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A Comprehensive Review on Nano-Emulgel Based Topical Delivery of Ketoconazole and Calotropis for Athlete's Foot

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ABSTRACT

Athlete's foot (tinea pedis) remains one of the most widespread fungal infections affecting people of all ages. While topical antifungal creams are commonly used, their effectiveness is often limited by poor solubility, insufficient skin penetration, and reduced retention at the infection site. Nano-emulgels an innovative blend of nanoemulsions and gel systems have emerged as a promising alternative to overcome these shortcomings. This review explores the potential of ketoconazole and Calotropis procera extract when formulated as a nano-emulgel, emphasizing their improved therapeutic performance, enhanced permeability, and patient-friendly profile.

Keywords : Nano-emulgel, Ketoconazole, Calotropis procera, Tinea pedis, Topical drug delivery, Antifungal therapy

1. INTRODUCTION

An infection may only occur when the body's defences are weakened or the number of pathogens reaches an unusually high density; otherwise, humans and the bacteria that surround them usually live in harmony. The agents that cause infections can cause the body to react, resulting in clinically noticeable signs and symptoms, but most infections remain unnoticed. This illness is referred to as an infectious sickness Ketoconazole is a well-studied antifungal agent known for its effectiveness against dermatophytes, yeasts, fungi can be classified as distinct organisms that are part of a different kingdom. Because of their larger cells than bacteria, membrane surrounding their nucleus, and molecular pathways that resemble those of plants and animals, fungi are categorised as eukaryotes. However, fungi nearly invariably have a stiff cell wall made of chitin products that encloses their plasma membrane, in contrast to mammalian cells. It is estimated that there are over 1.5 million fungal species in the world; however, over 69,000 species have been described over time.

2. Athlete's Foot

The most prevalent dermatophyte infection is athlete's foot, often known as tinea pedis. One the term "dermatophytes" describes a collection of three fungal genera: Microsporum, Epidermophyton, and Trichophyton that cause skin disorders in both humans and animals.

Figure 1: Athlete Foot

In 30 to 59% of instances, tinea pedis is linked to onychomycosis, a fungal nail infection that typically affects toenails more than fingernails. Males are more likely than females to have tinea pedis, and its prevalence typically increases with age. Men between the ages of 31 and 60 are more likely to have it. It is typically found Between the toes or in the interdigital areas of the foot, it is characterised by scaling, fissuring, and white, macerated skin. The toes that typically experience it are the third, fourth, and fifth. One or both feet may have minor erythema and scaling plaques on the soles, heels, and lateral aspect. are other possible manifestations of the disorder. Skin markings may appear white and disproportionate. There are usually no indications on the dorsal aspect of the foot. The risk of infection may be decreased by wearing protective footwear in public areas, as contact with infected scales on shower or pool floors might spread tinea pedis. Regular laundry washing would be a good preventative step to take because contaminated scales can be found on clothing. By producing warm, humid, macerating conditions that encourage the growth of dermatophytes, occlusive footwear contributes to the progression of disease. Therefore, after showering, bathing, or swimming, patients should try to reduce foot moisture by limiting the use of occlusive footwear and completely drying their feet and between their toes. When your feet or socks are moist, avoid putting them on. Wearing shoes that are spacious or aired to allow air to flow is another way to help prevent infection. You should also try to avoid sharing nail equipment, such as clippers and scissors, and shoes and towels.

3. Ketoconazole:

The well-known antifungal drug ketoconazole has strong biological action against a variety of fungi, including those that cause skin infections. Its mode of action involves inhibiting the formation of ergosterol, a crucial component of fungal cell membranes, and it is a member of the azole antifungal class. Ketoconazole's broad-spectrum action against filamentous fungi, yeasts, and dermatophytes prevents the growth and reproduction of these fungi, hence treating the infection. Ketoconazole is a useful therapy choice for fungal skin infections because of its biological activity against antifungal microorganisms.

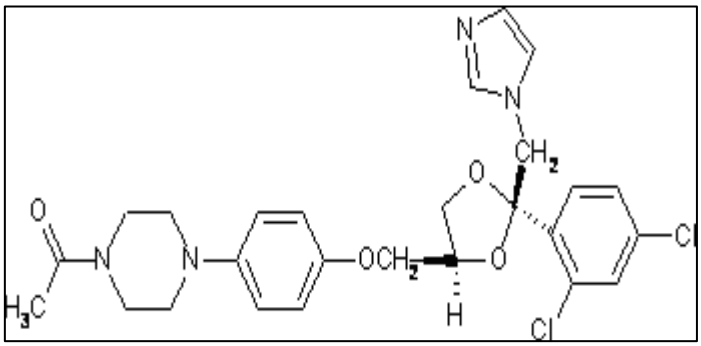

Figure 2: Structure of Ketoconazole

The topical dose form of ketoconazole has been utilised extensively. By applying ketoconazole topically rather than orally, one can prevent modifications in the way other medications are converted and lower the chance of liver harm. Class II of the Biopharmaceutical Classification System (BCS) includes ketoconazole. It is soluble in an acidic environment but insoluble in water.

