*Journal of Applied Pharmaceutical Research*
*Volume 14 Issue 3, Year of Publication 2026, Page 109 – 121*
*DOI: https://doi.org/10.69857/joapr.v14i3.1887*

Check for updates

**Research Article**

***JOURNAL OF APPLIED PHARMACEUTICAL RESEARCH | JOAPR***
***www.japtronline.com*** ***ISSN: 2348 – 0335***

# *DEVELOPMENT, IN-VITRO AND EX-VIVO EVALUATION OF HPMC E-15/XANTHAN GUM MUCOADHESIVE BUCCAL PATCH OF TELMISARTAN*

Hattaraki Shashank Shivanand, Preethi G. B.*, Shashank K, Subham Roy, Suhasini Rendale

***Article Information***
Received: 8th January 2026
Revised: 21st February 2026
Accepted: 23rd April 2026
Published: 15th May 2026

**Keywords**
*Telmisartan, Mucoadhesive Buccal patch, HPMC E-15, Xanthan gum, Kolliphor RH 40*

***ABSTRACT***

**Background:** Telmisartan, an antihypertensive drug, exhibits poor aqueous solubility and low oral bioavailability due to extensive hepatic first-pass metabolism. Buccal delivery offers a potential alternative route to bypass first-pass metabolism and achieve sustained drug release for better blood pressure control, particularly in nocturnal hypertension. The aim of the work was to formulate and evaluate a Telmisartan mucoadhesive buccal patch for sustained drug delivery. **Methodology:** Telmisartan solid dispersion with Kolliphor RH 40 was prepared by solvent evaporation, and mucoadhesive buccal patches (T1–T9) were formulated by solvent casting and optimized using a $3^2$ full factorial design with Xanthan gum (A) and HPMC E15 (B) at three levels each, followed by evaluation of physicochemical properties, mucoadhesion, swelling, drug release, permeation, and drug–excipient compatibility by FT-IR, DSC, and XRD. **Results & Discussion:** Based on statistical analysis, it was observed that Xanthan gum and HPMC E15 significantly ($p < 0.05$) affected all the responses, and T9 was selected as the optimized formulation with a desirable swelling index of 331% and strong mucoadhesive strength of 28.5 ± 0.5 g. Optimized formulation T9 showed sustained drug release of 94.87%, and *ex vivo* permeation of 1.773 ± 0.033 mg/cm²) with a flux of 0.221 mg/cm²/h). **Conclusion:** The optimized T9 patch exhibited enhanced swelling, adhesion, sustained release, and permeation, suggesting its potential as an effective alternative for managing nocturnal hypertension.

## *INTRODUCTION*

Hypertension, a chronic cardiovascular disorder, remains one of the major contributors to global morbidity and mortality. Uncontrolled hypertension predisposes individuals to severe complications such as stroke, myocardial infarction, and renal failure [1,2]. Long-term pharmacotherapy typically involves the daily administration of antihypertensive agents; however, challenges such as poor patient adherence, variable gastrointestinal absorption, and first-pass hepatic metabolism often result in suboptimal therapeutic control [3,4]. In addition, maintaining consistent plasma concentrations is critical in conditions such as nocturnal hypertension, in which blood pressure remains elevated at night [5]. To overcome the inherent limitations of conventional oral dosage forms, alternative drug delivery systems have gained significant attention. Among

*Department of Pharmaceutics, KLE College of Pharmacy, Rajajinagar, Bengaluru 560010, KLE Academy of Higher Education and Research, Belagavi 590010, Karnataka, India

***For Correspondence:** **preethigb_100@yahoo.com**

these, the buccal route has emerged as a promising non-invasive platform offering improved bioavailability and patient compliance [6]. Buccal patches are thin, flexible, mucoadhesive films designed to adhere to the buccal mucosa, enabling direct drug absorption through the highly vascularized epithelial membrane. This route effectively circumvents hepatic first-pass metabolism and enzymatic degradation in the gastrointestinal tract, thereby enhancing systemic bioavailability and allowing for either rapid or sustained drug release, depending on formulation design [7].

The buccal mucosa offers several advantages as a route for drug delivery due to its high permeability, rich vascularization, and relatively low enzymatic activity compared to other regions of the gastrointestinal tract. These characteristics facilitate rapid drug absorption and help bypass first-pass hepatic metabolism. Formulations designed for buccal administration commonly utilize bioadhesive polymers that promote close contact with the mucosal surface, thereby enhancing mechanical stability and enabling controlled drug release. Additionally, incorporating permeation enhancers, plasticizers, and nanocarrier systems can further improve drug permeability and prolong the formulation's residence time at the site of absorption. These advancements expand the potential of buccal delivery for a wide range of therapeutic agents, including peptides, hormones, and antihypertensive drugs [8–12]. Furthermore, the ease of administration and removal, along with the non-invasive nature of this route, significantly contributes to better patient compliance, particularly in the long-term management of chronic diseases [13,14].

Angiotensin II receptor antagonists like telmisartan are frequently used to treat hypertension. Its oral bioavailability is relatively low (42–58%) due to extensive first-pass hepatic metabolism, despite its elimination half-life of around 24 hours, which allows for a single dose. Buccal administration can overcome this constraint by avoiding first-pass metabolism, thereby increasing bioavailability, therapeutic efficacy, and patient compliance. [15,16].

Class II medications, according to the Biopharmaceutics Classification System, have high permeability and low water solubility [17,18], with absorption primarily governed by the dissolution rate [19]. Solid dispersion is an effective approach for increasing drug solubility and dissolution by dispersing the drug in hydrophilic carriers, resulting in smaller particle sizes, improved wettability, and partial or total amorphization. These impacts help to increase bioavailability [20-22].

Xanthan gum (XG) is a mucoadhesive polymer known for its bioadhesion strength, biocompatibility, and non-toxicity. XG, a high-molecular-weight polysaccharide, contains abundant hydroxyl and carboxyl groups that form strong hydrogen bonds with mucin glycoproteins on the buccal surface, ensuring prolonged residence time and sustained drug action. Upon hydration, XG swells to form a gel-like matrix that regulates drug diffusion, improves patch uniformity, and provides mechanical stability [23]. Hydroxypropyl methylcellulose (HPMC E-15) is a film-forming and release-modifying polymer. Its excellent film-forming capacity, transparency, and mechanical integrity ensure uniform, controlled hydration, leading to predictable, sustained drug release. Furthermore, HPMC exhibits synergistic mucoadhesion when combined with polysaccharides such as XG, improving both mechanical and adhesive characteristics [24,25]. Polyvinyl alcohol (PVA) serves as a supporting polymer that enhances the film's flexibility, tensile strength, and elasticity. It is a biocompatible, non-toxic polymer that can be combined with other polymers to maintain patch integrity and achieve a consistent release profile [26]. Understanding the importance of polymers discussed above, the present mucoadhesive buccal films of telmisartan were developed using natural polymer Xanthan gum in combination with HPMC and PVA, and evaluated for their *in vitro* and *Ex vivo* performance.

## *MATERIALS AND METHODS*

### Materials

Telmisartan was obtained as a gift sample from Micro Labs Ltd, Bengaluru, India. Xanthan gum and dialysis membrane 50 were sourced from HiMedia Lab Pvt. Limited, Mumbai. HMPC E-15, PVA, and other materials were purchased from S.D. Fine-Chem Ltd., Mumbai, India. All chemicals and reagents for this study met analytical-grade requirements.

### Methods

#### Phase Solubility Study

Phase solubility studies were carried out by preparing a series of phosphate-buffered saline (PBS) solutions (pH 6.8) containing increasing concentrations of the carriers Soluplus, Gelucire 44/14, Kolliphor RH 40, β-cyclodextrin, mannitol, polyethylene glycol 6000, and citric acid. Carrier concentrations were prepared at 0.1%, 0.25%, 0.5%, 0.75%, and 1% w/v. An excess

amount of telmisartan (TLM) was added to each solution to ensure saturation. The mixtures were vortexed and kept under continuous agitation at 60 rpm for 24 hours to reach equilibrium. After incubation, the samples were centrifuged at 10,000 rpm for 30 minutes to separate the supernatant. The clear supernatant was collected, suitably diluted, and analyzed using a UV–Visible spectrophotometer at 296 nm. The concentration of TLM in each sample was determined using a previously prepared calibration curve, with PBS containing the respective carrier concentrations serving as the blank [27,28].

