



Antifungal Activity of *Mentha × piperita* L. Essential Oil Against *Trichophyton mentagrophytes*

Carmelita AS¹, Wijaya L^{2*}, Surja SS³, Arieselia Z⁴ and Kambira PFA⁵

¹ School of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia, Jl. Pluit Raya No. 2, Jakarta Utara, 14440, DKI Jakarta

² Department of Dermatology and Venereology, School of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia, Jl. Pluit Raya No. 2, Jakarta Utara, 14440, DKI Jakarta

³ Department of Parasitology, School of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia, Jl. Pluit Raya No. 2, Jakarta Utara, 14440, DKI Jakarta

⁴ Department of Pharmacology, School of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia, Jl. Pluit Raya No. 2, Jakarta Utara, 14440, DKI Jakarta

⁵ Department of Pharmacy, School of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia, Jl. Pluit Raya No. 2, Jakarta Utara, 14440, DKI Jakarta

Carmelita AS, Wijaya L, Sem SS, Arieselia Z, Kambira PFA 2026 – Antifungal Activity of Peppermint (*Mentha × piperita* L.) Essential Oil Against *Trichophyton mentagrophytes*. Current Research in Environmental & Applied Mycology (Journal of Fungal Biology) 16(1), 24–31, Doi 10.5943/cream/16/1/2

Abstract

Dermatophytosis, a superficial fungal infection caused by dermatophytes such as *Trichophyton mentagrophytes*, has become increasingly difficult to manage due to rising resistance to synthetic antifungals like terbinafine. This study evaluates the potential of peppermint (*Mentha × piperita* L.) essential oil, rich in menthol, as a natural antifungal alternative. Peppermint oil was extracted through water distillation and tested at concentrations of 25%, 12.5%, 6.25%, 3.125%, 1.562%, 0.781%, 0.390%, and 0.195% to evaluate its inhibitory effects on three different strains of *T. mentagrophytes*. The Minimum Inhibitory Concentration (MIC) was determined using the microdilution method according to CLSI M38 guidelines. Antifungal activity was assessed based on medium turbidity, with itraconazole serving as a positive control. The findings revealed that peppermint oil at a concentration of 0.78125% suppressed the growth of two *T. mentagrophytes* variants, whereas a concentration of 12.5% was required to inhibit the third variant. These results suggest that peppermint essential oil could serve as a natural antifungal agent against *T. mentagrophytes*, justifying additional research as an alternative to synthetic therapies.

Keywords – dermatophytes – dl-Menthol – MIC determination – microdilution – peppermint oil

Introduction

Superficial fungal infections of the skin remain one of the most pressing and unrelenting public health concerns affecting millions of individuals all over the world. According to the World Health Organization, approximately 20% of the global population is affected by skin fungus and 60-70% of these are due to dermatophytes (Moskaluk & VandeWoude 2022). Dermatophytosis often known as Tinea or ringworm is a skin, hair and nails disease which is caused by dermatophytes, keratinophilic fungi (Brooks et al. 2013, Widaty et al. 2019). This makes tropical countries like Indonesia, to experience much higher incidence rates of this disease, as the warm and moist climate creates the

perfect conditions for the growth of fungi (Nurhidayah et al. 2021). Reports indicate that dermatophytes are responsible for 52% of superficial mycoses in Indonesia, with *Trichophyton rubrum* being the most common species (58.9%), followed by *T. mentagrophytes* (24.6%) (Hidayat 2018). However, recent data suggest a significant rise in *T. mentagrophytes* prevalence, now accounting for 90% of cases in some regions (Keshwania et al. 2023).

