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Garlic Plant (Allium sativum) in Ethnomedicine for the Treatment of Tinea Pedis (Athlete's Foot): A Systematic Literature Review of Antifungal Activity Against Trichophyton mentagrophytes

Muh. Faisal[1], Dea Numayang Sari[2], Yuli Fitriana[3], Della Hazma Aulya Permata[4], Destira Arlita[5], Devana Adinda Setiawan[6]
[1,2,3,4,5,6] Universitas Muhammadiyah Mataram, Indonesia

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A B S T R A C T

Skin fungal infections such as tinea pedis are among the most common dermatological diseases and are often caused by dermatophytes, especially *Trichophyton mentagrophytes*. The use of medicinal plants in ethnomedicine, including garlic (*Allium sativum*), has emerged as a potential therapeutic alternative due to their bioactive compounds, which possess antimicrobial activity. This study aims to analyse the potential of garlic as an antifungal agent for the treatment of tinea pedis using a systematic literature review. The research method employed a systematic literature review of scientific articles from Google Scholar, PubMed, and ScienceDirect databases, published between 2014 and 2024. Articles were selected based on inclusion criteria covering studies related to the antifungal activity of *Allium sativum* against dermatophytes, particularly *Trichophyton mentagrophytes*. The review found that garlic contains major bioactive compounds, such as allicin and ajoene, which exhibit antifungal activity by inhibiting fungal growth and damaging the cell membranes of dermatophytes. Therefore, garlic has the potential to be developed as an alternative herbal therapy for the treatment of tinea pedis. These findings provide a scientific basis for the development of natural-based antifungal products and encourage further research regarding their formulation and clinical effectiveness.

1. INTRODUCTION

The use of medicinal plants in ethnomedicinal practices is an important part of traditional healthcare systems in communities around the world. Ethnomedicine refers to local knowledge developed and passed down through generations about the use of natural resources, particularly plants, for therapeutic and disease-prevention purposes. Medicinal plants are known to contain various secondary metabolites, such as flavonoids, alkaloids, saponins, and essential oils, which possess biological activities against various pathogenic microorganisms. In recent decades, research on ethnomedicinal plants has continued to grow due to the potential of their bioactive compounds to be developed into modern natural-based medicines. One of the plants widely used in traditional medicine is garlic (*Allium sativum*), which is known to possess broad antimicrobial activity against pathogenic bacteria, viruses, and fungi (Bayan et al., 2014; El-Sabre Batiha et al., 2020; Sharifi-Rad et al., 2019).

One common fungal skin disease is tinea pedis, also known as athlete's foot. This is a dermatophyte infection that primarily affects the keratin layer of the feet and commonly occurs in the interdigital spaces between the toes. The major causative agents of this infection are dermatophyte fungi from the genus *Trichophyton*, particularly *Trichophyton mentagrophytes* and *Trichophyton rubrum*. This infection is characterised by itching, redness, cracked skin, and skin peeling. The high prevalence of tinea pedis is often associated with humid environmental conditions, prolonged use of closed footwear, and poor foot hygiene. Therefore, the development of alternative therapies based on natural ingredients, including ethnomedicinal plants with antifungal activity, has become an attractive approach for the treatment of skin diseases (Aala et al., 2014; Gupta et al., 2020; Havlickova et al., 2008).

*Corresponding author
E-mail addresses: devanaadindas159@gmail.com

Ethnomedicine is the study of traditional community knowledge in utilising medicinal plants as the primary theoretical basis for the development of alternative therapies for skin diseases. The use of various plant species in traditional practices is supported by the presence of secondary metabolites such as alkaloids, flavonoids, and essential oils, which play crucial roles in anti-inflammatory and antimicrobial mechanisms (Kaneria et al., 2017). For example, research on *Chassalia kolly* reported quantitative data showing a total flavonoid content of 30.29 ± 2.18 μg QE/mg DM and very strong antioxidant activity (IC50 = 0.05 μg/μL), demonstrating greater efficacy than aspirin in membrane stabilisation tests (Alain et al., 2021). Furthermore, testing of the alkaloid harmaline, isolated from *Ophiorrhiza nicobarica*, in Balb/C rat models demonstrated significant inhibition of HSV-1 viral replication by interfering with early viral gene transcription, making it a safe and non-toxic candidate for antiviral skin therapy (Pal et al., 2014). Therefore, the exploration of bioactive compounds, such as essential oils containing thymol and carvacrol, is highly important as an innovative solution for managing dermatological disorders and overcoming future challenges of drug resistance (Dominguez et al., 2021).

