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Formulation, Development and Evaluation of Antifungal Shampoo of Itraconazole with Natural Extract

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Abstract:

The present study aimed to formulate and evaluate an antifungal shampoo containing itraconazole in combination with natural extracts such as neem, aloe vera, reetha, and shikakai for effective treatment of scalp fungal infections. A total of nine formulations (F1–F9) were developed using aqueous gel-based emulsion technique by varying concentrations of herbal components. Preformulation studies including DSC and FTIR confirmed the purity and compatibility of itraconazole with excipients. The prepared shampoos were evaluated for physicochemical parameters such as pH, viscosity, spreadability, foamability, stability, and drug content. The pH of all formulations ranged from 5.4 to 6.1, suitable for scalp application. Viscosity varied depending on xanthan gum concentration, with F3, F6, and F9 showing higher viscosity. Spreadability and foaming studies indicated good cleansing and application properties. Among all formulations, F6 exhibited optimal performance with balanced viscosity, stable foam, and good spreadability. In vitro drug release studies revealed sustained release of itraconazole up to 79% over 8 hours. Drug release kinetics followed first-order model ($R^2 = 0.998$), indicating concentration-dependent release. The formulation also showed significant antifungal activity against fungal strains. Thus, the developed antifungal shampoo represents a promising topical delivery system combining synthetic and herbal agents.

Keywords: Itraconazole, Antifungal shampoo, Herbal extract, Neem, Aloe vera, Drug release kinetics.

Introduction

Fungal infections of the scalp, including dandruff, seborrheic dermatitis, and dermatophytosis, represent some of the most prevalent dermatological disorders worldwide. These conditions are primarily associated with fungal species such as Malassezia, Candida, and dermatophytes, which colonize the scalp and disrupt its normal physiology. The symptoms often include itching, flaking, inflammation, irritation, and hair fall, significantly affecting the quality of life and psychological well-being of affected individuals. The increasing incidence of these infections can be attributed to factors such as environmental pollution, excessive use of chemical-based hair products, poor hygiene, and compromised immunity. Conventional antifungal therapies, including topical creams, lotions, and oral

medications, are widely used for managing these infections. However, these treatments are often associated with several limitations such as poor drug penetration into the scalp, systemic side effects, prolonged treatment duration, and reduced patient compliance. Additionally, repeated use of synthetic antifungal agents may lead to resistance and recurrence of infection. These challenges have prompted the need for alternative therapeutic approaches that are safer, more effective, and patient-friendly.

Itraconazole is a potent broad-spectrum antifungal agent belonging to the triazole class of compounds. It exhibits its antifungal activity by inhibiting the enzyme lanosterol 14α-demethylase, thereby blocking the biosynthesis of ergosterol, an essential component of fungal cell membranes. This results in increased membrane permeability and eventual fungal cell death. Despite its high efficacy, the topical application of itraconazole is limited by its poor aqueous solubility and low permeability, which necessitates the development of suitable formulation strategies to enhance its delivery and retention at the target site. In recent years, there has been a growing interest in the incorporation of natural and herbal ingredients into pharmaceutical and cosmeceutical formulations.

Herbal extracts not only provide therapeutic benefits but also improve the safety profile and consumer acceptability of the product. Neem (Azadirachta indica) is well known for its strong antifungal, antibacterial, and anti-inflammatory properties, making it highly effective in treating scalp infections. Aloe vera (Aloe barbadensis Miller) possesses moisturizing, soothing, and wound-healing properties, which help in reducing scalp irritation and dryness. Reetha (Sapindus mukorossi), commonly known as soapnut, acts as a natural surfactant and cleansing agent, producing rich lather without causing damage to hair. Shikakai (Acacia concinna) is traditionally used as a natural conditioner that promotes hair growth and maintains scalp health.

The combination of itraconazole with these herbal ingredients offers a synergistic approach, where the synthetic drug provides potent antifungal action, while the natural extracts enhance therapeutic efficacy, improve scalp condition, and minimize side effects. Such polyherbal formulations align well with the current trend towards natural and sustainable healthcare products. Shampoos are among the most convenient and widely accepted dosage forms for scalp application. They not only cleanse the scalp and hair but also serve as effective carriers for delivering active pharmaceutical ingredients. Medicated shampoos provide localized drug delivery, prolonged contact time, and ease of application, thereby improving patient compliance. Moreover, shampoos can incorporate both hydrophilic and lipophilic components, making them suitable for complex formulations like itraconazole with herbal extracts.

