Frontiers in Health Informatics
ISSN-Online: 2676-7104
2024; Vol 13: Issue 8
www.healthinformaticsjournal.com
Open Access

Nano Siddha medicine: A New Era in Dermatophytosis Treatment- a Review

Saravanasingh Karan Chand Mohan Singh[*1], A. Jayakalaiarasi [2], V. Gowri[3], Anbarasan Balasubramanian[4], V. Indumathy[5], D.A. Kumarakurubaran[6], C. Vimala[7], S.P. Kopperundevi[8], V. sathiya[9], A. Elavarasi[10]

1. Assistant Professor, Department of Maruthuvam, National Institute of Siddha, Ministry of AYUSH, Govt of India, Chennai-47

2. Associate professor, Department of forensic medicine and toxicology, Santhigiri siddha medical college and research organization, Trivandrum, kerala -695589

3. Professor, Department of Marunthiyal, Maria siddha medical college & hospital, Thiruvattar

4. Assistant Professor, Department of Maruthuvam, National Institute of Siddha, Ministry of AYUSH, Govt of India, Chennai-47

5. Assistant Professor, Department of Maruthuvam, Sri Sairam siddha medical College and research center, Sai leo Nagar, Poonthandam, West tambaram, Chennai - 600 064.

6. Associate Professor, Department of Udal Koorugal, National Institute of Siddha, Ministry of AYUSH, Govt of India

7. Associate professor, Department of Noi Anuga Vidhi Ozhukkam, Maria siddha medical college & hospital, Thiruvattar

8. Lecturer, Department of Aruvai Thol Maruthuvam, JSA Medical College for Siddha and Research Centre, Ulundurpet, Kallakurichi – 606104

9. Associate professor, Department of udal koorugal, JSA Medical College for Siddha and Research Centre, Ulundurpet, Kallakurichi – 606104

10. Associate professor, Department of Noi Anuga Vidhi Ozhukkam, National Institute of Siddha, Ministry of AYUSH, Govt of India, Chennai-47

*Corresponding author

Dr. K. Saravanasingh M.D (SIDDHA), Ph.D
Assistant professor,
Department of Maruthuvam,
National Institute of Siddha,
Chennai-47
E.Mail: k.saravanasingh@gmail.com

Cite this paper as: Saravanasingh Karan Chand Mohan Singh, A. Jayakalaiarasi , V. Gowri, Anbarasan Balasubramanian, V. Indumathy, D.A. Kumarakurubaran, C. Vimala, S.P. Kopperundevi, V. sathiya, A. Elavarasi (2024), Nano Siddha medicine: A New Era in Dermatophytosis Treatment- a Review. *Frontiers in Health Informatics*, *13(8) 4496-4503*

Abstract
Dermatophytosis, commonly known as ringworm, is a widespread fungal infection that affects the skin, hair, and nails and is caused by dermatophytes (Trichophyton, Microsporum, and Epidermophyton). Traditional treatments rely on topical and systemic antifungal medications, which, despite their efficacy, often have limitations, including side effects and incomplete resolution in some cases. The emergence of Siddha medicine, an ancient traditional healing system from South India, provides an alternative therapeutic approach, especially with the advent of nanoformulations. Nano Siddha medicine utilizes nanotechnology to enhance the delivery, bioavailability, and efficacy of herbal compounds with antifungal properties, such as turmeric (Curcuma longa) and neem (Azadirachta indica). These formulations provide targeted delivery to infected regions, enhanced penetration into the cutaneous layers, and reduced dosage, thereby minimizing adverse effects. Preliminary studies have demonstrated promising antifungal activity, although clinical validation is limited. This review explores the etiology, clinical presentation, and conventional treatments for dermatophytosis, while highlighting the role of nano-Siddha medicine as a novel therapeutic modality. This emphasizes the advantages of nanoformulations, including enhanced bioavailability, sustainability, and reduced side effects, while addressing the current limitations and the need for further research. Integrating traditional knowledge with modern science through nano-Siddha medicine has the potential to revolutionize dermatophytosis management and improve patient outcomes.

