International Journal of PharmTech Research
CODEN (USA): IJPRIF ISSN : 0974-4304
Vol. 3, No.1, pp 516-525, Jan-Mar 2011

Development and *in-vitro* Evaluation of Buccoadhesive Metoclopramide Hydrochloride Tablet Formulations

Yadav Deepak R.*, T. Ayyappan, S. Shanmugam, K. Sundaramoorthy and T. Vetrichelvan.

Adhiparasakthi College of pharmacy, Melmaruvathur-603 319, Tamilnadu, India.

Corres.author: deep_y85@yahoo.com, Mobile No: 09029183994.

Abstract: Buccoadhesive tablets of Metclopramide Hydrochloride were fabricated with objective of avoiding extensive first pass metabolism and to prolong its duration of action with reduction in dosing frequency. The mucoadhesive polymers used in the formulations were Carbopol 934P, Chitosan, HPMC K4M and HPMC K15M. Tablets were prepared by direct compression method using polymer in different ratios. The tablets were evaluated for dimension (diameter and thickness), hardness, friability, 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 subjected to stability study. Formulation (F4) containing Carbopol 934P and HPMC K4M in the ratio of (1:1) showed good bioadhesive force and maximum drug release of 96.10% in 10 hours. The surface pH of all tablets was found to be satisfactory, close to buccal pH, hence no irritation would observe with these tablets. FTIR studies showed no evidence on interaction between drug and polymers. It was observed that the optimized formulation follows korsmeyer-peppas release kinetics.

Keywords: Buccoadhesive tablets, Metoclopramide Hydrochloride, Bioadhesion and *in-vitro* drug release.

Introduction

Buccal delivery of drugs provides an attractive alternative to the oral route of drug administration, particularly in overcoming the disadvantages associated with the later mode of dosing. Problems such as first pass metabolism and drug degradation in the harsh gastrointestinal environment can be circumvented by administering drug via buccal route. Moreover, the oral cavity is easily accessible for self medication and can be promptly terminated in case of toxicity just by removing the dosage form from buccal cavity. It is also possible to administer drug to patients who cannot be dosed orally via this route.[1-4]

Metoclopramide Hydrochloride is commonly used for the treatment of nausea and vomiting. This drug is highly water soluble and is rapidly absorbed after oral administration. It has a short biological half life (4.5 hours) and is usually administered in a dose of 10 to 15 mg four times daily in order to maintain effective concentrations throughout the day. In long - term therapy, fluctuation in the plasma concentration, with high concentration peaks are common for drugs with rapid absorption and elimination. The secondary effects of Metoclopramide Hydrochloride on the Central Nervous System in the form of extrapyramidal symptoms, if plasma levels markedly exceed therapeutic levels. Such characteristics make Metoclopramide Hydrochloride as best suitable drug candidates for controlled drug delivery.

In the present investigation, an attempt has been made to design efficacious and prolonged release buccoadhesive tablets of Metoclopramide Hydrochloride using various polymers to avoid first pass metabolism, to reduce dosing frequency and to improve patient compliance.

Materials and Methods

Materials

Metoclopramide Hydrochloride was received as a gift sample from Ipca laboratories (Mumbai, India). Carbopol 934P was procured from Loba chemie (Mumbai, India). HPMC K4M and HPMC K15M were received as a gift samples from Griffon Laboratories (Mumbai, India). Chitosan was procured from Ranbaxy research laboratories (Gurgaon, India). All other reagents and materials were of analytical or pharmacopoeial grade.

Fourier transforms infra-red (FTIR) spectroscopy[5, 6]

FTIR study was carried out to check compatibility of drug with polymers. Infrared spectrum of Metoclopramide Hydrochloride was determined on Fourier transform Infrared Spectrophotometer using KBr dispersion method. The base line correction was done using dried potassium bromide. Then the spectrum of dried mixture of drug and potassium bromide was run followed by drug with various polymers by using FTIR spectrophotometer. The absorption maximums in spectrum obtained with the substance being examined correspond in position and relative intensity to those in the reference spectrum.

Preparation of buccoadhesive tablets

Buccoadhesive tablets were formulated by direct compression method. All ingredients were passed through mesh no. 60. Required quantity of each was taken for particular formulation (Table1) and the blend was mixed by mortar and pestle. The powder blend was compressed using 16 stations tablet compression machine (Cadmach, Ahmadabad, India) to produce flat faced tablets weighing 150 mg each with the diameter of 9 mm.

Evaluation of buccoadhesive tablets[10]

The prepared buccoadhesive tablets were evaluated for Dimension (Diameter and Thickness) using 6 tablets (vernier calipers), uniformity of weight using 20 tablets (Shimadzu BL-220H analytical balance), hardness using 6 tablets (Monsanto hardness tester) and friability using 20 tablets (Roche type friabilator).

