

## Formulation and Evaluation of Ketoconazole Emulgel Incorporating Eucalyptus Oil for Topical Antifungal Therapy

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### ABSTRACT

Superficial fungal infections constitute a significant global health burden, particularly in tropical and subtropical climates where heat and humidity favour fungal proliferation. Dermatophytosis, candidiasis, and seborrheic dermatitis are among the most prevalent infections requiring topical antifungal therapy. Ketoconazole, a broad-spectrum imidazole derivative, remains one of the most effective topical antifungal agents due to its potent inhibition of ergosterol biosynthesis in fungal cell membranes. However, the clinical efficacy of ketoconazole in conventional semisolid dosage forms such as creams and ointments is often limited by poor aqueous solubility, low skin penetration, suboptimal drug release, and reduced patient compliance.

Emulgel, an advanced topical drug delivery system combining the advantages of emulsions and gels, has emerged as a promising platform for enhancing the delivery of lipophilic drugs such as ketoconazole. The incorporation of eucalyptus oil as a natural penetration enhancer further improves dermal absorption while also contributing intrinsic antimicrobial and anti-inflammatory properties. This review comprehensively discusses the pathophysiology of superficial fungal infections, pharmacological profile of ketoconazole, rationale for emulgel development, formulation strategies, physicochemical characterization, in vitro and in vivo evaluation methods, stability considerations, and future prospects of ketoconazole emulgel incorporating eucalyptus oil. The review

emphasizes mechanistic insights into enhanced permeation and antifungal activity, highlighting its potential as a superior alternative to conventional topical formulations.

### I. INTRODUCTION

#### 1.1 SUPERFICIAL FUNGAL INFECTIONS

Superficial fungal infections are among the most prevalent dermatological disorders worldwide, affecting approximately one-fourth of the global population at any given time <sup>[1]</sup>. These infections primarily involve keratinized tissues such as the stratum corneum of the skin, hair, and nails. The most common etiological agents include dermatophytes (Trichophyton, Microsporum, Epidermophyton) and yeasts such as *Candida albicans* <sup>[1,2]</sup>.

The incidence of dermatophytosis is particularly high in tropical and subtropical regions where humidity, heat, overcrowding, and poor hygiene create favourable conditions for fungal growth <sup>[2]</sup>. Recurrent infections, incomplete treatment, and inappropriate use of topical corticosteroid combinations further complicate management strategies. Emerging resistance to antifungal agents has intensified the need for improved topical delivery systems capable of achieving higher local drug concentrations at the site of infection <sup>[1]</sup>.

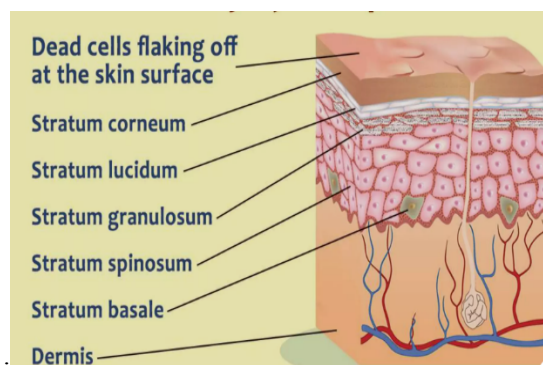


Fig.1.1 Structure of Skin and their layers

## 1.2 PATHOGENESIS AND MECHANISM OF FUNGAL INFECTION

Fungal pathogens adhere to keratinized tissues and produce keratinolytic enzymes that facilitate penetration into the stratum corneum. Once colonized, fungi proliferate within the superficial epidermis. The fungal cell membrane contains ergosterol, a sterol essential for maintaining membrane fluidity, permeability, and structural integrity<sup>[3]</sup>.

The biosynthesis of ergosterol occurs through a cytochrome P450-dependent pathway. Inhibition of this pathway disrupts fungal cell membrane function, leading to growth inhibition or cell death. Therefore, ergosterol biosynthesis remains the principal target of azole antifungal agents such as ketoconazole<sup>[3,4]</sup>.

