Title Page

# Design, Development and Characterization of Oral Mucoadhesive Gel Containing Benzydamine Hydrochloride

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**ABSTRACT**

**Oral mucoadhesive gels have emerged as one of the most promising platforms for both local and systemic drug delivery via the oral mucosa. These systems can significantly prolong the residence time of the dosage form at the site of absorption, thereby enhancing drug bioavailability and therapeutic efficacy. Delivery through the oral mucosa also offers distinct advantages, including bypassing hepatic first-pass metabolism, protection of the drug from gastrointestinal degradation, rapid onset of action through direct absorption into the systemic circulation, and improved patient compliance due to ease of application.**

**The primary objective of the present study was to design, develop, and characterize an oral mucoadhesive gel containing Benzydamine Hydrochloride, a locally acting non-steroidal anti-inflammatory and analgesic agent, for the treatment of oral lesions such as aphthous ulcers. A total of nine different gel formulations (F1 to F9) were developed using varying concentrations of Carbopol 934, HPMC K15M, and Sodium Alginate as mucoadhesive polymers, with glycerin and propylene glycol as co-solvents and penetration enhancers. Methyl paraben was incorporated as a preservative. The gels were prepared using mechanical stirring to ensure uniform dispersion and homogeneity.**

**Among all the formulations, Batch F4 was found to be the optimized batch with the best combination of mucoadhesive strength, viscosity, spreadability, and in-vitro drug diffusion. The formulation also showed stability over one month, confirming its potential for practical use. Thus, the study demonstrates that a well-designed mucoadhesive gel of Benzydamine Hydrochloride can serve as an effective, patient-friendly treatment option for oral ulcers and related conditions.**

**Keywords: Mucoadhesive gel, Benzydamine Hydrochloride, HPMC K15M, Oral ulcer, In-vitro study.**

**Introduction**

## Aphthous Stomatitis (Mouth Ulcer)

The term *aphthous* originates from the Greek word *aphtha*, meaning ulcer. Aphthous stomatitis, commonly known as recurrent aphthous stomatitis (RAS), is one of the most prevalent ulcerative conditions affecting the oral mucosa. It is characterized by extremely painful, recurrent solitary or multiple ulcers within the oral cavity and upper throat. These ulcers are typically small, round or ovoid with well-defined margins, featuring a gray or yellowish necrotic floor surrounded by an erythematous halo [1].

The condition was first described as early as 400 B.C. by Hippocrates. It remains widely recognized today under various names such as canker sores, cold sores (though technically distinct), recurrent aphthous stomatitis (RAS), or recurrent aphthous ulcers (RAU). RAS affects approximately 10–20% of the population, with a recurrence rate of around 50% within three months .The associated pain

significantly impacts daily activities such as eating, speaking, and swallowing, thereby reducing patients' quality of life[ 1].

Aphthous stomatitis is clinically classified into three forms: **minor aphthae**, **major aphthae**, and **herpetiform ulcers.**

.Minor aphthae are the most common subtype, accounting for 75–85% of all RAS cases. These ulcers typically measure less than 10 mm in diameter and heal spontaneously within 10–14 days without scarring. They predominantly occur on non-keratinized mucosal surfaces such as the buccal and labial mucosa and the floor of the mouth.[2]

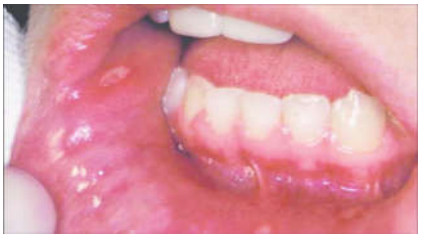


Fig no-1. minor. Aphthae

Major aphthae, also known as Sutton's disease, are a less common but more severe form of recurrent aphthous stomatitis. These ulcers typically exceed 10 mm in diameter, cause deeper mucosal ulceration, and often heal with scarring. Major aphthae account for approximately 10–15% of RAS cases. Healing time is prolonged compared to minor aphthae, with lesions persisting for 10–20 days or, in some cases, several weeks to months. They are commonly located on the soft palate, lips, and oropharyngeal region [2].

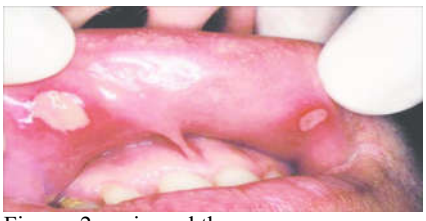
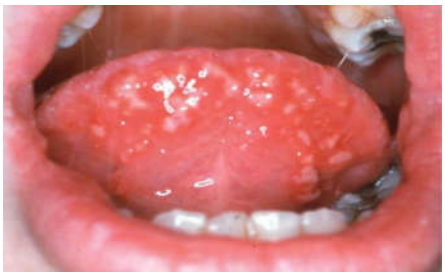


Fig no -2. major aphthae

Herpetiform aphthae represent a rare variant of recurrent aphthous stomatitis, accounting for approximately 7–10% of cases. These ulcers are typically very small, measuring about 2–3 mm in diameter, but are numerous — often appearing as clusters of up to 100 ulcers simultaneously. Individual lesions may coalesce, forming larger, irregular ulcerations. Despite their extensive presentation, herpetiform ulcers generally heal within 7–10 days without leaving scars [3].

Fig no-3 herpetiform aphthous



**Causes of Aphthous Stomatitis (Mouth Ulcers)**

The exact etiology of recurrent aphthous stomatitis (RAS) remains multifactorial and incompletely understood. Several predisposing and contributing factors have been identified, including genetic, environmental, nutritional, microbial, and immunological aspects.

**a) Genetic Predisposition**
A positive family history is observed in approximately 40% of patients with RAS, suggesting a genetic link. Individuals with a hereditary predisposition may develop ulcers at an earlier age and tend to experience more severe or recurrent episodes [4].

**b) Mechanical Injury**
Trauma from dental procedures, local anesthetic injections, sharp teeth, ill-fitting dentures, or aggressive tooth brushing can damage the oral mucosa, increasing susceptibility to ulceration. Reduced salivary flow may further compromise mucosal protection [5].

**c) Micronutrient and Vitamin B12 Deficiencies**
Deficiencies of hematinic factors such as folic acid, iron, and vitamin B12 have been implicated in RAS development. Individuals with RAS are reported to have these deficiencies up to twice as often as healthy controls, although findings vary due to genetic and dietary differences [6].

**d) Stress and Psychological Factors**
Psychological stress is a well-documented precipitating factor. Elevated stress levels often correlate with ulcer onset, and studies have shown reduced incidence following antidepressant therapy. Stress-induced parafunctional habits, such as cheek or lip biting, may also contribute [7].

