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Formulation, Development & Evaluation of Mucoadhesive Buccal Patches For Toothache Relief

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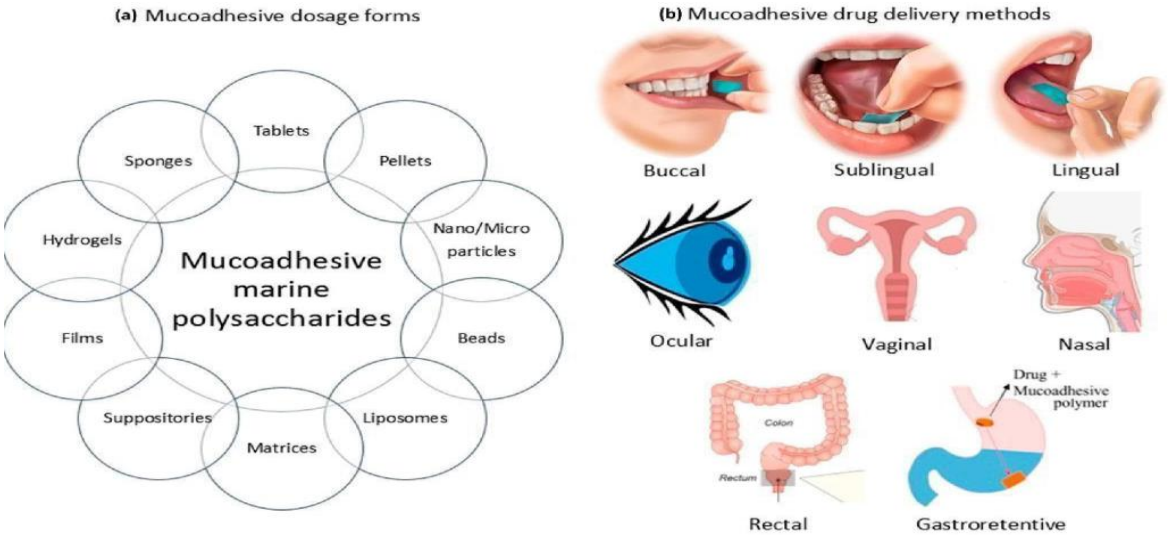
ABSTRACT

The present study focuses on the formulation and evaluation of mucoadhesive buccal patches using Thespesia populnea, a plant known for its significant analgesic, anti-inflammatory, and antimicrobial properties, for the effective relief of toothache. The extraction of bioactive constituents was carried out using the Soxhlet method, and the patches were prepared via the solvent casting technique using polymers such as HPMC E15 and sodium alginate. Preliminary and formulation batches were evaluated for various physicochemical parameters including thickness, weight uniformity, folding endurance, surface pH, swelling index, moisture loss, and eggshell membrane permeability. Among all, Batch F8 was found to be optimal, showing desirable mucoadhesive strength, flexibility, and drug permeation characteristics. The study concludes that Thespesiapopulnea mucoadhesive buccal patches offer a promising natural alternative for localized and effective toothache relief. Future prospects involve advanced testing models and in vivo studies to enhance therapeutic efficacy and bioavailability.

Keywords: *Thespesia populnea, mucoadhesive Buccal patches, HPMC E15, sodium alginate, polyethylene glycol 400, solvent casting technique.*

1. INTRODUCTION

Toothache is a common dental complaint that often requires immediate and localized therapeutic intervention. Conventional oral dosage forms, while effective, suffer from limitations such as poor bioavailability, first-pass metabolism, and systemic side effects. To overcome these challenges, buccal drug delivery systems have emerged as a promising alternative, offering several advantages including bypassing hepatic metabolism, rapid onset of action, and ease of administration. Among the various dosage forms, mucoadhesive buccal patches have gained attention due to their ability to adhere to the buccal mucosa, enabling controlled and sustained drug release at the site of action.



