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Development evaluation and characterization of Buccal patches containing Nebivolo using hydrophilic polymers

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Abstract
This study aimed to design and assess buccal patches for Nebivolo release, using mucoadhesive hydrophilic polymers such as sodium alginate and tamarind seed polysaccharide. The patches were constructed with a drug-free backing layer composed of 6% ethyl cellulose. The Nebivolo-loaded buccal patches were fabricated through the solvent evaporation technique, utilizing mucoadhesive hydrophilic polymers. The formulations were evaluated for various parameters, including patch thickness, weight variation, folding endurance, drug content, moisture content, moisture absorption, swelling percentage, surface pH, in vitro residence time, and mucoadhesive performance. Drug permeation studies were performed using a Franz diffusion cell with a goat buccal mucosal membrane in phosphate-buffered saline at pH 6.8. Characterization techniques such as FT-IR and SEM were employed to assess the formulation. Stability testing was carried out following ICH guidelines. The developed buccal patch formulations demonstrated consistent results in terms of average weight, thickness, drug content, moisture content, moisture absorption, swelling index, and surface pH. Among the seven formulations tested, F1exhibited the most favorable mucoadhesive strength (31.36±0.95 g), force of adhesion (0.31±0.04 N), highest swelling index (341±0.83%), and a residence time of over 24 hours. F1also showed the highest drug permeation rate (97.51%) over 24 hours and was stable. FT-IR analysis indicated no significant interaction between the drug and the polymer, and SEM analysis revealed a smooth surface texture of the patch. The formulated Nebivolo buccal patches hold significant potential for improving patient compliance and reducing the frequency of administration, offering a promising approach to controlled drug delivery.

Keywords: Tamarind seed polysaccharide, buccal patches, mucoadhesion, Nebivolo, ex vivo permeation

Introduction
The oral route is the most widely used and accepted method of drug administration globally due to its convenience. However, several challenges arise with this method, including presystemic metabolism, drug degradation in the gastrointestinal tract, and the poor bioavailability of certain drugs. These limitations have led to the exploration of alternative non-invasive routes such as buccal, transdermal, rectal, and inhalation drug delivery systems [1].

Among these alternatives, the buccal route stands out as a preferred option due to its distinct advantages. Drug delivery via the buccal mucosa bypasses the presystemic metabolism, leading to improved bioavailability. This method allows for sustained drug release, rapid onset of action, and the ability to terminate therapy quickly if needed. Additionally, it offers easier drug administration and higher patient acceptance compared to other non-invasive routes [2, 3].

Nebivolo, a β1-selective receptor antagonist, is widely prescribed for managing conditions such as hypertension, myocardial infarction, angina pectoris, and heart failure. Despite its efficacy, Nebivolo has a low water solubility, a daily dose range of 25 to 100 mg, and a relatively short half-life of 6 to 7 hours, with a bioavailability of only 40%.

Given its small dose, significant first-pass metabolism, and low bioavailability, Nebivolo is an ideal candidate for delivery through the buccal route [4-8].

Previous studies have demonstrated the development of oral disintegrating films of Nebivolo, produced using solvent casting techniques, which exhibit effective drug release and fast disintegration times. Similarly, bilayered buccal adhesive tablets of Nebivolo have shown enhanced bioavailability and unidirectional drug release. Floating matrix tablets of Nebivolo have also been developed to extend gastric residence time and regulate the drug release rate using different polymers. The objective of this study was to design and evaluate various mucoadhesive buccal patch formulations of Nebivolo, incorporating mucoadhesive polymers like sodium alginate and tamarind seed polysaccharide (TSP), to provide sustained treatment for hypertension [9-13].

Materials and Methods

Materials

Nebivolo was generously provided by M/S. P. D. I. L, India. Tamarind seed polysaccharide was derived from the seeds of Tamarindus indica. Glycerine was sourced from Raychem Pt. Ltd., India, while ethyl cellulose was obtained from Matrix Laboratories, India. Dibutyl phthalate was procured from Ranbaxy Laboratories, India. All other reagents used in the study were of analytical grade.

Methods

Extraction of Tamarind Seed Polysaccharide

To begin the extraction, the outer shell of the tamarind seeds was removed by soaking them in hot water. Afterward, the seeds were gently crushed to form a fine powder. A portion (20 g) of the powdered seeds was mixed with 200 mL of double-distilled water for 24 hours to create a slurry. This slurry was then poured into 800 mL of distilled water and heated for 20 minutes in a water bath to produce a clear solution. The solution was left overnight at room temperature. The resulting transparent liquid was centrifuged for 20 minutes at 6000 rpm to eliminate any remaining particulate matter. The supernatant was collected and mixed with twice its volume of 95% ethanol while stirring continuously. The precipitate obtained was dried in a hot air oven at 40°C for 12 hours. The dried tamarind seed polysaccharide was then ground into a fine powder and stored in a desiccator until further use [14-17].

Preparation of Backing Membrane

In this study, the backing membrane was prepared by dissolving 6% ethylcellulose in a mixture of acetone and isopropyl alcohol (65:35 ratio). To act as a plasticizer, dibutyl phthalate (10%) was added to the solution. This mixture was poured into a 38 cm² petri dish and left to dry at room temperature for 12 hours [18-20].

