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Research Article

# Formulation And Evaluation of Mucoadhesive Buccal Film for Mouth Ulcer by Using *Solanum Nigrum* Extract

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## ABSTRACT

The present research focuses on the formulation and evaluation of a mucoadhesive buccal film containing Solanum nigrum extract for the treatment of mouth ulcers. Solanum nigrum is a medicinal plant known for its anti-inflammatory, antioxidant, analgesic, and wound-healing properties, which can promote faster healing of oral mucosal lesions. The buccal films were prepared by the solvent casting method using Hydroxypropyl Methylcellulose (HPMC K15M) as the mucoadhesive polymer, Glycerin as a plasticizer and Sodium Saccharin as sweetener. The prepared formulations were evaluated for various physicochemical parameters such as appearance, thickness, weight uniformity, folding endurance, surface pH, swelling index, drug content uniformity, and in-vitro drug release. FT-IR studies confirmed no major drug–excipient interactions. The optimized formulation exhibited desirable mucoadhesive strength, good mechanical properties, and sustained release of the extract, ensuring prolonged retention at the site of application. The findings suggest that Solanum nigrum-based mucoadhesive buccal films can serve as a promising, safe, and effective herbal delivery system for the management of mouth ulcers.

## INTRODUCTION

### 1.1 Overview of Oral Ulcers

Oral ulcers, particularly aphthous ulcers (commonly known as canker sores), are painful, recurrent lesions that affect the non-keratinized mucosal regions of the oral cavity. They present as round or oval ulcers with a white or yellow base surrounded by an erythematous halo and are often accompanied by discomfort or pain, particularly while eating or speaking. These lesions can significantly impair the quality of life due to the pain and inconvenience they cause. While oral ulcers are generally self-limiting, their frequent recurrence, particularly in immunocompromised individuals or those with systemic conditions like Crohn's disease, HIV/AIDS, or Behçet's

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syndrome, necessitates therapeutic intervention. Moreover, repeated occurrences can also lead to chronic inflammation, secondary infection, or tissue damage. Mouth ulcers are common and are usually due to trauma, such as from ill-fitting den tures, fractured teeth, or fillings However, patients with an ulcer of over 3 weeks' duration should be referred for biopsy or other investigations to exclude malignancy or other serious conditions such as chronic infections [1]. Ulcers related to trauma usually resolve in about a week after removal of the cause and with the use of an anti-inflammatory and anaesthetic throat spray to provide symptomatic relief and chlorhexidine 0.2% aqueous mouthwash to maintain good oral hygiene. Recurrent aphthous stomatitis typically starts in childhood or adolescence with recurrent small, round, or ovoid ulcers with circumscribed margins, erythematous haloes, and yellow or gray floors. It affects at least 20% of the population, and its natural course is one of eventual remission. There are 3 main clinical types:

- Minor aphthous ulcers (80% of all aphthae) are less than 5 mm in diameter and heal in 7 to 14 days
- Major aphthous ulcers are large ulcers that heal slowly over weeks or months with scarring
- Herpetiform ulcers are multiple pinpoint ulcers that heal within about a month [2].

### 1.2 Causes of Mouth Ulcer

Various factors can contribute to the onset of oral ulcers, including mechanical trauma (e.g., from braces or ill-fitting dentures), nutritional deficiencies (particularly vitamin B12, iron, and folate), stress, hormonal imbalances, food sensitivities, microbial infections, and autoimmune responses. Despite the high prevalence of oral ulcers, treatment options are still limited, often focusing on symptomatic relief rather than addressing the underlying cause. Most conventional therapies involve topical corticosteroids, antiseptics, anaesthetics, and antibiotics. However, prolonged use of these agents can lead to adverse effects such as mucosal thinning, microbial resistance, hypersensitivity, and dysbiosis of the oral microbiota. This necessitates the development of novel, biocompatible, and effective therapeutic approaches with minimal side effects.

### 1.3 Botanical Overview of *Solanum Nigrum*

*Solanum nigrum* L., commonly known as Black Nightshade, is an annual herbaceous plant of the Solanaceae family. It is native to Eurasia but widely distributed across tropical and subtropical regions of Asia, Africa, and Europe. In India, it is locally known as "Manathakkali" in Tamil, "Makoy" in Hindi, and "Kakamachi" in Sanskrit. The plant typically grows up to 30–120 cm in height, with ovate leaves, small white flowers, and green-to-black berries upon ripening. Traditionally, it has been cultivated and foraged for its edible leaves and fruits, as well as for its extensive medicinal applications [3].

### 1.4 Rationale For Developing Mucoadhesive Buccal Film With *Solanum Nigrum* Extract

Mouth ulcers are painful inflammatory lesions of the oral mucosa that often cause discomfort and difficulty in eating or speaking. Conventional dosage forms such as gels, ointments, and mouthwashes provide only temporary relief because of their limited residence time and rapid washout by saliva. [36] To overcome these limitations, mucoadhesive buccal films offer an effective drug delivery system that can adhere to the buccal mucosa, prolong drug contact time, and provide controlled and localized drug release [4]. *Solanum nigrum* (Black Nightshade) is a

medicinal herb known for its anti-inflammatory, antioxidant, antimicrobial, and wound-healing properties, making it suitable for treating oral mucosal lesions [5, 6]. The presence of bioactive compounds such as flavonoids, alkaloids, and glycosides contributes to its therapeutic potential against ulcerative and inflammatory conditions [7]. By incorporating *Solanum nigrum* extract into a mucoadhesive buccal film, the localized drug delivery can ensure sustained release of phytoconstituents directly at the ulcer site, enhance therapeutic efficacy, minimize systemic side effects, and improve patient compliance. Thus, this novel herbal-based mucoadhesive formulation represents a safe and effective alternative for the management of mouth ulcers.

## 2. MATERIALS AND METHODS

### 2.1 MATERIALS

Fresh, green, and mature leaves of *Solanum Nigrum* was collected from local fields. Hydroxypropyl Methylcellulose (HPMC K15M) was selected as the primary film-forming polymer because of its biocompatibility, non-toxicity, and excellent mucoadhesive characteristics. Glycerin was incorporated as a plasticizer to impart flexibility and reduce brittleness, while saccharin sodium served as a sweetening agent to improve patient acceptability and taste masking. Analytical-grade solvents, including ethanol, methanol, and distilled water, were used throughout the study.