Standard treatment for dermatophytosis involves antifungal agents such as ketoconazole, itraconazole, griseofulvin, and terbinafine, which have demonstrated efficacy against *T. mentagrophytes* in vitro (Fernández-Torres et al. 2000). However, prolonged use of these drugs often results in adverse side effects and the emergence of drug-resistant fungal strains (Prastiyanto et al. 2021). Therefore, the research on natural, safe and effective antifungal agents has received increasing attention in the last few years. Peppermint (*Mentha × piperita* L.) essential oil and leaf extracts exhibit a broad spectrum of pharmacological activities beyond the antifungal, antibacterial, antiviral and antioxidant effects already noted. Recent reviews and chemical analyses report that peppermint oil is dominated by monoterpenes such as menthol and menthone but also contains limonene, pulegone, isopulegol and other terpenoids that together contribute to multiple bioactivities. These constituents have demonstrated antimicrobial and antifungal activity against yeasts, dermatophytes and a range of filamentous fungi, primarily via disruption of cell membranes, increased membrane permeability, leakage of intracellular constituents, inhibition of membrane-bound enzymes (e.g., PM-H⁺-ATPase) and induction of oxidative stress in microbial cells. (Hudz et al. 2023, Zhao et al. 2022, Leiva-Mora et al. 2025)

Beyond direct microbicidal effects, peppermint and its major constituent menthol exert anti-inflammatory, analgesic and spasmolytic effects that have clinical relevance (e.g., topical antipruritic/analgesic uses and oral formulations for gastrointestinal spasm and irritable bowel syndrome). In vitro and in vivo evidence also supports antiviral activity of some *Lamiaceae* essential oils and monoterpenes (including activity reported against certain respiratory viruses in cell-based assays), as well as notable antioxidant and anti-parasitic properties described for various *Mentha* spp. Importantly, safety and formulation considerations are critical: regulatory and safety reviews conclude peppermint-derived ingredients are generally safe for cosmetic and topical use at appropriate concentrations, but specific constituents (notably pulegone and high doses of menthone) show hepatotoxicity or neurotoxicity in animal studies at high oral doses, therefore clinical/topical application requires concentration control, standardized composition and consideration of dermal irritation potential. (Hudz et al. 2023, Johnson et al. 2023)

Composition of essential oils originating from *Mentha* genus varies depending on factors such as species, harvest time, their origin and the method of extraction used (Buleandra 2016). Tullio et al. (2019) proved that organic peppermint oil from Italy has reaction against various yeast strains and dermatophytes like *T. mentagrophytes*. Audreylia et al. (2020) supports this evidence by showing that peppermint leaves produced in Indonesia possess activities against the fungal *Candida* species. Nevertheless, research on the antifungal activity of peppermint essential oil originating from Indonesia specifically against *T. mentagrophytes* remains limited.

The purpose of this study is to assess the antifungal activity of peppermint essential oil prepared using water distillation against the growth of *T. mentagrophytes*. This study aims to address essential research questions: (1) Which organic compounds prevail in peppermint essential oil based on the GC-MS analysis? (2) Does peppermint essential oil influence the growth of *T. mentagrophytes*? (3) What is the optimal concentration of peppermint essential oil required for fungal inhibition? By exploring these questions, this research aims to contribute to the development of alternative treatments for dermatophytosis and provide insights into the use of peppermint essential oil as a natural antifungal agent.

Materials & Methods

This experimental study was conducted in the laboratory facilities of Department of Biochemistry and Parasitology, School of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia from December 2023 to September 2024. Ethical clearance for the study was

granted by the ethics committee under reference number 15/05/KEP-FKIKUAJ/2024. Gas chromatography–mass spectrometry (GC–MS) analysis was performed to determine the chemical composition of the peppermint (*Mentha × piperita* L.) essential oil. The analysis was conducted at the Regional Health Laboratory (Laboratorium Kesehatan Daerah; Labkesda), DKI Jakarta.

Distillation of peppermint essential oil

The distillation process for extracting peppermint essential oil involved meticulous preparation to ensure optimal yield and purity. Fresh peppermint (*Mentha × piperita* L.) leaves sourced from Hijos Farm, Banten, Indonesia, were first rinsed thoroughly with distilled water to remove impurities. After washing, the leaves were air-dried at room temperature and weighed precisely using a digital balance, with 60 grams prepared for each distillation cycle.