In recent years, interest in natural therapeutics has surged, driven by their favorable safety profiles and multifaceted pharmacological activities. Thespesiapopulnea, commonly known as the Indian Tulip Tree or Portia Tree, is a medium-sized evergreen plant found in tropical and coastal regions. Belonging to the family Malvaceae, it is well documented for its analgesic, anti-inflammatory, antimicrobial, and antioxidant properties (Solomon et al., 2015; Saxena Prasoon Kumar et al., 2010). Phytochemical investigations have revealed the presence of several bioactive constituents such as flavonoids, phenolic compounds, tannins, terpenoids, and alkaloids, all of which contribute to its therapeutic potential in dental ailments including toothache (Vishwakarma et al., 2022).

The buccal delivery of Thespesiapopulnea extract via mucoadhesive patches offers the dual advantage of site-specific action and sustained release, enhancing its efficacy in pain management. Prior studies have reported successful use of polymers like HPMC, PVA, and Carbopol 934 for developing such patches (Puratchikody et al., 2011). In this study, HPMC E15 and sodium alginate were selected as primary mucoadhesive polymers to formulate and evaluate buccal patches containing Thespesia populnea extract. The solvent casting method was employed for preparation, and the patches were subjected to thorough physicochemical and permeation evaluations to determine their suitability for clinical application.

This research aims to establish a novel, herbal-based mucoadhesive drug delivery system for effective toothache relief, offering an alternative to synthetic analgesics with potential improvements in patient compliance and therapeutic outcomes.

Mucoadhesive buccal patches' mechanism:

In order to release the medication in a controlled manner for either local or systemic absorption, mucoadhesive buccal patches adhere to the buccal mucosa, which is the inside lining of the cheek. Mucoadhesion and drug release are the two primary phases of the process.[8]

1. Mechanism of Mucoadhesion:

The adherence of a medication delivery system to the mucin layer of the mucosal surface is known as mucoadhesion. There are three successive stages to it:

a. Wetting and Swelling Stage (touch Stage):

Saliva and fluids come into touch with the patch. The patch's hydrophilic polymers swell come into close contact with the mucosal surface.

b. Adhesion Stage (Interpenetration):

The patch's polymer chains interact with the mucus layer's mucin glycoproteins. Ionic interactions, van der Waals forces, hydrogen bonds, and physical Appearance.

c. Consolidation Stage:

Durable adherence is guaranteed by robust chemical and physical interactions. The patch stays in place despite mechanical stress from tongue and cheek movement as well as salivary wash-out.

2. Drug Release Mechanism:

One or more of the following mechanisms releases the drug after adhesion is established: Diffusion: The medication enters the mucosa via diffusing through the enlarged polymer matrix. Dissolution: The medication penetrates the buccal membrane after dissolving in saliva. Erosion: The medication is released in certain regions as the polymer matrix eventually erodes.

3. Drug Absorption Pathway:

The medication enters the capillaries beneath the buccal epithelium. skips the first-pass metabolism and enters the systemic circulation immediately.

- **Phytochemical Constituents :**

Key bioactive compounds found in various parts (bark, leaves, flowers, fruits, roots):

a) **Flavonoids:** Gossypetin, kaempferol, quercetin Phenolic compounds: Gallic acid, ellagic acid Tannins

b) **Terpenoids Steroids:** β-sitosterol Gums, Mucilage Alkaloids .

- **Pharmacological Activities :**

a) Anti-inflammatory Antioxidant .

b) Antimicrobial (antibacterial, antifungal) Wound healing .

c) Hepatoprotective Antidiabetic Analgesic Anti-ulcer.

2. MATERIAL AND METHODS:

2.1. PREFORMULATION STUDY:

2.1. 1.Identification Test:

A. Thespesia Populnea:

- **Melting point:**

The melting point of Thespesia Populnea was determined by capillary method.

2.2. Thespesia populnea extraction with the Soxhlet apparatus:

1. Prepare the sample by drying the plant or solid material and then powdering it finely.
2. Fill the thimble: Put the sample into a cellulose thimble that is permeable.
3. Configure the device by placing the thimble inside the Soxhlet extractor.
4. Add solvent: Pour an appropriate solvent into the round-bottom flask.
5. Start heating: Warm the solvent until it evaporates, drips into the thimble, and condenses in the condenser.
6. Extraction cycle: Solvent enters the chamber, the chemical is extracted, and the chamber siphons back into the flask.
7. Repeat cycles: This cycle runs on autopilot for a number of hours.
8. Collect extract: To obtain the pure extract, remove the solvent from the flask after finishing.