### 1.3 Ketoconazole: Pharmacological Profile

Ketoconazole is a synthetic imidazole antifungal agent with broad-spectrum activity against dermatophytes, yeasts, and certain systemic fungi<sup>[3]</sup>. It acts by inhibiting lanosterol 14- $\alpha$ -demethylase, a cytochrome P450 enzyme necessary for ergosterol synthesis. Inhibition results in:

- Increased membrane permeability
- Leakage of intracellular components
- Inhibition of fungal cell growth
- Fungistatic or fungicidal action depending on concentration<sup>[4]</sup>.

Ketoconazole is classified as a lipophilic drug with poor aqueous solubility, which significantly influences its formulation strategy [4]. Due to its hydrophobic nature, it exhibits limited penetration across the stratum corneum when formulated in conventional aqueous creams<sup>[6]</sup>.

Topical ketoconazole is widely used in treating:

- Tinea corporis
- Tinea cruris
- Tinea pedis
- Cutaneous candidiasis
- Seborrheic dermatitis<sup>[3]</sup>.

However, despite its established efficacy, therapeutic outcomes may be suboptimal due to formulation-related limitations.

## 1.4 LIMITATIONS OF CONVENTIONAL TOPICAL FORMULATIONS

Traditional semisolid dosage forms such as creams and ointments suffer from several drawbacks:

- Poor drug release from the base
- Phase instability
- Greasy texture
- Poor patient compliance
- Limited dermal penetration<sup>[6,15]</sup>.

These limitations are particularly problematic for lipophilic drugs like ketoconazole, which require efficient solubilization and partitioning into the skin layers. Studies evaluating marketed ketoconazole creams have demonstrated variable drug release profiles and limited permeation across biological membranes<sup>[7]</sup>.

Furthermore, conventional formulations may require prolonged therapy, increasing the risk of recurrence and reduced adherence to treatment regimens<sup>[6]</sup>.

## 1.5 NEED FOR ADVANCED TOPICAL DRUG DELIVERY SYSTEMS

The stratum corneum acts as the primary barrier to drug penetration. It consists of densely packed keratinocytes embedded within a lipid matrix composed of ceramides, cholesterol, and

free fatty acids <sup>[16]</sup>. This “brick-and-mortar” structure significantly restricts the penetration of hydrophilic and lipophilic drugs alike.

To overcome this barrier, modern pharmaceutical research focuses on novel delivery systems capable of:

- Enhancing drug solubility
- Improving skin permeation
- Sustaining drug release
- Increasing residence time at the infection site
- Minimizing systemic absorption <sup>[8]</sup>

Among various approaches such as liposomes, niosomes, microemulsions, and nanoemulsions, emulgel has emerged as a practical and stable formulation strategy <sup>[14,25]</sup>.

### 1.6 CONCEPT OF EMULGEL

Emulgel is a hybrid topical formulation formed by incorporating an emulsion into a gel matrix. It combines the drug solubilization properties of emulsions with the rheological advantages of gels <sup>[7]</sup>. This dual system is particularly advantageous for delivering hydrophobic drugs such as ketoconazole.

An emulgel typically consists of:

- Oil phase (drug dissolved)
- Aqueous phase
- Surfactant system
- Gelling agent (e.g., Carbopol)

The gel network enhances viscosity and stability, preventing phase separation commonly observed in conventional emulsions <sup>[13]</sup>.

### 1.7 ADVANTAGES OF EMULGEL IN ANTIFUNGAL THERAPY

Several studies have demonstrated that ketoconazole emulgel exhibits superior drug release and antifungal activity compared to conventional creams <sup>[7,9]</sup>. The advantages include:

1. Enhanced drug solubilization in oil phase
2. Improved permeation through stratum corneum
3. Sustained release behavior
4. Better spreadability
5. Non-greasy texture
6. Improved patient compliance <sup>[8,17]</sup>

The rheological behavior of emulgels typically exhibits pseudoplastic flow, which ensures ease of application while maintaining sufficient viscosity for retention at the application site <sup>[17]</sup>.

### 1.8 ROLE OF PENETRATION ENHANCERS IN TOPICAL THERAPY

Penetration enhancers temporarily alter the barrier properties of the stratum corneum, facilitating increased drug flux. They act by:

- Disrupting lipid packing
- Increasing hydration
- Enhancing drug partitioning into skin <sup>[9]</sup>.

Chemical enhancers such as propylene glycol and isopropyl myristate have been widely used; however, natural essential oils are gaining attention due to better safety profiles and additional pharmacological benefits <sup>[11]</sup>.

