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Research Article

FORMULATION AND EVALUATION OF NIFEDIPINE BUCCAL TABLETS

K. Naga Raju*, P. Ramreddy, M. Chinna Eswaraiah
Department of pharmaceutics, Anurag Pharmacy College, Ananthagiri (V), Kodad (M), Nalgonda (Dt), Andhra Pradesh, India.508206

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Corresponding Author's email: **kandukoori007@gmail.com**

Abstract: The buccal mucoadhesive tablets of nifedipine were fabricated with objective of avoiding first pass metabolism and prolonging duration of action. The mucoadhesive polymers used in formulations were Carbopol (cp934), Hydroxyl Propyl methyl Cellulose (HPMCE15), Sodium Carboxy Methyl Cellulose (NaCMC). These formulations were characterized for physiochemical parameters, in vitro bioadhesive strength, swelling index, In vitro drug release, and in vitro drug permeation. The modified physical balance assembly was used to measure the bioadhesive strength of tablets with fresh sheep buccal mucosa as a model tissue. The best mucoadhesive performance and in vitro drug release profile were exhibited by the tablet contain Na CMC, HPMC E15 and Nifedipine in the ratio of 1:1.

Key words: Buccal mucoadhesive tablet, Bioadhesive Strength, swelling index, Nifedipine.

1. INTRODUCTION

Nifedipine[1, 2] a systemic calcium channel blocker, is a practically water insoluble and light sensitive drug used in angina pectoris and hypertension. As its biological half-life is about 2 h and is eliminated rapidly, repeated daily administrations are needed to maintain effective plasma levels. It shows a low and irregular bioavailability of about 50% after oral administration with a high first pass effect. It has been suggested that drugs with biological half-lives in the range of 2–8 h are good candidates for sustained-release formulations.

The short half-life and severe first pass metabolism of Nifedipine makes it suitable for administration via a buccal delivery system that provides controlled drug delivery, bypassing first pass effect. Successful buccal delivery requires at least three of the following: (a) a bioadhesive to retain the drug in the oral cavity and maximize the intimacy of contact with the mucosa; (b) a vehicle that releases the drugs at an appropriate rate under the conditions prevailing in the mouth; and (c) strategies for overcoming the low permeability of the oral mucosa[3]. Mucoadhesive drug delivery systems promote the residence time and act as sustained-release dosage forms. Three steps of formation of bioadhesive bonds are: (a) wetting and swelling of polymer; (b) entanglement of polymer and mucin chains; and (c) formation of weak chemical bonds between entangled chains[4].

The aim of this work was to develop and characterize a buccoadhesive sustained release tablet of Nifedipine. The buccal route was chosen because of its good accessibility, robustness of the epithelium, facile removal of the dosage form, relatively low enzymatic activity, and natural clearance mechanisms for elimination of the drug from buccal area, satisfactory patient acceptance and avoiding the hepatic first pass metabolism. Apart from the overall increased bioavailability, because of bypassing the first pass effect and sufficient time to produce therapeutic effect, an important advantage of buccal delivery for Nifedipine is also potentially better control of plasma levels, typically lower variation in bioavailability, reduced costs of the drug because of application of much lower doses than necessary for oral products.

2. MATERIALS AND METHODS

2.1 MATERIALS

Nifedipine was obtained as a gift sample from bari pharmaceuticals Lab, Carbopol (cp 934), Hydroxylpropyl methyl cellulose (HPMC E 15), Sodium carboxy methyl cellulose (Na CMC) was obtained from bari scientific traders. All other materials used are of analytical grade.

2.2 METHODOLOGY

1. PREFORMULATION STUDIES

A. DRUG AND EXCIPIENTS COMPATABILITY STUDIES [5]

The IR spectrums of physical mixtures of Nifedipine individual drug and drug with polymers were recorded using PerkinElmer FTIR (Tokyo, Japan) using pellet technique. The spectra were scanned over the wave number range of 4000 to 400 cm –1

B.CHARACTERIZATION OF FORMULATION BLEND

The formulation blend was characterized by determining bulk density, tapped density, angle of repose, Haussener's ratio and compressibility index.

2. FORMULATION DEVELOPMENT PREPARATION OF BUCCOADHESIVE BILAYERED TABLETS [6, 7]

The buccoadhesive bilayered tablets were prepared using different polymers either alone or in combinations with varying ratios as summarize. Bilayered tablets were prepared by direct compression. procedure involving two consecutive steps. The buccoadhesive drug/polymer mixture was prepared by homogeneously mixing the drug and polymers in a glass mortar for 15 min. Magnesium stearate (MS) was added as a lubricant in the blended material and mixed. The blended powder was then lightly compressed on 8 mm flat faced punch using rotary punch tablet compression machine , the upper punch was then allow to up wards and backing layer material ethyl cellulose was added over it and finally compressed at a constant compression force.

TABLE 4: Composition of Nifedipine Tablets

Formulations	Nifedipine	HPMC E15	Sodium CMC	Carbopol 934P	Starch	MCC	Mg Stearate	Ethyl cellulose
F_1	30 mg	30 mg	30 mg	-------	30 mg	75 mg	5 mg	50 mg
F_2	30 mg	30 mg	10 mg	---------	30 mg	95 mg	5 mg	50 mg
F_3	30 mg	20 mg	---------	20mg	30 mg	100mg	5 mg	50 mg
F_4	30 mg	20mg	30 mg	-------	30 mg	95 mg	5 mg	50 mg
F_5	30 mg	15 mg	--------	20 mg	30 mg	100mg	5 mg	50 mg
F_6	30 mg	15 mg	20 mg	--------	30 mg	110mg	5 mg	50 mg
F_7	30 mg	10 mg	--------	30 mg	30 mg	95 mg	5 mg	50 mg
F_8	30 mg	10 mg	30 mg	-------	30 mg	95 mg	5 mg	50 mg
F_9	30 mg	10 mg	20 mg	-------	30 mg	105mg	5 mg	50 mg
F_{10}	30 mg		50 mg	--------	30 mg	85 mg	5 mg	50 mg
F_{11}	30 mg	50 mg	-------	--------	30 mg	85 mg	5 mg	50 mg
F_{12}	30 mg		-------	50 mg	30 mg	85 mg	5 mg	50 mg

3. EVALUATION OF TABLETS

The formulated tablets were evaluated for the physicochemical parameters like weight variation, hardness, thickness and drug content and also evaluated for in-vitro mucoadhesion, in-vitro swelling, ex-vivo drug permeation and in-vitro drug release.

A. *In-vitro* mucoadhesion studies [8, 9]

Mucoadhesive strength of the buccal tablets was measured on the Modified Physical Balance method. The method used sheep buccal mucosa as the model mucosal membrane. The fresh sheep buccal mucosa was cut into pieces and washed with phosphate buffer pH 6.8. The both pans were balanced by adding an appropriate weight on the left- hand pan. A piece of mucosa was tied to the surface of the beaker and placed below the left pan which was moistened with phosphate buffer pH 6.8.The tablet was stuck to the lower side of left pan with glue. Previously weighed beaker was placed on the right hand pan and water (equivalent to weight) was added slowly to it until the tablet detach from the mucosal surface. The both pans were balanced by adding an appropriate weight on the left- hand pan. The weight required to detach the tablet from the mucosal surface gave the bioadhesive strength.

