World Journal of Pharmaceutical and Life Sciences
WJPLS
www.wjpls.org
SJIF Impact Factor: 6.129

FORMULATION AND EVALUTION OF MUCOADHESIVE BUCCAL FILMS OF MOSAPRIDE CITRATE

***Likhith H. S., Suresh V. Kulkarani*, K. Manjunath, Pawan C., Arjun K. L.**

Department of Pharmaceutics, Sree Siddaganga College of Pharmacy, B.H. Road, Tumkur – 572102 Karnataka, India.

Corresponding Author: Likhith H. S.
Department of Pharmaceutics, Sree Siddaganga College of Pharmacy, B.H. Road, Tumkur – 572102 Karnataka, India.

Article Received on 04/05/2020 **Article Revised on 25/05/2020** **Article Accepted on 15/06/2020**

ABSTRACT

Gastro-prokinetic medications are pharmacological agents that are used to treat Gastro-esophageal reflux disease. The aim of the present study is to formulate and evaluate mucoadhesive buccal film of Mosapride citrate. Mosapride buccal films were prepared by using different polymers like HPMC K100, HEC, HPC and Glycerol as plasticizer and saccharin as a sweetening agent and vanillin as a flavoring agent. Buccal films were prepared using solvent casting technique. The major problem with Mosapride was it belongs to class Ⅱ in BCS classification and have low solubility in biological fluids. In order to enhance the solubility of mosapride solid dispersion of mosapride were prepared by melting technique at different drug carrier (PEG 4000) weight ratios and evaluated. No interaction was found between the drug and the polymers by the FTIR studies. The buccal films were evaluated for Folding endurance, weight variation, Drug content, Thickness, permeation study and *in-vitro* drug release study Dissolution profile as studied in USP dissolution apparatus type 1 using pH 6.8simulated saliva. The influence of variable like polymer type, concentration, of Mosapride citrate release profile was studied. The formulation was optimized on the basis of various evaluation parameters like drug content and In-vitro drug release. Formulation F3 successfully sustained the release of drug within 7 hours. stability studies were as per ICH guide lines and result indicated that the selected formulation was stable.

KEYWORDS: Mosapride citrate, HPMC K100, HEC, HPC, PEG 4000, Buccal films.

INTRODUCTION

In the course of the most recent two decades mucoadhesion has happened to enthusiasm for its capability to improve confined medication conveyance, by holding a dosage form at the site of administration (e.g.: inside gastrointestinal tract) or systemic delivery, by retaining a formulation in close contact with the absorption site (e.g. the buccal cavity). Mucoadhesion might be characterized as a state where two materials, one of which is bodily fluid or a mucous film, is held together for broadened timeframe. Out of the different destinations accessible for mucoadhesive medication conveyance, buccal mucosa is the most fit one for local as well as systemic delivery of medications. It's anatomical and physiological highlights like nearness of smooth muscles with high vascular perfusion, shirking of hepatic first pass digestion and henceforth can possibly improve bioavailability are the special highlights which make it as a perfect course for mucoadhesive medication conveyance. Additionally, these dosage forms are economic and patient-friendly.The buccal mucosa allows a prolonged retention of a dosage form particularly with the utilization of mucoadhesive polymers absent a lot of obstruction in exercises, for example, discourse or rumination dissimilar to the sublingual course. Buccal film might be favored over adhesive tablet as far as adaptability and solace. Likewise, they can evade the generally short habitation time of oral gels on the mucosa, which are effortlessly washed away and evacuated by salivation. Additionally, the buccal films can ensure the injury surface, accordingly decreasing agony and rewarding oral ailments more effectively.

Advantages of buccal films include improved patient compliance, taste masking character, reduction in dose of drug, no need of water during film administration, no fear of chocking and enhanced stability. Hence, in the present study we made an attempt to develop mucoadhesive buccal films of mosapride citrate.

MATERIALS AND METHODS

Mosapride citrate from Yarrow chemicals, Hydroxypropyl methyl cellulose (HPMC K 100), Hydroxy propyl cellulose (HPC), Hydroxy ethyl cellulose (HEC), from Yarrow chemicals. All other chemicals used were of analytical grade.

Standard Curve of Mosapride citrate

Mosapride citrate is a white fine powder which was soluble in Simulated saliva pH 6.8. Though several methods are reported for its estimation, the UV spectrophotometric method was employed in the study. Mosapride citrate shows maximum absorbance at 270 nm in simulated saliva pH 6.8. Based on this information, a standard graph was constructed (Figure No.1).

