IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 5, Issue 9, May 2025
Impact Factor: 7.67

# Formulation and Evaluation of Antifungal Ketoconazole Emulgel

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**Abstract**: *Ketoconazole (KTZ) is a broad-spectrum antifungal agent and an imidazole derivative, commonly used to treat a range of fungal infections such as candidiasis, dermatophytosis, and dandruff. It works by disrupting the synthesis of the fungal cell membrane, making it effective against a wide variety of fungi. This research aimed to formulate ketoconazole into a topical emulgel to improve its effectiveness in treating localized fungal infections. Emulgels—gel-like emulsions—offer several advantages, including controlled drug release, enhanced skin penetration, and better formulation stability. In this study, different ketoconazole emulgel formulations were developed and evaluated through physical characterization, pH measurement, viscosity testing, in-vitro drug release studies, drug content analysis, and swelling index assessment. The goal was to optimize the formulation to ensure sustained and targeted delivery of ketoconazole at the infection site, ultimately leading to better therapeutic outcomes in the management of fungal infections*

**Keywords**: Ketoconazole, Emulgel , Topical Drug Delivery, AntiFungal Activity

## I. INTRODUCTION

Ketoconazole is a broad-spectrum antifungal agent that belongs to the imidazole class. It is widely used to treat fungal infections, particularly those caused by *Candida albicans* and *Malassezia* species. Its primary mode of action involves blocking the production of ergosterol, a crucial component of the fungal cell membrane. Without ergosterol, the membrane becomes unstable and more permeable, ultimately leading to the death of the fungal cells. When applied topically, ketoconazole is effective against a variety of skin conditions such as ringworm (*tinea corporis*), athlete's foot (*tinea pedis*), jock itch (*tinea cruris*), seborrheic dermatitis, and *pityriasis versicolor*. Like other azole antifungals, it can interfere with specific enzymes within fungal cells, making its action either fungistatic or fungicidal depending on the dose and the type of fungus. It is generally considered safe and well-tolerated when used on the skin, showing strong activity against yeasts, dermatophytes, and even some gram-positive bacteria. Due to its poor water solubility and lipophilic nature, developing a stable and effective topical formulation of ketoconazole remains a key focus in pharmaceutical research. Emulgels have emerged as a promising delivery system for such drugs. These are hybrid formulations that combine the properties of both emulsions and gels—making them ideal for drugs like ketoconazole. They offer improved drug solubility, stability, and absorption through the skin while being easy to apply and non-greasy.

In this study, ketoconazole was incorporated into emulgel formulations using different gelling agents (Carbopol 934). The research aimed to optimize various formulation factors such as the type of gelling agent, the amount of emulsifier, and the composition of the oil phase, all of which influence the texture, spreadability, and drug release behavior of the final product.

**Advantages of Emulgels for Ketoconazole:**

- **Better skin delivery** – Emulgels enhance the penetration and availability of lipophilic drugs like ketoconazole by merging the absorption power of emulsions with the adhesive properties of gels.

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- **Stable formulation** – Emulgels are more physically stable than standard emulsions and are less likely to separate over time.
- **User-friendly** – Their smooth, non-greasy texture makes them comfortable to use, especially over large or hairy areas of skin.
- **Limitations of Emulgels:**
- **Limited deep penetration** – Without enhancement techniques, the formulation may not reach deeper skin layers effectively.
- **Possible skin irritation** – Some users may react to ingredients like preservatives or gelling agents.
- **Residual stickiness** – In some cases, emulgels may leave a sticky feel, particularly in humid conditions or on body hair.

## II. FUNGAL INFECTION

Fungal infections have been increasingly reported in recent years, making them a growing public health concern. These infections often go unnoticed in the early stages, which allows them to worsen over time and makes treatment more challenging. Fungi have developed sophisticated ways to evade the body's immune defenses, allowing infections to spread and become more severe. To manage both superficial and deeper systemic fungal infections, a range of antifungal medications are used. With advancements in drug design and formulation technologies, newer and more effective antifungal treatments are being developed.