Force of adhesion (N) = (Bioadhesive strength/100) ×9.81

Bond strength (N/m^2) = force of adhesion/surface area of tablet

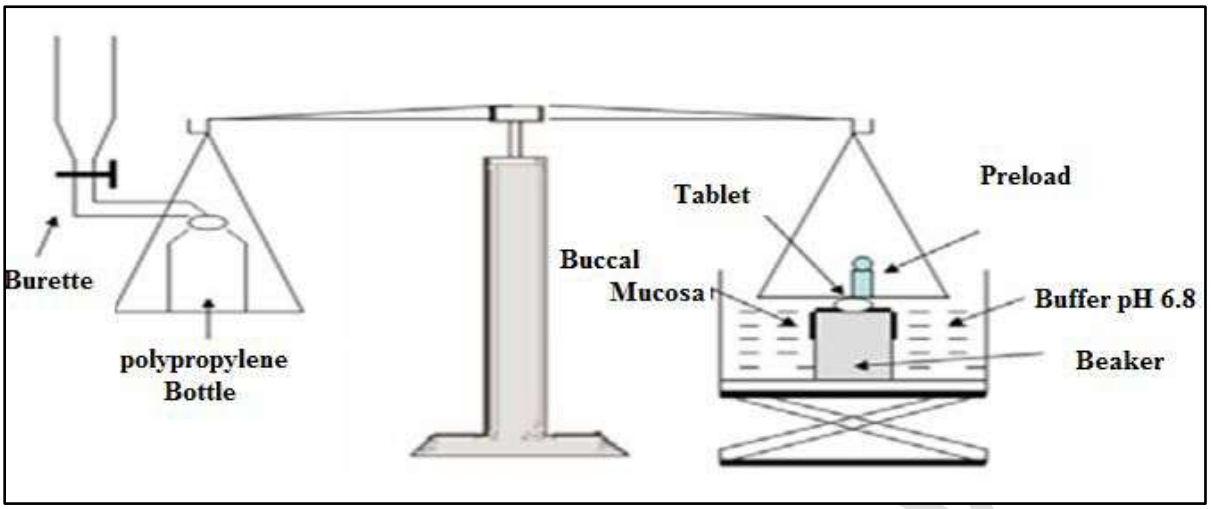


Figure 1. Modified physical balance for measurement of mucoadhesive strength

B. *In vitro* swelling studies of buccoadhesive tablets [10]

Buccal tablets were weighed individually (W1) and placed separately in 2% agar gel plates with the core facing the gel surface and incubated at 37°C ±1°C. At regular 1-hour time intervals until 6 hours, the tablet was removed from the Petri dish, and excess surface water was removed carefully with filter paper. The swollen tablet was then reweighed (W2) and the swelling index (SI) was calculated using the formula. The results listed in table 10, 11, 12.

% Swelling index = $[(W_2 - W_1)/W_1] \times 100$

C. Ex *vivo* permeation of buccal tablets

Tissue isolation:

Sheep buccal tissue was obtained from a local slaughterhouse and used within 2 hours of slaughter. The tissue was stored in Krebs buffer pH 6.8 at 4^0c after collection. The epithelium was separated from the underlying connective tissue with a surgical technique and de lipidized membrane was allowed to equilibrate for approximately one hour in receptor buffer to regain lost elasticity.

Study protocol:

Ex vivo permeation study of Nifedipine buccal tablets through the sheep buccal mucosa was performed using Franz-type[10,] diffusion cell. The freshly excised sheep buccal mucosal membrane was clamped between donor and receiver chambers of the Franz-type diffusion cell, facing the mucosal side towards the donor compartment. The receiver chamber was filled with fresh pH 6.8 buffer solution and added 0.5w/v tween60 after the buccal membrane was equilibrated for 30 min. The buccal tablet was placed in donor chamber and 1mL of buffer solution (pH 6.8) was added and the receptor compartment was maintained at 37 ± 0.2^0Cand continuously stirred at 50 rpm throughout the study. Aliquots (2mL) were collected at predetermined time intervals and filtered through a filter paper, and the amount of drug permeated through the buccal mucosa was then determined by measuring the absorbance at 238 nm using an UV spectrophotometer. The medium of the same volume (2mL), which was pre warmed at 37°C, was then replaced into the receiver chamber. the experiments were performed in triplicate (n = 3) and mean value was used to calculate the flux (J) and permeability coefficient (P).

J = (dQ/dt)/A

P = (dQ/dt)/ ΔCA

Where,

J is Flux (mg.hrs-1cm-2);

P is permeability coefficient (cm/h);

dQ/dt is the slope obtained from the steady state portion of the curve;

Δ C, the concentration difference across the mucosa and A the area of diffusion (cm2).

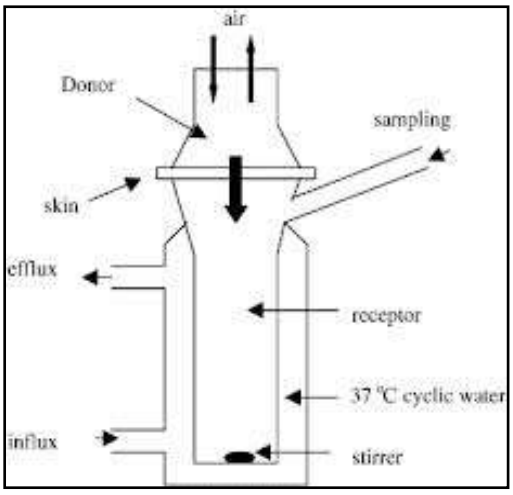


Fig 2: Franz type diffusion cell.

D. *IN VITRO* DISSOLUTION STUDIES OF TABLETS[11]

Dissolution studies were carried out for all the formulations combinations in triplicate, employing USP-II, paddle method and 900ml of pH 6.8 phosphate buffers as the dissolution medium and added 0.5% w/v tween 60. The medium was allowed to equilibrate to temp of 37°c + 0.5°c. Tablet was placed in the vessel and the vessel was covered the apparatus was operated for 8hrs in pH 6.8 phosphate buffer at 100 rpm. At definite time intervals i.e. 0.5,1,2,3,4,5,6,7,8 hrs of the aliquot of sample of 5 ml was withdrawn periodically and the volume replaced with equivalent amount of the fresh dissolution medium. The samples were analyzed spectrophotometrically at 238 nm using Uv-spectrophotometer. Cumulative drug release was calculated using the equation (y = 0.045x + 0.001) generated from Beer Lambert's Calibration curve in the linearity range of 2-10 µg/ml.

Dissolution parameters:

Apparatus	: USP-II,
Dissolution Medium	: pH 6.8 phosphate buffer
RPM	: 100
Sampling intervals	: 0.5,1,2,3,4,5,6,7,8 Hrs
Temperature	: 37°c + 0.5°c

Release Kinetics [12]

The drug release data was fitted in to different kinetic equations to know the drug release pattern and mechanism.

3. RESULTS AND DISCUSSION

1. PREFORMULATION RESULTS

A. Drug and Excipients Compatibility studies by FT IR Spctrophotometry

The infrared spctra of pure drug and mixture of polymers and excipients were studied by FT IR spectroscopy using the KBR. Here spectral changes in the mixture are the basis for the determination of compatibility. The obtained spectrums of different formulation combinations were shown below.

