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A Comprehensive Review on Topical Treatment Strategies for Tinea Pedis: Formulation Approaches and Clinical Outcomes

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A B S T R A C T

Tinea pedis, also called athlete's foot, is among the commonest superficial mycoses, mainly attributed to dermatophytes belonging to the genus Trichophyton. This disease affects a considerable number of people worldwide, mostly those living in hot and humid climates, wearing occlusive shoes, and with low hygienic standards. The condition can occur in different forms, namely interdigital, moccasin, and vesiculobullous forms, presenting symptoms such as pruritus, scaling, erythema, and pain. The identification process involves a clinical assessment alongside laboratory procedures like KOH microscopy, fungal culture, and molecular diagnostics. While topical antifungal medications represent the principal form of treatment due to their targeted nature, low side effects, and enhanced safety profile relative to oral formulations, the traditional antifungal drugs available, like azoles and allylamines, can suffer from several shortcomings. These include skin penetration issues, extended therapy periods, and rising drug resistance. In response to these limitations, numerous improvements have been made concerning the development of novel drug delivery technologies, incorporating nanocarrier systems, hydrogels, in-situ gels, and film-forming systems, among others.However, challenges like recurrence, resistance, and patient non-compliance continue to be a problem. This article presents an extensive discussion about the pathophysiology, diagnosis, and treatment modalities of tinea pedis using topical therapy. Formulation development is also highlighted in this paper, together with recent breakthroughs and future directions for this common skin disease.

Keywords:- Tinea pedis, topical antifungal therapy, nanocarrier drug delivery, skin penetration enhancement, dermatophyte infections

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INTRODUCTION

The tinea pedis, or athlete's foot, is among the most common forms of fungal infections affecting the upper layers of skin, and it affects about 15 to 25% of people globally. The infection is more frequent in warm and humid tropical and sub-tropical areas. Athlete's foot occurs more often in adults than in children and is also common among males since the condition thrives in warm, sweaty conditions provided by occlusive clothing. Groups such as athletes, soldiers, and industrial workers are more likely to suffer from this condition because of the long hours they spend wearing tight and occlusive shoes that do not breathe well. Moreover, it is becoming increasingly common with urbanization and changes in lifestyles that encourage more physical exercise and sport-related activities.[1,2]

Dermatophyte fungi constitute the main etiological causes of tinea pedis, more specifically those belonging to the genera Trichophyton. Trichophyton rubrum, which is responsible for chronic and generalized forms, and Trichophytoninterdigitale, a synonym for T. mentagrophytes, are the two dermatophytes most frequently isolated in acute and inflammatory cases. [3,4] The fungi contain keratinase enzymes, which allow them to penetrate keratinous tissues like stratum corneum of skin, hair, and nails. Direct contact with affected persons and indirect transmission through environmental reservoirs like floor surfaces, towel, and shoes are common routes of infection. Resistance of these fungi to moisture and warmth in addition to their immune evasion characteristics make them capable of causing persistent and recurrent infections.[5]

Several predisposing conditions have been implicated in the causation and perpetuation of tinea pedis. Environmental variables that include high humidity levels, excessive perspiration, and wearing of occlusive footwear are known to enhance the occurrence. Poor personal hygiene practices, sharing of personal items, and using of common facilities, for example, swimming pools, gyms, and lockers contribute to disease propagation. Patients with a weakened immune system, patients suffering from diabetes mellitus, and those with peripheral vascular disease have been shown to be more vulnerable to developing serious infection.[10] Tinea pedis may present itself in a variety of ways, which include interdigital, moccasin, and vesiculobullous forms. These types of lesions are characterized by specific manifestations that range from itchiness, peeling, fissures, and inflammation among others. The infection has been largely regarded as a trivial disease; however, failure to treat it may result in complications that involve the onset of bacterial infection, cellulitis, and even infections of other areas like the nail bed.[11]

