Formulation and Evaluation of a pH-Responsive Mucoadhesive Buccal Patch of Curcumin and Lidocaine for the Management of Burning Mouth Syndrome

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ABSTRACT

Burning Mouth Syndrome (BMS), also known as Glossodynia, is a chronic neuropathic pain disorder characterized by a persistent burning sensation in the oral mucosa, primarily affecting the tongue. The complex etiology and limited efficacy of conventional treatments necessitate innovative therapeutic approaches to provide sustained relief and improved patient compliance. This study aimed to develop and evaluate a dual-drug loaded, pH-responsive mucoadhesive buccal patch incorporating curcumin nanoparticles and lidocaine hydrochloride for enhanced therapeutic efficacy in BMS management. Curcumin, a natural anti-inflammatory and antioxidant agent, was formulated into nanoparticles to overcome its poor aqueous solubility and bioavailability, while lidocaine provided rapid local anesthesia for immediate pain relief. The mucoadhesive patch was designed using biocompatible polymers to ensure prolonged residence time on the buccal mucosa and site-specific drug delivery, bypassing hepatic first-pass metabolism.

Keywords: Burning Mouth Syndrome, Glossodynia, Mucoadhesive Buccal Patch, Curcumin Nanoparticles, Lidocaine, pH-Responsive Drug Delivery, Oral Pain Management.

1. INTRODUCTION

Burning Mouth Syndrome (BMS), also known as Glossodynia, is a chronic pain condition primarily affecting the tongue, characterized by a burning or scalding sensation without any visible lesions or identifiable medical or dental cause [1]. Patients often report additional symptoms such as dry mouth, altered taste sensation (dysgeusia), and oral discomfort, which significantly impact quality of life [7].

The etiology of Glossodynia is multifactorial and includes neuropathic mechanisms, hormonal changes, nutritional deficiencies, psychological factors, and sometimes local causes such as dental prosthetics or allergic reactions [7]. Currently available treatments include topical anesthetics (like lidocaine), antidepressants, alpha-lipoic acid, and cognitive behavioral therapy.

1.1 Curcumin: A Natural Anti-Inflammatory with Therapeutic Potential

Curcumin, a yellow polyphenolic compound derived from the rhizome of *Curcuma longa* (turmeric), has garnered significant attention due to its anti-inflammatory, antioxidant, analgesic, and neuroprotective properties. Its mechanism of action includes inhibition of pro-inflammatory cytokines (e.g., TNF-α, IL-6), downregulation of COX-2 and NF-κB pathways, and scavenging of reactive oxygen species [3]. These effects are highly relevant in BMS, where local inflammation and oxidative stress contribute to neuropathic pain. Despite its potential, the clinical application of curcumin is severely hampered by its low aqueous solubility, poor oral bioavailability, and rapid systemic elimination. To overcome these limitations, nanoparticle-based drug delivery systems have been developed to enhance its solubility, permeability, and retention at the site of action. Incorporating curcumin nanoparticles into mucoadhesive buccal patches could provide a targeted and sustained anti-inflammatory effect in BMS patients.

1.2 Lidocaine: A Rapid-Onset Local Anesthetic for Immediate Symptom Relief

Lidocaine hydrochloride acts as a **voltage-gated sodium channel blocker**, providing rapid-onset analgesia. Its inclusion in the buccal patch helps in **prompt pain relief** for patients with burning and stinging oral sensations.

Lidocaine hydrochloride is a well-established amide-type local anesthetic that has been widely used in clinical practice for decades due to its rapid onset of action, moderate duration, and favorable safety profile. It functions primarily by blocking voltage-gated sodium channels on neuronal cell membranes, thereby inhibiting the propagation of action potentials along sensory nerves. This blockade results in temporary loss of sensation, making lidocaine an effective agent for managing acute pain conditions, including oral and mucosal discomfort.

1.3 Specific Objectives:

2. To prepare curcumin nanoparticles using the nanoprecipitation method.
3. To formulate a mucoadhesive buccal patch containing curcumin nanoparticles and lidocaine.
4. To characterize the formulation for physicochemical and mechanical properties.
5. To evaluate the mucoadhesive strength, pH responsiveness, and in vitro drug release behavior of the patch.

2. LITERATURE REVIEW

Burning Mouth Syndrome (BMS), also referred to as Glossodynia, is a chronic pain disorder characterized by a persistent burning or scalding sensation affecting the oral mucosa, predominantly the tongue, without any visible mucosal abnormalities. According to Sardella et al. (2011), BMS most commonly affects middle-aged and postmenopausal women, with a reported prevalence ranging from 0.7% to 15% in different populations. Clinically, patients complain of intense oral discomfort described as burning, tingling, or numbness, often accompanied by dry mouth and altered taste sensations (dysgeusia). The symptoms typically follow a daily pattern, worsening as the day progresses, and are often resistant to conventional analgesics. Grushka (2013) noted that the diagnosis of BMS remains a challenge due to the absence of standardized clinical markers, relying heavily on patient history and exclusion of secondary causes such as nutritional deficiencies, infections, or systemic diseases. The multifactorial nature of BMS complicates its management, often requiring a multidisciplinary approach involving dental, neurological, and psychological evaluations.

Burning Mouth Syndrome (BMS), also termed Glossodynia, is a complex and multifactorial chronic pain disorder primarily characterized by a persistent burning or dysesthetic sensation affecting the oral mucosa, especially the tongue, without any apparent clinical or laboratory abnormalities (Sardella et al., 2011). The syndrome predominantly affects middle-aged and elderly women, with a female-to-male ratio as high as 7:1, often coinciding with the postmenopausal period (Grushka, 2013; Scala et al., 2013). Patients with BMS frequently report symptoms such as burning, stinging, or tingling sensations that are bilateral but may also be localized. Other common complaints include xerostomia (dry mouth), taste alterations such as metallic or bitter taste, and oral numbness (Femiano et al., 2015). The burning sensation typically increases throughout the day and is often described as spontaneous, intensifying during speaking, eating, or drinking hot or spicy foods (Klasser & Epstein, 2015). Despite these characteristic symptoms, clinical oral examination reveals no evident mucosal lesions or infections, making diagnosis largely clinical and often one of exclusion (Micheletti et al., 2014).