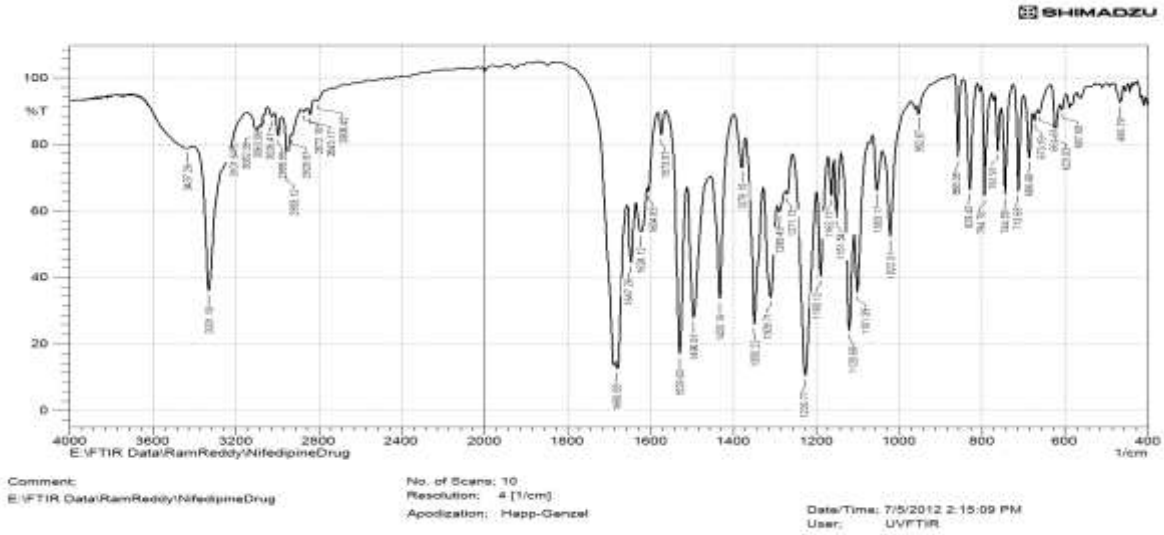


Fig3: IR spectrum of pure Nifedipine drug

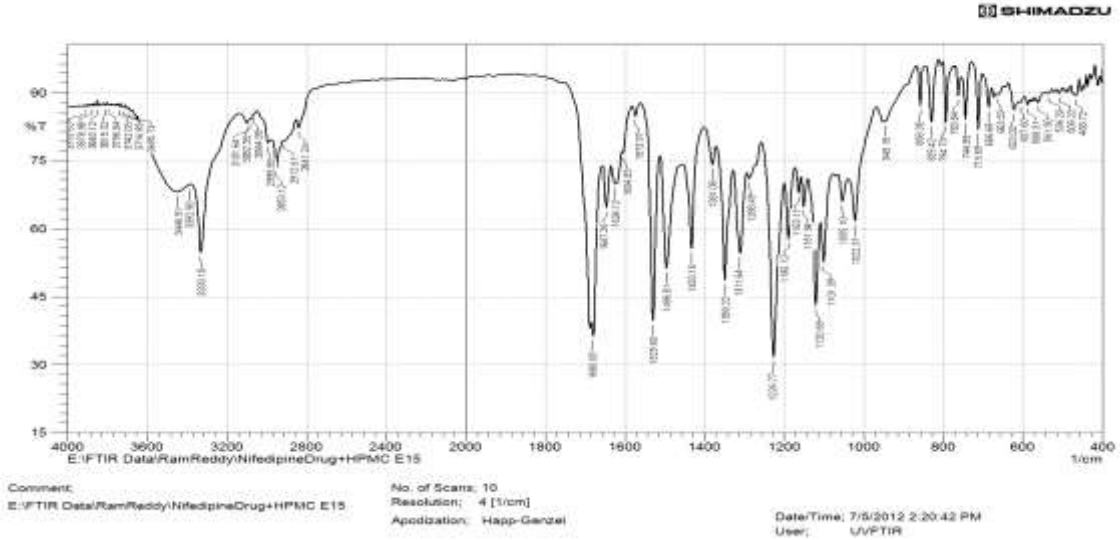


Fig 4 : IR spectrum of pure drug with HPMC E15:

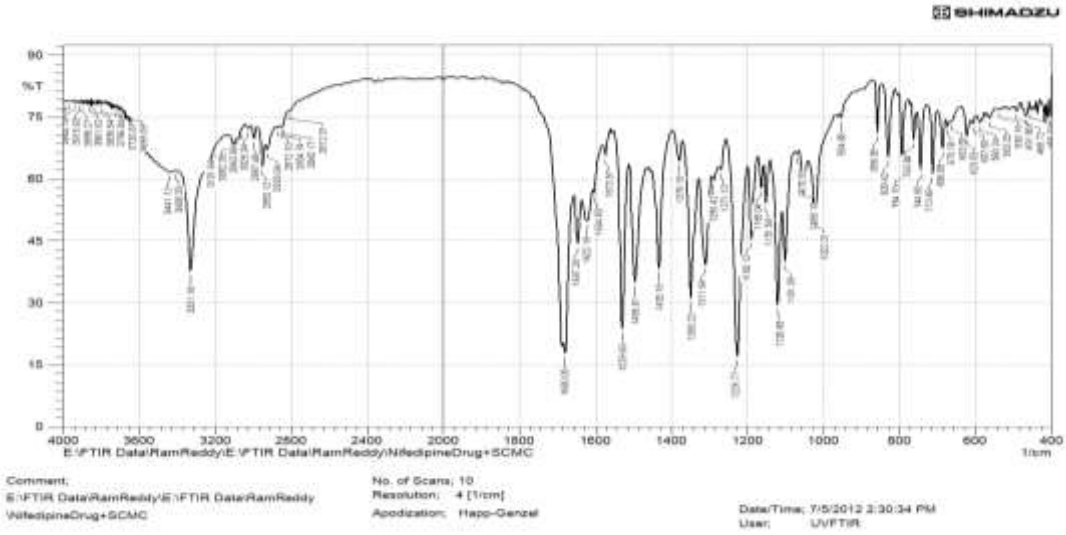


Fig 5: IR spectrum of pure drug with SCMC.

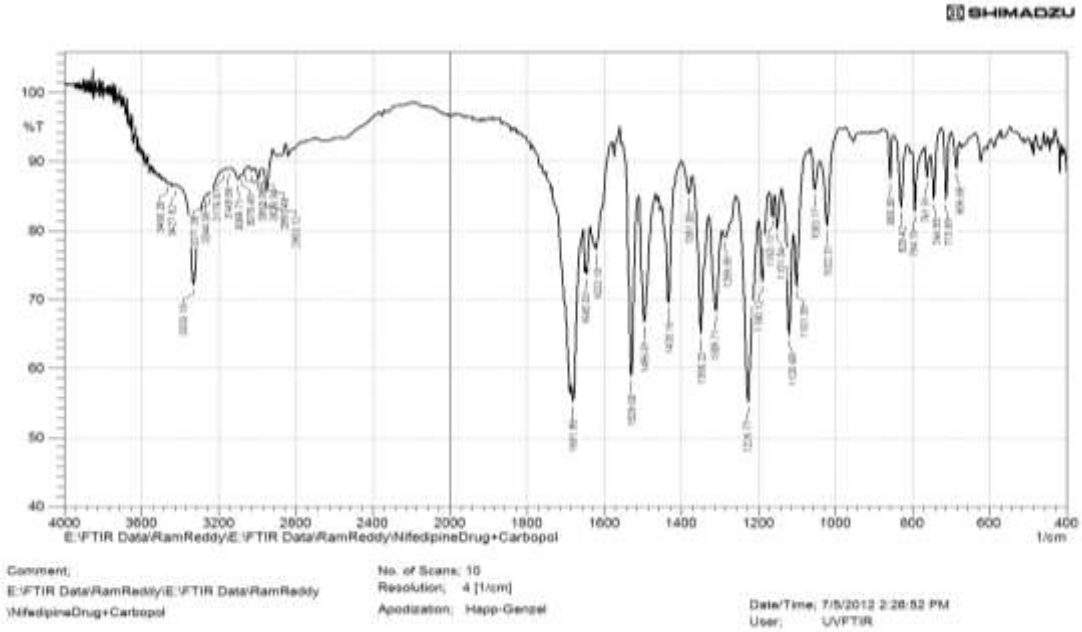


Fig6 : IR Spectrum of pure drug with Carbopol 934p

The IR spectra of pure drug Nifedipine and mixture of polymer and excipients were studied by FTIR spectroscopy using KBR. The results are indicated that there was no chemical incompatibility between drug –polymer, polymer-polymer, polymer and excipients.