One of the most common fungal infections in humans is candidiasis, which is caused by a type of yeast called *Candida*, particularly *Candida albicans*. Normally, this fungus lives harmlessly on the skin and inside the body—in areas like the mouth, throat, intestines, and vagina. However, under certain conditions, such as a weakened immune system or imbalance in the body's natural flora, *Candida* can grow excessively and cause infection. In more severe cases, it can even enter the bloodstream or affect internal organs such as the kidneys, heart, or brain.

**Common Types of Candida Infections:**

**Thrush:**

A yeast infection in the mouth and throat, seen as white patches or bumps. It is more common in babies, the elderly, and people with compromised immune systems.

**Vaginal Candidiasis (Yeast Infection):**

An overgrowth of yeast in the vaginal area causes itching, irritation, and thick white discharge. Common triggers include pregnancy, antibiotics, hormonal changes, and a weakened immune system.

**Oral Thrush:**

Also known as oral candidiasis, this appears as creamy white lesions on the tongue, inner cheeks, or throat. It can be triggered by stress, uncontrolled diabetes, or immune deficiencies.

**Invasive Candidiasis:**

A serious, potentially life-threatening infection where *Candida* enters the bloodstream and spreads to organs like the brain, bones, and heart. It mostly affects hospitalized patients, especially those using catheters or recovering from surgery.

**Treatment Options:**

**Oral medications:** Tablets or lozenges taken by mouth for internal infections.

**Topical medications:** Creams or ointments applied directly to the affected area for skin or mucosal infections.

## III. AIM AND OBJECTIVE

**Aim:** To Formulate and Evaluate Antifungal emulgel of Ketoconazoele.

**Objectives:**

- To improve patient acceptance.
- To enhance permeation of poorly water soluble drug.

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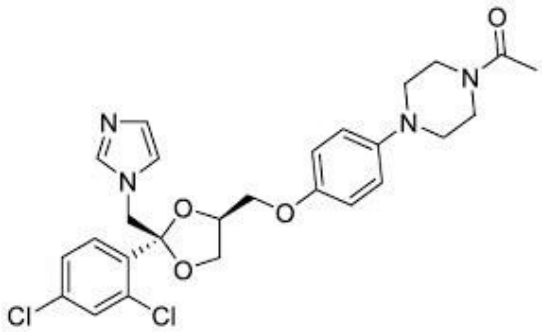
- To overcome limitation of conventional oral and parentral route of administration
- To prevent the first pass metabolism.
- To enhance the penetration of active ingredients through the skin by combining the emollient properties of oils with the water-soluble properties of gels, thereby facilitating better drug delivery.
- To be easily spreadable on the skin, allowing for convenient and uniform application over the affected area.

## IV. DRUG PROFILE

**Table No.1: Drug Profile of Ketoconazole**

| Parameter | Information |
|---|---|
| **Drug Name** | Ketoconazole |
| **Structure** |  |
| **Mol. Weight** | 531.437 gm/mol |
| **Chemical formula** | C26 H28 Cl2 N4 O4 |
| **IUPAC Name** | *cis*-1-acetyl-4-[[(2*RS*,4*RS*)-2-(2,4-dichlorophenyl)-2(1*H*imidazolw-1-ylmethyl)-1,3_dioxolan4yl}methoxyl]phenylpiperazine. |
| **Category** | Antifungal |
| **Dose** | For an Adult, 200 mg to 400 mg once daily with food for 14 days; for a child, 3 mg per kg body weight daily. |
| **Description** | A White to off-white, crystalline powder. |
| **Identification** | Determine by Infrared absorption spectrophotometery. Compare the spectrum with that obtained with ketoconazole RS or with the reference spectrum of ketoconazole<br>Melting range. 148° to 152° |
| **Solubility** | Ketoconazole is practically insoluble in water,<br>Sparingly soluble in alcohol,<br>Freely soluble in dichloromethane,<br>Soluble in methyl alcohol |
| **pKa value** | 8.8 |
| **Particle size** | Less than 100 nm |
| **Polymorphic form** | Form I |
| **Hygroscopicity** | Slightly hygroscopic in nature |
| **BCS class** | Class II |
| **T max** | 1 to 4 hour |
| **Solid state Stability** | Sparingly soluble in water Highly soluble in organic solvents. |
| **Melting Point** | 148° to 152° |


