Original Article

Formulation and Evaluation by Appling 3^2 (Three Squire) Factorial Design of Lercanidipine Hydrochloride Buccal Tablets with Mucoadhesive Polymers

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ABSTRACT

Aim: The aim of the present research work is to develop buccal tablets of Lercanidipine hydrochloride to reduce dosage frequency; obtain optimized and controlled therapy, better patient compliance. **Materials and Methods:** Lercanidipine HCl was obtained as a gift sample from Sun Pharma, Baroda, India. Other ingredients like Na-alginate, Carbopol 934 P, Micro Crystalline Cellulose, Mannitol, Magnesium stearate, Ethyl cellulose and Hydroxy Propyl Methyl CelluloseK4M were purchased from various sources. All other ingredients used were of analytical grade. Attempt was made by using mucoadhesive polymers HPMC K4 M, sodium alginate and carbopol 934 P in combination with Ethyl Cellulose as an impermeable backing layer. **Results:** Combination of polymer HPMC K4 M and sodium alginate release of drug was found in desired manner than other combinations. On the basis of the preliminary trials a 3^2 full factorial design was employed to study the effect of independent variables such as concentration of sodium alginate: HPMC K4M (X1) and type of filler (X2) on dependent variables. Factorial batches of F1 to F9 were formulated. HPMC K4M exhibited a much greater sustained effect on the release rate compared with sodium alginate. F4 shown the highest *f2* value 70.46 and also all the h drug release was within the specified range. Based on the *f2* value and targeted release profile the F4 batch was considered as optimized batch. Formulation F4 was subjected to an *in vitro* buccal permeation study. The results showed drug permeation of 99.04% in 12 h. The correlation between *in vitro* drug release rate and *in vitro* drug permeation across the chicken mucosa was found to be positive, with a correlation coefficient (R^2) of 0.9921. **Conclusion:** From kinetic modelling of the dissolution profile of the optimized formulation, it was concluded that there is erosion-controlled release of Lercanidipine from the buccal adhesive drug delivery system.

Key words: Lercanidipine hydrochloride, Buccal tablets, HPMC K4M, Buccal permeation study, Erosion controlled release.

INTRODUCTION

Hypertension is a medical condition where the blood pressure is chronically elevated is one of the commonly found diseases throughout the world. Lercanidipine belongs to the drug class known as calcium channel blockers. It relaxes and dilates the blood vessels thereby allowing blood to flow more freely throughout the body. Consequently, blood pressure is reduced and the heart is able to function more efficiently. The absolute bioavailability is reduced to approximately 10% because of extensive first pass metabolism to inactive metabolites. Mean half-live of Lercanidipine is about 4.4 h in humans after single dose of 20 mg. These pharmacokinetic parameters make Lercanidipine a suitable candidate for buccal delivery. Hence, in this research work an attempt was made to formulate buccal tablets of Lercanidipine hydrochloride to increase patient compliance by reducing dosing frequency and to achieve

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plasma concentration profile over 12 h. The primary aim is to protect the drug from an unfavourable environment in the gastrointestinal tract.

The buccal route has long been advocated as possible route of delivery of drugs having poor oral bioavailability because of high first pass metabolism or degradation in the gastrointestinal tract. The buccal mucosa reaching the heart directly via the internal jugular vein as this route is well vascularised with venous blood draining. Although, the drug fluxes via this route are less than that obtained with sublingual mucosa due to permeability barrier, the relative immobility of buccal musculature, as compared to that of sublingual route, makes this site ideally suited for delivery of drugs.

During development, sufficient information about the physical and chemical properties of the drug substance, composition of the product in terms of the drug substance, excipients and manufacturing process were gained and evaluated the critical parameters of the process those needed to be controlled in order to ensure batch to batch reproducibility.[1,2]

MATERIALS AND METHODS

Materials

Lercanidipine HCl was obtained as a gift sample from Sun Pharma, Baroda, India. Na-alginate was purchased from Finar Chemicals Pvt. Ltd., Ahmedabad, India. Lactose, Micro Crystalline Cellulose, Mannitol, Magnesium stearate were purchased from Chemdyes Corporation, Ahmedabad, India. Ethyl cellulose and Hydroxy Propyl Methyl Cellulose K4M, Carbopol 934 P were purchased from Yarrow Chem. Product, Mumbai, India. All other ingredients used were of analytical grade.