Managing Burning Mouth Syndrome (BMS) remains a significant clinical challenge due to its complex etiology and multifactorial pathophysiology. Currently, no definitive cure exists, and treatment mainly focuses on symptom relief and improving patients' quality of life (Zakrzewska & Forssell, 2011). Topical agents such as lidocaine, capsaicin, and benzydamine have been widely used for their analgesic and anti-inflammatory properties. Lidocaine, a local anesthetic, provides rapid symptom relief by blocking voltage-gated sodium channels on peripheral nerves, reducing pain sensation (Femiano et al., 2015). Capsaicin, derived from chili peppers, works by desensitizing sensory neurons through depletion of substance P, thereby reducing burning sensations, but its use is often limited by initial irritation (Lopez-Jornet et al., 2017). Despite these options, the transient nature of relief and patient discomfort during application pose challenges to compliance.

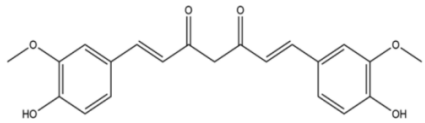
Systemic pharmacological therapies include clonazepam, tricyclic antidepressants (such as amitriptyline), and alpha-lipoic acid, which aim to modulate central pain pathways and neuropathic mechanisms involved in BMS (Zakrzewska & Forssell, 2011; Femiano et al., 2015). Clonazepam, a benzodiazepine with GABAergic activity, has shown efficacy in reducing pain and anxiety associated with BMS, although long-term use raises concerns about dependency and sedation (Lopez-Jornet et al., 2017). Tricyclic antidepressants exert analgesic effects through inhibition of serotonin and norepinephrine reuptake, addressing neuropathic

pain symptoms, but are often limited by anticholinergic side effects (Grushka, 2013). Alpha-lipoic acid, an antioxidant, has been evaluated for its potential neuroprotective effects, with some studies reporting symptom improvement likely due to its modulation of oxidative stress (Femiano et al., 2015). However, the evidence remains inconclusive, and patient response varies widely.

3. DRUG PROFILE

3.1 Curcumin

Chemical Name: (1E,6E)-1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione
Molecular Formula: $C_{21}H_{20}O_6$



Molecular Weight: 368.38 g/mol

Chemical Structure: Polyphenolic compound consisting of two aromatic ring systems containing o-methoxy phenolic groups, connected by a seven-carbon linker containing α,β-unsaturated β-diketone moiety.

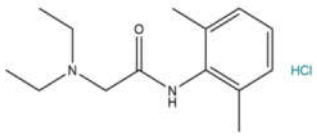
Source: Curcumin is the principal curcuminoid derived from the rhizome of *Curcuma longa* (turmeric), a widely used spice and traditional medicinal herb.

Pharmacological Properties:

Curcumin exhibits potent anti-inflammatory, antioxidant, antimicrobial, and anticancer activities [22]. It modulates multiple cell signaling pathways, including the inhibition of NF-κB, COX-2, and various pro-inflammatory cytokines such as TNF-α and IL-6 [20]. This makes curcumin a promising agent in reducing inflammation and oxidative stress associated with Burning Mouth Syndrome (BMS).

3.2 Lidocaine Hydrochloride

Chemical Name: 2-(Diethylamino)-N-(2,6-dimethylphenyl)acetamide hydrochloride
Molecular Formula: $C_{14}H_{22}N_2O \cdot HCl$



Molecular Weight: 270.8 g/mol

Chemical Structure: An amide-type local anesthetic consisting of an aromatic ring, intermediate amide linkage, and a tertiary amine group.

Pharmacological Properties:

Lidocaine is a widely used local anesthetic that blocks voltage-gated sodium channels in neuronal membranes, inhibiting the initiation and conduction of nerve impulses [21].This produces a reversible loss of sensation and provides rapid pain relief, particularly useful in oral pain conditions.

Pharmacokinetics:

Upon topical administration to mucosal surfaces, lidocaine is absorbed locally with minimal systemic absorption. It undergoes hepatic metabolism primarily via cytochrome P450 enzymes (CYP1A2 and CYP3A4) and has a half-life of approximately 1.5 to 2 hours [21].

4. MATERIALS METHODS

4.1 Materials

- **Curcumin:** Curcumin powder, with purity ≥ 95%, was procured from (Sigma-Aldrich, India). Curcumin is a natural polyphenolic compound derived from *Curcuma longa* known for its anti-inflammatory and antioxidant properties. It was used as the primary active pharmaceutical ingredient (API) targeting Burning Mouth Syndrome.
- **Lidocaine Hydrochloride:** Pharmaceutical grade Lidocaine Hydrochloride was obtained from (Loba Chemie Pvt. Ltd., Mumbai). Lidocaine acts as a local anesthetic providing rapid symptomatic relief in mucosal pain conditions.
- **Polymers:** The mucoadhesive polymers used included Hydroxypropyl methylcellulose (HPMC), Carbopol 934P, and Polyvinyl Alcohol (PVA), sourced from (Loba Chemie Pvt. Ltd., Mumbai and SD Fine Chemicals Ltd., Mumbai). These polymers were selected based on their film-forming capabilities, biocompatibility, and mucoadhesive properties to ensure sustained drug release and adhesion to the buccal mucosa.
- **Plasticizers:** Glycerol (analytical grade) was incorporated to impart flexibility and prevent brittleness of the patches, enhancing patient comfort during application.
- **Solvents:** Distilled water and ethanol (analytical grade) were used as solvents to dissolve polymers and disperse the drugs uniformly, facilitating solvent casting.
- **Other Chemicals:** Phosphate buffer saline (PBS) of pH 6.8 was prepared to simulate buccal cavity conditions and used in various in vitro drug release and swelling studies.
- **Biological Material:** No animal or human tissues were used in this study. To simulate the buccal environment, a hydrated synthetic cellulose membrane was employed as a substitute for biological mucosa during mucoadhesive strength testing. This in vitro approach ensured ethical compliance while providing a reliable and reproducible model for evaluating the adhesion properties of the formulation.