Tinea pedis is a chronic dermatophyte fungal infection of the feet that affects the keratinised tissues between the toes and on the soles, clinically characterised by pruritus (itching), scaly skin, and burning sensations (Nowicka & Nawrot, 2021). Epidemiologically, the global prevalence of this superficial fungal infection is estimated at 20–25% of the general population, with incidence rates in certain communities reported to reach nearly 70% (Sahoo & Mahajan, 2016). *Trichophyton mentagrophytes* has been identified as one of the major pathogens causing functional and cosmetic morbidity, with complications frequently involving nail involvement (onychomycosis) and significantly prolonging treatment duration (Nowicka & Nawrot, 2021). The health impact of this condition presents a major challenge to the medical field due to the limitations of current antifungal therapies, which are restricted to only four major drug classes, along with increasing reports of drug resistance and the lack of consistent international clinical guidelines for chronic case management (Sahoo & Mahajan, 2016). This phenomenon underscores the urgency of developing alternative antifungal agents to address therapeutic failure and the high recurrence rate among patients with dermatophytosis (Nowicka & Nawrot, 2021).

Based on various research findings, garlic has been shown to possess significant antifungal activity against various dermatophyte species that cause skin infections. However, existing studies are still scattered across experimental studies and pharmacological reviews discussing garlic's general antimicrobial activity. Until now, there have been limited studies that specifically integrate these findings in the form of a Systematic Literature Review focusing on the antifungal activity of garlic against *Trichophyton mentagrophytes*, the main causative agent of tinea pedis. Therefore, this study aims to conduct a Systematic Literature Review of various studies discussing the antifungal activity of garlic (*Allium sativum*) against *Trichophyton mentagrophytes* in the treatment of tinea pedis. The results of this review are expected to provide a comprehensive overview of garlic's potential as an ethnomedicine-based herbal therapy for skin diseases and to serve as a scientific basis for the development of future natural antifungal drugs.

2. METHOD

This study employed a Systematic Literature Review (SLR) with a qualitative-descriptive approach to identify, evaluate, and synthesise scientific findings on the antifungal activity of garlic (*Allium sativum*) against *Trichophyton mentagrophytes*, the causative agent of tinea pedis. The objective of this study was to systematically analyse scientific evidence concerning the potential antifungal activity of garlic against *Trichophyton mentagrophytes* based on relevant research publications. The data sources in this study were obtained from various scientific databases and academic literature search engines, namely Google Scholar, Elicit, Scite.ai, Scispace, Directory of Open Access Journals (DOAJ), and Scopus, which provide research articles published in reputable scientific journals. The SLR method was selected because it can provide a comprehensive and systematic synthesis of knowledge by following the stages of identification, selection, quality evaluation, and analysis of relevant literature (Shaffril et al., 2021; Kitchenham & Madeyski, 2022).

The literature collection process in this study used predetermined inclusion and exclusion criteria to ensure the relevance and quality of the data sources. The inclusion criteria in this study included: (1) research articles discussing the antifungal activity of *Allium sativum* against dermatophyte fungi, particularly *Trichophyton mentagrophytes*; (2) articles published in scientific journals or academic proceedings; (3) articles available in full text; and (4) articles published from 2016 to 2025. Meanwhile, the exclusion criteria included: (1) articles that did not directly discuss the antifungal activity of garlic against dermatophytes; (2) articles in the form of opinions, editorials, or non-scientific reports; (3) publications not available in full text; and (4) duplicate articles appearing across multiple databases. The literature search process was conducted using combinations of keywords such as "*Allium sativum*," "garlic extract," "antifungal activity," "*Trichophyton mentagrophytes*," and "tinea pedis," which were combined using Boolean operators (AND, OR) to obtain more specific and relevant search results (Butler et al., 2016; Booth, 2016).