### 2.2 Preparation Of *Solanum Nigrum* Extract

Fresh leaves of *Solanum nigrum* were collected from a verified local source and authenticated by a qualified botanist. The leaves were washed thoroughly with distilled water to remove adhering dust and impurities, shade-dried at room temperature for 7–10 days, and then pulverized using a mechanical grinder. The dried powder was subjected to extraction using 70% ethanol in a Soxhlet apparatus for 6 to 8 hours. The resulting extract was concentrated under reduced pressure using a rotary evaporator at 40–45°C and further dried in a hot air oven at a low temperature to obtain a semi-solid crude extract. This crude extract was stored in sterile amber-colored containers at 4°C until further use. The yield was calculated, and preliminary phytochemical screening was conducted to identify the presence of alkaloids, flavonoids, saponins, glycosides, tannins, and phenolic compounds.

### 2.3 Formulation Development Of Mucoadhesive Buccal Films

The mucoadhesive buccal films of *Solanum nigrum* were formulated using the solvent casting method. This technique allows uniform dispersion of the extract, smooth film formation, and reproducible drug loading. For the preparation, the accurately weighed amount of HPMC K15M was dispersed in ethanol and stirred for about one hour using a magnetic stirrer until a clear viscous gel was obtained. The *Solanum nigrum* extract was then added gradually to the polymeric dispersion with continuous stirring to ensure uniform distribution. Glycerin and saccharin sodium were subsequently incorporated and stirred until a smooth, homogenous solution was achieved. The prepared mixture was poured into clean, glycerin-coated glass Petri dishes and allowed to dry at room temperature (25 ± 2 °C) for 24–48 hours. After drying, the films were carefully peeled off and cut into 2 × 2 cm squares, each containing a uniform dose of *Solanum nigrum* extract equivalent to the therapeutic amount used in in vivo studies. The films were stored in a desiccator over silica gel until further evaluation. To obtain the optimal formulation, three preliminary trials (F1–F3) were prepared by varying the ratios of

extract, polymer, and plasticizer while maintaining the total solid weight of 150 mg (excluding solvent). This optimization aimed to determine the most suitable combination that provides adequate flexibility, mechanical strength, smoothness, and mucoadhesion without being sticky and brittle.

## 2.4 Evaluation of Formulated Mucoadhesive Buccal Film

### 2.4.1 Physicochemical Evaluation

#### 2.4.1.1 Film Thickness

The formulated films were subjected to preliminary physicochemical evaluation. The thickness of the films was measured using a digital micrometer at five different points.

#### 2.4.1.2 Folding Endurance

Folding endurance is a simple, widely used measure of a buccal/oral film's mechanical flexibility — it is defined as the number of times a small strip of film can be folded at the same place without showing cracks or breaking. To perform the test, cut three strips (commonly 2 × 2 cm) from each formulation and condition them as required by your lab SOP; take one strip, hold it between the thumb and forefinger and repeatedly fold it at the same point through ~180° until a visible crack or break appears, counting the number of folds. The reported folding endurance is the number of folds the film withstood; report the mean ± SD of the three replicates. For greater repeatability and for thicker or commercial films, an M.I.T.-type folding tester (or equivalent apparatus) may be used following standard procedures [8].

#### 2.4.1.3 Morphological Properties

The physical appearance of the films was visually examined for color, transparency, texture, and surface smoothness.

#### 2.4.1.4 Weight Variation

To evaluate uniformity, three films from each batch (2 cm × 2 cm) were randomly selected, weighed individually, and the mean and standard deviation were calculated.

#### 2.4.1.5 Percentage Moisture Loss

To determine moisture loss, films were weighed initially and then kept in a desiccator containing anhydrous calcium chloride for 72 hours. They were reweighed, and the percentage moisture loss was calculated using the formula:

**Percentage Moisture Loss (%)=($W_i - W_f$ / $W_i$)×100**

**Where:**

- $W_i$ = Initial weight of the film
- $W_f$ = Final weight of the film after desiccation

#### 2.4.1.6 SURFACE pH

The surface pH of a mucoadhesive buccal film is evaluated to ensure that the formulation will not cause irritation or discomfort to the buccal mucosa after application. The test is carried out by allowing the film to swell slightly in contact with distilled water. In this procedure, a film sample (usually 2 × 2 cm) is placed on the surface of 1 mL of distilled water and allowed to equilibrate for about 1 hour at room temperature. After swelling, the surface pH is measured by placing the tip of a pH electrode (previously calibrated with standard buffers of pH 4.0 and 7.0) gently on the surface of the moistened film. The measurement is repeated for at least three films per batch, and the mean ± SD value is reported. A surface pH value close to neutral (6.5 – 7.5) indicates compatibility with the buccal cavity and minimizes the risk of irritation [9, 10].

#### 2.4.1.7 Swelling Index

The swelling index of a mucoadhesive buccal film is determined to evaluate its ability to absorb moisture and swell upon contact with biological fluids, which influences drug release and mucoadhesive strength. In this procedure, a film sample of known initial weight ($W_1$) or initial area ($A_1$) (usually 2 × 2 cm) is placed in a Petri dish containing 5 mL of phosphate buffer (pH 6.8) and maintained at 37 ± 0.5 °C to simulate buccal conditions. At predetermined time intervals (e.g., 5, 10, 15, 30, 45, 60 min), the film is carefully removed, blotted gently with filter paper to remove excess surface water, and then weighed ($W_2$). The swelling index (SI) is calculated using the formula:

$$\text{Swelling Index (\%)} = \frac{(W_2 - W_1)}{W_1} \times 100$$

Alternatively, if based on area,

$$\text{Swelling Index (\%)} = \frac{(A_2 - A_1)}{A_1} \times 100$$

where $A_1$ and $A_2$ are the initial and final film areas. The mean of three determinations is reported as the swelling index (mean ± SD). A moderate swelling index indicates an optimal balance between hydration and mechanical strength, ensuring effective mucoadhesion without disintegration. [15, 59]

### 2.4.2 Drug Content Uniformity

The drug content uniformity of a mucoadhesive buccal film is determined to verify that each individual film contains the intended amount of active ingredient and that the drug is uniformly distributed across units. In a typical procedure, a specified number of films (commonly 3–10 units per formulation; many research reports use three replicates for assay and 10 units if applying pharmacopeial content-uniformity criteria) are accurately weighed and each film is transferred to a separate volumetric flask; a suitable solvent or extraction medium (e.g., phosphate buffer pH 6.8, dilute acetic acid, or a solvent that fully dissolves the drug and swells the polymer matrix) is added to each flask and the films are allowed to dissolve or are homogenized/sonicated for a fixed time (for example 1–5 h with intermittent shaking or 30–60 min sonication) to ensure complete extraction of drug from the polymeric matrix. The resulting solutions are diluted to volume, filtered (0.45 µm) if necessary, and an aliquot is analyzed by a validated assay method (UV spectrophotometry or HPLC, depending on drug specificity and matrix interference) against an appropriate calibration curve. Drug content for each unit is calculated as mg per film and expressed as percent of label claim; the mean ± standard deviation (and %RSD) of the tested units is reported [11].