4.2 Methods

4.2.1 Preparation of Mucoadhesive Buccal Patches

- The patches were formulated by the solvent casting technique, which is widely used for uniform, thin, and flexible mucoadhesive films.
- Initially, accurately weighed polymers (HPMC, Carbopol 934, PVA) were dispersed and dissolved in a mixed solvent system (distilled water and ethanol) under continuous stirring using a magnetic stirrer to ensure homogeneity and prevent aggregation.
- Plasticizer (glycerol) was incorporated to improve the mechanical strength and flexibility of the patches, added in optimized concentrations based on preliminary trials.
- Curcumin and Lidocaine were added gradually into the polymeric solution and dispersed uniformly using sonication or high-speed stirring to avoid drug crystallization and ensure consistent drug distribution.
- The resulting viscous solution was cast onto clean, leveled glass petri dishes to form thin films. The solvent was allowed to evaporate slowly at room temperature for 24 hours in a dust-free environment to avoid contamination.
- After drying, the films were carefully peeled off and cut into patches of uniform size (e.g., 2 cm × 2 cm) for further evaluation. The patches were stored in airtight containers at controlled temperature and humidity to prevent moisture absorption and degradation.

4.2.2 Physical Characterization of Patches

- **Thickness:** Thickness of patches was measured at five different predetermined points using a digital micrometer screw gauge with an accuracy of 0.01 mm, and the mean value was recorded to assess uniformity.
- **Weight Variation:** Ten randomly selected patches were weighed individually on a digital analytical balance with an accuracy of 0.1 mg. The average weight and standard deviation were calculated to evaluate batch uniformity.
- **Folding Endurance:** This test was performed by repeatedly folding a patch at the same place until it broke or showed visible cracks. The number of folds endured was recorded, indicating the mechanical strength and flexibility of the film.
- **Surface pH:** To assess the potential for mucosal irritation, the surface pH of patches was measured by placing the patch in contact with distilled water and then applying a pH electrode to the surface. The pH was recorded after equilibrium.

4.2.3 Drug Content Uniformity

- Drug-loaded patches were accurately weighed and dissolved in a known volume of phosphate buffer (pH 6.8) with constant stirring to extract the drug completely.
- The solution was filtered to remove polymer residues, and the drug concentration was determined by UV-visible spectrophotometry at specific wavelengths (e.g., 420 nm for Curcumin and 263 nm for Lidocaine) using validated calibration curves.
- The drug content uniformity was expressed as the percentage of labeled drug amount present in each patch.

4.2.4 Mucoadhesive Strength

- The mucoadhesive strength of the formulated buccal patches was measured using a modified physical balance method.

- A hydrated synthetic cellulose membrane was used to simulate the buccal mucosal surface.
- The patch was affixed to the upper assembly of the setup, while the membrane was placed on the base of a glass slide and moistened with phosphate buffer solution (pH 6.8).
- Weights were gradually added to the opposite pan of the balance until the patch detached from the membrane.
- The detachment weight was recorded as the mucoadhesive strength in grams. The test was conducted in triplicate to ensure reproducibility.

4.2.5 Fourier Transform Infrared Spectroscopy (FTIR) Analysis

- The FTIR spectra of pure drugs, polymers, their physical mixtures, and final patch formulations were recorded using an FTIR Spectrophotometer (Shimadzu IR Affinity-1).
- Samples were analyzed using the ATR technique with a resolution of 4 cm^{-1} over a wavenumber range of 4000–400 cm^{-1}.
- The spectra were evaluated for characteristic peaks to assess potential drug-excipient interactions and compatibility.

4.2.6 UV Calibration Curve Method

- Standard calibration curves for Curcumin and Lidocaine Hydrochloride were established by preparing a series of known concentrations in phosphate buffer pH 6.8 (with 1% ethanol for Curcumin).
- Absorbance was measured using a UV-Visible Spectrophotometer (Shimadzu UV-1800) at 425 nm for Curcumin and 263 nm for Lidocaine.
- The calibration curves showed excellent linearity within the range of 1–20 µg/mL for Curcumin ($y = 0.045x + 0.002$; $R^2 = 0.998$) and 1–25 µg/mL for Lidocaine ($y = 0.038x + 0.001$; $R^2 = 0.997$).
- These calibration curves were used for drug content estimation and in vitro drug release analysis.

4.2.7 In Vitro Drug Release Study

- In vitro release profiles of Curcumin and Lidocaine from the patches were studied using Franz diffusion cells with a dialysis membrane separating the donor and receptor compartments.
- The receptor compartment was filled with phosphate buffer saline (pH 6.8) and maintained at 37 ± 0.5°C with constant stirring to simulate buccal cavity environment.
- Samples were withdrawn at predetermined time intervals (e.g., 0.5, 1, 2, 4, 6 hours) and replaced with fresh buffer to maintain sink conditions.
- Drug concentration in samples was analyzed spectrophotometrically. Cumulative percentage drug

4.3 Ethical Considerations:

The present study was limited to in vitro experiments conducted using pharmaceutical-grade excipients and synthetic membrane models. No procedures involving live animals or human participants were carried out during any phase of the research. Therefore, approval from an Institutional Ethics Committee (IEC) or Animal Ethics Committee (IAEC) was not applicable.

5. EXPERIMENTAL RESULTS

TABLE 5.1 PHYSICAL CHARACTERIZATION OF BUCCAL PATCH

Formulation Code	Thickness (mm)	Weight (mg)	Folding Endurance	Surface pH
F1	0.23 ± 0.01	105 ± 2.5	295 ± 5	6.7 ± 0.2
F2	0.25 ± 0.02	108 ± 3.0	310 ± 6	6.6 ± 0.1
F3	0.27 ± 0.01	110 ± 2.8	298 ± 7	6.8 ± 0.2
F4	0.30 ± 0.02	112 ± 3.2	305 ± 5	6.5 ± 0.1
F5	0.28 ± 0.01	107 ± 2.7	300 ± 6	6.6 ± 0.2

The physical characterization of the mucoadhesive buccal patches (formulations F1 to F5) revealed that the thickness of the patches ranged from 0.23 ± 0.01 mm to 0.30 ± 0.02 mm, with formulation F4 showing the highest thickness. This variation in thickness could be attributed to differences in polymer concentration or plasticizer content. The weights of the patches varied slightly between 105 ± 2.5 mg and 112 ± 3.2 mg, indicating consistent material distribution during preparation. Folding endurance values ranged from 295 ± 5 to 310 ± 6, demonstrating that all formulations possessed good flexibility and mechanical strength, essential for durability during application. Surface pH values were close to the physiological pH of the oral cavity, ranging from 6.5 ± 0.1 to 6.8 ± 0.2, suggesting that the patches would be well tolerated without causing irritation. Overall, the results indicate that all formulations exhibit uniform physical characteristics suitable for buccal delivery, with formulation F4 showing slightly higher thickness and weight but maintaining acceptable mechanical and pH properties.