Introduction

Dermatophytosis is a common fungal infection caused by dermatophytes that affect the skin, hair, and nails. These infections require new treatment alternatives because of increasing resistance. Several studies have explored the use of natural extracts as potential antidermatophytic agents. The aqueous Azorean Black Tea (ABT) extract exhibited significant antidermatophytic activity against Trichophyton mentagrophytes, T. rubrum, and Microsporum canis, with fungicidal effects at relatively low concentrations (Fernandes et al., 2023). Similarly, the ethanolic extract of Withania chevalieri (WcCEE) demonstrated concentration-dependent fungicidal activity against dermatophytes, with potential synergistic effects when combined with terbinafine (Correia et al. 2023). Both extracts appeared to target the fungal cell wall, particularly β-1,3-glucan synthesis pathway. Interestingly, the p21-activated kinase (PAK) protein TrCla4 in T. rubrum was found to be crucial for mycelial growth and hyphal morphology, suggesting it as a potential therapeutic target for dermatophytosis (Ishii et al., 2023). Additionally, phenolic-rich extracts from various plant sources, including Olea europaea, Castanea sativa, Punica granatum, and Vitis vinifera, have been shown to significantly inhibit the growth of Trichophyton interdigitale and other pathogenic fungi (Lombardi et al., 2023). These studies highlight the potential of natural extracts and novel molecular targets for developing alternative treatments for dermatophytosis. The antidermatophytic, antioxidant, and anti-inflammatory properties of these extracts, combined with their low toxicity, make them promising candidates for pharmaceutical and dermocosmetic applications in the management of fungal skin infections.

This condition is prevalent worldwide and can affect individuals of all ages. The clinical manifestations of dermatophytosis vary depending on the site of infection and the specific species involved. The primary lesions typically include erythematous, scaly patches with a raised, advancing border (Pesqué et al., 2024). These infections can affect different parts of the body, including the skin, hair, and nails. Interestingly, recent research has highlighted the importance of accurate taxonomic delineation of etiologic agents responsible for dermatophytosis. A study in India revealed that the organism causing a recalcitrant dermatophytosis epidemic belongs to the "Indian ITS genotype," currently labeled as T. indotineae, a clonal offshoot of T. mentagrophytes (Rudramurthy et al., 2023). This finding emphasizes the role of specific species in determining the clinical course and severity of the infection. In conclusion, while the general clinical presentation of dermatophytosis involves erythematous, scaly lesions, the specific manifestations can vary

based on the anatomical site and the infecting species. The identification of T. indotineae as the causative agent in the Indian epidemic underscores the importance of accurate species identification in understanding and managing dermatophytosis outbreaks (Rudramurthy et al., 2023). Traditional treatment options include topical antifungals and systemic medications; however, there is growing interest in alternative therapies, including Siddha medicine, particularly its nano formulations. Traditional antifungal treatments face challenges due to increasing drug resistance and limited options, prompting interest in alternative therapies. Siddha medicine, an indigenous system, offers potential solutions through natural products and herbal formulations (Mandal et al., 2023).

The poly-herbal formulation Kabasura Kudineer from Siddha medicine was evaluated using computational approaches to identify potential inhibitors against SARS-CoV-2 targets. Top bioactive compounds like quercetin, gallic acid, and chrysoeriol showed promising binding affinities and stability against viral targets (Mandal et al., 2023). While this study focused on antiviral properties, it demonstrates the potential of Siddha formulations in addressing microbial infections.

In addition to Siddha medicine, other natural products have shown promise as antifungal agents. Plant-derived compounds like catechins enhanced the susceptibility of Candida glabrata to azole antifungals (Hervay et al., 2023). Essential oils, such as those from Lippia origanoides, demonstrated synergistic effects with fluconazole against resistant Candida tropicalis strains. Patchouli alcohol exhibited antifungal and antibiofilm activity against Candida albicans (Zhang et al., 2023).

These findings highlight the potential of traditional medicine systems and natural products as alternative or complementary therapies to conventional antifungal treatments. The integration of these approaches with modern drug development techniques may lead to more effective and less toxic antifungal strategies.