Preparation of Buccal Patches

A range of buccal patches were formulated by combining mucoadhesive polymeric layers of sodium alginate and tamarind seed polysaccharide (TSP) with 25 mg/cm² of Nebivolo and 10% glycerine (w/w) as a plasticizer. The process began by dissolving Nebivolo, sodium alginate, and tamarind seed polysaccharide in a suitable solvent, with the help of a magnetic stirrer. The mixture was further homogenized using a homogenizer for 15 minutes. Glycerine, representing 10% of the dry weight of the polymers, was added to the formulation as a plasticizer. To remove any air bubbles from the solution, it was sonicated for 30 minutes. The prepared solution was then poured into a 38 cm² petri dish containing the previously prepared backing membrane. The patches were allowed to dry at 50°C for 24 hours. After drying, the buccal patches were carefully removed from the petri dish and stored in a desiccator for later use [21-25].

Table 1 illustrates the composition of the various -loaded buccal patch formulations used in the study

Table 1: Formulation design of buccal patches

Formulation	Sodium alginate (mg)	Tamarind seed polysaccharide (mg)	Drug (mg/cm2)	Glycerin (%)	Double distilled water (ml)
F1	700	100	25	10	30
F2	600	200	25	10	30
F3	500	300	25	10	30
F4	400	400	25	10	30
F5	300	500	25	10	30
F6	200	600	25	10	30
F7	100	700	25	10	30

Compatibility study of drug with various polymers

To evaluate potential interactions between the drug and the excipients used in the study, and to authenticate the identity of the drug, compatibility tests were conducted using an FT-IR spectrophotometer. The FT-IR spectra of the pure drug and the physical mixtures of the drug with various polymers were obtained by mixing the samples with potassium bromide (KBr) and scanning the spectra in the range of 500 to 3500 cm-1 [26].

Determination of Average Weight

The average weight of the buccal patch formulations was determined by weighing three individual patches using a digital balance.

Thickness Measurement

The thickness of the patches was measured by a thickness gauge. Three randomly chosen patches from each formulation were tested at six different points to ensure accuracy.

Folding Endurance Test

The folding endurance of the buccal patches was manually tested by folding each patch at the same location until it either broke or withstood up to 300 folds without cracking. The number of times the patch could be folded at the same spot without breaking determined its folding endurance.

Drug Content Determination
To measure the drug content, a 1 cm² patch was dissolved in 100 ml of saline phosphate buffer solution and stirred for 24 hours at room temperature. After filtration using Whatman filter paper (No. 42), the solution was analysed via UV-VIS spectrophotometry at 274 nm. A calibration curve for drug concentrations ranging from 1 to 5 µg/ml was used for analysis, with the regression equation of Y=0.048X + 0.002 and $R^2 = 0.9990$ [27].

Surface pH Measurement
The surface pH of the buccal patch formulations was measured to assess the potential for irritation in the buccal cavity. A 1 cm² patch was placed in 1 ml of distilled water and allowed to swell for two hours at room temperature. The pH was measured using a pH meter with a surface electrode, and the procedure was repeated three times for consistency.

Moisture Content Evaluation
The moisture content of the patches was determined by placing accurately weighed patches in a desiccator containing anhydrous calcium chloride for three days. After this period, the patches were removed, reweighed, and the percentage moisture content was calculated [28].

Moisture Absorption Study
The moisture absorption of the patches was evaluated by storing three 1 cm² patches of each formulation in a desiccator containing a saturated aluminium chloride solution, maintaining a relative humidity of 76%. After three days, the patches were removed, reweighed, and the percentage moisture absorption was calculated.

Bio adhesive strength measurement
The mucoadhesive strength was determined by measuring the weight required to detach the patch from goat buccal mucosa. The procedure involved a physical balance with one side 5 grams heavier than the other. The patch was hydrated with phosphate buffer saline (pH 6.8), applied to the mucosa, and a weight was gradually added to the balance until the patch separated from the mucosal surface. The required weight for detachment was recorded as the mucoadhesive strength [29-31].

***In vitro* residence time evaluation**
The in vitro residence time of the buccal patches was tested using the USP disintegration apparatus. A piece of goat buccal mucosa was mounted on a glass slab, and the patch was moistened with phosphate buffer saline before being placed in contact with the mucosal surface. The apparatus was operated to simulate the buccal cavity's conditions. The time taken for complete detachment or erosion of the patch was recorded as the in vitro residence time [32].

Swelling Index Study
The swelling index was determined by measuring the increase in the patch's weight due to swelling. Patches of 1x1 cm were weighed and placed in a 50 ml phosphate buffer saline solution (pH 6.8). At hourly intervals for up to 6 hours, the swollen patches were withdrawn, excess water was removed, and the swelling index was calculated [33].

Ex *vivo* drug permeation study
Ex vivo drug permeation was conducted using a Franz diffusion cell with a 40 ml receptor compartment and an effective diffusion area of 1.74 cm². The receptor medium was filled with saline phosphate buffer (pH 6.8) maintained at 37±0.5°C. The buccal mucosa was mounted between the donor and receptor compartments, and the patch was placed in contact with the mucosa. The receptor medium was stirred at 50 rpm, and at regular intervals, 5 ml of the solution was withdrawn and analysed by UV-VIS spectrophotometry at 274 nm.

Stability Studies
Stability testing was carried out in compliance with ICH guidelines to assess the effects of environmental factors such as temperature, humidity, and light. The drug formulation was stored in nitrogen-flushed borosilicate glass bottles in a stability chamber at 40°C and 75% relative humidity for six months. The formulation was analysed periodically for drug content and ex vivo drug permeation [34].

