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FORMULATION AND EVALUATION OF PROMETHAZINE HYDROCHLORIDE BUCCAL TABLETS

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ABSTRACT

Mucoadhesive buccal tablets containing promethazine hydrochloride (25mg) were prepared using polymers such as Carbopol 934P, HPMC K4M and Chitosan in varying concentration by direct compression technique. The Prepared tablets were evaluated for thickness, hardness, friability, and weight variation, uniformity of content, surface pH study, In-vitro swelling study, matrix erosion study, In-vitro bioadhesion study, ex-vivo mucoadhesion time, in-vitro drug release study and stability study. The surface pH of all tablets was found to be satisfactory, close to buccal pH, hence no irritation would observe with these tablets. The formulation (F4) containing carbopol 934P and HPMC K4M in the ratio (1:1) showed good bioadhesive force and maximum drug release of 96.62% for 10 hours. It was observed that the optimized formulation follows korsmeyer-peppas release kinetics. The optimized formulation (F4) was found to be stable upon conducting stability studies as per ICH guidelines at 40^0C at 75 % RH.

KEYWORDS: Buccoadhesive tablets, Promethazine Hydrochloride, Bioadhesive strength, In vitro drug release, Release kinetics.

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INTRODUCTION

Buccal mucosa is a potential site for the delivery of drugs to the systemic circulation. A drug administered through the buccal mucosa enters directly to the systemic circulation, thereby minimizing the first passes hepatic metabolism and adverse gastrointestinal effect. Oral mucosal drug delivery is an alternative method of systemic drug delivery that offers several advantages over both injectables and enterable method. More over buccal drug absorption can be terminated promptly in case of toxicity by removing the dosage form the buccal cavity. It is also possible to administer the drug to patients who cannot be dosed orally to prevent accidental swallowing. Therefore mucoadhesive dosage forms were suggested for oral drug delivery which includes adhesive tablets, adhesive gels and adhesive patches[1]. Buccal delivery involves the administration of drug through buccal mucosal membrane (the lining in the oral cavity). Buccal drug delivery is the safer method of drug utilization because drug absorption is terminated in case of toxicity by removing the dosage from from the buccal cavity. The drug directly reaches to the systemic circulation through the internal jugular vein and bypasses the drugs from the hepatic first pass metabolism, which leads to high bioavailability. The other advantages of buccal drug delivery include: low enzymatic activity, suitable for drugs or excipients that mildly and reversibly damage or irritate the mucosa, painless drug administration, easy drug withdrawal, possible to include the permeation enhancer/enzyme inhibitor or pH modifier in the formulation. A suitable buccal drug delivery system should be flexible and should possess good bioadhesive properties, so that it can be retained in the oral cavity for the desired duration. In addition, it should release the drug in a controlled and predictable manner to elicit the required therapeutic response [2].

During the past decade, bioadhesive polymers have received considerable attention for platforms of buccal controlled delivery because of their ability to localize the dosage form in specific regions to enhance drug bioavailability. Bioadhesive polymers can not only cause the adhesion effects but can also control the release rate of the drug. From a technological point of view, an ideal buccal dosage form must have 3 properties. It must (1) maintain its position in the mouth for a few hours; (2) release the drug in a controlled fashion, and (3) provide the drug release in a unidirectional way toward the mucosa. If the mucoadhesive excipients are able to control drug release, the second requirement can also be achieved. The third objective can be fulfilled by preparing a system having uniform adhesiveness and impermeable backing layer[3]. Promethazine Hydrochloride (PMZ) is a first-generation H1 receptor antagonist of the phenothiazine chemical class used medically as an antihistamine antiemetic and is effective in preventing motion sickness. PMZ is well absorbed from the gastrointestinal tract and undergoes for extensive first-pass metabolism leading to poor bioavailability[4] (25%). From both, physicochemical (low molecular weight 320.9 g mol−1, low dose 25 mg) and pharmacokinetic (absolute bioavailability 25%) perspective, PMZ was considered to be a suitable candidate for buccal delivery.