Literature selection was carried out gradually through identification, screening, eligibility assessment, and article inclusion, following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines to ensure transparency and adherence to systematic review procedures. The initial stage involved identifying all articles obtained from the databases, followed by screening based on titles and abstracts to assess their relevance to the research topic. Articles meeting the criteria were then analysed in depth through full-text reading. The data from each article were subsequently analysed using thematic analysis and qualitative synthesis to identify research findings on the mechanisms and effectiveness of Allium sativum's antifungal activity against *Trichophyton mentagrophytes*. To ensure validity and reliability, the literature selection and analysis processes were conducted systematically, considering the methodological quality of the articles and the consistency of findings across studies (Pati & Lorusso, 2018; García-Peñalvo, 2022).

3. RESULT AND DISCUSSION

- **Potential of Garlic (*Allium sativum*) in Ethnomedicine for the Treatment of Skin Infections**

Interpretation of global ethnomedicinal practices indicates that *Allium sativum* (garlic) serves as a major pillar in traditional medicine across various cultures, ranging from communities in the Dominican Republic to traditional healers in Algeria, who consistently utilise it to treat skin infections and accelerate tissue regeneration (Batista et al., 2011; Belkebir et al., 2024). In-depth pharmacological evaluations confirm that its broad-spectrum antimicrobial activity originates from organosulfur compounds, particularly allicin, which acts synergistically by inhibiting pathogen proliferation through disruption of protein synthesis and the integrity of bacterial and fungal cell membranes (González et al., 2017). Synthetically, highly detailed laboratory evidence demonstrates that a 75% ethanol extract gel formulation of garlic was capable of producing an inhibition zone diameter of 20.6 mm against *Staphylococcus aureus*, a value statistically categorised as "very strong" antibacterial activity and proving garlic's potential as an alternative topical antibiotic (Dewi et al., 2020). Furthermore, in vivo testing on acute wound models in rats revealed significant healing mechanisms through stimulation of Vascular Endothelial Growth Factor (VEGF) expression and faster collagen deposition compared to controls, along with high fungicidal effectiveness against dermatophytes causing skin infections such as *Trichophyton rubrum* (Shibly et al., 2016; González et al., 2017). However, despite its efficacy, evaluative concerns remain regarding the risk of contact dermatitis in sensitive skin and the highly unstable nature of allicin, which is easily degraded. Therefore, dose standardisation and formulation technologies capable of maintaining the stability of the active compound are essential prerequisites for safe and effective clinical application (González et al., 2017).

Interpretation of the phytochemical profile of *Allium sativum* demonstrates that the antifungal efficacy of this plant originates from the diversity of organosulfur compounds, particularly allicin, ajoene, and diallyl sulfide, each of which contributes uniquely to the inhibition of skin pathogens. Evaluation of their molecular mechanisms reveals that these compounds act simultaneously by inhibiting essential enzymes containing thiol (-SH) groups and disrupting fungal cell membrane integrity by inhibiting ergosterol biosynthesis (Aala et al., 2014). Synthetically, highly detailed laboratory evidence confirms the remarkable potential of allicin against dermatophytes such as *Trichophyton rubrum*, with very low Minimum Inhibitory Concentration (MIC) values ranging from 0.097 to 1.56 μg/mL, and the ability to produce hyphal growth inhibition percentages exceeding 90% with statistical significance values of $p < 0.05$ (Aala et al., 2012; Yamada & Azuma, 1977). Although allicin is often regarded as the most active component, stability analyses indicate that this compound is highly susceptible to degradation. In contrast, ajoene—its transformation product—shows superior stability profiles and often stronger antifungal potential at lower doses in the treatment of chronic fungal infections (Yamada & Azuma, 1977). Additionally, the role of diallyl sulfide in suppressing fungal viability further broadens the biological protective spectrum of garlic, thereby integrating all these organosulfur compounds into a comprehensive and effective antifungal defence system to overcome the clinical challenges of dermatophytosis (Aala et al., 2010).