Scanning Electron Microscopy (SEM) Study
SEM was used to analyse the surface texture and morphology of the buccal patch formulations. This technique provided three-dimensional images of the surface relief and helped to evaluate the microstructure of the formulation containing the drug and polymer [35].

Results and Discussion
The objective of this study was to design, evaluate, and characterize buccal patches containing an antihypertensive drug. These patches incorporated the drug within a mucoadhesive polymeric layer made of sodium alginate and tamarind seed polysaccharide, while a drug-free backing layer was composed of 6% ethyl cellulose. The solvent evaporation method was used for formulation preparation.

Average Weight
The average weight of the different buccal patch formulations, each measuring 38 cm², ranged from 1.67±0.06 g for formulation F7 to 1.79±0.04 g for formulation F5 (Table 2).

Thickness: The thickness of the buccal patches was assessed using a thickness gauge. For formulations F1 through F7, the thickness varied between 0.54±0.03 mm (F1) and 0.63±0.05 mm (F5), (Table 2).

Folding Endurance
Folding endurance was determined manually by folding the patches at the same location until they either broke or showed significant deformation. The folding endurance was highest for formulation F1, with a value of 186±2, and lowest for formulation F4, with a value of 159±2 (Table 2). This test highlights the flexibility of the prepared buccal patches.

Drug Content
The uniformity of drug content across the different buccal patch formulations (F1 to F7) was measured by dissolving 1 cm² of each patch. The drug content was found to range from 99.06±0.09% in formulation F6 to 99.62±0.08% in formulation F1 (Table 2), indicating a consistent drug distribution throughout the formulations.

Table 2: Physico-chemical parameters of buccal patches

Formulation	Weight variation (g) n=3	Thickness (mm) n=3	Drug content (%) n=3	Folding endurance n=3	Surface pH n=3
F1	1.68±0.03	0.54±0.03	99.62±0.08	186±2	6.59±0.02
F2	1.71±0.02	0.58±0.02	99.36±0.11	175±3	6.66±0.01
F3	1.76±0.05	0.61±0.05	99.45±0.06	182±1	6.69±0.02
F4	1.74±0.08	0.59±0.06	99.48±0.09	159±2	6.55±0.03
F5	1.79±0.04	0.63±0.05	99.26±0.12	167±2	6.79±0.02
F6	1.70±0.05	0.57±0.06	99.06±0.09	169±3	6.63±0.01
F7	1.67±0.06	0.56±0.04	99.11±0.12	181±1	6.61±0.01

Data represent mean±SD

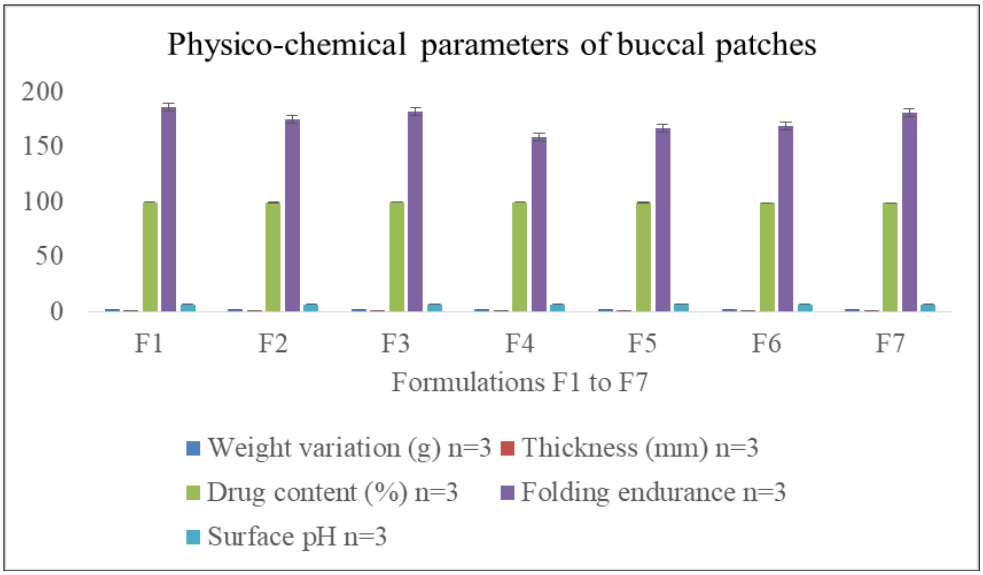


Fig 1: Physico-chemical parameters of buccal patches

Surface pH

The surface pH of the prepared buccal patches plays a crucial role in enhancing drug permeation and ensuring good mucoadhesion. An excessively acidic or alkaline pH may lead to irritation of the buccal mucosa. In this study, efforts were made to maintain the surface pH of the patches as close to the natural pH of the buccal cavity as possible by selecting suitable polymers for formulation. The surface pH of the buccal patch formulations, F1 to F7, ranged from 6.55±0.03 (F4) to 6.79±0.02 (F5), which is within the range favorable for buccal pH. This suggests that the patches are unlikely to cause irritation to the buccal mucosal tissue, as the pH of the patches is consistent with the normal buccal pH, making them suitable for safe senate Moisture Content and Absorption: ** The moisture content and absorption of the buccal patch formulations were evaluated to assess their physical stability under varying humidity conditions and their integrity when dry. The percentage moisture content for formulations F1 to F7 ranged from 1.31±0.02% for F1 to 1.92±0.04% for F5. The moisture absorption values varied from 5.35±0.04% for F1 to 6.89±0.06% for F5. These results suggest that the moisture absorption increases as the hydrophilic nature of the polymers used in the patches increases. The moisture content helps to prevent brittleness and reduces the risk of microbial contamination, ensuring the stability of the patches. Each experiment was conducted in triplicate, and the average values were recorded.