A. Characterization of pre formulation blend

Table7: Bulk density,Tapped density, % Compressibility index, Hausner's ratio and Angle of repose.

Pre-compression parameters :					
Formulations	**Bulk Density**	**Tap Density**	**Carr's Index**	**Hausner's ratio**	**Angle Of Repose(Θ)**
F_1	0.50	0.58	13.79	1.16	29.34
F_2	0.47	0.55	14.54	1.17	28.23
F_3	0.50	0.58	3.791	1.16	29.34
F_4	0.41	0.50	18	1.21	26.78
F_5	0.41	0.50	18	1.21	26.78
F_6	0.47	0.55	14.54	1.17	28.23
F_7	0.50	0.58	13.79	1.16	29.34
F_8	0.46	0.55	16.36	1.19	26.71
F_9	0.45	0.55	18.18	1.22	27.91
F10	0.44	0.52	13.28	1.19	29.64
F11	0.46	0.55	14.33	1.17	27.24
F12	0.49	0.57	14.21	1.18	25.76

The blend of ingredients was analyzed for physical characteristics the bulk density, tapped density, corr's index, hausner's ratio were found in the range of 0.41-0.50gm/cm^2,0.50-0.58gm/cm^2, 14.54-18.18%,1.16-1.22, 25.79-29.34^0.it shows that all formulation blends were having good flow characteristics and flow rates.

2. Evaluation of Tablets

A. Evaluation of Avg. Weight, Hardness, Friability, Drug content.

Table No: 8- Evaluation of Avg. Weight, Hardness, Friability, Drug content.

Formulation	**Avg. Weight (Mean±S.D) (n=20)**	**Hardness (Kg/cm$^{2)}$ (n=3)**	**Friability (n=20)**	**% Drug content (n=3)**
F1	249.6±1.14	4.6±0.1	0.64	98.36
F2	249 ± 1.58	4.63±0.15	0.48	98.56
F3	249± 1.58	5.60±0.10	0.48	98.48
F4	250.4 ± 1.140	5.43±0.20	0.64	98.15
F5	249.4± 1.58	6.60±0.26	0.48	98.76
F6	249.6 ±1.140	4.63±0.15	0.50	99.74
F7	249.4 ± 0.89	6.66±0.15	0.36	98.78
F8	249.4± 1.140	4.10±0.10	0.68	99.76
F9	249.8 ± 1.48	3.63±0.15	0.56	98.98
F10	249.6± 1.140	7.36±0.20	0.32	99.97
F11	249.8± 1.48	6.36±0.20	0.24	99.96
F12	250.4± 1.50	6.66±0.15	0.16	98.97

The average weight of the tablet was found to be between 249.0 mg and 250.4 mg. Buccoadhesive tablets containing Carbopol showed hardness in the range of 7.36 to 5.5 kg/cm ^{2} and it decreased with increasing amounts of SCMC. The hardness of the tablets containingNaCMC was

much lower, ranging from 4.60 to 7.2 kg/cm^2 and increased with increasing amounts of HPMC or Carbopol.Friability range between 0.16 and 0.68%.

The assayed drug content in various formulations varied between 98.15% and 99.97%.

***In-vitro* Mucoadhesion studies:**

Table 9 : In vitro Mucoadhesion strength of Nifedipine buccoadhesive tablets

Formulation	Bioadhesive strength(gm)
F1	**25.8**
F2	**18.9**
F3	**30.4**
F4	**23.6**
F5	**28.3**
F6	**19.7**
F7	**34.6**
F8	**24.3**
F9	**22.3**
F10	**28.6**
F11	**30.8**
F12	**40.9**

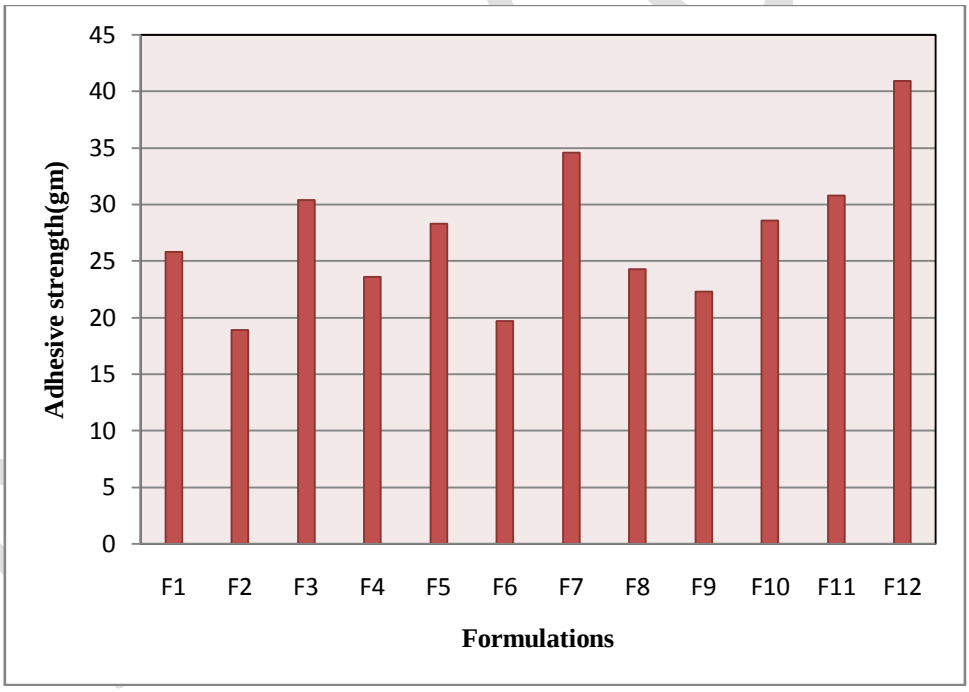


Fig 9: Bioadhesive profile of Nifedipine Mucoadhesive tablets from F1-F12

The bioadhesion characteristics were affected by the type and concentration of bioadhesive polymers. The highest detachment force was proposed by F12 and F7 containing carbopol 934p.

C.SWELLING INDEX:

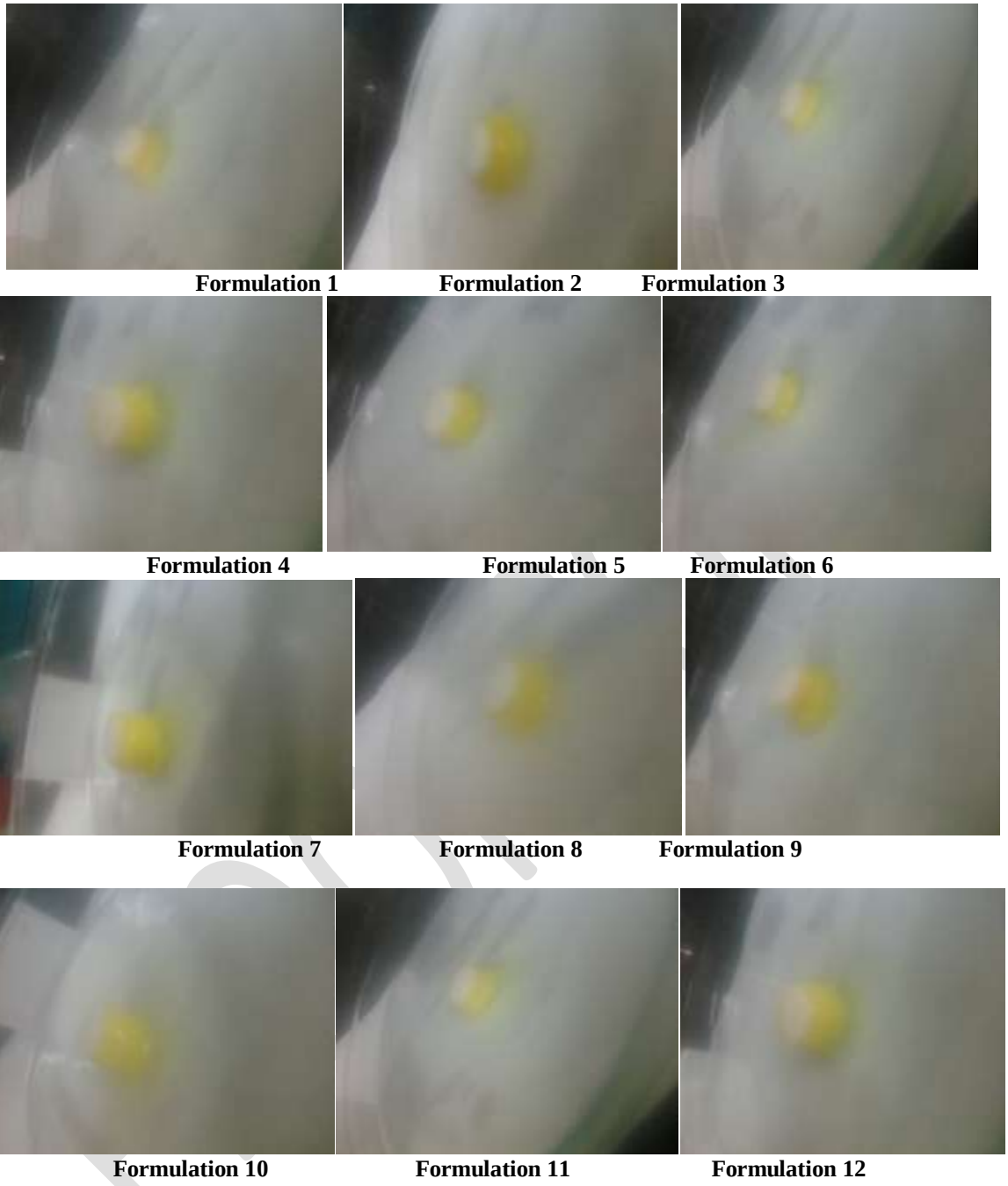


Fig 10: swelling Photo graphs of tablets at 6th Hr of formulations from F1 to F12

Table 10: swelling index results of Nifedipine buccoadhesive tablet formulations from F1-F4.

FORMULATION	0hr	1hr	2hr	3hr	4hr	5hr	6hr
F1	0	0.11	0.36	0.65	0.81	0.86	0.92
F2	0	0.08	0.12	0.19	0.23	0.45	0.68
F3	0	0.10	0.22	0.36	0.48	0.59	0.78
F4	0	0.09	0.15	0.39	0.64	0.75	0.89

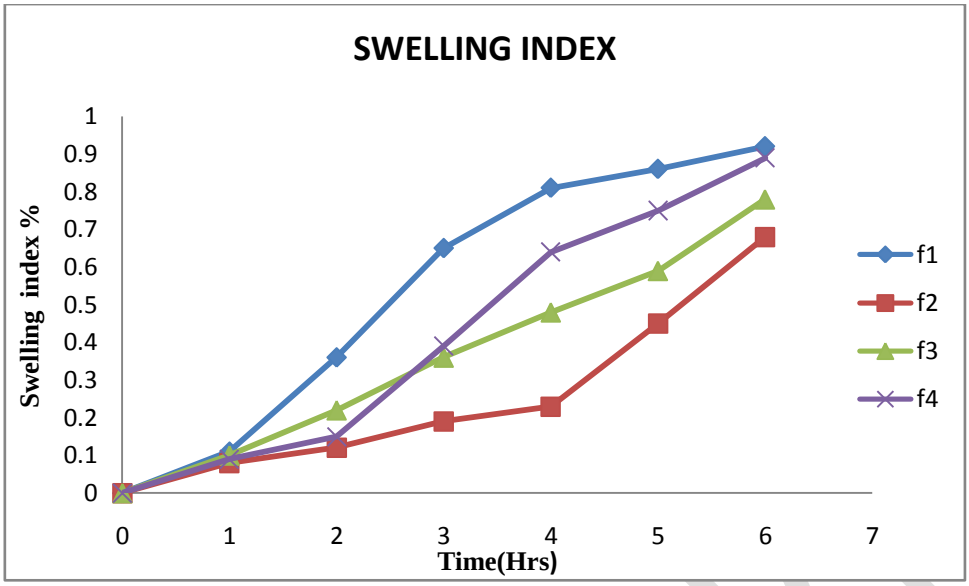


Fig 11:Graph of the Swelling index of formulations from F1 to F4

Table11: swelling index results of Nifedipine buccoadhesive tablet formulations from F5-F8.

Formulation	0hr	1hr	2hr	3hr	4hr	5hr	6hr
F5	0	0.07	0.11	0.36	0.45	0.66	0.82
F6	0	0.06	0.11	0.21	0.32	0.54	0.62
F7	0	0.11	0.38	0.63	0.76	0.89	0.96
F8	0	0.12	0.14	0.36	0.59	0.76	0.84

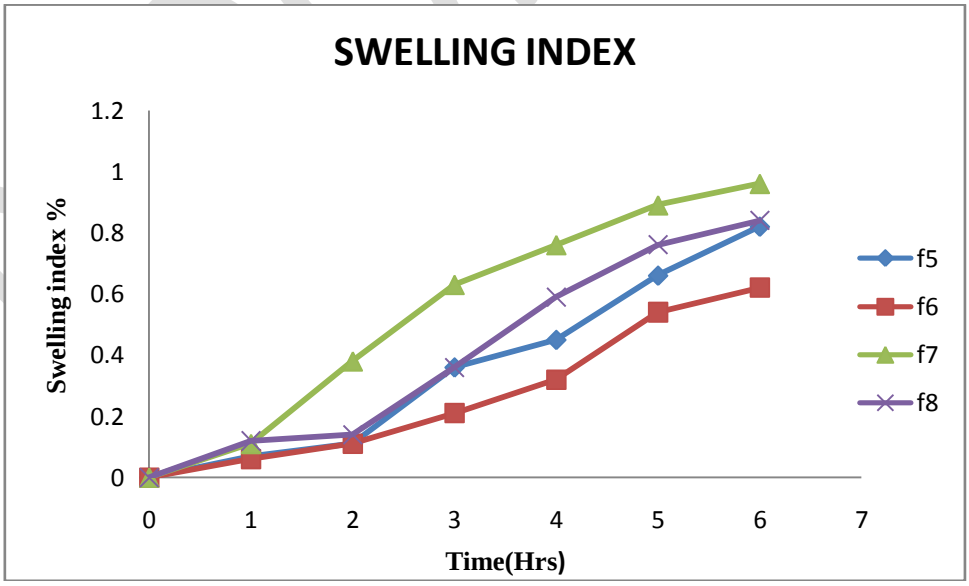


Fig 12: Graph of the Swellingindex of formulations from F5 to F8

Table12: swelling index results of Nifedipine buccoadhesive tablet formulations from F9-F12.

