2026 Volume: 02 Issue: 04 www.ijrpa.com ISSN 2456-9995 Research Article

International Journal Research Publication Analysis

Page: 01-13

DESIGN DEVELOPMENT AND OPTIMIZATION OF MUCOADHESIVE DRUG DELIVERY SYSTEM OF LERCANIDIPINE

*** [1]Pooja, [2]Dr. Gaurav Bhaduka, [3]Dr. Dilip Agrawal**

*[1]Research Scholar, Mahatma Gandhi College of Pharmaceutical Sciences, Jaipur- 302022.

[2]Professor, Mahatma Gandhi College of Pharmaceutical Sciences, Jaipur, Rajasthan- 302022.

[3]Principal, Mahatma Gandhi College of Pharmaceutical Sciences, Jaipur, Rajasthan- 302022.

Article Received: 05 March 2026
Article Revised: 23 March 2026
Published on: 13 April 2026

***Corresponding Author: Pooja**
Research Scholar, Mahatma Gandhi College of Pharmaceutical Sciences, Jaipur-302022.

DOI: https://doi-doi.org/101555/ijrpa.2435

ABSTRACT

Buccal route of drug delivery has significant attention to the systemic circulation through the jugular vein bypassing the first pass hepatic metabolism leading to high bioavailability. Such routes have expanded important notice due to their presystemic metabolism or instability in the acidic environment associated with the oral administration. Lercanidipine can be release and permeated through buccal mucosa rapidly at the first and then continuously for prolonged period. 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 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. Dissolution data for trial batches 1, 2,3,4,5 shown that drug release were found to be decreased as compared to trial batch 6 containing sodium alginate and HPMC combination. Similarity factor also calculated for batches 1 to 5 were F2 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.

KEYWORDS: Bioavailability, Buccal drug delivery, Muucoadhesive tablets, Lercanidipine.

INTRODUCTION

The most common modifiable risk factor for death and disability is hypertension, which includes stroke, accelerated coronary and systemic atherosclerosis, heart failure, chronic kidney disease, lowering blood pressure with antihypertensive drugs, and reducing target organ damage and the prevalence of the occurrence of cardiovascular disease. Amongst the various routes of drug delivery, oral route is perhaps the most preferred to the patient and the clinician alike. However, peroral administration of drugs has disadvantages such as hepatic first pass metabolism and enzymatic degradation within the GI tract, that prohibit oral administration of certain classes of drugs especially peptides and proteins. Consequently, other absorptive mucosae are considered as potential sites for drug administration. Transmucosal routes of drug delivery (i.e., the mucosal linings of the nasal, rectal, vaginal, ocular, and oral cavity) offer distinct advantages over peroral administration for systemic drug delivery. The first-line therapy for hypertension is lifestyle change, which includes weight loss, dietary sodium reduction, potassium supplementation, a healthy eating pattern, physical exercise, and moderate alcohol consumption. Thiazide or thiazidelike diuretics, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, and calcium channel blockers are first-line remedies when pharmacological therapy is required.

Advantages of Drug Delivery via the Buccal Lining:

1. Bypass of the gastrointestinal tract and hepatic portal system, increasing the bioavailability of orally administered drugs that otherwise undergo hepatic first-pass metabolism**.** In addition the drug is protected from degradation due to pH and digestive enzymes of the middle gastrointestinal tract.
2. Improved patient compliance due to the elimination of associated pain with injections; administration of drugs in unconscious or incapacitated patients; convenience of administration as compared to injections or oral medications.
3. Sustained drug delivery.
4. A relatively rapid onset of action can be achieved relative to the oral route, and the formulation can be removed if therapy is required to be discontinued.
5. Increased ease of drug administration**.**
6. Though less permeable than the sublingual area, the buccal mucosa is well vascularized, and drugs can be rapidly absorbed into the venous system underneath the oral mucosa.

Limitations of Buccal Drug Delivery:

Depending on whether local or systemic action is required the challenges faced while delivering drug via buccal drug delivery can be enumerated as follows.