Methods

Calculation of theoretical release profile of Lercanidipine hydrochloride

The theoretical release profile of Lercanidipine HCl was carried out by calculation of the immediate release dose and calculation of maintenance dose.

Calculation of the Immediate Release Dose

$$IR = Css \times \frac{Vd}{F} = 3.88 \text{ mg}$$

Where, IR = Immediate release,

C_{SS} = Concentration at steady state,

V_d = Volume of distribution,

F = Fraction bioavailable.

Calculation of Maintenance Dose (MD)

$$MD = IR\{(1 + 0.693t)\}/t_{1/2} \times 0.693$$

IR = Immediate release,

MD = Maintenance dose,

t = time up to which sustain release is required,

$t_{1/2}$ = half-life.

According to the theoretical profile the drug release in first h should be 3.88 mg (19.40%). In the remaining 11h, 16.12 mg (80.60%) drug should be released. So, after initial release 07.32% drug should release from the matrix of tablet each h approximately. This is summarized in Table 1.

Preparation of BADDS (Buccal Adhesive Drug Delivery System)

The preparation process of BADDS mainly involves 3 steps:

(1) Formation of core tablet: The composition of core[3] (fast and sustained release layers) and adhesive outer layer along with polymer ratios are presented in Table 2 (a) and Table 2 (b). All ingredients were passed through American Society for Testing Materials (ASTM) sieve no. 100 and blended separately in a mortar. The core containing fast and sustained release layers was prepared in 7 mm punch size using an electrically operated single station punching machine.

(2) Formation of Backing layer: Formation of Backing Layer[4] (using 11 mm punch). Then backing layer material was inserted in 11-mm die cavity and uniformly distributed in 11-mm die cavity by single rotation.

Table 1: Theoretical Drug Release Profile of Lercanidipine hydrochloride.

Time (h)	Amount of Drug Release	% of Drug Release
0	0	0
1	3.88	19.40
2	5.35	26.72
3	6.82	34.04
4	8.29	41.36
5	9.76	48.68
6	11.23	56.00
7	12.70	63.32
8	14.17	70.64
9	15.64	77.96
10	17.11	85.28
11	18.58	92.60
12	20.05	100

Table 2: (a) Formulae for tablet formulation.										
No.	First Layer			Second layer				Adhesive cup Layer		Backing Layer
	Drug	Mannitol	Filler	Drug	Carbopol 934P	HPMC K4M	Lactose	Carbopol 934P	HPMC K4M	EC
Trial 1	4	30	16	16	17	17	0	100	-	50
Trial 2	4	30	16	16	15	15	4	80	20	50
Trial 3	4	30	16	16	15	15	4	75	25	50
Trial 4	4	30	16	16	15	15	4	50	50	50
Trial 5	4	30	16	16	15	15	4	25	25	50

Table 2: (b) Formulae for Tablet Formulation.										
No.	First Layer			Second layer				Adhesive cup Layer		Backing Layer
	Drug	Mannitol	Filler	Drug	Sodium alginate	HPMC K4M	Lactose	Sodium alginate	HPMC K4M	EC
Trial 6	4	30	16	16	15	15	4	25	25	50

(3) Formation of BADDS: Formation of BADDS (using 11 mm punch): Then on prepared backing layer put core tablet of 7 mm sized in centre and buccal adhesive polymeric material inserted around the core tablet and then compressed using 11-mm flat-faced upper and lower punches.

Evaluation of tablets of trial batches

Weight variation test

To study weight variation twenty tablets of the formulation were weighed using a Sartorius electronic balance and the test was performed according to the official method.

Thickness

The thickness of the tables was determined by using micrometer. Five tablets were used and average values were calculated.

Drug content

Five tablets were weighed individually and the drug was extracted in phosphate buffer pH 6.8, the drug content was determined as described above.

The above parameters are expressed in Table 3.