**e) Food Allergies**
Certain foods, including chocolate, coffee, almonds, cereals, peanuts, strawberries, tomatoes, cheese, and gluten-containing products like wheat, have been reported as potential triggers for aphthous ulcers [8].

**f) Microbial Factors**
Although no definitive infectious agent has been linked to RAS, possible associations with L-form streptococci, adenoviruses, herpes simplex virus (HSV), varicella-zoster virus, and cytomegalovirus have been explored. Current evidence suggests that these microorganisms are unlikely to be direct causes; for example, antiviral agents such as acyclovir have shown no therapeutic benefit in RAS prevention [9].

**g) Tobacco Smoking**
Paradoxically, smoking has been associated with a lower prevalence and severity of RAS. Some individuals experience recurrence upon smoking cessation, and nicotine replacement has been suggested to reduce ulcer frequency [10].

**h) Immunopathogenesis**
RAS is believed to involve cell-mediated immune dysfunction. Patients may show increased antibody-dependent cellular cytotoxicity, elevated serum immunoglobulin levels, and altered T-cell subsets,

including increased T-helper cells and decreased T-suppressor cells. Histological evidence supports an active role of infiltrating T-lymphocytes in ulcer formation [11].

**i) Hormonal Factors**
Hormonal fluctuations may influence RAS occurrence, particularly in women. Some studies report ulcer exacerbation during menstruation and improvement during pregnancy, though findings remain inconsistent [12].

**j) Drug-Induced Ulcers**
Certain medications, including non-steroidal anti-inflammatory drugs (NSAIDs) such as diclofenac, and β-blockers, have been linked to ulcer development resembling RAS. These ulcers typically resolve upon discontinuation of the offending drug [12].

## Mucoadhesive Drug Delivery System

Mucoadhesive drug delivery systems utilize the bioadhesive properties of specific polymers that become adhesive upon hydration, enabling prolonged retention of the drug at the site of application. Bioadhesion refers to the attachment between two materials, at least one of which is biological, through interfacial forces. When the adhesion occurs between a polymer and the mucin layer of a mucosal tissue, the phenomenon is specifically termed *mucoadhesion*.

Mucoadhesive systems can be administered via various routes, including buccal, oral, vaginal, rectal, nasal, and ocular pathways. Such systems offer the advantages of targeted drug delivery, extended residence time, and improved therapeutic efficacy [13].

## Oral Mucosal Drug Delivery

Drug delivery through the oral mucosa has gained significant attention due to its easy accessibility and potential to bypass hepatic first-pass metabolism, thereby enhancing bioavailability and patient compliance. The buccal and sublingual routes are the most common, as the non-keratinized epithelium (e.g., buccal mucosa, floor of the mouth, ventral tongue) provides a relatively permeable barrier for drug transport. Hydrophilic and large molecules mainly use paracellular pathways, while lipophilic drugs permeate transcellularly. Mucoadhesive dosage forms — such as gels, tablets, films, patches, and mouthwashes — have been widely developed for local conditions like aphthous ulcers, periodontitis, and oropharyngeal infections. Studies have demonstrated that mucoadhesive patches and tablets can improve local retention, sustain drug release, and reduce side effects compared to conventional treatments. Recent clinical trials and products, including buccal patches for buprenorphine, mucoadhesive patches for photodynamic therapy, and novel buccal insulin aerosols, further highlight the versatility of this route for both local and systemic therapy [14-15].

## Mucoadhesion Theories

Several theories have been proposed to explain the mechanisms underlying mucoadhesion — the interaction between a mucoadhesive polymer and the mucosal surface.

The Wetting Theory suggests that adhesion depends on the ability of a polymer to spread and penetrate surface irregularities.

The Absorption Theory attributes adhesion to chemical interactions like hydrogen bonding and Van der Waals forces.

The Electronic Theory describes adhesion through electron transfer and the formation of an electronic double layer.

The Mechanical Theory involves interlocking of the adhesive into surface roughness, increasing contact area.

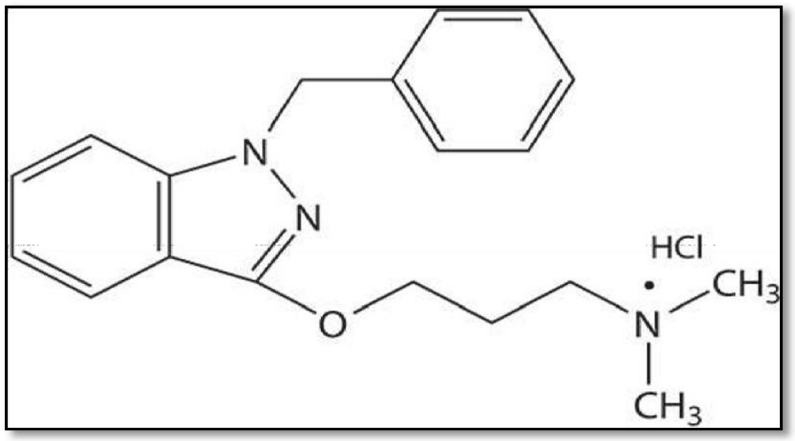
The Fracture Theory relates the adhesive bond strength to the force required for separation.

The Diffusion Theory explains mucoadhesion by interpenetration of polymer and mucus chains, forming an entangled layer that stabilizes the bond [16].

**Benzydamine Hydrochloride (BZH)[17-19]**

- **Generic Name:** Benzydamine Hydrochloride
- **Chemical Name:** 3-(1-benzylindazol-3-yloxy) propyldimethylamine hydrochloride
- **Empirical Formula:** $C_{19}H_{23}N_3O \cdot HCl$
- **Molecular Weight:** 309.84 g/mol
- **Appearance:** White crystalline powder
- **Solubility:** Very soluble in water; freely soluble in ethanol; practically insoluble in ether (BP, 2009)
- **Melting Point:** 161–164 °C

- **Pharmacological Action:** Locally acting NSAID with anti-inflammatory, local anesthetic, analgesic, antimicrobialand membrane-stabilizing effects (Krzeszowski et al., 2015).
- **Key Pharmacokinetics:** Well absorbed; peak plasma levels ~1.5 hrs; plasma half-life ~8 hrs; mainly metabolized by liver and excreted in urine.
- **Common Dosage:** 1–2 mg applied locally every 3 hrs as needed (adults); not recommended for children under 6 years.
- **Adverse Effects:** Mainly mild local reactions: oral numbness, burning sensation, dry mouth.
- **Drug Interactions:** No known significant interactions.