**Preparation of Telmisartan Mucoadhesive Buccal Patches**

Mucoadhesive buccal patches were prepared by the solvent casting method. Initially, Xanthan gum and polyvinyl alcohol were dispersed in hot distilled water with continuous stirring until a clear solution was obtained. The solution was allowed to cool to room temperature, after which HPMC E15 and propylene glycol were incorporated and stirred until fully dissolved, yielding a uniform polymeric matrix. Separately, Telmisartan solid dispersion was dissolved in 5 mL of methanol and then added gradually to the polymeric solution under continuous stirring. The resulting mixture was sonicated to eliminate entrapped air bubbles and poured onto a glass Petri plate. The cast films were dried in a hot air oven at 50 °C for 5 hours. After drying, the films were carefully peeled off and stored in a desiccator at room temperature until further evaluation. [29].

**Experimental Design ($3^2$ Factorial Design)**

The buccal films were formulated using a $3^2$ full factorial design. The two independent variables are Xanthan gum concentration (factor A) and HPMC E15 concentration (factor B). Each variable was studied at three levels. For Xanthan gum (A), the levels were 0.1% (low), 0.2% (medium), and 0.3% (high). For HPMC E15 (B), the levels were 1% (low), 1.5% (medium), and 2% (high). The dependent responses are swelling index ($Y_1$), film thickness ($Y_2$), and *in vitro* drug release ($Y_3$). The design generated nine experimental formulations based on the combinations of the selected factor levels (Table 1)

**Table 1: Composition of Telmisartan mucoadhesive buccal patches**

| Ingredients | T1 | T2 | T3 | T4 | T5 | T6 | T7 | T8 | T9 |
|---|---|---|---|---|---|---|---|---|---|
| **TS (mg)** | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 |
| **KH (mg)** | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 | 15 |
| **XG (%w/v)** | 0.1 | 0.2 | 0.3 | 0.1 | 0.2 | 0.3 | 0.1 | 0.2 | 0.3 |
| **HPMC E 15 (%w/v)** | 1 | 1 | 1 | 1.5 | 1.5 | 1.5 | 2 | 2 | 2 |
| **PVA (%w/v)** | 0.75 | 0.75 | 0.75 | 0.75 | 0.75 | 0.75 | 0.75 | 0.75 | 0.75 |
| **PG*** | 35 | 35 | 35 | 35 | 35 | 35 | 35 | 35 | 35 |
| **Water (ml)** | 40 | 40 | 40 | 40 | 40 | 40 | 40 | 40 | 40 |
| **Methanol (ml)** | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 | 60 |

**Amount of PG in terms of %w/w of the total dry polymer weight. PG: Propylene glycol, HPMC: Hydroxypropyl methylcellulose, XG: Xanthan gum, TLM: Telmisartan drug, KH: Kolliphor RH 40.*

***EVALUATION OF TELMISARTAN MUCOADHESIVE BUCCAL PATCHES***

**Thickness and Weight of Patches:** The buccal patch was divided into 2 cm x 2 cm sections and accurately weighed on a digital balance. The thickness of the patches was measured at three different locations using a Vernier caliper. The above procedure was repeated for all the trials [30].

**Drug Content Uniformity**: UV spectrophotometric analysis was performed to assess uniformity of drug content across the patches. Three different locations on the cast patches were selected, and 1cm 2 sections were cut. Each patch was dissolved in 100 mL of PBS at pH 6.8. The solution is filtered, and the absorbance is measured at 296nm. This procedure was repeated for 3 patches of each formulation, and the drug content was determined [31,32].

**Measurement of Folding Endurance**

Folding endurance was assessed to evaluate the mechanical strength of T-SD–containing buccal patches. Each patch was manually folded at the same position and in the same direction until it broke, and the number of folds required for breakage was recorded [33].

**Measurement of Moisture Content**

Moisture content of the MBPs was evaluated by weighing the patches, then storing them in desiccators containing anhydrous calcium chloride. The patches were reweighed after three days, and the percentage moisture loss was calculated using the following equation. [34]:

$$\textit{Moisture Content}\ (\%) = \frac{\textit{Initial Weight} - \textit{Final Weight}}{\textit{Initial weight}} x100$$

**Surface pH Measurement**

To measure the MBP surface pH. The patches were placed in Petri dishes with 5 mL of distilled water and allowed to swell fully for an hour. Each patch's pH was measured using a digital pH meter by touching the wet patch surface with the pH probe. The average pH value was obtained after this procedure was performed three times [35].

**Measurement of Swelling Index**

To determine the swelling index (SI) of the T-SD MBP, a PBS solution at pH 6.8 was used. Each patch was divided into 2 cm X 2 cm sections, and its initial weight (w1) was recorded. Subsequently, the patches were immersed in PBS, and at specific time intervals (10-60 min), they were removed, filtered, and weighed again (W2). The following formula was used to determine the swelling index percentage [36,37]:

$$\textit{Swelling Index}\ (\%) = \frac{\textit{final weight} - \textit{initial weitht}}{\textit{inital weight}} \times 100$$

**Fourier Transform Infra-Red (FT-IR) Spectroscopy**

Infrared spectrophotometry was performed using a Jasco 460 Plus (Japan) for the drug & excipients used in the formulation. The drug was mixed with the polymers; to check for any possible drug-excipient interactions, the IR spectrum of the pure drug, excipients, Telmisartan solid dispersion T-SD, and Physical Mixture PM were examined [38].

**Differential Scanning Calorimetry (DSC)**

A differential scanning calorimetry (DSC) experiment was conducted using a DSC-60 instrument (Shimadzu, Japan) by placing the samples weighing 2-10 mg into aluminum pans and sealing them. The samples were then heated to a temperature between 25 and 300ºC at a rate of 10 ºC/min while a nitrogen atmosphere was maintained [39].

**Powder X-ray Diffraction**

XRD of pure TLM, excipients, powdered PM, and T-SD were recorded using Rigaku Miniflex 600(5th gen). The samples were analyzed using Ni-filtered Cu ka radiation at 40kV/15mA with a 2θ range of 5-80[40,41].

***In vitro* Drug Release**

In vitro drug release from the TLM-containing mucoadhesive buccal patches (MBP) was evaluated using a USP dissolution apparatus Type I (basket method) under sink conditions. The study was conducted in 900 mL of pH 6.8 phosphate buffer solution at 37 ± 0.5 °C with a rotation speed of 50 rpm. A 2 cm × 2 cm patch was attached to the dissolution basket using double-sided adhesive tape, ensuring that the mucoadhesive layer remained in contact with the dissolution medium. Although the volume of dissolution medium exceeds the physiological volume of saliva present in the buccal cavity, this larger volume was used to maintain sink conditions and ensure consistent drug diffusion and accurate quantification during the release study. At predetermined time intervals, 5 mL samples were withdrawn and replaced with an equal volume of fresh dissolution medium to maintain constant volume. The collected samples were analyzed using a UV–visible spectrophotometer at 296 nm to determine the amount of TLM released from the patches [42,43].

**Kinetics of Drug Release**

Different kinetic models, including zero-order, first-order, Higuchi, and Korsmeyer-Peppas, were used to study the release pattern of TLM from the buccal patch matrix. These models were applied to the best formulation, based on in vitro drug release data, to determine the release mechanism. The model with the highest correlation coefficient was considered the best fit [44].

***Ex vivo* Mucoadhesive Strength**

The modified two-arm balance technique was followed to determine mucoadhesive strength. The buccal mucosa of a goat was obtained from a nearby slaughterhouse. The mucosal membrane, 2 mm thick, was prepared after removing fat and loose tissue, then washed with distilled water and PBS (pH 6.8) at 37°C. Using cyanoacrylate glue, a piece of buccal mucosa was attached to the bottom of a smaller beaker. A buccal patch was attached to the left-hand side pan of the balance, brought into contact with the mucosa, and covered with adhesive tape. After holding the balance in place for five minutes, the right-side pan's weight was steadily increased until the patch detached from the mucosal surface. Mucoadhesive strength, reported in grams, represents the weight required to separate the mucosa from the patch. Three duplicates of each experiment were run, and average results were reported [45].

