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FORMULATION AND EVALUATION OF A NATURAL EXCIPIENT–BASED ANTIFUNGAL GEL CONTAINING CLOTRIMAZOLE FOR TOPICAL APPLICATION

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ABSTRACT

Clotrimazole is a widely used imidazole antifungal agent effective against dermatophytes, yeasts, and molds; however, conventional topical formulations often suffer from poor patient compliance and limited residence time at the site of action. The present study aimed to formulate and evaluate a topical antifungal gel of clotrimazole using a combination of natural and synthetic excipients to enhance safety, spreadability, and drug release. Gels were prepared using natural gelling agents such as tragacanth and gelatin, along with polyethylene glycol 400, glycerin, aloe vera, vitamin E, and benzoic acid as a preservative. The formulations were evaluated for physicochemical properties including pH, spreadability, viscosity, washability, homogeneity, drug content, and in vitro drug release using simulated vaginal fluid. Among the prepared formulations, batch F2 demonstrated optimal spreadability, acceptable viscosity, and superior drug release characteristics. The results indicate that clotrimazole gel formulated with natural excipients can serve as a safe, effective, and patient-friendly topical antifungal delivery system.

Keywords: *Clotrimazole, Topical antifungal gel, Natural excipients, Drug release study, Spreadability and viscosity, Simulated vaginal fluid.*

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INTRODUCTION

Fungal infections of the skin and mucosal tissues represent a significant global health concern, particularly in tropical and subtropical regions. These infections are commonly caused by dermatophytes, Candida species, and other opportunistic fungi, leading to conditions such as candidiasis, ringworm, athlete's foot, and vaginal infections [1,2]. Topical antifungal therapy remains the preferred treatment approach due to its localised action, reduced systemic side effects, and improved patient compliance [3,4]. Clotrimazole is a broad-spectrum imidazole antifungal agent that exerts its action by inhibiting ergosterol synthesis, an essential component of fungal cell membranes. Although clotrimazole is available in various dosage forms such as creams, powders, and vaginal tablets, gel formulations offer distinct advantages, including non-greasy texture, ease of application, better spreadability, and enhanced patient acceptability [5-7].

Recently, there has been increasing interest in incorporating natural excipients into pharmaceutical formulations due to their biocompatibility, safety, and multifunctional therapeutic benefits. Natural polymers such as tragacanth and gelatin possess excellent gelling properties and are capable of forming stable semisolid systems. Additionally, excipients like aloe vera and vitamin E provide soothing, moisturizing, and antioxidant effects, which may further enhance therapeutic outcomes.The present study focuses on the development of a clotrimazole antifungal gel using natural and synthetic excipients, followed by systematic evaluation of its physicochemical properties and in vitro drug release behavior to identify an optimized formulation [8-15].

MATERIALS AND METHODOLOGY

Materials

The Drug Clotrimazole was Purchased from Dolphin Pharmacy Instrument PVT, Kalbadevi Road,Mumbai. Tragacanth, gelatin, polyethylene glycol 400 (PEG 400), glycerin, benzoic acid, aloe vera gel, vitamin E capsules, alcohol, and distilled water were used as excipients. All chemicals and reagents used were of analytical grade.

Method of Preparation of Clotrimazole Gel

The antifungal gel formulations were prepared by the dispersion and hydration method, using different concentrations of natural gelling agents.

Preparation Using Tragacanth (F1 & F2)

The required quantity of tragacanth was dispersed in alcohol and allowed to hydrate in distilled water under continuous stirring. Glycerin was added separately to distilled water and mixed thoroughly. Both mixtures were combined and allowed to stand for uniform gel formation. Aloe vera gel and vitamin E were incorporated, followed by gradual addition of clotrimazole dissolved in alcohol. Benzoic acid was added as a preservative, and the formulation was heated gently to ensure uniformity.

Preparation Using Gelatin (F3–F5)

Gelatin was dissolved in hot distilled water and mixed with PEG 400 under constant stirring. Glycerin was added, followed by aloe vera and vitamin E. Clotrimazole was incorporated slowly with continuous mixing, and benzoic acid was added as a preservative. The formulation was heated at controlled temperature to obtain a smooth, homogeneous gel.