The distillation was conducted using a "Wise Therm" heating mantle. A 900 mL volume of distilled water was added to the boiling flask containing the leaves. The temperature was maintained at 100°C for approximately 6 hours to ensure the complete release of essential oil. Distillation was monitored continuously, and the distillate (a mixture of water and essential oil) was collected in a receiving flask. The essential oil was stored at 4°C for further analysis and testing. This procedure was based on previously described distillation methods for peppermint leaves (Aziza et al. 2013, Batool et al. 2018, Dai et al. 2019).

The preparation of *Trichophyton mentagrophytes*

The strains of *Trichophyton mentagrophytes* used in this study were obtained from the Parasitology Laboratory, School of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia. The strains were inoculated on Sabouraud Dextrose Agar (SDA) and incubated at 25–30°C for 7 days to ensure optimal fungal growth.

For antifungal testing, the fungal concentration was standardized by preparing a suspension. A sterile cotton swab was used to scrape fungal colonies, which were then suspended in 0.9% sterile sodium chloride solution. The suspension was vortexed to achieve uniform distribution, and the concentration was adjusted to approximately 2×10^3 to 6×10^3 CFU/mL using a hemacytometer. The inoculum density range was selected based on the Clinical and Laboratory Standards Institute (CLSI) M38 reference protocol for filamentous fungi, which recommends preparing inocula equivalent to 1×10^3 to 3×10^3 CFU/mL following twofold dilution during microdilution setup (CLSI 2017a). The higher concentration prior to dilution ensures accuracy and comparable fungal load during antifungal susceptibility testing. Verification of fungal concentration was performed using the pour plate method, where colony counts between 10–30 per plate were targeted, corresponding to the final testing range. This dual verification approach enhances precision in measuring active cell concentration, thereby strengthening the reliability of the study's findings on the antifungal efficacy of peppermint essential oil.

Antifungal Activity Test

The antifungal activity of peppermint essential oil and itraconazole was evaluated using the broth microdilution method, following the guidelines outlined in CLSI M38 and all tests were performed in triplicate to ensure reliability and reproducibility. For each test, serial dilutions of the essential oil were prepared in RPMI 1640 medium (Gibco) to achieve concentrations ranging from 0.01% to 12.5%. Similarly, itraconazole (sourced from PT Dankos Farma) was prepared at concentrations ranging from 0.01 mg/mL to 1 mg/mL as a positive control. Each dilution was pipetted using micropipettes (Thermo) into 96-well microplates (Biologix), with 100 µL of fungal suspension added to each well. The plates were then incubated at room temperature (25–30°C) for 4 days. Minimum inhibitory concentration (MIC) was determined as the lowest concentration of antifungal agent that inhibited visible fungal growth in the wells. The antifungal efficacy of peppermint essential oil was compared with itraconazole.

Evaluation Metrics

The antifungal susceptibility testing was also assessed to investigate the effectiveness of peppermint essential oil compared to itraconazole. Daily turbidity measurements of the culture medium from four days were used as an estimate of fungal growth or inhibition. Increasing turbidity along with visible hyphal structures within the medium signaled fungal proliferation, while stable turbidity indicates inhibitory effect. The mean MIC values for peppermint essential oil and itraconazole were calculated to quantify their inhibitory potential against the three *Trichophyton mentagrophytes* variants.

Results

Yield and Chemical Composition of Peppermint Essential Oil

Environmental conditions of peppermint plants, including the quality of soil used, seasonal changes, as well as the methods of fertilization, influence the yield and chemical composition of the essential oil. These variables highlight the importance of considering cultivation and extraction parameters when analyzing essential oil productivity and quality.