DOI: 10.48175/IJARSCT-27064

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## V. MATERIALS AND METHOD

**5.1. Materials and Chemical:** Ketoconazole, Carbopol 940,Propylene glycol Ethanol(95%), Triethanolamine, Methyl paraben,Purifide water

**5.2. Instrument:** pH meter, Magnetic stirrer.

**5.3. Experimental work:**

**5.3.1. Formulation of Clotrimazole hydrogel.**

| Sr. No | Ingredient | F1 | F2 | F3 | F4 | F5 |
|---|---|---|---|---|---|---|
| 1 | Ketoconazole | 0.1 | 0..1 | 0..1 | 0.1 | 0.1 |
| 2 | Carbapol 934 | 0.5 | 0.5 | 0.75 | 0.75 | 1 |
| 3 | Tween 20 | 0.3 | 0.3 | 0.3 | 0.3 | 0.3 |
| 4 | Liquid Paraffin | 2.5 | 2.5 | 3 | 3 | 3.5 |
| 5 | Propylene Glycol | 2.5 | 2.5 | 2.5 | 2.5 | 2.5 |
| 6 | Methyl Paraben | 0.01 | 0.01 | 0.01 | 0.01 | 0.01 |
| 7 | Propyl Paraben | 0.03 | 0.03 | 0.03 | 0.03 | 0.03 |
| 8 | Methanol | 1.25 | 1.25 | 1.25 | 1.25 | 1.25 |
| 9 | Purified water | 50 | 50 | 50 | 50 | 50 |

**Procedure of Ketoconazole hydrogel:**

**Step 1: Preparation of Gel Base**

A gelling agent, such as Carbopol 934, is dispersed in purified water under continuous mechanical stirring to form a uniform gel base. The dispersion is allowed to swell, and the pH is adjusted to approximately 6.0–6.5 using triethanolamine, ensuring compatibility with skin and drug stability

**Fig No. 1: Carbapol Gel**

**Step 2: Formulation of the Emulsion**

**Oil Phase Preparation:**

Span 20 (a lipophilic surfactant) is mixed with light liquid paraffin to form the oil phase.

**Aqueous Phase Preparation:**

In a separate container, Tween 20 (a hydrophilic surfactant) is dissolved in purified water. Ketoconazole is separately dissolved in methanol, while preservatives like methylparaben and propylparaben are dissolved in propylene glycol. These solutions are then added to the aqueous phase with continuous stirring.

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**Emulsion Formation:**

Both the oil and aqueous phases are heated separately to around 70–80°C. The oil phase is gradually added to the aqueous phase with continuous stirring until a stable emulsion is formed, which is then cooled to room temperature.

**Step 3: Incorporation of Emulsion into Gel**

The prepared emulsion is added gradually into the gel base in a 1:1 ratio with constant stirring to ensure uniform distribution and consistency. The final formulation is stored in airtight containers to maintain stability.

**Fig No.2: Ketoconazole Emulgel**

**EVALUATION TEST**

**Physical Appearance** was evaluated to check color, consistency, and homogeneity, which are critical indicators of formulation stability and aesthetic acceptability.

**pH Measurement** was performed to ensure the emulgel's pH falls within the skin-friendly range (5.5–6.5), minimizing the risk of irritation or discomfort upon application.