All formulations were allowed to cool, packed in suitable containers, and stored for further evaluation.

Evaluation Parameters

The prepared clotrimazole gel formulations were evaluated for various physicochemical and performance characteristics to ensure their quality, stability, and suitability for topical application [16-23].

Physical Appearance and Homogeneity

The prepared gel formulations were visually inspected for color, clarity, presence of lumps, and homogeneity. A small quantity of gel was pressed between the thumb and forefinger to check for uniformity and absence of grittiness.

pH Determination

The pH of each gel formulation was measured using a digital pH meter. Approximately 1 g of gel was dispersed in 10 mL of distilled water and allowed to stand for 2 hours. The pH meter was calibrated using standard buffer solutions (pH 4.0 and 7.0), and the pH of the gel dispersion was recorded. All measurements were performed in triplicate.

Spreadability

Spreadability was determined using the slip and drag method. A fixed quantity of gel (about 1 g) was placed between two glass slides. A weight of 500 g was placed on the upper slide for 5 minutes to remove trapped air and form a uniform film. The time taken for the upper slide to move a specified distance under the influence of weight was noted. Spreadability was calculated using the formula:

$$S = \frac{M \times L}{T}$$

where

S = Spreadability,

M = Weight tied to the upper slide (g),

L = Length moved by the slide (cm),

T = Time taken (sec).

Viscosity

Viscosity of the gel formulations was measured using a Brookfield viscometer fitted with a suitable spindle at 25°C. The spindle was immersed in the gel sample, and readings were recorded at different rotational speeds. The average viscosity was calculated.

Extrudability

Extrudability was evaluated by filling the gel formulation in a collapsible tube. The tube was pressed from the crimped end, and the force required to extrude the gel from the nozzle was noted. Extrudability was expressed qualitatively as excellent, good, or poor based on ease of extrusion.

Washability

Washability of the gel was assessed by applying a small quantity of gel to the skin and washing it with running tap water. Ease and completeness of removal were observed and recorded.

Drug Content Uniformity

About 1 g of gel was accurately weighed and dissolved in a suitable solvent (methanol). The solution was sonicated for 15 minutes, filtered, and suitably diluted. Drug content was determined using a UV–Visible spectrophotometer at the predetermined λmax of clotrimazole. The drug content was calculated using the calibration curve.

In Vitro Drug Release Study

In vitro drug release was performed using a Franz diffusion cell with a suitable diffusion membrane. The receptor compartment was filled with simulated vaginal fluid and maintained at 37 ± 0.5°C. The gel formulation was placed in the donor compartment. Samples were withdrawn at predetermined intervals and replaced with fresh medium. The samples were analysed spectrophotometrically, and cumulative drug release was calculated.

RESULTS AND DISCUSSION

Five clotrimazole gel formulations (F1–F5) were successfully prepared using tragacanth (F1–F2) and gelatin (F3–F5) as gelling agents by the dispersion and heating method. All formulations resulted in smooth, homogeneous gels without visible lumps, indicating proper hydration and dispersion of polymers.

Formulations F1 and F2, prepared using tragacanth, produced translucent gels with moderate viscosity. F2, containing a lower concentration of tragacanth, showed improved spreadability and ease of application

compared to F1, suggesting that polymer concentration significantly influences gel consistency.

Formulations F3, F4, and F5, prepared using gelatin and PEG 400, resulted in clear and glossy gels. Among them, F4 exhibited optimum consistency and uniformity, whereas F3 showed higher viscosity due to increased gelatin content. F5, prepared at elevated temperature (80°C), demonstrated good gel formation but slightly increased thickness, indicating temperature-dependent polymer behaviour.

The incorporation of aloe vera and vitamin E improved the aesthetic appearance and moisturising characteristics of all formulations, while benzoic acid effectively acted as a preservative. Overall, variations in polymer type, concentration, solvent system, and processing temperature had a direct impact on gel texture, viscosity, and handling properties. Among all batches, F2 and F4 were found to be the most promising formulations for further evaluation based on their uniformity and ease of application.