In-vitro Drug Release

In vitro drug release studies were carried out using USP II (rotating paddle) dissolution apparatus (Elecrolab TDT 08L) with minor modifications. The dissolution medium consisted of 200 ml of phosphate buffer pH 6.8 with 2.5% polysorbate 80. The release study was performed at 37°C ± 0.5°C, with a rotation speed of 25 rpm. The backing layer of the buccal tablet was attached to the glass disk with cyanoacrylate adhesive. The disk was placed at the bottom of the dissolution vessel. Samples of 5 ml were withdrawn at predetermined time intervals and replaced with fresh medium. The samples were filtered through 0.2-µm Whatman filter paper and analyzed after appropriate dilution by UV spectrophotometer (Shimadzu, 1800) at 350 nm. Then compare the batches with theoretical profile and found the similarity factor f_2 value.

Comparison of dissolution profiles

The similarity factor (f_2) given by SUPAC guidelines[5] for modified release dosage form was used as a basis to compare dissolution profile. The dissolution profiles are considered to be similar when *f2* is between 50 and 100. The dissolution profiles of products were compared using *f2*. This similarity factor is calculated by following formula,

$$f_2 = 50 \log \{[1+\frac{1}{n}\sum_{n=1}^{n}(R_t-T_t)^2]^{-0.5} \times 100$$

Where, n is the number of dissolution time and R_j and T_j are the reference and test dissolution values at time *t*.

Observations of preliminary trials

Lercanidipine tablets were prepared by direct compression. HPMC, carbopol, sodium alginate were used as a release retarding agents in Lercanidipine tablets formulation. Drug content of all formulation was in the range of 98.00 to 100 % which passed the official requirement as per I.P. of all batches of preliminary trial batches was

Table 3: Evaluation of Preliminary trial formulation of Lercanidipine hydrochloride tablets.

Preliminary Batches	Weight (mg) (X±SD)	Thickness (mm) (X±SD)	Drug Content (%) (X±SD)
Trial 1	249.20±0.13	2.20±0.03	98.70±0.3
Trial 2	248.80±0.25	2.17±0.02	98.20±0.1
Trial 3	249.15±0.22	2.15±0.02	99.74±0.2
Trial 4	249.40±0.53	2.20±0.01	97.38±0.3
Trial 5	198.80±0.31	1.95±0.02	99.35±0.4
Trial 6	198.50±0.12	1.94±0.03	98.90±0.2

Data are represented as mean (X) ±standard deviation (SD), *n*=3.

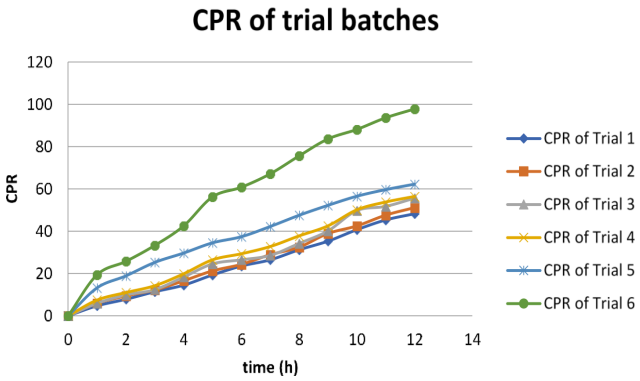

Figure 1: CPR of trial batches.

performed. Weight variation indicated that they were in range of official standards and no significant difference between individual weights of tablets from the average value. Dissolution of Lercanidipine tablet was carried out in USP type –II apparatus with some modification. In this method, phosphate buffer pH 6.8 was used a dissolution medium. All other conditions were kept as standards. Dissolution data for trial batches 1 to 5 shown that drug release were found to be decreased as compared to trial batch 6 containing sodium alginate and HPMC combination as shown in Figure 1. Similarity factor also calculated for batches 1 to 5 were f_2 value in the range of 25 to 40% which suggested that there was dissimilarity between theoretical drug release profile and trial batch using different polymer concentration. But in trial batch 6, there was similarity factor found above 50 % so the other formulation batches developed on the ratio of polymer used factorial design. After the results of preliminary batches of Lercanidipine tablet, it was concluded that the formulation of other factorial batches carried out on the polymer ratio used in trial batch no. 6.

