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ARTICLE

BIOACTIVITY OF ENDOPHYTIC FUNGI EXTRACTS RESIDING IN THE HAUSTORIA OF MISTLETOE (*Dendrophthoe pentandra* (L.) Miq.) ON THE LIME PLANT (*Citrus aurantifolia*)

[*Bioaktivitas Ekstrak Jamur Endofitik yang Diisolasi dari Haustorium Benalu (Dendrophthoe pentandra (L.) Miq.)*]

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ABSTRACT

Mistletoe (*Dendrophthoe pentandra* (L.) Miq.) is a parasitic plant that has traditional medicinal properties. This study examines the endophytic fungi found in mistletoe roots and their bioactivity. Endophytic fungal species are identified using their morphological traits. The potato dextrose broth (PDB) medium is utilized for both culture and extraction, with ethyl acetate as a solvent. The antioxidant test employed the DPPH method, whereas the antibacterial test used the paper disc diffusion method. Mistletoe haustoria yielded four endophytic fungal isolates (BR1–BR4). The findings of the morphological study revealed that BR1 (*Pythium* sp.), BR2 (*Trichoderma* sp.), BR3 (*Fusarium* sp.), and BR4 (*Mortierella* sp.). The endophytic fungus BR4 (*Mortierella* sp.) had the highest potential antioxidant and antibacterial activities. This endophytic fungal extract has the potential to be a source of novel medications through additional investigation by isolating the pure component and in vivo studies.

Keywords: Bioactivity; *Dendrophtoe pentandra* (L.) Miq.; Endophytic fungi; Haustoria of mistletoe

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ABSTRAK

Benalu (Dendrophthoe pentandra (L.) Miq.) merupakan tanaman parasit yang memiliki khasiat obat tradisional. Penelitian ini meneliti jamur endofit yang ditemukan pada haustorium benalu dan bioaktivitasnya. Spesies jamur endofit diidentifikasi menggunakan ciri morfologinya. Media potato dextrose broth (PDB) digunakan untuk kultur dan ekstraksi, dengan etil asetat sebagai pelarut. Uji antioksidan menggunakan metode DPPH, sedangkan uji antibakteri menggunakan metode difusi cakram kertas. Haustorium benalu menghasilkan empat isolat jamur endofit (BR1–BR4). Hasil studi morfologi menunjukkan bahwa BR1 (Pythium sp.), BR2 (Trichoderma sp.), BR3 (Fusarium sp.), dan BR4 (Mortierella sp.) teridentifikasi. Jamur endofit BR4 (Mortierella sp.) memiliki potensi aktivitas antioksidan dan antibakteri tertinggi. Ekstrak jamur endofit ini berpotensi menjadi sumber pengobatan baru melalui penyelidikan tambahan dengan mengisolasi komponen murni dan penelitian in vivo.

Kata kunci : *Bioactivitas; Dendrophtoe pentandra; Jamur Endofit; Haustorium Benalu*

INTRODUCTION

Medicinal plants are very popular as raw materials for traditional medicine and herbal medicine (Asase, 2023; Courric *et al*., 2023; Rojas *et al*., 2022). People believe that consuming plants with medicinal properties will improve the immune system because these plants have specific properties as medicinal plants that are preventive and promotive through their secondary metabolite content (Li *et al*., 2024; Mitropoulou *et al*., 2023; Sukhikh *et al*., 2023). Mistletoe is a plant that has medicinal properties but information about it has not been explored globally.

Mistletoe is a plant that is parasitic to the plant hosts. Mistletoe can be found easily on large trees in tropical areas. However, despite its detrimental nature, based on observation mistletoe is used by the community as a traditional medicine, especially the leaves and the haustoria as a medicine for fever, diarrhea, hemorrhoids, hypertension and cancer, especially mistletoe which lives on lime hosts (Gao *et al*., 2024; Paller *et al*., 2023; Pelzer *et al*., 2022; Staupe *et al*., 2023; Szurpnicka *et al*., 2020; Yousefvand *et al*., 2022). The ability of mistletoe as a traditional medicine cannot be separated from its secondary metabolite content, such as polyphenols, flavonoids, alkaloids and tannins (Itam *et al*., 2021; Mudgal *et al*., 2022; Nicoletti, 2023). Studies reveal that extracts from mistletoe parts, including the roots, stems and leaves of mistletoe are used as antibacterials for *Staphylococcus aureus, Salmonella typhi, Pseudomonas* and *Eschericia coli* because they contain flavonoids and quercetin (Bacińska *et al*., 2023; Sakyiamah *et al*., 2023; Szurpnicka *et al*., 2020). Apart from that, mistletoe extract can also be used as a source of antioxidants because it contains flavonoids and phenols (Kleszken *et al*., 2022; Olas, 2024; Pietrzak & Nowak, 2021). Based on these studies, mistletoe has good potential as a source of new medicinal ingredients. However, the insufficient number of mistletoe, especially mistletoe roots, is an obstacle to being used as a source of medicine even though mistletoe haustoria have great potential to be developed as medicinal raw materials. Therefore, another alternative is needed to meet the need for natural medicinal ingredients that do not disturb biodiversity, namely endophytic fungi.

