

# A Review on Luliconazole Cream : An Effective and Safe Treatment Option for Fungal Skin Infection

Roman Vaishnavi, Arote Sneha, Mr. Bhalekar S . M

Student, Department of Assurance Techniques

Samarth Institute of Pharmacy, Belhe, Maharashtra, India

**Abstract:** Luliconazole is an imidazole antifungal agent with a unique structure, as the imidazole moiety is incorporated into the ketene dithioacetate structure. Luliconazole is the R-enantiomer, and has more potent antifungal activity than lanoconazole, which is a racemic mixture. In this review, we summarize the in vitro data, animal studies, and clinical trial data relating to the use of topical luliconazole. Preclinical studies have demonstrated excellent activity against dermatophytes. Further, in vitro/in vivo studies have also shown favorable activity against *Candida albicans*, *Malassezia spp.*, and *Aspergillus fumigatus*. Luliconazole, although belonging to the azole group, has strong fungicidal activity against *Trichophyton spp.*, similar to that of terbinafine. The strong clinical antifungal activity of luliconazole is possibly attributable to a combination of strong in vitro antifungal activity and favorable pharmacokinetic properties in the skin. Clinical trials have demonstrated its superiority over placebo in dermatophytosis, and its antifungal activity to be at par or even better than that of terbinafine. Application of luliconazole 1% cream once daily is effective even in short-term use (one week for tinea corporis/cruris and 2 weeks for tinea pedis). A Phase I/IIa study has shown excellent local tolerability and a lack of systemic side effects with use of topical luliconazole solution for onychomycosis. Further studies to evaluate its efficacy in onychomycosis are underway. Luliconazole 1% cream was approved in Japan in 2005 for the treatment of tinea infections. It has recently been approved by US Food and Drug Administration for the treatment of interdigital tinea pedis, tinea cruris, and tinea corporis. Topical luliconazole has a favorable safety profile, with only mild application site reactions reported occasionally.

**Keywords:** Luliconazole, antifungal, emulgel, BCS class II, controlled release system

## I. INTRODUCTION

A cream is a topical preparation usually for application to the skin. Creams may be considered pharmaceutical products as even cosmetic creams are based on techniques developed by pharmacy and unmedicated creams are highly used in a variety of skin conditions. The use of the finger tip unit concept may be helpful in guiding how much topical creams is required to cover different areas.

### Luliconazole:

Luliconazole has anti-fungal activity. Luliconazole is inhibiting the enzyme lanosterol demethylase. Lanosterol demethylase is needed for the synthesis of ergo-sterol, which is a major component of the fungus cell membranes. For skin care and the topical treatment of dermatological diseases, a wide choice of vehicles including solid, semisolids and liquid Preparation is available to physician and patients. Within the major groups of semisolid preparations, the use of transparent emulgel has expanded, both in cosmetics and pharmaceuticals. Emulgel or jellified emulsion is stable one and better vehicle for hydrophobic or water insoluble drugs as Luliconazole. Also emulgel has a high patient acceptability since they possess the advantages of both emulsions and gels. Therefore, they have been recently used as vehicles to deliver various drugs to the skin.

**Formulation of Cream:**

- **Vehicle-** Comply with the ideal characteristics given in the Pharmacopeias.
- **Aqueous material-** The aqueous phases used is water, alcohol, etc
- **Emulsifiers-** Emulsifiers are used for preparation of emulsion. Classical examples are span 80, tween 80, stearic acid, sodium stearate.
- **Gelling agents-** Gelling agents are used to prepare gels, which enhances consistency and provides thickness to the preparation.
- **Penetration enhancers-** Penetration enhancers help to absorb drug to the skin. <sup>[6]</sup>

**II. MATERIALS AND METHODS**

luliconazole ,cetostearyl alcohol, liquid paraffin, (light), cetomacrogol, white soft paraffin, sodium hydroxide, benzoic acid, tween-80, sodium lauryl sulfate, sodium metabisulfate, propylene glycol, purified water,etc. were obtained from the laboratory of Samarth institute of pharmacy, Belhe. All chemical solvents were of analytical grade and used without further purifications.