Formulation of buccal tablet using 3^2 full factorial designs

It is desirable to develop an acceptable pharmaceutical formulation in shortest possible time using minimum number of man-hrs and raw materials.[6] Traditionally pharmaceutical formulations after developed by changing one variable at a time approach. The method is time consuming in nature and requires a lot of imaginative efforts. Moreover, it may be difficult to evolve an ideal formulation using this classical technique since the joint effects of independent variables are not considered. It is therefore very essential to understand the complexity of pharmaceutical formulations by using established statistical tools such as factorial design.

In addition to the art of formulation, the technique of factorial design is an effective method of indicating the relative significance of a number of variables and their interactions. The number of experiments required for these studies is dependent on the number of independent variables selected. The response/s (Yi) is/are measured for each trial and then either

A statistical model incorporating interactive and polynomial term was used to evaluate the response:

$$Y = b_0 + b_1X_1 + b_2X_2 + b_{12}X_1X_2 + b_{11}X_1^2 + b_{22}X_2^2$$

Where, Y is the dependent variables, b_0 is the arithmetic mean response of the nine runs and b_1 is the estimated coefficient for the factor X_1. The main effects (X_1 and X_2) represent the average result of changing one factor at a time from its low to high value. The interaction terms (X_1X_2) show how the response changes when two factors are simultaneously changed. The polynomial terms (X_{12} and X_{22}) are included to investigate non-linearity.

A 3^2 randomized full factorial design was used in this study.[7] In this design two factors were evaluated, each at three levels and experimental trials were performed at all nine possible combinations expressed in Table 4. Concentration of Sodium alginate: HPMC K4M (X_1) and type of Filler (X_2) were selected as independent

Table 4: Batches according to factorial design.

Factorial Batch	(Factor X_1) Sodium alginate: HPMC K4M	(Factor X_2) Type of Filler
F1 (-1,-1)	1:2	Lactose
F2 (-1,0)	1:2	MCC
F3 (-1,1)	1:2	Mannitol
F4 (0,-1)	1:1	Lactose
F5 (0,0)	1:1	MCC
F6 (0,1)	1:1	Mannitol
F7 (1,-1)	2:1	Lactose
F8 (1,0)	2:1	MCC
F9 (1,1)	2:1	Mannitol

Table 5: Composition of core layer and buccal adhesive cup along with code.										
No.	First Layer			Second layer				Adhesive cup Layer		Backing Layer
	D	M	F	D	S	H	F	S	H	EC
F1	4	30	16(A)	16	10	20	4(A)	16.66	33.33	50
F2	4	30	16(B)	16	10	20	4(B)	16.66	33.33	50
F3	4	30	16(M)	16	10	20	4(M)	16.66	33.33	50
F4	4	30	16(A)	16	15	15	4(A)	25	25	50
F5	4	30	16(B)	16	15	15	4(B)	25	25	50
F6	4	30	16(M)	16	15	15	4(M)	25	25	50
F7	4	30	16(A)	16	20	10	4(A)	33.33	16.66	50
F8	4	30	16(B)	16	20	10	4(B)	33.33	16.66	50
F9	4	30	16(M)	16	20	10	4(M)	33.33	16.66	50

Where D=Drug, A= Lactose, B=MCC, M=Mannitol, F=Filler, S=Sodium alginate, H=HPMC K4M, all weights are in mg.

Table 6: Physicochemical properties of BADDS of Lercanidipine.			
Formulation	Weight [a](mg)	Thickness [b](mm)	% Drug Content [b]
F1	195.8±1.40	1.94±0.01	99.03±0.35
F2	193.68±1.53	1.93±0.01	98.17±0.28
F3	192.9±1.33	1.94±0.01	97.67±0.23
F4	191.8±1.60	1.94±0.01	99.23±0.25
F5	190.8±1.64	1.93±0.02	100.17±0.47
F6	190.1±1.68	1.94±0.01	96.67±1.02
F7	188.7±2.02	1.94±0.01	97.9±0.78
F8	187.4±1.63	1.93±0.01	97.57±0.97
F9	187.55±1.70	1.95±0.01	95.07±0.41

[a] Mean (± SD) of 20 tablets, [b] Mean (± SD) of 3 tablets.

variables. The similarity factor f_2 was selected as dependent variables.

According to the factorial design the nine formulations were calculated and summarized in Table 5.

Tablets were then evaluated for % drug release profile to select the optimum concentration of release retarding agent.