Ftir Studies

FT-IR spectra of pure Mosapride citrate, and combination with HPMC K100, HEC, HPC, PEG 4000 is showed in (Figure 2a-2e). Pure Mosapride citrate showed principle absorption peaks at 1705-1725 cm-1 (C=O stretch) and 1000-1400 cm-1(C-N Stretch), 700-850 cm-1 (C-H Stretch), 800-600 cm-1(C-Cl Stretch),1000-1400 cm-1(C-F Stretch) Same peak of C=O Stretch, C-N Stretch, C-H Stretch, C-Cl Stretch, C-F Stretch bonds were present as that of pure drug without much shifting in the spectra of Mosapride citrate along with the polymers. This suggested no chemical interaction between the drug and polymer.

Preparation of Mosapride citrate solid dispersion

Mosapride citrate and PEG 4000 are mixed using mortar and pestle. PEG 4000 as carrier in different proportions 1:1 and 1:2 (drug: carrier). To accomplish a homogenous dispersion the mixture is heated at or above the melting point of all the components with constant stirring. It is then cooled to acquire a congealed mass. It is crushed and sieved.

Characterization of Mosapride citrate solid dispersion

1. Percentage Practical Yield

Percentage practical yield is calculated to know about percent yield, thus its help in selection of appropriate method of production. Solid dispersions were collected and weighed to determine practical yield (PY) from the following equation (Figure No.3)

$$\text{Percentage of practical yield} = \frac{\text{Practical yield}}{\text{Theoretical yield}} \times 100$$

2. Drug content

10 mg of solid dispersions were weighed accurately and dissolved in 10 ml of methanol. The solution was filtered, diluted suitably and drug content was analyzed at 270 nm by UV spectrophotometer. Each sample analyzed in triplicate (Figure No.4). Actual drug content was calculated for all batches using the equation as follows

$$\text{Percentage of drug content} = \frac{\text{Observed value}}{\text{Actual value}} \times 100$$

Drug-polymer interaction study of films

There is always a possibility of drug-excipients interaction in any formulation due to their intimate contact. The technique employed in this study to know drug- excipients interactions is IR spectroscopy. IR spectroscopy is one of the most powerful analytical techniques which offer the possibility of chemical identification. Infra-red spectra of pure drug Mosapride citrate and formulations were scanned by using FTIR, by a thin film method.

Evaluation of Mosapride citrate buccal films

a) Physical appearance and surface texture of films

This parameter was checked simply with visual inspection of films and evaluation of texture by feel or touch.

b) Weight uniformity of films

Three films of the size 2×2 cm was weighed individually using digital balance and the average weights were calculated.

c) Thickness of films

Thickness of the films was measured using screw gauge with a least count of 0.01mm at different spots of the films. The thickness was measured at three different spots of the films and average was taken.

d) Folding endurance of patches

The flexibility of films can be measured quantitatively in terms of what is known as folding endurance. Folding endurance of the films was determined by repeatedly folding a small strip of the films (approximately 2x2 cm) at the same place till it broke. The number of times films could be folded at the same place, without breaking gives the value of folding endurance.

e) Drug content uniformity of films

The drug content uniformity of films were tested by UV Spectrophotometric method. Films of 2×2 cm size were cut from three different places from the casted films. Each film was placed in 100 mL volumetric flask and dissolved in simulated saliva pH 6.8 and 5 mL is taken and diluted with water up to 10 ml. The absorbance of the solution was measured at λ max 270 nm using UV/ visible spectrophotometer (Shimadzu). The percentage drug content was determined.

f) *In-vitro* dissolution studies

The release rate of Mosapride citrate Buccal films was determined by using USP dissolution testing apparatus II at 50 RPM. The film with 2×2 cm was placed in the 300 mL of 6.8 pH simulated saliva as dissolution medium, and temperature was maintained at 37°C. From this dissolution medium, 2 mL of the sample solution was withdrawn at different time intervals. The samples were filtered through Whitman filter paper and absorbance was determined 270nm using double beam UV- Visible spectrophotometer.

g) Permeation study

The prepared Buccal films are placed in the diffusion cell on the upper membrane of the (donor compartment) and the receptor compartment contain a simulated saliva (20 ml) it can be contact with the dialysis membrane upper side of the donor compartment contain a film attach the film of length and width (2×2) cm it contain 10 mg of drug. And the receptor compartment it contain a simulated saliva and magnetic bead and this diffusion compartment placed in the magnetic stirrer the drug permeation start through the dialysis membrane and enter in to the receptor compartment the drug to be enter in the receptor compartment and this solution taken 2 ml at regular time intervals and maintain the sink condition by replace the 2ml of simulated saliva in to the receptor compartment and this every interval taken samples analyzed by (Shimadzu) UV-visible spectrophotometer.

h) Stability studies

The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors. To assess the drug and formulation stability, stability studies were done as per ICH guidelines. The formulated Buccal films were wrapped in aluminum foil and stored at 45 ± 0.5ºC for period of twelve weeks. After the period of three month, films were tested for appearance, drug content and In-vitro drug release.