MATERIALS

Promethazine hydrochloride purchased from Taj Phamaceuticals Ltd., Mumbai. Carbopol 943 P was purchased from Loba chemie, Mumbai. Chitosan and HPMC K4M were purchased from Griffon laboratories Pvt. Ltd., Mumbai. Lactose, Mannitol, Magnesium steatate and Talc was purchased from SD fine-chem limited, Mumbai. All other reagents and chemicals used were of analytical grade.

METHODS

Formulation of Promethazine Hydrochloride Buccal tablets

Mucoadhesive tablets of promethazine hydrochloride were prepared by direct compression techniques using different

grades of polymer with varying concentration showed in table 1. The tablets were prepared using Carbopol 934P and as primary polymers and chitosan, HPMC K4M used as secondary polymer as a penetration enhancer. The effect of secondary polymer on drug release and mucoadhesion was studied. The tablets were compressed using 8mm flat faced punch on a single stroke punching machine[5].

Table 1
Composition of Promethazine Hydrochloride buccal tablets

Ingredients (mg/tab)	F1	F2	F3	F4	F5	F6
Promethazine Hcl	25	25	25	25	25	25
Carbopol 934P	60	40	30	60	40	30
Chitosan	60	80	90	_	_	_
HPMC K4M	_	_	_	60	80	90
Lactose	35	35	35	35	35	35
Mannitol	14	14	14	14	14	14
Talc	3	3	3	3	3	3
Magnesium Stearate	3	3	3	3	3	3
Total (mg/tab)	200	200	200	200	200	200

Evaluation of Promethazine hydrochloride buccal tablet

1. Hardness test

The hardness of the tablets was determined using Monsanto Hardness tester. It is expressed in Kg/cm^2. Three tablets were randomly picked from each formulation and the mean and standard deviation values were calculated[6].

2. Thickness

Control of physical dimension of the tablets such as thickness, width and length is essential for consumer acceptance and to maintain tablet to tablet uniformity[7]. The thickness of three randomly selected tablets from each formulation was determined in mm using a Screw gauge.[6, 8].

3. Friability test

The friability of tablet was determined by using Roche Friabilator. It is expressed in percentage (%). Twenty tablets were initially weighed ($W_{initial}$) and transferred into friabilator. The friabilator was operated at 25 rpm for 4 minutes or run up to 100 revolutions in which tablet droped from 6 inch distance. The tablets were dusted weighed again (W_{final}). The percentage friability was then calculated by,

$W_{initial} – W_{final/} W_{initial\_} \times 100$ %

Friability of tablets less than 1% is considered acceptable [6].

4. Uniformity of weight

The weight variation test was performed as per procedure of Indian Pharmaceutical. The weight (mg) of each of 20 individual tablets, selected randomly from each formulation was determined by dusting each tablet off and placing it in an electronic balance. The individual weight was compared with average weight for determination of percent deviation[9].

5. Uniformity of drug content

Five tablets were powdered in a glass mortar and the powder equivalent to 10 mg of drug was placed in a stoppered 10 ml conical flask. The drug was extracted with 60% methanol with vigorous shaking and filtered into 10 ml volumetric flask. Further appropriate dilution were made by using phosphate buffer pH 6.8 to make 10 mcg/ml concentration and absorbance was measured at 254 nm against blank (phosphate buffer pH 6.8)[9, 10].

6. Surface pH study

A combined glass electrode is used for this purpose. The tablet is allowed to swell by

keeping it in contact with 1 ml of phosphate buffer pH 6.8 for 2 h at room temperature. The pH is identified by bringing the electrode into contact with the tablet surface and allowing equilibrating for 1 min[10].

7. Swelling studies

Five Buccal tablets were individually weighed (W1) and placed separately in each petri dishe with 5 ml of phosphate buffer (pH 6.8). At time intervals of 1, 2, 4 and 8hr. the tablet was removed from each Petri dish and excess surface water from the tablet was wiped out carefully with filter paper. Each swollen tablet was reweighed (W2) and the swelling index (SI) was calculated using the following formula[12].