Content uniformity[11]

The drug content in each formulation was determined by triturating 10 tablets and powder equivalent to 10 mg was added in 100ml of pH 6.8 phosphate buffer followed by stirring for 10 minutes. The solution was filtered through a 0.45µ membrane filter, diluted suitably and the absorbance of resultant solution was measured by using Shimadzu-1700 Pharmaspec UV-VISIBLE spectrophotometer at 309 nm using pH 6.8 phosphate buffers.

Surface pH study[12, 13]

The surface pH of the buccal tablet was determined in order to investigate the possibility of any side effects in an oral cavity. As an acidic or alkaline pH may irritate the buccal mucosa, attempt was made to keep the surface pH close to the buccal pH. The tablets were allowed to swell for 2 h in 1 ml of distilled water. The surface pH was measured by bringing the electrode in contact with the surface of the formulations and allowing it to equilibrate for 1 min.

***In- vitro* swelling study**[14, 15]

Three tablets were used from each formulation for the test. After recording the initial weights the tablets were placed over a 10 cm diameter wet filter paper disc soaked in purified water in a petridish at room temp. After the time interval of 1, 2, 4, 6 and 8 h., the tablets were removed and weighed individually. The percent water sorption was calculated using following formula:

% Swelling index = $[(w_2-w_1)/w_1] \times 100$

Where,

W_2: weight of tablet after particular time interval

W_1: initial weight of tablet

Table 1: Composition of bucccoadhesive tablets of Metoclopramide Hydrochloride

Ingredients (mg/tab)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Metoclopramide Hydrochloride	30	30	30	30	30	30	30	30	30
Carbopol 934P	49	32.6	24.5	49	32.6	24.5	49	32.6	24.5
Chitosan	49	65.4	73.5	-	-	-	-	-	-
HPMC K4M	-	-	-	49	65.4	73.5	-	-	-
HPMC K15M	-	-	-	-	-	-	49	65.4	73.5
Lactose	21	21	21	21	21	21	21	21	21
Magnesium Stearate	1	1	1	1	1	1	1	1	1

Matrix erosion study[14]

The swollen tablets were dried at 60° for 24 hr in an oven and kept in desiccators for 48 hr and reweighed. The percent matrix erosion were calculated by using following formula,

%Matrix erosion= $[(w_1-w_3)/w_3] \times 100$

Where, W1- Initial weight of tablet

W3-Weight of dried tablet after desiccation.

***in- vitro* bioadhesion study**[16, 17]

Bioadhesive strength of the tablets were measured on a modified physical balance using method described by Gupta et al. Measurement of adhesion force was determined by using bovine buccal mucosa which was obtained from slaughter house. The underlying tissues were separated and washed thoroughly with phosphate buffer solution (pH 6.8). The membrane was then tied to the bottom of the lower vial using rubber band. The vial was kept in glass bottle which was filled with phosphate buffer solution at 37 ± 1 ^{0}C in such way that buffer just reaches the surface of mucosal membrane and kept it moist. The tablet to be tested was stuck on the lower side of the hanging Glass vial by using adhesive tape and the weight (2 gm) on the right pan was removed. This lowered the left side of the pan along with the tablet over the mucosa. It was kept undisturbed for three minutes and the weights are added on right side of pan till the tablet just separated from the membrane surface. The excess weight on the right pan i.e. total weight minus 2 gm was taken as measure of bioadhesive strength. Bioadhesive force was calculated by using following equation.

$$\text{Bioadhesive force} = \frac{\text{Bioadhesive strength}}{1000} \times 9.81$$

***Ex-vivo* mucoadhesion time**[18]

The *ex-vivo* mucoadhesion time was examined after application of the buccal tablet on freshly cut bovine buccal mucosa. The fresh bovine buccal mucosa was tied on the glass slide and a mucoadhesive core side of each tablet was wet with 1 drop of phosphate buffer (pH 6.8) and pasted to the bovine buccal mucosa by applying a light force with a fingertip for 30 seconds. The glass slide was then put in the beaker, which was filled with 200 ml of the phosphate buffer and kept at 37 ^{0}C± 1 ^{0}C. After 2 minutes, a slow stirring rate was applied to stimulate the buccal cavity environment and tablet adhesion was monitored for 20 hours. The time for the tablet to detach from the bovine buccal mucosa was recorded as the mucoadhesion time.