***Ex vivo* Permeation Studies**

The *Ex-vivo* permeation study of the MBP formulation was conducted using the Franz diffusion cell method. Each patch was shaped into a circle with a diameter of 1.2 cm and a diffusion area of 0.75 cm2. PBS at pH 6.8 was used to fill the receptor chamber, which was then heated to 37 ºC using a water jacket

and stirred with a magnetic stirrer. The setup was then carefully adjusted to put the freshly cut goat buccal mucosa between the donor and receptor chambers. The goat mucosal membrane was subsequently covered with the patch formulation. During the experiment, at regular intervals, 1 ml samples were obtained and replaced with identical volumes of fresh PBS. The drug concentration in the samples was measured using a UV spectrometer at 296 nm. The permeation results were presented as the cumulative amount per area (mg/cm$^2$) plotted against time (hours), and the steady-state flux (mg/cm$^2$/h) was calculated by determining the slope of permeation by area of diffusion [46].

**Statistical evaluation**

Statistical analysis of the experimental data was performed using Design-Expert® software. Analysis of Variance (ANOVA) was applied to assess the significance of the developed model and the effect of individual factors.

## *RESULTS AND DISCUSSION*

**Phase Solubility Study**

As telmisartan (TLM) belongs to the BCS Class II drug, solid dispersion was explored as a strategy to improve its solubility [47]. Phase-solubility studies were carried out in a pH 6.8 phosphate buffer using different carriers. Solubility increased with increasing carrier concentration (Fig. 1). At 1% w/v, Kolliphor RH 40 showed the highest solubilizing capacity (38.2µg /mL), followed by Gelucire 44/14 (19.45µg/mL), citric acid (22.419µg/mL), Soluplus (21.75 µg/mL), mannitol (16.31µg/mL), PEG-6000 (13.161µg/mL), and β-cyclodextrin (9.405µg/mL). Based on these results, Kolliphor RH 40 was selected for preparing TLM solid dispersions. The dispersions were obtained by solvent evaporation using a 1:1 drug-to-carrier ratio & the dried product exhibited markedly improved solubility in both pH 6.8 buffer and water compared to the pure drug.

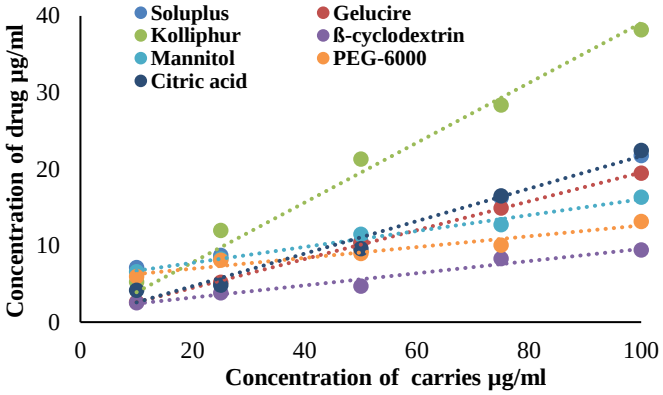


**Figure 1: Phase solubility studies**

**Evaluation of Telmisartan Mucoadhesive Buccal Patches**

The thickness of the TLM buccal patches for formulations T1 to T9 ranged from 0.60±0.03 mm to 0.77±0.005 mm, as shown in Table 2. An increase in patch thickness was observed as the concentrations of xanthan gum (XG) and HPMC E-15 increased. This can be attributed to the higher viscosity of xanthan gum, which forms a denser polymeric matrix during casting, resulting in thicker films. The weight of the prepared buccal patches ranged from 80.2±1.2 mg to 97.5±0.5 mg (Table 2). All formulations showed acceptable weight variation and complied with the limits reported for buccal patches in the current literature [48].

Folding endurance values for formulations T1-T9 ranged from 302 to 364. A proportional increase in folding endurance was noted with higher concentrations of HPMC E-15 and xanthan gum. This indicates that the patches possessed good flexibility and mechanical strength. The improved folding endurance can be attributed to the film-forming ability of HPMC E-15 and the plasticizing effect of propylene glycol, which together reduce brittleness and enhance the structural integrity of the patches. The DC uniformity values for formulations T-1 to T-9 ranged from 0.92±0.023mg to 1.11±0.001mg, as shown in Table 2. These values fell within the desired range, indicating that the formulations exhibit satisfactory uniformity of drug content [49].

**Surface pH Measurement**

All patches were determined by the surface pH to be within the range of 7 -6.9 (Table 2). Therefore, no mucosal irritation was anticipated from these prepared patches [33,34].

**Moisture Content**

The moisture content of the prepared TLM MBP was determined, and the results ranged from 1.08 ± 0.005% to 1.78 ± 0.27% (Table 2). The lesser moisture content observed in these patches is significant as it helps prevent microbial contamination. Moreover, it plays an important role in maintaining patch stability and preventing patches from becoming dry and brittle [50].

**Percentage Swelling Index**

The degree of swelling in mucoadhesive polymers plays a crucial role in mucoadhesion and prolonged release of the drug. The water absorption percentage (% swelling) of patches was evaluated to predict the polymer's hydration behavior. Overall results showed that at 37ºC, the swelling percentages after 1h increased from 196.6% to 331% with increasing concentrations

of Xanthan gum and HPMC-E15. This can be attributed to the hydrophobic and ionic properties of xanthan gum, which result in greater affinity for water & form a gel due to hydrogen bonding with water [51]. It shows the SI of TLM buccal patches from T1 to T9.

**Table 2: Thickness, weight variation, folding endurance, DC, moisture content, surface pH, Mucoadhesive Strength, and SI**

| Parameters | T1 | T2 | T3 | T4 | T5 | T6 | T7 | T8 | T9 |
|---|---|---|---|---|---|---|---|---|---|
| Thickness (mm)* | 0.60±0.03 | 0.61±0.01 | 0.71±.005 | 0.61±.005 | 0.73±.01 | 0.75±.005 | 0.63±.005 | 0.74±0.01 | 0.77±.005 |
| WV (mg)* | 80.2±1.2 | 81.3±1.5 | 90.3±1.1 | 86.6±.57 | 92.3±1.1 | 88.6±1.15 | 95.6±0.57 | 96.1±1 | 97.5±0.5 |
| FE | 302 | 301 | 295 | 316 | 306 | 310 | 321 | 340 | 364 |
| DC* (mg) | 0.92±.023 | 0.976±.005 | 1.03±.03 | 0.93±.002 | 0.90±.001 | 0.96±.005 | 1.18±.001 | 1.03±.001 | 1.11±.001 |
| MC* (%) | 1.08±.005 | 1.11±.002 | 1.30±.09 | 1.37±0.1 | 1.25±0.8 | 1.56±0.1 | 1.61±0.4 | 1.72±0.2 | 1.78±0.2 |
| SurfacepH* | 7 ±0.05 | 7 ± 0.05 | 6.9±0.1 | 6.8±0.05 | 6.5±0.1 | 6.5±.057 | 7.1±0.16 | 6.9±0.11 | 6.9±0.11 |
| MS *(gm) | 21.2±1 | 22.06±1 | 20.3±1.4 | 22±1 | 22.1±1.01 | 23.53±.5 | 25.9±0.8 | 27.2±0.2 | 28.9±0.5 |
| SI (%) | 196.6 | 198 | 201.5 | 249 | 264.7 | 270 | 277.5 | 318 | 331 |

**All values are mean ± SD, n=3*

### *In Vitro* Drug Release Study

As shown in Figure 2, the in *vitro* drug release of TLM buccal patches (T1–T9) ranged from 30.5±1.14% to 94.87±1.23%. Higher levels of HPMC E-15 and xanthan gum produced sustained release due to their hydrophilic swelling behavior. Patches T1–T7 disintegrated between 2 and 5 hours, while T8 and T9 remained intact for more than 6 hours, showing cumulative release of 90.86±0.80% and 94.87±1.23%, respectively, confirming the enhanced release from solid dispersion containing Kolliphor RH 40 [52].

