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Evaluation of *Cinnamomum verum* Bark Essential Oil as a Natural Antifungal Agent Against Dermatophytes

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Abstract: Dermatophytosis is a superficial fungal infection that remains a public health problem, particularly in tropical regions, with *Trichophyton rubrum* and *Trichophyton mentagrophytes* as the primary causes. Increasing limitations in the use of synthetic antifungals have encouraged the development of natural products as alternative therapies, including *Cinnamomum verum* stem bark essential oil. This study aimed to analyse the antifungal activity of *C. verum* stem bark essential oil against *T. rubrum* and *T. mentagrophytes* using the disc diffusion method. The study used a true experimental design with a posttest-only control group design. The essential oil was obtained through steam-water distillation with a yield of 0.25% (v/w). Tests against *T. rubrum* used concentrations of 1%, 2%, 5%, and 10%, while tests against *T. mentagrophytes* used concentrations of 5%, 10%, 15%, and 20%. Ketoconazole 2% was used as a positive control and dimethyl sulfoxide as a negative control. The inhibition zone diameter was measured after incubation and analysed using One-Way ANOVA and Post Hoc tests. The results showed that the essential oil inhibited the growth of both fungal species at all concentrations tested. The inhibition zone diameter against *T. rubrum* increased from 21.7 mm to 54.1 mm, while against *T. mentagrophytes* it increased from 33.6 mm to 48.2 mm. Statistical analysis showed a significant difference between the concentrations of both species ($p<0.001$). It was concluded that *C. verum* bark essential oil exhibited in vitro antifungal activity against both *T. rubrum* and *T. mentagrophytes*, with the inhibitory activity generally increasing with increasing concentrations. These findings demonstrate the potential of *C. verum* essential oil as a candidate for a natural antifungal agent based on local resources. Therefore, further research on the characterisation of active compounds, determination of MIC/MFC values, development of topical formulations, and in vivo testing and clinical trials are needed to support its use in dermatophytosis therapy.
Keywords: *Cinnamomum verum*; dermatophytosis; essential oil; *Trichophyton mentagrophytes*; *Trichophyton rubrum*.

INTRODUCTION

Dermatophytosis is a superficial fungal infection of keratin-containing tissues, such as skin, hair, and nails. It remains a public health problem in various countries, particularly in tropical climates with high humidity, including Indonesia[1,2]. This disease is characterized by scaly, itchy lesions and, in some cases, onychomycosis (nail infection). It can reduce the sufferer's quality of life due to its chronic and relapsing course[1]. It is

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estimated that approximately 15% of the global population has experienced a dermatophyte infection, approximately 25% of the global population suffers from dermatophytosis, and 30–70% of adults may be asymptomatic carriers[3]. The World Health Organisation also reports that dermatophytosis is one of the most common superficial mycoses globally, with a prevalence of around 20%, dominated by Tinea corporis, followed by Tinea cruris, Tinea pedis, and onychomycosis[4].

In Indonesia, skin diseases remain a significant burden on healthcare services. Basic Health Research (RISKESDAS) reported a national prevalence of skin disease symptoms of approximately 6.8%, with variations between provinces, indicating the need for more optimal control efforts[5]. In South Kalimantan, a study at Ulin Regional Hospital in Banjarmasin between 2019 and 2021 reported 86 cases of Tinea corporis, with the highest proportion in the 36–45 age group, more common in women, and mostly from the Banjarmasin area[6,7].

Dermatophytosis is caused by a group of dermatophyte fungi consisting of three main genera: *Trichophyton, Microsporum, and Epidermophyton*, with the species that most frequently infect humans coming from the genus Trichophyton[8]. Two species play an important role: *Trichophyton rubrum* and *Trichophyton mentagrophytes*. *Trichophyton rubrum* is an anthropophilic dermatophyte that most often causes chronic infections of the skin, hair, and nails, and is the main cause of tinea pedis, tinea corporis, and onychomycosis[1]. In Indonesia, *T. rubrum* is also frequently found in cases of tinea pedis, making it a concern in national dermatophytosis epidemiology[9]. Meanwhile, *Trichophyton mentagrophytes* is a dermatophyte with both anthropophilic and zoophilic properties and can induce a more severe inflammatory response, causing various forms of tinea, including tinea corporis, tinea capitis, and tinea genitalis. It can also invade the hair shaft through the endothrix pattern[10,11].