Swel Study

Swelling is an essential characteristic for mucoadhesive polymers, as it determines the extent to which the polymer can absorb water and form a gel-like structure. The swelling index of the buccal patch formulations was assessed to understand the water absorption rate and its impact on mucoadhesive strength. The swelling of patches varied across formulations, with F1 showing the highest swelling index of 341±0.83%, and F5 showing the lowest at 292±1.54%. The order of swelling index was F1 > F2 > F3 > F7 > F6 > F4 > F5, indicating that the polymer composition significantly influences the swelling properties of the patches.

***In vitro* Residence**

The in vitro residence time of the buccal patches was evaluated, with formulations F1 and F2 demonstrating the longest residence times of over 24 hours. The shortest residence time, 18.28±1.1 hours, was observed with formulation F5. This test indicates that the prepared buccal patches have a strong association with the buccal mucosa, providing prolonged retention time, which is beneficial for sustained drug release.

Ex *vivo*

Mucoadhesion Study vivo mucoadhesion study revealed that formulation F1 exhibited the highest mucoadhesive strength of 31.36±0.95 g, while formulation F5 showed the lowest mucoadhesive strength of 19.45±0.82 g. The force of adhesion was also recorded, with the highest being 0.31±0.04 N for formulation F1 and the lowest 0.19±0.04 N for formulation F5. The results indicate a strong mucoadhesive bond between the polymers in the patches and the buccal mucosal tissue, which is essential for the

efficient delivery and retention of the drug on the mucosal surface.

Table 3: Moisture content (%), Moisture uptake (%), swelling index study of different buccal patches

Formulation	Moisture content (%) n=3	Moisture uptake (%) (76%RH) n=3	Swelling Index (%) 6h n=3
F1	1.31±0.02	5.35±0.04	341±0.83
F2	1.48±0.02	5.89±0.03	338±0.63
F3	1.59±0.05	6.38±0.02	319±1.12
F4	1.71±0.06	6.55±0.05	305±0.39
F5	1.92±0.04	6.89±0.06	292±1.54
F6	1.88±0.02	6.81±0.08	308±1.19
F7	1.78±0.02	6.22±0.02	313±0.39

Data represent mean±SD

Table 4: *In vitro* residence time, *ex vivo* mucoadhesion study of different buccal patches

Formulation	*In vitro* residence time (h) n=3	Mucoadhesive strength (g) n=3	Force of adhesion (N) n=3
F1	24±1.4	31.36±0.95	0.31±0.04
F2	24±1	29.42±0.39	0.29±0.05
F3	23.16±1.2	25.59±0.85	0.25±0.02
F4	21.33±1	22.33±0.63	0.22±0.03
F5	18.28±1.1	19.45±0.82	0.19±0.04
F6	20.15±1.13	23.19±0.91	0.23±0.02
F7	20.55±1.1	24.86±0.58	0.24±0.03

Data represent mean±SD

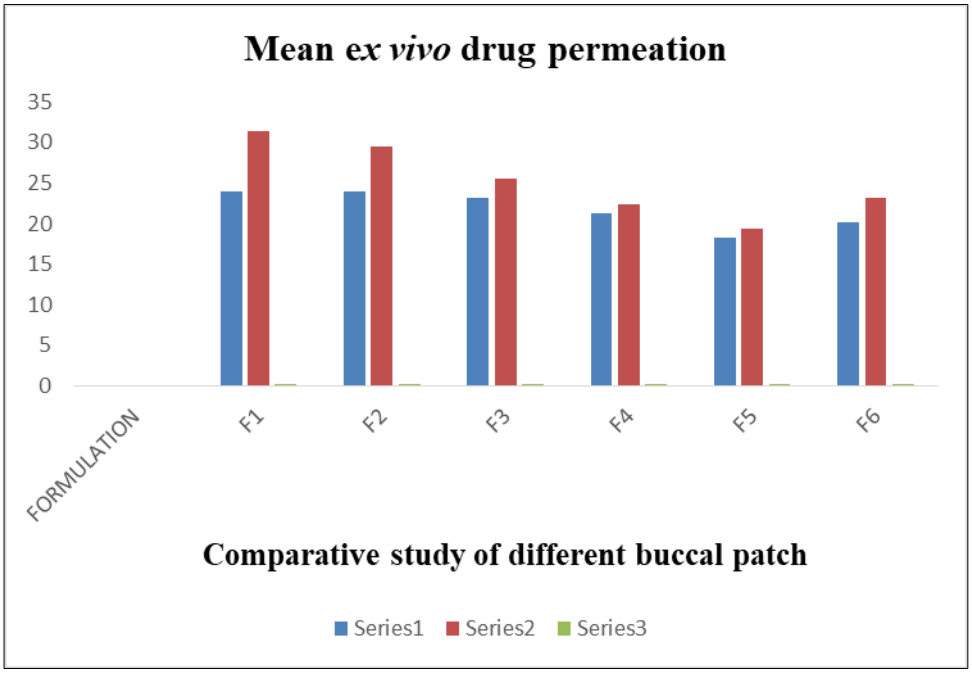


Fig 2: Mean ex *vivo* drug permeation comparative study of different buccal patch