### 2.4.3 Franz Diffusion Cell

The Franz diffusion cell method is commonly used to evaluate in-vitro drug release and permeation from mucoadhesive buccal films. In a typical procedure, the film (or a fixed area of the film, e.g., 1 cm²) is placed in the donor compartment either directly (for release studies) or mounted onto a suitable biological membrane (e.g., excised porcine buccal mucosa, or a synthetic membrane such as cellulose acetate/dialysis membrane) and clamped so that the film faces the receptor chamber. The receptor compartment is filled with a pre-warmed dissolution/permeation medium (commonly phosphate buffer pH 6.8 to simulate saliva; volume depends on cell size but is typically 5–12 mL) and maintained at 37 ± 0.5 °C with continuous stirring (magnetic bead or small stir-bar) to ensure homogeneity and sink conditions. At predetermined time points (for example 5, 15, 30, 60, 120, 240, 360 min and longer as appropriate),

aliquots (e.g., 0.5–1.0 mL) are withdrawn from the receptor compartment and immediately replaced with equal volumes of fresh, pre-warmed medium to maintain constant volume. Samples are filtered if required and analyzed by a validated assay (UV spectrophotometry or HPLC). Results are reported as cumulative amount of drug permeated per unit area (µg/cm²) or as percentage of the drug released versus time; data can be fitted to release/permeation models (e.g., Higuchi, zero-order, first-order) to elucidate the mechanism of drug release. Critical points to report are membrane type and thickness, exact donor film area, receptor medium composition and volume, temperature and stirring conditions, sampling schedule, analytical method (including validation), and whether sink conditions were maintained. This procedure provides comparative release/permeation profiles useful for formulation optimization and mechanistic interpretation [9, 12, 13].

### 2.4.4 Compatibility Study

The FT-IR analysis of *Solanum nigrum* extract and formulation excipients (HPMC, Glycerin, Saccharin sodium) is typically performed to detect potential interactions.

### 2.4.5 Pharmacological Evaluation

#### 2.4.5.1 Antioxidant Activity

The antioxidant activity of the extract-loaded films was evaluated using both in vitro and ex vivo models. For in vitro testing, DPPH radical scavenging assay and ABTS cation decolorization assays were employed. A known quantity of the film was dissolved in methanol, and varying concentrations of the solution were incubated with DPPH solution. The decrease in absorbance was measured at 517 nm after 30 minutes. The percentage inhibition and IC50 values were calculated. The ABTS assay involved generation of $ABTS^{\bullet+}$ radicals, followed by treatment with the film extract solution and measurement of absorbance reduction at 734 nm. Additionally, ferric reducing antioxidant power (FRAP) assays were performed and measurement of absorbance reduction at 700nm. Total antioxidant capacity was quantified and compared with standard antioxidants like ascorbic acid.

#### 2.4.5.2 Anti-Inflammatory Activity

The anti-inflammatory activity was evaluated using the in vitro human red blood cell (HRBC) membrane stabilization method and the protein denaturation assay. The HRBC method involves mixing the film extract solution with HRBC suspension and hypotonic saline. The mixture was incubated and centrifuged, and the absorbance of the supernatant was measured at 560 nm. Protection against hemolysis indicates membrane stabilizing (anti-inflammatory) potential. Diclofenac sodium was used as the reference standard in both assays. Percent inhibition of protein denaturation and RBC lysis was calculated and compared among different concentrations of the extract.

#### 2.4.5.3 Anticancer Activity

The anticancer activity was determined by in vitro cytotoxicity assays using human oral cancer cell lines MCF-7. The MTT assay was used to determine cell viability following treatment with various concentrations of the film extract. Cells were cultured in 96-well plates and treated with film extract solutions for 24–48 hours. MTT dye was added, and the formazan crystals formed were solubilized in DMSO. Absorbance was read at 570 nm. The $IC_{50}$ value was determined. Further apoptotic studies, including acridine orange/ethidium bromide (AO/EB) dual staining and caspase-3 expression by ELISA, were also

conducted. Reactive oxygen species generation and mitochondrial membrane potential loss were examined using flow cytometry. Untreated cells and doxorubicin-treated cells served as controls.

#### 2.4.5.4 Antimicrobial Activity

The antimicrobial potential of the formulated buccal films was evaluated against selected bacterial and fungal strains to assess their efficacy in controlling oral infections.

#### Antibacterial Activity

The antibacterial activity of the *Solanum nigrum* extract and the corresponding buccal films was assessed using the agar well diffusion method. Standard bacterial strains, including *Staphylococcus aureus* (Gram-positive), *Klebsiella pneumoniae* (Gram-negative), and *Helicobacter pylori* (Gram-negative), were cultured on nutrient agar plates. Wells of uniform size were prepared in the agar, and the film extract solutions of known concentrations were introduced. The plates were incubated at 37°C for 24 hours, after which the zones of inhibition were measured in millimetres. Tetracycline was used as the standard antibiotic control. Additionally, time-kill studies were performed to evaluate the bactericidal kinetics of the films over time, providing insight into the rate and extent of bacterial inhibition.

#### Antifungal Activity

The antifungal activity of the buccal films was evaluated using the agar well diffusion method against standard fungal strains, including *Candida albicans*, *Candida tropicalis*, and *Candida krusei*. Potato Dextrose Agar (PDA) plates were prepared, and wells of uniform size were made to introduce the film extract solutions of known concentrations. The plates were incubated at 28–30°C for 48 hours, and the zones of inhibition were measured in millimetres. Fluconazole was used as the standard antifungal control. Time-kill assays were also conducted to determine the fungicidal kinetics of the films over specified time intervals.

## 3. RESULTS

### 3.1 Compositions

**Table no.1: Formulation of Mucoadhesive buccal film of *Solanum nigrum* extract**

| Components | (F1) | (F2) | (F3) |
|---|---|---|---|
| *Solanum nigrum* Extract | 20 ml | 22.5 ml | 25 ml |
| HPMC K15M (Film former) | 98 mg | 95.5 mg | 93 mg |
| Glycerine (Plasticizer) | 29.5 mg | 29.5 mg | 29.5 mg |
| Saccharin Sodium | 2.5 mg | 2.5 mg | 2.5 mg |
| Ethanol | Q.S to 10 ml | Q.S to 10 ml | Q.S to 10 ml |
| Total Weight (excluding solvent) | 150 mg | 150 mg | 150 mg |

### 3.2 Formulation Observations and Suitability

#### Formula 1 (F1):

This formulation contained a higher proportion of polymer (HPMC K15M) and a lower extract concentration. The film formed was mechanically strong but lacked flexibility, becoming stiff and brittle upon drying. While the film showed good integrity, it was difficult to peel without cracking. Therefore, F1 was not selected for further evaluation due to poor folding endurance and reduced patient comfort.

