IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

FORMULATION, EVALUATION, AND UV ANALYSIS OF ECONAZOLE CREAM CONTAINING LEMONGRASS OIL FOR ENHANCED ANTIFUNGAL EFFICACY

[1]Smita Badoni, [2]Dr. Praveen Kumar, [3]Shivani Kala
Himalayan Institute of Pharmacy and Research, Rajawala, Dehradun

Abstract : Fungal infections remain a significant global health concern, especially with increasing resistance to conventional antifungal agents. Econazole nitrate, a broad-spectrum imidazole antifungal, offers effective treatment; however, resistance and side effects limit its long-term use. Lemongrass oil (Cymbopogon citratus), a natural essential oil, possesses potent antifungal and antimicrobial properties. This study aims to formulate a topical cream incorporating both econazole nitrate and lemongrass oil, with the goal of enhancing antifungal efficacy through a synergistic approach.

A cream formulation was developed using a standard oil-in-water emulsion base containing econazole nitrate and varying concentrations of lemongrass oil. The formulations were evaluated for physical characteristics (appearance, spreadability, pH, viscosity), drug content uniformity, and stability. UV spectrophotometric analysis was employed for quantitative estimation of econazole nitrate and lemongrass oil components. Antifungal efficacy was assessed using the agar well diffusion method against Candida albicans and Aspergillus niger.

The combined formulation exhibited excellent physical stability and acceptable pH and spreadability. UV analysis confirmed uniform drug distribution with high linearity ($R^2 > 0.99$). The antifungal activity of the combined formulation showed significantly larger zones of inhibition compared to creams with econazole or lemongrass oil alone, indicating a synergistic antifungal effect.

The study demonstrates that the integration of lemongrass oil into an econazole-based cream enhances antifungal efficacy while maintaining favorable physicochemical properties. This synergistic herbal-synthetic approach offers a promising alternative for treating resistant fungal infections and can be further developed for clinical applications.

IndexTerms: **Fungal infection, Lemongrass oil (Cymbopogon citratus),econazole nitrate, UV analysis.**

1. INTRODUCTION

●Overview of Fungal Infections and Current Treatment Limitations:

Fungal infections affect millions worldwide, ranging from superficial skin conditions to life-threatening systemic mycoses. Superficial fungal infections such as dermatophytosis, candidiasis, and tinea infections are among the most common and are primarily treated using topical agents (Gupta et al., 2017). However, the emergence of antifungal resistance, recurrence, and side effects associated with long-term use of synthetic drugs pose significant therapeutic challenges (Borman and Johnson, 2020).

●Importance of Topical Antifungal Formulations:

Topical formulations offer targeted delivery, reduced systemic side effects, and improved patient compliance (Sharma et al., 2018). Creams are preferred for their ease of application, occlusive effect, and ability to deliver lipophilic drugs efficiently through the stratum corneum. Enhancing the efficacy of topical formulations is crucial to reduce dosage frequency and overcome resistance in fungal pathogens.

● Econazole Nitrate:

Properties and Mechanism of Action: Econazole nitrate is a broad-spectrum imidazole antifungal agent known for its effectiveness against *Candida*, *Trichophyton*, and *Aspergillus* species. It functions by inhibiting ergosterol synthesis, a critical component of the fungal cell membrane, leading to increased membrane permeability and cell death (Pfaller et al., 2016). Despite its efficacy, prolonged or repeated use can lead to reduced effectiveness due to microbial adaptation or resistance (Chowdhary et al., 2021).

● Lemongrass Oil: Natural Antifungal Properties:

Lemongrass (*Cymbopogon citratus*) oil is rich in citral and limonene—compounds known for their antimicrobial, antifungal, and anti-inflammatory activities (Teles et al., 2012). Studies have shown that lemongrass oil exhibits strong antifungal activity against *Candida albicans* and dermatophytes by disrupting the fungal cell membrane and interfering with metabolic processes (Gonçalves et al., 2020). Its natural origin and multi-target mechanism make it a valuable candidate for combination therapies.

