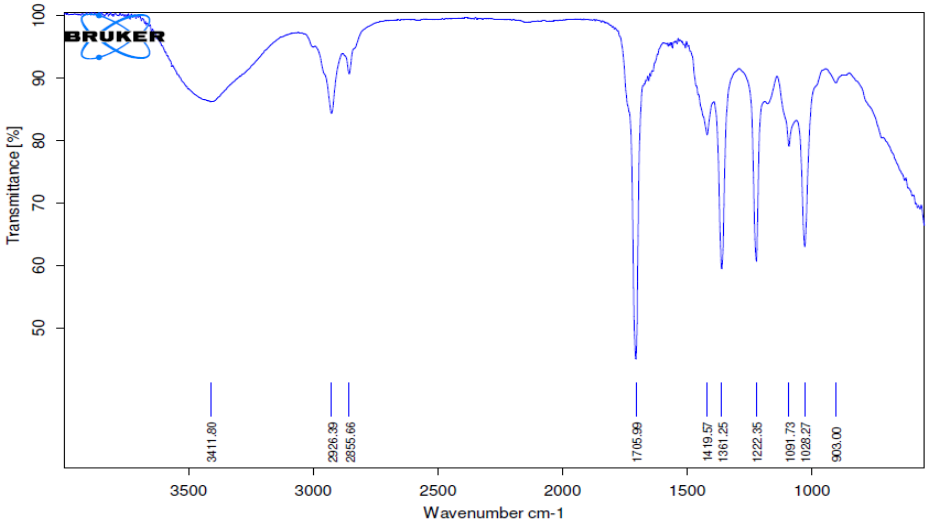

Fig-1: FTIR Studies of Esomeprazole

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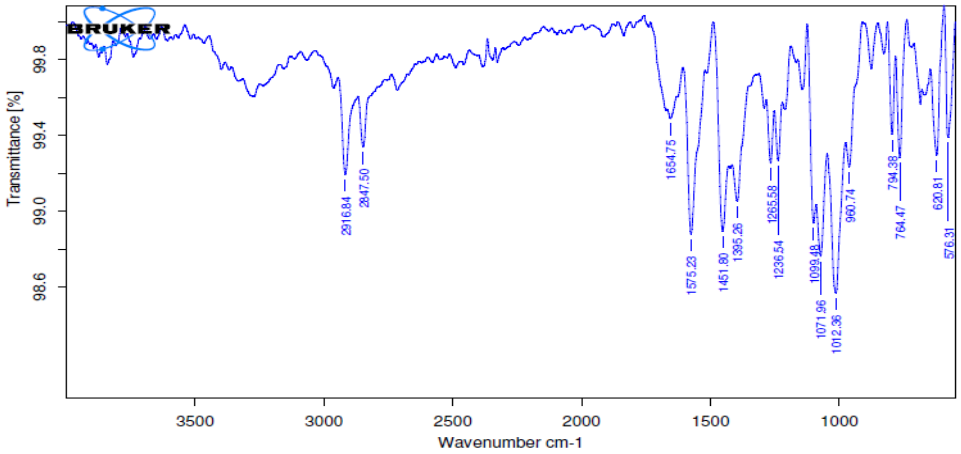

Fig-2: FTIR Studies of Physical mixture of drug and excipients

Physical appearance and surface texture of buccal patches:

These parameters were checked simply with visual inspection of patches and by feel or touch. The observation reveals that the patches are having smooth surface, and they are elegant in appearance.

Weight uniformity of buccal patches:

The weight of the patches was determined using digital balance and the average weight of all patches

Thickness of buccal patches:

The thickness of the patches was measured using screw gauge and the average thickness of all patches.

Folding endurance of buccal patches:

The folding endurance gives the idea of flexible nature of patches. The folding endurance was measured manually, patches were folded repeatedly till it broke, and it was considered as the end point. The folding endurance was found optimum, and the patches exhibited good physical and mechanical properties and the average folding endurance of all patches.

Drug content uniformity of buccal patches:

Esomeprazole buccal patches prepared with various polymers were subjected to the valuation for uniform dispersion of drug throughout the patch. In each case three patches were used, and the average drug content was calculated.

% moisture loss:

The moisture content in the buccal patches ranged from 8.75 to 8.96%. The moisture content in the formulations was found to be increased by increase in the concentration of polymers.