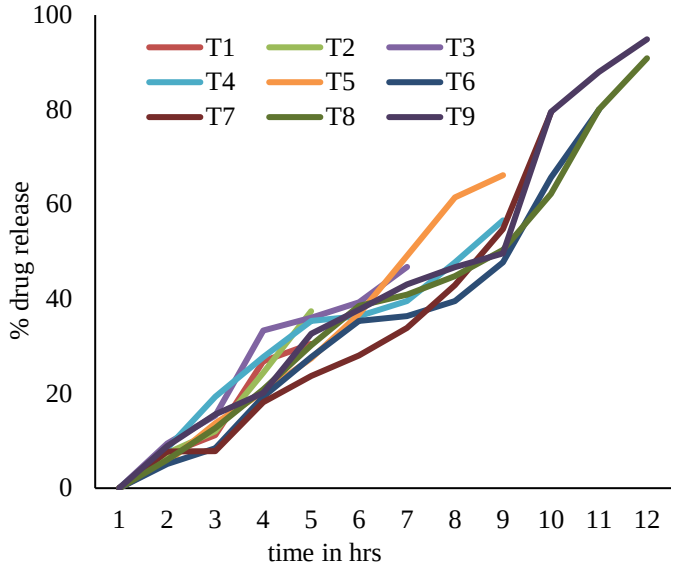


**Figure 2**: *In vitro* drug release profile of patches from T1 to T9

### *Optimization and Model Validation*

Using a $3^2$ factorial design, nine experimental runs were performed to evaluate the effects of two independent variables, Xanthan gum (A) and HPMC E15 (B), on the swelling index (Y1), thickness (Y2), and % in vitro drug release (Y3). The experimental results are summarized in Tables 3 and 4, and the response surface plots are shown in Figure 3. From the regression analysis, the swelling index (Y1) followed a two-factor interaction (2FI) model, whereas thickness (Y2) and in vitro drug release (Y3) followed linear models. All models were statistically significant. Statistical significance of factors was evaluated using ANOVA, where p-values < 0.05 and higher F-values denote significant model terms. The high $R^2$ values (Y1 = 0.9861, Y2 = 0.8657, Y3 = 0.9841) and the close agreement between Adjusted $R^2$ and Predicted $R^2$ confirmed good model fit and reliability. Table 3 shows that Xanthan gum (A) and HPMC E15 (B) significantly influenced all responses ($p < 0.05$). The interaction term (AB) was significant only for the swelling index, confirming the combined effect of the two polymers on swelling behavior.

The coded equations for the responses were:

$$Y1 = 256.26 - 13.23\,A + 55.07\,B + 12.15\,AB$$

$$Y2 = -0.6833 + 0.0650\,A + 0.0367\,B$$

$$Y3 = 64.73 + 9.19\,A + 25.07\,B$$

The response surface plots (Figure 3) support the statistical findings. The swelling index increased with increasing polymer concentrations, showing an interaction between A and B. The thickness increased linearly with polymer concentration, with Xanthan gum showing a slightly greater contribution. In vitro drug release increased markedly with increasing HPMC E15 concentration, indicating its dominant role in controlling drug release. Overall, Xanthan gum and HPMC E15 significantly affected the measure responses, with HPMC E15 exerting a stronger influence on swelling and drug release, while Xanthan gum contributed more prominently to thickness. T9 was selected as the optimized formulation and subjected to further evaluation following statistical evaluation.

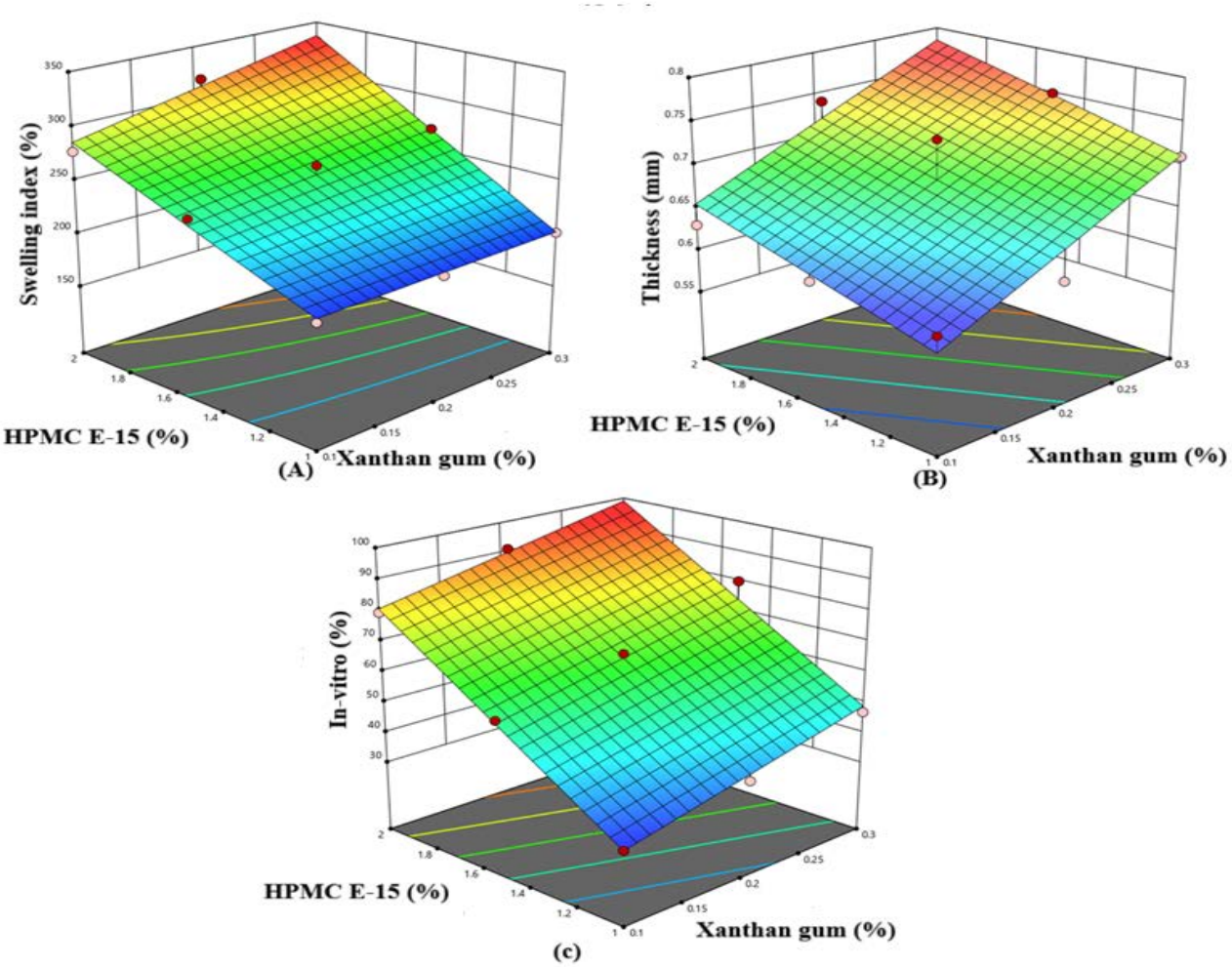


**Figure 3: Surface response Plot for the (A) Swelling index, (B) Thickness, (C) In-vitro drug release**

**Table 3: Fit model summary statistics of responses**

| Factors | Y1 | | | Y2 | | | Y3 | | |
|---|---|---|---|---|---|---|---|---|---|
| | CE | F-value | P-value | CE | F-value | P-value | CE | F-value | P-value |
| A | 13.23 | 18.85 | 0.0074 | 0.0650 | 29.34 | 0.0016 | 9.19 | 44.08 | 0.0006 |
| B | 55.07 | 326.39 | <0.0001 | 0.0367 | 9.34 | 0.0223 | 25.07 | 327.91 | <0.0001 |
| AB | 12.15 | 10.59 | 0.0226 | - | - | - | - | - | - |