Formulation	0hr	1hr	2hr	3hr	4hr	5hr	6hr
F9	0	0.08	0.33	0.54	0.65	0.87	0.92
F10	0	0.06	0.33	0.54	0.65	0.87	0.92
F11	0	0.11	0.22	0.29	0.31	0.49	0.55
F12	0	0.11	0.33	0.67	0.85	1.00	1.21

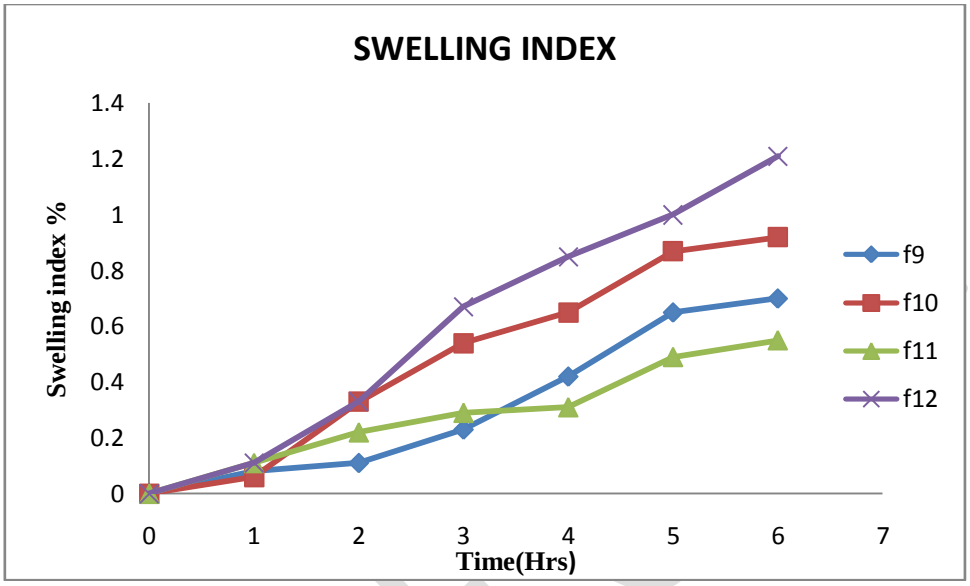


Fig 13: Graph of the Swelling index of formulations from F9 to F12

Swelling index increased as the weight gain by thetablets increased proportionally with the rate of hydration. In swelling study, it was found that the amount of carbopol plays an important role in swelling of the matrix and leads to the drug diffusion. The fastest hydration rate was obtainedfrom F12 (CP 934) and F9 (Na CMC) within 6 hr. It was observed that swelling rate increased with an increase in carbopol and Na CMC polymer content of the prepared tablets.

D. *Ex vivo* permeation of buccal tablets

Table13: *Ex vivo* permeation data of Nifedipine buccoadhesive tablets of F1, F2, F3, and F4formulations:

TIME (Hours)ss)	F1	F2	F3	F4
0	0	0	0	0
1	7.53	8.88	10.70	9.75
2	14.08	16.43	22.50	20.50
3	20.50	27.16	30.83	32.00
4	25.33	38.83	40.33	42.50
5	35.83	47.50	47.50	53.33
6	50.50	49.50	56.83	60.50
7	54.00	52.50	61.16	65.83
8	60.50	60.16	65.66	70.33

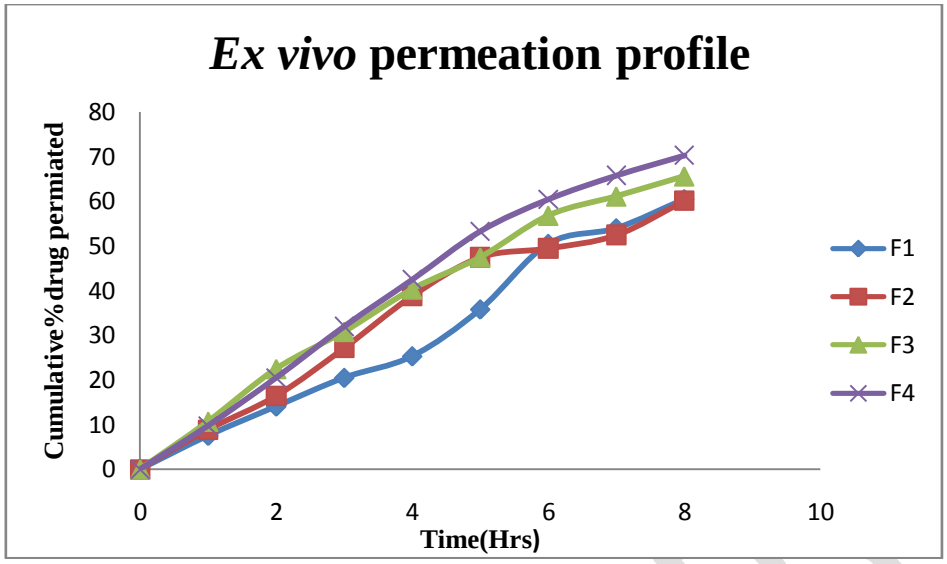


Fig 14: *Ex vivo* permeation profile of tablets of F1, F2, F3 and F4formulations:

Table 14: *Ex vivo* permeation data of Nifedipine buccoadhesive tablets of F5, F6, F7, and F8formulations:

TIME (Hours)	F5	F6	F7	F8
0	0	0	0	0
1	12.71	18.00	19.16	12.71
2	25.16	30.83	30.83	25.16
3	37.16	40.33	40.16	36.16
4	49.16	52.16	52.16	52.50
5	57.83	58.50	62.33	64.33
6	68.33	66.16	71.16	70.00
7	70.33	75.83	78.00	82.83
8	76.66	80.33	86.66	92.33

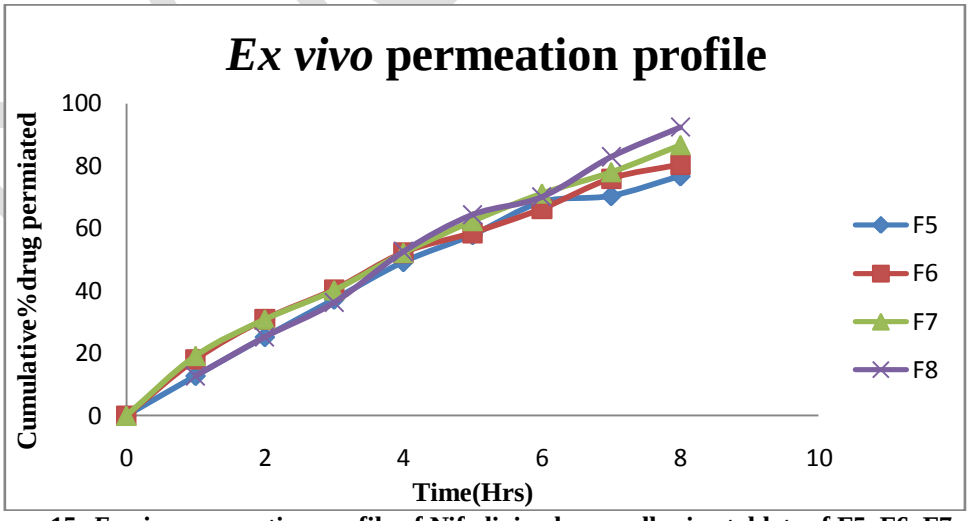
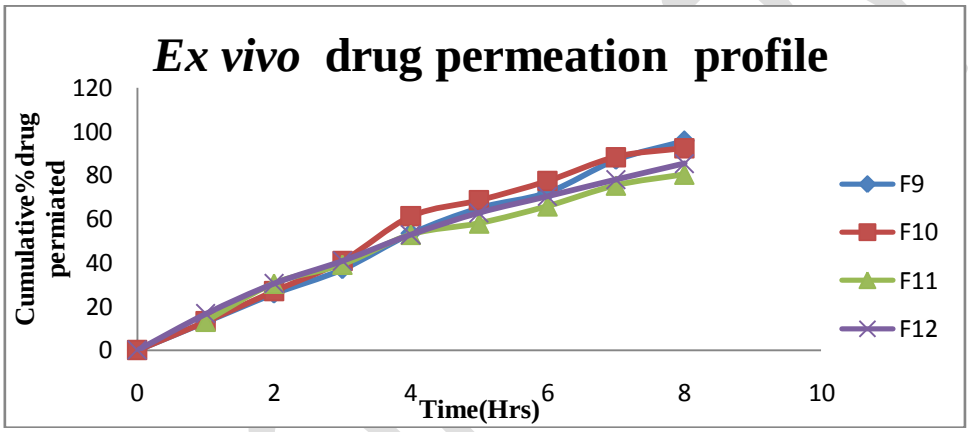