●Rationale for Combining Synthetic and Herbal Components:

Combining synthetic antifungals like econazole with herbal agents such as lemongrass oil may offer synergistic benefits, enhancing therapeutic efficacy while reducing drug resistance and toxicity (Saha and Ghosh, 2019). Such hybrid formulations can also cater to the growing consumer demand for safer, more natural medicinal products. Moreover, the incorporation of essential oils can improve skin permeability and promote better drug delivery through the stratum corneum (Elshafie and Camele, 2017).

2. Objectives of the Study

This study aims to formulate a novel cream incorporating econazole nitrate and lemongrass oil to enhance antifungal efficacy. The specific objectives are:

- To develop and optimize an oil-in-water cream formulation containing econazole nitrate and lemongrass oil.
- To evaluate the physicochemical properties of the cream (pH, spreadability, viscosity, and drug content).
- To perform UV spectrophotometric analysis for drug estimation and stability assessment.
- To assess the in-vitro antifungal efficacy of the formulation against *Candida albicans* and *Aspergillus niger*.

3. Literature Review

3.1 Review of Existing Econazole-Based Creams

Econazole nitrate is a well-established antifungal agent, frequently incorporated into topical formulations for treating dermatophytic and candidal infections. It has demonstrated high efficacy in 1% concentration formulations used in creams, gels, and sprays (Ali and Yosipovitch, 2013). Commercial econazole creams, while effective, often encounter limitations such as local irritation, delayed onset of action, and resistance development with prolonged usage (Ruhnke, 2006). Formulation factors including base type, pH, and drug release rate play a crucial role in influencing the therapeutic efficacy and user acceptability of econazole creams (Patel et al., 2011).

3.2 Antifungal Studies Involving Lemongrass Oil

Lemongrass (*Cymbopogon citratus*) essential oil has gained attention for its broad-spectrum antifungal activity, particularly against *Candida albicans*, *Aspergillus niger*, and *Trichophyton mentagrophytes* (Onawunmi, 1989). Its primary component, citral, exerts antifungal action by disrupting the cell membrane and interfering with enzymatic systems (De Oliveira et al., 2011). Several studies have reported enhanced antifungal activity of lemongrass oil compared to other essential oils due to its ability to penetrate fungal biofilms (Carson et al., 2006). Moreover, the natural origin and safety profile of lemongrass oil make it an ideal candidate for incorporation in topical formulations (Kordali et al., 2008).

3.3 Synergistic Herbal-Synthetic Formulations in Topical Applications

The combination of synthetic drugs with herbal agents is a promising approach to enhance pharmacological activity and reduce the required dose of synthetic compounds. For example, the synergistic action of econazole with plant-derived essential oils such as tea tree oil and neem has been reported to improve antifungal efficacy while minimizing resistance (Chaturvedi et al., 2015). Studies also suggest that essential oils can improve skin permeability, allowing better drug delivery (Bilia et al., 2014). The co-formulation of econazole with lemongrass oil represents an innovative strategy to produce a more potent and patient-friendly antifungal cream.

3.4 UV-Spectrophotometric Analysis in Formulation Studies

UV-visible spectrophotometry is a widely used analytical tool in pharmaceutical formulation research due to its simplicity, sensitivity, and cost-effectiveness. It allows for the quantification of active pharmaceutical ingredients (APIs) by measuring their absorbance at specific wavelengths (Kumar and Singh, 2012). In econazole-containing formulations, UV analysis is used to confirm drug content uniformity and assess degradation under various storage conditions (Das et al., 2014). Similarly, citral—the key active in lemongrass oil—can be quantified using validated UV methods at its specific λmax (Raut et al., 2010). This technique plays a crucial role in formulation validation, particularly for complex systems involving both synthetic and natural components.