Materials and Methods

Materials

Itraconazole was used as the active pharmaceutical ingredient due to its broad-spectrum antifungal activity. Natural components such as neem extract, aloe vera gel, reetha, and shikakai were incorporated to enhance therapeutic efficacy and provide additional benefits such as conditioning, moisturizing, and cleansing of the scalp.

Other excipients used in the formulation included glycerin as a humectant, propylene glycol as a solvent and penetration enhancer, ethanol as a solubilizer for itraconazole, citric acid for pH adjustment, xanthan gum as a thickening agent, methyl paraben and sodium benzoate as preservatives, and purified water as the base. All ingredients

were of analytical grade and selected based on their compatibility and functionality in shampoo formulation.

Method of Preparation

The antifungal shampoo was prepared using an aqueous gel-based emulsion method to ensure uniform distribution of both synthetic and herbal components while maintaining their stability. Initially, the shampoo base was prepared by heating distilled water to approximately 40°C, followed by the gradual addition of reetha and shikakai extracts under continuous stirring to obtain a uniform solution. Itraconazole was accurately weighed and dissolved in ethanol to enhance its solubility, and this solution was slowly incorporated into the prepared base with constant stirring to ensure even dispersion of the drug. Subsequently, neem extract and aloe vera gel were added gently to preserve their bioactive properties. In the final step, preservatives were incorporated, and the pH of the formulation was adjusted to the desired range of 5.5–6.5 using citric acid to match the natural pH of the scalp. The final formulation was mixed thoroughly and stored in suitable containers for further evaluation.

Evaluation Parameters

The formulated shampoos were evaluated for various physicochemical and performance parameters to ensure their quality, stability, and effectiveness. Organoleptic properties such as color, odor, appearance, and homogeneity were assessed visually to determine aesthetic acceptability. The pH of the formulations was measured using a digital pH meter to ensure compatibility with scalp conditions. Viscosity was determined using a viscometer to evaluate the flow behavior and consistency of the shampoo. Spreadability was assessed to determine the ease of application over the scalp surface. Foam height and stability were evaluated to measure the cleansing efficiency and lathering ability of the shampoo. The dirt dispersion test was performed to assess the cleaning capability, while wetting time was determined to evaluate the efficiency of surfactants. Surface tension measurements were carried out to study the spreading and wetting characteristics of the formulation. Antifungal activity was tested against fungal strains to confirm therapeutic efficacy. Additionally, stability studies were conducted under different conditions to evaluate the physical and chemical stability of the formulation over time.

Results and Discussion

Physicochemical Evaluation

All the prepared shampoo formulations were found to be smooth, homogeneous, and exhibited a green to yellow-green color with a pleasant herbal odor, indicating good aesthetic acceptability. No phase separation or lump formation was observed, confirming the stability and uniformity of the formulations. The pH of all formulations ranged from 5.4 to 6.1, which is considered suitable for scalp application and helps in maintaining the natural acid mantle of the skin. Viscosity studies revealed that the viscosity increased with an increase in xanthan gum concentration, indicating its significant role in determining the consistency of the formulation. Spreadability studies showed that formulation F6 exhibited balanced spreading behavior, ensuring ease of application and adequate retention on the scalp. Foaming studies indicated that formulation F3 produced the highest foam due to the presence of natural surfactants, while formulation F6 demonstrated stable and adequate foam, making it suitable for effective cleansing.

Analytical Studies: Analytical characterization of itraconazole confirmed its purity and compatibility with the excipients used in the formulation.

Differential Scanning Calorimetry (DSC) studies showed a sharp melting point in the range of 166–171°C, indicating the crystalline nature and purity of the drug. Fourier Transform Infrared (FTIR) spectroscopy revealed characteristic functional group peaks without any significant shift, confirming the absence of drug-excipient interactions and ensuring the stability of the formulation.

Calibration Curve

The calibration curve of itraconazole was prepared using UV-visible spectrophotometry, and the drug exhibited maximum absorbance (λmax) at 260 nm. The calibration curve showed good linearity within the selected concentration range, indicating the reliability and accuracy of the method for drug estimation in the formulation.