***in- vitro* drug release study**[12, 19]

The influence of technologically defined condition and difficulty in simulating *in- vivo* conditions has led to the development of a number of *in- vitro* release methods for buccal formulations, however, no standard method has yet been developed. *In-vitro* release rate of buccoadhesive tablets of Metoclopramide Hydrochloride was carried out using rotating basket apparatus (USP Type I). The dissolution medium consisted of 500 ml of phosphate buffer (pH 6.8). The release study was performed at 37 ^{0}C ± 0.5 ^{0}C with a rotation speed of 50 rpm. The sample (5 ml) was withdrawn at time interval of 30, 60 and 90 minutes up to 10 h and replaced with 5 ml of dissolution media. The amount of Metoclopramide Hydrochloride released was determined spectrophotometrically at 309 nm.

Kinetics of *in-vitro* drug release[20]

To study the release kinetics of *In-vitro* drug release, data was applied to kinetic models such as zero order, first order, Higuchi and Korsmeyer-Peppas.

Zero order: $C = K_0 t$

K_0 - zero-order rate constant expressed in units of concentration/time, t - time in hrs.

First order: $LogC = LogC_0 - Kt / 2.303$

Where, C_0 - is the initial concentration of drug, K - first order constant, t - time in hrs.

Higuchi: $Qt = Kt^{1/2}$

Where Q_t - amount of the release drug in time t, K- kinetic constant, t- time in hrs.

Korsmeyer peppas:

$$Mt / M\infty = Kt^n$$

Where

M_t - represents amount of the released drug at time t,

M_∞- Is the overall amount of the drug (whole dose) released after 12 hrs

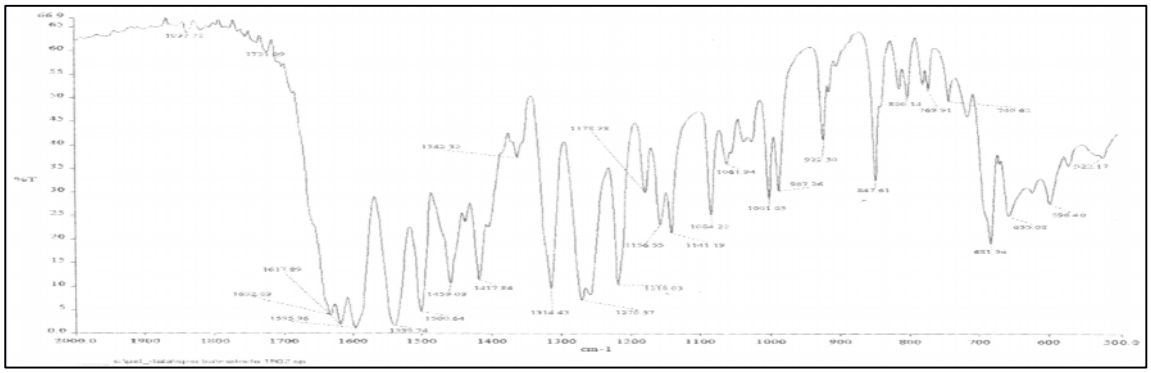
K- Is the diffusional characteristic of drug/ polymer system constant

n- Is a diffusional exponent that characterizes the mechanism of release of drug.

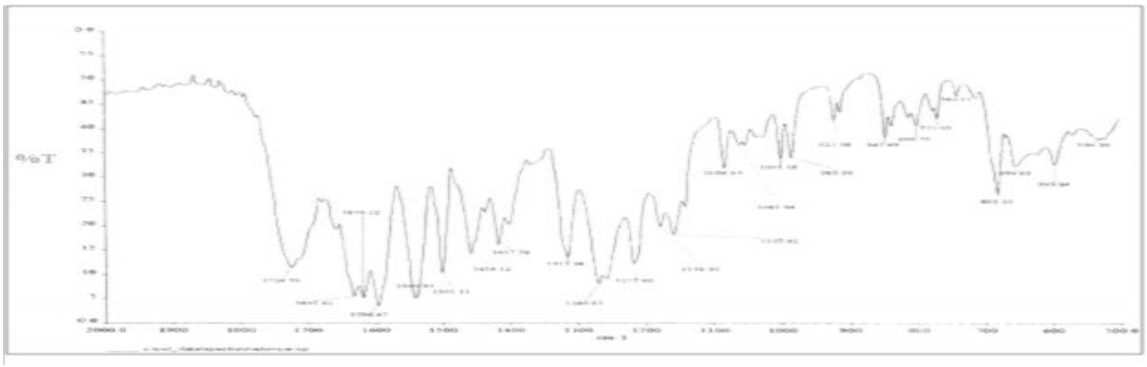
Stability studies[21]

Stability studies were carried out at 40°C / 75% RH as per ICH guidelines for the optimized formulation for 3 months. The tablets were stored at 40°C/75% RH in closed high density polyethylene bottles for 3 months. The samples were withdrawn after periods of 1 month, 2 months and 3 months. The samples were analyzed for its hardness, drug content and bioadhesive force and *in-vitro* drug release.