#### Formula 2 (F2):

This formulation balanced the polymer and extract ratios, resulting in a smooth, flexible, and transparent film with uniform thickness and good handling characteristics. The film exhibited adequate mucoadhesion, moderate tensile strength, and non-stickiness. It peeled off easily and remained stable during storage. Hence, F2 was considered the most optimized and suitable formulation for further physicochemical and biological evaluations.

**Formula 3 (F3):**

In this formulation, a higher extract concentration and reduced polymer content led to the formation of a sticky and gel-like film. The film was soft, lacked structural integrity, and was difficult to remove from the Petri dish. The excess extract and reduced polymer ratio compromised its mechanical properties, making it unsuitable for practical application. Therefore, F3 was rejected due to poor film-forming ability and excess stickiness.

***Fig.no.1:*** **Mucoadhesive buccal film of *Solanum nigrum* extract (F2)**

### 3.3 Physicochemical Evaluation

#### 3.3.1 Film Thickness

The mean thickness ranged from 0.24 mm to 0.28 mm**,** with a standard deviation of ±0.02 mm. This consistency in thickness is critical for uniform drug content, Mucoadhesion, and drug release behaviour**.**

#### 3.3.2 Folding Endurance

In this study, all formulations showed folding endurance values between 170–200 folds**, indicating** excellent flexibility and mechanical integrity**.** This ensures the films can resist breakage during handling and application inside the buccal cavity.

#### 3.3.3 Morphological Properties

The physical appearance of the films was visually examined for color, transparency, texture, and surface smoothness. All prepared films were:

- Pale green colour,
- Smooth,
- Transparent to translucent,
- Free from air bubbles, cracks, or particulate matter.

These characteristics reflect the homogeneity of the film matrix and confirm the successful incorporation of *Solanum nigrum* extract into the HPMC polymeric base.

#### 3.3.4 Weight Variation

The film weights ranged from 145.5 mg to 154.5 mg with standard deviations below 3%, confirming good uniformity in formulation and solvent casting process**.** Minor variation may be due to differences in solvent evaporation during drying.

#### 3.3.5 Percentage Moisture Loss

The moisture loss ranged from **3.2% to 5.8%**, indicating **adequate drying and stability**. Low

moisture content ensures longer shelf life and prevents microbial contamination.

### 3.3.6 Surface PH

The results revealed that all formulations exhibited surface pH values in the range of 6.5 ± 0.2 to 6.9 ± 0.1. The optimized formulation (F2) displayed a surface pH of 6.7 ± 0.1, which is nearly neutral and well within the acceptable physiological range. The slight variations observed among the formulations can be attributed to minor differences in polymer-to-extract ratio, which may influence the hydration and ionization behavior of the film matrix. This near-neutral pH suggests that the incorporation of *Solanum nigrum* extract and excipients such as Glycerin and saccharin sodium did not significantly alter the microenvironmental pH. Hence, the films are expected to be non-irritating, biocompatible, and comfortable for buccal application over extended durations.

### 3.3.7 Swelling Index

The swelling index values ranged between 21.4 ± 1.6% (F1) and 33.6 ± 1.8% (F3), with the optimized formulation (F2) showing a moderate and desirable swelling index of 28.9 ± 1.3%. Formulation F1, with higher polymer content and lower extract concentration, demonstrated limited swelling, likely due to the increased cross-linking density and reduced water penetration. Conversely, F3, containing higher extract levels and less polymer, showed excessive swelling and slight softening, which could compromise structural stability. F2 achieved an optimal balance between polymer and extract, maintaining sufficient hydration without disintegration. The moderate swelling behavior supports effective mucoadhesion and controlled release of the active constituents from the hydrated matrix. This swelling characteristic ensures adequate residence time at the ulcer site, enhancing drug absorption and therapeutic efficacy.

### 3.4 Drug Content Uniformity

The drug content was found to be uniformly distributed among all formulations, ranging from 96.4 ± 0.9% to 101.2 ± 1.1% of the theoretical value. The optimized formulation (F2) exhibited a content uniformity of 99.3 ± 0.8%, indicating excellent homogeneity in the dispersion of Solanum nigrum extract throughout the polymer matrix. The low standard deviation (<2%) across replicates confirms the reproducibility of the solvent casting process and proper mixing during formulation. The high level of uniformity also indicates that there was no drug migration during the drying phase, which can otherwise cause concentration gradients in the film. These findings ensure accurate dosing, consistent release kinetics, and reliable therapeutic performance of the formulated films.

### 3.5 Franz Diffusion Cell (In Vitro Drug Release Study)

The cumulative drug release values after 120 minutes were found to be 91.3 ± 1.7% (F1), 96.2 ± 0.9% (F2), and 88.5 ± 2.0% (F3). Among these, F2 demonstrated an optimal release profile with a sustained and consistent pattern suitable for buccal delivery. Kinetic modeling of the release data indicated that the optimized formulation followed Higuchi diffusion kinetics ($R^2$ = 0.984), confirming that drug release was primarily governed by diffusion through the hydrated polymer matrix. The Korsmeyer–Peppas exponent (n = 0.52) suggested non-Fickian diffusion, indicating that both polymer relaxation and diffusion mechanisms contributed to drug release. This sustained release profile ensures prolonged drug availability at the ulcer site, minimizing dosing frequency and enhancing local therapeutic

efficiency. Such controlled diffusion is advantageous for *Solanum nigrum* extract, which contains polyphenolic and alkaloidal compounds requiring steady exposure to achieve maximal anti-ulcer, anti-inflammatory, and antioxidant effects.