Evaluation of Buccal Tablets

Content Uniformity

Drug content uniformity[8] was determined by dissolving the tablets in acetone and filtering with Whatman filter paper (0.45 µm, Whatman). The filtrate was evaporated and the drug residue dissolved in 100 ml of phosphate buffer (pH 6.8) containing 2.5% w/w of Polysorbate 80. The 10 ml solution was then diluted with phosphate buffer (pH 6.8) containing 2.5% w/w of Polysorbate 80 up to 100 ml, filtered through 0.45-µm Whatman filter paper and analyzed at 350 nm using a UV spectrophotometer (Shimadzu 1800, Japan). The experiments were performed in triplicate and average values were reported (Table 6).

In vitro mucoadhesion strength measurement

Mucoadhesion Strength (MS) of BADDS with chicken intestinal mucosa was measured using a modified 2-arm balance. The chicken intestinal mucosa was fixed to the small beaker with cyanoacrylate adhesive and then placed in a large beaker. Phosphate buffer solution was added into the large beaker up to the upper surface of the buccal mucosa to maintain buccal mucosal viability during the experiments.[9] The BADDS was attached to the upper clamp of the apparatus and then the beaker was raised slowly until contact between chicken intestinal mucosa and BADDS was established. A preload of 50 g was placed on the clamp for 5 min (preload time) to establish adhesion bonding between BADDS and chicken intestinal mucosa. The preload and preload time were kept constant for all the formulations. After completion of the preload time, preload was removed from the clamp and water was then added into the Petri dish from the burette at a constant rate of 100 drops per min. The addition of water was stopped when BADDS was detached from chicken intestinal mucosa. The weight of water required to detach BADDS from buccal mucosa was noted as Mucoadhesion Strength (Table 7).

Swelling Studies

BADDS was weighed individually (recorded as W_1) and placed separately in Petri dish containing 5 ml of phosphate buffer (pH 6.8) solution.[10] At regular intervals (1, 2, 3, 4 and 5 h), the BADDS was removed from the Petri dish and excess surface water was removed carefully using the filter paper (Table 8). The swollen

Table 7: *In vitro* mucoadhesive study of BADDS of Lercanidipine.

Formulation	Mucoadhesion Strength (gram force)
F1	34.15
F2	33.24
F3	34.12
F4	28.69
F5	28.48
F6	28.35
F7	24.69
F8	23.76
F9	23.18

Table 8: Swelling index of BADDS tablets of batches from F1to F9.

Formulation	Swelling Index				
	1 h	2 h	3 h	4 h	5h
F1	0.94	1.47	1.82	2.23	2.42
F2	0.96	1.48	1.79	2.28	2.36
F3	0.94	1.42	1.78	2.32	2.40
F4	1.052	1.526	2.25	2.83	2.86
F5	1.128	1.496	2.28	2.64	2.68
F6	1.12	1.51	2.18	2.76	2.8
F7	2	2.78	3.21	3.26	3.42
F8	2.2	2.82	3.20	3.21	3.24
F9	2.08	2.80	3.11	3.14	3.17

BADDS was then reweighed (W_2) and swelling index (SI) was calculated using formula as

$$S1 = \frac{w2 - w1}{w1}$$

In vitro drug release

In vitro drug release studies were carried out using USP II (rotating paddle) dissolution apparatus (Elecrolab TDT 08L) with minor modifications. The dissolution medium consisted of 200 mL of phosphate buffer pH 6.8 with 2.5 % polysorbate 80. The release study was performed at 37°C ± 0.5°C, with a rotation speed of 25 rpm. The backing layer of the buccal tablet was attached to the glass disk with cyanoacrylate adhesive.[11] The disk was placed at the bottom of the dissolution vessel. Samples of 5 ml were withdrawn at predetermined time intervals and replaced with fresh medium. The samples were filtered through 0.2-µm Whatman filter paper and analyzed after appropriate dilution by UV spectrophotometer (Shimadzu, 1800) at 350 nm and represented in Figure 2.