**Table 4: Coefficients and ANOVA for the model of all the responses**

| Response | Model | p-value | SD | R2 | AR2 | PR2 |
|---|---|---|---|---|---|---|
| Y1 | 2FI | 0.0226 | 7.47 | 0.9861 | 0.9778 | 0.9247 |
| Y2 | Linear | 0.0024 | 0.0294 | 0.8657 | 0.8210 | 0.7386 |
| Y3 | Linear | <0.0001 | 3.39 | 0.9841 | 0.9788 | 0.9630 |
| | | | | | | |

**Fourier Transform Infra-Red (FT-IR) Spectroscopy**

A useful analytical method for examining the chemical interactions between the drug and other excipients used in the formulation is IR spectrophotometry [53]. The IR spectra were recorded for the pure drug, XG, HPMC E-15, PM (Physical mixture), and T-SD. Spectra are depicted in Figure 4 (a-e) and

were compared with each other for any possible drug excipient interactions. As depicted in the IR spectrum, T-SD and PM retained all functional group peaks, as in the pure drug. These results indicate no interaction between TLM and excipients.

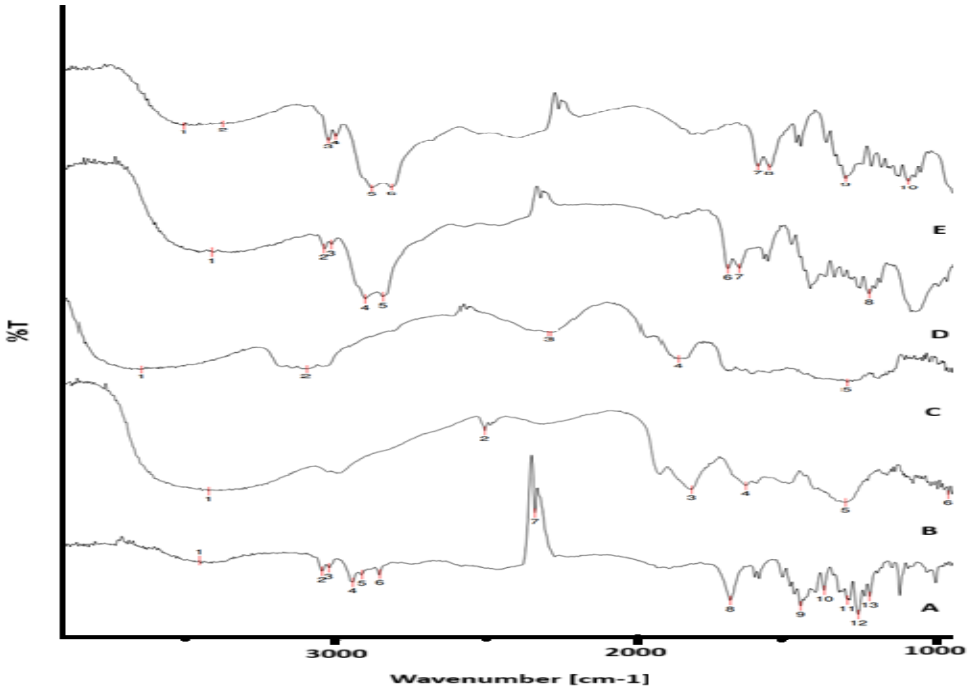


**Figure 4: FTIR of drug, excipient, physical mixture, and solid dispersion, where A is telmisartan, B is XG, C is HPMC E15, D is the physical mixture of A, B, and C, and E is the TLM Solid dispersion**

**Differential Scanning Calorimetry (DSC)**

The DSC analysis of TLM, T-SD, excipients HPMC E-15 and XG, and PM (drug and excipients) is done to understand the interaction of the drug and the excipient. The DSC thermograms shown in Figure 5 (a) indicate that pure TLM exhibits a sharp endothermic peak at approximately 270 °C, confirming its characteristic melting point and crystalline nature.

In physical mixture (Figure d), the slight shift in the TLM melting peak from 270.16°C to 267.21°C suggests melting point depression, which typically occurs when one component is mixed with another. Additionally, the reduced intensity of the drug peak in the PM indicates the absence of significant drug–excipient interaction.

In the thermogram of the T-SD formulation (Figure e), a decrease in the intensity of the drug peak around 262 °C was observed, which may be attributed to the partial transformation of TLM from a crystalline to an amorphous state. This result suggests that the solid dispersion system may enhance drug dispersion within the polymer matrix without causing chemical incompatibility, thereby enhancing the solubility of the poorly soluble drug [46,49,54].

**Powder X-ray Diffraction**

The XRD pattern of the pure drug TLM exhibited a strong and intense peak at diffraction 2θ of 20.198ºC, 21.319ºC at a range of 24ºC, indicating its crystalline nature (Figure 6a). The diffractogram of the excipient XG and HPMC E15 (Figure 6 b, c) displayed no sharp peaks but exhibited a large and broad peak, indicating its amorphous characteristics.

The XRD pattern of the physical mixture (Figure 6 d) displayed sharp and intense peaks, similar to those observed in the pure diffractogram. This indicates the absence of drug–excipient interaction in a physical mixture. XRD pattern of the solid dispersion (Figure 6 e) showed sharp peaks with decreased intensity, indicating a change from crystalline to amorphous form, which is responsible for enhanced solubility of TLM in 6.8 pH phosphate buffer.

***Ex vivo* Mucoadhesive Strength**

The mucoadhesive strength of the T1-T9 formulations was evaluated, and the results are shown in Figure 7, ranging from 21.2±1 to 28.9±0.5 g. Formulations T8 and T9 exhibited the highest mucoadhesive strengths, 27.2±0.2 g and 28.9±0.5 g, respectively, which can be attributed to their greater swelling

capacities of 318% and 331%, respectively. As the swelling index increases, mucoadhesion strength also increases, ensuring patch adherence at the site of administration. Along with XG, HPMC E-15 also influences the mucoadhesion strength due to its physical nature. [55].

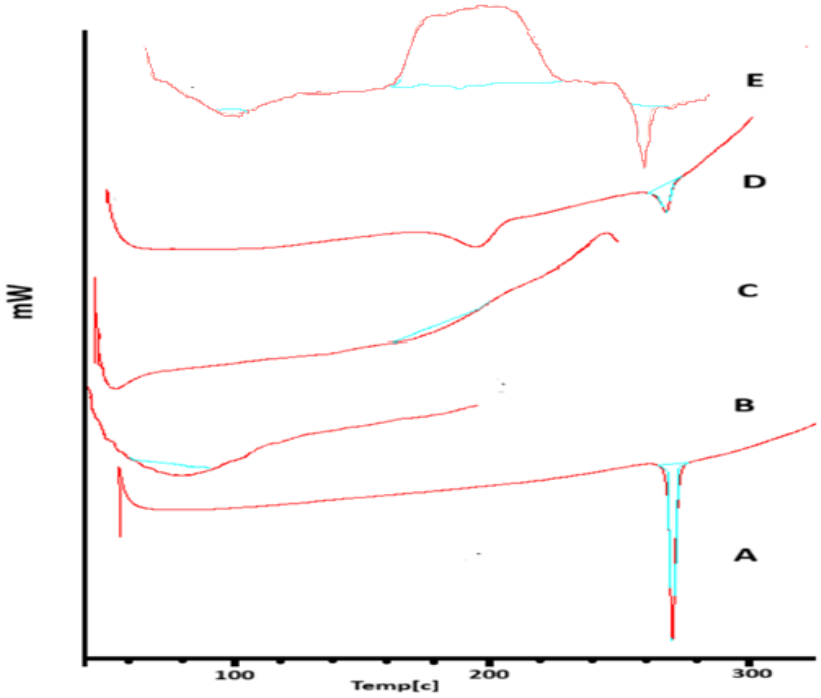


**Figure 5: DSC of drug, excipient, physical mixture, and solid dispersion, where A is telmisartan, B is XG, C is HPMC E15, D is the physical mixture of A, B, and C, and E is the TLM Solid dispersion**