**Table No.2: Physiochemical Analysis**

| Parameter | F1 | F2 | F3 | Remarks |
|---|---|---|---|---|
| **Surface pH** | 6.5 ± 0.2 | 6.7 ± 0.1 | 6.9 ± 0.1 | Within salivary pH; non-irritant |
| **Swelling Index (%)** | 21.4 ± 1.6 | 28.9 ± 1.3 | 33.6 ± 1.8 | Moderate swelling ensures Mucoadhesion |
| **Drug Content Uniformity (%)** | 96.4 ± 0.9 | 99.3 ± 0.8 | 101.2 ± 1.1 | Uniform drug distribution |
| **Cumulative Drug Release (120 min)** | 91.3 ± 1.7 | 96.2 ± 0.9 | 88.5 ± 2.0 | Sustained release pattern |

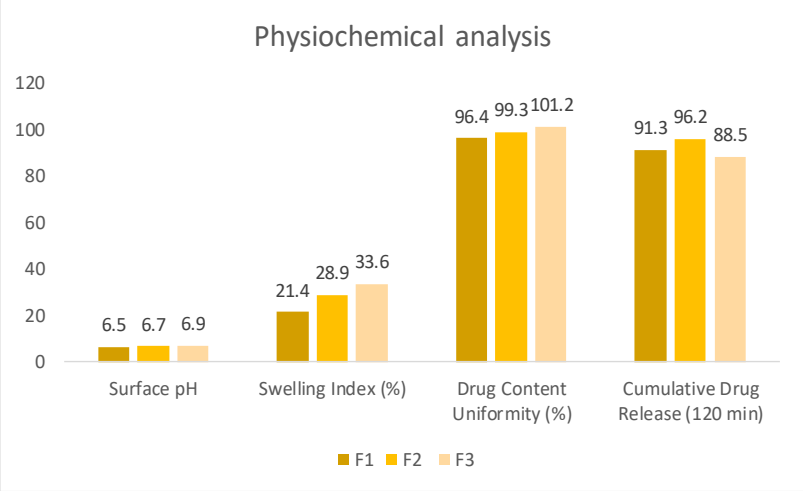



***Fig.no.2:*** **Physiochemical Analysis**

### 3.6 Compatibility Study

The IR Spectra of Solanum nigrum 2854.74 cm-1, 1319.36 cm-1, 1263.42 cm-1, 1107.18 cm 1 wave number as major peaks were found when it is mixed with excipients. There was no appearance or disappearance of any characteristic peak of the drug which confirm the absence of chemical interaction. Hence the excipients Hydroxypropyl Methylcellulose (HPMC K15M), Glycerin, Saccharin Sodium which were observed to be compatible with solanum nigrum were selected for the further development of the formulation.

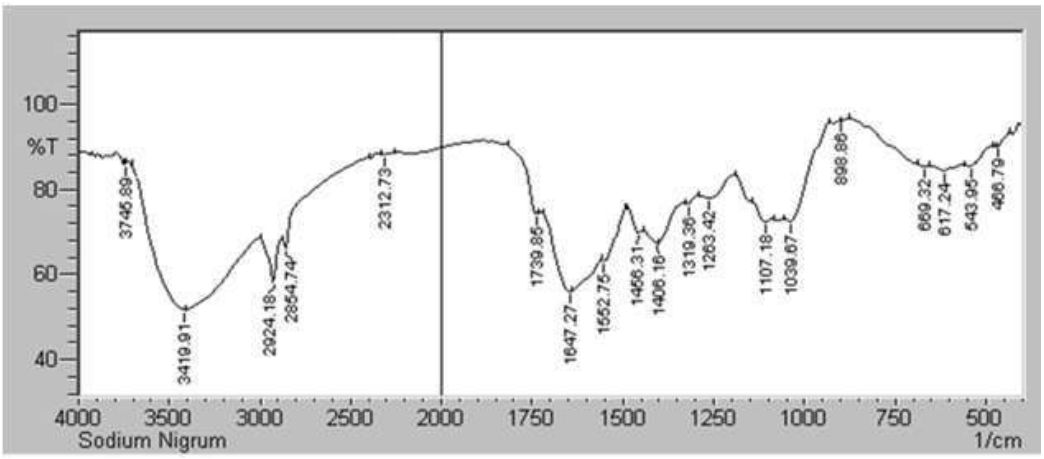



***Fig.no.3:*** **IR Spectra of *Solanum Nigrum***

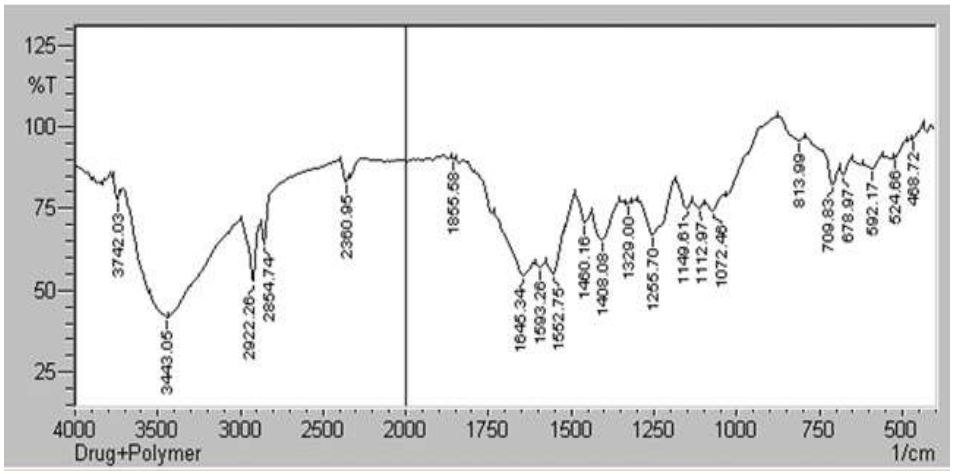



***Fig.no.4*:IR Spectra of *Solanum Nigrum* with Excipients**

### 3.7 Pharmacological Evaluation

#### 3.7.1 Antioxidant Activity

In all assays, radical scavenging and ferric-reducing activity increased in a concentration-dependent manner. At the highest concentration tested (120 µg/mL), the films produced 45.5 % inhibition in the DPPH assay, 88.6 % inhibition in the ABTS assay, and 27.9 % ferric ion reduction. These findings demonstrate potent free-radical scavenging and reducing properties, which can neutralize reactive oxygen species generated at ulcer sites and thereby accelerate mucosal repair. The particularly high ABTS inhibition suggests that the films are efficient at scavenging both hydrophilic and lipophilic radicals, likely due to the flavonoids and phenolic compounds present in *Solanum nigrum.*

**Table No.3: DPPH radical scavenging assay**

| S. No | Conc. (µg/mL) | Absorbance @517nm | % of Inhibition |
|---|---|---|---|
| 1 | Control | 0.224 | - |
| 2 | 20 | 0.179 | 20.08 |
| 3 | 40 | 0.155 | 30.80 |
| 4 | 60 | 0.153 | 31.69 |

| | | | |
|---|---|---|---|
| 5 | 80 | 0.148 | 33.92 |
| 6 | 100 | 0.131 | 41.51 |
| 7 | 120 | 0.121 | 45.51 |