2.3.Preparation for Mucoadhesive buccal patches:

The solvent casting process was used in this study to create mucoadhesive buccal patches. Using a range of polymers, including cellulose derivatives, acrylic polymers, and biodegradable lactide and glycolide polymers, this method has been widely utilized to prepare buccal patches.

2.4.Mucoadhesive buccal patches are prepared using the following method:

Solvent casting, which involves dissolving a polymer in a solvent and then evaporating the solvent to produce films or porous structures.

1. Dissolving: A suitable solvent was used to dissolve the medication and mucoadhesive polymers.
2. Blending: To guarantee a homogenous combination, the solution was well combined, frequently with the aid of a magnetic stirrer.
3. Plating: After that, the solution was transferred to an appropriate surface and allowed to dry.
4. Drying: After the film had dried, it was carefully trimmed to the appropriate size and shape.

2.5 Batches For Selection & Procurement of Polymer

INGREDIENTS	PO1	PO2	PO3	PO4	PO5	PO6
THESPESIA	20	20	20	20	20	20

POPULNEA(mg)						
ALOE GUM(mg)	200	300	400	-	-	-
HPMC E15	-	-	-	200	300	400
SODIUM ALGENATE(mg)	200	200	200	200	200	200
PEG(ml)	0.16	0.16	0.16	0.16	0.16	0.16
ETHANOL(ml)	5	5	5	5	5	5
WATER(ml)	25	25	25	25	25	25

Table 1: Preliminary batches of mucoadhesive buccal patches

2.6. Optimization of Mucoadhesive Buccal Patches Formulation Using 32 Full Factorial Designs:

Creating a pharmaceutical formulation that is acceptable in the shortest amount of time with the fewest possible man-hours and raw resources is ideal. Pharmaceutical formulations are typically generated by adjusting one variable at a time. The process is time-consuming and necessitates a great deal of creativity. Furthermore, because the joint effects of independent variables are not taken into account, it could be challenging to create an optimal formulation using this traditional method. Therefore, it is crucial to use well-established statistical tools like factorial design to comprehend the complexity of pharmaceutical formulations. The factorial design methodology is a useful way to show the relative importance of several variables and their interactions, in addition to the art of formulation.The number of independent variables chosen determines how many experiments are needed for these investigations. For every trial, the response (Yi) is assessed. Y=b0+b1X1+b2X2+b12X1X2+b11X1 +b X = 2 22 2 2 where bi is the estimated coefficient for the factor Xi, b0 is the arithmetic mean response of the nine runs, and Y is the dependent variable. The average outcome of adjusting one factor at a time from its low to high value is shown by the primary impacts (X1 and X2). When two factors are altered at the same time, the response changes, as indicated by the interaction terms (X1X2).

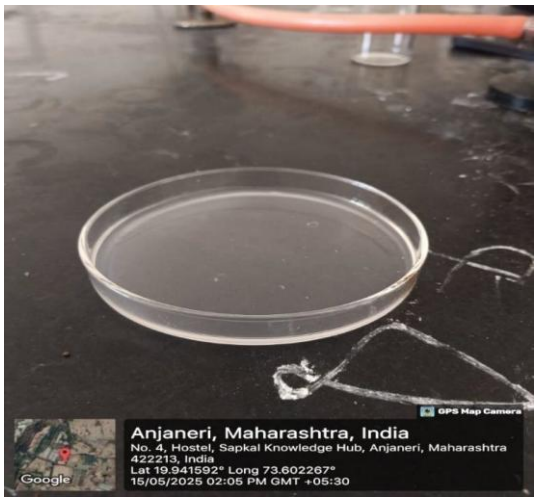
The current study used a 32-person randomized complete factorial design. In this approach, experimental trials were conducted at all nine potential combinations, and two factors were investigated at three levels each.