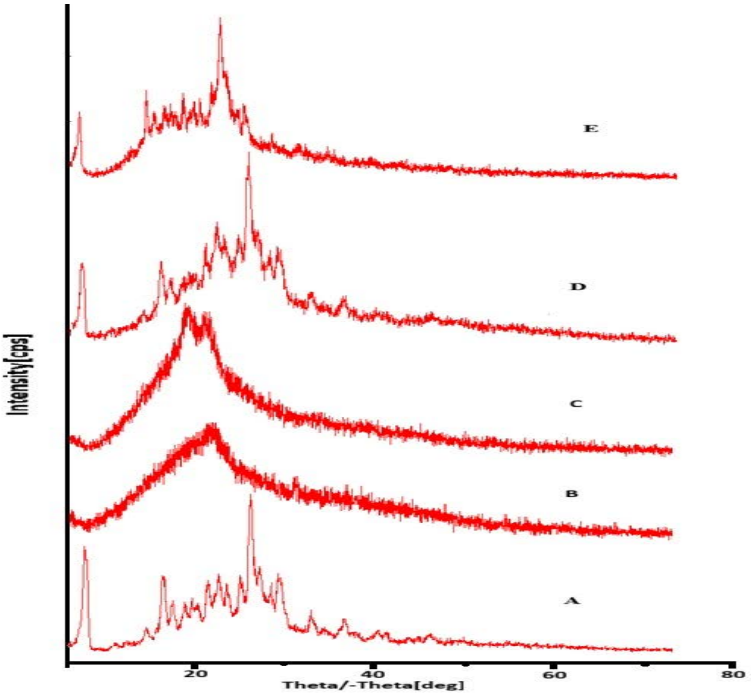


**Figure 6: XRD of drug, excipient, physical mixture, and solid dispersion, where A is telmisartan, B is XG, C is HPMC E15, D is the physical mixture of A, B, and C, and E is the TLM Solid dispersion**

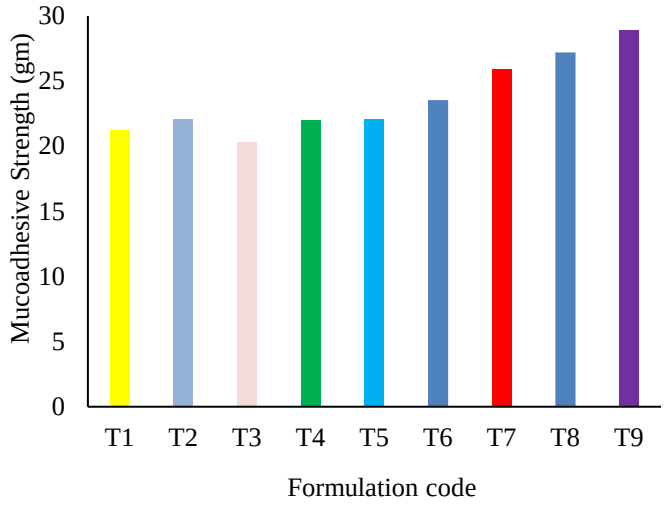


**Figure 7: *Ex vivo* mucoadhesive strength**

### *Ex vivo* Drug Permeation Study

*Ex vivo* drug permeation studies of mucoadhesive buccal patches containing pure drug (TLM) and formulation T9 were conducted using goat buccal mucosa, and the results are depicted in Figure 8. Permeation was evaluated in terms of cumulative amount permeated per unit area and steady-state flux. Formulation T9 exhibited a cumulative permeation of 1.773 mg/cm² over 8 hours with a steady-state flux of 0.221 mg/cm²/h. In comparison, the pure drug showed a significantly lower cumulative permeation of 1.378 mg/cm². The higher permeation observed with formulation T9 was statistically significant ($P < 0.0001$) and can be attributed to the presence of Kolliphor RH 40, which enhances drug permeation across the buccal mucosa [56]. *Ex vivo* permeation flux of formulation T9 at 1.77 mg/cm2 over 8 hours may be sufficient to achieve the required therapeutic plasma concentration of Telmisartan in humans. Still, in *vivo* pharmacokinetic studies are necessary to confirm clinical relevance.

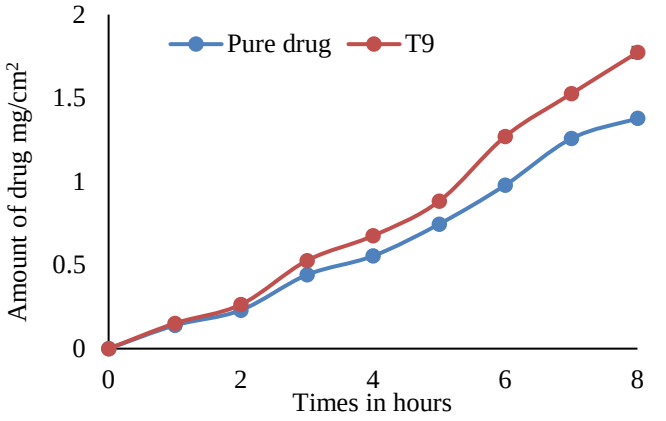


**Figure 8: *Ex vivo* permeation of optimized formulation T9**

### Release Kinetics

The in vitro drug-release profile of the T9 formulation was analyzed using various kinetic models, including the Zero-order, Higuchi, and Korsmeyer–Peppas models. The release data (Table 5) showed the best fit to zero-order kinetics, as indicated by the highest correlation coefficient ($R^2 = 0.9954$). Further evaluation using the Korsmeyer–Peppas model yielded an 'n' value of 1.503, which corresponds to a Super case II transport mechanism, suggesting that drug release is governed by both erosion and relaxation of the polymer chains [57].

**Table 5: Release kinetics of formulation T9**

| Release Model | | T9 |
|---|---|---|
| **Zero Order** | $R^2$ | 0.9913 |
| **First Order** | $R^2$ | 0.9482 |
| **Higuchi Matrix** | $R^2$ | 0.9596 |
| **Peppas Order** | $R^2$ | 0 .9954 |
| | n | 1.503 |

## *CONCLUSION*

The study successfully developed a telmisartan mucoadhesive buccal patch to overcome limitations related to poor solubility and first-pass metabolism. A 3² factorial design was used to optimize formulations, and ANOVA confirmed the significance of the developed models. Solid dispersion using Kolliphor RH 40 improved drug solubility and supported effective patch formulation. Compatibility studies confirmed the absence of drug–excipient interactions. The optimized formulation (T9) exhibited a high swelling index (331%), strong mucoadhesive strength (28.5 ± 0.5 g), sustained drug release (94.87%), and enhanced *ex vivo* permeation (1.773 ± 0.033 mg/cm²) with a flux of 0.221 mg/cm²/h. Overall, the optimized patch shows promise for managing nocturnal hypertension. Further stability and *in vivo* studies are required to confirm long-term efficacy and clinical applicability.

## *FINANCIAL ASSISTANCE*

NIL

## *CONFLICT OF INTEREST*

The authors declare no conflict of interest.

## *AUTHOR CONTRIBUTION*

Hattaraki, Shashank Shivannad, and Shashank K performed the bench experiments and contributed to drafting the manuscript. Preethi G B was responsible for study conceptualization, data analysis, and critical revision of the manuscript. Subham Roy conducted the literature review and contributed to manuscript

preparation. Suhasini Rendale assisted with the literature search and manuscript refinement.