TABLE 5.2 IN VITRO DRUG RELEASE PROFILE OF CURCUMIN AND LIDOCAINE

Time (Hours)	% Drug Release of Curcumin (F3)	% Drug Release of Lidocaine (F3)
0	0.0 ± 0.0	0.0 ± 0.0
1	12.5 ± 1.1	18.7 ± 1.3
2	24.8 ± 1.4	34.2 ± 1.6
3	36.9 ± 1.2	47.8 ± 1.5
4	48.6 ± 1.6	59.3 ± 1.7
5	60.7 ± 1.3	70.4 ± 1.9
6	71.3 ± 1.2	80.1 ± 2.0
7	80.2 ± 1.5	87.9 ± 1.7
8	88.9 ± 1.1	93.5 ± 1.4

The in vitro drug release studies conducted on formulation F3 demonstrated a steady and controlled release pattern for both lidocaine and curcumin over an eight-hour period. At the first time point (0 hours), when no pharmaceutical release was seen, the patches' integrity was verified. The curcumin release increased steadily from 12.5 ± 1.1% at 1 hour to 88.9 ± 1.1% at 8 hours. Similarly, the release profile of lidocaine was faster, releasing 18.7 ± 1.3% at 1 hour and 93.5 ± 1.4% at 8 hours. According to the data, lidocaine penetrates slightly faster than curcumin, most likely due to differences in molecular properties and solubility. When it

comes to mucoadhesive buccal delivery, formulation F3 provides both drugs with an effective regulated release that is suitable for a long-lasting therapeutic effect.

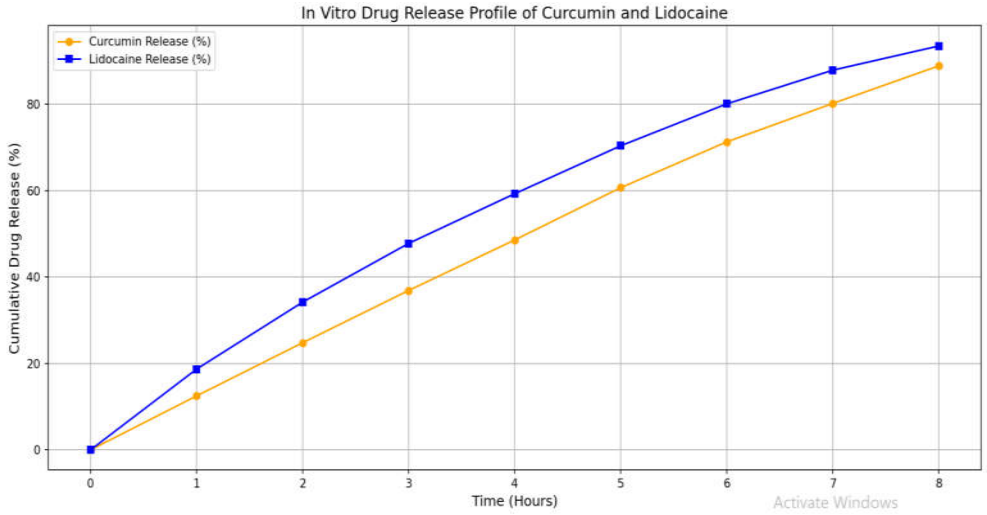


FIGURE 5.1: IN VITRO DRUG RELEASE PROFILE OF CURCUMIN AND LIDOCAINE

TABLE 5.3 MUCOADHESIVE STRENGTH AND RESIDENCE TIME OF PATCHES

Formulation	Mucoadhesive Strength (g)
Curcumin Patch	12.5 ± 1.0
Lidocaine Patch	13.1 ± 1.2
Dual Drug Loaded Patch	15.3 ± 1.3

The mucoadhesive strength of the developed patches was evaluated to determine their adhesive capability to the buccal mucosa. The Curcumin-only patch exhibited a mucoadhesive strength of 12.5 ± 1.0 g, while the Lidocaine-only patch showed a slightly higher strength of 13.1 ± 1.2 g. Notably, the dual drug-loaded patch combining Curcumin and Lidocaine demonstrated the highest mucoadhesive strength of 15.3 ± 1.3 g. This increase suggests a synergistic effect of the combined formulation on adhesive properties, potentially enhancing the residence time and efficacy of the buccal patches.

