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FORMULATION AND EVALUATION OF PANTOPRAZOLE MUCOADHESIVE BUCCAL FILMS

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ABSTRACT

The aim of present work deals with formulation and evaluation of Pantoprazole mucoadhesive films with film forming polymers like HPMC K100 and Sodium alginate by solvent casting technique. HPMC K100, Sodium alginate were used for sustained release polymers. FT-IR analysis was performed to study the interaction between the drug and polymer and also i*n-vitro* dissolution studies, surface pH, folding endurance test, disintegration and dissolving time tests were performed. From all the evaluation parameters, F2 and F4 formulation was found to be better showing sustained release when compared to other formulations.

Key words: Pantoprazole, HPMC K100, Sodium alginate, FT-IR.

INTRODUCTION:

Extensive research efforts have recently been focused on placing a drug delivery system in a particular region of the body for maximizing biological drug availability and minimizing dose-dependent side effects[1]. Bioadhesive formulations have a wide scope of applications, for both systemic and local effects of drugs. The concept of mucosal adhesion or mucoadhesive was introduced into controlled drug delivery area in the early 1980's, which is become a major part of novel drug delivery system in the recent era. Some of the potential sites for attachment of any mucoadhesive system are include buccal cavity, nasal cavity, eyes, vagina, rectal area, sublingual route and gastrointestinal area.

Moreover, the buccal films are able to protect the wound surface, thus reducing pain and treating oral diseases more effectively[2].

Advantages of Mucoadhesive Buccal Films[3]:

1. Rapidity of Action.
2. Medications administered through Buccal route bypass the first pass metabolism.
3. Medications administered through Buccal route directly enter systemic circulation without undergoing gastrointestinal degradation.
4. Buccal mucosa provides efficient blood supply and has relatively low enzymatic activity.
5. Moreover, the buccal mucosa is easily accessible and acceptable to patients; it allows the patient to interrupt drug administration by simply removing the drug delivery system.
6. The oral cavity is easily accessible for self medication and hence is well accepted by patients and is safe.
7. Drug can be administered and even removed from the site of application.
8. Terminating the input of drug whenever desired.
9. The sublingual and buccal delivery of a drug via thin film has the potential to improve the onset of action, lower the dosing, and enhance the efficacy and safety profile of the medicament.
10. Beneficial in cases such as motion sickness, acute pain, sudden episodes of allergic attack or coughing, where an ultra rapid onset of action required.

EXPERIMENTAL WORK

Materials:

Pantoprazole was received as a gift sample from Aurbindo labs, (Hyderabad), HPMC K100 was received as a gift sample from Himedia labs, (Mumbai). All other chemicals used in this study were of analytical grade.

METHOD

Solvent casting:

Mucoadhesive 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. Water soluble ingredients are dissolved in H_2O and API and other agents are dissolved in suitable solvent to form a clear viscous solution .Both the solutions are mixed resulting solution is cast as a film and allowed to dry film is collected

↓

Both the solutions are mixed

↓

Resulting solution is cast as a film and allowed to dry

↓

Film is collected

Characterization of Mucoadhesive buccal films[4-8]

Weight variation:

For weight variation three films of every formulation were taken weighed

individually on digital balance then average weight was calculated.

Thickness:

For thickness, three films of each formulation were taken and the films thickness was measured using Digital vernier caliper (Absolute Digimate) at six different places and the mean value was calculated.

Tensile strength:

This mechanical property was evaluated using Instron universal testing instrument (Model 1121, Instron Ltd., Japan, NITK, Suratkal) with a 5-kilogram load cell. Film strips in special dimension and free from air bubbles or physical imperfections were held between two clamps positioned at a distance of 3 cm. During measurement, the strips were pulled by the top clamp at a rate of 100 mm/m; the force and elongation were measured when the film broke. Results from film samples, which broke at and not between the clamps, were not included in the calculations. Measurements were run in triplicate for each film.

$$\text{Tensile strength} = \frac{\text{Force at break (N)}}{\text{Initial cross sectional area of the sample } (mm^2)}$$

Folding endurance:

The folding endurance was determined by repeatedly folding one patch at the same place till it broke. The number of times the film could be folded at the same place without breaking gives the value of the folding endurance.