The integration of ethnomedicinal evidence and phytochemical analysis demonstrates that *Allium sativum* possesses significant therapeutic potential as a natural antifungal agent in the treatment of skin infections, including dermatophytosis. Various traditional medicinal practices around the world have long utilised garlic to treat skin infections, and modern scientific findings increasingly support its use by identifying active organosulfur compounds, such as allicin, ajoene, and diallyl sulfide. These compounds act synergistically by inhibiting important enzymes containing thiol groups and disrupting ergosterol biosynthesis in fungal cell membranes, thereby effectively inhibiting the growth and proliferation of dermatophytes. Experimentally, various laboratory studies have shown that allicin can produce very low Minimum Inhibitory Concentration (MIC) values against pathogenic fungi, accompanied by high levels of hyphal growth inhibition, while ajoene provides advantages in terms of chemical stability and effectiveness in chronic infections. In addition to its antifungal activity, garlic extract also supports tissue healing processes by increasing growth factor expression and accelerating collagen deposition. Nevertheless, the clinical use of this plant still requires attention to potential side effects, such as contact dermatitis in individuals with sensitive skin, as well as challenges related to the stability of its active compounds. Therefore, the development of standardised formulations is an important step to ensure the safety and effectiveness of garlic-based therapy in modern medical practice.

- **Antifungal Activity of *Allium sativum* Against Dermatophytes Causing Tinea Pedis**

Interpretation of the pharmacological profile of allicin indicates that its efficacy as a broad-spectrum antifungal agent against dermatophytes is driven by its ability to perform thiol-disulfide exchange reactions with sulfhydryl (-SH) groups in various essential enzymes, which directly halts fungal cellular metabolism (Yamada & Azuma, 1977). Evaluation of its mechanism of action reveals that allicin specifically inhibits the ergosterol biosynthesis pathway, resulting in structural instability of the cell membrane and cytoplasmic leakage (Aala et al., 2014). Synthetically, highly detailed laboratory evidence from electron microscopy (SEM and TEM) provides visual confirmation of collapsed hyphal structures, cell wall deformation, and damage to internal organelles in *Trichophyton rubrum* following exposure to allicin (Aala et al., 2013). Quantitative data support this potential, with very low Minimum Inhibitory Concentration (MIC) values ranging from 0.097 to 1.56 μg/mL, which significantly ($p < 0.05$) reduced ergosterol levels and drastically inhibited fungal growth (Aala et al., 2012; Yamada & Azuma, 1977). Through synergistic interactions between thiol enzyme inhibition and membrane integrity disruption, allicin is a highly effective bioactive molecule that disrupts dermatophyte fungal homeostasis, making it a strong candidate for natural-based antifungal therapy capable of addressing the clinical challenges of chronic skin infections (Aala et al., 2010).

Interpretation of the in vitro effectiveness of *Allium sativum* demonstrates that garlic extract possesses significant antifungal potential against *Trichophyton mentagrophytes*. However, its efficacy remains substantially lower than that of standard antifungal agents such as ketoconazole (Aala et al., 2012). Evaluation of research data reveals that although garlic actively inhibits dermatophyte growth, there is high variability in results, influenced by extraction methods and testing protocols (Ayat Elahi Mousavi et al., 2009). Synthetically, detailed laboratory evidence confirms that garlic essential oil and aqueous extract are capable of inhibiting *T. mentagrophytes* with Minimum Inhibitory Concentration (MIC) values of 0.25 mg/mL and 0.5 mg/mL, respectively, and a Minimum Fungicidal Concentration (MFC) of approximately 1.0 mg/mL (Lora Cahuas et al., 2015; Hailu et al., 2017). In comparison, ketoconazole demonstrated much greater efficacy, with MIC50 and MIC90 values of 1 μg/mL and 2.5 μg/mL, respectively, indicating that the standard agent works at concentrations thousands of times lower than those of garlic extract (Akwuma, 2023). Although some studies reported dose-dependency at high concentrations (10–20 mg/mL), others found no significant differences across concentrations ($p > 0.05$), suggesting that inhibitory responses are highly dependent on the formulation used (Ayat Elahi Mousavi et al., 2009). Therefore, the antifungal profile of *Allium sativum* against *T. mentagrophytes* has proven effective at the milligram scale; however, dose standardisation and extraction methods remain major challenges in achieving consistent therapeutic potential (Lora Cahuas et al., 2015).