**Spreadability** testing was carried out to assess how easily the emulgel can be applied over the skin surface, which influences patient compliance and dosage uniformity.

**Viscosity** was measured to determine the formulation's flow behavior and structural integrity, essential for maintaining consistency during storage and use.

**Antifungal Activity** was examined using the cup plate method to evaluate the formulation's ability to inhibit the growth of *Candida albicans*, reflecting its therapeutic efficacy

## VI. RESULT AND DISCUSSION

Parameters like Physical appearance, pH determination, spreadability, Viscosity determination and antifungal study of all batches were performed. Batch F1, F4, F5 shows good consistency and homogeneity than batch F2 and F3. Phase separation was shown by batch F2. Batch F4 and F5 formulation was consider to be more preferable than 3 batches.

**Physical appearance:**

**Table No. 2:- Physical appearance of emulgel**

| Formulation Batch | Color | Consistency | Homogeneity | Phase separation |
|---|---|---|---|---|
| F1 | White | +++ | ++ | None |
| F2 | White | + | + | + |
| F3 | Shiny white | ++ | ++ | None |
| F4 | Shiny white | +++ | +++ | None |
| F5 | Shiny white | +++ | +++ | None |

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**pH Determination:**

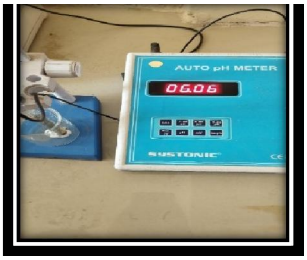


**Fig No. 3: pH determinatione**

**Table No. 3: pH determination**

| Formulation | pH |
|---|---|
| F1 | 5.83 |
| F2 | 5.84 |
| F3 | 5.97 |
| F4 | 6.06 |
| F5 | 6.10 |

**Spreadability**

**Fig No. 4: Spreadability**

**Table No. 4:- Spreadability**

| **Formulation** | **Spreadability** |
|---|---|
| **F1** | **4** |
| **F2** | **2.5** |
| **F3** | **4** |
| **F4** | **4.7** |
| **F5** | **4.8** |

**Viscosity determination:**

**Table No. 5:Viscosity**

| **Formulation** | **Viscosity** |
|---|---|
| **F1** | **1.26** |
| **F2** | **1.25** |
| **F3** | **1.30** |
| **F4** | **1.36** |
| **F5** | **1.36** |

**Antifungal study:**

The antifungal effect of the ketoconazole emulgel we prepared was tested using the cup plate method against Candida albicans, a common fungus that causes skin infections. The emulgel formed a clear zone where the fungus couldn't

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grow, showing that it was effective in killing or stopping the fungus. When compared to a regular, store-bought ketoconazole cream, our emulgel performed just as well—or even slightly better. This might be because the emulgel spreads more easily and stays on the skin longer, allowing the medicine to work more effectively. Overall, the test results suggest that our formulation could be a reliable and useful option for treating fungal skin infections.


**Fig No. 5: Antifungal study**

**Table No. 6 : Antifungal action**

| Formulation | Zone of inhibition |
|---|---|
| F2 | 36mm |
| F3 | 37mm |
| F4 | 43mm |
| F5 | 45mm |

## VII. CONCLUSION

In the present study antifungal emulgel of ketoconazole were successfully formulated by dispersion method. Developed formulations were characterized and F5 was selected as optimized formulation on the basis of pharmaceutical properties and percent drug release.On the basis of study, it can be concluded that emulgel for topical delivery of ketoconazole can be successfully developed.

## VIII. FUTURE DIRECTION

Future research should focus on exploring the long-term effects of emulgel, as well as their potential applications in various clinical populations, such as patients with fungal infections, dermatophytosis, tinea pedis,tinea crusis. Additionally, the emulgel form allows better absorption, less greasiness, and cooling effects compared to creams.

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DOI: 10.48175/IJARSCT-27064

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