Pathophysiology and Clinical Presentation

The tinea pedis pathogenesis starts from adhesion of dermatophyte fungi, particularly those of the Trichophyton genus, to keratinized layers of the epidermis. They secrete enzymes that act on keratin, including keratinases, lipases, and proteases, leading to keratinolysis and subsequent fungal penetration of the stratum corneum. In general, the causative microorganisms will continue growing within the uppermost layers of the skin without extending their growth beyond these layers in the absence of underlying complications for immunocompetent patients. Environmental factors that favor fungal growth, such as warmth, humidity, and occlusion, are known to contribute to the persistence of tinea pedis. Immune function plays an essential role in influencing the severity of the infection. Failure of immune mechanisms to respond to infection leads to a prolonged infection while, in some cases, it can contribute to infection-related inflammation. Furthermore, dermatophytes may employ mechanisms of immune evasion such as antigen masking.[6,7]

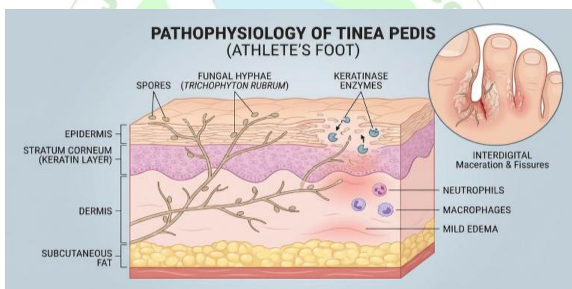

Figure 1: Pathophysiology of tinea pedis

There are various types of tinea pedis which have different pathological changes and etiological agents. The first type is interdigital which occurs commonly in between fourth and fifth toes and it is manifested through maceration, scaling, and fissures because of moisture accumulation in this area. The second type is known as moccasin type, which is mostly caused by chronic tinea pedis caused by Trichophyton rubrum. It is manifested through hyperkeratosis and scaling over the entire sole, heel, and sides of feet in a "moccasin distribution" [8]. This type is difficult to treat and chronic in nature. The third type is vesiculobullous which is caused by Trichophytoninterdigitale. It is inflammatory in nature and is characterized by the development of vesicles or bullae on the bottom surface and instep of the foot. [9]

The presentation of tinea pedis can range from one patient to another according to the type and extent of the infection but includes mainly itchiness [pruritus], a burning feeling, and pain in the infected areas. Symptoms start off with mild erythema and scaling on the involved skin surfaces, especially interdigitally. With continued progression, these lesions could be complicated by maceration, fissures, and an unpleasant odor due to secondary infections. For chronic conditions, such as moccasin tinea pedis, there may be the development of thick, scaly, dry skin [hyperkeratosis] involving the soles and the lateral surfaces of the foot. In vesiculobullous tinea pedis, the lesion is characterized by the presence of fluid-filled blistering that could result in pain and inflammatory reactions. Other complications associated with the condition include secondary infections that can worsen redness, swelling, and purulent discharge from the sores. There could also be a spread of the infection to the toenails [onychomycosis][12,13].

Diagnosis

Tinea pedis clinical diagnosis is mainly based on the symptoms and physical signs of the condition, together with a comprehensive patient history. Physical examination usually presents various skin lesions, including scales, redness, maceration, cracking, and occasionally vesicles or bullae development, which depend on the clinical types of the infection. The most common body areas prone to infection include the interdigital spaces, particularly between the fourth and fifth toes. Other factors that predispose patients to tinea pedis infection include excessive sweating, use of occlusive shoes, and contact with communal settings like gyms and swimming pools. While the diagnosis can be made effectively from clinical presentations in easy cases, there are some cases where it may pose difficulties because of similarity with other dermatological diseases.[10,13]

Confirmatory laboratory testing is key in making the diagnosis of tinea pedis. Potassium hydroxide [KOH] preparation is an efficient test that takes a short while to conduct and requires little expenditure. This method involves taking scrapes from the skin lesion and mixing it with potassium hydroxide, which dissolves keratin, thus allowing visualization of fungal elements, such as hyphae, using a microscope. Fungal culture is the preferred gold standard for species differentiation and involves putting a sample onto a selective growth medium, such as Sabouraud dextrose agar; unfortunately, it is a slow process since results can take many weeks. Recently, molecular diagnostic methods, such as the polymerase chain reaction [PCR], have become highly sensitive and specific approaches in detecting dermatophyte DNA and hence identifying fungi. Although PCR is fast and reliable, its main limitation lies in the fact that it is expensive to do and may not be available in all settings.[14,15]