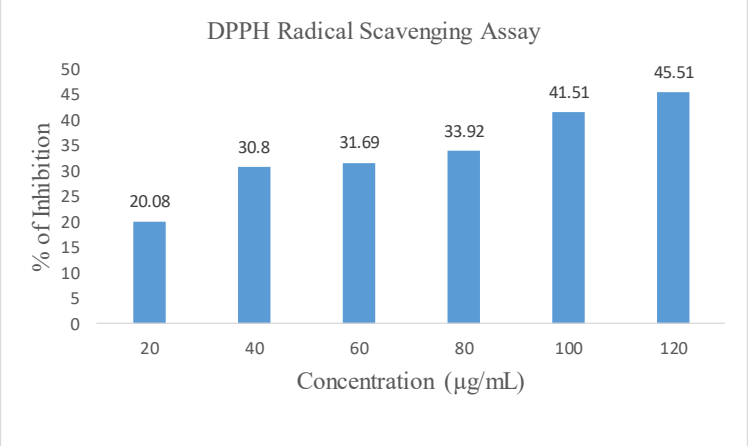



**Fig.no.5:IR Spectra of Solanum Nigrum with Excipients**

**Table No.4: DPPH radical scavenging assay graph comparison**

| S. No | Conc. (µg/mL) | Absorbance @734nm | % of Inhibition |
|---|---|---|---|
| 1 | Control | 0.132 | - |
| 2 | 20 | 0.099 | 25 |
| 3 | 40 | 0.067 | 49.24 |
| 4 | 60 | 0.051 | 61.36 |
| 5 | 80 | 0.045 | 65.90 |
| 6 | 100 | 0.022 | 83.33 |
| 7 | 120 | 0.015 | 88.63 |

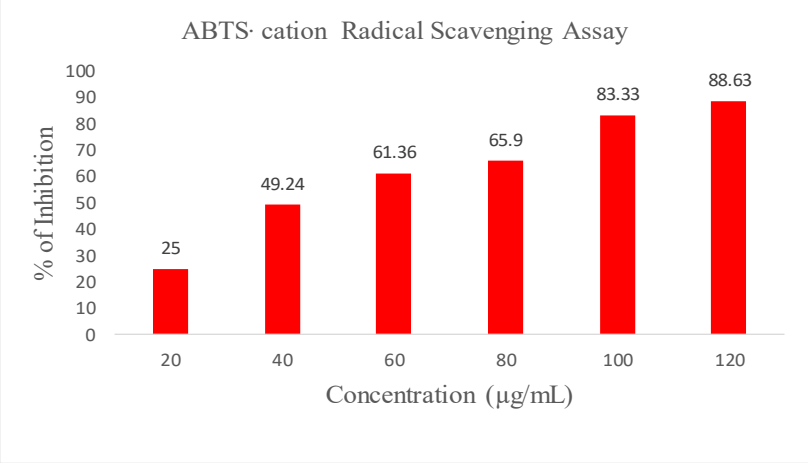



***Fig.no.6*: ABTS· cation radical scavenging assay graph comparison**

**Table No.5: Ferric reduction assay**

| S. No | Conc. (µg/mL) | Absorbance @700nm | % of Reduction |
|---|---|---|---|
| 1 | **Control** | **0.300** | - |
| 2 | 20 | 0.336 | 10.71 |
| 3 | 40 | 0.343 | 12.53 |
| 4 | 60 | 0.372 | 19.35 |

| | | | |
|---|---|---|---|
| 5 | 80 | 0.398 | 24.62 |
| 6 | 100 | 0.408 | 26.47 |
| 7 | 120 | 0.416 | 27.88 |

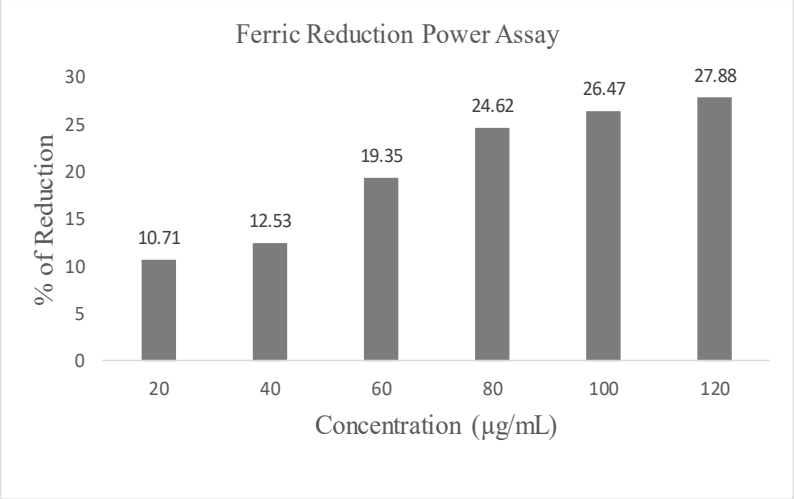



***Fig.no.7*: Ferric reduction assay graph comparison**

### 3.7.2 Anti-Inflammatory Activity

The observed anti-inflammatory activity can be attributed to the bioactive phytoconstituents present in *Solanum nigrum*, including steroidal alkaloids (solamargine and solasodine), flavonoids, tannins, and saponins. These compounds are known to inhibit cyclooxygenase (COX) and lipoxygenase (LOX) enzymes, reducing the synthesis of pro-inflammatory mediators such as prostaglandins and leukotrienes. Additionally, flavonoids stabilize cellular membranes and scavenge reactive oxygen species, further protecting tissues from oxidative damage and accelerating mucosal healing. The sustained release of these bioactives from the mucoadhesive film ensures prolonged anti-inflammatory action at the site of application, supporting its potential as an effective and patient-friendly therapy for oral ulcers.

**Table No.6: HRBC membrane stabilization assays**

| S. No | Conc. (µg/mL) | Absorbance @560nm | % of Inhibition |
|---|---|---|---|
| 1 | Control | 0.102 | - |
| 2 | 20 | 0.099 | 2.94 |
| 3 | 40 | 0.085 | 16.66 |
| 4 | 60 | 0.064 | 37.25 |
| 5 | 80 | 0.041 | 59.80 |
| 6 | 100 | 0.016 | 84.31 |
| 7 | 120 | 0.005 | 95.09 |