Swelling Index = [(W2-W1)/ W1] ×100

8. Matrix erosion

After swelling study, the swollen tablets were dried at 60°c for 24 h in an oven and kept in descicator for 48 h and reweighed (W3). Matrix erosion was calculated using following formula [13].

% Matrix erosion = [(W1-W3) ÷ W3] × 100

9. Measurement of mucoadhesive strength

The mucoadhesive strength of the tablets was measured on a modified physical balance. The apparatus consist of a modified double beam physical balance in which the right and left pan were with lighter pans. The left side of the balance was made heavier than the right side by placing a 5g weight on left side pan. Another Teflon block of 3.8 cm diameter and 2 cm height was fabricated with an upward protrusion of 2 cm height and 1.5 cm diameter on one side. This was kept in beaker, which was then placed below the left hand set of the balance. The goat gastric mucus membrane was used as the model membrane and pH 1.2 buffer solution was used as the moistening fluid. The goat stomach mucosa was kept in tyrode solution at 37^0C for hr. The underlying mucus membrane was separated and washed thoroughly glass slide and this slide was fixed over the Teflon block using a thread. The block was then kept in beaker containing pH 1.2 buffer solutions at a level that just touches the membrane so as to moisten the membrane. By keeping a 5 g weight on the right pan that two sides were balanced. The beaker with the Teflon block was kept below the left hand setup of the balance. The tablet was struck on to the lower side of the left hand side pan. The 5 g weight from the right pan was then removed. This lowered the left pan along with the tablet over the membrane with the weight of 5 g. This was kept undisturbed for 3 min. Then the weight on the right hand side was added in an increment of 0.5 g until the tablet just separates from the membrane surface. The excess weight on the right pan i.e. total weight minus 5 g was taken as the measure of the mucoadhesive strength from the mucoadhesive strength the force of adhesion was calculated using following formula[14].

10. Ex vivo residence time

The Ex vivo residence time was determined using a modified USP dissolution apparatus. The phosphate buffer of pH 6.8 is used as dissolution medium which is maintained at 37^0C± 2^0C. A segment of porcine buccal mucosa each of 4 cm length was glued to the surface of glass slide which was then vertically attached to the apparatus. Three tablets of each formulation were hydrated using 15µl pH 6.8 buffer on one side and hydrated surface was brought into contact with mucosal membrane. The tablets secured on the glass slide were completely immersed in the buffer solution. The paddle of the dissolution apparatus as adjusted at a distance of 5 cm from the tablet and rotated at 25 rpm the time for complete erosion or detachment from the mucosa was recorded[15].

11. In-vitro release studies

In-vitro release studies of promethazine hydrochloride bioadhesive tablet were determined using USP Dissolution Testing Apparatus-II (Paddle type). The dissolution test was performed by using 500ml of 6.8 phosphate buffer, at 37±0.5°c at 50 rpm.

Aliquot (5ml) of the solution was collected from the dissolution apparatus hourly for 10 hours and were replaced with fresh dissolution medium. Aliquot were withdrawn at one hour interval from a zone midway between the surface of the dissolution medium and the top of the rotating paddle not less than 1cm apart from the vessel wall[16]. The aliquots were filtered, and the absorbance was measured at 254nm spectrophotometrically.

12. Drug Release Kinetics

To analyze the mechanism of the drug release rate kinetics of the dosage form, the data obtained was fitted into a) Zero order kinetics; b) First order kinetics; c) Higuchi's square root model and d) Korsemeyer and Peppas model. The data obtained from stability study was also subjected to statistical analysis (student's t-test) in order to find out any significant difference in the drug content of optimum formulation[17].