A differential diagnosis of tinea pedis is necessary because of the clinical appearance of the condition that makes it similar to many other skin disorders. The most common diseases that mimic the clinical appearance of tinea pedis include eczema [in particular contact dermatitis], psoriasis, candidiasis, and erythrasma[a bacterium-caused infection]. For example, eczema presents itself as a condition accompanied by itching and scaling but usually follows allergic reactions. Psoriasis is a disease involving clearly defined patches with silvery scales. Candidiasis includes wet and macerated lesions but is usually diagnosed among immunocompromised patients and affects the groin, axillae, and intergluteal fold in addition to the foot. Erythrasma, which is a bacterial infection caused by Corynebacterium minutissimum, can look like interdigital tinea pedis, but it can be distinguished with the help of Wood's lamp test demonstrating coral red fluorescence.[16,17]

Rationale for Topical Therapy

Topical therapy is often regarded as the first-line treatment option for the vast majority of tinea pedis infections owing to its good safety and local nature of action. Contrary to the systemically administered antifungals, which are associated with side effects such as hepatotoxicity and gastrointestinal disorders, topical drugs are applied directly onto the affected areas and hence do not penetrate into the system, significantly decreasing the possibility of any adverse reactions. This approach is beneficial for patients with additional health problems or under the simultaneous therapy with other drugs since there is minimal interaction between topical medicines and other compounds and organs. Furthermore, topical formulations are usually easy to apply, increasing patients' adherence. Another significant advantage of this kind of treatment is that it is economical and does not require regular monitoring.[17,18]

One of the advantages of using topical medication is that topical drug delivery will help deliver the drug directly to the infected keratinized tissues. Localized drug delivery provides increased concentration of the drug at the site of infection in comparison to systemic delivery because of poor vascularization of the stratum corneum. Modern topicals include components that increase drug absorption and retention from topical drugs. In particular, for example, the use of penetration enhancers, lipids as drug delivery vehicles, and novel drug delivery systems like liposomes, nanoemulsions, and hydrogels are used to improve drug delivery into the skin. Such a strategy will not only increase the effectiveness of the anti-fungal treatment but also decrease the number of applications and total course of treatment. Moreover, localization of delivery leads to a low level of systemic absorption; hence, there is reduced risk of adverse reactions associated with systemic toxicity.[19]

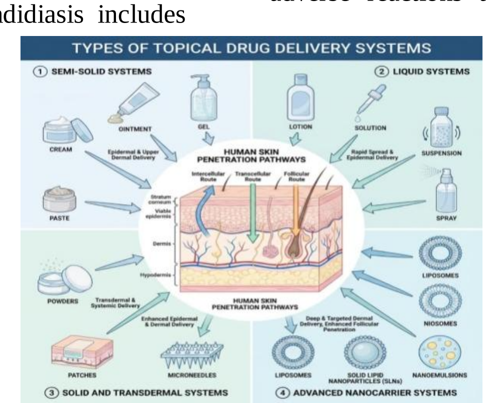

Figure 2: Types of topical delivery systems

However, although oral antifungal agents are efficacious when treating severe or difficult-to-treat cases of tinea pedis, there are numerous downsides to their application. Systemic antifungals such as terbinafine, itraconazole, and fluconazole pose a risk of adverse events like hepatotoxicity, gastrointestinal symptoms, skin reactions, and, in rare instances, serious systemic effects. Systemic antifungals, furthermore, may interact adversely with other drugs due to their capacity to induce changes in pharmacokinetics and drug metabolism in patients undergoing long-term treatment of chronic disorders. Another downside to taking oral antifungals is that they necessitate precise dosage schedules and in certain cases liver function tests, thereby posing obstacles for patients' medication adherence.[19] This risk becomes even greater for the vulnerable populations, including elderly patients, immunocompromised people, and individuals with liver or kidney pathologies. Lastly, systemic therapy may not always be appropriate in cases of localized tinea pedis infections, as it results in unnecessary exposure to medication where a topical antifungal treatment would suffice.[18,20]

