Development of bilayered mucoadhesive patches for buccal delivery of felodipine: *in vitro* and *ex vivo* characterization

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**Abstract**

Bilayered buccoadhesive patch for systemic administration of felodipine was developed using hydroxy propyl methyl cellulose as primary layer and Eudragit RLPO as secondary layer. *In vitro* drug permeation studies through porcine buccal membrane and buccal absorption studies in human volunteers were performed. Six formulations were developed by solvent casting technique and evaluated for *in vitro* drug release, moisture absorption, mechanical properties, surface pH, *in vitro* bioadhesion and *in vitro* permeation of felodipine through porcine buccal membrane from bilayered buccal patch. Formulation BB4 showed a drug release of 94.6 % with zero order release profile and permeated 41.6 % of drug with a flux of 0.113 mg h⁻¹cm⁻² through porcine buccal membrane. Formulation BB4 showed 3.42 N and 1.63 mJ peak detachment force and work of adhesion respectively. The physicochemical interactions between felodipine and polymer was investigated by Fourier transform infrared (FTIR) Spectroscopy. According to FTIR the drug did not show any evidence of an interaction with the polymer. A stability study of optimized patch BB4 was done in natural human saliva; it was found that both drug and buccal patches were stable in human saliva. The results indicate that suitable bilayered buccoadhesive patches with desired permeability could be prepared.

**Keywords:** Buccal patches, felodipine, bioadhesion, mechanical properties, buccal delivery

**Introduction**

Buccal delivery of drugs provides an attractive alternate to the oral route of drug administration, particularly in overcoming deficiencies associated with the oral route. Buccal mucosa has an excellent accessibility, an expanse of smooth muscle and relatively immobile mucosa, hence suitable for administration of retentive dosage forms. The direct entry of the drug into the systemic circulation avoids first-pass hepatic metabolism leading to increase in bioavailability (1, 2). Other advantages such as low enzymatic activity, painless administration, easy drug withdrawal, facility to include permeation enhancers/enzyme inhibitors or pH modifiers in the formulation and versatility in designing as multidirectional or unidirectional release systems for local or systemic actions (3). Various mucoadhesive formulations were suggested for buccal delivery that includes buccal patches (4, 5), adhesive tablets (6, 7) and adhesive gels (8). However, buccal films are preferred over adhesive tablets in terms of flexibility and comfort (9).

Felodipine (FDP), a calcium channel blocker belonging to dihydropyridines is used as a potent
peripheral vasodilator, which effectively reduces blood pressure when given at doses of 5–20 mg per day. After a single, 20 mg oral dose of FDP, peak plasma concentrations are achieved within 2.5–5 hours (10). It was reported to be well absorbed following oral administration, but undergoes extensive first pass metabolism; leading to poor bioavailability (11). From both, physicochemical (low molecular weight 384.3 g/mol, low dose 5-20 mg) and pharmacokinetic (absolute bioavailability about 10-25%) views, FDP is considered to be suitable for buccal delivery.

In the present study, matrix based bilayered buccoadhesive patches were developed and evaluated for in vitro drug permeation studies, buccal absorption, in vitro drug release, moisture absorption, mechanical properties, surface pH studies, in vitro bioadhesion and stability in human saliva.

Materials and Methods

Materials

Felodipine was gifted by Sun pharmaceuticals, Baroda, India. Hydroxypropyl methylcellulose E15 and Eudragit RLPO were gifted by Dr Reddys Laboratories Hyderabad, India. Polyester backing membrane was gifted by 3M, St. Paul, MI, USA. Mucin (Crude Type II) was procured from Sigma-Aldrich, Germany and was used without further purification. Phosphate buffer saline, Dulbecco’s and Phenol red were purchased from Hi Media, Mumbai, India. All reagents used were of analytical grade.

Tissue preparation (Isolation)

Porcine buccal tissue from domestic pigs was obtained from local slaughterhouse and used within 2 hours of slaughter. The tissue was stored in Krebs buffer at 4°C after collection. The epithelium was separated from the underlying connective tissue with surgical technique and the delipidized membrane was allowed to equilibrate for approximately one hour in receptor buffer to regain the lost elasticity.