Furthermore, it breaks down readily in the presence of light. Because of its poor solubility and difficulties entering diseased skin, ketoconazole poses obstacles despite its therapeutic promise. However, a possible remedy is provided by nanotechnology, more especially by drug delivery based on micro emulsions.

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4. Mechanism of Action

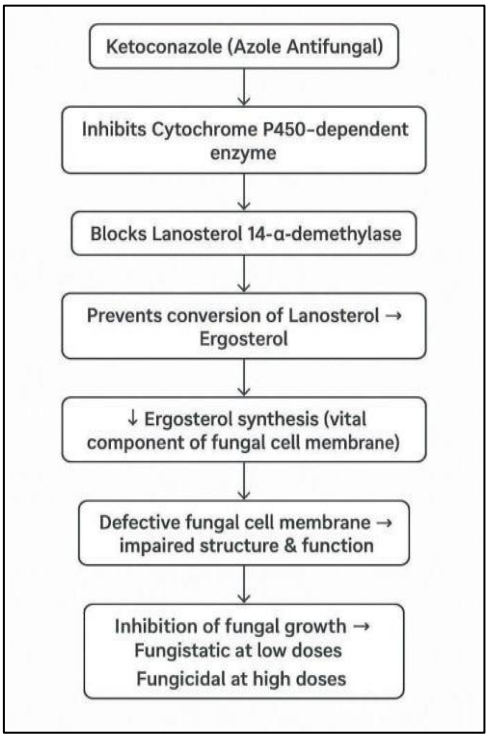

Figure 3: Mechanism of Action of Ketoconazole

5. Calotropis

Calotropis, also referred to as milkweed or Aak, is a member of the Apocynaceae family. Because various plant parts exude a white, sticky latex, plants in this genus are referred to as milkweeds. The two common species in the genus Calotropis, Calotropis procera (Rakta arka) and Calotropis gigantea (Sweata arka), are said to have essential pharmacological qualities species in the genus Calotropis, Calotropis procera (Rakta arka) and Calotropis gigantea (Sweata arka), are said to have essential pharmacological qualities for Ayurvedic toxicology and treatment. In the developing world, about 80% of people receive their primary medical care from herbal remedies. Plants are the source of many bioactive substances. Calotropis procera (C. procera) is one such plant that has been practically harvested because of its distinctive medicinal qualities. The Latin word "procera" means "leaves and stem cuticular wax," while the Greek word "Calotropis" means "beautiful," describing its flowers. It is a perennial shrub that belongs to the Apocynaceae family and is commonly referred to as aak, king's crown, rubber bush, sodom apple, and rubber tree. It is a softwood xerophytic, evergreen plant that grows all over the world, but particularly in arid and semi- arid tropical and subtropical regions of Asia and Africa.

TABLE 1: SCIENTIFIC CLASSIFICATION

Kingdom	- plantae	**Subclass**	- Asteridae
Subkingdom	- Tracheobionta	**Order**	- Gentianales
Superdivision	- Spermatophyta	**Family**	- Asclepiadoideae
Division	- Magnoliophyta	**Genus**	- Calotropis
Class	- Magnoliopsida	**Species**	- Calotropis procera

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Figure 4: ***Calotropis procera***

6. Nano-Emulgel

A dispersed system composed of small droplets uniformly distributed throughout an immiscible medium is called an emulsion. The term "macroemulsion," which refers to a droplet with a diameter of 1 to 100 µm, is also used to refer to conventional emulsions or colloids, which are emulsion kinds that are categorized based on their droplets. Generally speaking, it is unstable when water droplets or float with nearly the dispersion phase and medium phase and volatile when solid particles are absorbed on the surface. Microemulsion (droplet diameter between 10 and 100 nm) is an isotropic liquid system with more uniform size and better physicochemical properties, whereas nanoemulsion (droplet diameter 20–200 nm) is more stable. By incorporating the integrated nanoemulsion system into the hydrogel matrix, nanoemulgel a hydrogel based on nanoemulsion is created, improving skin penetration.