13. Stability testing

The stability experiments were conducted to investigate the influence of temperature and relative humidity on the drug content and dissolution profile of various mucoadhesive buccal tablets. The formulations were exposed to a temperature of 40°C and a relative humidity of 75 % RH. The sample was removed from the stability chamber at the end of 24 hours and the tablets were visually examined for any physical changes, analyzed for drug content for 90 days, and were subjected to dissolution study. Average of triplicate readings was taken. The observations were tabulated. The dissolution profiles were compared with dissolution profile performed on tablets kept at ambient conditions.[17]

14. Infrared spectra analysis

Compatibility of the Drug with the excipients was determined by subjecting the physical mixture of the drug and the polymers of the main formulation to infrared absorption spectra analysis. Any changes in chemical composition of the drug after combining it with the polymers were investigated with I.R. spectral analysis. Infrared spectrum of Promethazine HCl was determined on Fourier transform infrared spectrophotometer using KBr pellet method. The base line correction was done using dried Potassium bromide. Then the spectrum of the dried mixture of drug and Potassium bromide was done.

RESULTS AND DISCUSSION

Before designing various formulations, the drug polymer-excipient compatibility studies were conducted by FTIR spectroscopy and results indicate that they were no chemical incompatibility between drug-polymer, polymer-polymer and polymer- excipients. Total six different formulations (F1 to F6) of Promethazine buccal tablets were prepared by direct compression techniques using various proportions of polymers and excipients. In order to select the best formulations, various evaluation parameters were checked and subjected to in – vitro dissolution studies and their release profiles.

Table 2
Physico-Chemical Properties of Tablets

Form. Code	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Weight variation (%)	Drug content (%)	Surface pH
F1	2.08±0.01	10.01±0.05	0.22±0.01	2.32	101.55±0.36	6.69±0.02
F2	2.13±0.02	8.19±0.02	0.35±0.01	1.52	98.60±0.59	6.51±0.01
F3	2.10±0.02	7.23±0.07	0.40±0.01	1.42	100.44±0.40	6.66±0.02
F4	2.15±0.01	9.10±0.06	0.35±0.02	1.81	98.74±0.81	6.67±0.03
F5	2.08±0.01	8.25±0.03	0.43±0.01	1.64	98.36±0.34	6.74±0.02
F6	2.20±0.01	6.33±0.07	0.35±0.01	1.72	99.21±0.61	6.35±0.01

A difference in tablet hardness reflects difference in tablet density and porosity. Hardness of the tablet increased with increasing the amount of Carbopol 934P. The hardness of tablets was found to be in the range of 6.33±0.07 kg/cm^2 to 10.01±0.05 kg/cm^2. This indicates good tablet strength. Thickness, Friability, weight variation and drug content, that all formulations having as per limits in Indian pharmacopoeia (Table 2). Surface pH of all the tablets was within the range of 6.51±0.01 to 6.74±0.03; showed in Graph 1. These results indicated that there is no risk of mucosal damage or irritation while administering these formulations on buccal mucosal region.

Table 3
In-Vitro Swelling Study and Matrix Erosion Study

Form. Code	In-Vitro swelling Time (hours)					% Matrix erosion
	1	2	4	6	8	
F1	143.11±1.65	223.73±1.90	287.42±1.84	305.76±0.81	327.39±1.09	24.12±1.02
F2	162.92±1.72	237.54±1.72	296.85±1.57	318.39±0.82	344.01±1.62	26.18±0.99
F3	171.47±0.76	241.14±2.44	299.97±1.34	335.29±1.70	351.93±0.93	28.14±0.99
F4	85.36±1.85	161.85±1.89	217.8±2.14	247.32±1.21	263.9±1.05	11.16±1.01
F5	75.62±1.91	142.44±2.00	201.15±1.31	227.24±0.74	248.82±0.83	10.63±0.52
F6	71.10±1.61	132.61±2.18	195.46±1.45	214.33±0.81	235.39±1.10	13.06±0.52