## *REFERENCE*


[1] Wibowo A, Hastuti P, Susanti V. The association of angiotensin converting enzyme I/D and angiotensinogen M235T polymorphism genes with essential hypertension: A meta-analysis. *Open Access Maced J Med Sci*, **9(F)**, 739–746 (2021) https://doi.org/10.3889/oamjms.2021.7628

[2] Guerrero-García C, Rubio-Guerra AF. Combination therapy in the treatment of hypertension. *Drugs Context*, **7**, 212531 (2018) https://doi.org/10.7573/dic.212531

[3] Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. *Nat Rev Nephrol*, **16(4)**, 223–237 (2020) https://doi.org/10.1038/s41581-019-0244-2

[4] Hanif M, Zaman M, Chaurasiya V. Polymers used in buccal film: A review. *Des Monomers Polym*, **18(2)**, 105–111 (2015) https://doi.org/10.1080/15685551.2014.971389

[5] Abdalla M, Goldsmith J, Muntner P, Diaz KM, Reynolds K, Schwartz JE, Shimbo D. Is isolated nocturnal hypertension a reproducible phenotype? *Am J Hypertens*, **29(1)**, 33–38 (2016) https://doi.org/10.1093/ajh/hpv058

[6] Sabareesh M, Suma P, Venkata Ravi M, Balaji A. Nanoparticles loaded mucoadhesive buccal patches: Review. *J Pharm Res Int*, **34(46B)**, 24–38 (2022) https://doi.org/10.9734/JPRI/2022/v34i46B36388

[7] Montenegro-Nicolini M, Morales JO. Overview and potential of buccal mucoadhesive films as drug delivery systems for biologics. *AAPS PharmSciTech*, **18**, 3–14 (2017) https://doi.org/10.1208/s12249-016-0525-z

[8] Şenel S, Rathbone MJ, Cansız M, Pather I. Recent developments in buccal and sublingual delivery systems. *Expert Opin Drug Deliv*, **9(6)**, 615–628 (2012) https://doi.org/10.1517/17425247.2012.676040

[9] Malpure DR, Deore SL. Buccal mucoadhesive films: A review. *Syst Rev Pharm*, **8(1)** (2017) https://doi.org/10.5530/srp.2017.1.7

[10] Shipp L, Liu F, Kerai-Varsani L, Okwuosa TC. Buccal films: A review of therapeutic opportunities, formulations and relevant evaluation approaches. *J Control Release*, **352**, 1071–1092 (2022) https://doi.org/10.1016/j.jconrel.2022.10.058

[11] Vikhe S, Sukhadhane P, Vikhe R, Bornare SL, Dhavane SS. Antidiabetic effects of *Semecarpus anacardium* leaf extracts in streptozotocin-induced diabetes in rats. *Journal of Applied Pharmaceutical Research*, **12(6)**, 144–158 (2024) https://doi.org/10.69857/joapr.v12i6.736

[12] Salamat-Miller N, Chittchang M, Johnston TP. The use of mucoadhesive polymers in buccal drug delivery. *Adv Drug Deliv Rev*, **57(11)**, 1666–1691 (2005) https://doi.org/10.1016/j.addr.2005.07.003

[13] Morales JO, McConville JT. Manufacture and characterization of mucoadhesive buccal films. *Eur J Pharm Biopharm*, **77(2)**, 187–199 (2011) https://doi.org/10.1016/j.ejpb.2010.11.023

[14] Jacob S, Nair AB, Shah J. An updated overview of the emerging role of patch and film-based buccal delivery systems. *Pharmaceutics*, **13(8)**, 1206 (2021) https://doi.org/10.3390/pharmaceutics13081206

[15] Dubey A, Kharia AA, Chatterjee DP. Enhancement of aqueous solubility and dissolution of telmisartan using solid dispersion technique. *Int J Pharm Sci Res*, **5(10)**, 4478–4485 (2014) https://doi.org/10.13040/IJPSR.0975-8232.5(10).4478-85

[16] Patel K, Patel A, Dave J, Patel C. Absorbance correction method for estimation of telmisartan and metoprolol succinate in combined tablet dosage forms. *Pharm Methods*, **3(2)**, 106–111 (2012) https://doi.org/10.4103/2229-4708.103891

[17] Deppe S, Böger RH, Weiss J, Benndorf RA. Telmisartan: A review of its pharmacodynamic and pharmacokinetic properties. *Expert Opin Drug Metab Toxicol*, **6(7)**, 863–871 (2010) https://doi.org/10.1517/17425255.2010.494597

[18] Sharpe M, Jarvis B, Goa KL. Telmisartan: A review of its use in hypertension. *Drugs*, **61(10)**, 1501–1529 (2001) https://doi.org/10.2165/00003495-200161100-00009

[19] Isaac J, Ganguly S, Ghosh A. Co-milling of telmisartan with poly(vinyl alcohol): An alkalinizer-free green approach to ensure its bioavailability. *Eur J Pharm Biopharm*, **101**, 43–52 (2016) https://doi.org/10.1016/j.ejpb.2016.01.016

[20] Mehta S, Joseph NM, Feleke F, Palani S. Improving solubility of BCS class II drugs using solid dispersion: A review. *J Drug Deliv Ther*, **4(3)**, 7–13 (2014) https://doi.org/10.22270/jddt.v4i3.844

[21] Jadhav V, Kashid P, Otari K, Yadav M. Solubility enhancement by solid dispersion method: An overview. *Asian J Pharm Res Dev*, **12(4)** (2024) https://doi.org/10.22270/ajprd.v12i4.1450

[22] Dalvi PB, Gerange AB. Solid dispersion: Strategy to enhance solubility. *J Drug Deliv Ther*, **5(2)**, 20–28 (2015) https://doi.org/10.22270/jddt.v5i2.1060

[23] Sharma V, Pathak K. Modified xanthan gum as a hydrophilic disintegrating excipient for rapidly disintegrating tablets of roxithromycin. *Indian J Pharm Educ Res*, **47(4)**, 79–87 (2013) https://doi.org/10.5530/ijper.47.4.11

[24] Newton AM, Lakshmanan P. Effect of HPMC-E15 LV premium polymer on release profile and compression characteristics of chitosan/pectin colon targeted mesalamine matrix tablets and in vitro study on effect of pH impact on the drug release profile. *Recent Pat Drug Deliv Formul*, **8(1)**, 46–62 (2014) https://doi.org/10.2174/1872211308666140225143926

[25] Newton AM, Prabakaran L, Jayaveera KN. Formulation development, optimization, and study on drug release kinetics of Eudragit® L100-HPMC E15 LV mixed film-coated colon-targeted mesalamine tablets. *Asian J Pharm*, **6(3)** (2012) https://doi.org/10.22377/ajp.v6i3.53

[26] Blajovan R, Ledeți I, Vlase G, Ledeți A, Vlase T. Study of thermally induced excipient–excipient interactions: Polyvinyl alcohol and polyvinylpyrrolidone with other pharmaceutical excipients. *J Therm Anal Calorim*, **126**, 171–179 (2016) https://doi.org/10.1007/s10973-016-5348-3

[27] Park J, Cho W, Cha KH, Ahn J, Han K, Hwang SJ. Solubilization of the poorly water-soluble drug telmisartan using supercritical anti-solvent process. *Int J Pharm*, **441(1–2)**, 50–53 (2013) https://doi.org/10.1016/j.ijpharm.2012.12.020

[28] Rao M, Bajaj A, Khole I, Munjapara G, Trotta F. In vitro and in vivo evaluation of β-cyclodextrin-based nanosponges of telmisartan. *J Incl Phenom Macrocycl Chem*, **77**, 135–145 (2013) https://doi.org/10.1007/s10847-012-0224-7

[29] Shiledar RR, Tagalpallewar AA, Kokare CR. Formulation and in vitro evaluation of xanthan gum-based bilayered mucoadhesive buccal patches of zolmitriptan. *Carbohydr Polym*, **101**, 1234–1242 (2014) https://doi.org/10.1016/j.carbpol.2013.10.072

[30] Kraisit P, Limmatvapirat S, Luangtana-Anan M, Sriamornsak P. Buccal administration of mucoadhesive blend films saturated with propranolol loaded nanoparticles. *Asian J Pharm Sci*, **13(1)**, 34–43 (2018) https://doi.org/10.1016/j.ajps.2017.07.006

[31] Kayande K. Formulation, optimization, and evaluation of bioadhesive xanthan gum based buccal patch for sustained delivery of ropinirole hydrochloride. *Asian J Pharm*, **15(1)** (2021) https://doi.org/10.22377/ajp.v15i1.3956