Etiology and Pathophysiology

Dermatophytosis is indeed primarily caused by fungi belonging to the genera Trichophyton, Microsporum, and Epidermophyton. However, recent molecular techniques have expanded our understanding of dermatophyte taxonomy. According to (Pérez-Rodríguez et al., 2023), dermatophytes are now classified into seven genera: Trichophyton, Microsporum, Epidermophyton, Nannizzia, Paraphyton, Lophophyton, and Arthroderma. Genotypic analysis of clinical isolates revealed that Trichophyton was the most prevalent genus (63.8%), followed by Nannizzia (25.5%), Arthroderma (9.6%), and Epidermophyton (1.1%) (Pérez-Rodríguez et al., 2023). Interestingly, the taxonomic delineation of dermatophytes is still debated, particularly in the context of the ongoing epidemic in India. Rudramurthy et al., 2023 discusses the controversy surrounding the designation of T. indotineae, which is considered a clonal offshoot of T. mentagrophytes. This study highlights the importance of multigene sequence analysis in accurately identifying dermatophyte species and understanding their evolutionary relationships. This updated classification system provides a more nuanced understanding of dermatophyte diversity and may have implications for diagnosis and treatment strategies.

Dermatophytes are fungi that invade keratinized tissues, leading to inflammation and characteristic erythematous lesions in dermatophytosis infections. While the papers provided do not directly discuss dermatophytes, we can draw some relevant insights from the information given about skin structure and inflammatory skin conditions: Keratinized tissues in the skin, such as the stratum corneum, provide an important barrier function. As described in the epidermis of amniotes like humans contains a corneous layer composed of various corneous proteins that contribute to its protective properties. Invasion of these keratinized layers by dermatophytes disrupts this barrier (Hassan Z *et al, 2023*). The inflammatory response to fungal invasion likely involves some similar mechanisms as seen in other inflammatory skin conditions. For example, (Nenciarini S *et al*, 2023) discusses how atopic dermatitis involves increased levels of inflammatory markers like IL-4, IL-13, and IgE, as well as infiltration of inflammatory cells like eosinophils. A similar inflammatory cascade may occur in dermatophyte infections (Nenciarini S *et al*, 2023). While not

specifically about dermatophytes, (Alibardi L*et al*, 2023) provides some general insights into fungal interactions with host tissues. It notes that fungal extracellular vesicles can play a role in pathogenicity and mediating interactions with the environment. Such mechanisms may be involved in how dermatophytes invade and interact with keratinized tissues (Alibardi L*et al*, 2023). Dermatophytes are not explicitly discussed, the papers provide context on skin structure, inflammatory processes, and fungal-host interactions that help explain how dermatophyte invasion of keratinized tissues can lead to characteristic inflammatory lesions. Further research, specifically on dermatophyte pathogenesis, would be needed to elucidate the exact mechanisms.

Fungal infections like ringworm, caused by dermatophytes, can indeed spread through direct contact and shared items such as towels. This transmission is facilitated by the fungi's ability to thrive in moist environments (Flores et al., 2023; Weerden et al., 2023). Plant defensins, such as Ppdef1, show promise as a novel treatment for fungal infections, including those affecting skin and nails. Ppdef1 demonstrates potent fungicidal activity against various human fungal pathogens, including dermatophytes like Trichophyton rubrum, a major cause of onychomycosis. Its ability to rapidly penetrate human nails makes it a promising candidate for topical treatments (Van Der Weerden et al., 2023). Similarly, extracts from Fomitopsis officinalis, particularly from the apical part, exhibit strong antimicrobial properties against dermatophytic species, with MIC values below 100 µg/mL (Flores et al., 2023). Interestingly, while not directly related to fungal infections, the use of antibacterial detergents in laundering towels can reduce the abundance of malodor-producing bacteria and attenuate microbial exchange (Lam et al., 2023). This finding highlights the importance of proper towel care in preventing the spread of microorganisms. Additionally, for individuals with compromised immune systems, such as cancer patients undergoing L-methioninase treatment, maintaining proper hygiene and avoiding potential sources of infection becomes even more crucial (İpek et al., 2023). Direct contact and shared items like towels can facilitate the spread of fungal infections, emerging treatments such as plant defensins and natural extracts show promise in combating these pathogens. Proper hygiene practices, including the use of antibacterial detergents for towels, can help mitigate the risk of transmission. The pathophysiology involves the ability of these fungi to produce keratinases, enzymes that degrade keratin, facilitating their invasion into the host's skin.