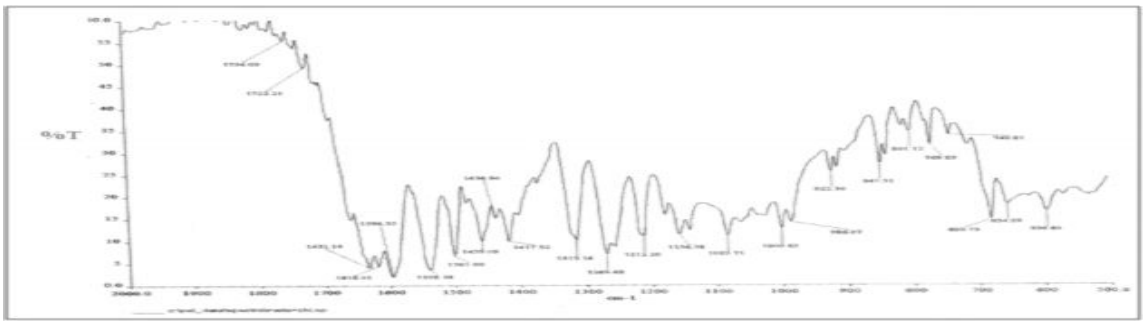
1A)



1B)



1C)



1D)

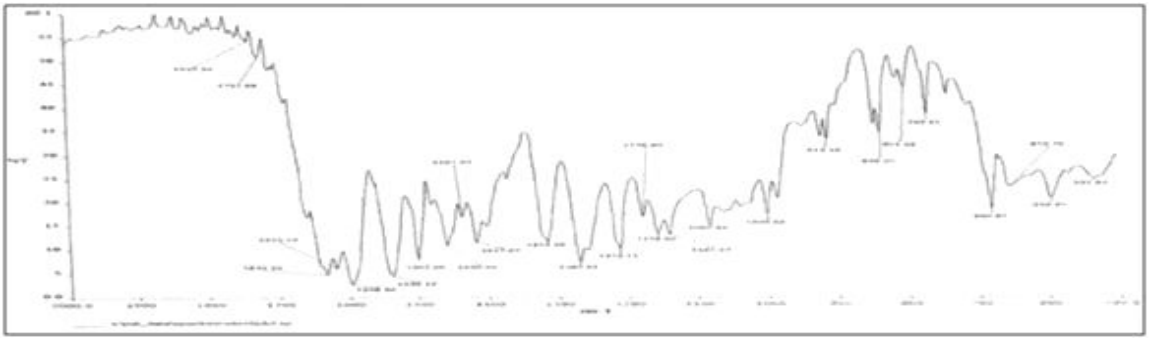


Fig. 1: FT-IR spectra of A) Metoclopramide Hydrochloride, B) Metoclopramide Hydrochloride + Carbopol 934P, C) Metoclopramide Hydrochloride + Chitosan, D) Metoclopramide Hydrochloride + HPMC.

Results and Discussion

Before designing various formulations, the drug-polymer compatibility study was conducted by FTIR spectroscopy. The results are present in figure1 and it indicates that there was no incompatibility between drug-polymers.

Total nine different formulations (F1-F9) of Metoclopramide Hydrochloride buccal tablets were prepared by direct compression technique using various proportions of polymers.All the studies were performed in triplicate, and results are expressed as mean ±SD.

The size (diameter) of the tablets of all formulations were found to be 9.0±0.0 mm and thickness ranged between 2.08±0.08mm to 2.25±0.14mm. Hardness of the tablet for each formulation was 6.33±0.25 kg/cm^2 to 10.16±0.25 kg/cm^2, Hardness of the tablet increased with increasing the amount of Carbopol 934P. The difference in the tablet strength are reported not to affect the release of the drug from hydrophilic matrices drug release is by diffusion through the gel layer and/ or erosion of this layer and is therefore independent of the dry state of the tablet.. The percent friability of all formulations was ranged from 0.24±0.03% to 0.45±0.01%. The percentage deviation from average tablet weight for all the formulations ranged from 1.14% to 2.42%. Drug content was found to be uniform for all formulations and ranged from 98.20±0.44% to 101.89±0.73%. The results given in the table and its graphical representation showed that the surface pH of all the tablets was within the range of 6.34±0.015 to 6.84±0.025. These results indicated that there is no risk of mucosal damage or irritation while administering these formulations on buccal mucosal region.

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. 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, and Carbopol 934 P with HPMC K15M, showed lower swelling index.

The swelling index values of tablets containing combination of Carbopol 934 P and Chitosan increased increased with increasing with increasing amount of Chitosan. The swelling indices of the tablets 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.

The tablets from Chitosan group showed faster hydration rate but they also showed maximum weight loss (erosion). The tablets containing HPMC were found to exhibit least matrix erosion.