RESULTS AND DISCUSSION

Among the two plans for solid dispersions i.e. F1 and F2, the optimized formulation was F2 which shows maximum drug content and percentage drug release compared to other formulations. These optimized mosapride citrate: Poly ethylene glycol 4000 solid dispersions (MOC: PEG 4000) at weight proportion of 1:2 arranged by dissolving strategy was chosen for this investigation. It was proposed to formulate and develop the sustained release buccal films of above solid dispersions to evaluate the efficacy of PEG 4000 solid dispersions. The formulated films were appeared to be clear, homogeneous; some are transparent and some are partially transparent. They were found be physically flexible and dry. The folding endurance was measured manually, by folding the films repeatedly at a point till it broke. The breaking time was considered as the end point. Folding endurance was found to be highest for FC 3 and lowest for FC 7. It was found that the folding endurance of the films was affected with increase of carrier concentration. The folding endurance values of the films were found to be optimum and therefore, the films exhibited the good physical and mechanical properties. The folding endurance of films was found to be in the range of 311 to 350 (Table No.3). As all the formulations contain different amount of polymers, the thickness was gradually increased with the amount of polymers. All the film formulations were found to have thickness in the range of 0.14 to 0.25 mm and were observed within the limits.

Weight variation

The randomly selected film strips about 2 × 2 cm areas were cut at different places from the casted film and weight was measured. Weight of film strip units varies from 47.24 to 54.78 mg. The results indicated that selected carriers used in method of solid dispersion preparation, proportion of carrier used have reduced the variation and improved the uniformity of the distribution in casted films (Table No.3).

Disintegration study

It was observed that in vitro dissolving/disintegration time varies from 36 to 47 sec for all the formulations (Table No.3). *In vitro* disintegration time of films was affected by polymers viz. HPMC K100, HPC and HEC. This is due to polymer's high-water absorption and retention capacities.

Drug content

The prepared film formulations were studied for their drug content. The drug was dispersed in the range of 91 % to 97 %. Suggesting that drug was uniformly dispersed in all films. (Table No. 3)

***In vitro* dissolution studies**

The *in-vitro* drug release profiles of the formulations in simulated saliva pH 6.8 show differences depending on their composition. The rate of drug release from the HPMC K100 films was significantly higher than the films containing HEC and HPC (Figure No.5-6). The formulation F3 films containing a HPMC K100 showing high percentage of drug release (97.39%) within 7 hours compare to that of films containing HEC and HPC as a polymer.

Drug permeation study

The formulation F3 containing HPMC K 100 has showed permeation of 94.08% in 8 hours, which is highest percentage with least time than the other formulations. (Table no. 5).

Table 1: *In-vitro* drug release data of solid dispersions.

Time (in mins.)	A1	A2
15	47.919944	54.113764
30	63.276889	69.755751
45	70.390934	75.980541
60	81.443111	88.938265

Table 2: Formulation details of mosapride mucoadhesive buccal films.

Formulation	Polymer and its composition (mg)				Glycerol (mL)	Sodium saccharin (mg)	Vanillin (mg)	D.water (mL)
	MOC:PEG4000	HPMC K 100	HPC	HEC				
F1	360	400			0.1	2	2	10
F2	360	450			0.1	2	2	10
F3	360	500			0.1	2	2	10
F4	360		400		0.1	2	2	10
F5	360		450		0.1	2	2	10
F6	360		500		0.1	2	2	10
F7	360			400	0.1	2	2	10
F8	360			450	0.1	2	2	10
F9	360			500	0.1	2	2	10

Table 3: Evaluation data for mucoadhesive buccal films.

Formulation Code	Weight variation(mg)	Thickness(mm)	Folding endurance	% drug content	Disintegration time (sec)
F1	47.85±0.737	0.14±0.008	344.00±0.81	91.7 ± 0.89	36.33±0.47
F2	53.23±0.286	0.20±0.169	343.33±0.942	95.6 ± 0.56	42.33±1
F3	54.78±0.428	0.24±0.004	350.00±0.816	97.4 ± 0.51	47.00±0.816
F4	47.24±0.331	0.14±0.008	315.00±2.94	93.3 ± 1.19	37.00±1.632
F5	48.80±0.454	0.21±0.012	322.67±0.942	91.8 ± 0.06	41.67±1.699
F6	50.13±0.249	0.22±0.004	339.00±1.632	92.9 ± 0.28	47.67±0.942
F7	49.84±0.299	0.17±0.008	311.00±1.632	95.8 ± 0.36	38.33±1.247
F8	52.18±0.245	0.23±0.008	317.67±0.471	97.0 ± 0.63	45.33±1.247
F9	53.89±0.255	0.25±0.008	322.67±2.05	94.3 ± 0.19	53.33±1.247

Cumulative % drug release from buccal films F1 to F9 prepared from HPMC K100, HPC, HEC

Table 4: *In-vitro* release data of various Mosapride citrate mucoadhesive buccal films prepared using HPMC K100, HPC, HEC.