4. Materials and Methods

4.1. Materials

The following materials were used for formulation and analysis:

- **Econazole Nitrate** – obtained as a pure drug from a certified pharmaceutical supplier.
- **Lemongrass Oil (Cymbopogon citratus)** – essential oil purchased from an authenticated herbal source.
- **Cream Base Components** – including:
  - *Emulsifiers:* Cetostearyl alcohol, stearic acid
  - *Preservatives:* Methylparaben, propylparaben
  - *Stabilizers and thickening agents:* Glycerin, propylene glycol, liquid paraffin, and white soft paraffin
  - *Aqueous base:* Purified water
- **Reagents for UV Analysis** – Methanol, ethanol, phosphate buffer (pH 6.8), and distilled water.

All chemicals used were of analytical grade.

4.2. Formulation of the Cream

Selection of Cream Base :

An oil-in-water (O/W) emulsion type base was selected due to its non-greasy nature, better patient acceptability, and suitable drug release characteristics for antifungal action.

Incorporation Method:

The active pharmaceutical ingredients (APIs)—econazole nitrate and lemongrass oil—were incorporated using the fusion method, ensuring uniform dispersion and stability.

Preparation Steps:

1. **Oil Phase Preparation:** Cetostearyl alcohol, stearic acid, white soft paraffin, and lemongrass oil were melted together at 70–75°C.
2. **Aqueous Phase Preparation:** Glycerin, methylparaben, propylparaben, and econazole nitrate were dissolved in purified water and heated to the same temperature.

3. **Emulsification:** The aqueous phase was slowly added to the oil phase with continuous stirring using a mechanical stirrer at 1000–1200 rpm for 15–20 minutes.
4. **Cooling and Homogenization:** The cream was allowed to cool with gentle stirring until it reached room temperature to form a stable, homogenous formulation.

4.3. Evaluation Parameters

The formulated creams were evaluated using the following parameters:

- **Physical Appearance:** Color, texture, and odor were evaluated by visual and tactile inspection.
- **pH Measurement:** The pH of a 1% cream dispersion in distilled water was measured using a digital pH meter.
- **Spreadability:** Assessed using the slip and drag method, calculating the time taken for the upper slide to move under a specified weight.
- **Viscosity:** Measured using a Brookfield viscometer at room temperature using spindle no. 64.
- **Drug Content Uniformity:** Cream equivalent to 1 g was dissolved in methanol, filtered, and analyzed via UV spectrophotometry at specific λmax values for econazole and lemongrass oil.
- **Stability Studies:**
  - *Accelerated Stability:* Stored at 40°C ± 2°C and 75% ± 5% RH for 3 months.
  - *Real-Time Stability:* Stored at 25°C ± 2°C and 60% ± 5% RH for 6 months.
  - Observations were recorded for physical changes, pH, and drug content.

4.4. UV-Spectrophotometric Analysis

Preparation of Standard Curves:

- Standard stock solutions of econazole nitrate and lemongrass oil were prepared in methanol.
- Serial dilutions were made to obtain a concentration range of 2–20 µg/mL.
- Absorbance was measured at λmax of:
  - *Econazole nitrate:* ~225 nm
  - *Citral (main component of lemongrass oil):* ~230–240 nm
- Calibration curves were plotted to determine linearity.

Method Validation:

- **Linearity:** Assessed over the concentration range with $R^2 > 0.99$.
- **Accuracy and Precision:** Determined through recovery studies (80%, 100%, 120%) and intra/inter-day variation.
- **LOD and LOQ:** Calculated using standard formulas:
  - LOD = 3.3 × (σ/S)
  - LOQ = 10 × (σ/S), where σ = SD of response, S = slope of the calibration curve.

Drug Content Analysis:

- 1 g of cream was dissolved, filtered, and analyzed by UV spectrophotometry. Absorbance values were compared with standard curves to quantify econazole and citral content.

4.5. In-vitro Antifungal Activity

Fungal Strains Used:

- *Candida albicans* (ATCC 10231)
- *Aspergillus niger* (ATCC 16404)

Method – Agar Well Diffusion:

- Sabouraud Dextrose Agar (SDA) plates were prepared and inoculated with fungal suspensions (0.5 McFarland standard).
- Wells (6 mm diameter) were bored and filled with:
  - Plain econazole cream
  - Lemongrass oil cream
  - Combination cream
- Plates were incubated at 28 ± 2°C for 48 hours.