Table 1: Formulation composition of clotrimazole antifungal gel prepared using natural and synthetic gelling agents (F1–F5).

INGREDIENTS	F1	F2	F3	F4	F5
Clotrimazole(gm)	1	1	1	1	1
Tragacanth(gm)	5.5	2.75	-	-	-
Gelatin(gm)	-	-	5.5	2.75	4.12
Alcohol(ml)	11	11	-	-	-
PEG 400(ml)	-	-	11	11	11
Glycerin(ml)	5	5	5	5	5
Aloe vera + vitamin E(gm)	2.5	2.5	2.5	2.5	2.5
Benzoic acid(gm)	0.25	0.25	0.25	0.25	0.25
Water(ml)	qs	qs	qs	qs	qs

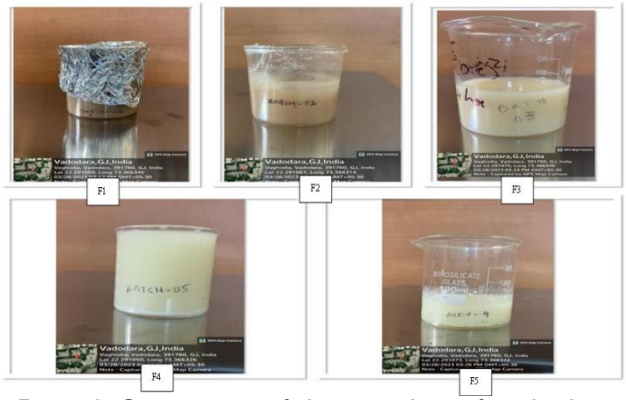

Figure 1: Composition of clotrimazole antifungal gel formulations (F1–F5) prepared using different concentrations of tragacanth and gelatin as gelling agents.

Evaluation Parameters

Spreadability

Spreadability is an important parameter that determines the ease of application of topical gels. The spreadability of clotrimazole gel formulations (F1–F5) was evaluated using a standard spreadability apparatus.

Formulation F1 showed the lowest spreadability due to higher polymer concentration. F2 exhibited optimum spreadability, making it easier to apply. Formulations F3–F5 showed higher spreadability, attributed to gelatin and PEG 400, which reduced gel rigidity. Among all, F2 demonstrated ideal spreadability for topical application

Table 2: Spreadability values of clotrimazole gel formulations (F1–F5)

Batch	Length moved (cm)	Time (sec)	Spreadability (g cm/sec)
F1	2.7	7	21.29
F2	6.6	3	121.42
F3	7.9	2	218.00
F4	6.8	2	187.65
F5	6.9	2	190.41

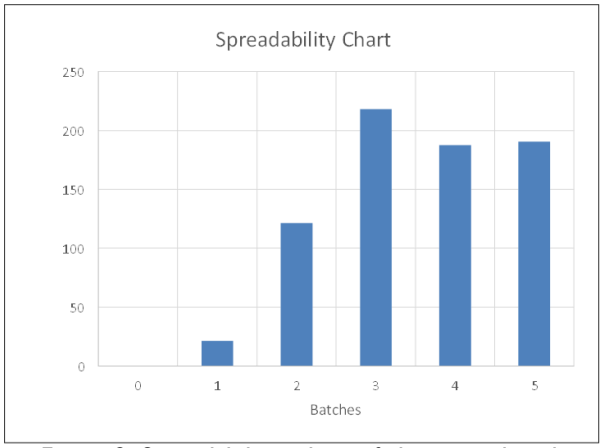

Figure 2: Spreadability values of clotrimazole gel formulations (F1–F5)

Viscosity Study

The viscosity of the prepared clotrimazole gels was measured using a Brookfield viscometer (Model LMDV60) at varying rotational speeds (0.3–30 rpm).

All formulations exhibited shear-thinning (pseudoplastic/dilatant) behaviour, where viscosity decreased with increasing shear rate. This behaviour is desirable for topical gels, ensuring easy application under shear and adequate consistency at rest. Gelatin-based formulations showed comparatively higher viscosity than tragacanth-based formulations.

pH Evaluation

The pH of all gel formulations was measured using a calibrated digital pH meter. Formulations F1–F4 showed pH values within the acceptable vaginal pH range (3.5–4.5), indicating suitability for vaginal application. F5 exhibited a higher pH, which may cause irritation and, hence, is less suitable. F2 and F4 were considered optimal in terms of pH compatibility.