In this study, peppermint (*Mentha × piperita* L.) essential oil was obtained through the water distillation method. The procedure yielded 10 mL of oil from 690 grams of fresh peppermint leaves procured from Banten with 1.45 % v/w of yield. The chemical compounds found in the peppermint essential oil, which were analyzed using gas chromatography-mass spectrometer (GC-MS) are shown below on Table 1 where the most abundant chemical compound was identified as *dl-Menthol*, which constituted 40.87% of the total composition. Menthol presence is consistent with this study and is in concordance with other research thereby proving its importance as one of the components in the oil with antifungal, antibacterial, and antiviral properties. The second most prominent compound was *Cyclohexanone, 5-methyl-2-(1-methylethyl)-, (2R-cis)*, which constituted 29.56%. This compound has demonstrated antibacterial activity, however, its antifungal properties remain unexplored, presenting an opportunity for further research.

Table 1 GC-MS Analysis of Peppermint Essential Oil (*Mentha × piperita* L.).

No.	Substance	Composition (%)
1.	<i>(1S)-2,6,6-Trimethylbicyclo[3.1.1]hept-2-ene</i>	3.78
2.	<i>Bicyclo[3.1.1]heptane, 6,6-dimethyl-2-methylene, (1S)</i>	3.16
3.	<i>D-Limonene</i>	8.22
4.	<i>Cyclohexanone, 5-methyl-2-(1-methylethyl)-, (2R-cis)</i>	29.56
5.	<i>Bicyclo[4.1.0]heptane, 3,7,7-trimethyl-, (1.alpha., 3.alpha., 6.alpha.)</i>	4.56
6.	<i>dl-Isopulegol</i>	1.40
7.	<i>dl-Menthol</i>	40.87
8.	<i>(1R,2R,5R)-5-Methyl-2-(prop-1-en-2-yl) cyclohexanol</i>	1.05
9.	<i>Pulegone</i>	1.65
10.	<i>2-Cyclohexen-1-one, 3-methyl-6-(1-methylethyl)</i>	1.05

Antifungal Activity Assessment

This study evaluated antifungal susceptibility using the microdilution technique, following the Clinical Laboratory Standards Institute (CLSI) M38 guidelines. This method involves adding the essential oil to a microplate containing a liquid medium with a fungal suspension, allowing for the identification of the lowest concentration that inhibits fungal growth. The layout of the 96-well

microplate is illustrated in Fig. 1, showing the arrangement of wells for various controls, peppermint essential oil concentrations, and itraconazole concentrations. The MIC is determined by visually observing the results, with the MIC being the lowest concentration of the antifungal agent in the well that remains clear, indicating fungal growth inhibition (Fig. 2). The microdilution method is highly recommended by CLSI due to its accuracy and sensitivity, making it the standard for antimicrobial testing for dermatophytes.