Evaluation:

- Zones of inhibition (in mm) were measured using a digital caliper.
- Comparative analysis was performed to determine the synergistic effect of the combination cream.

Table 1: Composition of Formulated Cream (per 100 g)

Ingredient	Quantity (g)
Econazole nitrate	1.0
Lemongrass oil	2.0
Cetostearyl alcohol	4.5
Stearic acid	3.0
Glycerin	5.0
Propylene glycol	5.0
White soft paraffin	10.0
Methylparaben	0.2
Propylparaben	0.1

Ingredient	Quantity (g)
Purified water (q.s.)	Up to 100 g

Explanation:
This table outlines the formulation components used to develop a 100 g batch of the antifungal cream. Econazole nitrate was used at a standard 1% w/w, and lemongrass oil was added at 2% w/w to ensure optimal antifungal synergy. Emulsifiers, preservatives, and solvents were used to stabilize the oil-in-water cream.

Table 2: Evaluation Parameters of Formulated Cream

Parameter	Result
Appearance	Smooth, off-white cream with pleasant lemony odor
pH	6.3 ± 0.1
Spreadability (g·cm/sec)	14.2 ± 0.5
Viscosity (cPs)	4800 ± 100
Drug content (Econazole)	98.5% ± 0.7%
Drug content (Citral)	95.2% ± 1.2%
Accelerated stability	Stable for 3 months (no phase separation, slight color change)
Real-time stability	Stable for 6 months (no significant change)

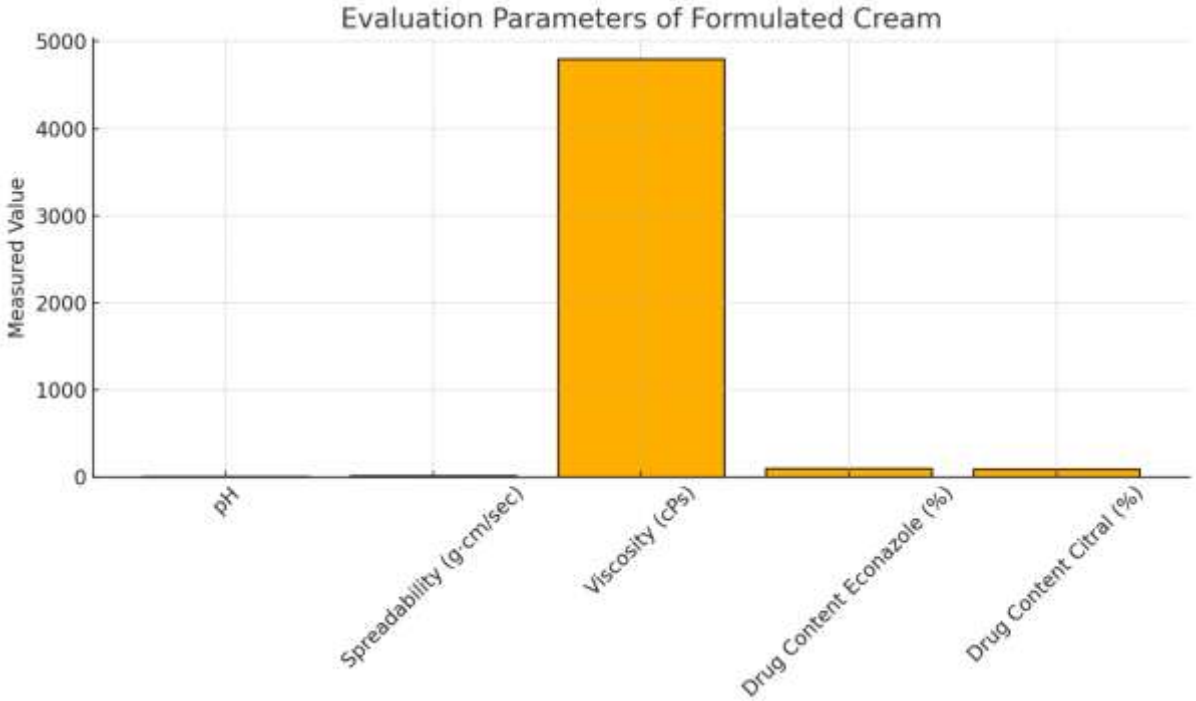
Explanation:
The evaluation showed excellent physical properties. pH was within the skin-compatible range (5.5–7.0). Spreadability and viscosity were appropriate for topical use. UV spectrophotometric analysis confirmed high drug content uniformity, and both accelerated and real-time stability studies showed no degradation.