The bioadhesive property of mucoadhesive tablets of Metoclopramide Hydrochloride 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 934P: HPMC K4M combination, this followed by F7 formulations containing Carbopol 934P: HPMC K15M combination. The reason for such findings might be ionization of Carbopol 934P at salivary pH which leads to improved attachments of the device to mucosal surface. Adhesion force decreased as another polymer is mixed with the Carbopol 934P.

The *ex-vivo* mucoadhesion time was examined after application of the buccal tablet on freshly cut bovine buccal mucosa. The result showed in Table 3, 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 bovine buccal mucosa ranged from 11.46±0.040 to 17.26±0.070 hours.

In-vitro drug release studies revealed that the release of Metoclopramide Hydrochloride from different formulations varies with the characteristics and composition of matrix forming polymers as shown in figure 4. 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 76.07%, 67.50% and 59.19% drug release respectively.

Table 2: Physicochemical properties of bucccoadhesive tablets

Code	Dimension		Hardness (kg/cm^2)	Friability (%)	Weight variation (%)	Drug content (%w/w)	Surface pH
	Diameter (mm)	Thickness (mm)					
F1	9.0±0.0	2.09±0.10	10.16±0.25	0.24±0.03	2.42	101.89±0.73	6.68±0.005
F2	9.0±0.0	2.16±0.12	8.33±0.25	0.34±0.07	1.42	98.67±0.26	6.50±0.025
F3	9.0±0.0	2.12±0.15	7.25±0.27	0.40±0.08	1.14	100.58±0.36	6.63±0.015
F4	9.0±0.0	2.17±0.07	9.08±0.20	0.37±0.07	1.93	98.70±0.55	6.64±0.025
F5	9.0±0.0	2.08±0.08	8.25±0.27	0.45±0.01	1.67	98.53±0.41	6.75±0.020
F6	9.0±0.0	2.25±0.14	6.33±0.25	0.34±0.04	1.72	99.53±0.56	6.34±0.015
F7	9.0±0.0	2.20±0.10	9.41±0.20	0.41±0.03	1.68	98.20±0.44	6.44±0.025
F8	9.0±0.0	2.15±0.15	7.16±0.25	0.32±0.10	2.02	98.96±0.49	6.37±0.025
F9	9.0±0.0	2.23±0.13	6.50±0.31	0.33±0.05	1.81	99.83±0.12	6.84±0.025

Table 3: Evaluation parameters of buccoadhesive tablets

Code	Swelling time (hours)	% Matrix erosion (%)	Bioadhesive strength (g)*	Bioadhesive force (N)	Mucoadhesion time (hours)	Cumulative % drug release
F1	325.11±3.54	24.06±1.189	17.53±0.060	1.71±0.005	14.20±0.040	76.07±0.27
F2	340.92±2.87	27.20±0.517	16.39±0.062	1.60±0.005	13.41±0.065	67.50±0.27
F3	351.41±1.54	28.17±0.484	14.91±0.055	1.46±0.007	11.46±0.040	59.19±0.12
F4	261.88±2.84	11.29±0.486	22.62±0.090	2.21±0.008	17.26±0.070	96.10±0.32
F5	251.67±1.86	10.95±0.556	21.39±0.060	2.09±0.006	15.31±0.055	89.81±0.22
F6	236.10±1.01	13.87±0.305	19.78±0.071	1.94±0.005	14.44±0.045	78.45±0.20
F7	250.89±0.69	12.65±0.200	21.61±0.070	2.12±0.006	16.41±0.066	87.38±0.54
F8	238.53±0.55	13.78±0.338	20.82±0.055	1.94±0.008	14.31±0.065	78.55±0.34
F9	224.93±0.55	15.50±0.337	17.41±0.058	1.70±0.009	13.15±0.060	70.77±0.33