The bioadhesion and drug release profile are dependent upon swelling behavior of the tablets. Swelling index was calculated with respect to time. Swelling index increased as the weight gain by the tablets increased proportionally with the rate of hydration, showed in table 3. The formulation batch containing combination of Carbopol 934 P with Chitosan showed higher swelling index while the formulation containing combination of Carbopol 934 P with HPMC K4M. The swelling index values of formulation batch F3 containing combination of Carbopol 934 P and Chitosan increased with increasing amount of Chitosan. The swelling index values of formulation batch F4 containing combination with Carbopol 934 P and HPMC increased with increasing amounts of Carbopol 934 P. It was observed that when tablet came in contact with aqueous medium, wetting occurred first at the lower surface of tablet and then progressed to whole. The rate of spreading of water was dependent on the ratio of two polymers used; results are showed in Graph 2. The tablets from Chitosan group showed faster hydration rate but they also maximum weight loss (erosion). These tablets showed matrix erosion values between 10.63±0.52 to 28.14±0.99; results are showed in Graph 3. The tablets containing HPMC were found to exhibit least matrix erosion (Table 3).

Table 4
In-Vitro Bioadhesion Study and Mucoadhesion time

Formulation Code	Bioadhesive strength (gm)	Bioadhesive force (N)	Mucoadhesion time (hrs)
F1	17.43±0.27	1.708±0.02	14.19±0.02
F2	16.71±0.21	1.634±0.02	13.17±0.03
F3	14.39±0.29	1.407±0.03	11.19±0.07
F4	22.39±0.22	2.192±0.02	17.29±0.11
F5	22.22±0.07	2.177±0.07	15.26±0.13
F6	19.43±0.31	1.904±0.03	14.34±0.17

The bioadhesive property of mucoadhesive tablets of Promethazine HCl containing varying proportions of polymers was determined with an insight to develop the tablets with adequate bioadhesivness without any irritation and other problems the bioadhesion characteristics were found to be affected by the nature and proportions of the bioadhesive polymers. The highest adhesion force that is highest strength of mucoadhesive bond was observed with the formulation F4 containing Carbopol 934 P: HPMC K4M combination. The reason for such findings might be ionization of Carbopol 934 P at salivary pH which leads to improved attachments of the device to mucosal surface. Adhesion force decreased as another polymer is mixed with the arbopol 934 P; results are showed in Graph 4.

Ex-Vivo Mucoadhesion time

The ex-vivo mucoadhesion time was examined after application of the buccal tablet on freshly cut bovine buccal mucosa. The result showed in Table 4, revealed that the mean adhesion time was increased in the formulation batches containing Carbopol 934 P: HPMC K4M combination followed by formulation containing Carbopol 934 P: HPMC K15M combination. This may be due to the flexibility of Carbopol 934 P chains, which easily diffuses and interpenetrates into the mucin and get entangled with that of mucin. The mucoadhesive time on porcine buccal mucosa ranged from 11.19±0.07 to 17.29±0.011 hours, showed in table 4.

Table 5
In-Vitro Drug Release Study of Promethazine HCL

Time	Cumulative % drug release Formulations					
	F1	F2	F3	F4	F5	F6
0	0.000±0.00	0.000±0.00	0.000±0.00	0.000±0.00	0.000±0.00	0.000±0.00
0.5	7.36±0.06	8.67±0.19	7.61±0.10	10.72±0.24	11.22±1.46	10.22±1.72
1	13.49±0.27	13.55±0.27	11.53±0.78	17.28±0.87	18.36±1.22	15.41±0.91
1.5	17.35±0.22	18.54±0.18	16.54±2.84	24.42±1.22	25.42±0.92	23.66±0.72
2	23.62±0.32	23.79±0.14	20.72±1.54	29.72±2.42	30.88±0.72	28.89±0.72
3	33.63±0.60	31.55±0.11	27.67±2.11	39.87±0.72	42.76±0.46	34.72±0.72
4	39.53±0.35	39.32±0.15	33.67±0.12	51.92±0.40	53.56±0.72	45.92±1.72
5	47.26±0.64	46.89±0.07	38.71±0.87	61.95±0.16	66.86±1.09	53.68±1.86
6	57.67±0.30	53.32±0.32	45.22±0.42	71.95±2.37	74.49±1.07	66.74±1.43
7	64.42±0.26	58.55±1.42	51.79±0.20	83.72±0.22	80.67±0.97	69.12±1.88
8	69.52±0.40	62.11±1.87	55.38±1.72	90.42±0.72	84.87±2.01	73.09±1.72
9	73.30±0.12	65.39±2.01	57.22±0.17	93.22±1.72	87.62±1.33	76.17±1.72
10	76.34±0.06	67.50±0.98	59.72±2.04	96.62±0.46	89.72±1.42	78.07±0.82