Figure 15: *Ex vivo* permeation profile of Nifedipine buccoadhesive tablets of F5, F6, F7 and F8formulations:

Table 15: *Ex vivo* permeation data of Nifedipine buccoadhesive tablets of F9, F10, F11, and F12 formulations:

TIME (Hours)	F9	F10	F11	F12
0	0	0	0	0
1	12.90	13.08	13.10	16.61
2	25.83	27.00	30.50	30.50
3	37.00	40.83	39.16	40.83
4	53.3	61.16	52.83	52.83
5	65.00	68.50	58.00	62.83
6	72.16	77.33	65.83	70.33
7	87.00	88.33	75.33	78.00
8	95.66	92.33	80.33	85.33



F9 formultion shows highest permeation throw buccal mucosa contain drug:poltmer ratio 1:1.

Figure 16: *Ex vivo* permeation profile of Nifedipine buccoadhesive tablets of F9, F10, F11 and F12formulations:

E. DISSOLUTION RESULTS:

Table16: Dissolution data of Nifedipine buccoadhesive tablets of F1, F2, F3, and F4 formulations.

TIME (Hours)	F1	F2	F3	F4
0	0	0	0	0
0.5	18.02	15.60	13.06	12.61
1	20.00	23.13	15.53	14.80
2	24.86	27.40	19.80	18.73
3	34.26	33.53	27.40	26.20
4	41.66	37.40	35.01	34.20
5	47.80	39.26	42.93	41.86
6	52.13	45.60	59.40	58.73
7	58.93	54.06	71.33	66.40
8	66.46	68.00	75.33	83.33

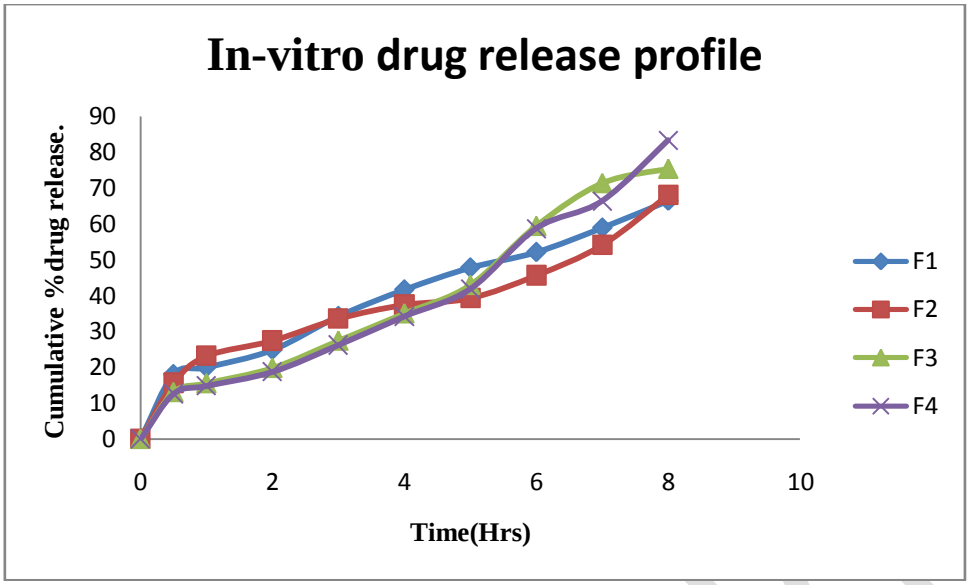


Figure 17: Dissolution profile of Nifedipine buccoadhesive tablets of F1, F2, F3, and F4formulations:

Table 17: Dissolution data of Nifedipine tablets of F5, F6, F7 and F8formulations:

TIME (Hours)	F5	F6	F7	F8
0	0	0	0	0
0.5	12.40	13.06	8.26	9.93
1	15.60	16.21	15.66	22.93
2	22.73	22.00	22.80	39.80
3	31.60	29.13	41.33	50.21
4	41.33	40.93	59.73	65.00
5	58.33	57.60	65.26	83.33
6	65.66	65.73	74.00	85.33
7	83.33	74.00	82.00	87.33
8	88.66	87.33	94.66	97.33

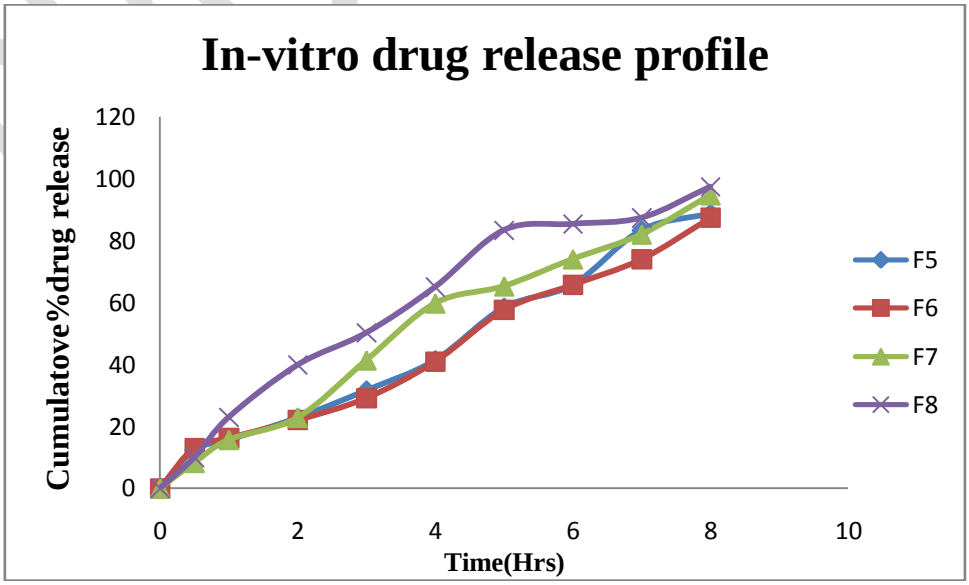


Figure 18: Dissolution profile of Nifedipine buccoadhesive tablets of F5, F6, F7 and F8 formulations.

Table 18: Dissolution data of Nifedipine buccoadhesive tablets of F9, F10, F11 and F12 formulations:

Time (Hours)	F9	F10	F11	F12
0	0	0	0	0
0.5	23.26	15	11.60	6.00
1	32.73	24.60	16.66	12.00
2	39.80	32.53	25.86	25.33
3	45.86	39.80	39.20	33.20
4	52.73	49.46	51.06	43.93
5	66.46	59.73	61.33	52.26
6	75.33	66.40	66.46	59.20
7	87.33	83.33	78.00	66.33
8	98.66	94.00	87.33	83.33