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Table 3: pH values of prepared clotrimazole gel formulations

Batch	pH
F1	3.21
F2	4.07
F3	3.84
F4	4.00
F5	7.69

Physical Evaluation

All formulations were smooth, homogeneous, washable, and free from phase separation, indicating good formulation stability.

Table 4: Physical evaluation parameters of clotrimazole gel formulations

Formulation	Spreadability	Washability	Color	Phase Separation	Odour
F1	Easy	Washable	Light brown	No	Characteristic
F2	Easy	Washable	Pale yellow	No	Characteristic
F3	Easy	Washable	White	No	Characteristic
F4	Easy	Washable	White	No	Characteristic
F5	Easy	Washable	White	No	Characteristic

Calibration Curve of Clotrimazole

The calibration curve of clotrimazole was constructed in the concentration range of 20–45 µg/mL using UV-Visible spectrophotometry. The calibration curve showed good linearity, confirming adherence to Beer-Lambert's law and suitability for quantitative drug analysis

Table 5: Calibration data of clotrimazole in simulated vaginal fluid

Concentration (µg/mL)	Absorbance
20	0.080
25	0.092
30	0.101
35	0.111
40	0.126
45	0.142

In-Vitro Drug Release Study

Drug release studies were carried out using simulated vaginal fluid (pH 4.5) and a semi-permeable cellophane membrane at 37 ± 5°C.Formulation F2 showed the highest cumulative drug release (84.41%), indicating superior drug diffusion and release behaviour. This may be attributed to optimal polymer concentration and gel consistency. Hence, F2 was selected as the optimised formulation.

Table 6: In-vitro drug release profile of clotrimazole gel formulations in simulated vaginal fluid

Time (min)	F1	F2	F3	F4	F5
0	0	0	0	0	0
10	9.25	8.67	10.08	11.50	9.08
20	23.00	22.33	23.08	23.33	18.50
30	35.67	36.25	26.42	35.92	28.58
40	48.08	51.58	50.58	48.92	39.08
50	63.92	67.67	64.75	63.00	59.00
60	79.58	84.42	80.50	78.08	79.58

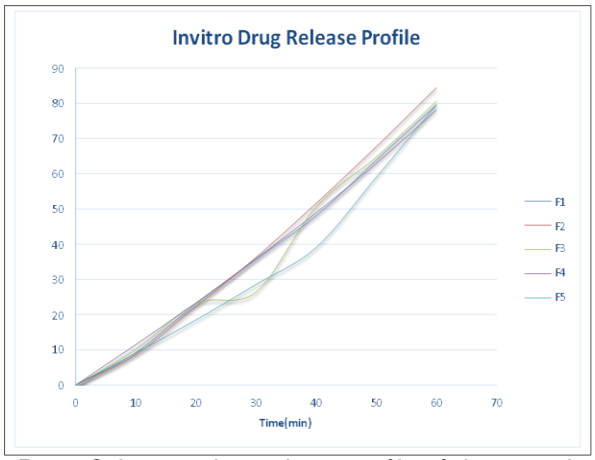

Figure 3: In-vitro drug release profile of clotrimazole gel formulations (F1–F5) in simulated vaginal fluid.

CONCLUSION

Clotrimazole gels prepared using natural and synthetic excipients showed satisfactory physicochemical properties. Among all formulations, F2 demonstrated optimum spreadability, acceptable pH, suitable viscosity, and superior drug release, making it the most promising formulation for antifungal therapy. The study confirms that combining natural polymers with suitable excipients enhances formulation performance while ensuring safety and effectiveness.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest regarding the publication of this paper. Acknowledgment

AUTHOR CONTRIBUTIONS

K. Sushma conceived and supervised the study and drafted the manuscript. Rajender Reddy Karnekanti, Konatham Teja Kumar Reddycontributed to data collection, analysis, and manuscript preparation. All authors reviewed and approved the final manuscript.

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