In-vitro drug release studies revealed that the release of Promethazine Hydrochloride from different formulations varies with the characteristics and composition of matrix forming polymers. The formulations F1, F2 and F3 contain the Carbopol 934 P 934P and Chitosan polymers in the ratio of 1:1, 1:2 and 1:3 respectively. The In-vitro cumulative drug release profile of formulations F1, F2 and F3 at 10 hours showed 76.34%, 67.50% and 59.72% drug release respectively. The formulation F4, F5 and F6 contain the Carbopol 934P and HPMC K4M polymers in the ratio of 1:1, 1:2 and 1:3 respectively, showed in table 5. The In-vitro cumulative drug release profile of formulations F4, F5 and F6 at 10 hours showed 96.62%, 89.72% and 78.07% drug release respectively; results are showed in Graph 5. The release rate of Promethazine Hydrochloride decreased with decreasing concentration of Carbopol 934P. Carbopol 934 P is more hydrophilic then HPMC, it can swell rapidly, therefore decrease of Carbopol 934 P content delays the drug release. Drug release rate was increased with increasing amount of hydrophilic polymers. The formulation F1 F2 and F3 containing different concentration of

Carbopol 934P in combination with Chitosan showed the lower drug release as compared to the formulations F4 to F6. The possible reason for observed reduction in total release of drug may be the interaction between two oppositely charged bioadhesive polymers that is cationic Chitosan and anionic Carbopol 934 P. It may be expected that inter polymer complex between carboxylic group of Carbopol 934 P and hydroxyl or amino group of Chitosan will be formed and the dissolution rate retarded by complex formation.

From the above evaluation parameters it was concluded that the formulation F4 having a good bioadhesive strength and high percentage of drug release in a sustained manner, so the formulation F4 was selected as the optimized formulation. Hence the formulation F4 was selected for the further stability study.

Table 6
Drug release kinetic studies of Buccoadhesive tablets

Form. code	Zero order plot R^2	First order Plot R^2	Higuchi R^2	Korsemeyer-Peppas		Best model
				R^2	N	
F4	0.977	0.947	0.971	0.652	0.67	Peppas

Further to characterize the release mechanism of Promethazine Hydrochloride from buccoadhesive tablets, the dissolution data was subjected to the different model such as zero- order, first order, Korsmeyer-peppas and matrix- Higuchi diffusion models. The release kinetic is best explained by the Korsmeyer- peppas and first order models. The values of n (diffusion exponent) were estimated by linear regression of log cumulative % drug release Vs log time (t) of different formulations; results are showed in Graph 6. The obtained values of n lie between 0.5 to 1.0 in all the formulations exhibiting a non- fickian release behavior controlled by combination of diffusion and chain relaxation mechanism. The optimized formulation F4 showed the sustained drug release according to the Korsmeyer- peppas diffusion model showed in table 6.

Stability Study:-

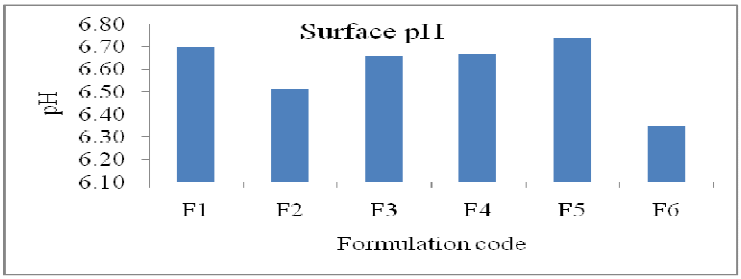
The optimized formulation (F4) was analyzed for various physical parameters.