Conventional Topical Antifungal Agents

The topical antifungal drugs commonly prescribed for tinea pedis can be categorized into three main classes: azoles, allylamines, and miscellaneous compounds, according to their chemistry and biological effects. Azoles, comprising both imidazoles like clotrimazole, miconazole, and ketoconazole, and triazoles like econazole, are some of the most frequently prescribed drugs due to their wide range of antifungal activity against dermatophytes, yeast fungi, and mold fungi. Allylamines, consisting of terbinafine and naftifine, are potent fungicidal drugs that are highly effective against dermatophytes and are favored due to their relatively short treatment periods and rapid effectiveness. Benzylamines, like butenafine, ciclopirox[hydroxypyridone], and tolnaftate[thiocarbamate] belong to other drug classes with varying antifungal activities that may be prescribed as alternatives or adjuncts to other treatments. [21,22]

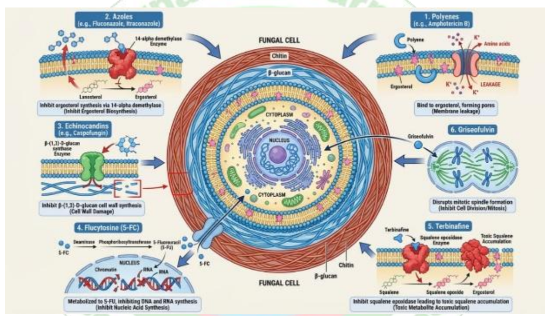

Figure 3: Mechanism of antifungal drug action

Mechanism of action of antifungals applied topically is mainly through the interference with the structure and integrity of the cell wall and inhibition of important biosynthetic pathways. Azole compounds act through the inhibition of lanosterol 14α-demethylase which interferes with the biosynthesis of ergosterol, an important component of the fungal cell membrane. Deficiency in ergosterol increases permeability of the cell membrane. Allylamine compounds inhibit squalene epoxidase enzyme involved in the formation of ergosterol and lead to toxic accumulation of squalene in the fungi cells. Unlike azoles which inhibit ergosterol formation allylamine compounds lead to accumulation of squalene in the fungal cells which is highly toxic. Ciclopirox is one antifungal agent whose mode of action is by interfering with the enzymes responsible for catalyzing reactions necessary for the growth and proliferation of the fungi. [21,23]

Table 1: Classification of Topical Antifungal Agents

Class	Sub-class	Examples	Mechanism of Action
Azoles	Imidazoles	Clotrimazole, Miconazole, Ketoconazole, Econazole	Inhibit ergosterol synthesis by blocking cytochrome P450 enzyme
	Triazoles	Fluconazole, Itraconazole	Inhibit ergosterol biosynthesis
Allylamines	—	Terbinafine, Naftifine, Butenafine	Inhibit squalene epoxidase → ergosterol depletion
Polyenes	—	Nystatin, Amphotericin B	Bind to ergosterol → increase membrane permeability
Echinocandins	—	Caspofungin, Micafungin	Inhibit β-[1,3]-D-glucan synthesis [cell wall]
Hydroxypyridones	—	Ciclopirox	Disrupt cellular transport and membrane integrity
Thiocarbamates	—	Tolnaftate	Inhibit ergosterol synthesis
Antimetabolites	—	Flucytosine	Interferes with DNA/RNA synthesis
Others	Fatty acids	Undecylenic acid	Alters membrane permeability
Newer Agents	—	Efinaconazole, Tavaborole	Inhibit fungal growth via novel mechanisms