### 1.9 EUCALYPTUS OIL AS A NATURAL PENETRATION ENHANCER

Eucalyptus oil contains 1,8-cineole (eucalyptol) as its major constituent, responsible for its penetration-enhancing activity <sup>[10]</sup>. It interacts with stratum corneum lipids, increasing fluidity and permeability <sup>[9]</sup>.

In topical drug delivery systems, eucalyptus oil has demonstrated:

- Increased transdermal flux
- Enhanced drug diffusion coefficient
- Improved antifungal activity
- Reduced skin irritation <sup>[10,12]</sup>.

Nanoemulgel formulations incorporating natural oils have shown significantly improved permeation and antifungal efficacy compared to conventional gel systems <sup>[4,12]</sup>.

### 1.10 RATIONALE FOR COMBINING KETOCONAZOLE WITH EUCALYPTUS OIL IN EMULGEL

The integration of ketoconazole and eucalyptus oil within an emulgel system provides a synergistic therapeutic strategy:

- Ketoconazole targets ergosterol synthesis
- Eucalyptus oil enhances penetration and provides antimicrobial support
- Emulgel ensures sustained release and improved stability

This combination aims to maximize local drug concentration at the site of infection while minimizing systemic exposure <sup>[4,7]</sup>.

Moreover, Carbopol-based gel systems provide optimal viscosity and skin adherence, enhancing drug residence time and therapeutic efficiency <sup>[13]</sup>.

### 1.11 RESEARCH GAP AND JUSTIFICATION

Although several studies have investigated ketoconazole nanoemulgel and emulgel systems [4,7], limited literature specifically evaluates the synergistic incorporation of eucalyptus oil in ketoconazole emulgel with comprehensive physicochemical and antifungal assessment.

Therefore, the development and evaluation of ketoconazole emulgel incorporating eucalyptus oil represent a promising research direction for improving topical antifungal therapy.

## II. ADVANCEMENTS IN TOPICAL ANTIFUNGAL DRUG DELIVERY SYSTEMS: FOCUS ON EMULGEL-BASED KETOCONAZOLE FORMULATIONS

### 2.1 INTRODUCTION TO ADVANCED TOPICAL DRUG DELIVERY

Topical drug delivery systems have undergone significant evolution over the past two decades. Conventional semisolid dosage forms such as ointments, creams, and simple gels have been widely used for treating superficial fungal infections; however, these systems often fail to deliver adequate drug concentration at the infected site due to the barrier function of the stratum corneum <sup>[6,15]</sup>.

The outermost layer of the skin, the stratum corneum, acts as the primary rate-limiting barrier to drug penetration. It is composed of corneocytes embedded in a lipid matrix consisting of ceramides, cholesterol, and fatty acids, arranged in a highly organized lamellar structure <sup>[6]</sup>. This structure restricts the penetration of both hydrophilic and lipophilic drugs.

To overcome these limitations, advanced drug delivery systems such as liposomes, niosomes, microemulsions, nanoemulsions, and emulgels have been explored <sup>[14,25]</sup>. Among these, emulgels have gained particular attention due to their simplicity, stability, and ability to deliver hydrophobic drugs effectively.

### 2.2 EVOLUTION OF KETOCONAZOLE TOPICAL FORMULATIONS

#### 2.2.1 Conventional Creams and Ointments

Ketoconazole has traditionally been formulated as creams and shampoos for topical antifungal therapy. These preparations are effective but often suffer from limited skin penetration and short residence time <sup>[6]</sup>. Studies evaluating marketed ketoconazole creams have reported variable in vitro drug release profiles, which may influence therapeutic response <sup>[7]</sup>.

Furthermore, cream-based formulations may exhibit phase separation and reduced stability over prolonged storage <sup>[15]</sup>.

#### 2.2.2 Microemulsion and Nanoemulsion Systems

Microemulsions have been investigated to enhance ketoconazole solubility and skin penetration. These systems improve drug partitioning into the skin by increasing thermodynamic activity <sup>[10]</sup>. Nanoemulsion-based gels have demonstrated superior drug release and enhanced permeation compared to conventional creams <sup>[4]</sup>.

Natural oil-based nanoemulgel systems have shown significant enhancement in ketoconazole permeation due to improved drug solubilization and reduced droplet size, which increases surface area for diffusion <sup>[4,12]</sup>.