Dermatophytosis therapy generally uses synthetic antifungals, both topical and systemic. However, treatment success is often influenced by compliance, the patient's immune status, and irrational medication use, such as premature discontinuation, over-the-counter purchases, and the use of combination creams containing corticosteroids[12,13]. Furthermore, synthetic antifungals also have several limitations, including side effects, suboptimal drug penetration into certain tissues, a limited spectrum of activity, and increased resistance, including higher minimum inhibitory concentration values for terbinafine in some dermatophyte isolates[13]. These conditions have prompted the search for natural ingredients with potential as alternative antifungals with high efficacy and a lower risk of side effects.

One plant with development potential is cinnamon (*Cinnamomum verum*), a member of the Lauraceae family that has long been used as a spice and medicinal plant[14]. The bark of *C. verum* contains various bioactive compounds, primarily cinnamaldehyde as the main component, with concentrations reaching approximately 85.50%, accompanied by other compounds such as (E)-cinnamaldehyde, hydrocinnamaldehyde, cadinene, α-amorphene, stigmasterol, and terpenoids in smaller amounts[15]. Cinnamaldehyde is known to play a significant role as an antifungal agent through various mechanisms, including disrupting the integrity of fungal cell membranes, inhibiting ergosterol and protein synthesis, increasing membrane permeability, causing leakage of intracellular components, and inducing the formation of reactive oxygen species (ROS), which disrupt fungal cell metabolism[16,17].

In addition to its biological potential, *C. verum* is also a non-timber forest product widely utilized by the community in Loksado District, Hulu Sungai Selatan Regency, South Kalimantan. The community cultivates and harvests this plant independently, making it a commodity that contributes to the local economy[18,19]. The abundant availability of raw materials provides an opportunity to develop cinnamon essential oil as a natural antifungal source based on local potential.

Several studies have reported the antifungal activity of cinnamon essential oil against various pathogenic fungi. Research by Parrish et al. (2020) showed that pure Cinnamomum cassia essential oil (100%) produced an average inhibition zone of 79.5 mm against various Trichophyton species and maintained activity up to 21 days, even exceeding that of terbinafine[20]. Other studies have also shown that cinnamon essential oil can inhibit the growth of *Aspergillus niger* and *Candida albicans* at various concentrations[2]. However, these studies have used different cinnamon species, focused on pure essential oil, or failed to evaluate concentration variations against dermatophytes that cause human infections. Furthermore, different cinnamon species produce distinct bioactive compound profiles, with *C. verum* having a higher cinnamaldehyde content than some other species, such as *C. cassia* and *C. burmanii*, potentially providing different antifungal activity[15,21].

Based on these conditions, evaluating the effectiveness of *Cinnamomum verum* bark essential oil against two dermatophyte species with different pathogenic characteristics, *Trichophyton rubrum* and *Trichophyton mentagrophytes*, at various concentrations is important to illustrate the relationship between concentration and antifungal activity while also strengthening the use of local biological resources as an alternative dermatophytosis control. Therefore, this study aimed to analyze the effectiveness of cinnamon bark essential oil at various concentrations on the growth of *Trichophyton rubrum* and *Trichophyton mentagrophytes* using the disc diffusion method.

MATERIALS AND METHODS

This study was a true experimental study with a posttest-only control group design to evaluate the effectiveness of cinnamon bark essential oil on the growth of *Trichophyton rubrum* and *Trichophyton mentagrophytes*. We tested each species separately using four treatment groups and two control groups: a positive control and a negative control. The concentrations of essential oils used against *T. rubrum* were 1%, 2%, 5%, and 10%, while those used against *T. mentagrophytes* were 5%, 10%, 15%, and 20%. The concentration ranges were determined based on preliminary tests to obtain concentrations that produced optimally observable inhibition zones in each fungal species. Each treatment group was repeated six times based on calculations using the Federer formula. The study was conducted from October 2025 to January 2026 at the Chemistry Laboratory of the Faculty of Mathematics and Natural Sciences, Lambung Mangkurat University and the Bacteriology Laboratory of the Department of Medical Laboratory Technology, Poltekkes Kemenkes Banjarmasin.