Clinical Presentation

Nano Siddha Medicines are a potential antifungal drug used to treat various forms of dermatophytosis, including tinea pedis (athlete's foot), tinea cruris (jock itch), and tinea corporis (red scaly rash on the skin) (Hussain et al., 2023). These conditions align with the clinical presentation of dermatophytosis mentioned in the question, which typically includes symptoms such as itching, redness, and scaling. The provided context does not directly address the diagnosis of dermatophytosis through clinical examination or laboratory tests like KOH microscopy or fungal culture, it does offer insights into the treatment of various forms of dermatophytosis using Nano Siddha Medicines are. The development of a precise analytical method for Nano Siddha Medicines quantification could contribute to more effective treatment strategies and monitoring of antifungal therapies for dermatophytosis.

Conventional Treatment Options

Conventional treatments for dermatophytosis, while effective, face challenges such as drug resistance and side effects, prompting research into alternative and complementary approaches. The aqueous Azorean Black Tea (ABT) extract has shown promising antidermatophytic activity against common dermatophytes like Trichophyton and Microsporum species. It demonstrated fungicidal effects at relatively low concentrations and exhibited an additive effect when combined with terbinafine. The extract's mechanism of action appears to target β-1,3-glucan synthesis in the fungal cell wall, suggesting its potential to enhance the efficacy of conventional topical treatments (Fernandes et al., 2023). Interestingly, novel drug delivery systems are being

explored to improve the efficacy of existing antifungals. For instance, miconazole-loaded microemulsions have shown enhanced skin permeation, drug deposition, and antifungal activity against Candida albicans compared to conventional creams (Phechkrajang et al., 2023). Similarly, buccal films loaded with both lidocaine and miconazole nitrate have been developed for treating oral candidiasis, offering controlled release of the antifungal agent and potentially reducing the frequency of applications (Tejada et al., 2023). In conclusion, while conventional antifungal treatments remain the mainstay for dermatophytosis, research is advancing on multiple fronts to address their limitations. Natural products like ABT extract, innovative drug delivery systems, and combination therapies are showing promise in enhancing treatment efficacy and potentially overcoming drug resistance. These developments may lead to more effective and patient-friendly treatment options for dermatophytosis in the future.

Siddha Medicine: An Overview

Siddha medicine, an ancient healing system from South India, aligns with the growing interest in natural and holistic approaches to healthcare. While the provided context does not specifically discuss Siddha medicine, it offers insights into related areas of herbal medicine and nanotechnology that are relevant to recent developments in Siddha practice.

Herbal medicine, which forms a core component of Siddha, has been shown to have numerous pharmacological activities and is often considered safer and more cost-effective than synthetic alternatives. However, herbal medicines face challenges such as low solubility, stability, and bioavailability. To address these issues, nanotechnology-based systems like nanohydrogels have been developed to enhance the delivery and efficacy of herbal compounds (Lestari et al., 2023). This aligns with the emerging interest in nano formulations within Siddha medicine. Interestingly, the integration of metallic elements with herbal compounds in nanoparticles and metal-organic frameworks has shown promise in reducing toxicity while increasing therapeutic effects (Tang et al., 2023). This synergistic approach could potentially be applied in Siddha medicine to enhance its traditional formulations. Siddha medicine was not explicitly mentioned in the provided context, the advancements in herbal medicine delivery systems and the combination of natural compounds with nanotechnology offer promising avenues for enhancing the efficacy of Siddha remedies. These developments could potentially bridge the gap between traditional Siddha practices and modern scientific approaches, leading to more effective and tailored treatments for patients.

Nano Siddha Medicine in Dermatophytosis

Gandhaga parpam, Nandhi Mezhugu, Vaan Mezhugu, Rasa Kenthi Mezhugu, and Parangi Pattai Choornam these Siddha drugs have been evaluated for their antifungal properties, particularly in treating candidiasis. They are traditional formulations used in Siddha medicine to combat fungal infections (Suresh B *et al,* 1994). Nano Siddha medicine employs nanoparticles to improve the delivery of therapeutic agents in treating dermatological conditions like dermatophytosis. These formulations can enhance the penetration of active ingredients into the skin layers, potentially increasing their antifungal activity while minimizing side effects. For instance, herbal extracts known for their antifungal properties can be encapsulated in nanoparticles for targeted delivery.