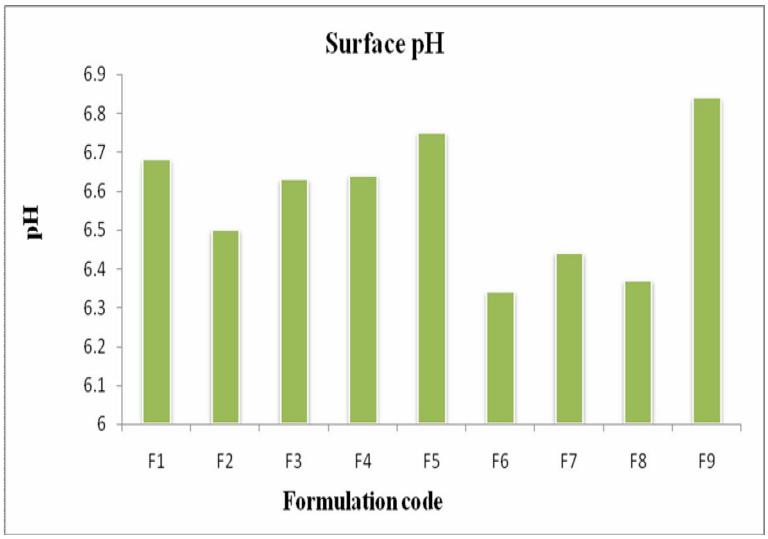


Fig. 2: Surface pH of buccoadhesive tablets

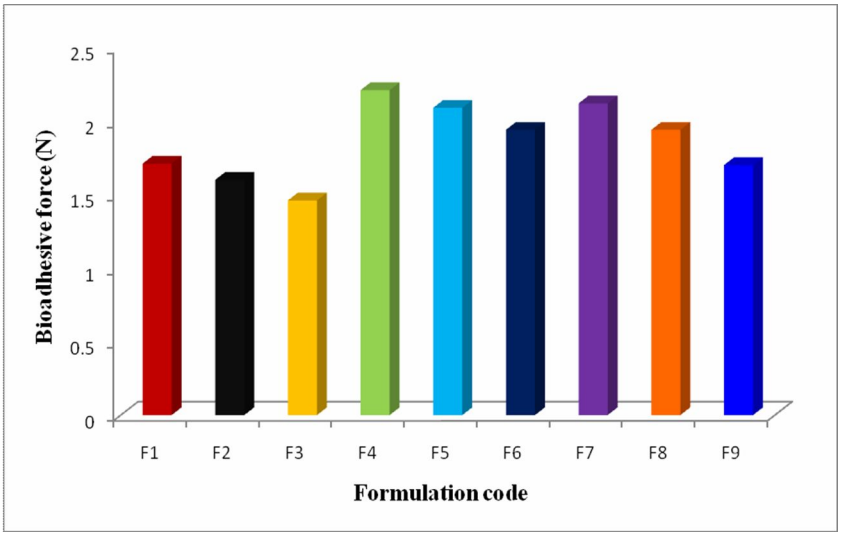


Fig. 3: Effect of bioadhesive polymers on bioadhesive force

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. The *In-vitro* cumulative drug release profile of formulations F4, F5 and F6 at 10 hours showed 96.10%, 89.81% and 78.45% drug release respectively. Similarly, the formulation F7, F8 and F9 contain the Carbopol 934P and HPMC K15M polymers in the ratio of 1:1, 1:2 and 1:3 respectively. The *In-vitro* cumulative drug release profile of formulations F7, F8 and F9 at 10 hours showed 87.38%, 78.55% and 70.77% drug release respectively.

The release rate of Metoclopramide 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 F9. 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.

It could be speculated that the extent of hydrogen bonding between Carbopol 934 P and Chitosan in the inter polymer complex depends on the pH of the medium, causing differences in dissolution degree. Therefore, there is possibility of formation of compact complex structure composed of ammonium ion of Chitosan and carboxylate ion of Carbopol 934 P at pH 6.8, which leads to decreased dissolution. At pH 4.0, below the pKa value of Carbopol 934 P the carboxylic group in polymer complex is in unionized state and Chitosan exists as ammonium ion. Thus, due to dissociation of intermolecular ammonium salt the dissolution degree increases at pH 4.0. At pH 7.0 amine of Chitosan is in the form of non protonated and Carbopol 934 P exist in ionized form resulting in even higher dissolution degree than that at pH 6.8.

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.

Kinetics for Drug Release

Further to characterize the release mechanism of Metoclopramide 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. 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.

Table 4: Drug release kinetic studies of Buccoadhesive tablets

Code	Zero order		First order		Higuchi		Korsemeyer- Peppas		Best fit model
	R^2	K_0 (mg/h^{-1})	R^2	K_1 (h^{-1})	R^2	K (mg$h^{-1/2}$)	R^2	n	
F1	0.9783	8.6743	0.9972	0.1435	0.9686	22.5546	0.9985	0.7957	Peppas
F2	0.9563	7.9286	0.9958	0.1205	0.9813	20.8056	0.9977	0.7134	Peppas
F3	0.9610	6.9175	0.9930	0.0976	0.9800	18.1255	0.9983	0.7133	Peppas
F4	0.9762	11.0773	0.9652	0.2742	0.9695	28.8290	0.9988	0.7693	Peppas
F5	0.9501	10.7455	0.9964	0.2258	0.9798	28.2303	0.9970	0.7152	Peppas
F6	0.9531	9.3129	0.9952	0.1615	0.9788	24.4424	0.9958	0.7110	Peppas
F7	0.9677	10.0865	0.9919	0.1974	0.9766	26.3608	0.9985	0.7333	Peppas
F8	0.9187	9.6531	0.9906	0.1695	0.9831	25.5583	0.9888	0.7117	1st order
F9	0.9313	8.4535	0.9873	0.1332	0.9814	22.3106	0.9780	0.7445	1st order