- **Figure no-4. Chemical Structure of Benzydamine Hydrochloride**

## 2. Materials and Methods

### 2.1 Materials

| Sr. No | Materials | Supplied By |
|---|---|---|
| 1 | Benzadamine hydrochloride | Swapnarooppharmacuticles chh.sambhajinagar |
| 2 | Hpmc K100m | Prayoginalaboratories |
| 3 | Carbapol 934 | Tharmosil fine chem industrise |
| 4 | Sodium alginate | Yarrow chem pharma pvt ltd |
| 5 | Methyl Paraben | Tharmosil fine chem industrise |
| 6 | Glycerine | Prayoginalaboratories |
| 7 | Propyline glycol | Prayoginalaboratories |
| | Sodium hydroxide | Prayoginalaboratories |
| 9 | Citric acid | Prayoginalaboratories |

**TABLE 1: List of drug and chemical used and their manufacturers**

**Equipment used**

| Sr.No. | Equipments | Manufacturer |
|---|---|---|
| 1 | Eelectronic weighing balance | Citizen scales pvt ltd |
| 2 | Digital balance | Hanna instuments,mumbai |
| 3 | Magnetic stirrer | Rem motors ,mumbai |
| 4 | Uv-visible spectrophotometer | Thermo alpha helios,mumbai |
| 6 | Stability chamber | Remi electronics, limited, vasai-401208 |
| 7 | Digital PH metre | Testmak , turkey |
| 8 | Viscometer | Brookfield engineering laboratories |
| 9 | Franz diffusion test apparatus | Meditech technologies |

**Table No 2: List of the instrument and their manufactures**

## 2.2 Preformulation Studies

Preformulation studies were conducted to evaluate the basic physical and chemical properties of Benzydamine Hydrochloride (BZH) and its compatibility with selected excipients.

Physical Characterization:
BZH was obtained from Swapnaroop Pharmaceuticals (Chhatrapati Sambhajinagar) and identified as a white crystalline powder. The melting point was determined using the capillary method and found to be within the standard range.

UV Absorption Spectroscopy:
A 2 µg/ml solution of BZH was prepared in phosphate buffer pH 6.8 and scanned from 200–800 nm to confirm the characteristic absorption maximum.[20-21]

Drug-Excipient Compatibility:
Compatibility of BZH with Carbopol 934, HPMC K15M, and sodium alginate was assessed by FT-IR spectroscopy. IR spectra of the pure drug, individual polymers, and their physical mixtures were recorded. No significant shifts in peaks indicated the absence of major interactions, confirming excipient compatibility.

Calibration Curve: A standard calibration curve for Benzydamine Hydrochloride was established in phosphate buffer (pH 6.8). The buffer was prepared by mixing 0.2 M potassium dihydrogen phosphate and 0.2 M sodium hydroxide solution, adjusting the pH to 6.8.

A stock solution (100 µg/ml) was prepared by dissolving 10 mg of Benzydamine Hydrochloride in phosphate buffer and making up the volume to 100 ml. Serial dilutions were prepared to obtain concentrations of 2, 4, 6, 8, and 10 µg/ml. The absorbance of each solution was measured at 254 nm using a UV-Visible spectrophotometer. The standard curve was plotted by graphing absorbance versus concentration, showing linearity within this range.[22]

**Preparation of Phosphate Buffer (pH 6.8):**

- **0.2 M Sodium Hydroxide:** 8 g of sodium hydroxide was dissolved in distilled water and the volume was adjusted to 1000 ml.
- **0.2 M Potassium Dihydrogen Phosphate:** 27.218 g of potassium dihydrogen phosphate was dissolved in distilled water and the volume adjusted to 1000 ml.
- **Phosphate Buffer (pH 6.8):** 50 ml of 0.2 M potassium dihydrogen phosphate was mixed with 22.4 ml of 0.2 M sodium hydroxide in a 200 ml volumetric flask and the volume was made up with distilled water. The pH was adjusted to 6.8 using 0.2 M sodium hydroxide solution if necessary.[23]

**Preparation of Standard Curve:**
A stock solution (100 µg/ml) was prepared by dissolving 10 mg of Benzydamine Hydrochloride in phosphate buffer (pH 6.8) and making up to 100 ml. Serial dilutions were made to obtain concentrations of 2, 4, 6, 8, and 10 µg/ml. Absorbance was measured at 254 nm using a UV-Visible spectrophotometer. A standard calibration curve was plotted by graphing absorbance against concentration.[24]

### 2.3 Formulation of Oral Mucoadhesive Gel

Composition of different formulations (F1–F9) of oral mucoadhesive gel

| **Ingredients (mg/ml)** | **F1** Carbopol | **F2** Carbopol | **F3** Carbopol | **F4** HPMC | **F5** HPMC | **F6** HPMC | **F7** Sodium alginate | **F8** Sodium alginate | **F9** Sodium alginate |
|---|---|---|---|---|---|---|---|---|---|
| Benzyadamine HCL | 50 mg | 50 mg | 50 mg | 50 mg | 50 mg | 50 mg | 50 mg | 50 mg | 50 mg |
| Carbopol 934 | 500 mg | 550 mg | 600 mg | | | | | | |
| HPMC K15M | | | | 500 mg | 750 mg | 1000 mg | | | |
| Sodium alginate | | | | | | | 800 mg | 900 mg | 1000 mg |
| $Cacl_2$ | | | | | | | 25 mg | 25 mg | 25 mg |
| Propylene glycol | 2.5 ml | 2.5 ml | 2.5 ml | 2.5 ml | 2.5 ml | 2.5 ml | 2.5 ml | 2.5 ml | 2.5 ml |
| Glycerin | 2.5 ml | 2.5 ml | 2.5 ml | 2.5 ml | 2.5 ml | 2.5 ml | 2.5 ml | 2.5 ml | 2.5 ml |
| Methyl paraben | 50 mg | 50 mg | 50 mg | 50 mg | 50 mg | 50 mg | 50 mg | 50 mg | 50 mg |
| Ph adjuster | q.s (NaOH) | q.s (NaOH) | q.s (NaOH) | q.s (citric acid) | q.s (citric acid) | q.s (citric acid) | q.s (NaOH) | q.s (NaOH) | q.s (NaOH) |

Table no-3 formulation table

**Method of Preparation of Mucoadhesive Oral Gel [25]**

The required amount of polymer was weighed accurately and gradually dispersed into 30 ml of distilled water in a beaker under continuous stirring at 400–600 rpm for 1 hour until a clear solution formed, avoiding the formation of lumps. Benzydamine Hydrochloride was then added to the polymer solution and stirred for an additional 3–4 hours to obtain a homogeneous dispersion. Separately, glycerin and propylene glycol were mixed and slowly incorporated into the gel under continuous magnetic stirring at 500–700 rpm. The final volume was adjusted to 50 g with distilled water. Care was taken to avoid air entrapment during mixing. The formulation was allowed to stand to remove any air bubbles, and the pH was adjusted to 6.75 ± 0.05.