In Vitro Drug Release

The in vitro drug release study demonstrated that formulation F6 exhibited a sustained release profile, releasing approximately 79% of itraconazole over a period of 8 hours. This sustained release behavior is advantageous for prolonged antifungal activity and improved therapeutic effectiveness.

Drug Release Kinetics

The drug release data were analyzed using different kinetic models to understand the release mechanism. The zero-order model showed a correlation coefficient (R^2) of 0.963, indicating a moderately linear release pattern. The first-order model exhibited the highest correlation coefficient ($R^2 = 0.998$), suggesting that the drug release was concentration-dependent. The Higuchi model ($R^2 = 0.983$) indicated diffusion-controlled release, while the Korsmeyer–Peppas model ($R^2 = 0.978$) suggested a non-Fickian diffusion mechanism. Overall, the results confirmed that the drug release followed a concentration-dependent mechanism with diffusion as a major contributing factor.

Antifungal Activity

The antifungal activity of the formulated shampoo was evaluated against fungal strains such as Candida albicans and Malassezia species. The results showed significant zones of inhibition, confirming the effectiveness of the formulation.

The combination of itraconazole with herbal extracts enhanced the antifungal activity, demonstrating a synergistic therapeutic effect.

Table 1: Formulation Table

Ingredients per 100 ml	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9
Itraconazole (gm)	1	1	1	1	1	1	1	1	1
Neem Extract (ml)	5	6	8	6.5	7	10	9	8.8	5
Aloe Vera Gel (ml)	10	10	15	20	18	15	10	20	15
Reetha Extract (ml)	2	2.5	3	-	-	-	-	-	-
Shikakai Extract(ml)	-	-	-	2	2.5	3	-	-	-
Reetha+ Shikakai (1:1)	-	-	-	-	-	-	2	3	4
Glycerin(ml)	5	5	5	5	5	5	5	5	5
Propylene Glycol (ml)	2	2	2	2	2	2	2	2	2
Ethanol (ml)	5	5	5	7.5	5	5	7.5	5	7.5
Citric Acid	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
XanthanGum	0.3	0.4	0.5	0.3	0.4	0.5	0.3	0.4	0.5
Sodium Benzoate	0.5	0.5	0.5	0.5	0.5	0.5	05	0.5	0.5
Purified water	q.s.	q.s	q.s	q.s	q.s.	q.s.	q.s.	q.s.	q.s.

Table 2: pH value of formulations

Formulation	pH Value
F1	5.9
F2	6.0
F3	5.8
F4	5.7
F5	5.6
F6	5.8
F7	6.1
F8	6.0
F9	5.9

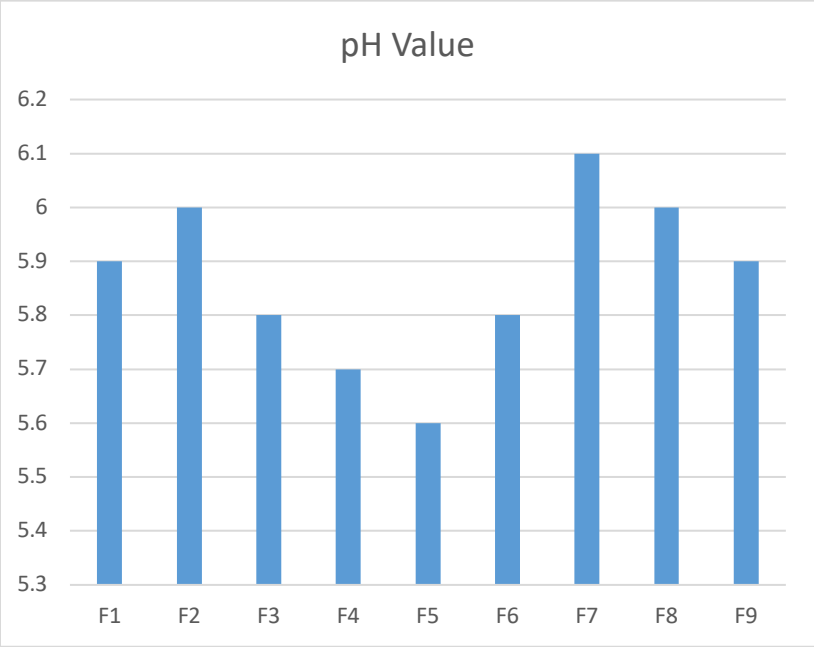


Fig 1: Graph showing pH level

Table 3: spreadibilty

Formulation	Spreadability (g·cm/sec)	Remarks
F1–F3	High	Fast spreading
F4–F6	Moderate	Controlled, easy application
F7–F9	Moderate to low	Slightly thicker formulations