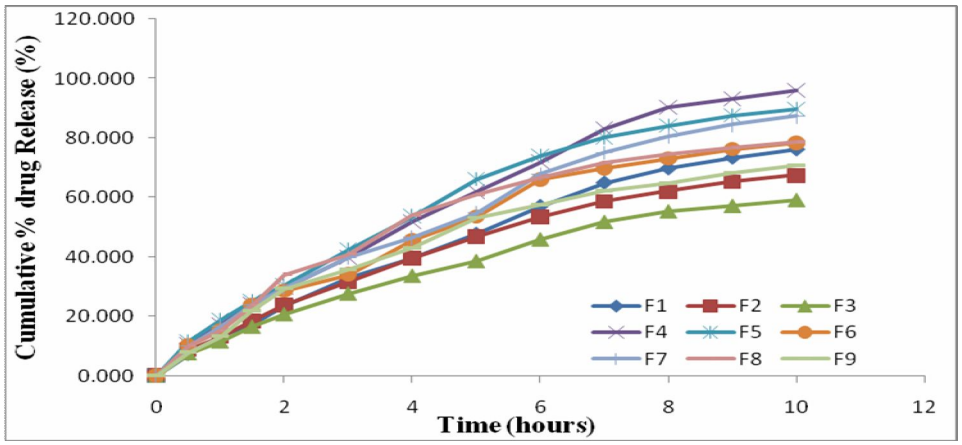


Fig. 4: Comparative drug release profile of all buccoadhesive tablets.

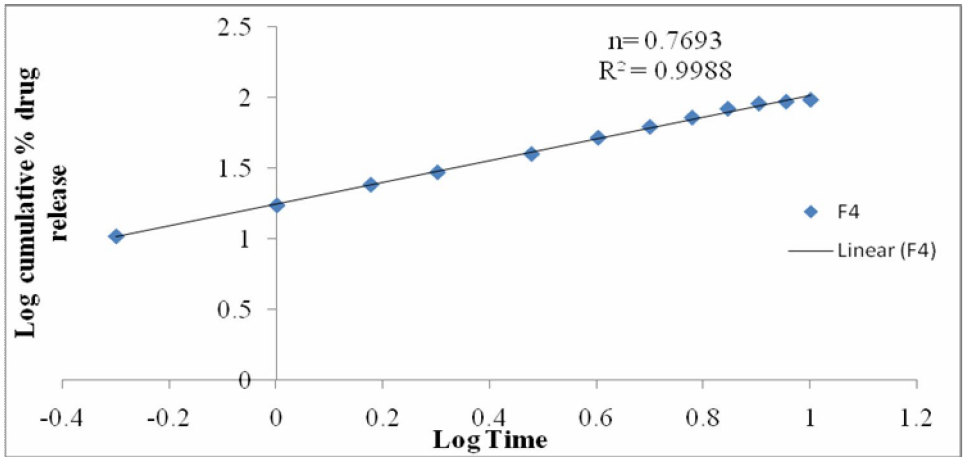


Fig. 5: Peppas curve of formulation F4

Table 5: Stability studies of buccoadhesive tablets

Characteristic	Initials	1 Month	2 Month	3 Month
Hardness (kg/cm^2)	9.08±0.20	9.08±0.19	9.08±0.20	8.91±0.21
Drug content (mg/tablet)	98.70±0.55	98.29±0.52	97.74±0.35	96.97±0.20
Bioadhesive force (N)	2.21±0.08	2.15±0.04	2.10±0.05	2.03±0.03
In-vitro drug release at 10 hour	96.10±0.32	95.78±0.32	95.55±0.10	95.25±0.17

Stability Study

After storage, the optimized formulation (F4) was analyzed for various physical parameters; results are showed in Table 5.

No major difference was found between evaluated parameters before and after storage and all are in acceptable limits. The tablets showed satisfactory physical stability at 40 ^{0}C at 75 % RH.

Conclusion

The present work was aimed to develop the buccoadhesive tablet of Metoclopramide Hydrochloride to reduce the dosing frequency of drug. The bioavailability of drug can also be improved with this buccoadhesive drug delivery system by avoiding extensive first pass effect, increasing efficacy, compliance and better clinical usefulness of patients. The optimized formulation (F4) had shown the satisfactory release of drug and excellent bioadhesive properties. Hence, from the results obtained, it was observed that the formulation had feasibility of formulating buccal drug delivery in the form of buccal tablet of Metoclopramide Hydrochloride as; it can help to bypass extensive hepatic first pass metabolism and thus increasing efficacy of Metoclopramide Hydrochloride. Hence, from overall results, it can be concluded that the objective of this study is achieved.