## 2.4 Evaluation

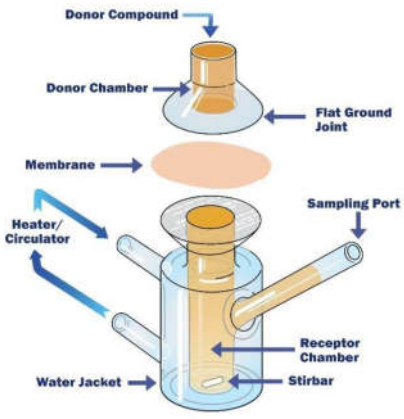
## Evaluation of Oral Mucoadhesive Gel [26-27]

Spreadability Test:
Spreadability was evaluated for all formulations to ensure ease of application. Spreadability indicates how easily the gel spreads with minimal shear. An increase in polymer concentration generally decreased spreadability, demonstrating the gel's behavior during dispensing.

pH Measurement:
The pH of each formulation was measured using a digital pH meter. For this, a solution was prepared by dispersing the gel in 100 ml of distilled water and allowing it to stand for 2 hours. The pH was measured in triplicate, and the average was calculated.

In Vitro Diffusion Study:
In vitro drug diffusion studies were carried out using a modified Franz diffusion cell with a dialysis membrane (flat width: 28.46 mm; diameter: 17.5 mm; length: 1 m). The membrane was soaked in phosphate buffer pH 6.8 for 9–12 hours before use. Mucoadhesive gel was uniformly spread onto the membrane and placed in contact with 25 ml of phosphate buffer in the receptor compartment. The assembly was maintained at 37 °C with continuous stirring on a magnetic stirrer. Samples (2 ml) were withdrawn at predetermined intervals and replaced with fresh buffer. Samples were analyzed spectrophotometrically at 322 nm, and cumulative drug release was calculated. A blank was used for correction

fig.no.5. Franz Diffusion cell



Viscosity Determination:
Viscosity was measured using a Brookfield Viscometer with spindle no. 3 (LV) at 20 and 30 rpm. The corresponding dial readings were recorded for each speed.

Stability Study:
Stability testing was performed according to ICH guidelines. Formulations were stored at 40 °C and 75% RH for one month. Appearance, pH, drug content, and in vitro drug release were evaluated at regular intervals.

Drug Content:
Drug content was determined by dissolving an accurately weighed 100 mg of gel in 100 ml of phosphate buffer (pH 6.8). The solution was stirred continuously for 24 hours, then sonicated and filtered. The drug concentration was estimated spectrophotometrically after suitable dilution.

Mucoadhesive Strength Test:
Mucoadhesive strength was measured using freshly excised goat oral mucosa and a modified physical balance method:

1. Preparation of Mucosa: Fresh goat oral mucosa was cleaned with saline, trimmed to appropriate size, and stored in simulated oral fluid (SOF, pH 6.4).
2. Simulated Oral Conditions: Mucosa was moistened with SOF before testing.
3. Mounting the Mucosa: Two glass slides were each affixed with mucosal tissue. One slide was fixed to the lower arm of the balance and the other to the upper movable arm.
4. Application of Gel: A fixed amount of gel was placed between the mucosal tissues. Gentle pressure was applied for 30 seconds to ensure adhesion.
5. Measuring Strength: Water was added dropwise to the opposite pan until detachment occurred.
6. Calculation: Mucoadhesive strength (N) was calculated as:
   Mucoadhesive Strength (N) = (Detachment Weight (g) × g) / Area Exposed

## 3. Results and Discussion

Preformulation Study

Preformulation studies were conducted to investigate the fundamental physical and chemical properties of the drug substance alone and in combination with selected excipients. These studies applied biopharmaceutical principles to assess key physicochemical parameters, supporting the rational design of an optimal and stable dosage form. The results confirm that preformulation is an essential step before developing various dosage forms.

**Physical Characterization of Drug**

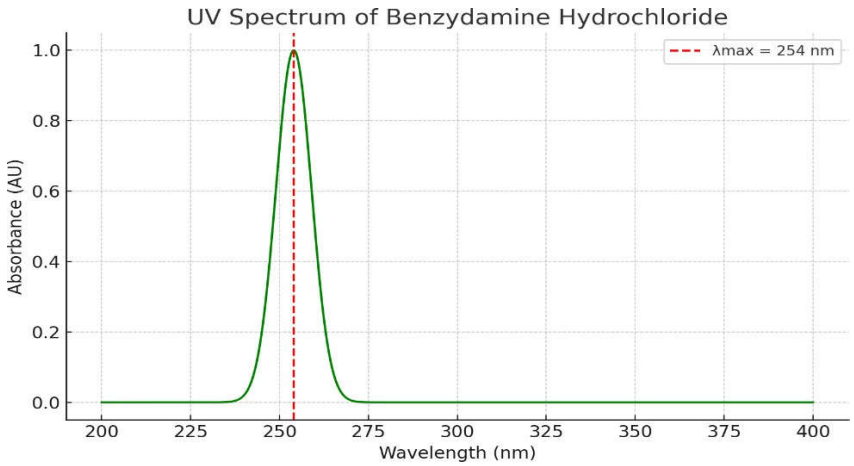
The received sample of **Benzydamine Hydrochloride** was characterized for its key physical and chemical properties as part of the preformulation studies.

**Description:**

- **Nature:** White or almost white crystalline powder.

- **Melting Point:** 161–164 °C (determined by the capillary method).
- **Solubility:** Freely soluble in water; highly soluble in ethanol (95%).