In vitro drug permeation studies

The buccal epithelium was carefully mounted between the two compartments of a Franz diffusion cell with an internal diameter of 2.1 cm (3.46 cm² area) with a receptor compartment volume of 25.0 mL. Phosphate buffer saline (PBS) pH 7.4 containing 40% v/v of polyethylene glycol (PEG 400) and 10% v/v alcohol was placed in the receptor compartment. The donor compartment contained 4 mL solution of PBS pH 7.4 and PEG 400 (1:1) in which 5 mg of FDP was dissolved. The donor compartment also contained phenol red a non absorbable marker compound at a concentration of 20 µg mL⁻¹. The entire set up was placed over magnetic stirrer and temperature was maintained at 37°C. Samples of 1 mL were collected at predetermined time points from receptor compartment and replaced with an equal volume of fresh solution (12, 13).

Buccal absorption studies

Buccal absorption test was performed for FDP solution in 8 healthy male volunteers aged between 24 and 29 years and weighing between 60 to 75 kg. The ethics committee of the University College of Pharmaceutical Sciences, Kakatiya University, India, approved the protocol. This method uses phenol red, a non absorbable marker for determining saliva volumes. Phenol red is lost neither by absorption nor by swallowing (14, 15). Before the test, volunteers were asked to moisten their mouth with 20 mL of buffer solution. PBS pH 6.6 (20 mL) containing 4 mg FDP and phenol red (20 µg mL⁻¹) was given to volunteers and were asked to swirl the solution about 60 swirling min⁻¹. The samples of 1 mL were collected from the floor of the mouth at 2, 4, 6, 8, 10, 12, 14, and 16 min using a micropipette.
While collecting the samples, volunteers were asked to stop swirling momentarily. After the last sample was collected, all the solution was expelled into beaker. Volunteers were asked to rinse their mouth twice with 20 mL of PBS pH 6.6 and the washings were pooled with the original sample. Volume was noted and the quantity of FDP present in the samples was estimated by high performance liquid chromatography (HPLC). Phenol red was estimated colorimetrically by making the solution alkaline with sodium hydroxide.

**Estimation of drug content by HPLC**

Analysis of samples was performed using HPLC. The HPLC system (Shimadzu, Kyoto, Japan) consisting of a LC-10AT solvent module, SPD10A UV–visible detector with LC10 software. The analytical column used was C18 column (Inertsil, 150mm x 4.6mm i.d., particle size 5 µm) at an ambient temperature. The mobile phase used was a mixture of (66:34) of acetonitrile and water. The flow rate was 1 mL min⁻¹ and detection was carried out at 240 nm. A calibration curve was plotted for FDP in the concentration range of 0.5-10 µg mL⁻¹. A good linear relationship was observed between the concentration of FDP and the peak area of FDP with a correlation coefficient \( r^2 = 0.999 \). The required studies were carried out to estimate the precision and accuracy of the HPLC method.

**Preparation of bilayered mucoadhesive buccal patches**

Bilayered mucoadhesive buccal patches were prepared using solvent casting technique with HPMC E15 as primary polymeric layer, Eudragit RLPO as secondary polymeric layer and propylene glycol as plasticizer. Primary polymer was added to 25 mL of solvent mixture (dichloromethane and methanol, 1:1) and allowed to stand for 6 hr to swell. Propylene glycol and FDP were dissolved in 5 mL of solvent mixture and added to the polymeric solution. This was set aside for 2 hr to remove entrapped air, transferred to a Petri plate, and dried at room temperature. The secondary polymeric solution was prepared by dissolving 600 mg of Eudragit RLPO and 120 µL of propylene glycol in 15 mL of solvent mixture and poured on the primary polymer layer and allowed for drying at room temperature. The developed patches were removed carefully, cut to size (each having an area of 1.13 cm²), and stored in a desiccator. The composition of the patches was shown in Table 1. Patches were subjected to weight variation, thickness variation and content uniformity. Patches with any imperfections, entrapped air, differences in weight were excluded from further studies.