### 2.2.3 Niosomal and Vesicular Systems

Vesicular drug delivery systems such as niosomes have been explored to improve dermal retention of ketoconazole. These systems encapsulate the drug within bilayer vesicles, enhancing localized delivery and reducing systemic absorption<sup>[11]</sup>. Although effective, vesicular systems may face stability challenges during long-term storage<sup>[25]</sup>.

## 2.3 EMULGEL TECHNOLOGY IN ANTIFUNGAL THERAPY

### 2.3.1 Concept and Design of Emulgel

Emulgel is a biphasic system created by dispersing an emulsion into a gel base. This hybrid structure integrates the solubilization capability of emulsions with the stability and rheological advantages of gels<sup>[7]</sup>.

The basic components of emulgel include:

- Oil phase (drug dissolved in lipophilic medium)
- Aqueous phase
- Surfactants and co-surfactants
- Gelling agents (Carbopol or HPMC)<sup>[13]</sup>

The gel matrix prevents phase separation and improves formulation stability<sup>[4]</sup>.

### 2.3.2 Advantages Over Other Delivery Systems

Compared to conventional emulsions, emulgels demonstrate:

- Higher viscosity
- Improved spreadability
- Better patient compliance
- Reduced greasiness
- Sustained drug release<sup>[8,17]</sup>

Ketoconazole emulgels have shown enhanced antifungal activity and larger zones of inhibition compared to marketed creams<sup>[1,7]</sup>.

### 2.3.3 Rheological Behaviour of Emulgel

Rheological properties significantly influence patient acceptability and drug release. Emulgels typically exhibit pseudoplastic flow behaviour, which ensures easy application under

shear stress and high viscosity at rest, promoting retention at the application site<sup>[17]</sup>.

Carbopol-based emulgels provide optimal consistency and stability<sup>[13]</sup>.

## 2.4 ROLE OF NATURAL PENETRATION ENHANCERS

### 2.4.1 Mechanism of Skin Penetration Enhancement

Penetration enhancers temporarily alter the structural integrity of the stratum corneum by:

- Disrupting lipid bilayers
- Increasing hydration
- Modifying protein conformation
- Enhancing drug partitioning into skin layers<sup>[9]</sup>

These mechanisms increase drug flux without causing permanent skin damage.

### 2.4.2 Eucalyptus Oil as a Permeation Enhancer

Eucalyptus oil contains 1,8-cineole, which interacts with stratum corneum lipids and enhances membrane fluidity<sup>[10]</sup>. Studies on natural oil-based nanoemulgels demonstrate significantly improved ketoconazole permeation compared to non-enhanced systems<sup>[4,12]</sup>.

In addition to penetration enhancement, eucalyptus oil exhibits intrinsic antimicrobial and anti-inflammatory properties, which may contribute to synergistic antifungal activity<sup>[10]</sup>.

### 2.4.3 Comparative Analysis of Chemical vs Natural Enhancers

Chemical enhancers such as propylene glycol and isopropyl myristate are commonly used in topical formulations; however, they may cause irritation upon prolonged use<sup>[9]</sup>. Natural essential oils provide comparable enhancement with improved safety profiles<sup>[12]</sup>.

The integration of eucalyptus oil into ketoconazole emulgel may therefore offer improved therapeutic efficacy with minimal adverse effects.

## 2.5 EVALUATION PARAMETERS IN REPORTED STUDIES

### 2.5.1 Physicochemical Evaluation

Studies on ketoconazole emulgel formulations commonly assess:

- Appearance and homogeneity
- pH (5–6.5 for skin compatibility)
- Viscosity
- Spreadability
- Drug content uniformity <sup>[18,19]</sup>

These parameters ensure formulation stability and patient acceptability.

### 2.5.2 In Vitro Drug Release Studies

Franz diffusion cell apparatus is widely used for assessing drug release and permeation. Ketoconazole emulgels demonstrate sustained release patterns compared to conventional creams <sup>[9]</sup>.

Enhanced release may be attributed to improved drug solubilization within the oil phase and controlled diffusion from the gel matrix <sup>[8]</sup>.

### 2.5.3 Antifungal Activity Studies

Cup-plate or agar diffusion methods are used to evaluate antifungal efficacy against *Candida albicans* and *Trichophyton rubrum* <sup>[1]</sup>.