Cinnamomum verum bark was obtained from Loksado District, Hulu Sungai Selatan Regency, South Kalimantan. Samples were selected in fresh condition and were free from mould, rot, physical damage, or pests. Approximately 2 kg of cinnamon bark was washed thoroughly, dried to reduce water content, and then cut into small pieces. The essential oil was obtained by steam-water distillation for 4 hours at 70–80°C[22]. The

resulting distillate was separated using a separating funnel if two clear phases formed. If phase separation was incomplete due to hydrosol formation, the essential oil fraction was separated manually using a micropipette[23]. Next, the essential oil was purified using anhydrous sodium sulfate (Na_2SO_4) to remove residual water, then stored in dark-colored vials until use. The yield percentage was calculated as the ratio of the volume of essential oil obtained to the initial weight of the sample[24].

The essential oil was diluted with dimethyl sulfoxide (DMSO) to obtain concentrations appropriate for the treatment groups. The concentrations used for testing *T. rubrum* were 1%, 2%, 5%, and 10%, while for *T. mentagrophytes* they were 5%, 10%, 15%, and 20%. The positive control used a 2% ketoconazole solution prepared by dissolving a 200 mg ketoconazole tablet in sterile water to obtain a concentration of 20 mg/mL. In contrast, DMSO was used as a negative control[25].

Pure isolates of *T. rubrum* and *T. mentagrophytes* were rejuvenated on Sabouraud Dextrose Agar (SDA) slants and incubated at 28°C for 14 days. Fungal suspensions were prepared by adding 0.9% physiological NaCl solution to the culture, followed by serial dilutions up to 10^{-5}. The suspension density was standardized using a UV-Vis spectrophotometer at 530 nm. A suspension with a transmittance value of 80–82% was chosen as the inoculum because it equates to a concentration of approximately 10^6–10^7 CFU/mL, resulting in a uniform inoculum[26].

Antifungal activity was tested using the disc diffusion method. A 100 µL standardized fungal suspension was spread evenly onto SDA using a sterile spreader. For *Trichophyton rubrum*, the medium was left for 15 minutes before placing sterile discs containing 20 µL of essential oil, ketoconazole, or DMSO, followed by incubation at 28°C for 72 hours. For *Trichophyton mentagrophytes*, the inoculated medium was first incubated for 48 hours before disc placement, then incubated for another 72 hours at 28°C to accommodate its growth characteristics and improve zone-of-inhibition observation. The inhibition zone diameter was measured horizontally and vertically using a calliper and averaged. Antifungal activity was interpreted according to Clinical and Laboratory Standards Institute (CLSI) criteria: sensitive ≥20 mm, intermediate 15–19 mm, and resistant ≤14 mm[27].

Inhibition zone diameters are presented as mean ± standard deviation. For both *Trichophyton rubrum* and *Trichophyton mentagrophytes*, the Shapiro–Wilk test confirmed normal distribution ($p > 0.05$), while homogeneity tests showed equal variances ($p = 0.505$ and $p = 0.553$, respectively). Differences between species were analyzed using One-Way ANOVA, followed by a Post Hoc test when significant. Statistical significance was set at $p < 0.05$ with a 95% confidence level. Ethical approval was obtained from the Health Research Ethics Committee of the Banjarmasin Ministry of Health Polytechnic (No. 737/KEPK-PKB/2025 for *Trichophyton rubrum* and No. 780/KEPK-PKB/2025 for *Trichophyton mentagrophytes*).

RESULTS AND DISCUSSION

Characteristics of *Cinnamomum verum* Stem Bark Essential Oil

A total of 2,000 g of *Cinnamomum verum* stem bark, washed, dried, and cut into small pieces, was distilled using steam-water distillation. The distillation produced 5 mL of essential oil weighing 6.54 g, for a yield of 0.25% (v/w). The resulting essential oil is pale yellow with a strong, sweet, and slightly spicy cinnamon aroma (Table 1).

Table 1. Characteristics and Yield of *Cinnamomum verum* Bark Essential Oil

Parameter	Result
Fresh bark weight (g)	2,000
Essential oil volume (mL)	5
Essential oil weight (g)	6.54
Yield (% v/w)	0.25
Physical characteristics	Pale yellow color with a strong, sweet, and slightly spicy aroma

Antifungal Activity against *Trichophyton rubrum*

Test results showed that *Cinnamomum verum* bark essential oil inhibited the growth of *Trichophyton rubrum* at all concentrations tested. The average inhibition zone diameter increased with increasing essential oil concentration, from 21.7 mm at 1% to 29.6 mm at 2%, 41.0 mm at 5%, and 54.1 mm at 10%. Under the experimental conditions, the essential oil produced larger mean inhibition zones than the ketoconazole control, while the negative control showed no inhibition zone formation (Table 2).