Even though they are effective, topical antifungal treatments suffer from certain drawbacks that might affect the effectiveness of the treatment process. One of these drawbacks relates to antifungal resistance, which might emerge as a result of excessive and improper use of azole-based treatments, leading to decreased susceptibility to the drug in question. Moreover, the ability of topical antifungal medications to diffuse through the stratum corneum layer and achieve appropriate concentrations in the affected area might also be hindered by such factors as poor drug formulation, excessive removal of the medication, and others. Another issue is related to patient adherence; because patients are usually expected to continue using the treatment for long periods of time without experiencing significant results, they might discontinue its use. Other issues include local irritations, burning, and even allergies, which may also lead to non-adherence to the therapy regimen.[24,25]

Formulation Approaches

Topical dosage forms continue to be the mainstay of treatment in tinea pedis owing to their simplicity, accessibility, and familiarity to the patients. The most frequently used dosage form is creams, which provide an ideal balance between oil and water phases, making it easy to dissolve drugs and apply them to moist or weeping lesions. Gels are either aqueous or hydroalcoholic and they offer non-greasy formulation, fast absorption, and improved acceptability by the patients when applied in a humid environment. [25]Ointments are greasy in nature and they provide a good contact time for drug delivery while at the same time providing moisture to the horny layer, increasing the rate of drug delivery; their main disadvantage is that they can reduce patient acceptability because of their greasy nature. Sprays and powders are more advantageous in the treatment of large lesions or difficult-to-reach areas as well as ensuring dryness in the interdigital space, limiting fungal growth.[26]

Several advanced drug delivery systems have been formulated to solve the problems associated with conventional topical formulations. For example, liposomes are drug carriers composed of phospholipids. The system is known to allow for better deposition of the active compound in the skin layer since it is capable of transporting lipophilic and hydrophilic compounds. However, unlike liposomes, niosomes are vesicles formed from non-ionic surfactants. In comparison to liposomes, niosomes are less expensive, stable, and more permeable with an extended period of drug release. Another advanced system that has been formulated includes solid lipid nanoparticles [SLNs]. This system creates a solid lipid matrix and hence allows for better drug stabilization, controlled release, and skin occlusion, thus facilitating skin hydration and penetration. Nanoemulsions have also been developed. The system has smaller droplets and higher surface areas; therefore, the system facilitates better solubilization and deeper penetration of antifungal compounds through the stratum corneum.[27-29]

Thanks to the recent innovations in the field of topical delivery of drugs, several systems that exhibit enhanced therapeutic efficacy and compliance have been developed. Hydrogels are 3D water-retaining hydrophilic polymeric networks that provide a cooling and soothing effect on the skin, as well as a controlled release of drugs. These systems are appropriate for use with inflamed or irritated skin. In situ gels are liquid formulations that are transformed into gels under physiological stimuli, like changes in temperature, pH, or ionic strength. As a result, these systems are easily applied to the treatment area and can stay there for a long period of time[30]. Film forming systems are an innovation in topical drug delivery that involves liquid formulations being converted into an adhesive film following the evaporation of the solvent. With such preparations, it is possible to ensure enhanced retention of drugs, reduced losses of medications due to washing, sweating, and fewer applications. [32,31]

Penetration Enhancement Strategies

Chemical penetration enhancers have been extensively used in topical anti-fungals for increasing drug delivery through the stratum corneum, which acts as the major barrier to the transdermal absorption of pharmaceutical products. Chemical enhancers increase drug diffusion across the skin barrier by modifying its structure via processes such as alteration of the lipid structure of skin barrier, denaturing of proteins in skin and increasing drug solubility in skin. The most common chemical enhancers that have been used include alcohols [ethanol, isopropanol], fatty acids [oleic acid], surfactants, terpenes, and DMSO[33]. These enhancers promote drug delivery either through increased skin fluidity through alterations in intercellular lipids or through interactions with keratin. In antifungal therapy, chemical enhancers have shown great benefit due to the poor solubility of many drugs and their inability to reach greater depths of epidermis. However, their use needs to be optimized because excessive amounts of chemical enhancers can cause skin irritation and other undesirable effects on skin barrier.[34,35]