Table 7
Stability studies of Buccal tablets

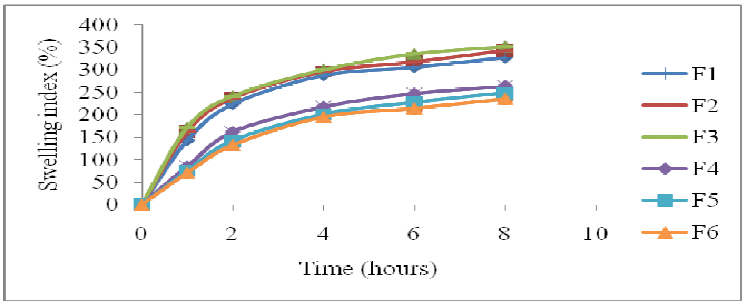
Characteristic	Initials	1 Month	2 Month	3 Month
Hardness (kg/cm2)	9.10±0.06	9.10±0.05	9.09±0.04	8.73±0.09
Drug content(mg/tab)	98.74±0.81	98.51±0.83	98.08±0.37	97.04±0.07
Bioadhesive Force(N)	2.192±0.02	2.174±0.03	2.148±0.03	2.094±0.05
In-vitro drug release	96.62±0.46	95.78±0.32	95.55±0.10	95.25±0.17

Comparisons of cumulative % drug released at the end of 10 hours for formulation F4 with initial and different periods of stability. No major difference was found between evaluated parameters before and after storage and all are in acceptable limits, showed in table 7. The tablets showed satisfactory physical stability at 40^0C at 75 % RH; results are showed in Graph 7 and 8.

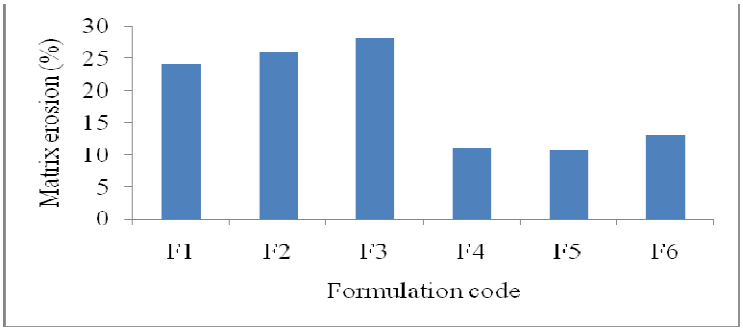
Graph 1
Surface pH of Buccal Tablets



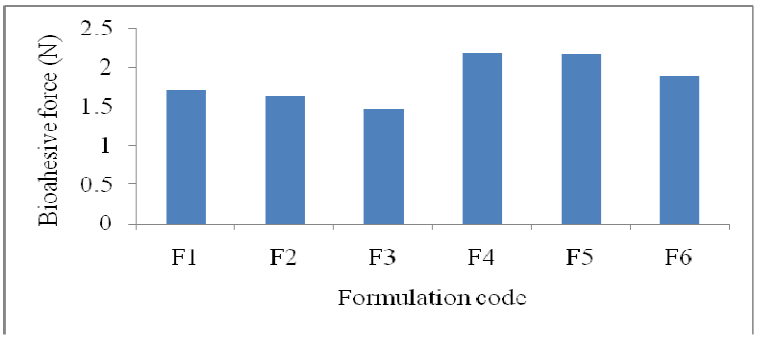
Graph 2
In-Vitro Swelling Study



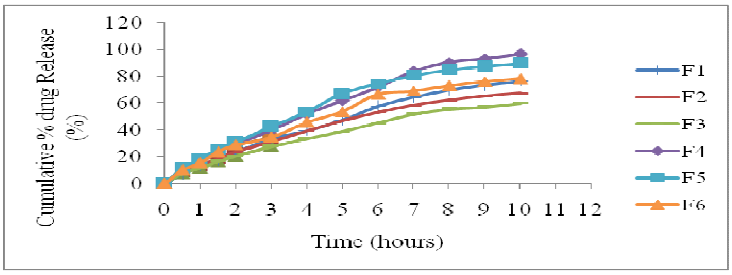
Graph 3
Matrix erosion of Buccal Tablets