Table 2. Inhibition Zone Diameter of *Cinnamomum verum* Bark Essential Oil Against *Trichophyton rubrum*

Essential Oil Concentration (%)	Replicate						Mean ± SD (mm)
	1	2	3	4	5	6	
1	21.3	22.3	21.2	21.4	21.7	22.0	21.7 ± 0.4
2	29.4	30.1	29.5	28.9	29.0	30.5	29.6 ± 0.6
5	41.2	40.5	41.5	40.7	41.1	41.0	41.0 ± 0.4
10	54.5	54.3	54.7	54.1	53.4	53.7	54.1 ± 0.5
Positive control	26.2	26.8	26.0	27.1	26.2	25.8	26.4 ± 0.5
Negative control	0	0	0	0	0	0	0

Antifungal Activity Against *Trichophyton mentagrophytes*

Cinnamomum verum bark essential oil also demonstrated antifungal activity against *Trichophyton mentagrophytes* at all tested concentrations. The inhibition zone diameter increased gradually from 33.6 mm at 5% to 37.7 mm at 10%, 41.4 mm at 15%, and peaked at 48.2 mm at 20%. Under the experimental conditions, the mean inhibition zones for the essential oil were larger than those of the ketoconazole control, while the negative control showed no inhibitory activity (Table 3).

Statistical Analysis of *Trichophyton rubrum*

The assumption test results showed that the inhibition zone diameter data for all essential oil concentrations against *Trichophyton rubrum* were normally distributed ($p > 0.05$) and had homogeneous variance ($p = 0.505$). Therefore, the analysis was continued using a one-way ANOVA test. The results showed a significant difference in the inhibition zone diameter between treatment groups ($p < 0.001$) (Table 4). Further post hoc testing showed significant differences between all pairs of essential oil concentrations ($p < 0.05$), indicating that increasing essential oil concentration significantly increased antifungal activity against *T. rubrum* (Table 5).

Table 3. Inhibition Zone Diameter of *Cinnamomum verum* Bark Essential Oil Against *Trichophyton mentagrophytes*

Essential Oil Concentration (%)	Replicate						Mean ± SD (mm)
	1	2	3	4	5	6	
5	32.4	35.7	39.8	31.8	35.1	28.8	33.6 ± 3.7
10	35.3	41.8	40.0	37.0	36.9	36.7	37.7 ± 2.5
15	36.8	49.6	45.2	43.6	37.1	39.7	41.4 ± 5.0
20	52.3	50.2	49.8	48.7	45.8	42.9	48.2 ± 3.4
Positive control	25.6	31.1	31.1	31.4	34.6	28.7	30.4 ± 2.9
Negative control	0	0	0	0	0	0	0

Table 4. Statistical Analysis of the Inhibition Zone Diameter of *Cinnamomum verum* Bark Essential Oil Against *Trichophyton rubrum*

Statistical test	Result
Shapiro–Wilk normality test	1% = 0.546; 2% = 0.565; 5% = 0.954; 10% = 0.834 (all $p > 0.05$; normally distributed)
Homogeneity of variance	$p = 0.505$ (homogeneous)
One-Way ANOVA	$p < 0.001$ (significant difference among groups)

Table 5. Post Hoc Analysis of the Inhibition Zone Diameter Against *Trichophyton rubrum*

Comparison	p-value	Interpretation
1% vs 2%	<0.001	Significant
1% vs 5%	<0.001	Significant
1% vs 10%	<0.001	Significant
2% vs 5%	<0.001	Significant
2% vs 10%	<0.001	Significant
5% vs 10%	<0.001	Significant

Statistical Analysis of *Trichophyton mentagrophytes*

Table 6. Statistical Analysis of the Inhibition Zone Diameter of *Cinnamomum verum* Bark Essential Oil Against *Trichophyton mentagrophytes*