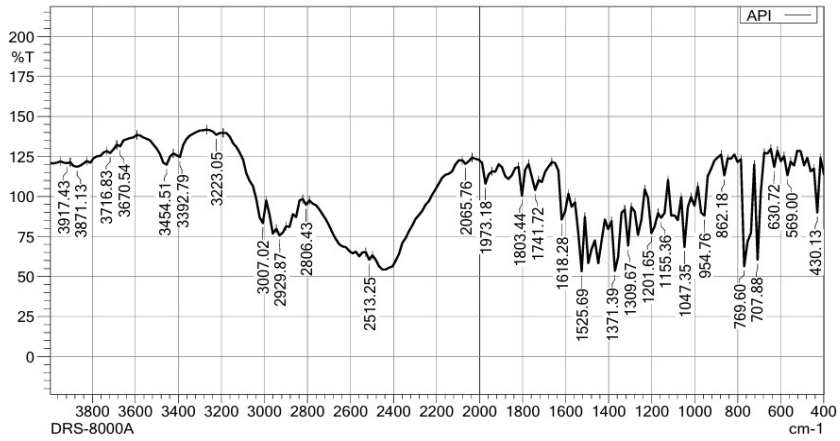
**Identification by UV-Visible Spectrophotometry:**
The absorption maximum (λmax) of Benzydamine Hydrochloride was determined by scanning the sample solution in a UV-Visible spectrophotometer. The characteristic peak was observed at **254 nm**, confirming the drug's identity.




## FT-IR STUDY

FT-IR Spectrum of Benzydamine Hydrochloride

*Figure X* shows the FT-IR spectrum of pure Benzydamine Hydrochloride (API). Characteristic absorption bands were observed at key wavenumbers, indicating the presence of functional groups consistent with the drug's structure. Notable peaks include broad bands around 3392–3917 $cm^{-1}$, attributed to O–H or N–H stretching, and peaks near 1618–1525 $cm^{-1}$, corresponding to C=C aromatic ring stretching. Additional bands in the fingerprint region (below 1500 $cm^{-1}$) further confirm the chemical identity of Benzydamine HCL




Figno 6-FTIR OF BENZADAMINE HCL

FT-IR Analysis of Benzydamine Hydrochloride with Carbopol 934

The FT-IR study was performed to assess any potential interaction between Benzydamine Hydrochloride and Carbopol 934. The observed characteristic peaks confirm the presence of key functional groups of both the drug and the polymer, indicating compatibility without significant shifts or disappearance of major peaks.

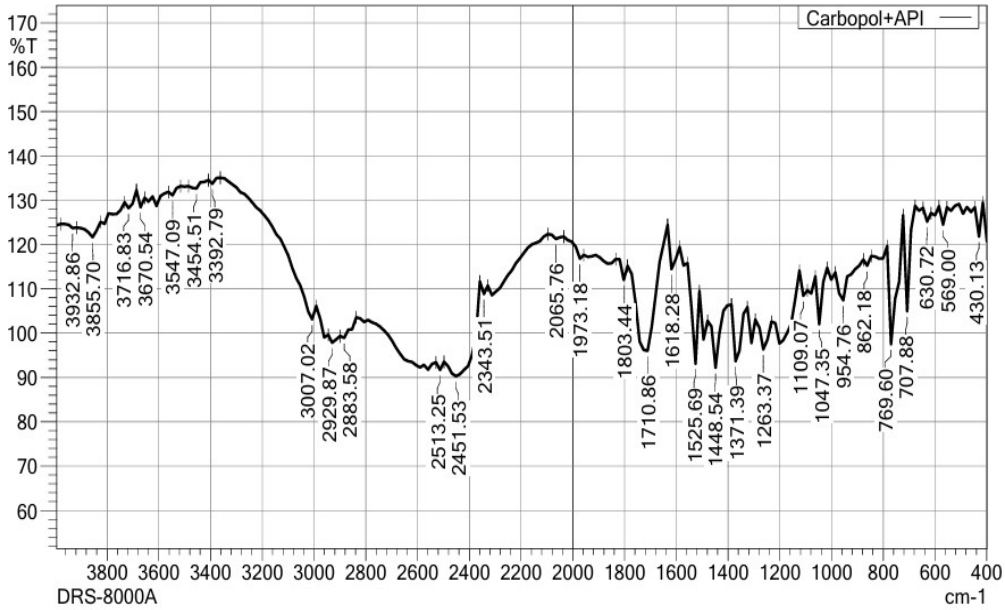
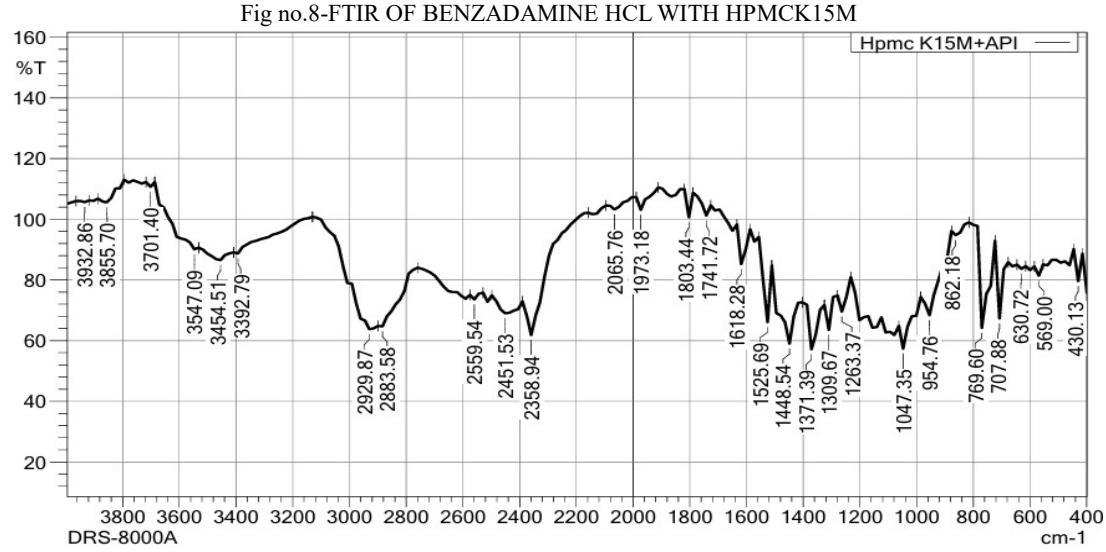



Fig no 7 —FTIR OF BENZADAMINE HCL WITH CARBAPOL-934

FT-IR Analysis of Benzydamine Hydrochloride with HPMC K15M

The FT-IR spectrum was analyzed to assess potential interactions between Benzydamine Hydrochloride and HPMC K15M. The characteristic absorption peaks indicate the presence of functional groups from both the drug and the polymer. The absence of significant shifts or disappearance of major peaks suggests good compatibility between the drug and HPMC K15M.