Endophytic fungi live symbiotically in host plant tissue, creating no problems or symptoms (Hashem *et al*., 2023; Wijesekara & Xu, 2023). Endophytic fungi may duplicate and change molecules from their host plants, allowing them to create bioactive substances that are either the same or different from them (Alam *et al*., 2021; Ebadi *et al*., 2024; Toppo *et al*., 2024). Many findings reveal that endophytic fungi extracts derived from plants, notably species with therapeutic qualities, exhibit outstanding bioactivity comparable to or even better than their hostplants (Elfita *et al*., 2023; Galindo-Solís & Fernández, 2022; Oktiansyah *et al*., 2024; Santra & Banerjee, 2022; Shen *et al*., 2023). As a result, the extraction and isolation of compounds from endophyticfungi is successful and efficient due to the short culture time, allowing the bioactive compounds to be employed when needed. The endophytic fungus from mistletoe haustoria is hypothesized to create bioactive chemicals with antioxidant activity, preventing free radicals from causing illness. This endophytic fungal technique uses extremely little plant biomass, so it does not harm nature conservation, and the bioactive chemicals are generated in a short period. This study examines the endophytic fungi found in mistletoe roots and their bioactivity.

MATERIALS AND METHODS

Plant Sample

The mistletoe (*D. pentandra*) used was a parasite that lives on lime. People believe that the mistletoe that lives in lime (*Citrus aurantifolia*) has medicinal properties. Mistletoe haustoria were obtained from Ogan Ilir Regency, South Sumatra. The plant has rootbeen identified in the Generasi Biologi Indonesia with number 302/UN9.1.7/4/EP/2021. Samples were taken fresh. Isolation of endophytic fungi was performed using haustoria tissue. Based on information from the local community, they usually used the leaves and haustoria as traditional medicine. However, the leaves part has been studied related to the host and its endophytic fungi. Therefore, this study used the haustoria to isolate its endophytic fungi and explore its bioactivity.

Table 1. Information about sample (Informasi tentang sampel).

Name of Sample (*Nama Sampel*)	**Latitude** (*Lintang*)	**Longitude** (*Bujur*)	**Altitude** (*Ketinggian*) **(m)**	**Soil pH** (*pH Tanah*)	**Temperature** (*Suhu*) **(℃)**	**Humidity** (Kelembaban) **(%)**	**Sample Colector** (*Kolektor Sampel*)	**Date** (*Tanggal*)	**Time** (*Waktu*)
Dendrophtoe pentandra	-3.207183	104.645507°	52	6,2	29	79	Ummi Hiras Habisukan	13 January 2023	09.00 WIB

Isolation of Endophytic Fungi

Endophytic fungal isolation begins with disinfection of *D. pentandra*'s haustoria surface. The haustoria were thoroughly cleansed with running water for around 5 minutes. Then, soak in 70% alcohol for around two minutes. Rinse briefly with sterile distilled water, then soak for one minute in 3% (w/v) sodium hypochlorite (NaOCl). The sterilized haustoria surface was aseptically cut. Samples were inoculated on potato dextrose agar plates and cultivated for one to two weeks at room temperature. The observation were made every day until the mold was visible. The fungal colonies that form around the haustoria on plates containing PDA medium with varying morphological properties (color, size, and texture) are purified. The mycellia was extracted from the colony, transferred to a plate with new PDA media, and cultured at room temperature for 48 hours. Purified fungal colonies are then put into the culture media (Gakuubi *et al*., 2021; Hapida *et al*., 2022).

Morphological Identification of Endophytic Fungi

Morphological characteristics of endophytic fungi were identified using both microscopic and macroscopic methods. Colony traits to look for include the colour of the colonies, the texture of the colony, the presence of exudate drop, radial lines, and concentric circles. Microscopic characterization analysis uses the slide culture technique, which involves investigating hyphae, spore, colour, and other specific features under a microscope at up to 1000X magnification. The macroscopic and microscopic characterizations were then matched to the several literatures (Walsh *et al*., 2018; Watanabe, 2010) and other relevant identification journals.

