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Formulation And Evaluation Of Ketoconazole Loaded Liposomal Gel For in treatment of fungal infections - A Review

***[1]Rohini K. Pundge *[2]Sameer S. Sheaikh *[3]Milke U. R**
***[1] Student *[2]Principal,**(Research Guide) ***[3]HOD**
Department Of Pharmaceutics
Durgamata Institute Of Pharmacy, Parbhani, India

***Abstract*:-**Fungal infections constitute a significant global health burden, encompassing both superficial and systemic forms. Superficial fungal infections (SFIs) are among the most prevalent infectious diseases worldwide, affecting approximately 1.73 billion individuals annually. These infections are particularly prevalent in tropical regions, where the hot and humid climate provides an ideal environment for fungal growth.Topical formulations of ketoconazole, such as creams, gels, and shampoos, provide targeted antifungal therapy with reduced systemic exposure. However, they are associated with several limitations. These limitations highlight the need for advanced drug delivery systems that can improve ketoconazole solubility, enhance skin penetration, provide sustained drug release, and minimize adverse effects. Liposomal gel systems offer a promising approach

Introduction

History Of fungal infection

According to recent estimates, invasive fungal infections afflict about 6.5 million people yearly and cause over 3.8 million deaths, making fungal infections a major cause of mortality from infectious diseases. With an estimated 1.57 million cases worldwide each year and a mortality rate of up to 63.6%, invasive candidiasis, which is caused by Candida species, is especially worrisome. Effective therapy is hampered by a number of issues even with the availability of antifungal medications. Drug resistance is a growing problem because organisms including dermatophytes and Candida spp. Show resistance to widely used medications, making treatment plans more difficult. Effective treatment of these infections is further hampered by problems including drug penetration and recurrence. These drawbacks highlight the necessity of developing novel drug delivery methods to improve the effectiveness of antifungal therapies.

Fungi are eukaryotic organisms that can be found all over the planet in a variety of habitats, from soil and decaying vegetation to harsh settings like deep sea sediments and deserts. Despite the fact that more than 100,000 species of fungi have been identified, the Kingdom Fungi is thought to include about 5 million species.[1] The World Health Organization's 2022 2 4 publication of the fungal pathogen priority list was a significant recognition of the significance of these pathogens and the challenges we face in treating the diseases they cause, including the few 6 available diagnostic and treatment options. Our knowledge and comprehension of the pathophysiology of fungal infections have significantly increased during the last ten years. [2] In terms of burden, fungal skin infections are most common in lower- and middle-income nations worldwide, with the highest incidence rates found in Asia. Forecasts regarding the incidence and frequency of fungal infections in the future indicate that they will continue to rise, highlighting the necessity of interventions, such as medicines.[3]

The shortcomings of traditional topical formulations, such as low solubility, insufficient penetration into the stratum corneum, and unpredictable treatment effect, were overcome by the development of advanced delivery systems for ketoconazole. Because the ketoconazole molecule is highly lipophilic, it is imperative to improve its distribution to deeper skin layers and hair follicles in order to treat diseases that are dominated by both dermatophytes and Malassezia.Enhancing medication solubilization, increasing local bioavailability, minimizing discomfort, and guaranteeing prolonged release are the main goals of contemporary technologies. In dermatological applications, a number of novel systems have shown notable advantages.[4]

Drug Profile

Ketoconazole is a synthetic imidazole chemical that inhibits lipid and sterol formation in fungi and blocks several cytochrome P450-dependent processes in humans. Its biological activity extends to both endocrine and antifungal systems. By interfering with endoplasmic reticulum-based enzymatic pathways responsible for fatty acid assembly, glycerolipid production, and the formation of phosphatidic acid, the precursor of major phospholipid classes required for bilayer integrity, ketoconazole disrupts the bios ynthesis of essential membrane lipids in fungi, including phospholipids and triglycerides [5]