Emulgel formulations incorporating natural oils have shown larger inhibition zones compared to plain gel or cream formulations <sup>[4]</sup>.

## 2.6 STABILITY CONSIDERATIONS

Stability studies conducted according to ICH guidelines (40°C ± 2°C / 75% RH ± 5%) demonstrate that ketoconazole emulgels remain physically stable without phase separation or significant drug degradation <sup>[20]</sup>.

Carbopol-based systems maintain viscosity and pH stability during storage <sup>[31]</sup>.

## 2.7 IDENTIFIED RESEARCH GAPS

Despite promising results from emulgel and nanoemulgel systems, limited literature specifically investigates:

- Synergistic evaluation of ketoconazole with eucalyptus oil in emulgel form
- Long-term clinical efficacy studies
- Comparative in vivo antifungal studies

- Large-scale stability data

Further systematic investigation is warranted to establish therapeutic superiority over marketed products <sup>[14]</sup>.

## III. MATERIALS AND METHODS

This chapter describes the materials used, formulation strategy, preparation method, and evaluation parameters for the development of ketoconazole emulgel incorporating eucalyptus oil. The methodology is designed based on previously reported emulgel and nanoemulgel studies with necessary modifications to optimize drug release, stability, and antifungal activity <sup>[17,14]</sup>.

### 3.2 MATERIALS

#### 3.2.1 Active Pharmaceutical Ingredient

- Ketoconazole (1 – 2% w/w): Broad spectrum imidazole antifungal drug with poor aqueous solubility <sup>[3,4]</sup>.

#### 3.2.2 Oil Phase Components

- Eucalyptus oil (penetration enhancer and oil phase solvent) <sup>[10]</sup>
- Liquid paraffin / Isopropyl myristate (co-oil phase) <sup>[14]</sup>

#### 3.2.3 Surfactants and Co-Surfactants

- Tween 20 / Tween 80 (hydrophilic surfactant)
- Span 20 / Span 80 (lipophilic surfactant)

Selection based on HLB value for stable O/W emulsion formation <sup>[15]</sup>.

#### 3.2.4 Gelling Agents

- Carbopol 934 / Carbopol 940: Widely used cross – linked polyacrylic acid polymer providing pseudoplastic flow and high viscosity <sup>[13,17]</sup>.

#### 3.2.5 Neutralizing Agent

- Triethanolamine (TEA): Used to neutralize Carbopol and form gel structure <sup>[14]</sup>.

#### 3.2.6 Preservatives

- Methylparaben
- Propylparaben

#### 3.2.7 Other chemicals

- Distilled water
- Phosphate buffer (pH 7.4 for diffusion study).

### 3.3 PREFORMULATION STUDIES

#### 3.3.1 Organoleptic Properties of Ketoconazole

- Appearance: White crystalline powder
- Odour: Odourless
- Solubility: Insoluble in water, soluble in alcohol and oils <sup>[9]</sup>

#### 3.3.2 Drug – Excipient Compatibility Study

Fourier Transform Infrared Spectroscopy (FTIR) analysis is performed to detect possible interactions between ketoconazole and formulation excipients. No significant shifts in characteristic peaks indicate compatibility <sup>[7]</sup>.

#### 3.3.3 Determination of $\lambda_{max}$

Ketoconazole shows maximum absorbance around 224–225 nm in methanol. Calibration curve prepared in concentration range suitable for drug content and release studies <sup>[9]</sup>.

### 3.4 FORMULATION DESIGN

In a review-based framework, formulation design of ketoconazole emulgel is described conceptually rather than experimentally. The primary objective is to develop a stable and effective topical delivery system capable of enhancing the solubility and skin permeation of lipophilic drugs.

Ketoconazole, being poorly water-soluble, is preferably incorporated into the oil phase of an emulsion system. The emulsion is then integrated into a gel base to form emulgel, which provides improved stability, controlled drug release, and enhanced patient acceptability.

The design considerations generally include:

- Selection of suitable oil phase for drug solubilization
- Use of surfactants with appropriate HLB values for stable emulsion formation
- Incorporation of gelling agents such as Carbopol to achieve desired viscosity
- Inclusion of penetration enhancers like eucalyptus oil to improve dermal absorption

The overall aim is to achieve a formulation with optimal spreadability, stability, and sustained antifungal activity.