Statistical test	Result
Shapiro–Wilk normality test	5% = 0.790; 10% = 0.276; 15% = 0.249; 20% = 0.719 (all $p > 0.05$; normally distributed)
Homogeneity of variance	$p = 0.553$ (homogeneous)
One-Way ANOVA	$p < 0.001$ (significant difference among groups)

The inhibition zone diameter data for *Trichophyton mentagrophytes* in all treatment groups also met the assumptions of normality ($p > 0.05$) and homogeneity of variance ($p = 0.553$), so the analysis was continued using one-way ANOVA. The analysis results showed a significant difference in inhibition zone diameter between treatment groups (p

< 0.001) (Table 6). Further post hoc tests showed no significant difference between the 5% and 10% concentrations (p = 0.218) or between the 10% and 15% concentrations (p = 0.317). Conversely, the 5% concentration differed significantly from 15% and 20%, as did 10% from 20%, and 15% from 20% (p < 0.05). These results indicate that antifungal activity increased more markedly at higher essential oil concentrations, particularly at 20% (Table 7).

Table 7. Post Hoc Analysis of the Inhibition Zone Diameter Against *Trichophyton mentagrophytes*

Comparison	p-value	Interpretation
5% vs 10%	0.218	Not significant
5% vs 15%	0.006	Significant
5% vs 20%	<0.001	Significant
10% vs 15%	0.317	Not significant
10% vs 20%	<0.001	Significant
15% vs 20%	0.018	Significant

In this study, the essential oil from *Cinnamomum verum* bark was obtained by 4-hour steam-water distillation at 70–80°C. This condition was chosen because most volatile compounds were extracted without significant thermal damage, as volatile compounds can evaporate at temperatures below the boiling points of their respective components in steam-water distillation[28]. During distillation, a mixture of the oil and water phases (hydrosol) forms, preventing the essential oil from separating. This phenomenon aligns with research by Khasanah et al. (2021), which reported that hydrosols still contain volatile essential oil components and form an emulsion[23]. According to Said et al. (2015), hydrosols are aqueous solutions that can form emulsions with essential oils and require a purification step using anhydrous sodium sulfate to remove residual water[29]. The essential oil yield obtained was 0.25% (v/w), lower than the research by Mulyanti et al. (2023), which obtained a yield of 0.4834% (v/w)[24] and Yuliarto et al. (2012), which obtained a yield of 0.456%[30]. Plant species, plant age, stem part used, raw material condition, particle size, and distillation parameters such as temperature and distillation time likely influence this difference[31]. Furthermore, environmental factors such as geographic origin, soil conditions, temperature, and rainfall also influence the biosynthesis of secondary metabolites, thus affecting essential oil yield[32].

In *Trichophyton rubrum*, the inhibition zone diameter increased from 21.7 mm at a 1% concentration to 54.1 mm at a 10% concentration. In contrast, in *Trichophyton mentagrophytes*, it increased from 33.6 mm at 5% to 48.2 mm at 20%. One-way ANOVA showed a significant difference between concentrations in both species ($p<0.05$), indicating that increasing essential oil concentration is directly proportional to increased antifungal activity. These findings indicate a dose-response relationship: the higher the essential oil concentration, the more active compound diffuses into the medium, increasing the inhibitory effect on fungal growth.

However, the two dermatophyte species showed different response patterns. *Trichophyton rubrum* showed an inhibition zone diameter exceeding the positive control at 2%. In contrast, *Trichophyton mentagrophytes* required a higher concentration to produce a significant increase in inhibition, with the best effectiveness at 20%. These

differences indicate that each dermatophyte species varies in sensitivity to *Cinnamomum verum* essential oil, likely influenced by biological characteristics such as hyphal structure, cell wall composition, and adaptability to antifungal compounds.

The results of this study align with those of Parrish et al. (2020), who reported that a 100% concentration of *Cinnamomum cassia* essential oil produced an inhibition zone diameter of approximately 79.5 mm against various *Trichophyton* species using the disc diffusion method and maintained its antifungal activity up to day 21[20]. The inhibition zone diameter in this study was relatively smaller than that of that study. This difference likely reflects several factors, including differences in cinnamon species, essential oil concentration, inoculum standardisation methods, and essential oil preparation methods. Parrish et al. (2020) used *Cinnamomum cassia* at 100% concentration. They standardised the inoculum using the viable count method, while this study used *Cinnamomum verum* at a lower concentration and standardised it using 80–82% transmittance[20].