Ex vivo drug permeation study

Table 5: *Ex vivo* drug permeation study of different buccal patch formulations

Time (h)	F1% CDP	F2 % CDP	F3 % CDP	F4 % CDP	F5 % CDP	F6 % CDP	F7 % CDP
0	0	0	0	0	0	0	0
0.5	5.12±0.05	5.98±0.11	4.39±0.08	3.65±0.11	3.25±0.16	3.71±0.03	4.19±0.12
1	10.35±0.89	11.26±0.52	11.91±0.25	12.35±0.15	13.65±0.33	12.88±0.09	7.06±0.28
2	17.68±0.58	18.19±0.26	20.15±0.33	21.44±0.58	23.12±0.21	22.36±0.12	11.35±0.43
3	23.34±0.25	25.08±0.49	26.32±0.51	29.98±0.64	30.59±0.19	29.68±0.19	17.29±0.68
4	29.66±0.63	30.98±0.18	31.85±0.69	34.83±0.31	36.38±0.65	37.24±0.25	21.25±0.85
5	36.15±0.19	37.11±0.57	38.31±0.34	38.56±0.49	40.24±0.58	42.18±0.75	29.31±0.59
6	41.09±0.38	43.36±0.08	42.44±0.29	41.95±0.92	44.12±0.61	45.49±0.68	35.62±0.79
8	48.84±1.02	48.96±0.14	49.35±0.72	47.38±0.38	50.09±0.86	53.76±0.83	44.16±0.84
12	64.61±0.85	61.36±0.9	59.99±0.48	59.36±0.26	58.46±0.88	62.14±0.95	61.38±0.98
24	97.51±1.15	95.18±0.94	92.96±1.01	91.43±1.04	88.89±1.12	90.06±1.08	90.48±1.21

% CDP-% Cumulative Drug Permeated, Data represent mean±SD, N=3

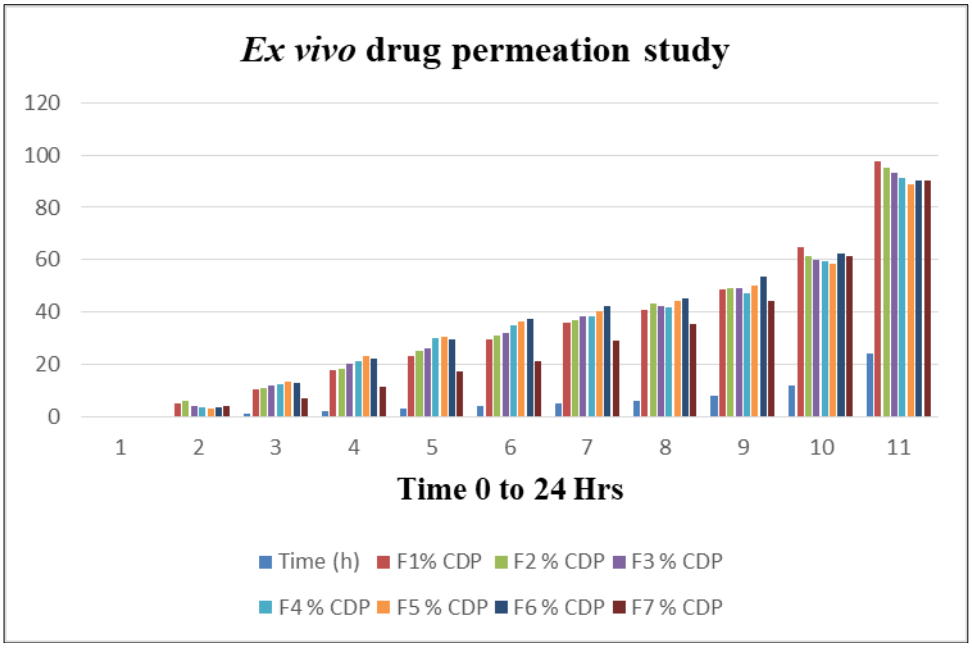
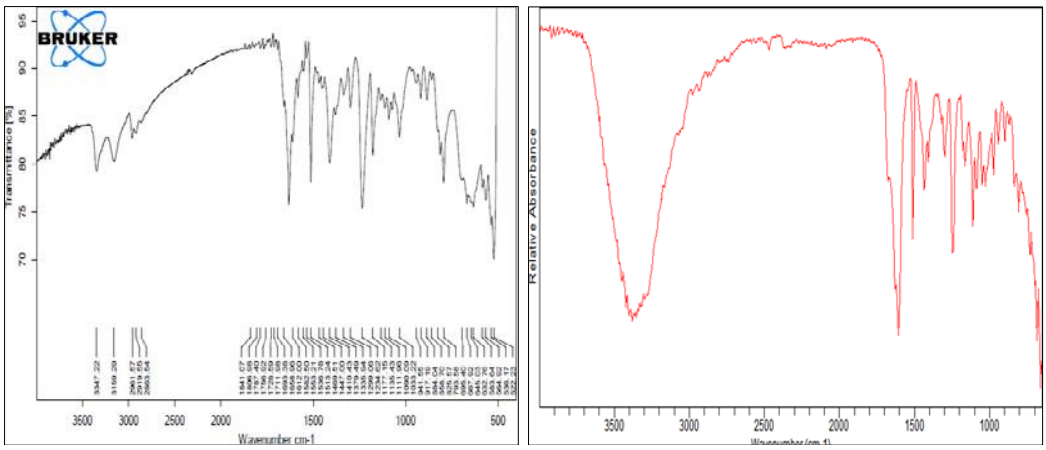