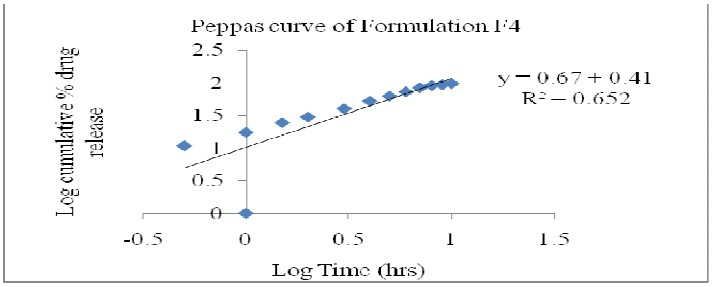
Graph 4
Effect of Bioadhesive polymers on Bioadhesive force



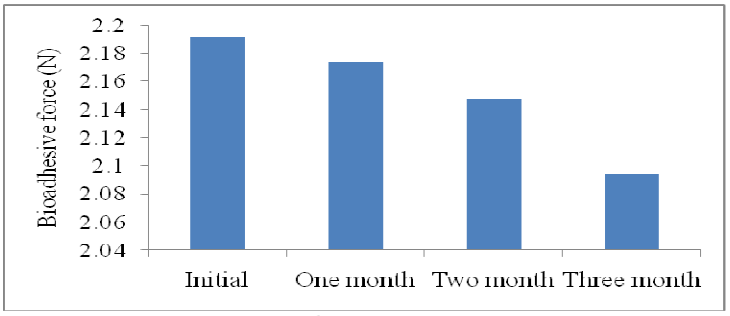
Graph 5
In-Vitro Drug Release Study



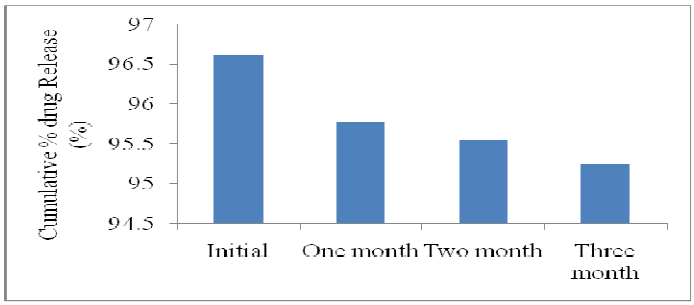
Graph 6
Peppas curve of formulation (F4)



Graph 7
Comparisons of Bioadhesive force (N) for formulation F4 with initial and different periods of stability



Graph 8
Comparisons of cumulative % drug released at the end of 10 hours for formulation F4 with initial and different periods of stability



CONCLUSION

The Mucoadhesion time of all batches was studied and result showed that the mean adhesion time was increased in the formulation containing Carbopol 934P with HPMC K4M was good than formulation containing Carbopol 934P with Chitosan. The detachment force observed with formulation containing Carbopol 934P with HPMC K4M was good than formulation containing Carbopol 934P with Chitosan. The results of In-vitro drug release study indicated that the formulation containing Carbopol 934P with HPMC K4M extended the release of the Promethazine HCl and these formulations also shown good bioadhesion. Hence, Formulation F4 was the most promising formulation as it gives satisfactory release (96.62%) for 10 hours and required more bioadhesive force (2.19 N) as compare to other batch formulations. The optimized formulation (F4) had shown the satisfactory release of drug and excellent bioadhesive properties. Hence, as the results obtained, it was observed that the formulation had feasibility of formulating buccal drug delivery in the form of buccal tablet of Promethazine Hydrochloride. Hence, from overall results, it can be concluded that the objective of this study is achieved.

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