Fig no.8-FTIR OF BENZADAMINE HCL WITH HPMCK15M




FT-IR Analysis of Benzydamine Hydrochloride with Sodium Alginate

The FT-IR analysis was carried out to investigate possible interactions between Benzydamine Hydrochloride and sodium alginate. The observed absorption peaks confirm the presence of characteristic functional groups of both the drug and the polymer. The results indicate no significant shifts or disappearance of major peaks, demonstrating compatibility between Benzydamine Hydrochloride and sodium alginate.

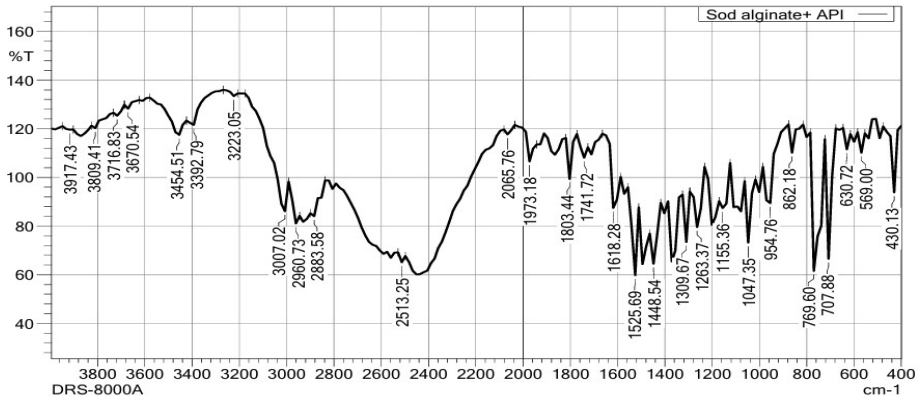



FIG NO.9-FTIR OF BENZADAMINE HCL WITH SODIUM ALGINATE

**Calibration Curve of Benzydamine Hydrochloride in Phosphate Buffer (pH 6.8)**

The calibration curve for Benzydamine Hydrochloride was established in phosphate buffer (pH 6.8) over a concentration range of 2–10 µg/ml. The standard curve passed through the origin and showed a linear relationship between concentration and absorbance. The results are presented in Table and Figure .

| Sr. No | Concentration (ug/ml) | Absorbance (nm) |
|---|---|---|
| 1 | 2 | 0.175 |
| 2 | 4 | 0.310 |
| 3 | 6 | 0.459 |
| 4 | 8 | 0.601 |
| 5 | 10 | 0.735 |

**TABLE NO 4**

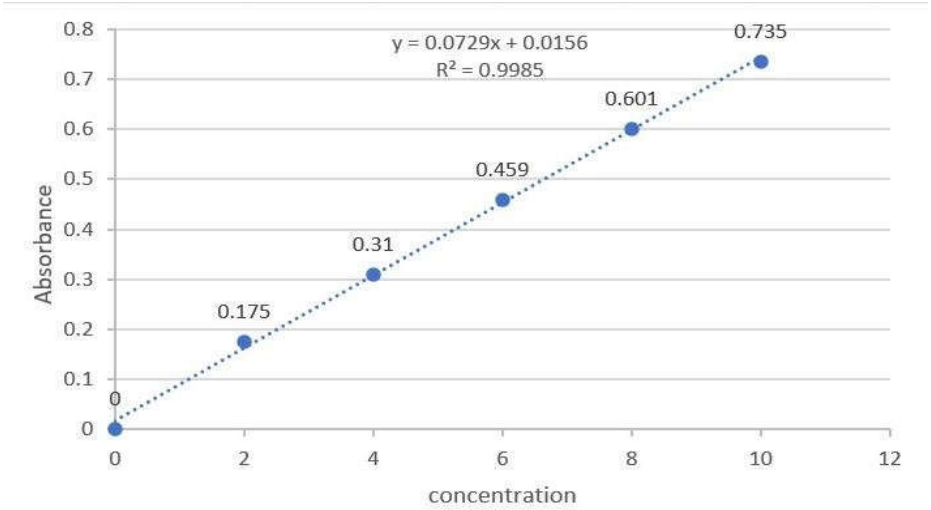



FIG NO 10 -Calibration curve of benzadamine HCL

## Characterization of Mucoadhesive Oral Gel

### pH of the Formulations

The pH of each prepared mucoadhesive oral gel formulation was measured using a calibrated digital pH meter. All formulations exhibited pH values within an acceptable range (approximately pH 6.6–6.9), indicating suitability for application to the oral mucosa without causing irritation

| Formulation code | pH |
|---|---|
| F1 | 6.6 |
| F2 | 6.9 |
| F3 | 6.8 |
| F4 | 6.9 |
| F5 | 6.9 |
| F6 | 6.9 |
| F7 | 6.9 |
| F8 | 6.9 |
| F9 | 6.9 |

**Table No 5: pH prepared formulation**

### Physical Characterization of Mucoadhesive Oral Gel

The prepared mucoadhesive oral gel formulations were evaluated for physical parameters including colour, Odor, washability, and consistency. All batches showed acceptable characteristics suitable for oral application.

| Batch | Colour | Odour | Washability | Consistency |
|---|---|---|---|---|
| F1 | Transparent | No | Washable | Better |
| F2 | Transparent | No | Washable | Excellent |
| F3 | Transparent | No | Washable | Excellent |
| F4 | Slightly white | No | Washable | Good |
| F5 | Slightly white | No | Washable | Better |
| F6 | Slightly white | No | Washable | Better |
| F7 | Slightly yellowish | No | Washable | Good |
| F8 | Slightly yellowish | No | Washable | Good |
| F9 | Slightly yellowish | No | Washable | Good |

**Table no 6- physical characterization**

**Viscosity Determination**

The viscosity of all mucoadhesive oral gel formulations was measured using a calibrated Brookfield viscometer equipped with spindle no. 3, operated at 20 to 30 rpm. The results demonstrated that the viscosity varied with the type and concentration of polymer used. This parameter is critical for ensuring suitable gel consistency, ease of application, and prolonged residence time at the site of administration.

| Sr. No | Formulation | Viscosity (Centipoise) |
|---|---|---|
| 1 | F1 | 16000 |
| 2 | F2 | 19800 |
| 3 | F3 | 21300 |
| 4 | F4 | 15000 |
| 5 | F5 | 17400 |
| 6 | F6 | 20000 |
| 7 | F7 | 11000 |
| 8 | F8 | 14000 |
| 9 | F9 | 15000 |