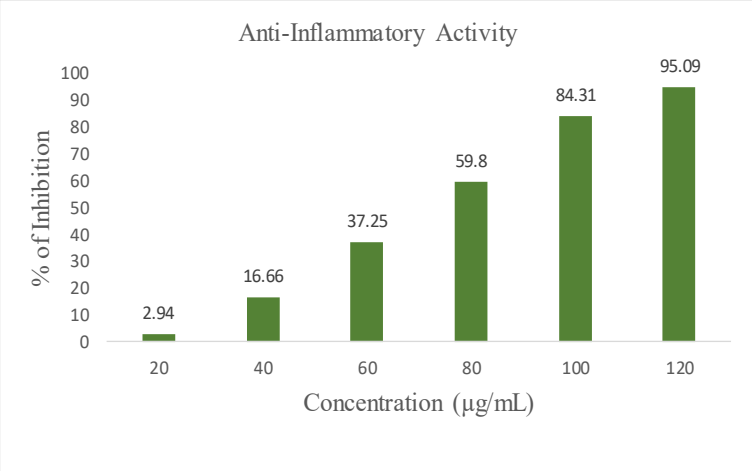



***Fig.no.8*: HRBC membrane stabilization assays graph comparison**

### 3.7.3 Anticancer Activity

Cytotoxicity studies on MCF-7 oral cancer cell lines revealed an IC50 of 54.2 µg/mL with up to 72.4 % cell death at 100 µg/mL. This indicates significant anticancer potential of *Solanum nigrum*'s steroidal alkaloids (solamargine, solasodine), which are known to induce apoptosis in cancer cells. While anticancer activity was not the primary objective of this formulation, the finding suggests a broader therapeutic potential, especially for oral precancerous lesions.

**Table No.7: Cytotoxicity studies**
**$IC_{50}$= 54.23 µg/ml**

| Concentrations (µg/mL) | % Cell viability | % Cell death |
|---|---|---|
| **Control** | 100 | 0 |
| 1.56 | 97.986 | 2.014 |
| 3.125 | 94.859 | 5.141 |
| 6.25 | 91.573 | 8.427 |
| 12.5 | 85.532 | 14.468 |
| 25 | 77.954 | 22.046 |
| 50 | 53.789 | 46.211 |
| 100 | 27.556 | 72.444 |

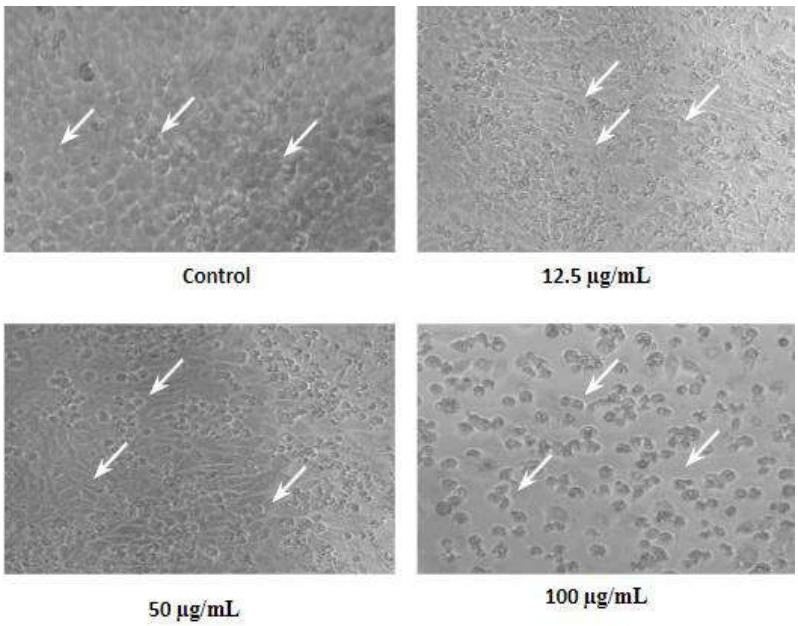


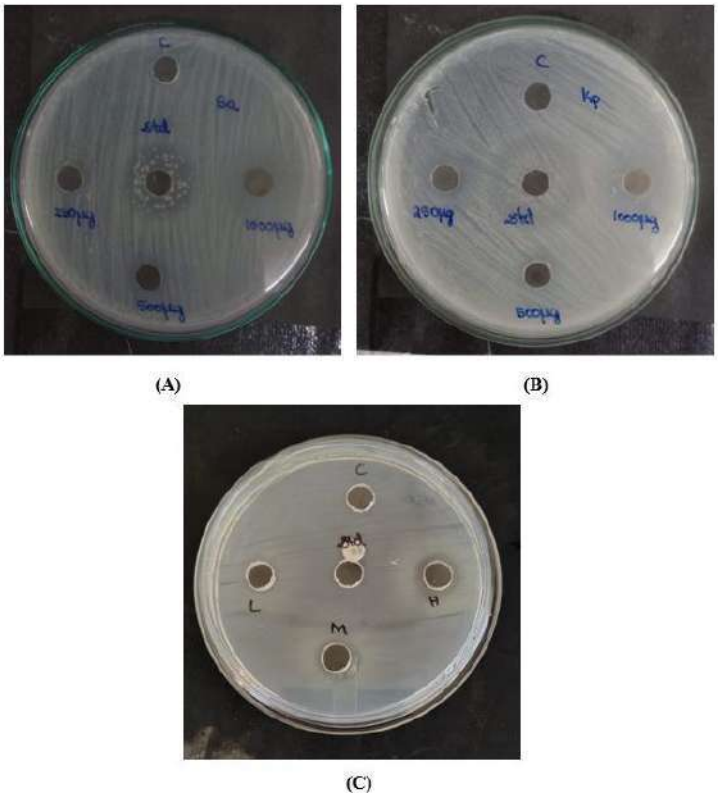

***Fig.no.9*: Oral Cancer Cell lines**

### 3.7.4 Antimicrobial Activity

The antibacterial and antifungal evaluations confirmed broad-spectrum antimicrobial activity. The films inhibited Staphylococcus aureus, Klebsiella pneumonia, and H. pylori with zones of inhibition up to 14 mm at 1000 µg, and also inhibited Candida albicans, Candida tropicalis, and Candida krusei with zones up to 13 mm. This property is particularly beneficial for preventing secondary infections in ulcerated tissues, which is a major drawback of conventional corticosteroid therapy

**Table No.8: Antibacterial activity**

| S.No. | Pathogen | Zone of Inhibition (mm) | | | |
|---|---|---|---|---|---|
| | | 250 µg | 500 µg | 1000 µg | STD |
| 1. | *Staphylococcus aureus* | 10 | 11 | 14 | 17 |
| 2. | *Klebsiella pneumonia* | 10 | 11 | 12 | 16 |
| 3. | *H. pylori* | - | 11 | 13 | 10 |




(A) (B) (C)

***Fig.no.10*: Microbial test of *Staphylococcus aureus* (A), *Klebsiella pneumonia* (B) & *H. pylori* (C)**

**Table No.9: Antifungal activity**

| S. No. | Pathogen | Zone of Inhibition (mm) | | | |
|---|---|---|---|---|---|
| | | 250 µg | 500 µg | 1000 µg | STD |
| 1. | *Candida albicans* | - | 10 | 13 | 10 |
| 2. | *Candida tropicalis* | - | - | 10 | 10 |
| 3. | *Candida krusei* | - | - | 13 | 10 |