1. For local action the rapid elimination of drugs due to the flushing action of saliva or the ingestion of foods stuffs may lead to the requirement for frequent dosing.
2. The non-uniform distribution of drugs within saliva on release from a solid or semisolid delivery system could mean that some areas of the oral cavity may not receive effective levels.
3. For both local and systemic action, patient acceptability in terms of taste, irritancy and 'mouth feel' is an issue.

Table 1: Mucoadhesive polymers in buccal delivery.

Criteria	Categories	Examples
Source	Semi-natural/natural	Agarose, chitosan, gelatin, Hyaluronic acid Various gums (guar, Xanthum, gellan, carragenan, pectin, and sodium alginate)
	Synthetic	*Cellulose derivatives* [CMC, sodium CMC, HEC, HPC, HPMC, MC] *Poly(acrylic-acid)-based polymers* [CP, PC, PAA, Polyacrylates] *Others :*Poly(N-2-hydroxypropyl methacrylamide) (PHPMAm), polyoxyethylene, PVA, PVP
Aqueous solubility	Water-soluble	CP, HEC, HPC (waterb38 8C), HPMC (cold water), PAA, sodium CMC, sodium alginate
	Water-insoluble	Chitosan (soluble in dilute aqueous acids), EC, PC
Charge	Cationic	Aminodextran, chitosan, trimethylated chitosan
	Anionic	Chitosan-EDTA, CP, CMC, pectin, PAA, PC, sodium alginate, sodium CMC, Xanthum gum
	Non-ionic	Hydroxyethyl starch, HPC, poly(ethylene oxide)
Potential bioadhesive forces	Covalent	Cyanoacrylate
	Hydrogen bond	Acrylates [hydroxylated methacrylate, poly(methacrylic acid)], CP, PC, PVA
	Electrostatic interaction	Chitosan

There are the various drugs are given through buccal route. The list is below as

Table 2: List of Drugs investigated for buccal delivery.

Acetretin	Acyclovir
Arecoline	Buprenorphine
Buserelin	Buspirone
Captropril	Carbamazepine

Carvedilol	Diltiazem
Danazol	Ergotamine
Diclofenac sodium	Lidocaine
Fentanyl	Metoprolol tartrate
Ketoprofen	Pilocarpine
Metronidazole	Prednisolone
Nifedipine	Propranolol
Pentazocine	Theophylline
Pindolol	verapamile
Silymarin	testosterone

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.

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.

Lercanidipine is completely absorbed after oral administration. Peak plasma levels of 3.30ng/mL ± 2.09 s.d and 7.66 ng/mL ± 5.90 s.d occur 1.5-3 hours after dosing with 10mg and 20mg, respectively.

The absolute bioavailability of lercanidipine is about 10%, because of high first pass metabolism. The bioavailability increases 4-fold when lercanidipine is ingested up to 2 hours after a high fat meal, and about 2-fold when taken immediately after a carbohydrate-rich meal. Consequently, lercanidipine should be taken at least 15 minutes before a meal.

MATERIAL AND METHOD:

Lercanidipine is obtained from Sun Pharma, Baroda, India. Methanol, Ethanol, Chloroform, Hydrochloric acid (HCl), KH2PO4, NaOH, HPMC K-4, Carbopol, Na Alginate, Citric acid, Talc, Lactose, Magnesium stearate were obtained from S.D. Fine Pvt. Ltd. Mumbai & Loba Chemie Pvt Ltd, Mumbai.