Physical enhancement methods provide another technique that does not target any physiological changes in the body to help improve drug absorption in the skin by providing temporary disruption of the stratum corneum barrier function. Iontophoresis is a drug delivery process where a mild electric current is introduced to transport the drug molecules across the skin through the process of electrorepulsion and electroosmosis. Microneedles [solid, coated, dissolving, and hydrogels] provide an avenue through which drug delivery is achieved through the creation of microchannels in the skin that do not touch nerve endings, thus facilitating painless drug administration. The creation of microchannels improves the permeation process and enhances sustained drug delivery, especially for antifungal drugs. In tinea pedis infections, microneedle drug delivery techniques are promising, as they can effectively deliver drugs even in thickened and hyperkeratotic skin, as seen in moccasin type infections.[36]

Nano-carrier systems play an important role in the improvement of the topical application of antifungal agents through increasing the drug solubility, stability, and penetration properties. The use of nanocarriers such as liposomes, niosomes, solid lipid nanoparticles, nanostructured lipid carriers, and polymeric nanoparticles allows interacting with the skin at the nano-level. This interaction is achieved due to their small size and increased surface area that increases the possibility of penetrating intercellular lipid pathways, even hair follicles in some situations. This property allows nanocarriers to be considered as drug depots for prolonged and controlled release. Nanocarriers also help in protecting drugs from degradation and decreasing local irritation through controlled release. In the treatment of tinea pedis, nano-carriers proved to increase the therapeutic activity against the causative dermatophytes by ensuring prolonged therapeutic drug levels in infected skin areas.[37,38]

Evaluation of Topical Formulations

Evaluation of physicochemical characteristics plays a crucial role in the preparation of antifungal formulations. Appearance, color, homogeneity, consistency, and lack of phase separation are some of the vital factors that point towards the homogeneity of the formulation. The pH value of the formulation is crucial as the formulation must have a pH value close to the physiological pH range [4.5–6.5]. Evaluation of viscosity and rheology of the formulation can provide information about the flow characteristics of the formulation and its drug release rate. Spreadability and extrudability of the formulation are important in determining the ease of administration. Uniformity of drug content is another essential factor that determines whether the API is uniformly distributed throughout the formulation. Apart from these, other physicochemical properties like particle size, zeta potential [for nanoformulations], and moisture content can also be evaluated.[39,40]

The release and permeation studies are crucial in quantifying the extent of drug release from topical dosage forms and the ability to penetrate through the skin barrier. The release study involves the use of diffusion cells. The Franz diffusion cell is one such example. The device comprises two chambers with an appropriate membrane between the two chambers. The dosage form is placed in one chamber [donor chamber], while the drug is collected in another chamber. The amount of the drug in another chamber can be used to determine the parameters of drug release. In permeation studies, excised skin [animal or human skin] can be used to quantify the permeation of the drug through the stratum corneum and deeper parts of the skin. There are several parameters that can be evaluated during permeation studies. Some of them include the cumulative drug permeation, flux, permeability coefficient, and lag time.[41,42]

Testing for antifungal activity is essential in validating the effectiveness of the product in dealing with the dermatophytes that cause tinea pedis. Methods that can be used include those that are microbiological in nature, such as the agar diffusion technique [zones of inhibition] and the broth dilution technique [minimum inhibitory concentration – MIC], and the time-kill technique. These methods are useful in establishing the effectiveness of the product relative to marketed and standard products. The process of assessing the stability of the formulation is equally important, since stability ensures that the physical, chemical, and microbiological characteristics of the formulation are maintained through time. Stability testing is done under various environments, which may include various temperatures and humidity conditions based on regulations. Some of the parameters that are analyzed during stability testing include drug content, pH value, viscosity, and appearance of the formulation.[43,44]