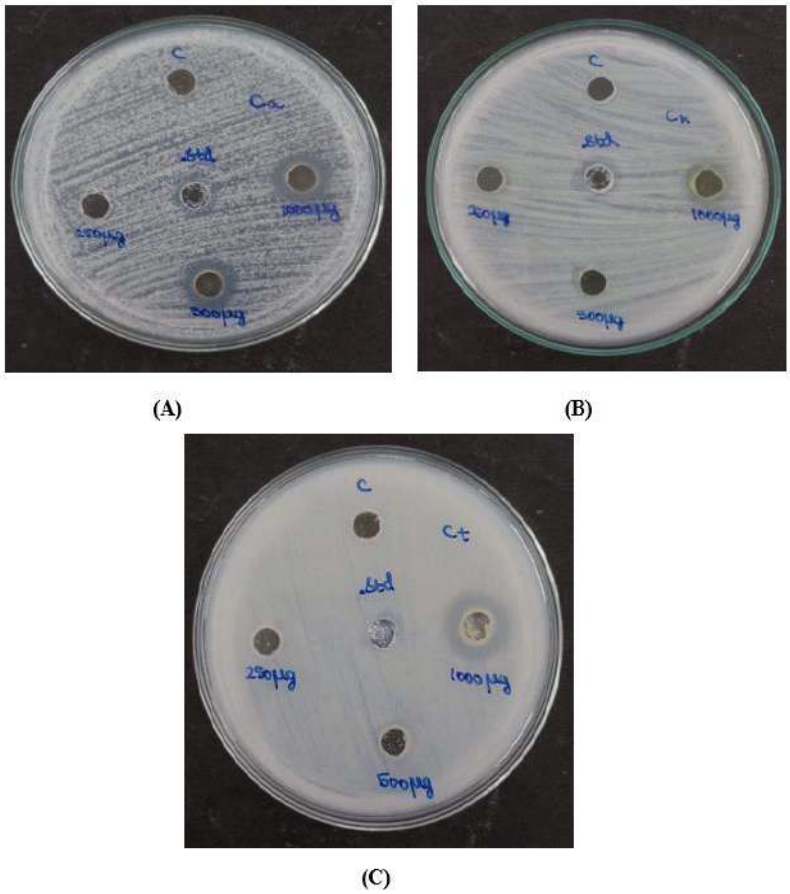



***Fig.no.11*: Microbial test of *Candida albicans* (A), *Candida tropicalis* (B) & *Candida krusei* (C)**

## 4. DISCUSSION

The present study was designed to develop and evaluate a novel mucoadhesive buccal film incorporating *Solanum nigrum* leaf extract for the treatment of mouth ulcers, with additional systemic pharmacological benefits. The findings of this research highlight the dual advantage of the formulation: localized therapeutic efficacy at the site of ulceration and systemic benefits due to the diverse phytochemical profile of *Solanum nigrum*. The extraction process using ethanol successfully yielded a phytochemically rich extract containing flavonoids, alkaloids, tannins, and phenolics, compounds well-documented for their anti-ulcer, antioxidant, and anti-inflammatory activities. The incorporation of the extract into an HPMC-based mucoadhesive film via solvent casting produced films that were uniform, flexible, and met the required physicochemical standards, including consistent weight, thickness, pH, folding endurance, and drug content uniformity. These results suggest that the chosen polymer–plasticizer combination was suitable for achieving the desired film quality and stability. The in vitro drug release studies demonstrated a rapid yet sustained release within 5.5 to 7.2 minutes, making the film particularly advantageous for oral ulcer management where quick relief and prolonged action are desirable. The mucoadhesive nature of the formulation ensures prolonged residence time at the site of action, reducing the frequency of administration and improving patient compliance. The pharmacological evaluation further strengthened the therapeutic potential of the formulation. Anti-ulcer studies in *H. Pylori* revealed significant mucosal healing and regeneration, correlating well with the traditional

use of *S. nigrum* in gastrointestinal disorders. Antioxidant assays confirmed the ability of the formulation to scavenge free radicals, which is vital in mitigating oxidative stress-associated tissue damage. Similarly, anti-inflammatory activity demonstrated through HRBC and protein denaturation models supports its role in reducing ulcer-associated inflammation.

Interestingly, the formulation also showed promising cytotoxic activity against oral cancer cells, with evidence of apoptosis, suggesting potential application in chemoprevention. Furthermore, the antibacterial, antifungal and anti-inflammatory activities recorded expand the therapeutic spectrum of the formulation, making it a multifunctional drug delivery system. These results underscore the holistic pharmacological properties of *S. nigrum* and justify its selection as the active therapeutic agent.

When compared with conventional treatments for mouth ulcers, the mucoadhesive buccal film offers multiple advantages. Current topical agents often require frequent reapplication and lack systemic benefits, while the developed formulation provides sustained release, multifunctional activity, and ease of administration. The integration of herbal medicine into modern dosage forms such as buccal films bridges traditional knowledge with contemporary pharmaceutical technology, supporting the concept of patient-friendly, green, and biocompatible drug delivery systems.

Nevertheless, certain limitations should be acknowledged. The study was limited to preclinical evaluations, and human trials are necessary to validate the clinical relevance of the findings. Moreover, large-scale stability and long-term storage studies are required to confirm its commercial feasibility. Despite these limitations, the present study provides a strong foundation for further research and potential translation into clinical practice.

## 5. CONCLUSION

The present study on the formulation and evaluation of mucoadhesive buccal films containing *Solanum nigrum* extract aimed to develop an effective, patient-friendly, and convenient dosage form for the treatment of mouth ulcers. The prepared films exhibited desirable physicochemical characteristics, including uniform thickness, smooth surface, acceptable folding endurance, and controlled drug release. The use of Solanum nigrum extract provided significant anti-inflammatory, antioxidant, antimicrobial, anticancer and wound-healing properties that helped accelerate mucosal repair and reduce ulcer discomfort. These results not only validate the traditional medicinal use of *Solanum nigrum* but also highlight its potential when incorporated into a novel dosage form that enhances bioavailability, patient compliance, and therapeutic efficacy. The study signifies a step toward sustainable, plant-based drug delivery systems that are cost-effective, biocompatible, and capable of addressing complex conditions where multiple therapeutic actions are required. Overall, the research indicated that the incorporation of Solanum nigrum extract into mucoadhesive buccal films is a promising approach for localized treatment of mouth ulcers, minimizing systemic side effects while improving patient compliance and comfort.

## 6. Conflict Of Interest Statement

We declare that we have no conflict of interest.

## 7. ACKNOWLEDGMENTS

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