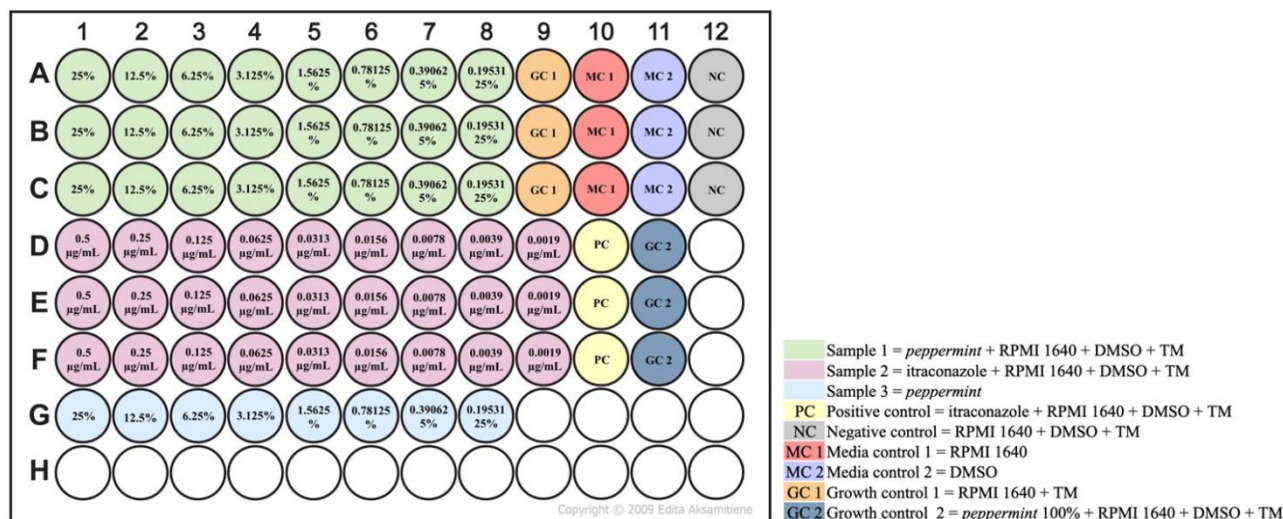


Fig. 1 – Illustration of the 96-well microplate layout used for antifungal activity assessment.



Fig. 2 – Antifungal activity of three *Trichophyton mentagrophytes* strains (TM A, TM B, TM C) using the microdilution method on 96-well microplates.

The results of the microdilution test of peppermint essential oil (*Mentha × piperita* L.) with 3 replications against 3 strains of *T. mentagrophytes* (TM A, TM B, and TM C) confirmed that peppermint essential oil exhibited antifungal activity against all three fungal variants tested. The oil showed MIC values of 0.78% for TM A and TM B, and 12.5% for TM C (Table 2). This variation indicates differences in sensitivity among the fungal strains, possibly due to genetic or phenotypic differences.

Table 2 Minimum Inhibitory Concentration (MIC) of peppermint essential oil (*Mentha × piperita* L.) against *Trichophyton mentagrophytes*.

Fungal strain	Microdilution replication	MIC (%)	Average MIC (%)
TM A	1	0.78125	0.78
	2	0.78125	
	3	0.78125	

Table 2 Continued

Fungal strain	Microdilution replication	MIC (%)	Average MIC (%)
TM B	1	0.78125	0.78
	2	0.78125	
	3	0.78125	
TM C	1	12.5	12.5
	2	12.5	
	3	12.5	

Antifungal Susceptibility Testing (AFST) with Itraconazole

Antifungal Susceptibility Testing (AFST) with itraconazole served as a positive control. The MIC values for itraconazole were 0.25 mg/mL for TM A and TM B, and 0.1 mg/mL for TM C (Table 3). This aligns with Clinical Laboratory Standards Institute (CLSI) M61 guidelines, which report an MIC range of 0.03–0.25 µg/mL for itraconazole against *T. mentagrophytes*.

Table 3 Minimum Inhibitory Concentration (MIC) of itraconazole (*Mentha × piperita* L.) against *Trichophyton mentagrophytes*.

Fungal strain	Microdilution replication	MIC (%)	Average MIC (%)
TM A	1	0.25	0.25
	2	0.25	
	3	0.25	
TM B	1	0.25	0.25
	2	0.25	
	3	0.25	
TM C	1	0.125	0.1
	2	0.125	
	3	0.0625	

Discussion

Peppermint essential oil, rich in menthol, presents a promising natural alternative for the treatment of *Trichophyton mentagrophytes* infections. Safety considerations suggest that peppermint essential oil, when applied topically at 1-5% concentrations, is generally safe and well tolerated. Nevertheless, higher concentrations (>10%) may cause skin irritation or dermatitis (Johnson et al. 2023). These findings align with the MIC values of TM A and TM B (0.78%), making the oil a good candidate for topical treatment of dermatophytosis. In contrast, the substantially higher MIC observed for TM C (12.5%) indicates reduced susceptibility. This raises concerns, as the required MIC for TM C exceeds the generally safe topical application range for peppermint oil.