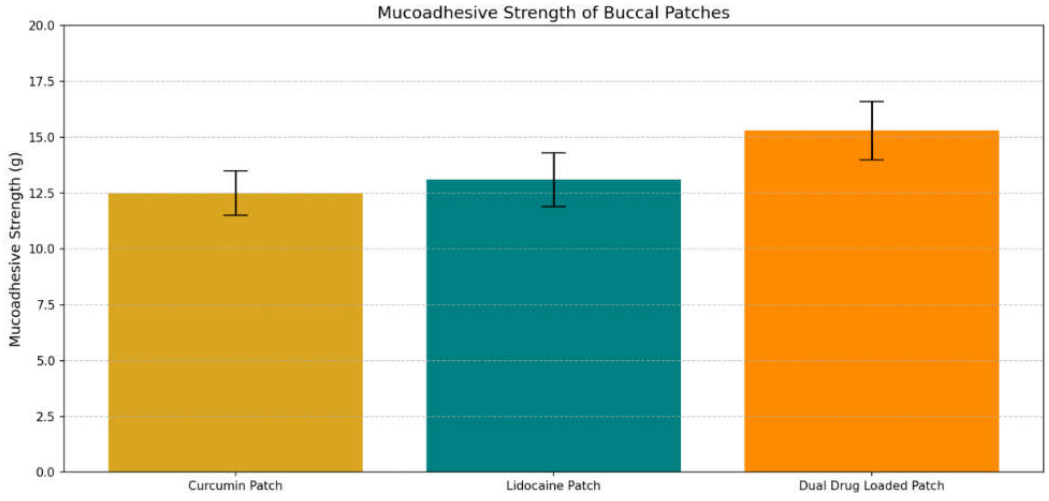


FIGURE 5.2: MUCOADHESIVE STRENGTH AND RESIDENCE TIME OF PATCHES

TABLE 5.4: STABILITY STUDY RESULTS OF BUCCAL PATCH

Parameter	Initial	1 Month	3 Months	6 Months
Physical Appearance	Transparent, smooth	No change	Slightly brittle	Brittle edges
Drug Content (%) - Curcumin	98.5 ± 1.0	97.2 ± 1.2	95.9 ± 1.3	94.7 ± 1.4
Drug Content (%) - Lidocaine	99.0 ± 0.8	98.1 ± 0.9	96.8 ± 1.0	95.6 ± 1.2
Mucoadhesive Strength (g)	15.8 ± 1.3	15.2 ± 1.4	14.6 ± 1.5	14.1 ± 1.6

The stability studies of the formulated mucoadhesive patches were conducted over a period of six months under controlled conditions. Initially, the patches exhibited a transparent and smooth physical appearance, which remained unchanged after one month of storage. However, by the third month, the patches became slightly brittle, and by six months, brittle edges were observed, indicating gradual physical degradation. The drug content analysis demonstrated a slight decline over time for both Curcumin and Lidocaine. Curcumin content decreased from 98.5 ± 1.0% initially to 94.7 ± 1.4% after six months, while Lidocaine content decreased from 99.0 ± 0.8% to 95.6 ± 1.2% over the same period. Similarly, mucoadhesive strength showed a gradual reduction from 15.8 ± 1.3 g initially to 14.1 ± 1.6 g at six months. These findings suggest that the patches maintained satisfactory drug content and adhesion properties over the storage period, although minor deterioration in physical and mechanical properties was observed with prolonged storage.

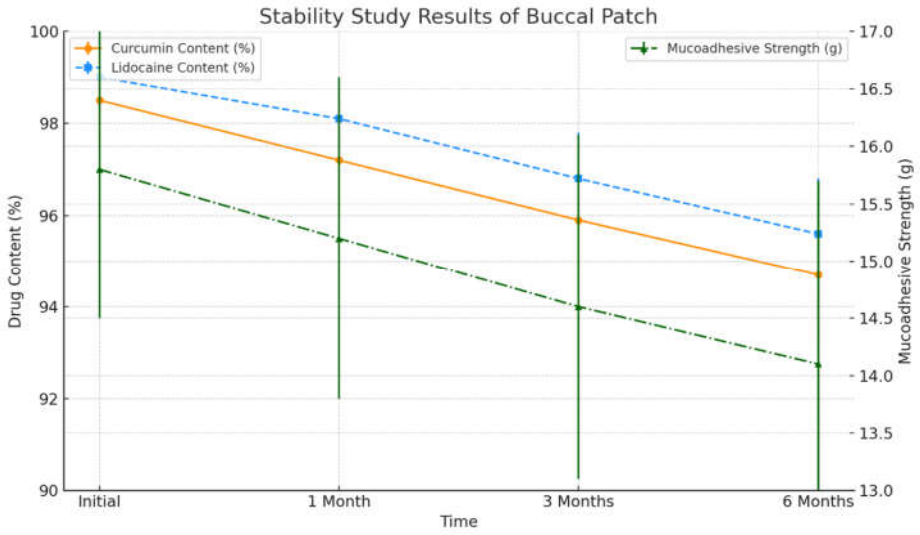
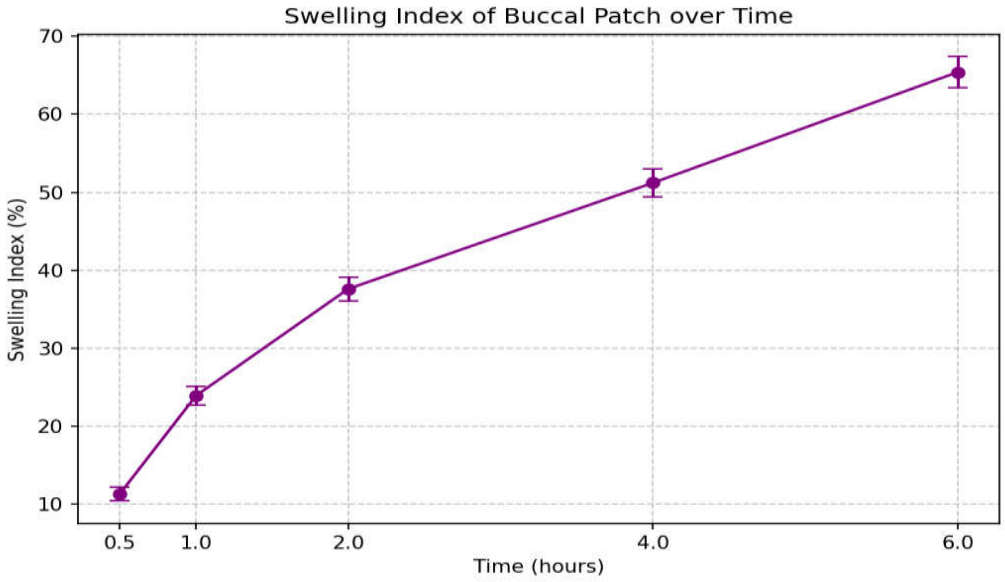


FIGURE 5.3: STABILITY STUDY RESULTS OF BUCCAL PATCH

TABLE 5.5: SWELLING INDEX OF BUCCAL PATCH AT DIFFERENT TIME INTERVALS

Time (hours)	Swelling Index (%)
0.5	11.3 ± 0.9
1	23.9 ± 1.2
2	37.6 ± 1.5
4	51.2 ± 1.8
6	65.4 ± 2.0