Extraction and Cultivation

To develop endophytic fungal isolates, 6 pure culture agar blocks (diameter ± 6 mm) were placed in 300 cc potato dextrose broth medium. Each isolate was grown in 15 culture bottles with a maximum capacity of 300 mL. The culture was then kept at room temperature in static conditions for four weeks. Filter paper was used to separate medium from biomass. The growing medium was then partitioned and extracted three times using ethyl acetate solvent (1:1). A rotary evaporator was used to extract the ethyl acetate. An oven set at 45°C was used to concentrate the extract (Habisukan *et al*., 2021; Simamora *et al*., 2021).

Antioxidant Activity Test

The DPPH technique was used to determine the antioxidant activity. Endophytic fungal ethyl acetate extracts were diluted in methanol to concentrations of 1000, 500, 250, 125, 62.5, 31.25, and 15.625 µg/mL. 0.2 mL of extract was mixed with 3.8 mL of 0.5 mM of DPPH. The liquid was homogenized before being stored in a dark tube for 30 minutes. A UVVis spectrophotometer was used to detect the absorption at λmax 517nm. The antioxidant standard in this test was ascorbic acid. Percent inhibition of DPPH and the IC_{50} value were used to determine the antioxidant activity (Abbas *et al*., 2021; Molyneux P, 2003):

$$\% \text{ Inhibition} = \frac{A_k - A_s}{A_s}$$

A_k = Absorbance of control
A_s = Absorbance of samples

Antibacterial Activity Test.

The Kirby-Bauer technique was used to determine antibacterial activity on MHA (Muller Hinton Agar) medium. The bacterial was *E. coli*, *S. typhi*, *S. aureus*, and *B. subtilis*. A 400 µg dose of endophytic fungal extract was dripped onto blank paper discs. DMSO was used to dilute the mushroom extract. Tetracycline (at 30 µg/disc) was employed as the positive control. The test disc paper was put on MHA medium infected with bacteria. The plate was then placed in 37°C for 1x24 hours, after which the inhibitory zone was seen. A caliper was used to measure the diameter of the resulting inhibitory zone. The criteria for assessing the antibacterial activity of the sample and the width of the inhibition zone are obtained using the following formula (Aini *et al*., 2022; Syarifah *et al*., 2021):

strong: $\frac{A}{B}$x 100% > 70 %; medium: 50 % <$\frac{A}{B}$x 100% ≤ 70 %; weak: $\frac{A}{B}$x 100% <50 %

A: Inhibition zone of sample
B: Inhibition zone of antibiotic as standard

RESULTS

Isolation and Identification of Endophytic Fungi

Isolation of endophytic fungi in haustoria of *D. pentandra* found four isolates (codes BR1-BR4). The colonies of the Four endophytic fungal isolates had different macroscopic features (shapes and colour) and unique microscopic properties (Figure 1). The colonies that formed were cream-colored, brownish-white, and black. Tables 2 and 3 show the findings of macroscopic and microscopic observations of the properties of endophytic fungal isolates, respectively.

Table 2. Characteristics of Endophytic Fungi Colonies Isolated from Haustoria of Mistletoe (*Karakteristik Jamur endofit yang diisolasi dari haustorium benalu*)

Code (*Kode*)	**Surface Colony** (*Warna Permukaan koloni*)	**Reverse Colony** (*Warna Sebalik Koloni*)	**Structure** (*Struktur*)	**Elevation** (*Bentuk Puncak*)	**Pattern** (*Pola*)	**Exudate Drops** (*Tetes Eksudat*)	**Radial line** (*Garis Radial*)	**Concentric circle** (*Lingkaran Konsentris*)
BR1	White (*Putih*)	White (*Putih*)	Cottony (*Berbulu*)	Rugose (*Berkerut*)	Zonate (*Membentuk Zonasi*)	-	-	√
BR2	Brown to yellow (*Coklat Kekuningan*)	Brown to yellow (*Coklat Kekuningan*)	Cottony (*Berbulu*)	Umbonate (*Memuncak pada bagian tengah*)	Zonate (*Membentuk Zonasi*)	-	√	√
BR3	White (*Putih*)	White (*Putih*)	Cottony (*Berbulu*)	Umbonate (*Memuncak pada bagian tengah*)	Zonate (*Membentuk Zonasi*)	-	-	-
BR4	Black (*Hitam*)	Black (*Hitam*)	Cottony (*Berbulu*)	Umbonate (*Memuncak pada bagian tengah*)	Zonate (*Membentuk Zonasi*)	-	-	-

Table 3. Microscopic Characteristics of Endophytic Fungi Colonies Isolated from Haustoria of Mistletoe (*Karakteristik Mikroskopis kolobi Jamur endofit yang diisolasi dari haustorium benalu*)