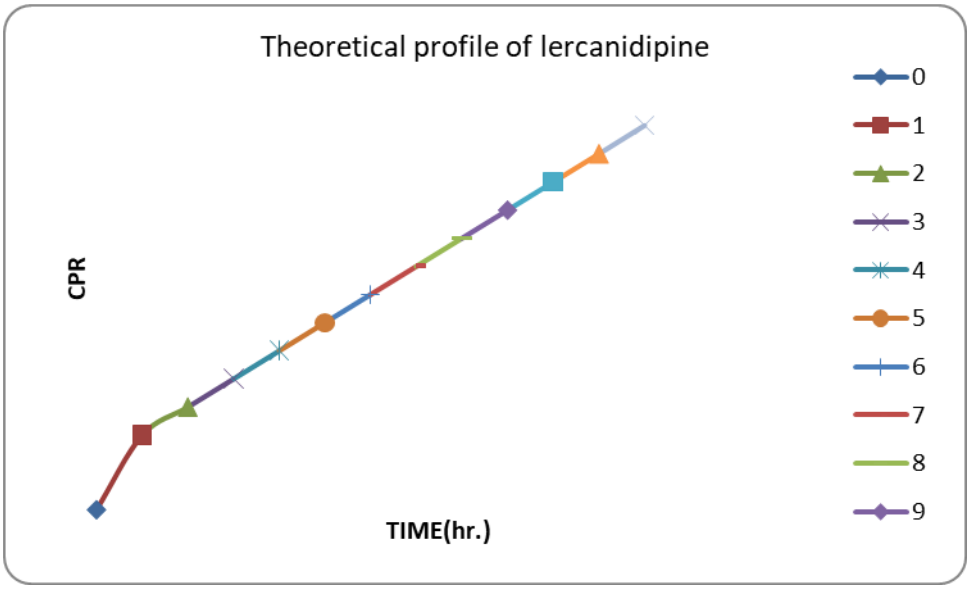

FIG- 1: Theoretical Drug Release Profile Lercanidipine.

Preparation of BADDS (Buccal Adhesive Drug Delivery System)

The preparation process of BADDS mainly involves 3 steps:

(1) Formation of core tablet,

(2) Formation of Backing layer and

(3) Formation of BADDS. The composition of core (fast and sustained release layers) and adhesive outer layer along with polymer ratios are presented in Table 3. All ingredients were passed through American Society for Testing Materials (ASTM) sieve no. 100 and blended separately in a mortar.

Table 3: Formula for tablet formulation.

S. 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

S. 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

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.

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.

Thickness:

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

Table 4: Dissolution Profile of Trial Batches.

Time(hr)	CPR of Trail Batches					
	Trial 1	Trial 2	Trial 3	Trial 4	Trial 5	Trial 6
0	0.00	0.00	0.00	0.00	0.00	0.00
1	4.75	5.88	5.94	7.45	13.22	19.39
2	7.84	9.42	9.87	11.02	18.90	25.77
3	11.42	12.20	12.41	14.24	25.27	33.31
4	14.52	16.56	18.34	19.86	29.68	42.51
5	19.34	21.25	24.57	26.47	34.52	56.27
6	23.58	24.31	26.51	29.34	37.41	60.85
7	26.50	28.89	28.57	32.75	42.23	67.17
8	31.25	32.42	34.24	37.78	47.54	75.64
9	35.32	38.89	40.15	42.51	52.24	83.66
10	40.74	42.47	49.78	50.09	56.54	88.17
11	45.36	47.56	51.78	53.78	59.67	93.69
12	48.30	51.12	55.65	56.42	62.25	97.85