Table 4: Foam Index

Formulation	Foam Height (ml)	Remarks
F1–F3	150–160 ml	High foam (Reetha)
F4–F6	110–130 ml	Moderate, stable foam
F7–F9	20–140 ml	Balanced foam

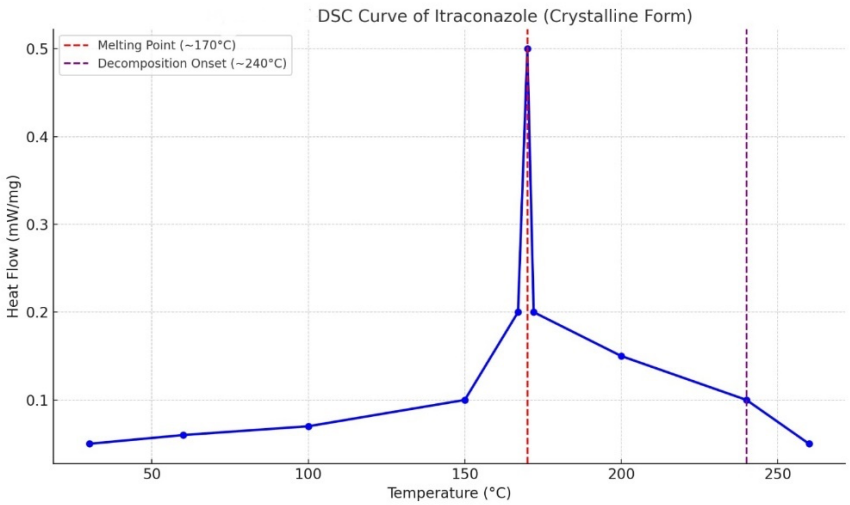


Fig 2: DSC

FTIR of itraconazole

Table 5: FTIR of itraconazole

Wavenumber (cm^{-1})	Functional Group / Vibration	Interpretation
~3120 – 3060 cm^{-1}	Aromatic C–H stretching	Due to aromatic rings in the structure
~2960 – 2850 cm^{-1}	Aliphatic C–H stretching	From alkyl groups
~1700 – 1650 cm^{-1}	C=N stretching (Imidazole ring)	Strong absorption, indicates imidazole
~1600 – 1500 cm^{-1}	C=C stretching (Aromatic ring)	Indicates presence of phenyl rings
~1450 – 1400 cm^{-1}	C–H bending (methyl/methylene groups)	Aliphatic bending vibrations
~1260 – 1000 cm^{-1}	C–O–C stretching (ether linkage)	From triazole and dioxolane rings
~850 – 750 cm^{-1}	Aromatic C–H bending	Out-of-plane deformation in phenyl groups