Efficacy of Nano Formulations

Several studies have explored natural sources for antifungal agents, including plants and invertebrates. For instance, extracts from mollusk species have shown inhibitory effects against Cryptococcus neoformans, impacting its virulence factors such as biofilm and capsule production (Gutierrez-Gongora et al., 2023). Similarly, Azorean Black Tea extract demonstrated antidermatophytic activity against common fungal pathogens like Trichophyton mentagrophytes and Trichophyton rubrum (Fernandes et al., 2023). Interestingly, some natural compounds have shown potential in combating drug-resistant fungal strains. For example, lecanoric acid, derived from the lichen Parmotrema austrosinense, exhibited significant antifungal

activity against tea fungal pathogens, outperforming some systemic and botanical fungicides (Rajendran et al., 2023). This aligns with the growing interest in natural compounds as alternatives to conventional antifungal treatments, especially in the face of increasing antimicrobial resistance. While the context does not specifically address nano formulations of Siddha medicine, it does highlight the potential of natural products in antifungal treatments. The studies suggest that plant-derived compounds and extracts can offer effective alternatives or complementary approaches to existing antifungal therapies, potentially with fewer side effects. This trend in research supports the exploration of traditional medicine systems, like Siddha, for novel antifungal formulations.

Advantages of Nano Siddha Medicine

1. Enhanced Bioavailability: Nanoparticles improve the solubility and absorption of herbal compounds.
2. Targeted Delivery: Nano formulations can deliver active ingredients directly to affected areas.
3. Reduced Side Effects: Lower dosages may lead to fewer adverse reactions compared to conventional treatments.
4. Sustainability: Utilizing natural resources aligns with sustainable healthcare practices.

Limitations and Future Directions

Despite promising results, research on nano Siddha medicine for dermatophytosis is still in its infancy. Most studies are limited to laboratory settings with few clinical trials validating efficacy in human subjects. Further systematic research involving larger populations is necessary to establish standardized protocols for integrating nano Siddha formulations into mainstream dermatological practice.

Conclusion

Dermatophytosis remains a significant public health concern due to its prevalence and impact on quality of life. While conventional treatments are effective, alternative approaches such as nano Siddha medicine offer exciting possibilities for enhancing therapeutic outcomes. Continued research into the efficacy and safety of these formulations could pave the way for innovative treatment strategies that harness traditional knowledge alongside modern scientific advancements.

Conflict of Interest

The authors declare no conflict of interest related to this review article.

References

1. Correia, E. E. M., Barros, L., Rodrigues, L., Pinela, J., Salgueiro, L., Fernandes, C., Gonçalves, T., Figueirinha, A., & Calhelha, R. C. (2023). The Chemical Profile, and Antidermatophytic, Anti-Inflammatory, Antioxidant and Antitumor Activities of Withania chevalieri A.E. Gonç. Ethanolic Extract. *Plants*, *12*(13), 2502. https://doi.org/10.3390/plants12132502
2. Fernandes, C., Calheiros, D., Salgueiro, L., Lenha-Silva, A. F., Correia, E., Gonçalves, T., Sousa-Baptista, J., & Figueirinha, A. (2023). Azorean Black Tea (Camellia sinensis) Antidermatophytic and Fungicidal Properties. *Molecules*, *28*(23), 7775. https://doi.org/10.3390/molecules28237775
3. Ishii, M., Matsumoto, Y., Ohata, S., Katada, T., Uga, H., & Yamada, T. (2023). TrCla4 promotes actin polymerization at the hyphal tip and mycelial growth in Trichophyton rubrum. *Microbiology Spectrum*, *11*(6). https://doi.org/10.1128/spectrum.02923-23
4. Lombardi, A., Campo, M., Papalini, M., Pizzetti, M., Vignolini, P., & Bernini, R. (2023). Phenolic-Rich Extracts from Circular Economy: Chemical Profile and Activity against Filamentous Fungi and Dermatophytes. *Molecules*, *28*(11), 4374. https://doi.org/10.3390/molecules28114374
5. Pesqué, D., Aerts, O., Bizjak, M., Gonçalo, M., Dugonik, A., Simon, D., Ljubojević-Hadzavdić, S., Malinauskiene, L., Wilkinson, M., Czarnecka-Operacz, M., Krecisz, B., John, S. M., Balato, A., Ayala, F., Rustemeyer, T., & Giménez-Arnau, A. M. (2024). Differential diagnosis of contact dermatitis: A practical