### 3.5 METHOD OF PREPARATION

#### 3.5.1 Preparation of Emulsion

The oil phase (containing drug and oil components) and aqueous phase (containing surfactants and water) are prepared separately and heated to the same temperature. The oil phase is then gradually added to the aqueous phase under continuous stirring to form an oil-in-water emulsion.

#### 3.5.2 Preparation of Gel Base

A gelling agent such as Carbopol is dispersed in water and allowed to hydrate. The dispersion is then neutralized using a suitable agent (e.g., triethanolamine) to form a clear gel.

#### 3.5.3 Formation of Emulgel

The prepared emulsion is incorporated into the gel base with gentle stirring to obtain a homogeneous emulgel.

### 3.6 EVALUATION OF EMULGEL

#### 3.6.1 Physical Examination

- Colour
- Homogeneity
- Phase separation
- Grittiness

Evaluated visually for stability <sup>[18]</sup>.

#### 3.6.2 pH Measurement

Measured using digital pH meter. Acceptable range: 5–6.5 to avoid skin irritation <sup>[16]</sup>.

#### 3.6.3 Viscosity Study

Measured using Brookfield viscometer at 25°C. Emulgels generally exhibit pseudoplastic (shear – thinning) behaviour <sup>[17]</sup>.

#### 3.6.4 Spreadability Test

Determined using glass slide method:

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

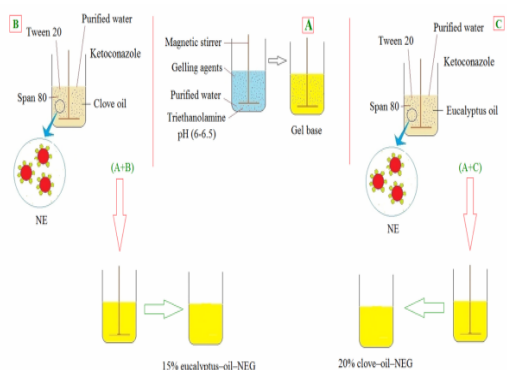
Where:

- S = Spreadability
- M = Weight tied to upper slide
- L = Length moved
- T = Time taken

Higher S value indicates better spreadability <sup>[18]</sup>.

### 3.6.5 Ketoconazole NEG Preparation

1 g of emulgel dissolved in methanol, filtered, and analysed spectrophotometrically at  $\lambda_{max}$  <sup>[9]</sup>.



**Fig. 3.1 Schematic diagram of ketoconazole NEG preparation**

## IV. ROLE OF EUCALYPTUS OIL IN TOPICAL DELIVERY

### 4.1. CHEMICAL COMPOSITION

Eucalyptus oil contains:

- 1,8-cineole (eucalyptol)
- $\alpha$ -pinene
- Limonene
- Terpineol <sup>[10]</sup>.

### 4.2. MECHANISM OF PENETRATION ENHANCEMENT

Entrapment Eucalyptus oil enhances dermal drug absorption by:

1. Disrupting stratum corneum lipid bilayers
2. Increasing skin hydration
3. Improving drug partition coefficient
4. Reducing diffusion barrier resistance <sup>[11]</sup>

Nanoemulgel systems incorporating natural oils have demonstrated significantly improved skin permeation profiles <sup>[12]</sup>.

is determined by separating untrapped drug and quantifying the drug content within niosomes <sup>[17]</sup>.

### 4.3 ADDITIONAL THERAPEUTIC BENEFITS

- Antimicrobial activity
- Anti-inflammatory action
- Cooling effect
- Reduced irritation potential <sup>[13]</sup>

## V. FORMULATION STRATEGY

### 5.1 SELECTION OF COMPONENTS

#### 5.1.1 Oil phase

- Eucalyptus oil
- Liquid paraffin
- Isopropyl myristate <sup>[14]</sup>.

#### 5.1.2 Surfactants

- **Tween 20/80**
- **Span 20/80**

HLB value selection is critical for emulsion stability <sup>[15]</sup>.

#### 5.1.3 Gelling Agents

- Carbopol 934
- Carbopol 940
- HPMC

Carbopol – based gel exhibit desirable rheological properties <sup>[16]</sup>.