Clinical Outcomes and Challenges

The effectiveness of topical antifungal agents for the treatment of tinea pedis is high, especially in mild to moderate cases, with success rates varying between 60% and 90%, depending on the specific drug family, preparation, and length of therapy. Allylamines like terbinafine usually show better effectiveness and faster relief than azoles due to their fungicidal effects, whereas azoles offer wide-spectrum activity and effectiveness against mixed infections. Treatment success depends on various aspects, such as the severity and nature of the infection, patient cooperation with treatment, and proper administration. The use of shorter courses of highly effective drugs is associated with higher patient compliance and greater success rates. On the other hand, chronic forms of the disease or those characterized by hyperkeratosis, such as moccasin-type tinea pedis, can be treated more successfully with long-term therapy or in combination. Hence, the choice of the proper preparation and therapy duration is critical for successful treatment.[45,46]

Table 2: Summary of Recent Clinical Studies on Topical Treatment of Tinea Pedis

Author [Year]	Study Design	Drug/Formulation	Sample Size	Duration	Key Findings
Gupta et al. [2022]	Randomized controlled trial	Luliconazole 1% cream	120	2 weeks	High mycological cure rate [>85%] with good tolerability
Elewski et al. [2021]	Multicenter clinical trial	Efinaconazole topical solution	98	4 weeks	Significant improvement in clinical symptoms and fungal clearance
Kircik[2021]	Comparative study	Terbinafine vs Clotrimazole cream	150	2–4 weeks	Terbinafine showed faster symptom relief and higher cure rates
Del Rosso [2022]	Observational study	Ketoconazole 2% cream	85	3 weeks	Effective in mild to moderate cases with minimal side effects
Verma et al. [2022]	Clinical study	Sertaconazole cream	75	3 weeks	Demonstrated anti-inflammatory and antifungal dual action
Nenoff et al. [2021]	Prospective study	Ciclopirox olamine cream	60	4 weeks	Broad-spectrum activity with good patient compliance
Singh et al. [2023]	Randomized trial	Nanoemulsion-based terbinafine gel	90	2 weeks	Enhanced penetration and improved efficacy compared to conventional gel
Sharma et al. [2022]	Comparative clinical study	Liposomal ketoconazole gel	70	3 weeks	Improved skin retention and reduced dosing frequency
Patel et al. [2023]	Clinical evaluation	Niosomalitraconazole gel	65	2–3 weeks	Sustained drug release and better therapeutic outcomes
Kumar et al. [2024]	Pilot clinical study	Hydrogel-based luliconazole	50	2 weeks	Improved hydration and faster healing of lesions
Ahmed et al. [2022]	Clinical trial	Combination [terbinafine + salicylic acid]	80	3 weeks	Enhanced efficacy in hyperkeratotic [moccasin type] infections
Zhang et al. [2023]	Randomized study	SLN-based antifungal formulation	60	2 weeks	Superior drug delivery and reduced recurrence rates

Topical antifungals are typically safe to use and produce only a few side effects due to their limited systemic absorption. Some local reactions include skin irritation, burning, redness, or itching, but these effects are temporary and do not interfere with the ongoing therapy process. Because of their good safety profile, topical medications are more favorable for prolonged use and for certain populations, such as elderly people and individuals with additional medical conditions. Patient compliance is another important aspect that impacts treatment effectiveness, and non-adherence can result in ineffective treatment and disease reoccurrence. Several factors can affect patient compliance, including convenience, formulation cosmesis, frequency, and duration of therapy. Novel formulations and dosage regimens that provide sustained drug delivery can help enhance compliance rates. In addition, patient education concerning proper hygiene and treatment adherence is also vital for the desired outcomes.[47]

However, despite the availability of topical antifungal agents, there are various limitations that still affect the ability to successfully manage the disease. One of these problems is recurrence of the disease due to inadequate treatment, reinfection of the disease or survival of fungal spores in shoes and their environment. Drug resistance is another emerging problem that results from the prolonged use of antifungal medications, mainly azoles, making them ineffective in treating the disease. Poor permeation of drugs into the skin due to its hyperkeratotic nature, especially in cases of moccasin-type tinea pedis, is a limiting factor when it comes to drug treatment. This is made even more difficult by the presence of sweat and constant washing which may wash away some of the medication on the feet.[48]