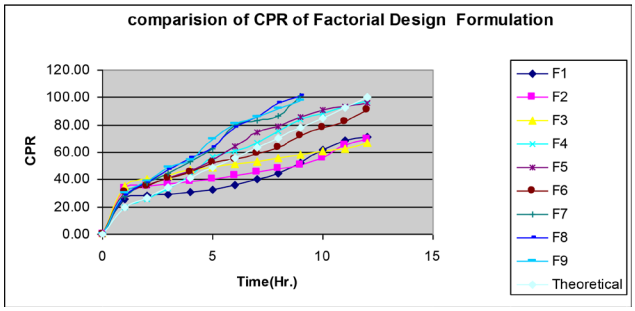

Figure 2: Comparison of factorial batches with theoretical profile.

Table 9: Similarity factor values of factorial batches.

Formulation	f_2 value
F1	35.22
F2	35.23
F3	37.23
F4	70.46
F5	56.71
F6	56.45
F7	41.31
F8	39.06
F9	30.96

Similarity factor (f_2): The dissolution profiles of products were compared using *f2* by using the similarity factor calculation and as shown in Table 9.

In vitro drug permeation

The *in vitro* buccal drug permeation study of Lercanidipine hydrochloride through the Chicken mucosa was performed using a modified diffusion cell[12] at 37°C ± 0.2°C has shown in Table 10.

Kinetics Modeling of Drug Dissolution Profiles

The *in vitro* release data obtained was fitted to various kinetic equations.[13] Correlation coefficients of batch F4 with applied equation are given in Table 11. Batch showed higher correlation with zero order than Higuchi plot and first order. So predominant drug release mechanism is followed erosion-controlled release.

RESULTS AND DISCUSSION

Tablets were found to be satisfactory when evaluated for average weight, thickness and drug content.

The average weight of the tablet was found to be between 187.55 mg to 195.8 mg and maximum % deviation was found to be ± 2.02 from all formulations. The thickness of all tablets was found to be between 1.93

Table 10: *In vitro* diffusion study of BADDS of Lercanidipine.

Time (h)	Percentage Cumulative Drug Diffused
1	18.49
2	25.23
3	33.98
4	42.93
5	50.32
6	56.37
7	69.58
8	73.83
9	82.08
10	87.22
11	95.56
12	99.04

Table 11: Correlation coefficients of drug release curves for Lercanidipine batch F4 based on kinetic models.

Model	Correlation coefficients of Batch F4
Zero order	0.996231
First order	0.989508
Higuchi	0.988253
Release mechanism	Erosion controlled

to 1.95 mm ± 0.01 to 0.02. Percent drug content was found to be 95- 100%.

HPMC K4M and Na-alginate were selected as the bioadhesive polymers because of their excellent bioadhesive properties. EC has recently been reported to be an excellent backing material given its low water permeability, hydrophobicity and moderate flexibility. So, it was chosen as an impermeable backing layer.[14] D-mannitol was used to improve the release of drug from polymer matrices and the concentration was optimized during the preliminary trial to find the best formulation of buccal tablets.

The *ex vivo* mucoadhesive strength of the tablets was determined for using chicken intestinal mucosa. Tablets containing a higher proportion of Na-alginate showed higher mucoadhesion at initial stage. This finding is owing to the hydrophilic nature of Na-alginate; it is hydrated easily with less contact time and forms a strong gel that entangles tightly with the mucin molecules. This high mucoadhesive strength of HPMC K4M may be due to formation of secondary mucoadhesive bonds with mucin because of rapid swelling and interpenetration of the polymer chains in the interfacial region, while other polymers undergo only superficial bioadhesion. Formulation F4 showed good mucoadhesive strength (28.69 g). The effect of HPMC K4M was more significant than the effect of Na alginate. The increase in concentration of HPMC K4M in series from formulation F9 to F1, showed a gradual rise in mucoadhesion time, while Na-alginate, which is also a good mucoadhesive polymer, showed a decrease in mucoadhesion time.

Appropriate swelling behavior of a buccal adhesive system is essential for uniform and prolonged release of the drug and effective mucoadhesion. Swelling index was calculated with respect to time. The swelling index increased as the weight gain by the tablets increased proportionally with rate of hydration as shown in to the Table 8.