Table 6: Absorbance

S. No.	Concentration µg/ml	Absorbance
1	0	0
2	2	0.1316
3	4	0.2419
4	6	0.3516
5	8	0.4615
6	10	0.5612

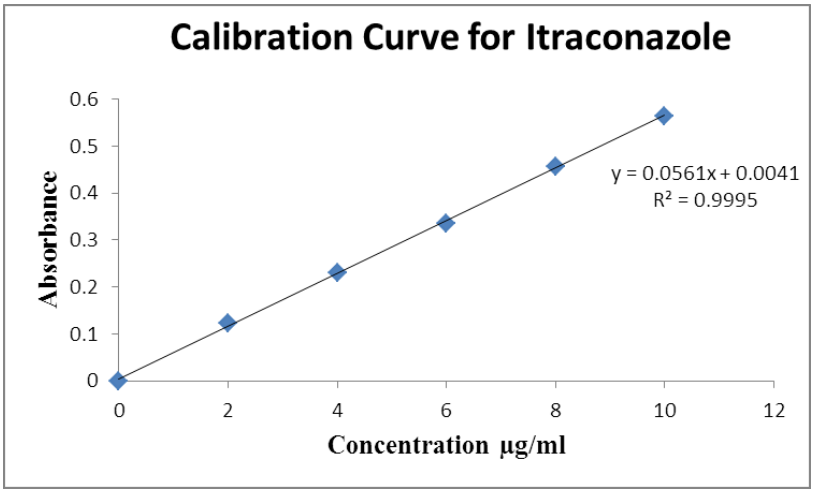


Fig 3: calibration curve

In Vitro Drug Release

Table 7: Drug Release

Time (hr)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	15	16	17	16	18	18	17	16	18
2	28	30	29	31	33	31	30	29	32
3	39	41	42	43	45	43	42	40	44
4	47	50	51	52	54	52	51	49	53
5	56	59	60	61	62	61	59	57	62
6	63	66	67	68	69	67	66	64	68
7	69	72	73	74	75	73	72	70	74
8	75	78	79	80	81	79	78	76	80

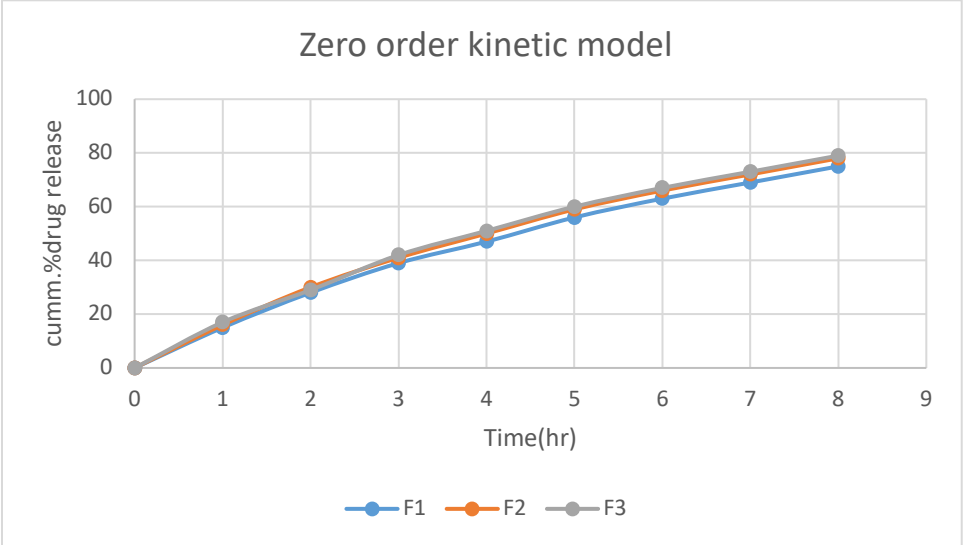
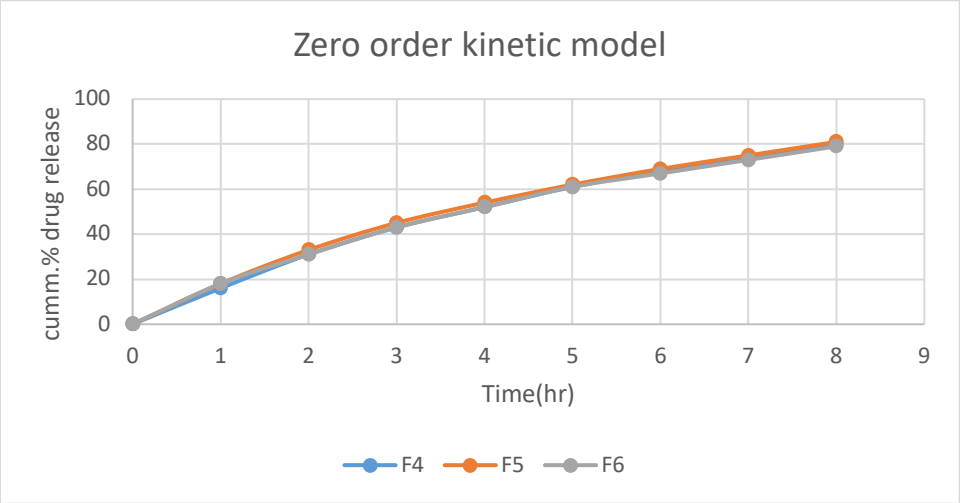