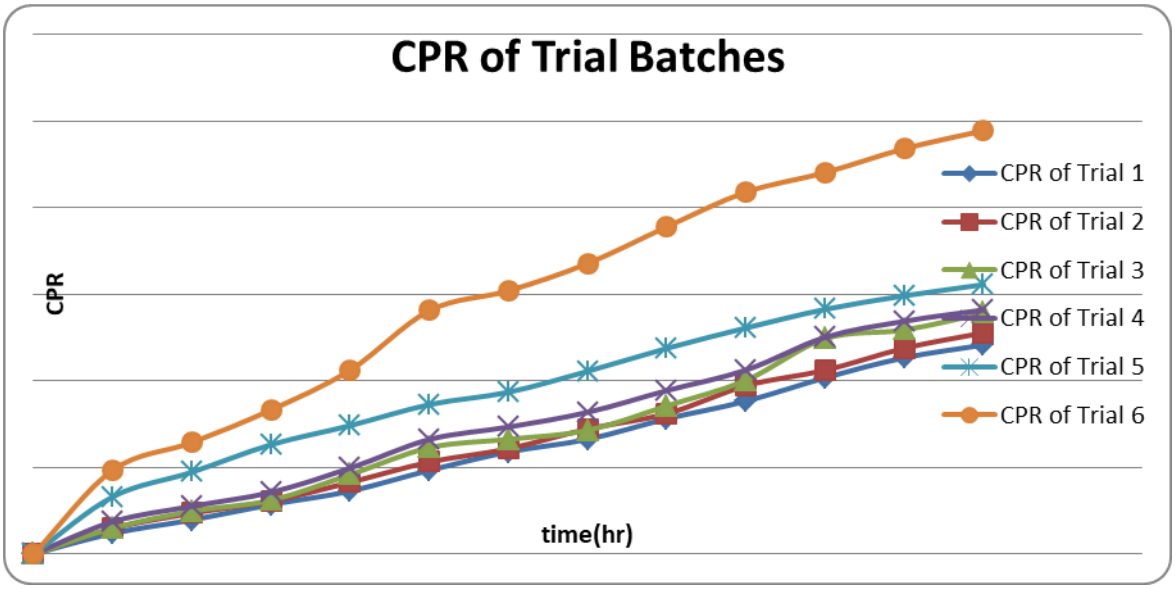

FIG. 2: CPR of trial Batches.

Result and Discussions 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 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, 2,3,4,5 shown that drug release were found to be decreased as compared to trial batch 6 containing sodium alginate and HPMC combination. Similarity factor also calculated for batches 1 to 5 were F2 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.

Swelling Studies:

BADDS was weighed individually (recorded as W1) and placed separately in Petri dish containing 5 mL of phosphate buffer (pH 6.8) solution. At regular intervals (1, 2, 3, 4 and 5 hours), the BADDS was removed from the Petri dish and excess surface water was removed

carefully using the filter paper. The swollen BADDS was then reweighed (W2), and swelling index (SI) was calculated using formula as

$$\text{Swelling Index} = \frac{(W2 - W1)}{W1}$$

Table 5: Swelling Index of BADDS Tablets of Batches from F1 TO F9.

Formulation	swelling Index at				
	1 hr.	2 hr.	3 hr.	4 hr.	5hr.
F1	0.94	1.47	1.82	2.023	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		
F8	2.2	2.82	3.20		
F9	2.08	2.80	3.11		

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.

Table 6: CPR Value of Factorial Batches.

Time(hr)	CPR of Factorial batches								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1	25.93	33.13	35.56	19.39	28.46	31.26	27.33	28.64	29.58
2	28.07	35.17	40.46	25.77	35.62	35.41	38.11	37.77	38.73
3	29.51	37.15	43.23	33.31	40.88	40.95	44.46	46.92	48.46
4	31.25	38.24	46.74	42.51	46.20	45.54	53.08	55.38	54.13
5	32.71	40.25	48.92	56.27	53.82	52.03	62.76	63.63	69.25
6	35.68	42.66	51.49	60.85	64.04	54.54	79.37	78.42	80.21
7	40	45.61	53.47	67.17	74.66	59.33	83.47	85.43	85.98

8	44.75	47.75	55.82	75.64	79.27	63.24	86.17	95.76	91.89
9	52.35	50.86	58.54	83.66	85.98	71.58	100.78	101.07	97.67
10	61.91	55.58	61.28	88.17	90.64	77.67			
11	68.3	65.39	62.9	93.69	93.24	82.69			
12	71.21	69.67	66.75	97.85	96.03	90.61			