Dissolving time:

The dissolving time was determined by placing the film in a beaker containing 50 ml of phosphate buffer (pH 7.4). Time required by the film to dissolve completely was noted.

Disintegration time:

Test was performed using disintegration test apparatus. 5cm2 film was placed in the basket, raised and lowered it in such a manner that the complete up and down movement at a rate to achieve equivalent to thirty times a minute. Time required by the film to achieve no trace of film remaining above the gauze was noted.

Swelling index:

A drug-loaded patch of 1x1 cm2 was weighed on a pre weighed cover slip. It was kept in a Petridis and 50 ml of phosphate saline buffer, pH 7.4 was added. After every five min, the cover slip was removed and weighed up to 30 min. The difference in the weights gives the weight increase due to absorption of water and swelling of patch.

The percent swelling, % S was calculated using the following equation:

$$\% S = \frac{X_t - X_o}{X_o} \times 100$$

where Xt is the weight of the swollen patch after time t and Xo is the original patch weight at zero time.

Surface pH:

The film to be tested was placed in a petridish and was moistened with 0.5 ml of phosphate buffered saline and kept for 1 h. The pH was noted after bringing the electrode of the pH meter in contact with the surface of the formulation and kept for 1 min to allow equilibrium condition.

Drug content:

A circular film of 2.5cm diameter was cut and placed in a beaker. 100 ml of phosphate buffered saline solution (pH 7.4) was placed. The contents were stirred in magnetic stirrer to dissolve the film. The contents were transferred to a volumetric flask (100 ml).

The absorbance of the solution was measured against the corresponding blank solution at 295 nm. As the absorbance noted above 1mcg/ml, 1ml of the stock was further diluted to 10ml of phosphate buffered saline solution (pH7.4) and absorbance was measured at 295nm.

In vitro dissolution studies:

Dissolution apparatus USP type II rotating paddle method was used to study drug release from buccal films. The dissolution medium consisted of 900ml of phosphate saline buffer [pH 7.4]. The study was performed at 37 C with 100 rpm. One side of each buccal film (3 films) (2.5 cm diameter) was attached to glass slide with cynoacrylate glue.

The glass slide was put to bottom of the vessel so that film remained on the upper side of the glass slide. Sample (5 ml) was withdrawn at predetermined time interval of 40, 80, 120, 160, 200, 240 minutes and replaced with fresh medium. The samples were filtered through whatmann filter paper and assayed by UV spectrophotometer at 295nm.