Time	F1	F2	F3	F4	F5	F6	F7	F8	F9
15m	13.99	20.98	22.98	12.99	14.99	15.98	11.99	16.98	17.98
30m	29.12	36.14	42.17	24.10	22.09	32.13	28.11	30.12	35.14
1h	43.17	45.18	56.22	37.15	38.15	41.16	45.18	41.16	48.19
2h	52.21	58.23	64.26	46.18	48.19	51.20	54.22	49.20	59.24
3h	65.26	70.28	72.29	51.20	57.23	56.22	62.25	61.24	71.28
4h	73.29	77.31	80.32	61.24	68.27	67.27	69.28	74.30	79.32
5h	82.33	85.34	87.35	73.29	77.31	78.31	78.31	81.32	85.34
6h	88.35	90.36	91.36	77.31	83.33	88.35	84.34	87.35	93.37
7h	94.38	95.38	97.39	86.34	89.36	97.39	90.36	92.37	

Table 5: Drug permeation study data of F1-F9.

Time	F1	F2	F3	F4	F5	F6	F7	F8	F9
30 m	25.85	28	33.6	18.4	22.4	24.8	22.4	25.6	28
1h	43.84	44.16	49.92	34.56	35.52	41.28	39.36	46.08	44.16
2h	51.06	50.88	58.56	41.28	46.08	48	47.04	53.76	55.68
3h	60.48	60	71.04	48.96	55.68	56.64	55.68	61.44	65.28
4h	67.2	69.12	78.72	56.64	62.4	64.32	62.4	68.16	72
5h	72.96	75.84	83.52	64.32	72	73.92	66.24	72	78.72
6h	79.68	81.6	87.36	71.04	73.92	74.88	73.92	77.76	82.56
7h	83.52	84.48	90.24	74.88	81.6	83.52	77.76	81.6	87.36
8h	86.4	89.28	94.08	79.68	84.48	85.44	82.56	86.4	89.28

Table 6: *In-vitro* release data of stability study of formulation F3.

Time (in hours)	% CDR			
	1st Day	After 4 weeks	After 6 weeks	After 12 weeks
30	21.96	22.32	21.96	23.12
1hr	40.33	42.66	41.96	42.12
2hr	56.11	56.32	56.15	56.21
3hr	68.31	68.28	68.31	68.22
4hr	77.36	77.25	77.21	77.36
5hr	84.31	84.36	84.3	84.69
6hr	91.34	90.98	91.97	91.56
7hr	97.21	97.38	97.49	97.18

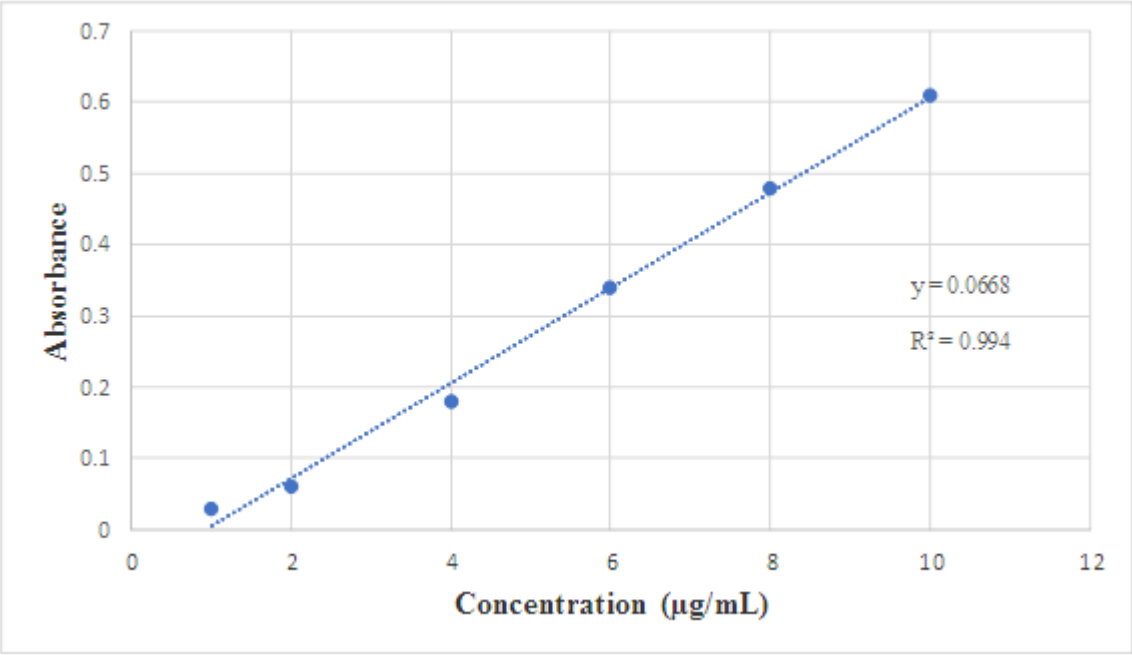

Figure 1: The standard graph of Mosapride citrate using simulated saliva buffer of pH 6.8.