Fig 3: Ex vivo drug permeation Formulations (F1to F7)

The ex vivo permeation study of the drug from various buccal patch formulations through goat buccal mucosa is presented. Among all the formulations (F1 to F7), formulation F1 demonstrated the highest ex vivo permeation, with 97.51±1.15% of the drug permeating through the goat buccal mucosa over 24 hours. In contrast, formulation F5 showed the lowest permeability at 88.89±1.12%, as shown in Table 4 and Figure 2. The drug permeation profile for the formulations followed the order: F1 > F2 > F3 > F4 > F7 > F6 > F5. The study indicated a gradual and consistent drug release from the buccal patches over time. Notably, formulations with higher swelling characteristics exhibited improved drug permeation. The ex vivo permeation results suggest that the drug was effectively absorbed through the goat buccal mucosa within 24 hours, indicating the potential for similar permeation through human buccal membranes.

Drug-polymer compatibility study



Pure drug Formulation F1

Fig 4: FT-IR spectra of pure drug and containing buccal patch formulation, F1

The FT-IR spectra of the drug and the buccal patch formulation F1 are depicted in Figure 2. The FT-IR spectrum of the pure drug showed distinct peaks: a broad O-H stretching vibration at 3347.22 cm-1, a C-H stretching vibration at 2961.57 cm-1, an N-H stretching band at 3159.29 cm-1, a C=C stretch at 1513.24 cm-1, a C=O stretch at 1693.38 cm-1, and an aromatic C-H stretch at 825.57 cm-1. The FT-IR analysis of the drug-excipient mixture revealed that all the characteristic peaks of the pure drug were preserved in the spectrum of the buccal patch formulation F1, indicating no significant interaction or chemical incompatibility between the drug and the excipients such as sodium alginate and tamarind seed polysaccharide used in the formulation.

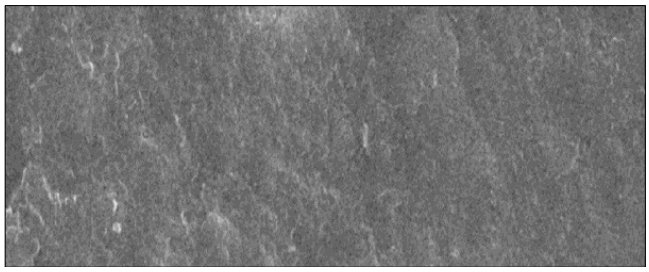
Stability studies

Table 6: Stability study of buccal patch formulation F1for six months

Time	Drug content (%)(n=3)	Cumulative % drug permeation (n=3)
Initial	99.62±0.06	97.51±1.3
1 Mo	99.14±0.08	96.14±0.8
3 Mo	98.39±0.09	95.98±1.2
6 Mo	97.81±0.12	95.06±1.2

Data represent mean±SD

Out of the seven different buccal patch formulations, formulation F1, consisting of 25 mg/cm² of the drug, 700 mg of sodium alginate, 100 mg of tamarind seed polysaccharide, and 10% w/w glycerine, was identified as the most optimal formulation. It exhibited the highest drug content, superior drug release profile (ex vivo), the largest swelling index, longest in vitro residence time, and the strongest mucoadhesive properties. This formulation was selected for stability testing. To assess its stability, F1 was placed in borosilicate glass containers, purged with nitrogen, and stored in a stability chamber at 40 °C and 75% relative humidity for six months. Samples from the stored formulation were analyzed at predetermined intervals for drug content and ex vivo permeation through goat buccal mucosa. The stability test results showed no significant variation in drug content or ex vivo permeation, confirming the stability of formulation F1 over the testing period.



Surface morphology study

Fig 5: SEM study of buccal patch formulation, F1

The SEM images of the buccal patch formulation F1, which consists of 25 mg/cm² of the drug, 700 mg of sodium alginate, 100 mg of tamarind seed polysaccharide, and 10% w/w glycerin, displayed a smooth and uniform surface. The mucoadhesive polymers, sodium alginate and tamarind seed polysaccharide, were well-laminated onto the ethyl cellulose backing membrane. This observation suggests that the drug was evenly distributed within the polymeric matrix of the buccal patches and demonstrates strong adhesion between the drug-containing mucoadhesive layer and the backing membrane, ensuring a solid bond and stability.

Conclusion

This study aimed to develop a novel antihypertensive buccal patch formulation for effective drug delivery. Based on various evaluation parameters, formulation F1 emerged as the most optimal among the seven tested formulations. It was found that F1 did not show any interactions with the selected polymers and remained stable under the storage conditions recommended by ICH guidelines. The findings of this research suggest that the use of mucoadhesive hydrophilic polymers in bilaminated buccal patches is a viable approach. These patches are not only safe and stable but also capable of sustaining drug release through the buccal mucosa, making them a promising solution for the treatment and prevention of hypertension.