The integration of molecular mechanism analysis of allicin with in vitro testing against *Trichophyton mentagrophytes* demonstrates that the antifungal potential of *Allium sativum* is influenced not only by the presence of active compounds but also by the extract form and concentration used. Pharmacologically, allicin acts by catalysing thiol-disulfide exchange reactions with sulfhydryl groups on essential fungal enzymes, thereby disrupting ergosterol biosynthesis and destabilising cell membranes, triggering cytoplasmic leakage and cell death. Electron microscopy evidence even demonstrates cell wall deformation, collapse of hyphal structures, and damage to internal organelles in dermatophytes following allicin exposure. These findings are reinforced by the very low Minimum Inhibitory Concentration (MIC) values of allicin against certain dermatophytes. However, when applied in the form of whole garlic extract against *Trichophyton mentagrophytes*, its effectiveness generally requires higher concentrations, with MIC values of approximately 0.5 mg/mL for aqueous extract and 0.25 mg/mL for essential oil, as well as a Minimum Fungicidal Concentration (MFC) value of approximately 1.0 mg/mL. Compared to synthetic antifungals such as ketoconazole, which act at microgram concentrations, the activity of garlic extract is relatively lower, suggesting that the biological efficacy of its active compounds may decrease due to variability in extraction methods, compound stability, and phytochemical composition across preparations. Therefore, although allicin has been shown to possess a very strong antifungal mechanism at the molecular level, optimisation of extraction methods, formulation, and dose standardisation is crucial to ensure the consistency of *Allium* *sativum's* effectiveness as an alternative therapy for the treatment of dermatophyte infections such as *T. mentagrophytes*.

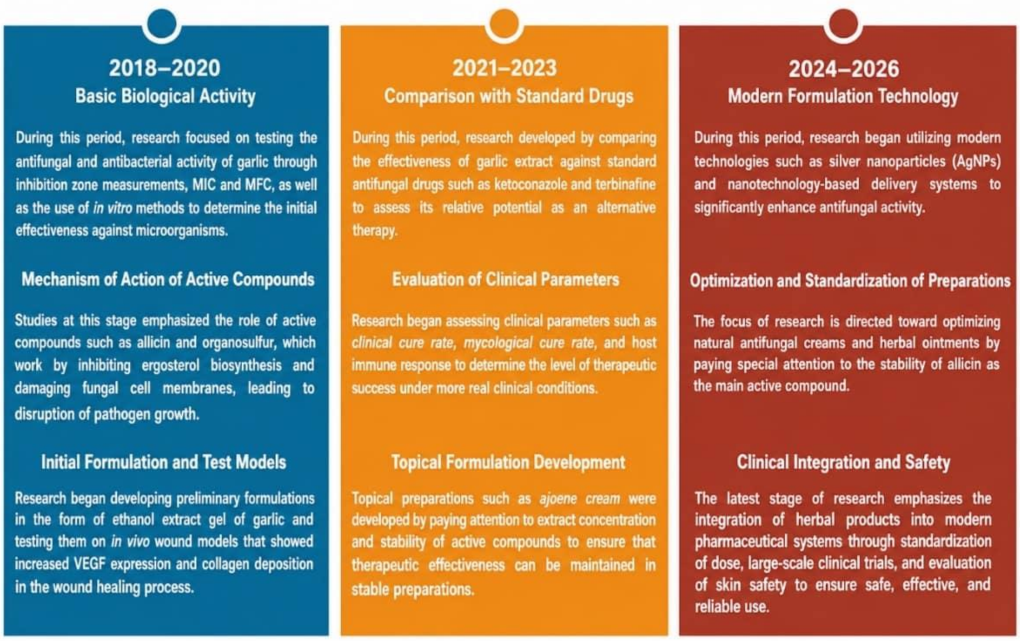
- **Development of *Allium sativum* as an Herbal Therapy for Tinea Pedis**