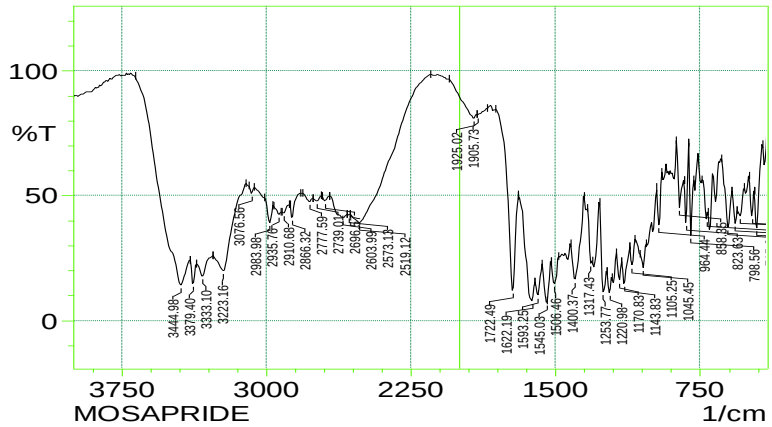

Figure 2(a): FTIR Spectrum of pure drug (Mosapride citrate).

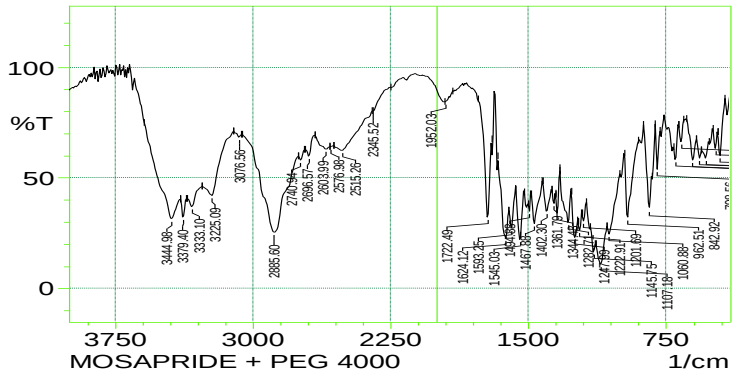

Figure 2 (b): FTIR Spectrum of Mosapride+ PEG 4000

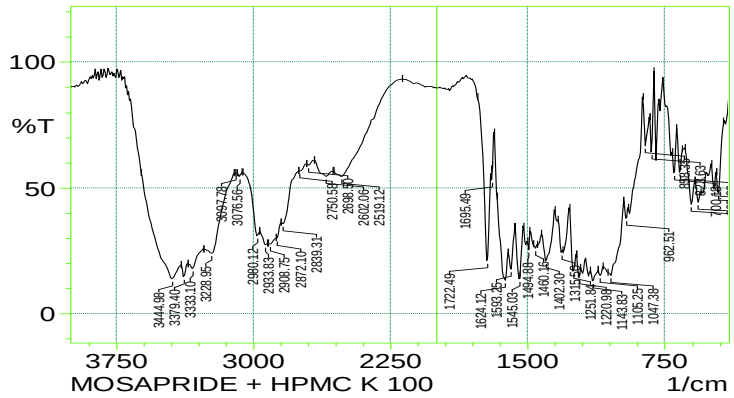

Figure: 2 (c): FTIR Spectrum of Mosapride + HPMC

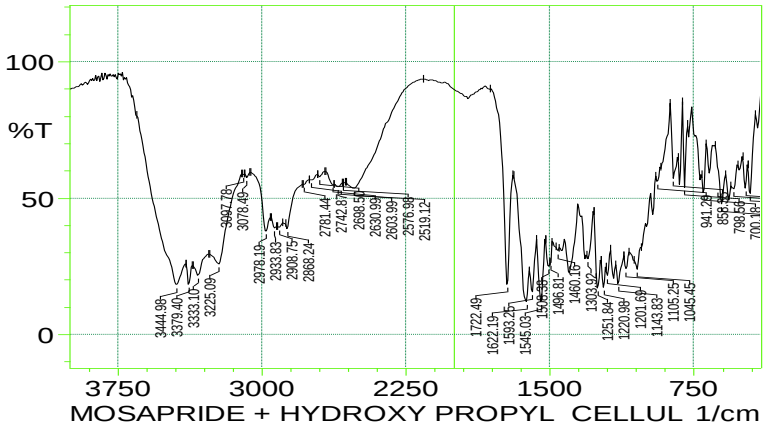

Figure 2 (d): FTIR Spectrum of Mosapride+ HPC.