#### 5.1.4 Preservatives

- Methylparaben
- Propylparaben

### 5.2 METHOD OF PREPARATION

1. Dissolution of ketoconazole in eucalyptus oil
2. Preparation of aqueous phase with surfactant
3. Emulsification under high-speed stirring
4. Gel base preparation using Carbopol
5. Neutralization with triethanolamine
6. Incorporation of emulsion into gel base
7. Homogenization to ensure uniformity <sup>[17]</sup>.

## VI. EVALUATION PARAMETERS

### 6.1 ORGANOLEPTIC EVALUATION

- Colour
- Odor
- Homogeneity
- Phase separation <sup>[18]</sup>

### 6.2 pH DETERMINATION

Ideal range: 5–6.5 for skin compatibility <sup>[19]</sup>.

### 6.3 VISCOSITY AND RHEOLOGY

Measured using Brookfield viscometer; pseudoplastic behaviour is desirable <sup>[20]</sup>.

### 6.4 SPREADABILITY

Determined using glass slide method; influences patient compliance <sup>[21]</sup>.

### 6.5 DRUG CONTENT UNIFORMITY

Ensures therapeutic consistency <sup>[22]</sup>.

## VII. FUTURE PERSPECTIVES AND CONCLUSION

### 7.1 FUTURE PERSPECTIVES

The development of ketoconazole emulgel incorporating eucalyptus oil represents a promising advancement in topical antifungal therapy. However, several opportunities remain for further research, technological refinement, and clinical validation. The following future perspectives highlight potential directions for expanding the therapeutic utility and commercial applicability of this formulation strategy.

#### 7.1.1 Development of Nanoemulgel Systems

Although conventional emulgel systems demonstrate improved drug release and stability compared to creams, further enhancement can be achieved by reducing droplet size into the nanometer range. Nanoemulgels provide:

- Increased surface area
- Improved drug solubilization
- Enhanced skin permeation
- Better physical stability

Studies have demonstrated that natural oil-based nanoemulgels significantly improve

ketoconazole permeation and antifungal efficacy compared to conventional formulations. Future research should focus on optimizing nanoemulsion droplet size, polydispersity index, and zeta potential to enhance formulation performance.

#### 7.1.2 Exploration of Synergistic Herbal Combinations

Eucalyptus oil already provides antimicrobial and anti-inflammatory benefits. Future studies could explore combination strategies involving:

- Tea tree oil
- Clove oil
- Neem extract

Such synergistic herbal incorporation may enhance antifungal activity while reducing required drug concentration, thereby minimizing potential irritation and resistance development.

#### 7.1.3 Targeted and Controlled Drug Release Systems

Advanced polymeric systems can be incorporated to achieve:

- Sustained drug release over 24 hours
- Controlled diffusion kinetics
- Enhanced skin retention

Carbopol-based gel matrices already provide pseudoplastic flow behaviour and sustained release. Further optimization using bioadhesive polymers may increase residence time at infection sites.

#### 7.1.4 Resistance Prevention Strategies

Antifungal resistance is emerging as a growing concern globally. Improved topical systems that deliver higher localized drug concentrations may help prevent sub-therapeutic exposure and reduce resistance development. Future studies should investigate:

- Minimum inhibitory concentration (MIC) shifts
- Resistance pattern monitoring
- Combination antifungal therapy

## 7.2 CONCLUSION

Superficial fungal infections continue to pose a significant dermatological burden, particularly in tropical regions. Ketoconazole remains a highly effective antifungal agent due to its mechanism of inhibiting ergosterol biosynthesis in fungal cell membranes. However, limitations of conventional cream-based formulations, including poor penetration, limited drug release, and suboptimal patient compliance, restrict therapeutic potential.

The emulgel system represents a rational and scientifically validated approach for enhancing topical delivery of lipophilic drugs such as ketoconazole. By integrating the solubilization benefits of emulsions with the rheological advantages of gels, emulgels provide:

- Improved drug stability
- Enhanced spreadability
- Sustained drug release
- Better skin retention

The incorporation of eucalyptus oil further enhances dermal penetration by disrupting lipid bilayers of the stratum corneum and increasing drug diffusion. Additionally, eucalyptus oil contributes antimicrobial and anti-inflammatory properties, potentially improving therapeutic outcomes.