A gel base formation containing nanoemulsion is called nanoemulgel. In order to improve skin penetration, a nanoemulsion system is incorporated into a gel matrix. The drug's release from the inner phase to the outer phase and beyond is influenced by the drug reservoirs in this nanoemulgel mixture. When the skin while the skin remains intact, oil droplets are discharged from the nanoemulgel.

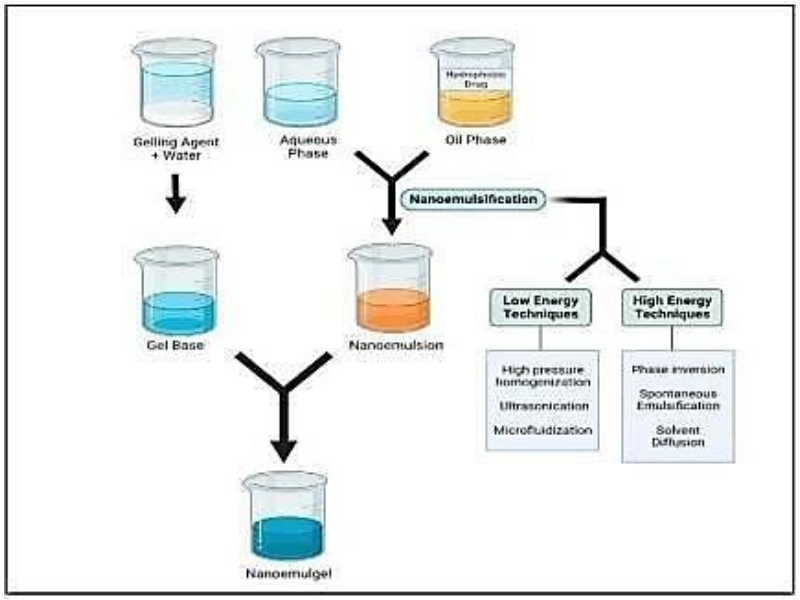

Figure 5: Nano-Emulgel

These precipitation drops deliver the drug to the intended site by penetrating the dermal capillaries in the skin. Because of its high drug solubilization in the oil phase and strong adhesion qualities, which produce a larger concentration gradient, the drug has a higher chance of penetrating the skin when applied in nanoemulsion-gel form.

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7. Benefits of Nano-Emulgel for Treating Athlete's Foot

• Improved solubility and stability of ketoconazole
• Enhanced penetration through the stratum corneum
• Sustained and controlled drug release
• Better spreadability and non-greasy feel
• Greater patient acceptance and convenience
• Increased antifungal potency due to nano-sized droplets
• Ability to combine synthetic and herbal agents in a single system

8. FORMULATION

The combination of two distinct systems, a gel system and a nanoemulsion, is known as nanoemulgel. Both water-in-oil and oil-in-water nanoemulsions can be used as drug delivery vehicles. It is composed of an oil phase, an aqueous phase, a surfactant, and occasionally a cosurfactant in both situations. This section provides an overview of the main, frequently used ingredients in nanoemulgel formulation.