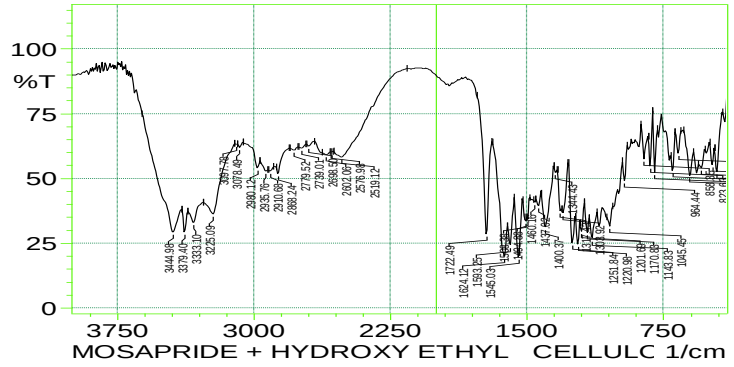

Figure 2 (e): FTIR Spectrum of Mosapride+ HEC

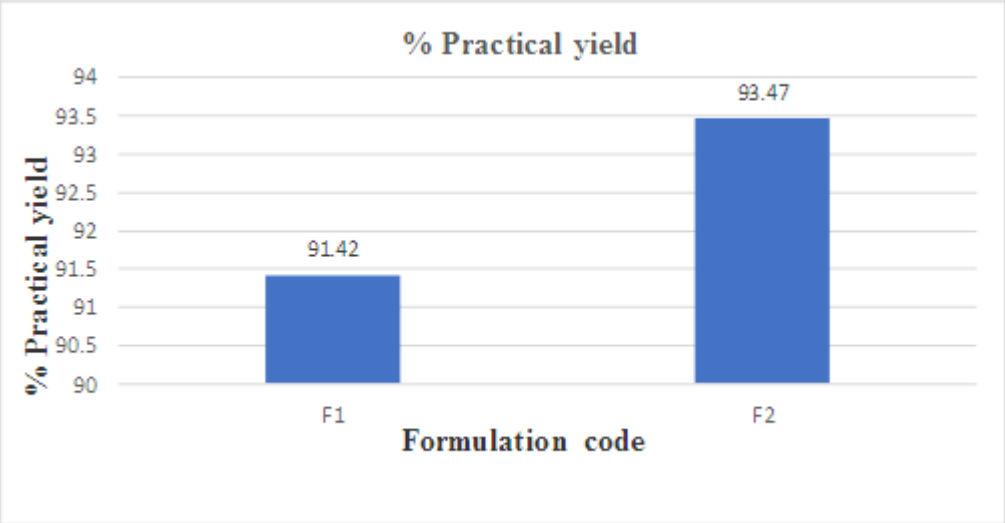

Figure 3: % Practical yield of solid dispersions.