Conflict of Interests: Nil

References

1. Khairnar G, Naik J, Mokale V. A statistical study on the development of micro particulate sustained drug delivery system for Losartan potassium by 3² factorial design approach. Bull Fac Pharm Cairo Univ. 2017;55:19-29.
2. Khan R, Arora R, Ojha A, Chopra H, Upadhayaya K. Formulation and evaluation of floating microspheres of levofloxacin. Int Res J Pharm. 2018;9(7):186-91.
3. Nath B, Nath KL, Kumar P. Preparation and in vitro dissolution profile of Zidovudine loaded microspheres made of Eudragit RS 100, RL 100 and their combinations. Acta Pol Pharm Drug Res. 2011;68(3):409-415.
4. Gopaiah KV, Kumar JN, Teja MR, Lokesh T, Sruthi DS, Roja M, *et al*. Development and assessment of hydroxypropyl methylcellulose-based floating tablets for ciprofloxacin HCl using direct compression technique. J Pharm Res Int. 2024 Mar 26;36(3):47-62.
5. Gopaiah KV, Gowtham M, Pracheta K. Development and assessment of rapid-dissolving enalapril malate tablets utilizing co-processed super disintegrates. Int J Innov Sci Res Rev. 2024 Oct 10;6(10):7181-7185.
6. Pandey N, Negi AS, Mahara K. Formulation and evaluation of floating microspheres of nateglinide. Int J Pharma Sci Res. 2016;7(11):453-464.
7. Devi AN, Vijendar C, Goud AK, Kumar AD, Khaja M, Anil A. Preparation and evaluation of floating microspheres of cefdinir in treatment of otitis media and respiratory tract infections. J Pharmaco. 2016;4(3):1-4.
8. Gopaiah KV, Medarametala RT, Kumar JNS, Niharika K, Sai NV, Pavani V, *et al*. Innovations and techniques in oral controlled release systems: A comprehensive review of tablet characterization methods. J Curr Pharm Res. 2024 Sep 9;20(9):16-24.
9. Gopaiah KV, Gowtham M, Pracheta K, Medarametla RT. Synergistic elegance: Harnessing liposomes as advanced cosmetic drug delivery systems with phospholipids and phenolic components. Pharm Sci Anal Res J. 2024 Aug 24;6(3):1-8.
10. Purohit K, Garud N. Formulation and evaluation of floating microspheres of losartan potassium using sodium alginate and HPMC by solvent evaporation method. J Drug Deliv Ther. 2019;9(1-s):60-6.
11. Patil P, Singh S, Sarvanan J. Preparation and evaluation of microspheres of flurbiprofen. Int J Pharm Sci Res. 2018;9(12):5388-5393.
12. Khairnar G, Naik J, Mokale V. A statistical study on the development of micro particulate sustained drug delivery system for Losartan potassium by 3² factorial design approach. Bull Fac Pharm Cairo Univ. 2017;55:19-29.
13. Khan R, Arora R, Ojha A, Chopra H, Upadhayaya K. Formulation and evaluation of floating microspheres of levofloxacin. Int Res J Pharm. 2018;9(7):186-91.
14. Nath B, Nath KL, Kumar P. Preparation and in vitro dissolution profile of Zidovudine loaded microspheres made of Eudragit RS 100, RL 100 and their combinations. Acta Pol Pharm Drug Res. 2011;68(3):409-15.
15. Gopaiah KV, Kumar JN, Teja MR, Lokesh T, Sruthi DS, Roja M, *et al*. Development and assessment of hydroxypropyl methylcellulose-based floating tablets for ciprofloxacin HCl using direct compression technique. J Pharm Res Int. 2024 Mar 26;36(3):47-62.
16. Gopaiah KV, Gowtham M, Pracheta K. Development and assessment of rapid-dissolving enalapril malate