As no phenotypic or genotypic characterization was performed in this study, explanations regarding strain heterogeneity remain hypothetical. Possible contributing factors may include differences in fungal cell wall structure, membrane composition, or efflux pump activity, which could alter permeability and antifungal uptake. Another potential explanation is laboratory adaptation, as TM C had been preserved longer than TM A and TM B, and prolonged in vitro maintenance may induce metabolic adjustments that influence antifungal response. These assumptions warrant further investigation.

On the other hand, the lower MIC value of itraconazole for TM C indicates that this isolate still responds to synthetic antifungal agents differently from peppermint oil. The proposed antifungal mechanism of menthol, namely membrane disruption, increased permeability, leakage of intracellular contents, and induction of oxidative stress was not evaluated in the present study and is inferred from previously published literature. Zore et al. (2022) demonstrated these effects in

Candida albicans, showing that menthol destabilizes the fungal cell membrane, induces oxidative stress, and subsequently leads to growth inhibition and apoptosis. This activity differs from itraconazole which works by the inhibition of lanosterol 14 α -demethylase, an important enzyme involved in ergosterol synthesis which is required for integrity of fungal cell membranes. The ability of menthol and itraconazole to be used through different pathways indicates the possibility of enhancing antifungal medications' effectiveness (Keshwania et al. 2023, Zore et al. 2022).

This study has some limitations that should be noted. The authors of this study focused on one specific dermatophyte species, *Trichophyton mentagrophytes*, meaning the findings cannot be generalized to other dermatophyte fungus. Furthermore, the safety and potential side effects of peppermint essential oil at antifungal concentrations were not assessed, which is an important factor for its clinical application. Therefore, further studies involving a wider variety of fungal species are needed, particularly to explore strategies for improving the efficacy of peppermint essential oil against resistance strains like TM C while ensuring its safety for topical application as a therapeutic agent for dermatophytosis.

Conclusion

Peppermint essential oil at concentrations of 0.78125% effectively inhibited the growth of two *Trichophyton mentagrophytes* variants, showing antifungal activity comparable to itraconazole at concentrations of 0.25 mg/mL. However, the third variant, peppermint oil required a significantly higher concentration of 12.5% to achieve similar inhibition, whereas itraconazole remained effective at 0.1 mg/mL. These findings suggest that peppermint essential oil may have antifungal potential against certain *T. mentagrophytes* strains, although its effectiveness appears strain-dependent and may be limited by concentration-related safety considerations. Further research is required to improve its efficacy, assess safety profiles, and evaluate potential formulation strategies before clinical application can be considered.

Acknowledgements

The author gratefully acknowledges PT Dankos Farma for providing itraconazole, which significantly supported the success of this study. The author also expresses gratitude to Mr. Agus and Ms. Linda, laboratory staff in the Departments of Parasitology and Biochemistry at the School of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia, for their assistance with all laboratory procedures involved in this study.

References

- Audreylia E, Budiman Y, Surja SS. 2020 – *Mentha piperita* extract, a potential antifungal agent against *Candida albicans* and *Candida krusei*. *Current Research in Environmental & Applied Mycology* 10, 236–241.
- Aziza SAN, Retnowati R, Suratmo S. 2013 – Isolasi dan karakterisasi terhadap minyak mint dari daun mint segar hasil distilasi uap. *Jurnal Ilmu Kimia Universitas Brawijaya* 2, 580–586.
- Batool I, Iqbal MS, Ahmad M, Murtaza G. 2018 – Extraction, production and analysis techniques for menthol: a review. *Journal of Essential Oil Bearing Plants* 21, 82–95.
- Brooks GF, Carroll KC, Butel JS, Morse SA et al. 2013 – Jawetz, Melnick & Adelberg's medical microbiology (26th ed.). McGraw-Hill, 671–678.
- Buleandra M, Oprea E, Popa DE, David IG et al. 2016 – Comparative chemical analysis of *Mentha piperita* and *M. spicata* and a fast assessment of commercial peppermint teas. *Natural Products Communications* 11, 551–555.
- Clinical and Laboratory Standards Institute (CLSI). 2017a – Reference method for broth dilution antifungal susceptibility testing of filamentous fungi (3rd ed.). CLSI standard M38. Wayne, PA: Clinical and Laboratory Standards Institute.