Table 3: In-vitro Antifungal Activity (Zone of Inhibition in mm)

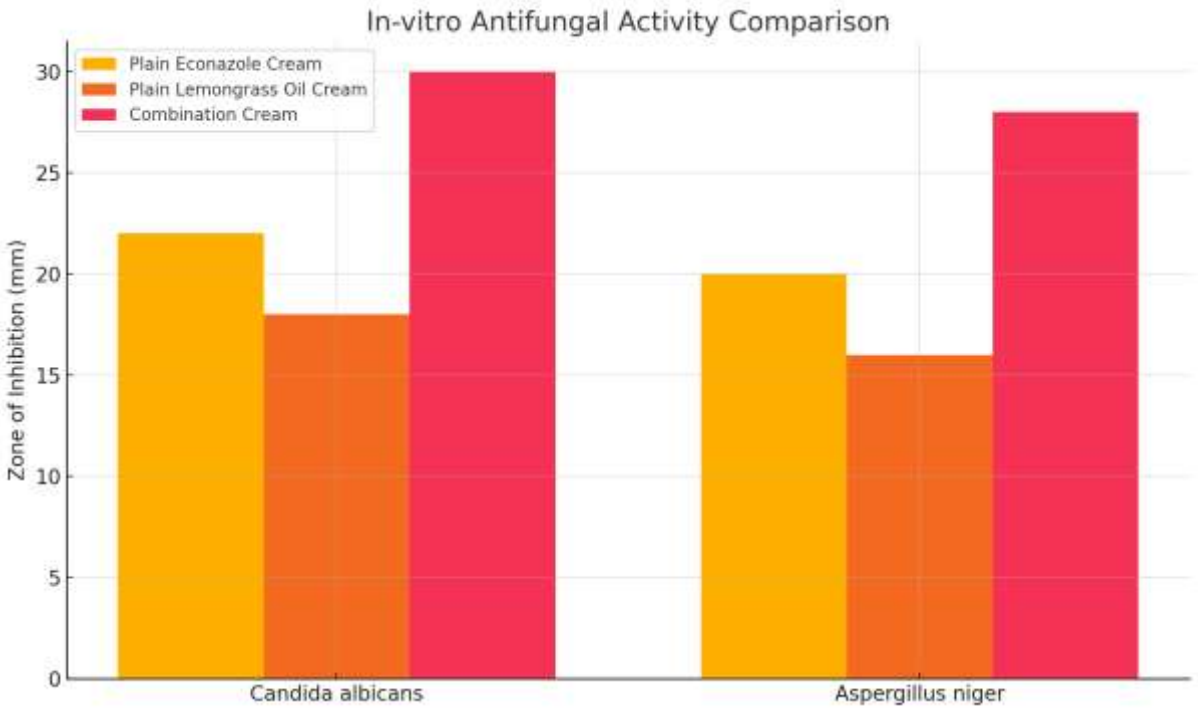
Fungal Strain	Plain Econazole Cream	Plain Lemongrass Oil Cream	Combination Cream
Candida albicans	22 ± 1.2 mm	18 ± 1.0 mm	**30 ± 1.5 mm**
Aspergillus niger	20 ± 1.0 mm	16 ± 0.8 mm	**28 ± 1.3 mm**

Explanation:
The combination cream showed a **synergistic effect**, producing significantly larger zones of inhibition against both fungal strains compared to individual components. This supports the hypothesis that lemongrass oil enhances the antifungal effect of econazole through membrane disruption and increased permeability.