%moisture absorption:

The moisture absorption in the buccal patches ranged from 7.14to 7.47 %.

Swelling index:

The swelling index in the buccal patches ranged from 14.50 to 15.47 %.

Table -2: Physicochemical evaluation data of Esomeprazole Buccal Patches

Formulation Code	F1	F2	F3	F4
Thickness (mm)	0.32	0.27	0.30	0.28
Weight variation (mg)	44.89	45.24	46.90	47.89
Drug content Uniformity	96.30	93.86	94.25	92.59
Folding endurance	80	79	82	83
% moisture loss	7.56	7.41	7.82	7.47
%moisture absorption	8.37	8.19	8.20	8.14
Swelling index	14.86	14.50	15.47	15.10

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Drug release studies

Table-3: *In vitro* release data of film F_1 to F_4

Time (hrs.)	F_1	F_2	F_3	F_4
0	0	0	0	0
1	15.12	14.16	13.48	15.28
2	25.79	25.91	27.50	26.91
3	38.82	37.82	38.93	39.55
4	49.18	47.93	45.12	48.26
5	62.85	69.15	68.55	67.24
6	77.45	72.15	72.11	76.18
7	88.93	87.80	86.07	82.14
8	95.90	92.66	91.52	93.58

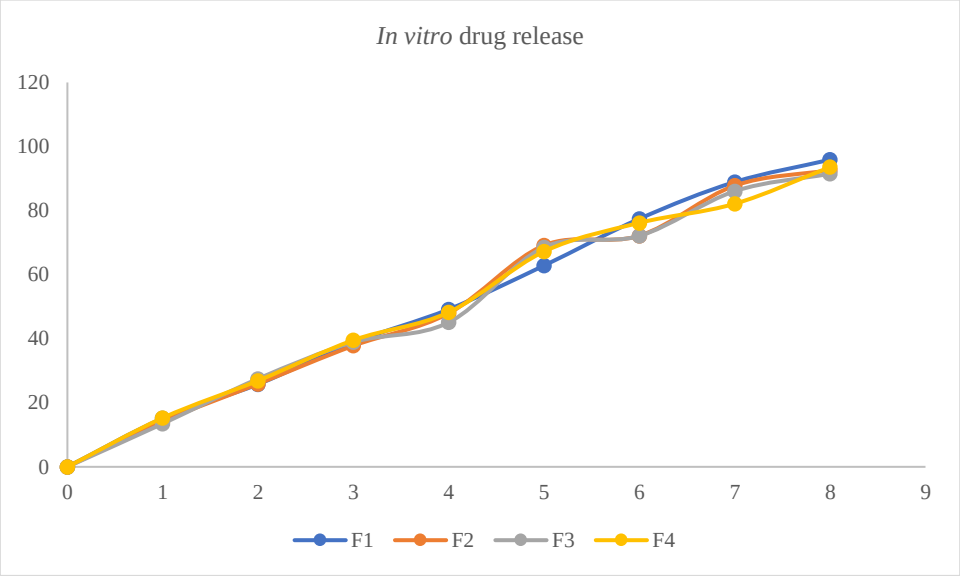

Fig-3: *In vitro* drug release of (F1- F4) formulation

Stability studies:

Optimized formulations F1 was selected for accelerated stability studies as per ICH guidelines. The patches were observed for color, appearance and flexibility for a period of three months. The folding endurance, weight, drug content, % cumulative drug release of the formulation was found to be decreasing. This decrease may be attributed to the harsh environment (40^0C) maintained during the studies.

Table-4: Stability studies of optimized formulations

S.NO	Time in days	Physical changes	Mean % drug release		
			Esomeprazole		
			25^0C/60%	30^0C/75%	40^0C/75%
1.	01	No Change	95.90	95..90	95.90
2.	90	No Change	94.15	94.09	93.99

CONCLUSION

The patches prepared were elegant in appearance and smooth surface. The weight, thickness of patches was uniform. The patches had good flexibility. The patches show uniform swelling index. There was no drug-excipients interaction between the drug and excipients used in the formulation. The drug was distributed throughout the patch uniformly.

More than 85 % of the drug was released from all the formulations at the end of 8 hrs. In short term stability studies indicate there were no significant changes in the drug content and *in-vitro* drug release for the period of three month. From the result and conclusion of the research work we can summarize that Esomeprazole can be delivered via buccal route.

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