<table>
<thead>
<tr>
<th>Component</th>
<th>BB1</th>
<th>BB2</th>
<th>BB3</th>
<th>BB4</th>
<th>BB5</th>
<th>BB6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Felodipine (mg)</td>
<td>320</td>
<td>320</td>
<td>320</td>
<td>320</td>
<td>320</td>
<td>320</td>
</tr>
<tr>
<td>HPMC E15 (mg)</td>
<td>1750</td>
<td>2000</td>
<td>2250</td>
<td>2500</td>
<td>2750</td>
<td>3000</td>
</tr>
<tr>
<td>Propylene glycol (µL)</td>
<td>262.5</td>
<td>300</td>
<td>337.5</td>
<td>375</td>
<td>412.5</td>
<td>450</td>
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<tr>
<td>Eudragit RLPO (mg)</td>
<td>600</td>
<td>600</td>
<td>600</td>
<td>600</td>
<td>600</td>
<td>600</td>
</tr>
<tr>
<td>Propylene glycol (µL)</td>
<td>120</td>
<td>120</td>
<td>120</td>
<td>120</td>
<td>120</td>
<td>120</td>
</tr>
</tbody>
</table>

Mucoadhesive patches for buccal delivery of felodipine
In vitro release studies

The drug release from buccal patches was studied using USP type II dissolution test apparatus (Lab India dissolution test apparatus, Disso 2000, Mumbai, India) equipped with an auto sampler and fraction collector for the collection and replenishment of the sample and dissolution medium, respectively. Patches (1.13 cm$^2$) were meant to release drug from one side only; therefore, an adhesive impermeable polyester backing layer was placed on the other side of patch. The assembly for release studies was prepared by sandwiching the patch between dialysis membrane 50 KD (Hi Media, Mumbai, India). A piece of glass slide was placed as support to prevent the assembly from floating. The dialysis tubing with patch inside was secured from both ends using dialysis closure clips and placed in the dissolution apparatus. The dissolution medium was 500 mL of 0.5 % w/v of sodium lauryl sulphate solution at 25 rpm and temperature was maintained at 37°C. Samples of 5 mL were collected at predetermined time intervals and analyzed spectrophotometrically at 240 nm.

Moisture absorption studies

The moisture absorption studies give an indication about the relative moisture absorption capacities of polymers and an idea whether the formulations maintain their integrity after absorption of moisture. Moisture absorption studies were performed in accordance with the procedure reported earlier (16). Briefly, 5 % w/v agar in distilled water, which in hot condition was transferred to Petri plates and allowed to solidify. Then 6 patches from each formulation were weighed and placed over the surface of the agar and left for 2 hr at 37°C and the patch was weighed again. The percentage of moisture absorbed was calculated using the formula:

\[
\text{% Moisture absorbed} = \left( \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \right) \times 100
\]

Measurement of mechanical properties

Mechanical properties of the patches were evaluated using a microprocessor based advanced force gauze with a motorized test stand (Ultra Test, Mecmesin, West Sussex, UK) and fitted with a 25 kg load cell. Strips from the patch with dimensions of 60 x 10 mm and no visual defects were cut and positioned between two clamps separated by a distance of 3 cm. Clamps were designed to secure the patch without crushing it. During test, lower clamp was held stationary and the strips were pulled apart by the upper clamp moving at a rate of 2.0 mm/sec until the strip broke. The force and elongation of film at the point when the strip broke were recorded. The tensile strength and elongation at break values were calculated using the formula:

\[
\text{Tensile strength (kg.mm}^{-2}\text{)} = \frac{\text{Force at break (kg)}}{\text{Initial cross sectional area of the sample (mm}^2\text{)}}
\]

\[
\text{Elongation at break (\%)mm}^{-2}\text{)} = \frac{\text{Increase in length (mm)} \times 100}{\text{Original length} \times \text{Cross-sectional area (mm}^2\text{)}}
\]

Surface pH study

The method adopted by Bottenberg et al. (17) was used to determine the surface pH of the patches. A combined glass electrode was used for this purpose. The patches were allowed to swell by keeping them in contact with 1 mL of distilled water (pH 6.5 ± 0.1) for 2 h at room temperature, and pH was noted down by bringing the electrode in contact with the surface of the patch, allowing it to equilibrate for 1 minute.

In vitro bioadhesion measurement

The adhesive binding of the patches containing FDP to porcine buccal mucosa was studied in triplicate with the same equipment as the one used for measurement of mechanical properties except that a load cell of 5 kg was used for this study. In this test, porcine buccal
membrane was secured tightly to a circular stainless steel adaptor and the buccal patch to be tested was adhered to another cylindrical stainless steel adaptor similar in diameter using a cyanoacrylate adhesive. During test, 100 µL of 1% w/v mucin solution was spread over the surface of the buccal mucosa and the patch was immediately brought into contact. A force of 0.5 N was applied for 180 sec to enhance the contact of the patch with the mucosa. At the end of the contact time, upper support was withdrawn at a speed of 0.5 mm sec⁻¹ until the patch was completely detached from the mucosa (18). The work of adhesion was determined from the area under force-distance curve while the peak detachment force was the maximum force required to detach the patch from the mucosa.