Allium sativum is considered suitable for development into natural antifungal ointments and creams, and for integration into plant-based pharmaceutical products, as both in vitro and clinical evidence demonstrate significant antifungal activity and favourable acceptance of topical formulations. The following discussion summarises key findings supporting such development. For example, an ethanol ointment formulation containing 15% garlic extract produced an average inhibition zone of 10.45 mm compared to 14.3833 mm for miconazole ointment (Fahdi & Sari, 2022). In a study involving dermatophyte isolates from 60 children with tinea capitis, methanolic garlic extract demonstrated inhibition zones ranging from 12.93 to 25.87 mm, indicating broad-spectrum activity against various dermatophyte species (Otegwu et al., 2019). Comparable clinical evidence for garlic-derived pharmaceutical compounds was observed with 0.4% ajoene cream, which achieved clinical and mycological cure in 27 out of 34 patients (79%) within 7 days, with all patients cured after an additional 7 days of treatment (Ledezma et al., 1996). Furthermore, a randomised controlled trial involving 60 subjects reported cure rates of 77% with 0.6% ajoene compared with 75% with 1% terbinafine after 30 days of evaluation (Ledezma et al., 2011). In a comparative tinea pedis study, among 70 recruited subjects (47 available for final evaluation), the 60-day mycological cure rates were 72% for 0.6% ajoene, 100% for 1% ajoene, and 94% for 1% terbinafine, further emphasising the pharmaceutical potential of garlic-derived formulations (Ledezma et al., 2000). Mechanistic and activity-enhancing data were also identified in vitro, where *Allium sativum* extract exhibited a Minimum Inhibitory Concentration (MIC) of approximately 0.04 mg/mL. In comparison, silver nanoparticles (AgNPs) demonstrated 94% inhibition at 0.08 mg/mL. The combination of garlic extract with AgNPs enhanced antimycotic activity even at fractional MIC levels, which is highly relevant for the development of high-performance topical preparations (Robles Martínez et al., 2019). Additionally, studies on onychomycosis reported an MIC value of 120 mg/mL, causing ultrastructural damage to fungal pathogens, along with antioxidant and anti-inflammatory effects that may support tissue healing, thereby supporting the concept of formulations combining antifungal activity with inflammation modulation (Pârvu et al., 2019). Additional in vitro evidence showed that aqueous garlic extract inhibited the growth of *Trichophyton mentagrophytes* by up to 100% at 10% and suppressed keratinase activity by approximately 91% at 8%, supporting the use of measured concentrations in topical ointment or cream formulations (Abd AL Khaliq, 2011). Overall, evidence from subject numbers (e.g., n=34; n=60; n=47 final evaluation), inhibition zones (10.45 mm; 12.93–25.87 mm), MIC values (0.04 mg/mL; 120 mg/mL), and clinical cure rates (79% within 7 days; up to 100% for 1% ajoene) strongly supports the feasibility of further developing herbal ointments, natural antifungal creams, and plant-based pharmaceutical products derived from *Allium sativum*, while recommending further studies on formulation standardization, skin toxicity testing, and controlled clinical trials to establish optimal dosage.

The development of herbal therapies for tinea pedis offers promising opportunities for clinical effectiveness but also faces challenges related to data standardisation and long-term safety. Clinical studies have shown significant potential, including the use of 1% ajoene (an organosulfur compound derived from garlic), which achieved a 100% mycological cure rate within 60 days in the final evaluation of 47 subjects, surpassing the effectiveness of 1% terbinafine at 94% (Ledezma et al., 2000). In addition, a randomised controlled trial involving 158 subjects using tea tree oil solutions at concentrations of 25% and 50% reported clinical cure rates of 72% and 68%, respectively, significantly outperforming the placebo group, which achieved only 39%. However, safety concerns emerged as contact dermatitis in 3.8% of patients (Satchell et al., 2002). Meanwhile, a study involving 101 subjects using *Solanum chrysotrichum* extract demonstrated clinical improvement rates of up to 96.08%, statistically comparable to 2% ketoconazole (91.67%; $p > 0.38$) with good tolerability (Herrera-Arellano et al., 2003). Despite these opportunities, the need for further large-scale clinical trials, more comprehensive reporting of p-values, and more systematic monitoring of side effects remains a major challenge in integrating herbal products into mainstream pharmaceutical therapy standards.