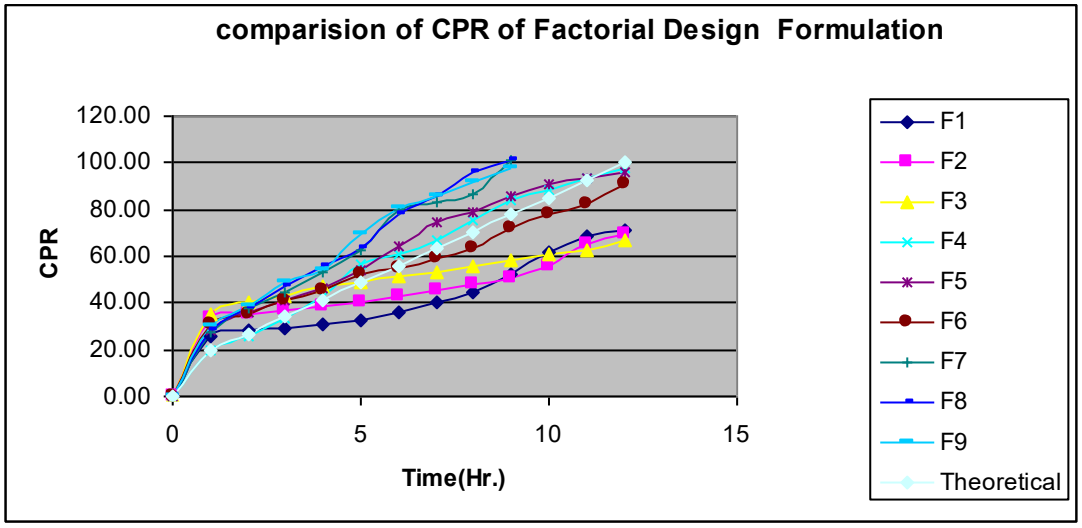

FIG.-3: Comparison of Factorial Batches with Theoretical Profile

The similarity factor (f2) given by SUPAC guidelines 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,

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

Where, n is the number of dissolution time and Rj and Tj are the reference and test dissolution values at time t.

Table 7: Similarity Factor Value of Factorial Batches.

Formulation	F2 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

In Vitro Drug Permeation:

The in vitro buccal drug permeation study of Lercanidipine-HCL through the Chicken mucosa was performed using a modified diffusion cell at 37°C ± 0.2°C. Fresh Chicken mucosa was mounted between the donor and receptor compartments. The tablet was placed with the core facing the mucosa, and the compartments were clamped together. The donor compartment was filled with 1 mL of phosphate buffer pH 6.8 with 2.5 % polysorbate 80. The receptor compartment was filled with phosphate buffer pH 6.8 with 2.5 % polysorbate 80 and the hydrodynamics in the compartment was maintained by stirring with a magnetic bead at uniform slow speed. 5 mL samples were withdrawn at predetermined time intervals and analyzed for drug content by UV spectrophotometer (Table 8).

Table 8: In Vitro Diffusion Study of BADDS of Lercanidipine.

Time(hr)	CPR(Diffusion)
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

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 mm to 1.95 mm and % deviation in thickness was found to be 0.01 to 0.02. Percent drug content was found to be 95- 100%(table 8.6).

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. 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.

CONCLUSION:

This designed BADDS can 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 at the first and then continuously for prolonged period.

In trial batches, tablets were prepared using mucoadhesive polymer HPMC K4M, sodium alginate and carbopol 934P. These polymers were used in combination.

Then all preliminary batches were evaluated for weight variation, thickness and drug content. Release of drug was not in desired manner in batch using combination of polymer HPMC K4M and carbopol 934P. But release of drug was in desired manner using HPMC K4M and sodium alginate in combination.

So, the factorial design of formulation was carried out on polymer ratio of HPMC K4M and sodium alginate.

On the basis of the preliminary trials in the present study, 3^2 full factorial design was employed to study the effect of independent variables, i.e. Concentration of Sodium alginate: HPMC K4M (X1) and type of Filler (X2) on dependent variables like similarity factor.