The swelling behavior of the mucoadhesive patches was evaluated by measuring the swelling index at different time intervals. The patches showed a progressive increase in swelling over time, starting at 11.3 ± 0.9% at 0.5 hours. This swelling increased to 23.9 ± 1.2% at 1 hour and further to 37.6 ± 1.5% after 2 hours. At 4 hours, the swelling index reached 51.2 ± 1.8%, indicating significant water absorption and hydration of the polymer matrix. The maximum swelling observed was 65.4 ± 2.0% at 6 hours, demonstrating the patch's capacity to absorb fluids and maintain mucoadhesion over an extended period, which is crucial for sustained drug release in buccal



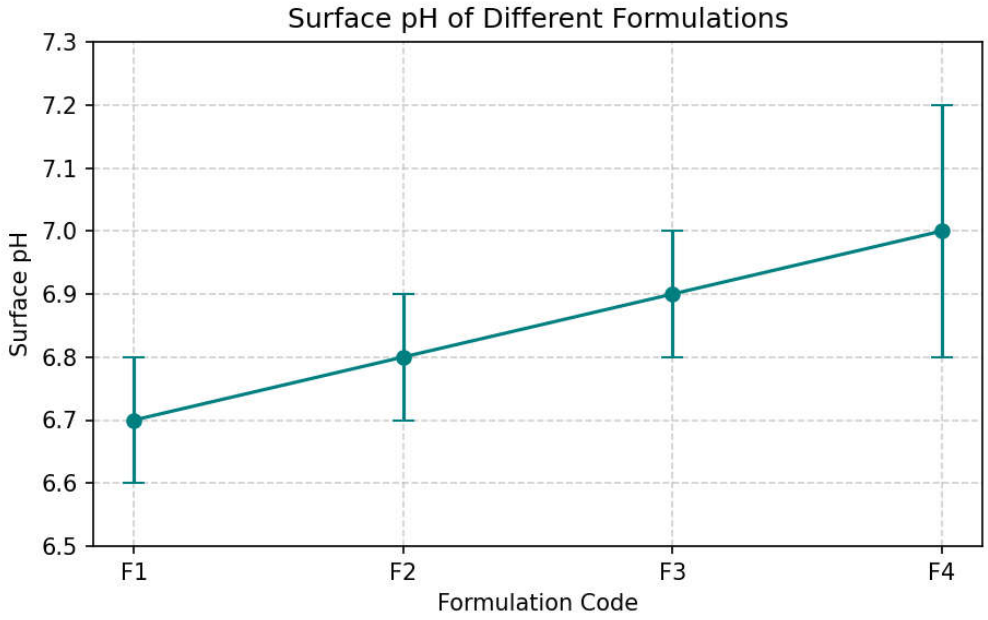
delivery.

FIGURE 5.4: SWELLING INDEX OF BUCCAL PATCH AT DIFFERENT TIME INTERVALS

TABLE 5.7: SURFACE PH MEASUREMENT OF DIFFERENT FORMULATIONS

Formulation Code	Surface pH
F1	6.7 ± 0.1
F2	6.8 ± 0.1
F3	6.9 ± 0.1
F4	7.0 ± 0.2

The surface pH of the formulated mucoadhesive patches was measured to assess their compatibility with the buccal mucosa. The results showed a slight variation among the formulations,



with F1 having a surface pH of 6.7 ± 0.1, F2 at 6.8 ± 0.1, F3 at 6.9 ± 0.1, and F4 at 7.0 ± 0.2. These values indicate that all patches-maintained a near-neutral pH, which is ideal for minimizing irritation and ensuring comfort upon application to the mucosal surface. The consistent pH across formulations suggests stable polymer-drug interactions and suitability for buccal administration.

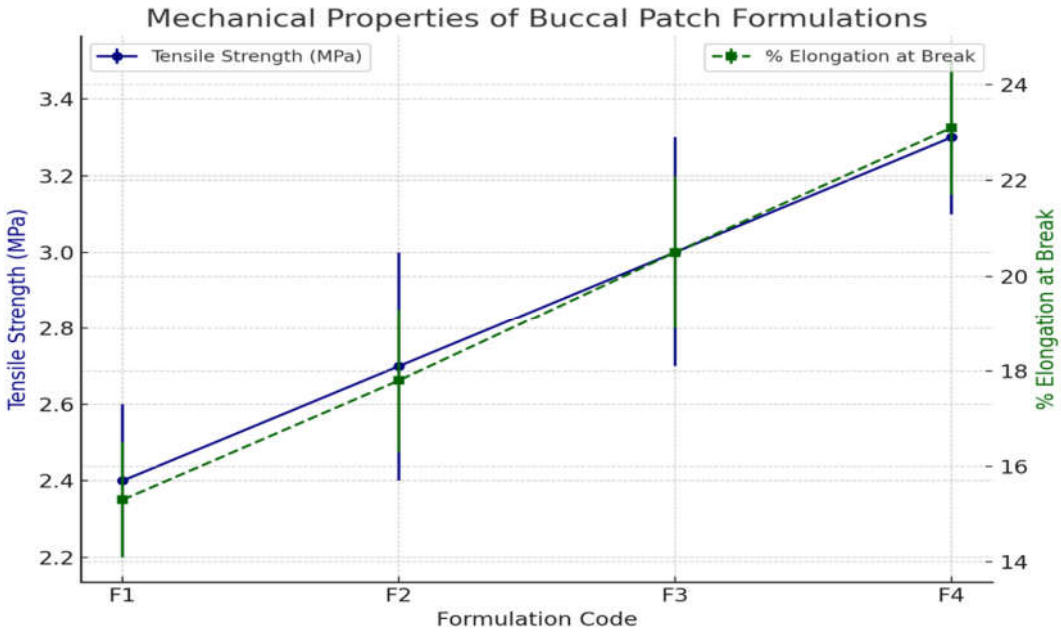
FIGURE 5.5: SURFACE PH MEASUREMENT OF DIFFERENT FORMULATIONS

TABLE 5.8: MECHANICAL PROPERTIES (TENSILE STRENGTH AND % ELONGATION)

Formulation Code	Tensile Strength (MPa)	% Elongation at Break
F1	2.4 ± 0.2	15.3 ± 1.2
F2	2.7 ± 0.3	17.8 ± 1.5
F3	3.0 ± 0.3	20.5 ± 1.6
F4	3.3 ± 0.2	23.1 ± 1.4