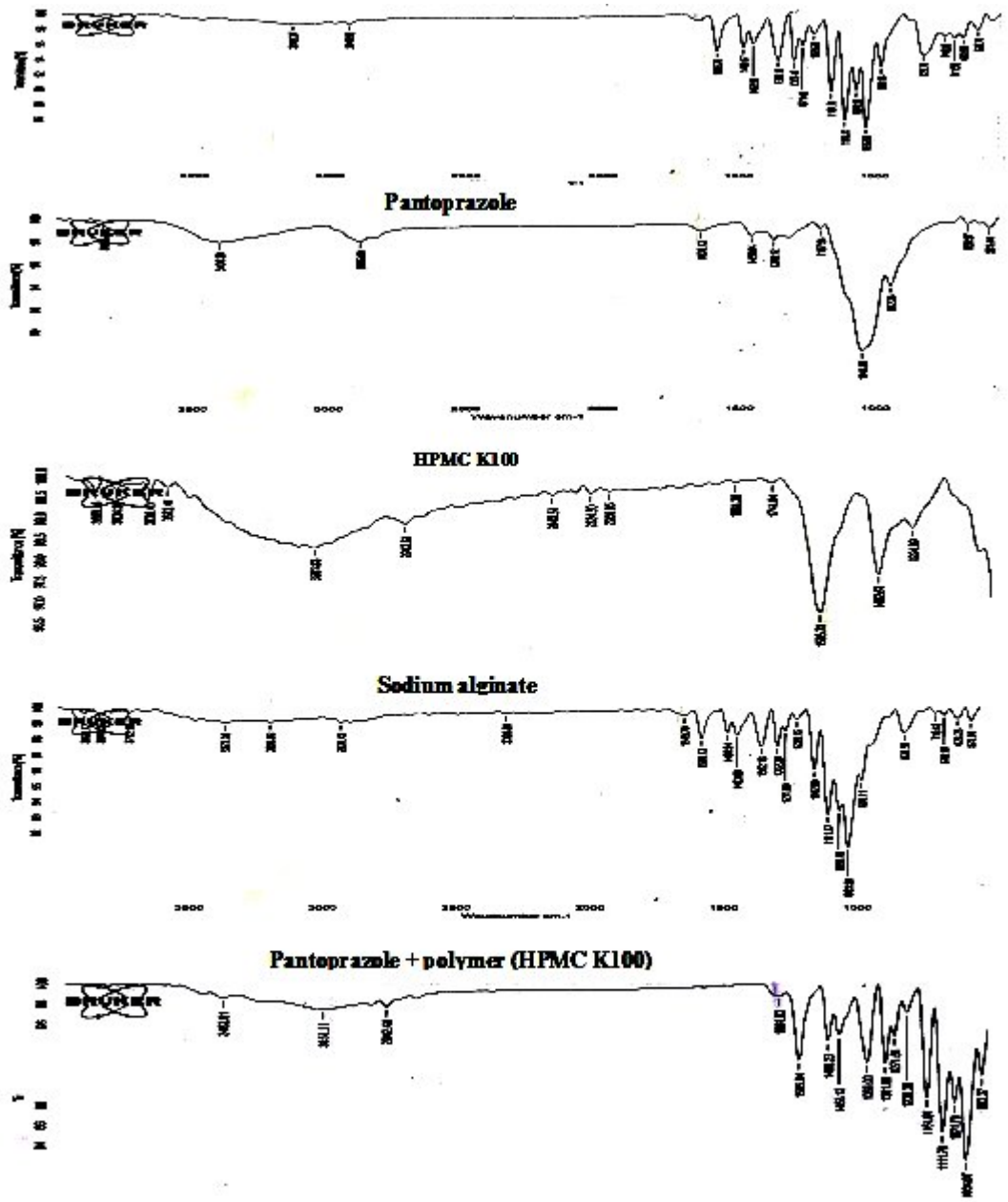
RESULTS AND DISCUSSION

Pre formulation studies:

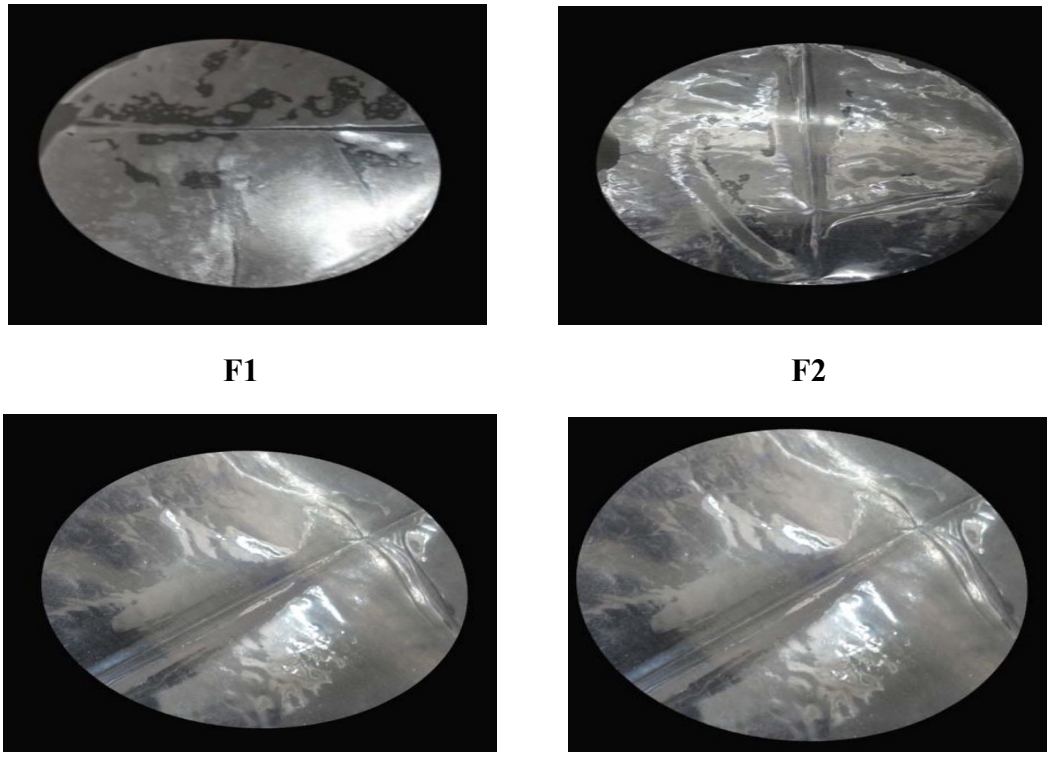
Fourier Transformed Infra Red (FT-IR) spectroscopic analysis:

FT-IR spectra of pure Pantoprazole, HPMC K100, and physical mixture of Pantoprazole with HPMC K100 and Pantoprazole formulation were analysis. The peaks and patterns produced by pure drug were compared with physical mixture and formulation.

Fig 1: Fourier transforms infrared (FTIR) spectroscopic studies of formulations



PHOTOGRAPHS OF FILMS OF DIFFERENT FORMULATIONS



F1 **F2**

F3 **F4**

Fig.No.2 Film photos of different formulations

All the prepared films were found to be non tacky. Three films each of 1 cm^2 were cut at three different places from the casted film and weight variation was determined. Weight variation varies from 19mg to 24mg. It was observed that *in-vitro* disintegration time varies from 120 to 160 min for all the formulations. *In-vitro* disintegration time of the films was found to be increased with increase in the amount of the polymer.

Folding endurance of film was found to be in the range of 207 to 226. The prepared film formulations were assayed for drug content. Results of drug content showed the uniformity of the drug and less loss of drug content. The surface pH of the films was ranging from 7.14 to 7.48 the surface pH of the films was found to be neutral.

The *In-vitro* drug release profiles of the formulations in phosphate buffer pH 7.4 show differences depending on their composition[13-17]. A rapid dissolution of all the film preparations was observed by the dissolution test. The drug release order of Pantoprazole mucoadhesive films prepared by solvent casting technique are given as follows F1> F3> F2> F4 drug release was more sustained in films containing more amount of polymer ratio because of the sustained action of the polymer.

Table No. 1: ***Formulation of Mucoadhesive buccal films of Pantoprazole*** [9-12]

Formulation	Pantoprazole (mg)	HPMC K100 (mg)	Sodium alginate (mg)	PEG (ml)	Glycerine (ml)	Distilled water (ml)
F_1	100	200	-	0.4	0.2	10
F_2	100	300	-	0.4	0.2	10
F3	100	-	200	0.4	0.2	10
F_4	100	-	300	0.4	0.2	10

Table No. 2: ***Evaluation tests for Pantoprazole Mucoadhesive buccal films***

S No.	Evaluation parameters	Formulations			
		F_1	F_2	F_3	F_4
1	Weight variation (%)	20	23	19	24
2	Thickness	0.693	0.827	0.420	0.760
3	Tensile strength	1.889	1.963	1.534	1.654
4	Folding endurance	222	226	207	213
5	Dissolving time (Min)	190	245	225	258
6	Disintegration time (Min)	120	154	136	160
7	Surface pH	7.48	7.14	7.24	7.32
8	Drug content (%)	96.34	94.07	95.04	93.13