Table no 7 – viscosity of formulation

**Drug Content Determination**

The drug content of the prepared mucoadhesive oral gel formulations was analyzed using a UV–Visible spectrophotometer at 254 nm. The percentage of drug content ranged from **56.17% to 88.10%**, demonstrating good entrapment efficiency across the batches. Formulation batch **F4** showed the highest drug content, indicating effective incorporation of the active ingredient.

| Sr. No | Formulation | Drug Content (%) |
|---|---|---|
| 1 | F1 | 78.49 |
| 2 | F2 | 75.18 |
| 3 | F3 | 79.11 |
| 4 | F4 | 88.10 |
| 5 | F5 | 82.64 |
| 6 | F6 | 78.74 |
| 7 | F7 | 56.17 |

| | | |
|---|---|---|
| 8 | F8 | 65.75 |
| 9 | F9 | 75.75 |

**Table no .8- Drug content**

## Spreadability

The spreadability of all mucoadhesive oral gel formulations was evaluated by applying approximately 1 g of gel on the oral mucosa. All formulations exhibited smooth and uniform spreading, indicating acceptable rheological behavior for patient use. Good spreadability ensures ease of application, improved patient compliance, and uniform drug distribution over the application site.

## In-Vitro Diffusion Study

An in-vitro drug diffusion study was conducted for all mucoadhesive oral gel formulations over an 8-hour period. The cumulative percentage drug release was measured at regular time intervals using a Franz diffusion cell with a dialysis membrane in phosphate buffer (pH 6.8).

The results indicate that formulation F4 achieved the highest percentage of drug diffusion, demonstrating superior release characteristics compared to other batches. This suggests that the choice and concentration of polymer significantly influence the release profile.

The detailed diffusion data for all batches are presented in Table and Figures

| **Time (min)** | **F1 (%)** | **F2 (%)** | **F3 (%)** | **F4 (%)** | **F5 (%)** | **F6 (%)** | **F7 (%)** | **F8 (%)** | **F9 (%)** |
|---|---|---|---|---|---|---|---|---|---|
| **15 min** | 41.90 | 36.77 | 9.77 | 47.27 | 30.97 | 28.22 | 36.18 | 34.13 | 22.79 |
| **30 min** | 43.85 | 46.97 | 18.00 | 56.76 | 47.23 | 34.62 | 45.56 | 42.36 | 37.96 |
| **45 min** | 53.67 | 54.23 | 26.83 | 67.40 | 57.36 | 44.51 | 55.36 | 50.30 | 41.74 |
| **60 min** | 61.42 | 63.18 | 31.48 | 75.81 | 66.78 | 53.88 | 63.80 | 57.74 | 56.60 |
| **75 min** | 71.83 | 70.64 | 40.84 | 79.76 | 77.44 | 67.88 | 75.87 | 73.41 | 63.06 |
| **90 min** | 78.16 | 75.30 | 60.95 | 86.81 | 80.04 | 78.88 | 82.72 | 80.10 | 75.79 |

Table no 9-in vitro drug release .

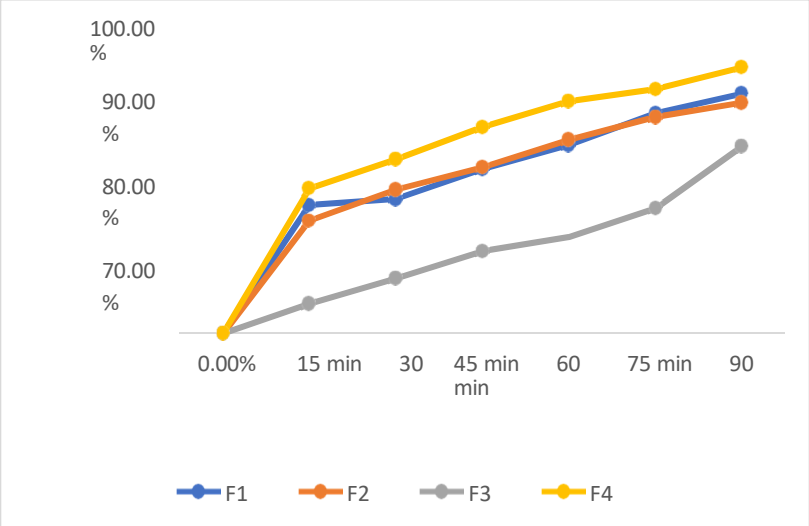



**Fig no – 11% cumulative drug formulation F1 to F4**

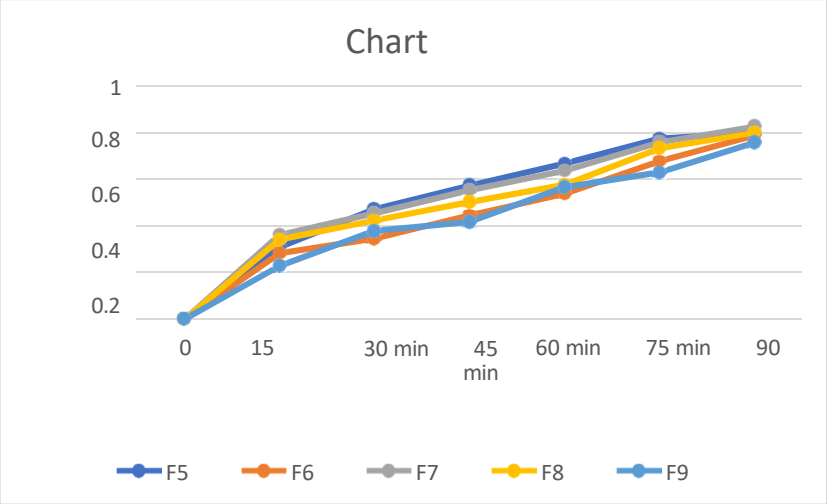



**Fig no – 12 % cumulative drug formulation F5 to F9**

## Mucoadhesive Strength

The mucoadhesive strength of each formulation was evaluated using a modified physical balance method with freshly excised goat oral mucosa. The results demonstrated that the mucoadhesive strength varied across batches, depending on the type and concentration of polymer used.

Among all batches, **F6** and **F9** showed the highest mucoadhesive strength (**11.0 g/cm²**), indicating good retention potential at the site of application, which is desirable for prolonged drug release and better therapeutic efficacy.

| batch | Mucoadhesive strength(gm/cm$^2$) |
|---|---|
| F1 | 8.5 |
| F2 | 9.2 |
| F3 | 10.1 |
| F4 | 8.0 |
| F5 | 10.2 |
| F6 | 11.0 |
| F7 | 8.8 |
| F8 | 10.1 |
| F9 | 11.0 |

**Table no .10**

**Stability Studies**

The stability of the optimized mucoadhesive oral gel formulations was evaluated over a period of **one month** at **40 °C ± 2 °C and 75% RH ± 5%**, following ICH guidelines. Critical quality attributes such as pH and viscosity were measured after the storage period to assess the formulations' physical stability.