approach review by the EADV Task Force on contact dermatitis. *Journal of the European Academy of Dermatology and Venereology : JEADV*, *38*(9). https://doi.org/10.1111/jdv.20052
6. Rudramurthy, S. M., Shaw, D., Dogra, S., Shankarnarayan, S. A., & Abhishek, A. (2023). Comprehensive Taxonomical Analysis of Trichophyton Mentagrophytes/Interdigitale Complex of Human and Animal Origin from India. *Journal of Fungi*, *9*(5), 577. https://doi.org/10.3390/jof9050577
7. Mandal, S. K., Rehman, M. M.-U., Katyal, A., Rajvanshi, K., Kannan, M., Garg, M., Murugesan, S., & Deepa, P. R. (2023). In silico anti-viral assessment of phytoconstituents in a traditional (Siddha Medicine) polyherbal formulation – Targeting Mpro and pan-coronavirus post-fusion Spike protein. *Journal of Traditional and Complementary Medicine*, *14*(1), 55–69. https://doi.org/10.1016/j.jtcme.2023.07.004
8. Hervay, N. T., Elias, D., Habova, M., Jacko, J., Morvova, M., & Gbelska, Y. (2023). Catechin potentiates the antifungal effect of miconazole in Candida glabrata. *Folia Microbiologica*, *68*(6), 835–842. https://doi.org/10.1007/s12223-023-01061-z
9. Zhang, Q., Zhang, J., Zhang, Y., Sui, Y., Du, Y., Yang, L., & Yin, Y. (2023). Antifungal and anti-biofilm activities of patchouli alcohol against Candida albicans. *International Journal of Medical Microbiology*, *314*, 151596. https://doi.org/10.1016/j.ijmm.2023.151596
10. Zapata-Zapata, C., Luque, D., Quintero, W., Mesa-Arango, A. C., García, L. T., Terrón, M. C., & Rojas-López, M. (2023). Lippia origanoides Essential Oil or Thymol in Combination with Fluconazole Produces Damage to Cells and Reverses the Azole-Resistant Phenotype of a Candida tropicalis Strain. *Journal of Fungi*, *9*(9), 888. https://doi.org/10.3390/jof9090888
11. Pérez-Rodríguez A, Duarte-Escalante E, Acosta Altamirano G, et al. Phenotypic and Genotypic Identification of Dermatophytes from Mexico and Central American Countries. *Journal of fungi (Basel, Switzerland)*. 2023;9(4):462. doi:10.3390/jof9040462
12. Hassan Z, Hassan T, Abu- Raghif A. Evaluation the Effect of Phytosterol Fraction of Chenopodium Murale in Comparison with Tacrolimus on Mice Induced Atopic Dermatitis. *Iraqi Journal of Pharmaceutical Sciences (P-ISSN 1683 - 3597 E-ISSN 2521 - 3512)*. 2023;32(1):84-91. doi:10.31351/vol32iss1pp84-91
13. Nenciarini S, Cavalieri D. Immunomodulatory Potential of Fungal Extracellular Vesicles: Insights for Therapeutic Applications. *Biomolecules*. 2023;13(10):1487. doi:10.3390/biom13101487
14. Alibardi L. General aspects on skin development in vertebrates with emphasis on sauropsids epidermis. *Developmental Biology*. 2023;501:60-73. doi:10.1016/j.ydbio.2023.05.007
15. Suresh B, Kalyanaraman VR, Dhanashekaran S, Dhanraj SA, Dube R. Evaluation of certain siddha drugs in the treatment of candidiasis. Anc Sci Life. 1994 Jul;14(1-2):16-20. PMID: 22556670; PMCID: PMC3336504.
16. Flores, G. A., Acquaviva, A., Libero, M. L., Blasi, F., Di Simone, S. C., Ianni, F., Emiliani, C., Orlando, G., Ferrante, C., Zengin, G., Menghini, L., Venanzoni, R., Cusumano, G., Cossignani, L., Angelini, P., Nilofar, N., & Pellegrino, R. M. (2023). Fomitopsis officinalis: Spatial (Pileus and Hymenophore) Metabolomic Variations Affect Functional Components and Biological Activities. *Antibiotics*, *12*(4), 766. https://doi.org/10.3390/antibiotics12040766
17. Van Der Weerden, N. L., Poon, S., Hayes, B. M., Bleackley, M. R., Mckenna, J. A., Parisi, K., Quimbar, P., Brown, M. B., Baker, M. J., Harvey, P. J., Anderson, M. A., Mccorkelle, O., Gaspar, Y. M., Guarino, R., Wevrett, S. R., Veneer, P. K., Craik, D. J., Turner, R. B., & Vasa, S. (2023). The Plant Defensin Ppdef1 Is a Novel Topical Treatment for Onychomycosis. *Journal of Fungi (Basel, Switzerland)*, *9*(11), 1111. https://doi.org/10.3390/jof9111111
18. Lam, T., Goo, J., Dai, Y., Iuchi, F., Lim, L., Ishida, Y., Huang, Y., Liu, J., Du, K., Wu, J., Liu, Y., & Xu, J. (2023). Impact of antibacterial detergent on used-towel microbiomes at species-level and its effect on malodor control. *IMeta*, *2*(3). https://doi.org/10.1002/imt2.110
19. İpek, S. L., Özdemir, M. D., & Göktürk, D. (2023). Cytotoxic Effect of L-Methioninase from