Isolate (*Isolat*)	**Spore** (*Spora*)	**Shape** (*Bentuk*)	**Hyphae** (*Hifa*)	**Characteristic** (*Karakteristik*)	**Species of Identification** (*Spesies Identifikasi)*
BR1	Conidia (*Konidia*)	Subglobose	Septate (*Bersekat*)	Hyaline chlamydospores. (*Klamidospora hialin*)	*Pythium* sp.
BR2	Conidia (*Konidia*)	Subglobose	Septate (*Bersekat*)	Conidia are formed in small groups, septate hyphae, hyaline hyphae. (*Konidia terbentuk dalam kelompok kecil, hifa bersepta, hifa hialin*)	*Trichoderma* sp.
BR3	Conidia (*Konidia*)	Cylinder	Septate (*Bersekat*)	Hyaline septate hyphae, monophialid conidiophores. (*Hifa bersepta hialin, konidiofor monofialid*)	*Fusarium* sp.
BR4	Spore (*Spora*)	Subglobose	Septate (*Bersekat*)	Sporangiofor tegak bercabang, Septated hyphae are dark colored. (*Sporangiofor tegak bercabang, hifa bersepta berwarna gelap*)	*Mortierella* sp.

Tables 2 and 3 summarize the morphological properties of endophytic fungal colonies collected from the haustoria of mistletoe (*D. pentandra*) for each isolate. There were four genera of endophytic fungus detected, namely Pythium (BR1), Trichoderma (BR2), Fusarium (BR3), and Mortierella (BR4). Four isolates of endophytic fungus were identified based on the morphological traits that showed (both macroscopic and microscopic).

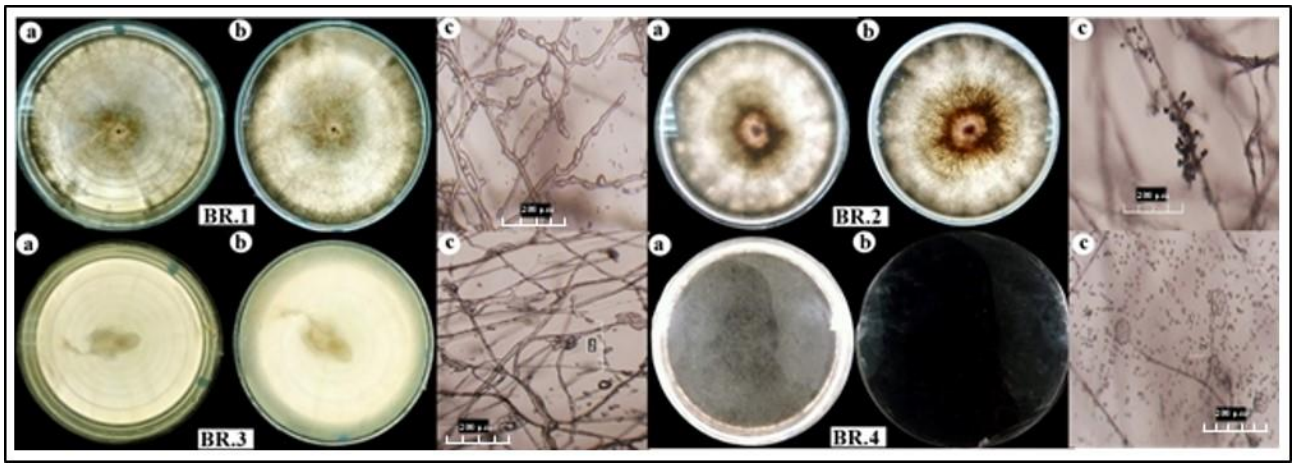

Figure 1. Morphology of Endophytic Fungi from Mistletoe Haustoria, Notes: a. Front view of the colony; b. Reverse appearance of the colony; c. Microscopic characteristics (100x/0.65); Video Digital Microscope Hyrox. (*Morfologi Jamur Endofit dari Haustorium Benalu, Catatan: a. Tampak depan koloni; b. Tampak belakang koloni; c. Karakteristik mikroskopis (100x/0,65); Mikroskop Digital Video Hyrox.*).

Antioxidant and Antibacterial Activity of Endophytic Fungi Extract

Endophytic fungi isolated from mistletoe haustoria using ethyl acetate solvent have antibacterial and antioxidant activities (Table 4). The studied extract shown antibacterial activity against *S. typhi*, *E. coli*, *B. subtilis*, and *S. aureus*, as well as significant antioxidant activity. One endophytic fungal extract revealed excellent antibacterial activity against the four tested pathogens, as well as highly strong antioxidant activity (IC_{50} < 20 µg/mL), namely isolate BR4 (*Mortierella* sp.).