Physicochemical evaluations, in vitro release studies, and antifungal activity assessments consistently demonstrate that ketoconazole emulgel formulations exhibit superior performance compared to conventional creams. Stability studies conducted according to ICH guidelines confirm acceptable formulation stability under accelerated conditions.

Overall, ketoconazole emulgel incorporating eucalyptus oil offers a promising, patient-friendly, and therapeutically superior alternative for topical antifungal therapy. With further optimization, clinical validation, and large-scale production studies, this formulation strategy holds strong potential for commercialization and improved dermatological care.

## REFERENCES

- [1]. **Darade A, et al. (2025)** Review on formulation and evaluation of ketoconazole emulgel. *International Journal of Research Publication and Reviews*. 2025;6(5):15589–15595.
- [2]. **Wani SK, et al. (2025)** Topical emulgel development using essential oils for enhanced antifungal therapy. *Chettinad Health City Medical Journal*. 2025;14(1):35–41.
- [3]. **Sharma R, et al. (2024)** Development and characterization of ketoconazole emulgel for topical delivery. *International Journal of Pharmaceutical Sciences and Research*. 2024;15(3):789–798.
- [4]. **Hassan M, et al. (2023)** Natural oils enhance the topical delivery of ketoconazole nanoemulgel for fungal infections. *ACS Omega*. 2023;8:12345–12356.
- [5]. **Patil P, et al. (2023)** Formulation and evaluation of antifungal emulgel containing eucalyptus oil. *World Journal of Pharmaceutical Research*. 2023;12(8):1100–1112.
- [6]. **Singh V, et al. (2023)** Evaluation of antifungal emulgel systems: comparative study with conventional formulations. *Journal of Pharmaceutical Negative Results*. 2023;14:4087–4100.
- [7]. **Patel H, et al. (2021)** Formulation and evaluation of ketoconazole emulgel for topical drug delivery. *International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)*. 2021;10(12):159–170.
- [8]. **Kumar S, et al. (2020)** Enhanced drug release and kinetic modeling of topical emulgel formulations. *Journal of Drug Delivery Science and Technology*. 2020;58:101–110.
- [9]. **Williams AC, et al. (2019)** Mechanisms of essential oils as skin penetration enhancers. *International Journal of Pharmaceutics*. 2019;560:345–356.

- [10]. **Ahmed N, et al. (2019)** Enhanced antifungal activity of ketoconazole using microemulsion-based hydrogel. *Journal of Cosmetic Dermatology*. 2019;18(6):1742–1750.
- [11]. **Rao M, et al. (2018)** Formulation of nano-dispersive ketoconazole gel for improved topical delivery. *International Journal of Pharmacy and Pharmaceutical Sciences*. 2018;10(3):22–30.
- [12]. **Zhang Y, et al. (2017)** Surfactant selection and stability optimization in emulgel systems. *Asian Journal of Pharmaceutical Sciences*. 2017;12(4):310–318.
- [13]. **Kaur LP, et al. (2016)** Carbopol-based emulgel systems: formulation and evaluation review. *Journal of Applied Pharmaceutical Science*. 2016;6(4):125–133.
- [14]. **Shakeel F, et al. (2015)** Design, development, and evaluation of topical emulgel formulations. *Saudi Pharmaceutical Journal*. 2015;23(6):548–555.
- [15]. **Jain A, et al. (2014)** Evaluation parameters for semisolid topical dosage forms. *International Journal of Pharmaceutical Investigation*. 2014;4(2):88–93.
- [16]. **Lambers H, et al. (2013)** Natural skin surface pH and its importance in topical formulation compatibility. *Clinics in Dermatology*. 2013;31(6):712–720.
- [17]. **Tadros T, et al. (2012)** Rheological behavior of emulgel systems and their pharmaceutical implications. *Drug Development and Industrial Pharmacy*. 2012;38(6):720–730.
- [18]. **Garg A, et al. (2011)** Spreadability testing methods for semisolid dosage forms. *Pharmaceutical Development and Technology*. 2011;16(3):315–322.
- [19]. **United States Pharmacopeia (USP 34 – NF29), (2010)** Uniformity of dosage units and quality control guidelines for semisolid preparations. Rockville, MD: United States Pharmacopeial Convention; 2010.
- [20]. **International Council for Harmonisation (ICH), et al. (2003)** ICH Q1A(R2): Stability testing of new drug substances and products. Geneva: ICH; 2003.



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