**Preformulation studies:**

- **Melting point determination:** The melting point of the sample is done to check the purity of the sample. Melting point is defined as the temperature at which a solid substance transits its state from solid to liquid. Melting point of luliconazole was found by using the digital melting point apparatus.
- **Solubility analysis:** Solubility is defined as the ability of a solute to dissolve in a liquid (solvent) to form a homogeneous solution. Factors affecting solubility are; type of solvent used, temperature and pressure. <sup>[11]</sup> Solubility analysis was primarily performed in order to find out a suitable solvent to dissolve the API, lipid and excipients used for formulation preparation.
- **Partition Coefficient of the Drug:** Partition coefficient is the measure of the lipophilic and hydrophilic nature of a drug substance. It is defined as the extent to which a substance is distributed between two liquid phases, one being the aqueous phase and other being the oily phase. The majorly used phases are water and n-octanol (oil phase) in the ratio 1:1. <sup>[12]</sup>

$$P_{o/w} = C(\text{n-octanol}) / C(\text{water})$$

**Preparation of luliconazole Cream:**

**Preparation of oil phase:**

The Oil phase ingredients were weighed and heated in the 250 ml borosilicate beaker at the temperature 75 -800C to form uniform liquid.

(Liq. Paraffin, beeswax, white soft paraffin, API)

**Preparation of Aqueous phase:**

The water phase ingredients were weighed and heated with continuous stirring in the 250 ml borosilicate beaker at the temperature 75-800C to form uniform liquid.

(borax, water, methyl paraben)

Table.1: Composition of Different Formulation Batches (%w/w).

Ingredients	F1	F2	F3	F4
Luliconazole	0.100	0.100	0.100	0.100
Cetostearyl alcohol	1.254	1.192	1.208	1.224
Liquid Paraffin	0.450	0.470	0.440	0.480
Cetomacrogol 1000	0.3	-	-	-
White soft paraffin	-	0.270	0.272	0.275
Sodium hydroxide	-	-	0.150	-
Benzoic acid	-	-	0.150	-

Tween 80	-	-	-	0.25
Sodium lauryl sulfate	0.100	0.100	0.100	0.100
Sodium metabisulfite	0.010	1.010	0.010	0.010
Propylene glycol	1.400	6.208	6.320	6.161
Purified Water	q.s.	q.s.	q.s.	q.s.
Total weight (gm)	10.00	10.00	10.00	10.00

#### Evaluation of prepared luliconazole Cream:

- **Physical appearance:** The prepared gel was examined for clarity, colour, homogeneity, odour, feel upon application (greasiness, grittiness) and texture.
- **pH:** For pH measurements, freshly prepared solutions were kept at 25±2°C for a period of 30 min. After pH measurement, each solution was placed in a water bath and heated gradually up to 60 °C. The pH was determined using digital pH meter.
- **Drug Solubility:** The shake-flask method was employed for the drug solubility experiment. The drug was solubilized in each solvent by stirring at room temperature. The sample solutions were filtered (0.45µm, Millipore, MA) before they attained the maximum solubility of Luliconazole in varying solvents.
- **Viscosity:** The viscosity of the prepared cream was carried out using a Brookfield viscometer using T-bar spindle (spindle-L4). The speed of 6 rpm was maintained for spindle rotation and the values were measured when the gel level was stabilized.

$$\text{Viscosity (mPa.S)} = \text{Dial Reading} \times \text{Factor}$$

- **Spreadability:** 10g cream was placed within a circle of 1 cm diameter premarked on a glass plate over which a second glass plate was placed. A weight of 500 gm was allowed to rest on the upper glass plate for 5 minutes. The increase in the diameter due to spreading of the cream was noted from the formula:

$$S = M \cdot L / T$$

Where, S is the spreadability (gm.cm/sec), M is the mass placed on the pan, L is the length of the slide (cm), and T is the time (in seconds) required to move the upper slide.

- **Extrudability:** The test was performed using a clean aluminum collapsible tube (20 g capacity) with a tip opening diameter of 1 cm. The extrudability was evaluated in by measuring the weight of gel sample ejected from the tube opening upon pressing with fingers, while holding the tube in hands.

### III. RESULT AND DISCUSSION

Luliconazole, has been studied for its potential benefits in treating fungal infection due to its anti funagal properties. Research indicates that cream derived from luliconazole may help treat fungal infections, relieve symptoms, prevent fungal growth, improve skin condition.

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