Table 4. Antibacterial activity of mistletoe haustoria endophytic fungus extract compared with tetracycline and antioxidant activity compared with ascorbic acid as a standard antioxidant (*Aktivitas antibakteri ekstrak jamur endofit haustorium benalu dibandingkan dengan tetrasiklin dan aktivitas antioksidan dibandingkan dengan asam askorbat sebagai antioksidan standar*)

Code Isolate (*Kode Isolat*)	**Genus/Identified Species** (*Genus/Spesies yang teridentifikasi*)	**Weight of extract** (*Berat Ekstrak*) **(gr)**	**% Antibacterial Activity** (*% Aktivitas Antibakteri*)				**IC_{50} (µg/mL)**
			E. coli	***S. typhi***	***S. aureus***	***B. subtilis***	
Methanol extract of host plant		2.8	71.6 ± 0.22 ***	71.40 ±0.35 ***	74.45 ±0.05 ***	75.53 ±0.31 ***	16.68****
BR1	*Pythium* sp.	1.2	65.16± 0.35 **	64.35 ±1.68 **	75.9 ± 0.35 ***	76.4±1.68 ***	44.56 ***
BR2	*Trichoderma* Sp.	1.2	66.8±0.18 **	65.2 ±0.05 **	74.7 ± 0.62 ***	72.4 ±1.68 ***	24.34 ***
BR3	*Fusarium* sp.	1.4	61.3 ±1.11 **	62.6±0.11 **	68.1 ± 0.72 **	65.3 ±0.39 **	82.19 ***
BR4	*Mortierella* sp.	1.2	78.1 ± 0.72 ***	72.6 ± 0.84 ***	80.6 ± 0.75 ***	79.6±0.11 ***	19.09 ****
	Positive Control (Kontrol Positif)		Tetracyclin 100 ***	Tetracyclin 100 ***	Tetracyclin 100 ***	Tetracyclin 100 ***	Ascorbic Acid 10,08****

Note: Antibacterial activity percentage: *** strong (≥ 70%), **moderate (50-70%), and *weak (< 50%). Antioxidant activity IC_{50} (µg/mL): ****very strong < 20 µg/mL ***strong < 100 µg/mL; **moderat 100-500 µg/mL; * weak > 500 µg/mL. (*Catatan: Persentase aktivitas antibakteri: *** kuat (≥ 70%), **sedang (50-70%), dan *lemah (< 50%). IC50 aktivitas antioksidan (µg/mL): ****sangat kuat < 20 µg/mL ***kuat< 100 µg/mL; **sedang 100-500 µg/mL; *lemah > 500 µg/mL*).

Table 4 shows the bioactivity of endophytic fungal extracts obtained from haustoria of *D. pentandra* and their host plants. The methanol extract of the host plant showed stronger antibacterial and antioxidant activity when compared with the endophytic fungal extract. Endophytic fungal extracts provided antibacterial effects in various categories ranging from moderate to strong against the four tested bacteria. BR4 exhibited the most potential bioactivity. However, when compared with standards, the antibacterial percentage and IC_{50} of endophytic fungal extracts are still lower. The percentage of antibacterial activity and IC_{50} value of the endophytic fungal isolate BR4 are closest to the values of tetracycline and ascorbic acid as standards.

DISCUSSION

Based on morphological identification, the BR4 isolate was *Mortierella* sp. The *Mortierella* genus is a fungus that is often found in soil habitats, including the alpine and subalpine zones (Huymann *et al*., 2024; Probst *et al*., 2024; Zuo *et al*., 2022). The characteristic of spores that spread easily through the air (aerosol) has the potential to be a means of spreading the fungus of the genus *Mortierella* (Hough *et al*., 2023; Wang *et al*., 2022). This fungus has been reported to be non-pathogenic to humans and animals, but several species of this fungus are pathogenic to plants. Even though it is pathogenic to plants, research has revealed that the ability of the fungus of the *Mortierella* genus spreads quickly and can be associated with medicinal plants (Corbu *et al*., 2023; Nicola *et al*., 2021; Probst *et al*., 2024). Endophytic fungi can develop secondary metabolite molecules due to their fungal invasion capacity. Fungi isolated from medicinal plants have been shown in investigations to exhibit high bioactivity (Hashem *et al*., 2023; Jamal *et al*., 2022; Manganyi & Ateba, 2020; Muthukrishnan *et al*., 2022; Toppo *et al*., 2024). This demonstrates that the *Mortierella* genus present in mistletoe haustoria may produce secondary metabolites found in the host plant. Several investigations have indicated that the *Mortierella* genus isolated from medicinal plants has great bioactivity because the chemicals they contain have comparable structures to their hosts.