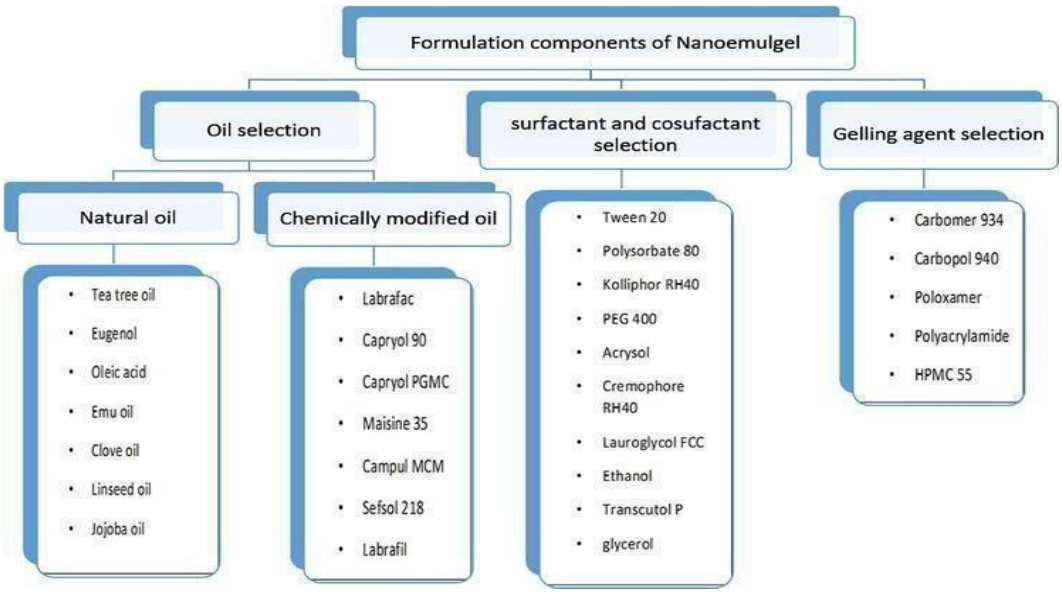

Figure 6: Formulation of Nano-Emeulgel

9. PREPARATION

Nano-emulgel, a non-equilibrium formulation of structured liquids, can be created with surfactant, energy, or both. They are made spontaneously by mixing the materials. This is achieved by either reducing the interfacial tension between the interfaces of the two immiscible phases or by increasing the energy contained in the biphasic system.

There are a number of published nano-emulgel preparation methods that vary depending on the sequence in which the oil and aqueous phase are mixed. According to Figure 3A, Lupi et al. (2014) separately dissolved the drug in the oil phase and the gelling agent in the water phase. An emulsion is made by adding the oil phase to the aqueous gel phase while stirring and then homogenising the mixture. The gelling ingredient in the emulsion changes from its sol form to gel by a number of procedures, including the addition of a complexing agent or the correct pH adjustment. .Dong et al. (2015) separated the total amount of water needed for the preparation into two sections, as shown in Figure 3B. The pre- emulsion is made with one half of the divided quantity, and the gel is made with the other half. These two ingredients are subsequently combined while being stirred. The emulsion and gel were prepared independently by Jeengar et al. (2016), and then they were combined in a proportion of 1:1 w/w. In order to prepare nano-emulgel, the oil (oil + drug) phase is added to the aqueous (water + gelling agent) phase in (A), and the nano-emulsion In (B), a gelling agent and water are combined to form an emulsion.

Two more categories can be distinguished in the development of nano-emulgel formulations based on the application of high-energy and low-energy emulsification processes.

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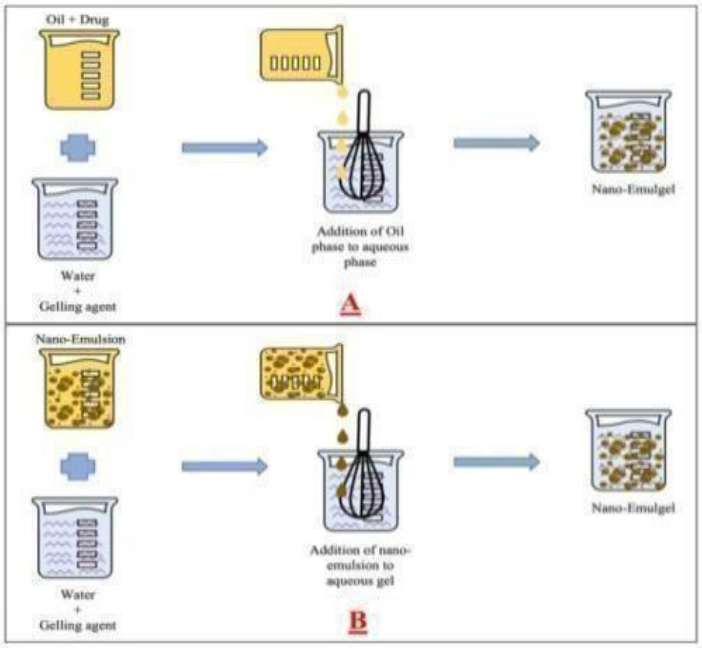

Figure 7: Preparation of Nano-Emulgel

10.Application of Nanoemulgel:

- Used as an anti-inflammatory agent
- used as anti-psoriatic
- used as an anti-fungal agent
- Used in alopecia.

11. Evaluation

1.physical examination

2.viscosity

3.drug content

4.spreadability

5. In -Vitro Diffusion Study

12. Conclusion

Nano-emulgel technology offers a modern, patient-friendly, and highly effective approach to treating fungal infections such as athlete's foot. By combining the proven antifungal strength of ketoconazole with the natural healing properties of Calotropis procera, this formulation addresses limitations seen in traditional topical therapies. Future research and clinical trials will further clarify its long-term benefits and potential for widespread use.

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