**In vitro permeation of felodipine through porcine buccal membrane from bilayered buccal patch**

*In vitro* permeation of FDP from bilayered buccal patches for the selected formulation (BB4) through porcine buccal membrane was studied. Buccal membrane was isolated as described in tissue preparation section. The membrane was mounted over a Franz diffusion cell whose internal diameter is 2.1 cm. The buccal patch was sandwiched between the buccal mucosa and the dialysis membrane, so as to secure the patch tightly from getting dislodged from the buccal membrane. The entire set up was placed over magnetic stirrer and temperature was maintained at 37°C. Samples of 1 mL were collected at predetermined time points from receptor compartment and replaced with an equal volume of fresh solution.

**Stability in human saliva**

The stability of optimized patches was performed in natural human saliva which was collected from humans aged between 18 to 35 years and filtered. Patches were placed in separate Petri plates containing 5 mL of human saliva and kept at a temperature controlled oven (Sheldon Manufacturing Inc., Cornelius, USA) at 37 ± 0.2°C for 6 h. At regular time intervals (0, 0.5, 1, 2, 4 and 6 h), the patches were examined for changes in color and shape, collapse of the patch and drug content. Drug content was determined by appropriate dilution of human saliva in phosphate buffer pH 6.8 and analyzed by spectrophotometry at 240 nm (19).

**FTIR studies**

The FDP, HPMC E 15 and physical mixture of FDP were prepared. The samples were prepared by grounding the pure drug, polymer and physical mixture with KBr separately. The IR spectra for the samples were obtained using KBr disk method using an FTIR spectrophotometer (PERKIN ELMER FT-I Insf. USA).

**Results and Discussion**

**Drug penetration studies through porcine buccal membrane**

Porcine buccal mucosa has been the most frequently chosen model for *in vitro* permeation studies because of its similarity to human tissue and is available in large quantities from slaughterhouses. Cumulative percentage amount permeated in 6 h was found to be 65.2 ± 2.48 % and the flux was calculated to be 0.153 mg h⁻¹ cm⁻². The penetration of drug through the porcine buccal epithelium was found to be rapid up to first 3 hours followed by a slow penetration in the next 3 hours (Fig.1). The tissue could be isolated successfully because no detectable levels of phenol red (marker compound) was found in the receiver compartment, where as FDP could penetrate freely.

**Buccal absorption study**

Buccal absorption study was conducted to substantiate the results from the *in vitro* permeation studies. In addition, it gives...
information regarding the irritant nature of the drug to oral mucosa. The results of buccal absorption study are shown in Fig. 2. It was observed that about 56.24% of the drug was absorbed through the buccal membrane in 16 min. The drug was absorbed at a rapid rate for the first 2 min, after which the drug absorption continued at a uniform rate. The total amount of phenol red present in 8 collected samples was found to be the same when compared to the initial collected samples of phenol red (400 µg) in solution. This indicated that the volunteers did not swallow the solution. The total amount of saliva secreted during 16 min of study was found to be averaging 26.42 mL. The volunteers reported numbness in the mouth for about 15 to 20 min after the test. The results of buccal absorption study revealed that FDP could penetrate through the oral cavity.

The drug was diffused from the patches on to the surface. Therefore to overcome the problem, bilayered patches were developed using Eudragit RLPO as secondary layer. The drug diffusion from patches was prevented by the secondary layer composed of Eudragit RLPO. The prepared patches were smooth in appearance, uniform in thickness, mass, and drug content and showed no visible cracks. The mass of patches ranged from 62 ± 2 to 72 ± 2 mg and the thickness ranged from 510.0 ± 7.1 to 580.2 ± 4.3 µm. The drug content in the buccal patches ranged from 96.7 ± 0.5 to 99.6 ± 0.2 %, indicating the favorable drug loading and patches uniformity with respect to drug content.