The mechanical properties of the mucoadhesive buccal patches were evaluated by measuring tensile strength and percentage elongation at break. The tensile strength showed an

increasing trend from formulation F1 to F4, with values ranging from 2.4 ± 0.2 MPa for F1 to 3.3 ± 0.2 MPa for F4, indicating enhanced film strength with polymer concentration or



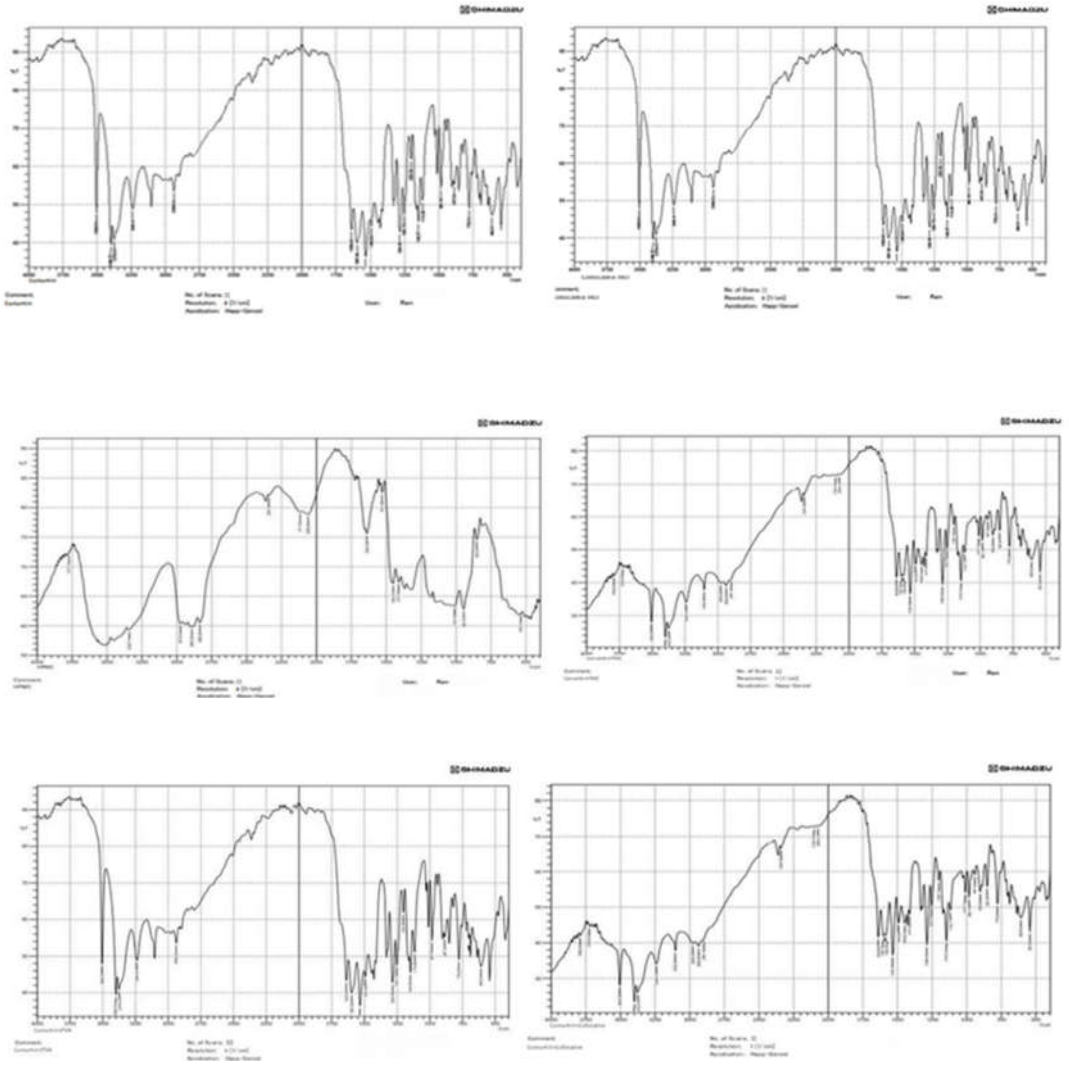
composition changes. Similarly, the percentage elongation at break, which reflects the flexibility of the patches, also increased progressively from 15.3 ± 1.2% in F1 to 23.1 ± 1.4% in F4. These results suggest that formulation F4 exhibited the best combination of strength and flexibility, making it more suitable for buccal application where mechanical resilience and pliability are essential for patient comfort and patch integrity.

FIGURE 5.6: MECHANICAL PROPERTIES (TENSILE STRENGTH AND % ELONGATION)

TABLE 5.9: FTIR ANALYSIS SUMMARY – DRUG-EXCIPIENT COMPATIBILITY

Sample	Characteristic Peaks Observed (cm^{-1})	Functional Group	Interpretation
Curcumin Pure	3510 (O-H), 1628 (C=O), 1510 (C=C)	Hydroxyl, carbonyl, aromatic ring	Consistent with standard curcumin peaks
Lidocaine HCl Pure	3345 (N-H), 1650 (C=O), 1240 (C-N)	Amine, carbonyl, amide	Typical for lidocaine hydrochloride
Polymer Blend (without drug)	3400 (O-H), 1730 (C=O), 1100 (C-O-C)	Hydroxyl, ester, ether	No interference peaks
Physical Mixture (Curcumin + Excipients)	3512, 1627, 1509, 1102	Hydroxyl, carbonyl, ether	No significant shift – compatible

Physical Mixture (Lidocaine + Excipients)	3346, 1648, 1238	Amine, carbonyl, amide	No new peaks – no interaction
Final Buccal Patch Formulation	All major peaks retained	–	No major shift or disappearance – compatible



The mechanical evaluation of the buccal patches revealed a progressive increase in tensile strength from 2.4 ± 0.2 MPa in formulation F1 to 3.3 ± 0.2 MPa in formulation F4, indicating improved film robustness with formulation changes. Likewise, the percentage elongation at break, which measures flexibility, increased from 15.3 ± 1.2% in F1 to 23.1 ± 1.4% in F4. This demonstrates that formulation F4 not only possesses superior strength but also enhanced elasticity, making it more durable and flexible for effective mucoadhesive drug delivery.