Based on available research, *Allium sativum* shows strong potential for development into natural topical antifungal formulations, such as herbal ointments and plant-based pharmaceutical creams, for the treatment of fungal skin infections, including tinea pedis. In vitro studies have shown consistent antifungal activity; for example, an ointment formulation containing 15% garlic extract produced an average inhibition zone of 10.45 mm. Although this result was still lower than miconazole at 14.38 mm, it nevertheless demonstrated biologically relevant effectiveness as a candidate herbal therapy (Fahdi & Sari, 2022). Broad-spectrum activity was also reported in a study involving 60 dermatophyte isolates from patients with tinea capitis, in which methanolic garlic extract produced inhibition zones ranging from 12.93 to 25.87 mm, indicating inhibitory activity against various dermatophyte species (Otegwu et al., 2019). In addition, clinical evidence from the use of ajoene, one of garlic's active compounds, demonstrated high cure rates in dermatophyte infections, such as 79% clinical cure within 7 days among 34 patients and cure rates up to 77% at a concentration of 0.6%, relatively comparable to 1% terbinafine (Ledezma et al., 1996; Ledezma et al., 2011).

Nevertheless, literature evaluation reveals variations in extraction methods, active compound concentrations, and research designs, indicating the need for formulation standardisation, skin toxicity evaluation, and larger-scale clinical trials to ensure long-term effectiveness and safety in clinical application. Synthetically, numerous studies demonstrate that the development of topical pharmaceutical products based on *Allium sativum* has a strong scientific foundation, both pharmacological and clinical. Experimental data indicate that garlic extract possesses an MIC value of approximately 0.04 mg/mL against dermatophytes. In comparison, combinations with silver nanoparticles (AgNPs) can enhance antifungal activity, reaching 94% inhibition at 0.08 mg/mL, indicating potential synergy in modern antifungal formulations (Robles-Martínez et al., 2019). Moreover, studies on pathogens causing onychomycosis reported MIC values around 120 mg/mL, which cause ultrastructural damage to fungal cells and provide additional antioxidant and anti-inflammatory effects that may support tissue healing (Pârvu et al., 2019). Other studies also demonstrated that aqueous garlic extract could inhibit the growth of *Trichophyton mentagrophytes* by up to 100% at 10% and suppress keratinase enzyme activity by approximately 91% at 8%, which is an important factor in dermatophyte pathogenesis (Abd AL Khaliq, 2011). Overall, the combination of evidence from inhibition zones (10.45–25.87 mm), MIC values (0.04–120 mg/mL), and clinical cure rates reaching up to 100% with 1% ajoene formulations demonstrates that *Allium sativum* possesses substantial potential for development into herbal ointments, natural antifungal creams, and plant-based pharmaceutical products. However, further studies are still needed to establish formulation standards, determine optimal dosing, assess active compound stability, and evaluate long-term safety in the treatment of fungal skin infections.



The diagram illustrates the progressive development of research on the use of *Allium sativum* as an antifungal agent from 2018 to 2026. During the 2018–2020 period, research focused on basic biological activities through antifungal and antibacterial testing, as well as investigations into the mechanisms of action of active compounds such as allicin, which plays a role in inhibiting ergosterol biosynthesis and damaging fungal cell membranes, accompanied by the development of initial formulations and in vivo testing models. Subsequently, in the 2021–2023 period, research advanced toward the therapeutic validation stage through comparisons with standard antifungal drugs, evaluations of clinical parameters such as clinical cure rate and mycological cure rate, and the development of topical formulations that accounted for extract concentration and active compound stability. In the 2024–2026 period, the direction of research advanced further through the application of modern formulation technologies, such as silver nanoparticles and nanotechnology-based delivery systems, followed by the optimisation and standardisation of herbal preparations and the integration of products into modern pharmaceutical systems through large-scale clinical trials and safety evaluations. This progression demonstrates a transition from basic research to more comprehensive, standardised clinical applications.