[32] Gupta KR, Pounikar AR, Umekar MJ. Drug–excipient compatibility testing protocols and characterization: A review. *Asian J Chem Sci*, **6(3)**, 1–22 (2019) https://doi.org/10.9734/ajocs/2019/v6i319000

[33] Yedurkar P, Dhiman MK, Petkar K, Sawant K. Mucoadhesive bilayer buccal tablet of carvedilol-loaded chitosan microspheres: In vitro, pharmacokinetic and pharmacodynamic investigations. *J Microencapsul*, **29(2)**, 126–137 (2012) https://doi.org/10.3109/02652048.2011.630109

[34] Hasnain MS, Guru PR, Rishishwar P, Ali S, Ansari MT, Nayak AK. Atenolol-releasing buccal patches made of *Dillenia indica* L. fruit gum: Preparation and ex vivo evaluations. *SN Appl Sci*, **2**, 1756 (2020) https://doi.org/10.1007/s42452-019-1756-x

[35] Semalty M, Semalty A, Kumar G. Formulation and characterization of mucoadhesive buccal films of glipizide. *Indian J Pharm Sci*, **70(1)**, 43–48 (2008) https://doi.org/10.4103/0250-474X.40330

[36] Patil S, Bhargav S. Formulation and evaluation of a bifonazole-loaded chitosan-honey invasomal hydrogel for enhanced topical antifungal activity. *Journal of Applied Pharmaceutical Research*, **13(4)**, 36–44 (2025) https://doi.org/10.69857/joapr.v13i4.1301

[37] El-Maghraby GM, Abdelzaher MM. Formulation and evaluation of simvastatin buccal film. *J Appl Pharm Sci*, **5(4)**, 70–77 (2015) https://doi.org/10.7324/JAPS.2015.50412

[38] Tran PH, Tran HT, Lee BJ. Modulation of microenvironmental pH and crystallinity of ionizable telmisartan using alkalizers in solid dispersions for controlled release. *J Control Release*, **129(1)**, 59–65 (2008) https://doi.org/10.1016/j.jconrel.2008.04.001

[39] Chella N, Narra N, Rama Rao T. Preparation and characterization of liquisolid compacts for improved dissolution of telmisartan. *J Drug Deliv*, **2014**, 692793 (2014) https://doi.org/10.1155/2014/692793

[40] Khanfar M, Al-Remawi M, Al-Akayleh F, Hmouze S. Preparation and evaluation of co-amorphous formulations of telmisartan-amino acids as a potential method for solubility and dissolution enhancement. *AAPS PharmSciTech*, **22**, 1–13 (2021) https://doi.org/10.1208/s12249-021-01952-9

[41] Zhong L, Zhu X, Luo X, Su W. Dissolution properties and physical characterization of telmisartan-chitosan solid dispersions prepared by mechanochemical activation. *AAPS PharmSciTech*, **14**, 541–550 (2013) https://doi.org/10.1208/s12249-013-9937-1

[42] Bhattarai M, Gupta AK. Fast dissolving oral films: A novel trend to oral drug delivery system. *Sunsari Tech Coll J*, **2(1)**, 58–68 (2015) https://doi.org/10.3126/stcj.v2i1.14802

[43] Abu-Huwaij R, Obaidat RM, Sweidan K, Al-Hiari Y. Formulation and in vitro evaluation of xanthan gum or carbopol 934-based mucoadhesive patches loaded with nicotine. *AAPS PharmSciTech*, **12(1)**, 21–27 (2011) https://doi.org/10.1208/s12249-010-9534-5

[44] Mircioiu C, Voicu V, Anuța V, Tudose A, Celia C, Paolino D, Fresta M, Sandulovici R, Mircioiu I. Mathematical modeling of release kinetics from supramolecular drug delivery systems. *Pharmaceutics*, **11(3)**, 140 (2019) https://doi.org/10.3390/pharmaceutics11030140

[45] Verma N, Chattopadhyay P. Effect of novel mucoadhesive buccal patches of carvedilol on isoprenaline-induced tachycardia. *J Adv Pharm Technol Res*, **5(2)**, 96–103 (2014) https://doi.org/10.4103/2231-4040.133436

[46] Devi JR, Das T, Kalita B, Sahariah BJ. Design and optimization of chitosan microspheres loaded with green tea phytosomes for sustained release. *Journal of Applied Pharmaceutical Research*, **13(5)**, 74–90 (2025) https://doi.org/10.69857/joapr.v13i5.1188

[47] Yildiz Pekoz A, Erdal MS, Okyar A, Ocak M, Tekeli F, Kaptan E, Sagirli O, Araman A. Preparation and in vivo evaluation of dimenhydrinate buccal mucoadhesive films with enhanced bioavailability. *Drug Dev Ind Pharm*, **42(6)**, 916–925 (2016) https://doi.org/10.3109/03639045.2015.1091470

[48] Singh S, Jain S, Muthu MS, Tiwari S, Tilak R. Preparation and evaluation of buccal bioadhesive films containing clotrimazole. *AAPS PharmSciTech*, **9**, 660–667 (2008) https://doi.org/10.1208/s12249-008-9083-3

[49] Al-Japairai KA, Alkhalidi HM, Mahmood S, Almurisi SH, Doolaanea AA, Al-Sindi TA, Chatterjee B. Lyophilized

amorphous dispersion of telmisartan in a combined carrier-alkalizer system: Formulation development and in vivo study. *ACS Omega*, **5(50)**, 32466–32480 (2020) https://doi.org/10.1021/acsomega.0c04588

[50] Perioli L, Ambrogi V, Rubini D, Giovagnoli S, Ricci M, Blasi P, Rossi C. Novel mucoadhesive buccal formulation containing metronidazole for the treatment of periodontal disease. *J Control Release*, **95(3)**, 521–533 (2004) https://doi.org/10.1016/j.jconrel.2003.12.018

[51] Pawar O, Godge R, Shinde G, Barde K, Vikhe A. Design, development, and optimization of mucoadhesive buccal films of ganaxolone for enhanced bioavailability. *Journal of Applied Pharmaceutical Research*, **13(2)**, 95–107 (2025) https://doi.org/10.69857/joapr.v13i2.943

[52] Kumar C, Nanda A. Novel microwave-assisted solid dispersion technology enhances piroxicam dissolution and therapeutic efficacy: An in vitro and in vivo study. *Journal of Applied Pharmaceutical Research*, **13(1)**, 49–61 (2025) https://doi.org/10.69857/joapr.v13i1.921

[53] Kyaw Oo M, Mandal UK, Chatterjee B. Polymeric behavior evaluation of PVP K30-poloxamer binary carrier for solid dispersed nisoldipine by experimental design. *Pharm Dev Technol*, **22(1)**, 2–12 (2017) https://doi.org/10.3109/10837450.2015.1116568

[54] Jaouen V, Brayner R, Lantiat D, Steunou N, Coradin T. In situ growth of gold colloids within alginate films. *Nanotechnology*, **21(18)**, 185605 (2010) https://doi.org/10.1088/0957-4484/21/18/185605

[55] Rossi S, Ferrari F, Bonferoni MC, Caramella C. Characterization of chitosan hydrochloride-mucin rheological interaction: Influence of polymer concentration and polymer:mucin weight ratio. *Eur J Pharm Sci*, **12(4)**, 479–485 (2001) https://doi.org/10.1016/S0928-0987(00)00194-9

[56] Erdal MS, Gürbüz A, Tan SB, Güngör S, Özsoy Y. In vitro skin permeation and antifungal activity of naftifine microemulsions. *Turk J Pharm Sci*, **17(1)**, 43–50 (2020) https://doi.org/10.4274/tjps.galenos.2018.87699

[57] Hesaraki S, Barounian MH, Borhan S, Shahrezayee M, Nezafati N. Controlled release of a non-steroidal anti-inflammatory drug from a photocurable polymeric calcium phosphate cement. *J Biomater Sci Polym Ed*, **20**, 1–8 (2023) https://doi.org/10.1080/09205063.2023.2193495