HPMC K4M exhibited a much greater sustained effect on the release rate compared with sodium alginate. In formulation containing 1:1(Sodium alginate: HPMC K4M), drug was completely release in 12 hrs with desired release rate.

Factorial batch F4 gave the highest f2 value 70.46. Based on the f2 value and targeted release profile, batch F4 was optimized. From kinetic modeling of the dissolution profile of optimized formulation F4, concluded that there was erosion controlled release of drug from the buccal adhesive drug delivery system.

REFERENCES:

1. Chiang, B.N., Perlman, L.V. & Epstein, F.H. (2017) Overweight and hypertension: A review. Circulation, 39, 403–421.
2. Oliveros, E., Patel, H., Kyung, S., Fugar, S., Goldberg, A., Madan, N. & Williams, K.A. (2020) Hypertension in older adults: Assessment, management, and challenges. Clinical

Cardiology, 43, 99–107.

3. Jackson, R.E. & Bellamy, M.C. (2015) Antihypertensive drugs. BJA Education, 15, 280–285.
4. Ram, C.V. (2021) Antihypertensive drugs: An overview. American Journal of Cardiovascular Drugs, 2, 77–89.
5. Cutler, D.M., Long, G., Berndt, E.R., Royer, J., Fournier, A.A., Sasser, A. & Cremieux, P. (2007) The value of antihypertensive drugs: A perspective on medical innovation. Health Affairs, 26, 97–110.
6. Das NG, Das SK. Controlled Release of Oral Dosage forms. Pharm. Tech. 2015;6:10-16.
7. Berressem P. The Birth of New Delivery Systems, Chem. Britain. 2009;35(2):29-32.
8. Shojaei AH. Buccal Mucosa As A Route For Systemic Drug Delivery: A Review Pharm Pharmaceutics Sci 2010;1(1):15-30.
9. Gandhi RE,Robinson JR. Bioadhesion in drug delivery; Ind. J. Pharm. Sci. 2010;50:145-152.
10. Harris D,Robinson JR. Drug delivery via the mucous membranes of the oral cavity, J. Pharm. Sci., 2009; Reproduced with permission of the American Pharmaceutical Association;81:1-10.
11. Stanciu C, Bennett JR.; Alginate/antacid in the reduction of gastrooesophageal reflux. *Lancet* 1974; i: 109–111.
12. Boisson-Vidal C, Haroun F, Ellouali M, *et al*.; Biological activities of polysaccharides from marine algae. *Drugs Future* 1995; 20(Dec): 1247– 1249.
13. Joseph I, Venkataram S. Indomethacin sustained release from alginategelatin or pectin-gelatin coacervates. *Int J Pharm* 1995; 125: 161–168.
14. Machluf M, Regev O, Peled Y, *et al*.; Characterization of microencapsulated liposome systems for the controlled delivery of liposome-associated macromolecules. *J Control Release* 1997; 43: 35– 45.
15. Murata Y, Sasaki N, Miyamoto E, Kawashima S. Use of floating alginate gel beads for stomach-specific drug delivery. *Eur J Pharm Biopharm* 2000; 50(2): 221–226.
16. Lewis G, Kuczynska J. A Summary of Calcium Channel Blocker Preparations. South West Medicines Information and Training 2004;3:1-12
17. Gasser R, Klein W, Koppel H. Lercanidipine, a new third generation Ca-antagonist in the treatment of hypertension. Journal of Clinical and Basic Cardiology 1999;2(2):69-174
18. Datasheet of Lercanidipine. New Zealand medicine and medical devices safety authority 2010 available at http://www.medsafe.govt.nz/profs/Datasheet/z/Zanidiptab.htm

19. Desai KGH. Preparation and Evaluation of a Novel Buccal Adhesive System.AAPS Pharm Sci Tech 2004;5(3);35:1-9
20. Patel VM, Prajapati BG. Mucoadhesive Bilayer Tablets of Propranolol Hydrochloride. AAPS Pharm Sci Tech 2007;8(3);77:E1-E6