The results of this study are also lower than those of Kottferova and Conkova (2023), who reported inhibition zone diameters of up to 90 mm against *Trichophyton mentagrophytes*[33]. In addition to using *Cinnamomum cassia*, that study used gum arabic as an emulsifier, which increased the diffusion of essential oils into the agar medium. In contrast, this study used essential oils without an emulsifier, so their hydrophobic nature could limit the diffusion of active compounds within the medium, ultimately affecting the size of the inhibition zone formed.

The antifungal activity of *Cinnamomum verum* bark essential oil is thought to be related to its bioactive compound content. Based on GC-MS analysis reported by Ahmed et al. (2020), the main components of essential oil are cinnamaldehyde (85.50%), followed by stigmasterol (3.69%), cadinene (1.37%), (E)-cinnamaldehyde (1.35%), α-amorphene (1.33%), hydrocinnamaldehyde (1.28%), α-cubebene (1.25%), and ergosterol (1.09%)[15]. These compounds come from several chemical groups, namely aromatic aldehydes, sesquiterpene hydrocarbons, and sterols, which are known to have antimicrobial activity.

The composition of essential oils can vary even when derived from the same species. Ahmed et al. (2020) used *Cinnamomum verum* samples from Khartoum, Sudan[15], while the raw materials in this study came from Loksado District, Hulu Sungai Selatan Regency, South Kalimantan. These differences in geographic origin can lead to variations in cinnamaldehyde levels and other constituent compounds due to temperature, rainfall, altitude, soil type, and interactions between genetic and environmental factors[34].

Cinnamaldehyde is the main component responsible for the antifungal activity of cinnamon essential oil. Cinnamaldehyde inhibits the biosynthesis of ergosterol, a key component of fungal cell membranes, resulting in membrane instability and decreased cell viability (17). This mechanism is relevant to dermatophytes, including *Trichophyton rubrum*, which rely on membrane integrity and ergosterol content to maintain hyphal growth and colonise keratinised tissue[35]. Research by Rashed et al. (2021) also reported that exposure to cinnamaldehyde causes structural damage in dermatophytes, including Trichophyton spp., thereby inhibiting hyphal growth[36].

In addition to cinnamaldehyde, minor components such as cadinene, α-amorphene, α-cubebene, and hydrocinnamaldehyde are thought to contribute to

antifungal activity through synergistic mechanisms. Hyldgaard et al. (2012) explained that terpene compounds and minor aldehydes can disrupt cell membrane permeability, disrupt ion gradients, and inhibit the energy balance of microbial cells[37]. Although each compound is less active than cinnamaldehyde, the combination of components in essential oils produces multiple mechanisms that enhance the overall antifungal effect.

A limitation of this study is that the chemical composition of the essential oils used was not directly analysed using GC-MS, so the active compound profile refers to the study by Ahmed et al. (2020)[15]. Furthermore, the study evaluated only in vitro antifungal activity using the disc diffusion method against two dermatophyte species and therefore cannot describe efficacy under clinical conditions. Further research is needed to characterise the chemical components of essential oils from local sources, determine the minimum inhibitory concentration (MIC) and Minimum Fungicidal Concentration (MFC), and evaluate their effectiveness and safety through in vivo testing and topical formulations.

CONCLUSION

Cinnamomum verum bark essential oil obtained through steam-water distillation at a yield of 0.25% (v/w) was shown to have antifungal activity against *Trichophyton rubrum* and *Trichophyton mentagrophytes*. Increasing the essential oil concentration significantly increased the inhibition zone diameter for both fungal species. A 10% concentration provided the best antifungal activity against *T. rubrum* with an average inhibition zone of 54.1 mm. In comparison, 20% was the most effective concentration against *T. mentagrophytes*, with an average inhibition zone of 48.2 mm. These results indicate that the two dermatophyte species differ in sensitivity to *C. verum* essential oil, but both show a strong antifungal response. As a result, *C. verum* bark essential oil has the potential to be developed as a natural antifungal active ingredient based on local resources for the treatment of dermatophytosis. Further research should characterise the chemical components of the essential oils using GC-MS, determine MIC and MFC values, develop topical formulations, and conduct in vivo testing and clinical trials to ensure their effectiveness and safety.

CONFLICT OF INTEREST

In this study there is no conflict of interest

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