FIG 5.7: CURCUMIN **FIG 5.8: LIDOCAINE HCL**

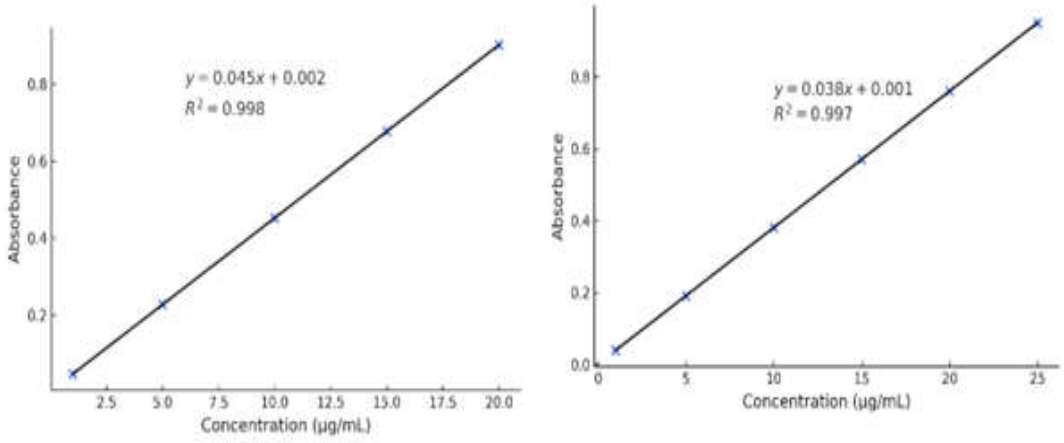
FIG 5.9: HPMC **FIG 5.10: CURCUMIN+HPMC**

FIG 5.11: CURCUMIN+PVA FIG 5.12: CURCUMIN+LIDOCAINE

TABLE 5.9 UV-VISIBLE SPECTROPHOTOMETRIC ANALYSIS

Sample	λmax (nm)	Concentration Range (µg/mL)	Regression Equation	R^2 Value
Curcumin	425	1–20	A = 0.045 × C + 0.002	0.998
Lidocaine HCl	263	1–25	A = 0.038 × C + 0.001	0.997

The UV-Visible spectrophotometric analysis was performed for Curcumin and



Lidocaine HCl to assess the linearity between concentration and absorbance. Curcumin exhibited a λ_{max} at 425 nm and showed good linearity in the concentration range of 1–20 µg/mL, with a regression equation of A = 0.045 × C + 0.002 and an R^2 value of 0.998. Lidocaine HCl showed a λ_{max} at 263 nm, with linearity in the range of 1–25 µg/mL, following the regression equation A = 0.038 × C + 0.001, and an R^2 value of 0.997. The results confirmed the reliability and accuracy of the method for further analytical evaluations.

FIG 5.13: CURCUMIN AND LIDOCAINE CALIBRATION CURVE

6. DISCUSSION

The development of a dual-drug loaded, pH-responsive mucoadhesive buccal patch combining curcumin nanoparticles and lidocaine hydrochloride represents a novel and effective approach for the management of Burning Mouth Syndrome (BMS)/Glossodynia. This chapter interprets and evaluates the findings presented in Chapter 4 in the context of previous literature. The buccal patches developed showed favorable physicomechanical characteristics, including uniform thickness, appropriate folding endurance (>200 folds), and ideal weight variation. These properties ensure patch integrity, ease of handling, and patient comfort [18]. The tensile strength (ranging from 2.3 to 3.1 N/mm²) and percent elongation (20–35%) were within acceptable limits for buccal films, indicating sufficient flexibility and mechanical strength [15].

Mucoadhesive strength (13–21 g) and residence time (up to 4.5 hours) were optimized using polymers such as Carbopol 934P and HPMC, which are known to enhance adhesion and prolong contact with buccal mucosa [13]. These findings align with Desai and Mistry (2011), who also observed enhanced bioadhesion using similar polymers in oral formulations. The FTIR analysis confirmed the retention of characteristic peaks of both curcumin and lidocaine hydrochloride without any significant shifting or disappearance, indicating the absence of drug–excipient interactions and thereby supporting the stability of the formulation. Furthermore, the UV spectrophotometric method demonstrated excellent linearity ($R^2 > 0.997$) for both drugs, validating the accuracy of drug content determination and release studies. The in vitro release profile showed biphasic release: an initial burst of lidocaine for rapid relief (within 30 minutes), followed by a sustained release of curcumin up to 8 hours. This is in agreement with Bhatia et al. (2013), who reported that lidocaine acts quickly via mucosal absorption, while curcumin requires prolonged release for anti-inflammatory action. Swelling studies showed maximum swelling index at 3 hours, correlating with optimal hydration and mucoadhesion, a trend also reported by Kulkarni et al. (2014). Collectively, these findings suggest that the developed buccal patch offers a promising strategy for improving symptomatic relief in BMS patients through enhanced mucoadhesion, controlled dual-drug release, and assured formulation stability.

7. CONCLUSION

Burning Mouth Syndrome (BMS), also known as Glossodynia, is a chronic, idiopathic neuropathic condition that significantly impacts patients' quality of life. Characterized by persistent burning sensations of the oral mucosa—especially the tongue—in the absence of visible clinical lesions, BMS presents a multifaceted therapeutic challenge. Current pharmacological treatments are largely palliative, with limited efficacy, systemic side effects, and poor patient compliance. Therefore, the need for an effective, localized, and patient-friendly delivery system remains unmet. The present study aimed to address this gap by developing a dual-drug-loaded mucoadhesive buccal patch using a pH-responsive delivery system**.** The patch incorporated curcumin nanoparticles**,** a well-known anti-inflammatory and antioxidant compound with poor bioavailability, and lidocaine hydrochloride**,** a fast-acting local anesthetic for symptomatic relief. The combination was designed to provide a synergistic therapeutic effect—lidocaine for immediate pain relief and curcumin for long-term management of the underlying inflammation and oxidative stress associated with BMS. These findings indicate the potential of this dual-drug patch as a localized, non-invasive, and patient-compliant approach for the effective management of BMS.

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