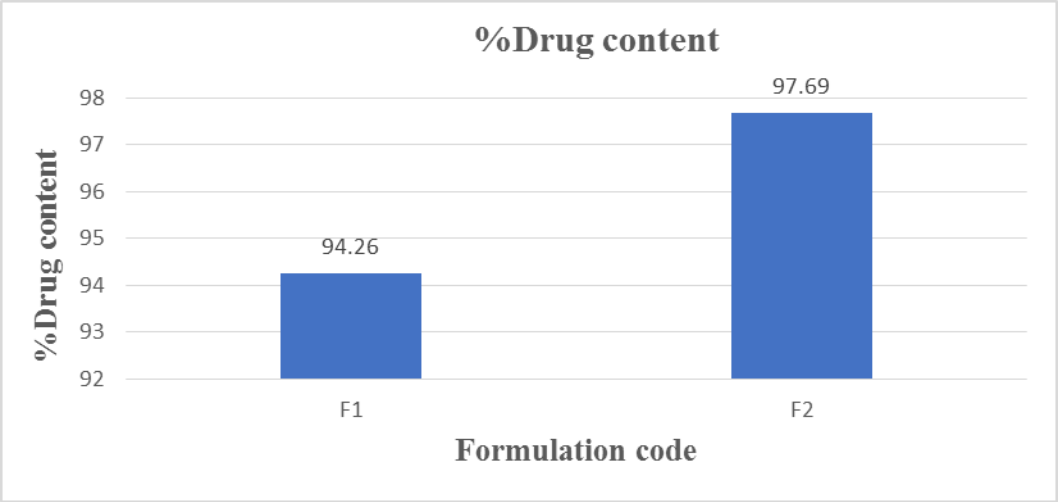

Figure 4: % Drug content of solid dispersions

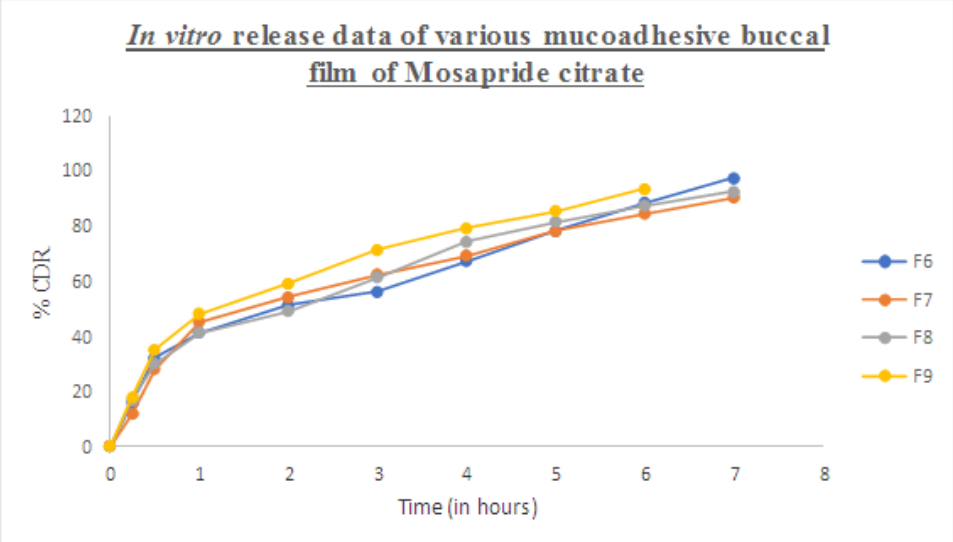

Figure 5: *In vitro* drug release profile of formulations F1-F5

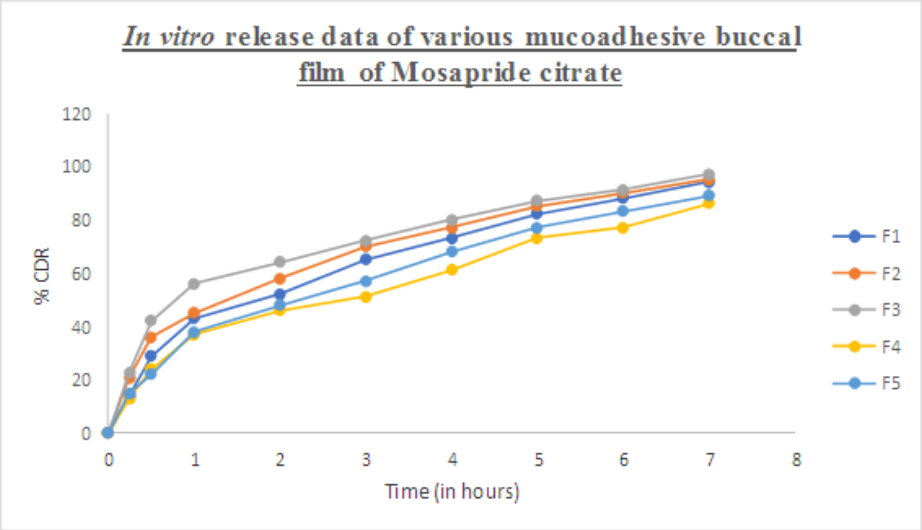

Figure 6*: In vitro* drug release profile of formulations F6-F9.