2.7.Formulation batches of Mucoadhesive Buccal Patches using *Thespesia populnea*:

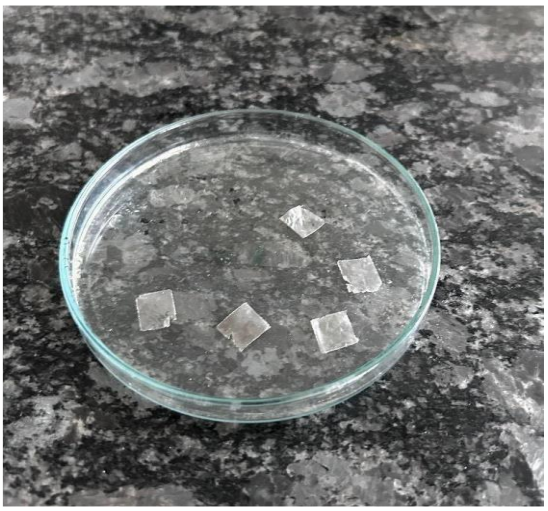
Batch code	**HPMC (mg)**	**Sodium Alginate (mg)**	**Thespesia Populnea (mg)**	**PEG400 (ml)**	**Ethanol (ml)**	**Water (ml)**
F1	150	150	20	0.16	5	25
F2	150	200	20	0.16	5	25
F3	150	250	20	0.16	5	25
F4	200	150	20	0.16	5	25
F5	200	200	20	0.16	5	25
F6	200	250	20	0.16	5	25
F7	250	150	20	0.16	5	25
F8	250	200	20	0.16	5	25
F9	250	250	20	0.16	5	25

Table 2: Formulation batches of MucoadhesiveBuccal Patches using *Thespesiapopulnea*

2.7.1. Formulation mucoadhesive buccal patches :



2.7.2. Prepared mucoadhesive buccalpatches:



2.8. EVALUATION OF PREPARED THESPESIA POPULNEA:

As stated in the protocol, drug-loaded mucoadhesive buccal patches were made using the solvent casting process. The following evaluation criteria were applied to prepared mucoadhesive buccal patches.

Preliminary evaluation tests:

2.8.1.Physical appearance: A visual inspection of the mucoadhesive buccal patches was conducted

2.8.2. Patch consistency in thickness: Three patches of each formulation were reserved so that the thickness of the patches could be measured at three distinct locations using a micrometer screw gauge. After then, the mean value was noted.

2.8.3. The patches' uniform weight:Three patches of each formulation were weighed separately on an ATX 224 digital scale (Shimadzu, Japan) in order to assess the patch weight. After that, the mean weight for every formulation was determined.

2.8.4. Folding endurance: A sharp blade was used to cut three patches of each formulation that were larger in size, measuring 2 × 2 cm. A tiny strip of patch was folded repeatedly at the same spot until it broke in order to measure folding durability. The folding endurance rating was determined by counting the number of times the patch could be folded in the same spot without breaking. After calculation, the mean value was noted.

2.8.5 Surface pH: Three patches of each formulation were placed on an agar plate and left to swell for two hours in order to measure the surface pH. Using the previously described technique, pH paper was applied to the surface of the swollen patch to test the surface pH. Three readings on average were noted

2.8.6Studies on the Mucoadhesive Buccal Patches' swelling: After being weighed (W1), the buccal patch was put in 2% agar gel plates and incubated for two hours at 37C. At regular 30minute time intervals, the patch was removed from the petri dish and excess surface water was removed gently using the filter paper. The enlarged patch was then reweighed (W2) and swelling index (SI) was calculated.

2.8.7.Percentage of Moisture Absorbed and Loss: The percentage of moisture absorbed and moisture lost for each formulation.