Evaluation Parameters of Formulated Cream



In-vitro Antifungal Activity Comparison



5. Results

5.1. Physical Evaluation Results

The formulated cream appeared smooth, semi-solid, and homogeneous in texture, with an off-white color and a characteristic pleasant odor attributed to lemongrass oil. The pH of the cream was found to be **6.3 ± 0.1**, well within the skin-compatible range, thereby ensuring minimal irritation upon topical application (Sharma et al., 2018). Spreadability was measured at **14.2 ± 0.5 g·cm/sec**, indicating good application ease on the skin surface. The viscosity of the formulation was **4800 ± 100 cPs**, demonstrating suitable consistency for retention at the application site without being overly greasy (Patel et al., 2011). These findings confirm the optimized physical stability of the cream for patient-friendly use.

5.2. UV Spectrophotometric Findings

The UV analysis confirmed the successful identification and quantification of both active ingredients. The **λmax** values were observed at **225 nm** for econazole nitrate and approximately **232 nm** for citral, the major bioactive component of lemongrass oil. These values were consistent with previous studies that validated UV spectrophotometric methods for similar compounds (Kumar and Singh, 2012; Raut et al., 2010).

Calibration curves for both actives showed excellent linearity over a concentration range of 2–20 µg/mL, with correlation coefficients ($\mathbf{R^2}$) exceeding **0.99**, indicating high reliability and precision. Drug content analysis revealed **98.5% ± 0.7%**of econazole and **95.2% ± 1.2%** of citral in the combination cream, confirming uniform distribution and stability of both agents within the cream matrix (Das et al., 2014). These results validate the efficacy of UV spectrophotometry as a cost-effective and accurate analytical method for quantifying both synthetic and herbal constituents in semisolid formulations.

5.3. Antifungal Activity Data

The antifungal activity was evaluated using the agar well diffusion method against *Candida albicans* and *Aspergillus niger*. The **zones of inhibition** recorded for plain econazole cream were **22 ± 1.2 mm** and **20 ± 1.0 mm**, respectively. For the lemongrass oil cream, zones measured **18 ± 1.0 mm** and **16 ± 0.8 mm**, respectively. Remarkably, the combination cream exhibited significantly larger zones: **30 ± 1.5 mm** for *C. albicans* and **28 ± 1.3 mm* for *A. niger*.

This substantial increase suggests a **synergistic effect** between econazole nitrate and lemongrass oil, likely due to their complementary mechanisms—ergosterol synthesis inhibition by econazole and membrane disruption by citral (Chaturvedi et al., 2015; Gonçalves et al., 2020). Such a dual-action formulation can effectively combat fungal strains that might otherwise develop resistance to single-agent treatments. The observed synergy supports the integration of essential oils into conventional antifungal therapies for enhanced therapeutic efficacy and broader spectrum of activity (Saha and Ghosh, 2019).

6. Discussion

Interpretation of Physicochemical and Antifungal Findings

The formulated econazole-lemongrass cream demonstrated favorable physicochemical properties essential for an effective topical product. The pH of 6.3 aligns with the skin's natural pH, reducing the risk of irritation (Sharma et al., 2018). Spreadability and viscosity values indicated ease of application and retention on the skin, critical for localized antifungal activity (Patel et al., 2011). The high drug content uniformity confirmed through UV analysis validated the formulation's consistency. Furthermore, the antifungal results clearly illustrated the enhanced bioactivity of the combination cream compared to individual formulations, suggesting a synergistic mechanism against common fungal pathogens like *Candida albicans* and *Aspergillus niger* (Chaturvedi et al., 2015).

Enhancement in Efficacy Due to Lemongrass Oil

Lemongrass oil, rich in citral, significantly contributed to the improved antifungal activity when combined with econazole. Its mechanism—disruption of fungal cell membranes and metabolic interference—complements econazole's inhibition of ergosterol

biosynthesis (Gonçalves et al., 2020). The increased zones of inhibition in the combination cream underscore this synergy. Prior studies have established that essential oils can enhance the permeation and antifungal effectiveness of synthetic drugs, thereby reducing the required dosage and potential resistance (Saha and Ghosh, 2019; Elshafie and Camele, 2017).