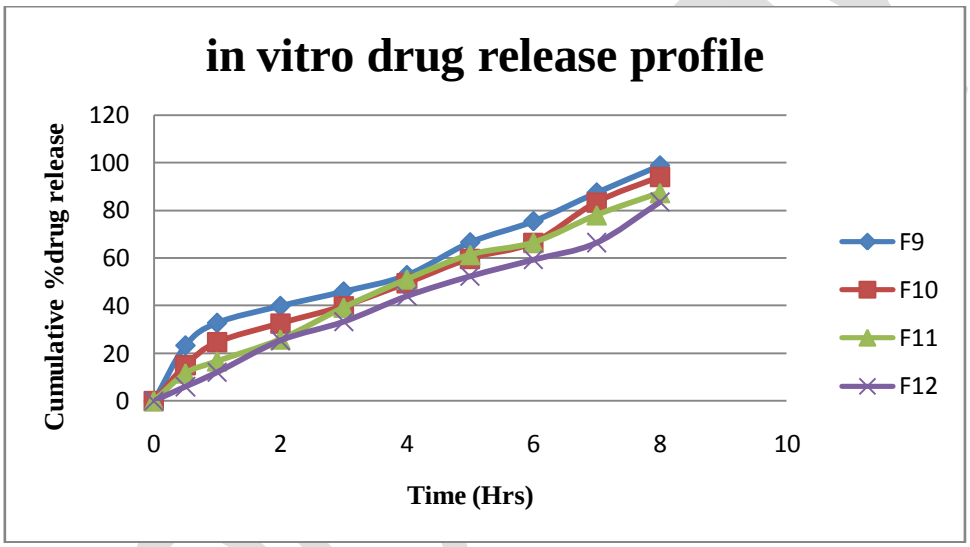


Figure 19: Dissolution profile of Nifedipine buccoadhesive tablets of F9, F10, F11 and F12formulations:

In vitro drug release studies revealed that the release of Nifedipine from different formulations varies with characteristics and composition of matrix forming polymers as shown intable no 6. The release rate of Nifedipine decreased with increasing concentration of HPMC E15 respectively. These findings are in compliance with the ability of HPMC to form complex matrix network which leads to delay in release of drug from the device. Carbopol is more hydrophilic than HPMC; it can swell rapidly, therefore decrease of Carbopol content decrease the drug release in F3 and F5 to F7. Drug release rate was increased with increasing amount of hydrophilic polymer. The maximum cumulative percent release of Nifedipine from formulation F9 could be attributed due to ionization of sodium car boxy methylcellulose at pH environment of the dissolution medium. Ionization of sodium carboxymethycellulose and carbopol leads to the development of negative charges along the backbone of the polymer. Repulsion of like charges uncoils the polymer into an extended structure. The counter ion diffusion inside the gel creates an additional osmotic pressure difference across the gel leading to the high water uptake. This water uptake leads to the considerable swelling of the polymer. The continued swelling of polymer matrix causes the drug to diffuse out from the formulation at a faster rate. Formulations F9, F8,F7,F10 showed relatively high rate of release of Nifedipine which is due to rapid swelling and erosion of NaCMC and carbopol. Further, the increase in rate of drug release could be explained by the ability of the hydrophilic polymers to absorb water, thereby promoting the dissolution, and hence the release, of the highly water soluble drug. Moreover, the hydrophilic polymers would leach out and hence, create more pores and channels for the drug to diffuse out of the device. Formulation F10 which contains high amounts of NaCMC gets eroded during dissolution study before stipulated study period. The results it was concluded that the increasing the rate controlling polymer concentration the release of drug might be slower.

F. Release Kinetics

Several kinetic models describing drug release from immediate and modified released dosage forms. The model that best fits the release data was evaluated by correlation coefficient (r). The correlation coefficient (r) value was used as criteria to choose the best model to describe the drug release from the buccoadhesive tablets. The 'r' values obtained for fitting the drug release data to zero order, indicating that the drug release mechanism follows zero order kinetics. From zero equation, the high values of correlation coefficient 'r' indicating that the drug release mechanism from these tablets was diffusion controlled.From the above results it is concluded that the drug release from the formulated buccoadhesive tablets of Nifedipine followes zero order kinetics.

CONCLUSION

In conclusion, the aim of the present study was to develop b sive drug delivery system for Nifedipine with a pro studies. From the foregoing investigation it may be conclude that the release rate of drug from the buccal tablets can be governed by the concentration of the polymer employed in the preparation of tablets. Regulated drug release in zero order manner attained in the current study indicates that the hydrophilic matrix tablets of Nifedipine, prepared by using HPMC E15, Carbopol 934P and Na CMC can successfully be employed as a buccoadhesive controlled released during delivery system. Good bioadhesive streangth of the formulation is likely to increase it's buccal residence time, and eventually, improve the extent of bioavailability. However, appropriate balancing between various levels of the two polymers is imperative to acquire proper controlled release and bioadhesion. Formulation F9 had good bioadhesion along with good swelling behavior and in-vitro drug release. Formulation F9 contain drug: polymer ratio is 1:1 containing Nifedipine (30 mg), HPMC E 15 (10 mg), Na CMC (20 mg) are considered as a optimized formulation with respected to bio adhesive strength (22.3 gm),swelling index (0.92), and in vitro drug release (98.66).the drug release pattern of this formulation was found to be fickian and approaching zero order kinetics.

REFERENCES

1. Bhavani patel, piyush patel, ashok bhosale, shrawaree hardikar, swati mutha, ganesh chaulang. Evaluation of tamarind seed polysaccharide (TSP) as mucoadhesive and sustained release component of nifedipine buccoadhesive tablet &comparision with HPMC and Na CMC, *Int.j. Pharm Tech Res*, **2009**; 1(3).
2. J.Varshosaz, Z.Dehghan. Development and characterization of buccoadhesive nifedipine tablets, *European journal of pharmaceutics and biopharmaceutic*s, **2002**; 54: 135-141.
3. SA Sreenivas , KV Pai Thiolated Chitosans. Novel Polymers for Mucoadhesive Drug Delivery ,*A Review Tropical Journal of Pharmaceutical Research*, **2008**; 7 (3): 1077-1088
4. K.P.R. Chowdary, B.Suresh, B.Sangeeta and G.Kamalakara Reddy. *Design and Evaluation of Diltiazem Mucoadhesive Tablets for Oral Controlled Release*, *Saudi Pharmaceutical Journal*, **2003**; 11(4):
5. Han Gon Choi, J.Jung, C.S.Yong, C.Rhee, M.Lee, J.Han, K.Park, C.Kim. Formulation and invivo evaluation of omiprazole buccaladhesive tablet, *Journal Of Controlled Release***, 2000**; 68: 405-412.
6. B.taylan, Y.capan ,O.guven, S.Kes, A.Atilla hincal. Desion and Evaluation of Sustained release and buccal adhesive propranolol hydrochloride tablets, *Journal of controlled release* , **1996**; 38 :11-20.
7. M.Chandira , Mehul, Debjit, Chiranjib, Kumudhavalli, B.Jayakar. Formulation, Desion and Development of buccoadhesive tablets of virapamil hydrochloride, *International journal of pharmatech and research*, **2009**; 1(4): 1663-167
8. V.Nahid Sharmin, Md. Elias-al-Mamun, Md.Saiful Islam and Reza-ul Jail. Preparation and Charecterization of lidocaine double layer buccal tablet using mucoadhesive Carbopol Polymers, Dhaka *Univ .J.Pharm.Sci.* **2011**; 10(1):29-34.
9. Ganesh G. N. K. Design and development of buccal drug delivery system for labetalol using natural polymer; *ijprd*, **2011**; 3(3):37 - 49).
10. Harikrishna.B, N.Ravikumar, Pranav b.,Dennis. Controlled release from directly compressible theophylline buccal tablets colloids and surfaces .*J. biointerfaces*, **2010**; 77: 227-233.
11. 1R Manivannan1, A Balasubramaniam1, DC Prem Anand1, G Sandeep and Rajkumar.Formulation and *In-Vitro* Evaluation of Mucoadhesive Buccal Tablets of Diltiazem Hydrochloride, *Research J. Pharm. and Tech,* **2008**; 1(4)
12. G.ikinci, S.Senel, C.G.Wilson, M.Summu. Development of a buccal bioadhesive nicotine tablet formulation for smooking cessatlon, *International Journalof Pharmaceutics*, **2004**; 277: 173-178.