% Absorption of Moisture = Mi - Mf / Mi × 100

where Mi is the patch's initial weight

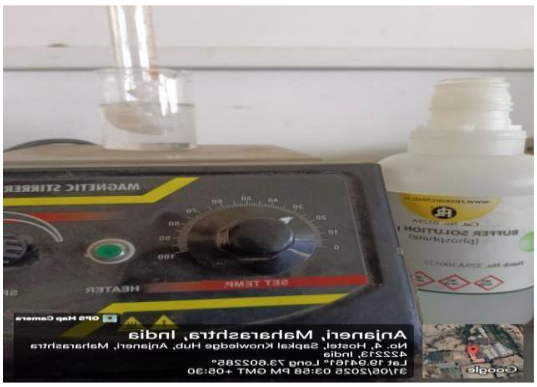
and Mf is its final weight.

2.8.8. Percentage Moisture Loss (PML): This test was used to evaluate the patches' integrity while they were dry. Three patches of one centimeter in diameter were cut out, precisely weighed, and stored in desiccators that contained fused anhydrous calcium chloride. The patches were taken out and weighed after 72 hours.

2.8.9Method of Eggshell Permeability Testing :

a. Decalcify the Eggshell: Gently crack the egg and take out its contents. To get rid of the calcium carbonate shell layer and preserve the eggshell membrane, soak the shell in 0.6% hydrochloric acid (HCl) for a whole day. Use distilled water to rinse well.

b. Cut and Mount the Membrane: Cut the membrane into a round piece that is only a little bit bigger than the test tube or diffusion cell's opening.



3. RESULT AND DISCUSSION:

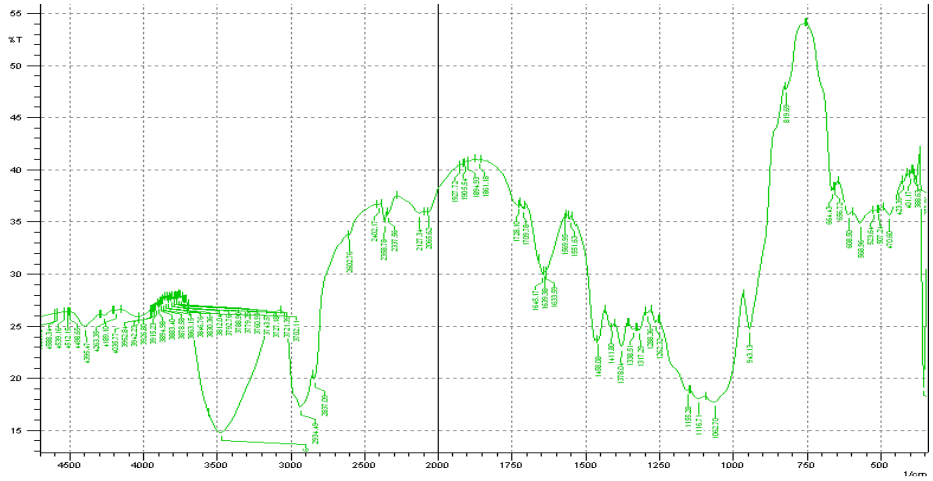
3.1Physical appearance:

It was observed that the fabricated mucoadhesive buccal patches were thin, transparent and visually smooth surfaced.

- **Melting point:**

The melting point of ThespesiaPopulnea was determined by capillary method and was found to be 58 – 600 C.

FTIR Spectroscopy of HPMC E15:



2.2.Thespesiapopulnea extraction with the soxhlet apparatus:

3.2. Thickness uniformity of the patches:

3.2.1. Thickness uniformity of trial batches formulation

Sr. No.	Trial batches code	Average thickness(mm)
1	PO1	0.12±0.010
2	PO2	0.12±0.010
3	PO3	0.13±0.011
4	PO4	0.38±0.007
5	PO5	0.37±0.070
6	PO6	0.36±0.023

Table 3.Thickness Uniformity of Trial Batches formulation

3.2.2.Data of Thickness of The Mucoadhesive Buccal Patches.