Acknowledgements

The authors would like to thank Adhiparasakthi college of pharmacy, Melmaruvathur, India, for providing the necessary facilities for carrying out this research.

References

1. Shojaei A.H., Buccal mucosa as a route for systemic drug delivery: A review. J. Pharm. Pharmaceut. Sci., 1998, 1(1), 15-30.
2. Giunchedi P., Juliano C. and Sorrenti M., Formulation and in vivo evaluation of Chlorhexidine buccal tablets prepared using drug loaded Chitosan microspheres.Eur. J. Pharm. Biopharm., 2002, 53, 233-9.
3. Agarwal S. P., Rajesh K. and Alka A., Preparation and evaluation of bioerodible Buccal Tablets containing Clotrimazole. Int. J. Pharm., 1996, 138, 67-73.
4. Asha S. J., Sathesh B. P., Divakar G., Manoj K. J. and Kapil K. P., Development and evaluation of buccoadhesive drug delivery system for Atorvastatin Calcium. J. Current Pharm. Res., 2010, 1, 31-38.
5. Robert M. Silverstein., Spectrometric identification of organic compounds, 6th edn. 2003, 71-144.
6. Becket A. H. and Stenlake J. B., Practical pharmaceutical chemistry. 4th edn. CBS. Publishers, New Delhi, II, 2005, 278-280.
7. Chatwal G. R. and Anand S. K., Instrumental methods of chemical analysis. Himalaya publishing house, Mumbai, 2007, 2.747-2.750.
8. Ansel S. C., Allen L. V. and Popovich N. G., Pharmaceutical dosage form and drug delivery systems. 8th edn., Lippincott Williams & Wilkins, New York, 2009, 234-238.
9. Aulton, M.E. Pharmaceutics: The science of dosage form design. 3rd edn. Churchill Livingstone, New York, 2007, 168-179, 461-464.
10. Lachmann L., Lieberman H. A. and Kanig J. L., The theory and practice of Industrial pharmacy. 3rd edn., Varghese Publishing House, Mumbai, 1987; 67, 293-373.
11. Anonymous. Indian Pharmacopoeia. 5 th edn., Government of India, Ministry of Health and Family Welfare, The Indian Pharmacopoeial commission, Ghaziabad, 2007, 1, 2, 179-183, 662-663, 1378 - 1380.
12. Ayyappan T. and Kasture P.V., Development and in vitro evaluation of a buccoadhesive Ondansetron Hydrochloride tablet formulation. Indian Drugs, 2005, 43(2), 92-95.
13. Parvez, N., Ahuja A. and Khar R. K., Development and evaluation of mucoadhesive buccal tablet of Lignocaine Hydrochloride. Indian J. Pharm. Sci., 2002, 64(6), 553-567.
14. Ramana M. V., Nagda C. and Himaja M., Design and evaluation of mucoadhesive buccal drug delivery systems containing Metoprolol Taratarate. Indian J. Pharm. Sci., 2007, 69(4), 515-518.
15. Nakhat P. D., Kondawar I. B., Rathi L. G. and Yeole P. G., Studies on buccoadhesive tablets of Terbutaline Sulphate. Indian. J. Pharm. Sci., 2007, 69 (4) 505-510.
16. Gupta A., Garg S. and Khar R.K., Measurement of bioadhesive strength of mucoadhesive buccal tablets: design of an in vitro assembly. Indian Drugs, 1992, 30, 152-155.
17. Cafaggi S., Leardi R., Parodi B., caviglioli G. and Bignardi G., Preparation and Evaluation of a Chitosan salt-poloxamer 407 based matrix for buccal drug delivery. J. Control. Rel., 2005, 102, 159-169.
18. Patel V. M., Prajapati B. G., Patel H. V. and Patel K. M., Formulation, evaluation and comparison of bilayered and multilayered mucoadhesive buccal devices of Propranolol Hydrochloride. AAPS

Pharm. Sci. Tech., 2007, 8 (1), 1- 8.

19. Rahman-Abdul, Mahorous M. G. and Mahmoud E. B., Preparation and comparative evaluation of sustained release Metoclopramide Hydrochloride matrix tablets. Saudi Pharm. J. 2009, 17 (4), 295-301.
20. Brahmankar D.M. and Jaiswal S.B., Biopharmaceutis and Pharmacokinetics: A treatise. 2nd edn., Vallabh Prakashan, New Delhi, 2006, 64-65, 335-357.
21. Nakhat P. D., Babla I. B., Rathi L. G., Yeole P. G. and Ghule B. V., Design and characterization of buccoadhesive tablets of Promethazine Hydrochloride. Indian Drugs, 2007, 44 (7), 520-528.

*****