Table 4 demonstrates the bioactivity of endophytic fungal extracts derived from the haustoria of *D. pentandra* and their host plants. The extract from the host plant outperforms the endophytic fungal extract in terms of antibacterial and antioxidant activity. This is largely due to the more complex and diverse secondary metabolite content in the host plant. These secondary metabolites, including polyphenols, flavonoids, alkaloids and tannins, play a crucial role in protecting the plant against pathogens and environmental stress (Itam *et al*., 2021; Mudgal *et al*., 2022; Nicoletti, 2023). These compounds also have strong antibacterial and antioxidant properties, which contribute to the plant's effectiveness in combating microorganisms and neutralizing free radicals. This is because plants have developed more sophisticated chemical defense systems over time. These compounds often have broader modes of action, enabling plants to combat a wide range of bacteria and withstand oxidative stress. Some plants produce antimicrobial compounds that target bacterial cell walls or interfere with bacterial metabolic processes, offering effective protection against infections (Bouslamti *et al*., 2022; Fitri *et al*., 2023; Jamal *et al*., 2022; Roy *et al*., 2024; Singh *et al*., 2024; Witoyo & Utoro, 2023).

In contrast, while endophytic fungi can also produce bioactive compounds, they typically have a simpler secondary metabolite composition than the host plant. Endophytic fungi primarily focus on their symbiotic relationship with the host plant, generating compounds that support the growth or defense of the plant, but with more limited antibacterial and antioxidant capacity (Kumari *et al*., 2023; Ozyigit *et al*., 2023; Qiu *et al*., 2023). Moreover, the ability of endophytic fungi to produce bioactive compounds depends greatly on the species and environmental conditions, so their activity is not always consistent or as potent as that of the host plant (Peng *et al*., 2021; Santra & Banerjee, 2022). Overall, while the extracts from endophytic fungi show promise in terms of bioactivity, the host plant extracts tend to be more effective due to their more complex and varied secondary metabolites. This makes the host plant a superior source for producing stronger and more effective antibacterial and antioxidant compounds capable of fighting pathogens and preventing oxidative damage.

Research shows that the extract produced by *Mortierella* has very strong antioxidant activity and strong antibacterial activity against the testing bacteria (Table 3). Various studies show that the endophytic fungi of the genus *Mortierella* contain secondary metabolite compounds including carotenoids, flavonoids and phenolics as their dominant secondary metabolites (Ozimek & Hanaka, 2021; Samadlouie *et al*., 2014; Wani *et al*., 2017; Zhu *et al*., 2002). Phenolic compounds exhibit structural variety, including the presence, quantity, and location of hydroxyl group substitution, as well as the length of saturated side chains, which provide these compounds the capacity to operate as antioxidants and antibacterials (Arnold *et al*., 2023; Kauffmann & Castro, 2023; Kruk *et al*., 2022; Lobiuc *et al*., 2023). According to this biological mechanism, the endophytic fungi of the genus *Mortierella* isolated from the haustoria of mistletoe *D. pentandra*, can be exploited as a prospective source of natural compounds for medical reasons, with necessary additional investigation.

CONCLUSION

This study identified four endophytic fungi, namely *Pythium* sp., *Trichoderma* sp., *Fusarium* sp., and *Mortierella* sp.. The fungus *Mortierella* sp. has very strong antioxidant and strong antibacterial activity. In future studies, isolation of antioxidant and antibacterial compounds will be carried out which have not been reported yet for use in advanced research, such as in vivo tests.

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AUTHOR CONTRIBUTIONS

ROk: designed the research and supervised all the processes. UHH: collected and analyzed the data. N; SSAN; IF; and ROc; assisted with the laboratory work.

REFERENCES

Abbas, S., Shanbhag, T., Kothare, A. 2021. Applications of bromelain from pineapple waste towards acne. *Saudi Journal of Biological Sciences*, *28*(1), pp.1001–1009.

Aini, K., Elfita, Widjajanti, H., Setiawan, A., Kurniawati, A.R. 2022. Antibacterial activity of endophytic fungi isolated from the stem bark of jambu mawar (*Syzygium jambos*). *Biodiversitas*, *23*(1), pp.521–532.

Alam, B., Lǐ, J., Gě, Q., Khan, M.A., Gōng, J., Mehmood, S., Yuán, Y., Gǒng, W. 2021. Endophytic Fungi: From Symbiosis to Secondary Metabolite Communications or Vice Versa? *Frontiers in Plant Science*, *12*, pp.1–24.

Arnold, W. A., Blum, A., Branyan, J., Bruton, T.A., Carignan, C.C., Cortopassi, G., *et al*. 2023. Quaternary Ammonium Compounds: A Chemical Class of Emerging Concern. *Environmental Science and Technology*, *57*(20), pp.7645–7665.

Asase, A. (2023). Ghana's herbal medicine industry: prospects, challenges and ways forward from a developing country perspective. *Frontiers in Pharmacology*, *14*, pp.1–9.