Sr. No.	Formulation code	Average thickness (mm)*
1	F1	0.38±0.007
2	F2	0.37±0.070
3	F3	0.36±0.023
4	F4	0.44 ±0.01
5	F5	0.43±0.01
6	F6	0.39±0.0278
7	F7	0.53 ±0.01
8	F8	0.48 ±0.01
9	F9	0.53 ±0.01

Table 4.Patch Thickness of Mucoadhesive Buccal Patch was found to be best in F8 Batch.

3.3Weight uniformity of the patches

Data of Weight Variation Sr. No.	Formulation code	Average weight (gm)*
1.	F1	160.32±0.996
2.	F2	181.48±0.996
3.	F3	198.43±0.577
4.	F4	254.23±0.996
5.	F5	277.53±0.571
6.	F6	299.24±0.571
7.	F7	381.67±0.571
8.	F8	360.29±0.571
9.	F9	398.76±o.577

Table 5: Weight uniformity of the patches

From above data we conclude F8 Batch was has required range weight uniformity range

3.4.Folding Endurance:

3.4.1.Folding Endurance of Aleo Gum Batches

Sr. No.	Trial batch code	Folding endurance
1	PO1	*
2	PO2	*
3	PO3	*
4	PO4	*
5	PO5	**
6	PO6	*

Table 6: Folding Endurance of Aleo Gum Batches

* =Flexible ** = Very flexible

3.4.2 .Data of Folding Endurance of TheMucoadhesiveBuccal Patches

Sr. No.	Formulation code	Folding endurance*
1.	F1	*
2.	F2	*
3.	F3	*
4.	F4	*
5.	F5	*
6.	F6	*
7.	F7	*

8.	F8	**
9.	F9	*

Table 7. Folding Endurance of TheMucoadhesiveBuccal Patches

From above data we conclude F8 batch was found to be best for folding Endurance as it contains best concentration of used polymers.

3.5.Surface pH:

Ordinary surface pH figure of prepared mucoadhesive buccal patch

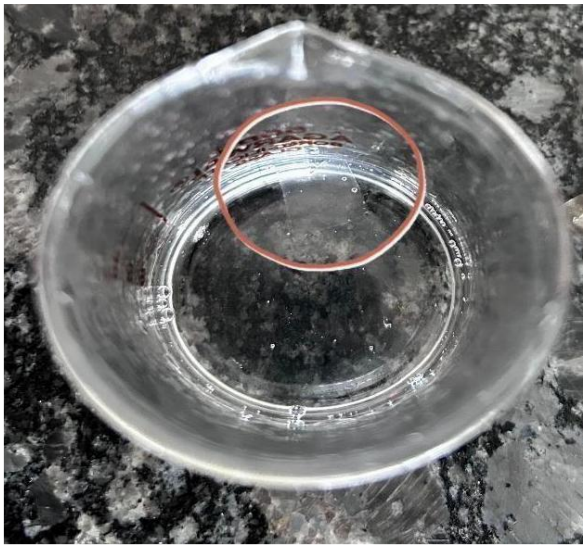
3.5.1Data of Surface pH of Mucoadhesive Buccal Patches

Sr. No.	Formulation code	Surface pH
1.	F1	6.54±0.01
2.	F2	6.46±0.01
3.	F3	6.44±0.00
4.	F4	6.86±0.01
5.	F5	6.84±0.02
6.	F6	6.76±0.01
7.	F7	6.92±0.01
8.	F8	6.99±0.01
9.	F9	6.9±0.01

Table 8:Surface pH of prepared MucoadhesiveBuccal Patches

Surface pH of prepared Mucoadhesive Buccal Patches were found between 5-6, which is best suitable for Mucoadhesive buccal drug delivery.

3.6.Swelling studies of the Mucoadhesive Buccal Patches:



Swelling studies for formulation of mucoadhesive buccal patches

3.6.1. Data of Swelling studies of Mucoadhesive Buccal Patches

Sr. No.	Formulation code	Swelling Index
1.	F1	84.2±0.4
2.	F2	92.32±0.893
3.	F3	99.08±0.01
4.	F4	82.4±0.01
5.	F5	90.48±0.503
6.	F6	98.18±0.012
7.	F7	90.23±0.012
8.	F8	80.8±0.0187
9.	F9	97.32±0.159

Table 9.Swelling Index of Formulated Buccal Patches was found.

