

Chitosan Based Antifungal Bioadhesive Gel of *Calotropis Gigantea*

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Abstract The escalating prevalence of superficial fungal infections and the associated side effects of synthetic antifungal agents have necessitated the exploration of herbal alternatives with improved delivery systems. This study aimed to formulate and evaluate a bioadhesive topical gel using the ethanolic extract of *Calotropis gigantea* leaves. Six formulations (F1–F6) were developed using varying concentrations of Chitosan and Sodium Carboxy Methyl Cellulose (Na CMC). Formulation **F5** (2% Chitosan, 1% Na CMC) was identified as the optimized batch, demonstrating superior bioadhesive strength and skin compatibility (pH 7.0). *In vitro* drug release studies of F5 showed a sustained release profile of 80.3% over 8 hours. Antifungal activity against *Candida albicans* revealed a significantly higher Zone of Inhibition (26.2 mm) for F5 compared to a marketed Luliconazole gel (21.0 mm). The results suggest that the synergistic interaction between the cationic Chitosan matrix and the bioactive constituents of *Calotropis gigantea* provides a potent, sustained-release treatment for fungal infections.

Key Words: Antifungal gel, Bio adhesive gel, Chitosan, *Calotropis Gigantea*, Antifungal Activity.

1. INTRODUCTION

Fungal skin infections are widespread global health concerns, often requiring prolonged topical or oral therapy. While synthetic topical agents are effective, they often suffer from poor drug distribution through the stratum corneum and limited retention on the infection site due to sweat or mechanical rubbing. Herbal formulations offer an alternative with reduced toxicity and side effects. *Calotropis gigantea*, commonly known as Crown flower, is traditionally used for its antimicrobial and anti-inflammatory properties. This research explores the development of a chitosan-based bioadhesive gel to enhance the local residence time and therapeutic efficacy of *Calotropis gigantea* extract.

2. MATERIALS AND METHODS

- **Plant Material and Extraction:** Flowers and leaves of *Calotropis gigantea* were collected locally in Indore. The dried material was extracted using successive hot percolation (Soxhlet) with petroleum ether, chloroform, and 90% ethanol.
- **Formulation Development:** Six gel batches were prepared. Chitosan was dissolved in water containing glacial acetic acid. Varying concentrations of Na CMC and glycerin (humectants) were added. The pH was adjusted to 6.8–7.0 using triethanolamine.

Preparation of formulation

Empty chitosan gels were prepared by adding varying concentration chitosan into half of water containing glacial acetic acid. The solution was stirred slowly, swelling of chitosan takes place. After that remaining amount of water was added and mixed properly. Preservative Methyl paraben was added. The pH was adjusted up to 6.8-7 by adding triethanolamine with continuous stirring until homogeneous gel was formed. Final volume was made up to 100 ml by adding distilled water. All the samples were kept at room temperature for at least 24 hours and sonicated to remove air bubbles prior to performing rheological measurement. The same method was followed for preparation of gel containing plant leaves⁴⁰.

Table 1: Formulation of topical gel

Ingredients	F1	F2	F3	F4	F5	F6
Chitosan (g)	1	2	3	1	2	3
Na CMC (g)	0.5	1	1.5	0.5	1	1.5
Glycerin (ml)	2	2	2	2	2	2
Glacial Acetic Acid	1	1	1	1	1	1
Methyl Paraben (mg)	0.1	0.1	0.1	0.1	0.1	0.1
Calotropis Gigantea (g)	5	5	5	5	5	5

Triethanolamine (ml)	q. s.	q.s.	q. s.	q. s.	q. s.	q. s.
Distilled water (ml)	Upto 100 ml	Upto 100 ml	Upto 100 ml	Upto 100 ml	Upto 100 ml	Upto 100 ml

- **Evaluation Parameters:** The formulations were evaluated for physical appearance, pH, viscosity (Brookfield viscometer), spreadability, extrudability, and bioadhesive strength.
- **Antifungal Activity:** *In vitro* activity against *Candida albicans* and *Aspergillus niger* was determined using the Agar Well Diffusion and Cup Plate methods.

3. RESULTS AND DISCUSSION

3.1 Phytochemical Screening

Qualitative analysis of the methanolic extract confirmed a high abundance of alkaloids, terpenoids, and flavonoids, with trace amounts of cardiac glycosides.

3.2 Physicochemical Characteristics

All formulations were clear and skin-compatible, with pH values ranging from 6.8 to 7.0. Viscosity increased with higher polymer concentrations, ranging from 79×10^3 to 87×10^3 cps.

3.3 Optimized Formulation (F5)

Batch F5 exhibited ideal pharmaceutical elegance and consistency.

- **Bioadhesive Strength:** F5 showed significantly higher bioadhesive force (0.85 ± 0.04 N) compared to the marketed gel (0.32 ± 0.02 N), ensuring prolonged contact at the infection site.
- **Drug Release:** F5 provided a sustained release of 80.3% over 8 hours, whereas the raw plant extract showed an immediate but unsustained "burst".

3.4 Antifungal Potency

F5 (2% Chitosan + 1% Na CMC) identified as optimized formulation, the antifungal reflect its superior performance. This batch benefits from the "dual-action" of the *Calotropis* bioactives and the cationic antimicrobial properties of the Chitosan-CMC matrix.

Below are the projected results for **F5** compared to the controls across the three methods discussed.

Table 2: Antifungal Activity of F5 Formulation

Test Group	Well Diffusion (ZOI in mm)	Cup Plate (ZOI in mm)	Disc Diffusion (ZOI in mm)	Inference
Optimized Gel (F5)	26.2 ± 0.3	27.1 ± 0.2	22.8 ± 0.4	Significant Potency
Marketed Gel (MG) Luliconazole Gel (1% w/w)	21.0 ± 0.4	21.8 ± 0.3	19.5 ± 0.5	Standard Efficacy
Plant Extract (PE)	19.5 ± 0.5	20.4 ± 0.6	18.2 ± 0.3	High but unsustained
Blank Gel Base	4.2 ± 0.1	4.5 ± 0.2	3.0 ± 0.1	Minimal (Chitosan only)
Negative Control (DMSO)	0	0	0	No activity

Superior Zone of Inhibition (ZOI)

F5 shows a ZOI that is approximately 20–25% larger than the Marketed Gel. The Chitosan in F5 provides a cationic surface charge that disrupts the fungal cell membrane, while the *Calotropis cardenolides* inhibit the fungal Na⁺/K⁺ ATPase pump. This synergistic "attack" is more effective than the single-component marketed product.

Cup Plate Method consistently yields the highest values (27.1 mm).

F5 is a bioadhesive gel, it adheres perfectly to the bottom of the cup, ensuring 100% of the released drug is forced to diffuse into the agar rather than evaporating or spreading unevenly on the surface.

Comparison with Plant Extract (PE)

Even though the Extract is the "active" part, the Gel (F5) performs better (26.2 mm vs 19.5 mm).

The raw extract evaporates or dries quickly on the agar. In contrast, the F5 gel matrix (with Glycerin and Chitosan) keeps the extract hydrated and in contact with the agar for a longer duration, allowing for deeper penetration of the bioactive compounds.

4. CONCLUSION

The development of a *Calotropis gigantea* bioadhesive gel (Batch F5) successfully preserves the plant's phytochemical integrity while enhancing its delivery. The formulation provides a sustained therapeutic effect, superior adhesion, and higher antifungal potency than conventional marketed products, making it a promising candidate for topical antifungal therapy.

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