Table No. 3: ***Swelling Index***

Time(min)	Swelling Index (%)			
	F1	F2	F3	F4
5	100	103	91	94
10	101	105	92	96
15	102	109	93	99
30	109	112	98	105

Table No. 4: ***Dissolution profile for comparative study***

S.No	Time (Min)	Percentage of Drug release (%)			
		F_1	F_2	F_3	F_4
1	0	0	0	0	0
2	40	20.23	18.62	19.68	17.28
3	80	40.35	36.71	38.72	35.77
4	120	60.43	57.89	59.09	58.15
5	160	79.19	75.17	77.85	76.78
6	200	89.91	81.47	88.71	79.86
7	240	97.42	84.55	95.04	82.68

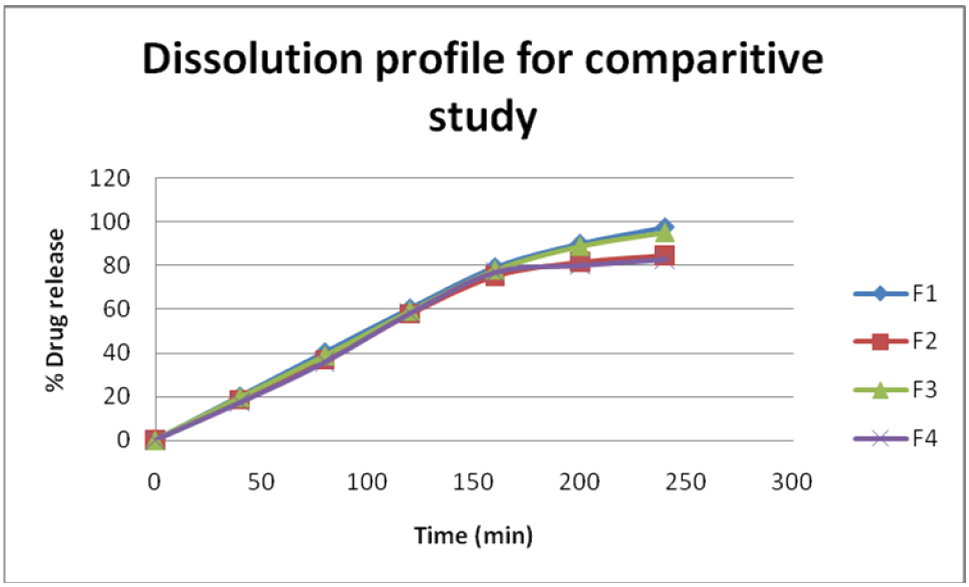


Fig.No.3: Comparative *In-vitro* dissolution profile of films.

CONCLUSION

Pantoprazole mucoadhesive buccal films were prepared by solvent casting technique it is a proton pump inhibitor used for the treatment of Gastro esophageal reflux disease (GERD). PEG600 acts as co solvent for inducing solubility of drug and also as plasticizer. The drug release from Mucoadhesive buccal films varied with respect to the polymer composition and nature. An increase in drug release from the Mucoadhesive buccal films was found with increasing concentration of polymers that are more hydrophilic in nature.

By varying the different concentrations of different polymers formulations i.e., F1, F2, F3, F4 were prepared, among that F2, F4 formulations consists of more amount of polymer ratio showing more sustained rate of drug release. From the characterisation studies like invitro dissolution studies , it says that F2, F4 formulation shows the optimum drug release rate as it is sustained release formulation, when compare to other formulations(the order of drug release is F1>F3>F2>F4).

From the present investigation, it can be concluded that such Mucoadhesive buccal films of Pantoprazole may provide buccal delivery for prolonged periods in the management of gastro esophageal reflux disease, which can be a good way to bypass the extensive hepatic first-pass metabolism.

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