Bacińska, Z., Baberowska, K., Surowiak, A.K., Balcerzak, L., Strub, D.J. 2023. Exploring the Antimicrobial Properties of 99 Natural Flavour and Fragrance Raw Materials against Pathogenic Bacteria: A Comparative Study with Antibiotics. *Plants*, *12*(21). https://doi.org/10.3390/plants12213777

Bouslamti, M., El Barnossi, A., Kara, M., Alotaibi, B. S., Al Kamaly, O., Assouguem, A., Lyoussi, B., Benjelloun, A.S. 2022. Total Polyphenols Content, Antioxidant and Antimicrobial Activities of Leaves of *Solanum elaeagnifolium* Cav. from Morocco. *Molecules*, *27*(13). https://doi.org/10.3390/molecules27134322

Corbu, V.M., Gheorghe-Barbu, I., Dumbravă, A. Ștefania, Vrâncianu, C.O., Șesan, T.E. 2023. Current Insights in Fungal Importance—A Comprehensive Review. *Microorganisms*, *11*(6), pp.1–52.

Courric, E., Brinvilier, D., Couderc, P., Ponce-mora, A., Vanessa, M., Sylvestre, M., Jeannie, H.,

Vaillant, J., Rousteau, A., Bejarano, E., Cebrian-torrejon, G. 2023. *An Ethnopharmacological Approach*. pp.1–19.

Ebadi, M., Ahmadi, F., Tahmouresi, H., Pazhang, M., Mollaei, S. 2024. Investigation the biological activities and the metabolite profiles of endophytic fungi isolated from Gundelia tournefortii L. *Scientific Reports*, *14*(1), pp.1–11.

Elfita, Oktiansyah, R., Mardiyanto, Widjajanti, H., Setiawan, A., Nasution, S.S.A. 2023. Bioactive Compounds of Endophytic Fungi *Lasiodiplodia theobromae* Isolated From The Leaves of Sungkai (*Peronema canescens*). *Biointerface Research in Applied Chemistry*, *13*(6). https://doi.org/10.33263/BRIAC136.530

Fitri, Y., Yusni, Y., Suryadi, T., Mudatsir, M. 2023. Characteristic and bioactivities value of Nypa fruticans from coastal area in West Aceh District, Indonesia as a candidate antidiabetic agent. *Biodiversitas*, *24*(10), pp.5260–5269.

Gakuubi, M.M., Munusamy, M., Liang, Z.X., Ng, S.B. 2021. Fungal endophytes: A promising frontier for discovery of novel bioactive compounds. *Journal of Fungi*, *7*(10). https://doi.org/10.3390/jof7100786

Galindo-Solís, J.M., Fernández, F.J. 2022. Endophytic Fungal Terpenoids: Natural Role and Bioactivities. *Microorganisms*, *10*(2), pp.1–22.

Gao, H., Huang, W., Zhao, C., Xiong, Y. 2024. An ethnoveterinary study on medicinal plants used by the Bai people in Yunlong County northwest Yunnan, China. *Journal of Ethnobiology and Ethnomedicine*, *20*(1), pp.1–14.

Habisukan, U.H., Elfita, Widjajanti, H., Setiawan, A., Kurniawati, A.R. 2021. Diversity of endophytic fungi in syzygium aqueum. *Biodiversitas*, *22*(3), pp.1129–1137.

Hapida, Y., Elfita, Widjajanti, H., Salni. 2022. Tritirachium oryzae and Other Endophytic Mediated Jambu Bol (*Syzygium malaccense*) are Potential as an Antioxidant. *Science and Technology Indonesia*, *7*(2), pp.220–227.

Hashem, A.H., Attia, M.S., Kandil, E.K., Fawzi, M.M., Abdelrahman, A.S., Khader, M.S., Khodaira, M.A., Emam, A.E., Goma, M.A., Abdelaziz, A.M. 2023. Bioactive compounds and biomedical applications of endophytic fungi: a recent review. *Microbial Cell Factories*, *22*(1), pp.1–23.

Hough, B., Steenkamp, E., Wingfield, B., Read, D. 2023. Fungal Viruses Unveiled: A Comprehensive Review of Mycoviruses. *Viruses*, *15*(5). https://doi.org/10.3390/v15051202

Huymann, L. R., Hannecker, A., Giovanni, T., Liimatainen, K., Niskanen, T., Probst, M., Peintner, U., Siewert, B. 2024. Revised taxon definition in European Cortinarius subgenus Dermocybe based on phylogeny, chemotaxonomy, and morphology. *Mycological Progress*, *23*(1). https://doi.org/10.1007/s11557-024-01959-z

Itam, A., Wati, M.S., Agustin, V., Sabri, N., Jumanah, R.A., Efdi, M. 2021. Comparative Study of Phytochemical, Antioxidant, and Cytotoxic Activities and Phenolic Content of *Syzygium aqueum* (Burm. f. Alston f.) Extracts Growing in West Sumatera Indonesia. *Scientific World Journal*, *2021*. https://doi.org/10.1155/2021/5537597

Jamal, H.A.A., Husaini, A., Sing, N.N., Roslan, H.A., Zulkharnain, A., Akinkunmi, W.A. 2022. Characterization of bioactive compounds produced by endophytic fungi isolated from *Gynura procumbens* (Sambung Nyawa). *Brazilian Journal of Microbiology*, *53*(4), pp.1857–1870.