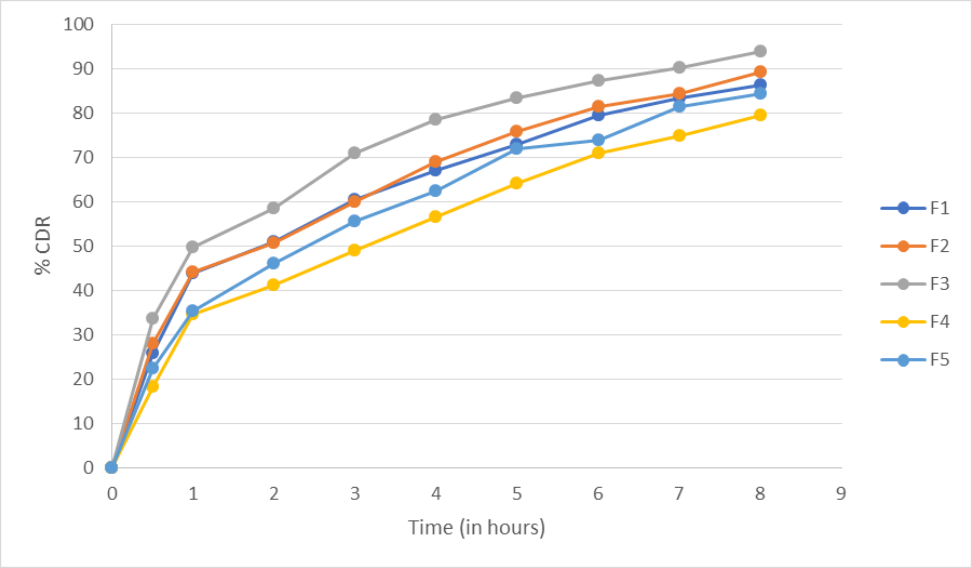

Figure no. 7: *In-vitro* permeation profiles of F1-F5.

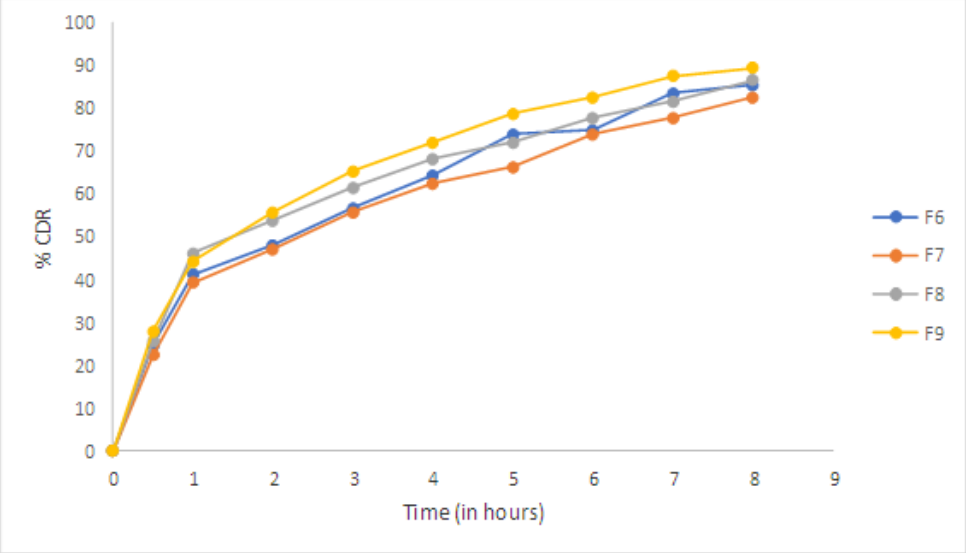

Figure no. 8: *In-vitro* permeation profiles of F6-F9.

CONCLUSION

- All the formulation showed acceptable quality control property formulation F3 having polymer concentration HPMC K100 showed better drug release rate over period of 7 hours thus formulation F6 was found to be the most promising formulation on the basis of acceptable evaluation property and the *In-vitro* drug release rate of 97.39%. Based on the FTIR studies appear to be no possibility of interaction between the Mosapride citrate and polymers of other excipients used in the films.
- Stability studies were conducted for the optimized formulation as per ICH guidelines for a period of 90 days which revealed that the formulation were stable. The result suggests that the developed mucoadhesive buccal film of Mosapride citrate could perform the better than conventional dosage form leading to improved efficacy and better patient compliance.

BIBLIOGRAPHY

1. Smart JD. The basics and underlying mechanisms of mucoadhesion. Adv Drug Deliv Rev., 2005; 57: 1556-68.
2. Shaikh R, Raj Singh TR, Garland MJ, Woolfson AD, Donnelly RF. Mucoadhesive drug delivery systems. J Pharm Bioallied Sci., 2011; 3(1): 89-100.
3. Nafee NA, Ismail FA, Boraie NA, Mortada LM. Mucoadhesive buccal patches of miconazole nitrate: *In-vitro/in-vivo* performance and effect of ageing. Int J Pharm, 2003; 264: 1-14.
4. Semalty A, Semalty M, Nautiyal U. Formulation and evaluation of mucoadhesive buccal films of enalapril maleate. Ind J Pharm Sci., 2010; 72(5): 571-5.
5. Rajaram DM, Laxman SD. Buccal mucoadhesive films: A review. Sys Rev Pharm. 2017;8(1):31-8
6. Sangeetha S, Venkatesh DN, Krishan PN, Saraswathi R. Mucosa as a route for systemic drug delivery. Res J Pharm Bio Chem Sci., 2010; 1(3): 178-87.