- Clinical and Laboratory Standards Institute (CLSI). 2017b – Performance standards for antifungal susceptibility testing of filamentous fungi (1st ed.). CLSI supplement M61. Wayne, PA: Clinical and Laboratory Standards Institute.
- Dai J, Mumper RJ. 2019 – Extraction of polyphenols from aromatic and medicinal plants: an overview of the methods and the effect of extraction parameters. In: *Polyphenols in Plants*. Elsevier, 243–259.
- Fernández-Torres B, Vázquez-Veiga H, Llovo X, Pereiro M et al. 2000 – In vitro susceptibility to itraconazole, clotrimazole, ketoconazole, and terbinafine of 100 isolates of *Trichophyton rubrum*. *Chemotherapy* 46, 390–394.
- Hidayat R. 2018 – Hubungan kebersihan diri (personal hygiene) dengan kejadian penyakit dermatofitosis di desa Lereng wilayah kerja puskesmas Kuok. *Jurnal Ners* 2, 86–94.
- Hudz NH, Shyichuk A, Kovalyova AM, Isayev OY et al. 2023 – *Mentha piperita*: Phytochemistry and biological activities. *Phytotherapy Research* 37, 1235–1252.
- Johnson W, Bergfeld WF, Belsito DV, Hill RA et al. 2023 – Amended safety assessment of *Mentha piperita* (peppermint)-derived ingredients as used in cosmetics. *International Journal of Toxicology* 42, 1175–1185.
- Keshwania P, Kaur N, Chauhan J, Sharma G et al. 2023 – Superficial dermatophytosis across the world's populations: Potential benefits from nanocarrier-based therapies and rising challenges. *ACS Omega* 8, 31575–31599.
- Leiva-Mora M, Bustillos D, Arteaga C, Hidalgo K et al. 2025 – Antifungal mechanisms of plant essential oils: A comprehensive literature review for biofungicide development. *Agriculture* 15, 2303.
- Widaty S, Budimulja U. 2019 – Dermatofitosis. In: Menaldi SL, Bramono K, Indriatmi W (Eds.), *Ilmu penyakit kulit dan kelamin* (7th ed.). Badan Penerbit FKUI, 109–116.
- Moskaluk AE, VandeWoude S. 2022 – Current topics in dermatophyte classification and clinical diagnosis. *Pathogens* 11, 957.
- Nurhidayah A, Dhanti KR, Supriyadi S. 2021 – Identifikasi jamur patogen penyebab dermatofitosis pada jari kaki petani di desa Bojongsari, Banyumas. *Jurnal Laboratorium Medika* 5, 8–17.
- Prastiyanto ME, Rohmah N, Efendi L, Arifin R et al. 2021 – Antifungal activities of the rhizome extract of five member Zingiberaceae against *Candida albicans* and *Trichophyton rubrum*. *Biodiversitas: Journal of Biological Diversity* 22, 1463–1469.
- Tullio V, Roana J, Scalas D, Mandras N. 2019 – Evaluation of the antifungal activity of *Mentha x piperita* (Lamiaceae) of Pancalieri (Turin, Italy) essential oil and its synergistic interaction with azoles. *Molecules* 24, 3148.
- Zhao H, Ren S, Yang H, Tang S et al. 2022 – Peppermint essential oil: its phytochemistry, biological activity, pharmacological effect and application. *Biomedicine & Pharmacotherapy* 154, 113559.
- Zore G, Thakre A, Abdulghani M, Bhosle K et al. 2022 – Menthol inhibits *Candida albicans* growth by affecting the membrane integrity followed by apoptosis. *Evidence-Based Complementary and Alternative Medicine* 2022, 1–10.