Parameter	Details
Drug Name	Ketoconazole
Chemical Name	1-acetyl-4-[4-[[2-(2,4-dichlorophenyl)-2-(1H-imidazol-1ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]piperazine
Chemical Structure	Imidazole ring attached to bisphenyl and dioxolane moieties
Molecular Formula	C26H28Cl2N4O4
Molecular Weight	531.44 g/mol
Solubility	Practically insoluble in water; soluble in ethanol, dimethylformamide
Mechanism of Action	Inhibits cytochrome P450 14α-demethylase → blocks ergosterol synthesis → disrupts fungal cell membrane
Pharmacological Class	Azole antifungal
Therapeutic Uses	Dermatophytosis, candidiasis, tinea versicolor, seborrheic dermatitis; also systemic fungal infections (restricted use)
Route of Administration	Oral, topical (cream, gel, shampoo)
Absorption	Poor and variable orally; improved in acidic medium
Bioavailability	Oral: ~70%; Topical: minimal systemic absorption
Protein Binding	~96%
Metabolism	Hepatic, primarily via CYP3A4
Half-Life	Oral: 2–8 hours; Topical: negligible systemic half-life
Excretion	Feces (~50%), urine (~13–16%)

Fig 1. Drug profile

Liposomal Gel

Liposomal gel systems are a novel hybrid drug delivery approach that combines the benefits of gel bases with the advantages of liposomal vesicles. By adding liposomes to a gel matrix, bioadhesion is improved, enabling the formulation to stick to the skin's surface more successfully. This improves drug retention and promotes long-lasting therapeutic activity Additionally, the gel foundation increases spreadability, which is crucial for treating superficial fungal infections since it allows for constant drug delivery and uniform distribution over the affected area.[6]

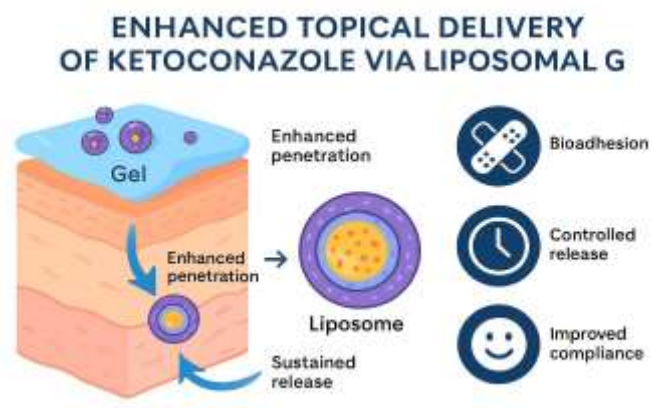

Fig 2.Mechanism Of Ketoconazole

Preparation Of liposomal gel

Using a rotary flash evaporator and the thin film hydration approach, multilamellar vesicles of KTZ were prepared . Soy lecithin (neutral charge), cholesterol (neutral charge), and tocopheryl acetate were used in the thin-film hydration process to create the liposomes. The impact of changing a number of process variables, including temperature, hydration time, vacuum, and rotational speed, on the development of a homogeneous thin lipid layer was assessed. [7]

Evaluation Of liposomal Gel

Physical examination The prepared gel formulations were inspected visually for Their color, homogeneity, consistency, and spreadability

pH

The pH values of 1% aqueous solutions of the prepared gels Were measured by a pH meter

Viscosity

Viscosity of prepared gels were measured by Brookfield DV-II+Pro Viscometer.

In-vitro drug release study

The rate at which the medicine is released from the carrier is a crucial factor in the assessment of drug delivery. Studies on skin penetration using liposomal formulations containing KTZ were conducted. The outcomes were contrasted with basic medication gel.

Skin retention Study

Study on skin retention In vitro skin deposition of KTZ was also computed since liposomal encapsulation of KTZ exhibits a drug reservoir effect in skin.

Conclusion

The present study indicates When compared to simple drug gel and plain drug cream, liposomal encapsulation demonstrated greater drug retention. The increased drug skin retention in the case of liposomal gel could be attributed to the formation of a drug reservoir effect in the skin as a result of other liposome components being deposited into the skin along with the drug, hence boosting the skin's ability to retain the drug.

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