4. CONCLUSION AND RECOMMENDATION

Based on the integration of various ethnomedicinal evidence, phytochemical analyses, and experimental and clinical studies, *Allium sativum* (garlic) shows strong potential as a natural antifungal agent for the treatment of dermatophyte skin infections, including *Trichophyton mentagrophytes* and *Trichophyton rubrum*. Garlic has long been utilised in traditional medicine to treat various skin infections, and modern studies have identified that its biological activity mainly originates from bioactive organosulfur compounds, including allicin, ajoene, diallyl sulfide, and diallyl disulfide. These compounds possess broad-spectrum antimicrobial activity and inhibit the growth of various pathogenic microorganisms, including dermatophyte fungi (Negri et al., 2014; Ojha et al., 2025).

Mechanistically, allicin, as the primary active component of garlic, acts through thiol-disulfide exchange reactions with sulfhydryl groups in essential fungal enzymes, resulting in disruption of fungal cellular metabolic functions. In addition, this compound can inhibit ergosterol biosynthesis, which is the main component of fungal cell membranes, thereby causing membrane instability, cytoplasmic leakage, and disturbances in hyphal growth. These structural damages have been confirmed by electron microscopy, which showed cell wall deformation, internal organelle damage, and hyphal collapse after exposure to allicin or garlic extract (Aala et al., 2014; Negri et al., 2014). Functionally, this mechanism is similar to several synthetic antifungal drugs that also target fungal ergosterol biosynthesis pathways (Davis, 2005; Chatterjee, 2023).

Various in vitro studies have demonstrated that garlic extract possesses significant antifungal activity against dermatophytes. Several studies reported that allicin can produce low Minimum Inhibitory Concentration (MIC) values and effectively inhibit dermatophyte hyphal growth, indicating strong pharmacological potential as a natural antifungal agent. In addition, allicin derivatives, such as ajoene, are known to offer greater chemical stability, making them more suitable for the development of topical formulations. Clinical studies have even shown that topical ajoene can achieve high cure rates in dermatophyte infections such as tinea pedis, with effectiveness in some cases comparable to that of synthetic antifungal drugs such as terbinafine (Ledezma & Apitz-Castro, 2006; Pintas & Lio, 2018).

In addition to its direct antifungal activity, garlic extract also possesses anti-inflammatory, antioxidant, and tissue-regenerative properties, which may help accelerate the healing of infected skin. Several studies have shown that bioactive compounds in garlic can enhance local immune responses and support wound healing by stimulating growth factors and collagen deposition. The combination of antifungal activity and tissue-healing effects makes *Allium sativum* a promising candidate for the development of natural-based topical pharmaceutical products, such as herbal ointments or antifungal creams (Negri et al., 2014; Borgohain, 2020).

However, the utilisation of garlic as an antifungal therapy still faces several scientific limitations. The biological activity of garlic extract may be influenced by extraction methods, concentrations of active compounds, the relatively low chemical stability of allicin, and variations in the phytochemical composition of plant materials. In addition, several studies indicate that whole garlic extract often requires higher concentrations than synthetic antifungals to produce similar inhibitory effects. Therefore, the development of garlic-based therapy requires standardisation of raw materials, extraction methods, and appropriate pharmaceutical formulations to ensure greater consistency in effectiveness and safe use in clinical practice.

In the context of future scientific development, further studies are necessary to optimise pharmaceutical formulation technologies that enhance the stability and bioavailability of active compounds such as allicin and ajoene, thereby maintaining their antifungal activity in topical preparations. Furthermore, controlled clinical trials involving larger sample sizes, as well as long-term dermatological safety evaluations, are also extremely important to ensure the effectiveness and safety of *Allium sativum* as an alternative therapy for the treatment of dermatophyte infections in humans.

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