Recent Advances and Future Perspectives

Innovative methods of enhancing the effectiveness of topical antifungal treatment through nanotechnology have shown promise by addressing the shortcomings associated with current preparations. Delivery mechanisms including liposomes, niosomes, SLNs, NLCs, and nanoemulsions are capable of improving the dissolution properties, stability, and specificity in delivering the medication deep into the layers of the infected skin. The high surface-to-volume ratio of these nanoparticles allows them to penetrate further into the stratum corneum and deposit in the epidermis and hair follicles where the medicine is stored for sustained release. Moreover, these nanoparticles can help minimize irritation and minimize system-wide effects by regulating the release rate of the drug. Research studies have confirmed that the application of nanomedicines leads to better outcomes in terms of antifungal effectiveness and quicker resolution than conventional medications. Another major advantage of using nanotechnology for delivery purposes is the ability to incorporate several drugs into the formula.[49,50]

Combination therapy has proved to be a highly useful technique to boost the efficiency of the treatment for tinea pedis by dealing with the various components of the disease together. The technique usually makes use of a variety of anti-fungal medications along with anti-inflammatory drugs, keratolytics, or antibiotics. Using anti-fungal medicines in combination with corticosteroids, for instance, can help reduce the inflammation and erythema of the skin in addition to the symptoms of itchiness. Additionally, using keratolytic drugs like salicylic acid or urea can assist in shedding off hyperkeratosis skin, thus improving the absorption of other medications into the deeper layers of the skin. Combination therapy is known to decrease the chances of resistance to medications through the use of drugs with distinct modes of action.[51,53]

Herbal preparations are becoming more popular in treating fungi due to their natural origin, safe nature, and broad spectrum of antimicrobial activity. Different herbal preparations such as tea tree oil, neem, aloe vera, and eucalyptus oil are known to possess antifungal properties against various dermatophytes. Natural products contain different active chemicals that prevent the growth of fungi by disrupting their cell membrane functions. The use of herbal preparations can be done through cream and gel forms or even in nanotechnology-based forms. Their benefits include their low toxicity levels and higher patient compliance. However, their usage is associated with certain limitations such as their inconsistency due to their variable nature, lack of standardization, and less clinical evidence on their effectiveness.[52]

There is an increasing trend of using herbal preparations to treat fungi because of the advantage of being from nature, safe, and having broad antimicrobial activities. Herbal preparations like tea tree oil, neem, aloe vera, and eucalyptus oils are some that are found to have antifungal activity against several dermatophytes. Natural products have different kinds of active ingredients that inhibit the growth of fungi by disrupting their cell membrane functions. The application of herbal preparation can be applied through creams and gels, as well as in nanotechnology formulations. There are advantages of using herbal preparation such as low toxicity and increased patient compliance. However, there are certain limitations that may occur like the variability of herbal preparation, which makes it inconsistent.[55,54]

CONCLUSION

Tinea pedis still is one of the most frequent superficial fungal infections, presenting major challenges from a medical perspective as well as a public health point of view because of its high rate of recurrence, chronicity, and high infectivity. The paper emphasizes that topical antifungal treatments are still considered to be a key aspect in the treatment of tinea pedis and have certain advantages when compared to oral medications due to better targeting of the affected area, lower toxicity levels, and greater patient safety. Standard antifungal agents show high efficiency, but there are some problems with their use. The emergence of novel formulation approaches such as those involving nanocarriers, hydrogels, in situ gelling, and film formation, among others, has greatly advanced drug delivery methods by improving permeation and retention as well as providing controlled release. Not only are the results of this enhanced drug delivery positive, but it has also helped improve patient adherence to treatment regimes. Moreover, techniques for overcoming the challenges of hyperkeratotic infections have been developed. Even with these improvements, problems like recurrence, drug resistance, and compliance issues remain, underscoring the importance of further investigation and improvement of topical treatments. Research efforts moving forward should concentrate on creating new antifungal drugs, intelligent drug delivery systems, and natural products based on scientific evidence. In general, the combination of pharmaceutical science with personalized medicine could be highly advantageous for the successful management of tinea pedis.

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