tablets utilizing co-processed super disintegrates. Int J Innov Sci Res Rev. 2024 Oct 10;6(10):7181-7185.
17. Pandey N, Negi AS, Mahara K. Formulation and evaluation of floating microspheres of nateglinide. Int J Pharma Sci Res. 2016;7(11):453-464.
18. Devi AN, Vijendar C, Goud AK, Kumar AD, Khaja M, Anil A. Preparation and evaluation of floating microspheres of cefdinir in treatment of otitis media and respiratory tract infections. J Pharmaco. 2016;4(3):1-4.
19. Gopaiah KV, Medarametala RT, Kumar JNS, Niharika K, Sai NV, Pavani V, *et al*. Innovations and techniques in oral controlled release systems: A comprehensive review of tablet characterization methods. J Curr Pharm Res. 2024 Sep 9;20(9):16-24.
20. Gopaiah KV, Gowtham M, Pracheta K, Medarametla RT. Synergistic elegance: Harnessing liposomes as advanced cosmetic drug delivery systems with phospholipids and phenolic components. Pharm Sci Anal Res J. 2024 Aug 24;6(3):1-8.
21. Purohit K, Garud N. Formulation and evaluation of floating microspheres of losartan potassium using sodium alginate and HPMC by solvent evaporation method. J Drug Deliv Ther. 2019;9(1-s):60-6.
22. Patil P, Singh S, Sarvanan J. Preparation and evaluation of microspheres of flurbiprofen. Int J Pharm Sci Res. 2018;9(12):5388-93.
23. Gopaiah KV, Medarametala RT, Kumar JS, Sahithi C, Prasanna DE, Sathwik G, *et al*. Comprehensive analysis of nizatidine: Pharmacodynamics and pharmacokinetics in anti-ulcer treatment. World J Adv Res Rev. 2024;23(3):2260-6.
24. Gopaiah VK, *et al*. Solid lipid nanoparticles of naftopidil: Formulation design & in vitro evaluation for improved oral absorption. Pharm Sci Anal Res J. 2024;6(2):180061.
25. Gopaiah KV, Mandadapu G, Kolli P. Impact of metformin on cardiac autonomic function in recently diagnosed type-2 diabetic patients at a specialized medical center. TIJER Int Res J. 2024 May 5;11(5):b331-6.
26. Medarametla RT, Gopaiah KV, Kumar JN, Sai AK, Chari GM, Kiran AK, *et al*. Clinical investigation of valsartan sustained-release matrix tablets: Formulation design and performance evaluation. J Pharm Res Int. 2024 Mar 9;36(2):39-54.
27. Mandadapu G, Kolli P, Gopaiah KV, Medarametla RT, Rajesh G. Formulation of fenofibrate capsules by dropping method using PEG 6000 and PEG 4000 to enhance solubility. World J Biol Pharm Health Sci. 2024;19(1):95-102.
28. Chukka AK, Gopaiah V, Ch S, Chowdary D, Irfan SK. A review of synthesis, biological activity, and docking studies of anti-tubercular agents. J Innov Appl Pharm Sci. 2023 Dec 7:45-50.
29. Bhuvaneswari S, Manivannan S, Akshay M, Nify F. Formulation and evaluation of gastroretentive microballoons of acebrophylline for the treatment of bronchial asthma. Asian J Pharm Clin Res. 2016;9(5):105-11.
30. Ramu S, Suresh P, Rao S, Ramakrishna G. Formulation and evaluation of floating microspheres of rosiglitazone. Int J Pharm Chem Biol Sci. 2015;5(4):907-18.
31. Medarametla R, Gopaiah V, Ch G, Neelima L, Reddy A, Sudheer B. Formulation and evaluation of tenoxicam ethosomes as a novel drug carrier. UPI J Pharm Med Health Sci. 2023 Nov 8:12-8.
32. Medarametla RT, Gopaiah V. A comprehensive study on the review of virosomes as a novel drug delivery system. UPI J Pharm Med Health Sci. 2023 Oct 15:1-6.
33. Gopaiah V, Brahmam G, Harika R, Pujitha V. Formulation and evaluation of Cefuroxime oral suspension for pediatrics. Int J Curr Innov Adv Res. 2023 Apr 27;60-7.
34. Gopaiah KV, Mandadapu G, Kolli. A study on method development for detection of different viral antibodies and virus by using RT-PCR method. World J Pharm Res. 2023 Mar 3;12(4):316-33.
35. Gopaiah KV, Mandadapu G, Kolli, Bhavana T. Diagnosing feline and canine disease by RT-PCR screens. Int J Res Anal Rev. 2023 Feb 8;10(1):590-603.
36. Gopaiah KV, Mandadapu G, Kolli, Patibandal S. A clinical study on chronic obstructive pulmonary disorder. J Emerg Technol Innov Res. 2023 Oct 1;10(1):b393-453.
37. Mandadapu G, Kolli P, Gopaiah KV, Teja R. Formulation and evaluation of Econazole nitrate nanoemulsion for fungal topical use.
38. Mandadapu G, Kolli P, Gopaiah KV, Medarametla RT, Rajesh G. Formulation of fenofibrate capsules by dropping method using PEG 6000 and PEG 4000 to enhance solubility. World J Biol Pharm Health Sci. 2024;19(1):95-102.
39. Shrivastava B. Topical combination delivery of benzoyl peroxide and adapalene niosomal gel for acne treatment. Asian J Pharm. 2019 Nov 7;13(4).
40. Gopaiah MK. Design, formulation, and evaluation of sustained release tablets for antihyperlipidemic agent. Asian J Pharm. 2018 Nov 11;12(4).
41. Mandadapu G, Kolli P, Gopaiah KV, Teja R. Formulation and evaluation of Econazole nitrate nanoemulsion for fungal topical use.
42. Gopaiah KV, Kumar JN, Teja MR, Lokesh T, Sruthi DS, Roja M, Rushitha N, Vahedunnisa SK. Development and assessment of hydroxypropyl methylcellulose-based floating tablets for Ciprofloxacin HCl using direct compression technique. J Pharm Res Int. 2024 Mar 26;36(3):47-62.
43. Mandadapu G, Kolli P, Gopaiah KV, Bhavana T. Diagnosing feline and canine disease by RT-PCR screens [Internet]. 2023.
44. Medarametla RT, Gopaiah KV, Kumar JN, Sai AK, Chari GM, Kiran AK, Naik BK, Rani KS. Clinical investigation of Valsartan sustained-release matrix tablets: formulation design and performance evaluation. J Pharm Res Int. 2024 Mar 9;36(2):39-54.
45. Gopaiah KV, Medarametla RT, Kumar JS, Sahithi C, Prasanna DE, Sathwik G, Sravani G, Murali K. Comprehensive analysis of nizatidine: pharmacodynamics and pharmacokinetics in anti-ulcer treatment. World J Adv Res Rev. 2024;23(3):2260-6.
46. Kamalakkannan V, Kumaran AKSG, Babu CS, Muthukumaran T, Raman SV. Preparation and in-vitro evaluation of diltiazem hydrochloride microspheres by using eudragit RL100, eudragit RS100 as polymers. J Chem Pharm Res. 2015;7(5):1111-20.