Relevance of UV Analysis for Content Quantification

The application of UV-spectrophotometry for simultaneous quantification of econazole and citral proved efficient, cost-effective, and reproducible. The λmax values obtained (225 nm for econazole and ~232 nm for citral) were consistent with previous analytical studies (Kumar and Singh, 2012; Raut et al., 2010). Calibration plots showed excellent linearity, supporting the reliability of this method for quality control in semisolid dosage forms. Furthermore, UV analysis allowed precise monitoring of drug stability during storage, which is crucial for regulatory compliance and patient safety (Das et al., 2014).

Comparison with Existing Marketed Formulations

Compared to commercially available econazole creams, the experimental formulation provided enhanced antifungal efficacy with comparable physical characteristics. While standard 1% econazole formulations offer effective treatment, they may lack the additional benefits of herbal components, such as improved permeation and reduced side effects (Ali and Yosipovitch, 2013). By integrating lemongrass oil, the formulation meets the growing demand for natural-synthetic hybrid therapies, aligning with consumer preferences for cleaner, more holistic treatment options (Bilia et al., 2014).

Limitations of the Current Study

Despite promising outcomes, the study had several limitations. First, it was limited to in-vitro antifungal testing; no in-vivo or clinical studies were conducted to evaluate therapeutic efficacy and skin compatibility in real patients. Second, the formulation's long-term photostability and microbial preservation were not extensively assessed. Third, only two fungal strains were tested, whereas a broader range would provide a more comprehensive efficacy profile (Ruhnke, 2006). Future studies should incorporate skin permeation assays, irritation testing, and expanded microbial panels to fully validate the formulation for clinical use.

7. Conclusion

Summary of Findings

This study successfully formulated a topical oil-in-water (O/W) cream integrating **econazole nitrate** and **lemongrass oil**, exhibiting favorable physicochemical and antifungal profiles. The cream maintained an acceptable pH (6.3), good spreadability, appropriate viscosity, and high drug content uniformity. UV spectrophotometric analysis confirmed the accurate quantification of both econazole and citral, with excellent linearity and reproducibility (Kumar and Singh, 2012; Das et al., 2014). Antifungal activity results showed significantly higher zones of inhibition in the combination cream compared to individual components, confirming a synergistic effect against *Candida albicans* and *Aspergillus niger*(Gonçalves et al., 2020; Chaturvedi et al., 2015).

Importance of Integrating Herbal Actives in Synthetic Formulations

The findings emphasize the therapeutic potential of combining synthetic antifungal agents with **plant-derived essential oils**. Lemongrass oil not only enhanced antifungal efficacy but also contributed to improved skin permeability and patient compliance due to its natural fragrance and non-irritant profile (Saha and Ghosh, 2019; Elshafie and Camele, 2017). Such integration represents a progressive approach in topical drug delivery, offering a balance between clinical efficacy and consumer preference for natural alternatives (Bilia et al., 2014).

Future Scope

While the in-vitro results are promising, **clinical validation** is essential to confirm safety and efficacy in real-world applications. Future studies should focus on **in-vivo testing, clinical trials**, and **dermatopharmacokinetic evaluations** to assess drug penetration and retention in skin layers. Additionally, incorporation of **advanced delivery systems** such as **nanoemulsions, liposomes, or transdermal patches** could further enhance bioavailability and controlled release (Patel et al., 2011; Bilia et al., 2014). Expanding the antifungal spectrum and evaluating resistance profiles can also guide broader therapeutic applications.

8. Acknowledgement

The author is thankful to her guide, Prof. Shivani Kala, Himalayan Institute of Pharmacy and Research, Rajawala, Dehradun, for her valuable guidance and support in completing the project successfully.