\textbf{In vitro drug release studies}

The drug release profiles of FDP from buccal patches are shown in Fig. 3. It was clear from the plots, the drug release was governed by polymer content. No lag time was observed as the patch was directly exposed to the dissolution medium. An increase in the polymer content was associated with decrease in drug release rates. The description of drug release profiles by a model

\begin{figure}[h]
\centering
\includegraphics[width=0.8\textwidth]{fig2.png}
\caption{Buccal absorption of FDP in healthy human volunteers, the values represented mean ± S.D (n=8)
}\end{figure}
function has been attempted using zero order and first order; release pattern using Korsmeyer et al (20)

\[ \frac{M_t}{M_{\text{a}}} = K \cdot t^n \]

Where \( \frac{M_t}{M_{\text{a}}} \) is the fractional release of drug, \( M_t \) is the amount released at time \( t \), \( M_{\text{a}} \) is the total amount of drug contained in the patches, \( t \) is the release time, \( K \) is the kinetic constant and \( n \) is the release exponent indicative of the operating release mechanism.

Formulation BB1 showed maximum drug release among the formulations. The drug release ranged from 67.1% (BB6) to 99.8% (BB1). However, the difference among the formulations (BB1, BB2, BB3 and BB4) was statistically insignificant. Formulations BB1, BB2 and BB3 \( (r^2 > 0.98) \) followed first order release kinetics, whereas BB4, BB5 and BB6 \( (r^2 > 0.99) \) showed zero order release kinetics as it was evidenced from correlation coefficients. All formulations showed non-fickian release pattern as it was evidenced from release exponent \( (n > 0.51) \) (21). Increasing the amount of the polymer in the patches produced the water-swollen gel-like state that could substantially reduce the penetration of the dissolution medium into the patches and so the drug release was delayed. The Eudragit layer minimizes the diffusion of the drug molecules from the patches. In addition, Eudragit layer could control the release of the drug from the patches. This was evidenced from the release studies of the monolayer patches where the drug release was rapid. Therefore, a rate controlling membrane could be used to control the release. The formulation that showed maximum amount of drug release with zero order release kinetics was selected as the optimized formulation and further was used for the evaluation of in vitro permeation studies across porcine buccal membrane and in vitro bioadhesion studies.
Moisture absorption studies

Moisture absorption studies evaluated the integrity of the formulation upon exposure to moisture. The results of moisture absorption studies, mass, thickness, drug content and surface pH were presented in Table 2. Results showed that there are differences in moisture absorption with BB1 to BB6 the percentage moisture absorbed ranged from about 60.4 to 77.9 % w/w for various formulations. When the patches were placed without backing membrane complete swelling followed by erosion was observed indicating that the drug release mechanism involves swelling of the polymer initially followed by drug release from the swollen matrix by diffusion.

Mechanical properties of films

Ideal buccal film, apart from good bioadhesive strength, should be flexible, elastic, and strong enough to withstand breakage due to stress caused during its residence in the mouth. The tensile strength (TS) and elongation at break (E/B) shows the strength and elasticity of the film. A soft and weak polymer is characterized by a low TS and E/B; a hard and brittle polymer is defined by a moderate TS, and low E/B; a soft and tough polymer is characterized by a moderate TS and a high E/B; whereas a hard and tough polymer is characterized by high TS and E/B (22). An ideal buccal film should have a relatively high TS and E/B (9). The results of the mechanical properties, i.e., TS and E/B, are presented in Table 2. TS and E/B increased with the increase in polymer content. Maximum TS was exhibited by BB6 (12.1 ± 2.5 kg.mm⁻²) which was statistically significant different (p<0.05) compared to BB1 (2.8 ± 0.1 kg.mm⁻²). Formulation BB4 showed 8.45 Kg. mm⁻² and 22.2 % mm⁻² of TS and E/B respectively. Maximum E/B was seen with BB6 (56.4 ± 5.5 % mm⁻²) and the least was observed with BB1 (17.7 ± 3.2 % mm⁻²).

Surface pH studies

The surface pH of the patches was determined in order to investigate the possibility of any side effects, in vivo. Since an acidic or alkaline pH may cause irritation to the buccal mucosa, we attempted to keep the surface pH as close to neutral as possible. The surface pH of all the patches (BB1 to BB6) was near 6 and hence, these patches should not cause any irritation in the buccal cavity.