Brevibacterium linens BL2 in Combination with Etoposide against Glioblastoma Cells. *Applied Sciences*, *13*(16), 9382. https://doi.org/10.3390/app13169382
20. Hussain, A., Khuroo, T., Altamimi, M. A., & Ramzan, M. (2023). Hansen Solubility Parameters and QbD-Oriented HPLC Method Development and Validation for Dermatokinetic Study of a Miconazole-Loaded Cationic Nanoemulsion in Rat Model. *ACS Omega*, *8*(38), 34746–34759. https://doi.org/10.1021/acsomega.3c03713
21. Phechkrajang, C., Nuchtavorn, N., Phiphitphibunsuk, W., Leanpolchareanchai, J., & Sukthongchaikool, R. (2023). Development of Miconazole-Loaded Microemulsions for Enhanced Topical Delivery and Non-Destructive Analysis by Near-Infrared Spectroscopy. *Pharmaceutics*, *15*(6), 1637. https://doi.org/10.3390/pharmaceutics15061637
22. Tejada, G., Lamas, C., Morri, M., Álvarez, V. A., Calvo, N. L., Leonardi, D., & Sortino, M. (2023). Miconazole Nitrate Microparticles in Lidocaine Loaded Films as a Treatment for Oropharyngeal Candidiasis. *Materials*, *16*(9), 3586. https://doi.org/10.3390/ma16093586
23. Lestari, U., Chaerunisaa, A. Y., Sujarwo, W., & Muhaimin, M. (2023). Improved Solubility and Activity of Natural Product in Nanohydrogel. *Pharmaceuticals*, *16*(12), 1701. https://doi.org/10.3390/ph16121701
24. Tang, X., You, G., Li, X., Kang, J., & Li, L. (2023). Metallic elements combine with herbal compounds upload in microneedles to promote wound healing: a review. *Frontiers in Bioengineering and Biotechnology*, *11*. https://doi.org/10.3389/fbioe.2023.1283771
25. Rajendran, K., Karuppiah, P., Gnanamangai, B. M., Ponmurugan, P., Shaik, M. R., Shaik, B., Khan, M., & Khan, M. (2023). Bioefficacy of Lecanoric Acid Produced by Parmotrema austrosinense (Zahlbr.) Hale against Tea Fungal Pathogens. *Horticulturae*, *9*(6), 705. https://doi.org/10.3390/horticulturae9060705
26. Gutierrez-Gongora, D., Raouf-Alkadhimi, F., Prosser, R. S., & Geddes-Mcalister, J. (2023). Differentiated extracts from freshwater and terrestrial mollusks inhibit virulence factor production in Cryptococcus neoformans. *Scientific Reports*, *13*(1). https://doi.org/10.1038/s41598-023-32140-3