Fig 4:



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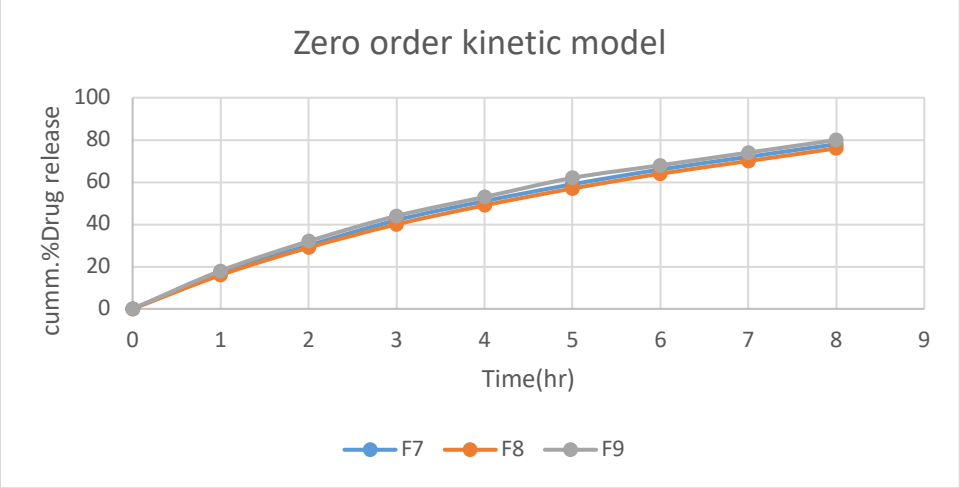

Fig 6:

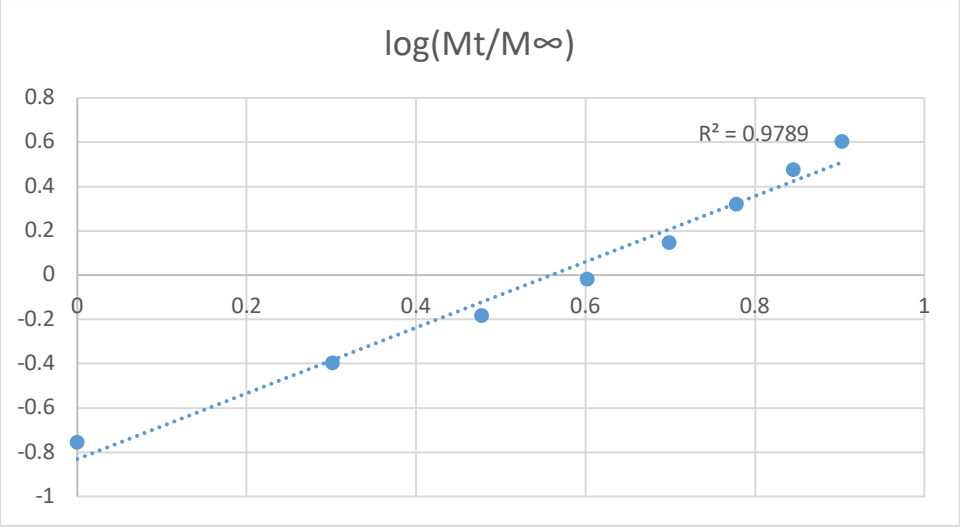

Fig 7:

Table 8: R^2 value for the F6 formulation

Formulation name	zero order	First order	Higuchi	Peppas
F6	0.963	0.998	0.983	0.9789

Conclusion

The present study successfully developed a polyherbal antifungal shampoo containing itraconazole in combination with natural extracts such as neem, aloe vera, reetha, and shikakai. All the formulations exhibited acceptable physicochemical properties, including suitable pH, viscosity, spreadability, and foam characteristics, ensuring good stability and user acceptability. Among all the formulations, F6 was identified as the optimized formulation due to its ideal pH of 5.8, balanced viscosity and spreadability, stable foam properties, high drug content of approximately 98%, sustained drug release of 79% over 8 hours, and significant antifungal activity. The study clearly demonstrates that the combination of synthetic antifungal agents with herbal extracts can provide a safe, effective, and cosmetically acceptable formulation for the treatment of scalp fungal infections.

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