3.7.Percentage moisture Absorbed and Loss:

The percentage moisture absorbed and moisture loss of all formulation was determine

3.7.1.Data of % Moisture Absorbed And % Moisture Loss of The Mucoadhesive Buccal Patches:

Sr. No.	Formulation code	Percent moisture absorbed*	Percent moisture loss*
1.	F1	3.24 ±0.15	5.98 ±0.01
2.	F2	3.263±1.235	7.6 ±0.01
3.	F3	3.00 ±0.12	8.62±0.002
4.	F4	3.97 ±0.14	5.67±0.01

5.	F5	3.738 ±1.509	6.16±0.03
6.	F6	3.847 ±1.347	8.45±0.01
7.	F7	3.907±1.34	6.15±0.01
8.	F8	4.324 ±0.24	5.51±0.01
9.	F9	5.235±1.211	7.8±0.01

Table 10: % Moisture Absorbed And % Moisture Loss

All values are expressed as mean ± SD (n=6).

From above data we conclude that Batch F8 was found to be ideal batch for preparation of mucoadhesive buccal patches.

3.7.2.DATA OF MOISTURE LOSS OF PRILIMINARY ALEO GUM BATCHES:-

Sr. No.	Trial batches	Percent moisture content	Percent moisture loss
1	PO1	2.34±0.12	3.12±0.32
2	PO2	2.36±0.11	3.02±0.20
3	PO3	2.35±0.12	3.3±0.13

Table 11: Data of moisture loss of preliminary aloe gum batches

3.8.Eggshell Permeability Testing Method:

The Pharmacognostic testing of F8 Batch was carried out to confirm the presence of secondary metabolites in the formulation.

Sr.No.	Test	Ideal Result	Obtained Result
1.	**Test For Tannins:** 1– 2 drops of $FeCl_3$ + solution.	Blue-black or greenish color indicates tannins.	Solution turns greenish black indicating presence of tannins
2.	**Test For Flavonoids:** 2-3 ml solution + small amount magnesium+ few drops conc. HCL	A reddish-pink, orange or red coloration indicates presence of flavonoids.	Solution turns pinks indicating presence of flavonoids
3.	**Test For Alkaloids:** 2 ml solution + few drops dragendorff's reagent	Orange color indicates presence of alkaloids	Solution turns yellow indicating presence of alkaloids
4.	**Test For Triterpenoids:** 2 ml solution + 2 ml chloroform + 3 ml conc. H2SO4	Reddish brown at interface indicates triterpenoids	Reddish brown color at interface indicated presence of triterpenoids

Table 12: Pharmacognostic testing

3.9. DISCUSSION

VALIDATION OF OPTIMIZED FORMULATION:

Optimized Formula For Formulation of Mucoadhesive Buccal Patches Using Thespesia Populnea

Ingredients	F8
Thespesia populnea (mg)	20
HPMC E15 (mg)	250
Sodium alginate (mg)	200
PEG 400(ml)	0.16
Ethanol (ml)	5

Table 13: Optimized Formula ForFormulation of MucoadhesiveBuccal Patches

We conclude Batch F8 was found to be optimized batch.

4. CONCLUSION

Sodium alginate and the polymer HPMC were used to successfully create the mucoadhesive buccal patches. Therefore, Batch F8 has a high enough concentration of polymers to distribute Thespesia Populnea by mucoadhesion. Populnea Thespesia The solvent casting process was used to create mucoadhesive buccal patches, as it was determined to be the most effective approach for doing so. As the percentage of polymer grew, so did the average thickness and weight of buccal polymeric patches. The F9 included two polymers at maximum concentrations and was the thickest and heaviest. The patches were assessed for swelling, and the results show that the recipes with the highest concentrations of sodium alginate and HPMC E-15 had the most swelling. Therefore, we draw the conclusion that Thespesia populnea can satisfy the optimal criteria for buccal delivery, which may be a useful treatment for toothaches.

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