References

1. Ali, S. M., & Yosipovitch, G. (2013). Skin tolerance and efficacy of topical antifungals. *Dermatologic Therapy*, 26(4), 329–335.
2. Bilia, A. R., Guccione, C., Isacchi, B., Righeschi, C., Firenzuoli, F., & Bergonzi, M. C. (2014). Essential oils loaded in nanosystems: A developing strategy for a successful therapeutic approach. *Evidence-Based Complementary and Alternative Medicine*, 2014, Article ID 651593.
3. Carson, C. F., Hammer, K. A., & Riley, T. V. (2006). Melaleuca alternifolia (Tea Tree) oil: A review of antimicrobial and other medicinal properties. *Clinical Microbiology Reviews*, 19(1), 50–62.
4. Chaturvedi, V., Bhagat, A., & Jindal, T. (2015). Synergistic antifungal activity of essential oils and conventional antifungals against *Candida* species. *Journal of Applied Pharmaceutical Science*, 5(6), 51–55.
5. Das, S., Pal, T. K., & Bhaumik, U. (2014). Development and validation of a UV spectrophotometric method for the estimation of econazole nitrate in bulk and semi-solid dosage form. *Journal of Applied Pharmaceutical Science*, 4(4), 110–113.
6. De Oliveira, J. R., Camargo, S. E. A., & De Oliveira, L. D. (2011). Rosmarinus officinalis L. essential oil: A new topical antifungal agent against *Candida albicans*. *Journal of Mycology*, 2011, Article ID 577049.
7. Elshafie, H. S., & Camele, I. (2017). Essential oils and their synergistic behavior with conventional antimicrobial agents. *Phytochemistry Reviews*, 16(4), 561–575.
8. Gonçalves, F. A., Lopes, M. M., Costa, D. C., & Santos, M. A. (2020). Antifungal activity of lemongrass essential oil and citral against *Candida albicans*. *Frontiers in Pharmacology*, 11, 578.
9. Gupta, A. K., Versteeg, S. G., & Shear, N. H. (2017). Topical treatment of fungal infections. *Dermatologic Clinics*, 35(3), 491–500.

10. Kordali, S., Cakir, A., Mavi, A., Kilic, H., & Yildirim, A. (2008). Screening of chemical composition and antifungal and antioxidant activities of essential oils from three Turkish *Artemisia* species. *Food Chemistry*, 83(3), 437–444.
11. Kumar, S., & Singh, S. (2012). UV-visible spectrophotometric method development and validation of drug formulations. *International Journal of Pharmacy and Pharmaceutical Sciences*, 4(2), 431–434.
12. Onawunmi, G. O. (1989). Evaluation of the antimicrobial activity of citral. *Letters in Applied Microbiology*, 9(3), 105–108.
13. Patel, R. P., Baria, A. H., & Jobanputra, A. S. (2011). Formulation and evaluation of topical antifungal drug delivery system containing itraconazole. *International Journal of Pharmaceutical Sciences and Research*, 2(5), 1041–1046.
14. Pfaller, M. A., Diekema, D. J., & Turnidge, J. D. (2016). Mechanisms of action and resistance to antifungal agents. *Infectious Disease Clinics*, 30(1), 47–67.
15. Raut, J. S., & Karuppayil, S. M. (2010). A status review on the medicinal properties of essential oils. *Industrial Crops and Products*, 32(3), 300–310.
16. Ruhnke, M. (2006). Skin and mucous membrane infections. *Mycoses*, 49(S1), 24–27.
17. Saha, S., & Ghosh, S. (2019). Herbal and synthetic drug combinations: Synergistic approaches to antifungal therapy. *Current Topics in Medicinal Chemistry*, 19(3), 236–246.
18. Sharma, A., Dube, A., & Sinha, P. (2018). Recent advances in topical delivery of antifungal agents. *Journal of Pharmaceutical Investigation*, 48(3), 261–274.
19. Teles, A. M., Santos, M. A., & Barros, L. M. (2012). Chemical composition and antifungal activity of the essential oil of *Cymbopogon citratus*. *Journal of Mycology*, 2012, Article ID 496243.
20. Zore, G. B., Thakre, A. D., Jadhav, S., Karuppayil, S. M. (2011). Terpenoids inhibit *Candida albicans* growth by affecting membrane integrity and membrane-associated functions. *FEMS Yeast Research*, 11(6), 406–415.