The order of swelling observed in these polymers could indicate the rates at which the preparations are able to absorb water and swell. Maximum liquid uptake and swelling of sodium alginate was achieved after 3 h and then gradually decreased due to erosion. HPMC K4M reached maximum swelling after 5 h and this was maintained until the end of the experiment. This finding may have been because of the fast-swelling property of Na alginate compared with HPMC K4M. The maximum swelling index was found in batch F7 (3.21), containing a higher proportion of Na-alginate and the lowest in F2 (2.36).

In dissolution profile of factorial batches HPMC K4M exhibited a much greater sustained effect on the release rate compared with sodium alginate. All formulations containing 1:2 (Sodium alginate: HPMC K4M) exhibited similar release of drug in 12 hrs up to 71.21%. In formulations containing 2:1 (Sodium alginate: HPMC K4M) the drug was completely released after 9 h from tablets. But in formulation containing 1:1(Sodium alginate: HPMC K4M) drug was completely release in 12 h with desired release rate. Formulation containing 1:1(Sodium alginate: HPMC K4M) was impressive since these formulations showed effective desired release pattern. Incorporation of loading dose (2 mg) along with sustained release dose into the BADDS resulted in faster release at the initial period and controlled release pattern in the later period.

Formulation F4 was optimized based on *in vitro* drug release (97.85 at 12 h), swelling index (2.86 at 5 h) and *ex vivo* mucoadhesive strength (28.69 g). It showed good drug release with sufficient mucoadhesion. Formulation F4 was subjected to an *in vitro* buccal permeation study using a diffusion cell. The results showed drug permeation of 99.04% in 12 h. The correlation between *in vitro* drug release rate and *ex vivo* drug permeation across the chicken mucosa was

found to be positive, with a correlation coefficient (R^2) of 0.9921.

CONCLUSION

This designed BADDS could overcome the disadvantage of poor and erratic oral bioavailability of Lercanidipine. BADDS has also overcome the drawback associated with conventional buccal adhesive tablets. BADDS consists of fast and sustained release layers, Lercanidipine can be release and permeated through buccal mucosa rapidly[15] at the first and then continuously for prolonged period.

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CONFLICT OF INTEREST

The author declare no conflict of interest.

ABBREVIATIONS

HPMC: Hydroxy Propyl Methyl Cellulose; **IR:** Immediate release; **MD:** Maintenance dose; **BADDS:** Buccal Adhesive Drug Delivery System; **ASTM:** American Society for Testing Materials; **MS:** Mucoadhesion Strength.

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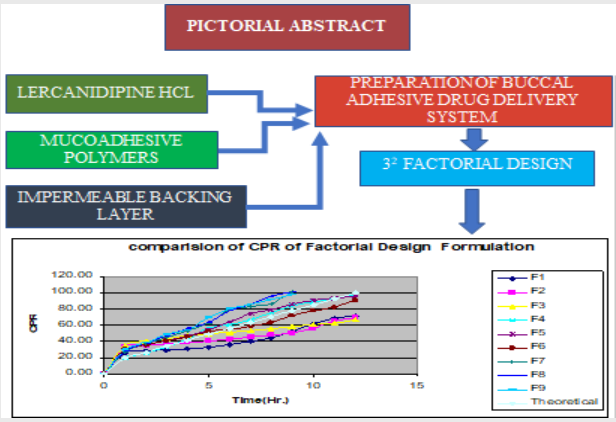
SUMMARY

Lercanidipine is a calcium antagonist of the dihydropyridine group and selectively inhibits the transmembrane influx of calcium into cardiac and vascular smooth muscle, with a greater effect on vascular smooth muscle than on cardiac smooth muscle. The anti-hypertensive action is due to a direct relaxant effect on vascular smooth muscle which lowers total peripheral resistance and hence blood pressure. Lercanidipine has a prolonged anti-hypertensive activity because of its high membrane partition coefficient. Lercanidipine has absolute bioavailability is reduced to 10% because of the extensive first pass metabolism to inactive metabolites. Lercanidipine hydrochloride is the best candidate for buccal drug delivery. In the present study, it was studied the effect of Sodium alginate and HPMC K4M and observed that drug permeation of 99.04% in 12 hr. The correlation between *in vitro* drug release rate and *ex vivo* drug permeation across the chicken mucosa was found to be positive, with a correlation coefficient (R^2) of 0.9921. Hence the effect of Sodium alginate and HPMC K4M were clearly established.

PICTORIAL ABSTRACT



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