**Tests after stability testing for one month**

pH After Stability Testing

The pH of all formulations remained within the acceptable range (6.6–6.9) after one month, indicating that the formulations retained suitable acidity levels for oral application without causing mucosal irritation.

| Formulation code | pH |
|---|---|
| F1 | 6.6 |
| F2 | 6.9 |
| F3 | 6.8 |

| | |
|---|---|
| F4 | 6.9 |
| F5 | 6.9 |
| F6 | 6.9 |
| F7 | 6.9 |
| F8 | 6.9 |
| F9 | 6.9 |

Table no-11.PH AFTER STABILITY

Viscosity After Stability Testing

The viscosity of all formulations showed minimal variation after one month of storage, demonstrating good physical stability and consistent gel structure.

| Sr. No | Formulation | Viscosity (Centipoise) |
|---|---|---|
| 1 | F1 | 17000 |
| 2 | F2 | 20800 |
| 3 | F3 | 22300 |
| 4 | F4 | 16000 |
| 5 | F5 | 18400 |
| 6 | F6 | 21000 |
| 7 | F7 | 12000 |
| 8 | F8 | 15000 |
| 9 | F9 | 16800 |

Table no 12-viscosity after viscosity

## 4. Summary and Conclusion

Oral mucoadhesive gels have emerged as an advanced and promising platform for local and systemic drug delivery via the oral mucosa. By prolonging the residence time of the formulation at the site of absorption, these systems can significantly enhance drug bioavailability and therapeutic efficacy. The oral mucosal route offers multiple clinical advantages, including avoidance of hepatic first-pass metabolism, protection of the drug from degradation in the gastrointestinal tract, rapid onset of action through direct systemic absorption, and improved patient compliance due to ease of administration and minimal discomfort.

The primary aim of this research was to develop and systematically evaluate an oral mucoadhesive gel containing Benzydamine Hydrochloride, a locally acting non-steroidal anti-inflammatory and analgesic agent, intended for the management of oral inflammatory conditions such as aphthous ulcers. A total of nine formulations (F1–F9) were prepared by varying the concentration and type of mucoadhesive polymers (Carbopol 934, HPMC K15M, and Sodium Alginate), combined with glycerin and propylene glycol as co-solvents and penetration enhancers, and methyl paraben as a preservative. The gels were formulated by a controlled mechanical stirring technique to ensure uniformity, homogeneity, and optimum gel consistency.

All formulations were physically stable, homogenous in appearance, washable, and exhibited pH values within the acceptable physiological range for oral mucosal application. Notably, Batch F4 demonstrated the most favorable balance of key characteristics, including optimal mucoadhesive strength, suitable viscosity, excellent spreadability, and the highest cumulative drug release profile (88.10% over 8 hours). The in-vitro drug diffusion results highlighted the formulation's potential for sustained release and enhanced therapeutic effect.

Importantly, the optimized formulation (F4) also showed excellent stability under accelerated conditions for one month, with no significant changes in its physicochemical properties, confirming its robustness and suitability for future scale-up and commercial development.

In conclusion, this study successfully demonstrated that an oral mucoadhesive gel containing Benzydamine Hydrochloride can be effectively formulated using HPMC K15M and other suitable excipients to deliver sustained local therapy for oral lesions. The developed gel system provides prolonged drug release, improved retention at the site of action, and enhanced patient acceptability compared to conventional dosage forms. Overall, this mucoadhesive gel represents a promising, patient-friendly approach for the targeted treatment of recurrent aphthous stomatitis, oral mucositis, and other localized oral inflammatory conditions — ultimately improving therapeutic outcomes and patient quality of life.

## 5. Future Scope

The present research focused on the design, development, and characterization of a mucoadhesive oral gel containing Benzydamine Hydrochloride, formulated with various polymers including Sodium Alginate, Carbopol 934, and HPMC K15M. Among these, the optimized formulation based on HPMC K15M demonstrated excellent mucoadhesive strength, desirable viscosity, sustained drug release, and patient-friendly application properties, indicating its strong potential as a local therapy for oral lesions.

Moving forward, several promising directions can be pursued to build upon and extend the outcomes of this work. One area involves the comparative evaluation of HPMC K15M with other grades of HPMC and cellulose derivatives to fine-tune viscosity, swelling behavior, and drug release kinetics. Additionally, blending HPMC K15M with other bioadhesive or biodegradable polymers may yield synergistic effects, further enhancing mucosal adhesion, formulation stability, and controlled release profiles.

Another significant avenue for advancement is the incorporation of nanocarrier systems, such as nanoparticles or nanoemulsions, into the HPMC K15M gel matrix. This hybrid strategy could substantially improve drug permeation through the mucosal layers, reduce dosing frequency, and enable more effective targeting of deeper tissues, particularly in persistent or severe conditions like recurrent aphthous stomatitis or oral lichen planus.

To translate the in vitro findings into clinical practice, comprehensive in vivo animal studies and subsequent clinical trials are essential. These investigations should assess the optimized gel's therapeutic efficacy, pharmacokinetics, and local safety, along with practical considerations such as patient taste acceptability, ease of application, and retention time under real-life oral conditions.

From an industrial perspective, the scale-up potential of the optimized HPMC K15M gel should be systematically evaluated to ensure reproducibility, packaging compatibility, microbial stability, and a robust shelf-life. Careful optimization of preservative systems and long-term physicochemical stability will be critical for successful commercial development.

Moreover, the mucoadhesive gel platform developed in this study holds substantial promise for adaptation to other therapeutic agents that require localized treatment of oral conditions — including antifungals, corticosteroids, and antimicrobial agents — using HPMC K15M as a versatile base polymer. This adaptability broadens its potential to meet diverse clinical needs.

Tailored formulations can also be designed to address the unique requirements of pediatric and geriatric patients, further enhancing user convenience, dosing accuracy, and patient compliance. Additionally, sustainability should be prioritized through the use of environmentally friendly excipients and biodegradable packaging materials to minimize ecological impact.

In summary, this study establishes a solid foundation for future innovation in localized oral drug delivery systems. With its demonstrated superior performance, HPMC K15M stands out as a highly promising polymer for the continued development of advanced mucoadhesive gel formulations, offering substantial scope for therapeutic improvement and industrial translation**.**

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