In vitro bioadhesion studies

In vitro bioadhesion measurements are performed routinely for mucoadhesive dosage forms, and the most commonly used technique for evaluation of buccal patches is the measurement of adhesive strength (23). Work of adhesion, calculated from area under the force distance-curve, is a measure of work that must be done to remove a patch or film from the tissue. Peak detachment force is the maximum applied force at which the patch detaches from tissue. The peak detachment force and work of adhesion for the BB4 patch was calculated as 3.42 ± 0.54 N and 1.63 ± 0.16 mJ respectively. The work of adhesion and peak detachment force values was within the range for suitable bioadhesion as reported for various films (9). In addition, all the formulations were found to have similar values since the basic surface environment of the patch, which is essential for the bioadhesion, remains the same and it is only the thickness that varies. However, differences do exist due to change in the polymer type or composition of the film.

In vitro permeation of FDP through porcine buccal membrane from bilayered buccal patch

Formulation BB4 was selected for the in vitro permeation studies due to its superior drug release properties in terms of percentage drug released, its capacity to retain the structure in
moisture absorption studies, and bioadhesion studies *in vitro*. The results (Fig. 4) indicated that the drug permeation was slow and about 41.6 % of FDP could permeate through the buccal membrane with a flux of 0.113 mg h⁻¹cm⁻² in 6 hours. The results of drug permeation reveal that FDP was released from the formulation and permeated through porcine buccal membrane and hence could possibly permeate through the human buccal membrane.

![Fig. 4](image)

**Fig. 4** *In vitro* permeation of FDP from patch BB4 through porcine buccal mucosa, the values represented mean ± S.D (n=3)

**Stability of patches in human saliva**

Stability studies are usually performed in phosphate buffer solution whose pH pertains to the buccal cavity, but stability studies performed in normal human saliva would be more appropriate to mimic the stability of drug and device in the oral cavity *in vivo*. Therefore, the stability study of optimized patches (BB4) was examined in human saliva and their appearance characteristics, such as color, shape and drug content in natural human saliva were evaluated (Table 3). Thickness and diameter of patches increased to 20.2 and 5.4 % owing to swelling in human saliva in 6 h studies. No color changes were observed. The recovery of the drug from all patches was found to be 97.9 % indicating maximum utilization of the drug incorporated.

**FTIR Studies**

To study any interaction between drug and polymers used in the preparation of patches IR spectroscopic studies were carried out. Figs 5a–c shows IR spectra of the FDP, HPMC E15 and physical mixture (BB4). FDP alone showed principal peaks at 1699.85, 1496.31, 1205.39, and 1098.30 cm⁻¹. HPMC E15 was not showed any characteristic peaks except few broad peaks at 1062.2, 2931.4 and 3471.5 cm⁻¹. The IR spectra of the physical mixture showed the same absorption bands as the pure drug, illustrating absence of interaction between FDP and HPMC E15.

**Table 3.** Stability study of optimized bilayered buccal patch (BB4) in human saliva

<table>
<thead>
<tr>
<th>Sampling time (h)</th>
<th>Thickness (mm)ᵃ</th>
<th>Diameter (mm)ᵇ</th>
<th>Drug recovered (%)ᵇ</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.46 ± 0.05</td>
<td>12.0 ± 0.1</td>
<td>99.6 ± 0.2</td>
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<tr>
<td>0.5</td>
<td>0.48 ± 0.06</td>
<td>12.1 ± 0.1</td>
<td>97.8 ± 0.4</td>
</tr>
<tr>
<td>1</td>
<td>0.53 ± 0.08</td>
<td>12.2 ± 0.1</td>
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</tr>
<tr>
<td>2</td>
<td>0.56 ± 0.05</td>
<td>12.2 ± 0.2</td>
<td>98.4 ± 0.5</td>
</tr>
<tr>
<td>4</td>
<td>0.58 ± 0.06</td>
<td>12.4 ± 0.2</td>
<td>98.8 ± 0.3</td>
</tr>
<tr>
<td>6</td>
<td>0.60 ± 0.03</td>
<td>12.5 ± 0.3</td>
<td>99.3 ± 0.2</td>
</tr>
</tbody>
</table>

ᵃ Mean ± SD, n = 3.
Conclusions

Bilayered buccoadhesive patches for buccal delivery of felodipine could be prepared. Formulation BB4 using the mucoadhesive polymer at a ratio 1:8 showed significant bioadhesive properties with an optimum release profile and could be useful for buccal delivery. Further work is recommended to support its efficacy claims by long term pharmacokinetic and pharmacodynamic studies in human beings.

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