Kauffmann, A.C., Castro, V.S. 2023. Phenolic Compounds in Bacterial Inactivation: A Perspective from Brazil. *Antibiotics*, *12*(4), pp.1–24.

Kleszken, E., Purcarea, C., Pallag, A., Ranga, F., Memete, A.R., Miere, F., Vicas, S.I. 2022. Phytochemical Profile and Antioxidant Capacity of *Viscum album* L. Subsp. album and Effects on Its Host Trees. *Plants*, *11*(22), pp.1–19.

Kruk, J., Aboul-Enein, B. H., Duchnik, E., Marchlewicz, M. 2022. Antioxidative properties of phenolic compounds and their effect on oxidative stress induced by severe physical exercise. *Journal of Physiological Sciences*, *72*(1), pp.1–24.

Kumari, P., Deepa, N., Trivedi, P.K., Singh, B.K., Srivastava, V., Singh, A. 2023. Plants and endophytes interaction: a “secret wedlock” for sustainable biosynthesis of pharmaceutically

important secondary metabolites. *Microbial Cell Factories*, *22*(1), pp.1–19.
Li, H., Huang, C., Li, Y., Wang, P., Sun, J., Bi, Z., Xia, S., Xiong, Y., Bai, X., Huang, X. 2024. Ethnobotanical study of medicinal plants used by the Yi people in Mile, Yunnan, China. *Journal of Ethnobiology and Ethnomedicine*, *20*(1). https://doi.org/10.1186/s13002-024-00656-1
Lobiuc, A., Pavăl, N. E., Mangalagiu, I. I., Gheorghiță, R., Teliban, G. C., Amăriucăi-Mantu, D., & Stoleru, V. 2023. Future Antimicrobials: Natural and Functionalized Phenolics. *Molecules*, *28*(3). https://doi.org/10.3390/molecules28031114
Manganyi, M.C., Ateba, C.N. 2020. Untapped potentials of endophytic fungi: A review of novel bioactive compounds with biological applications. *Microorganisms*, *8*(12), pp.1–25.
Mitropoulou, G., Stavropoulou, E., Vaou, N., Tsakris, Z., Voidarou, C., Tsiotsias, A., Tsigalou, C., Taban, B. M., Kourkoutas, Y., Bezirtzoglou, E. 2023. Insights into Antimicrobial and Anti-Inflammatory Applications of Plant Bioactive Compounds. *Microorganisms*, *11*(5), pp.1–15.
Molyneux, P. 2003. The use of the stable free radical diphenylpicryl-hydrazyl (DPPH) for estimating antioxidant activity. *Songklanakarin Journal of Science and Technology*, 50, pp.211–219.
Mudgal, G., Kaur, J., Chand, K., Parashar, M., Dhar, S.K., Singh, G.B., Gururani, M.A. 2022. Mitigating the Mistletoe Menace: Biotechnological and Smart Management Approaches. *Biology*, *11*(11). https://doi.org/10.3390/biology11111645
Muthukrishnan, S., Prakathi, P., Sivakumar, T., Thiruvengadam, M., Jayaprakash, B., Baskar, V., Rebezov, M., Derkho, M., Zengin, G., Shariati, M.A. 2022. Bioactive Components and Health Potential of Endophytic Micro-Fungal Diversity in Medicinal Plants. *Antibiotics*, *11*(11). https://doi.org/10.3390/antibiotics11111533
Nicola, L., Landínez-Torres, A.Y., Zambuto, F., Capelli, E., Tosi, S. 2021. The mycobiota of high altitude pear orchards soil in colombia. *Biology*, *10*(10), pp.1–17.
Nicoletti, M. 2023. The Antioxidant Activity of Mistletoes (*Viscum album* and Other Species). *Plants*, *12*(14). https://doi.org/10.3390/plants12142707
Oktiansyah, R., Widjajanti, H., Setiawan, A., Elfita. 2024. Antioxidant and Antibacterial Activity of Endophytic Fungi Isolated from Fruit of Sungkai (*Peronema canescens*). *Science and Technology Indonesia*, *9*(1), pp.17–27.
Olas, B. 2024. *The cardioprotective potential of selected species of mistletoe*. *Front Pharmacol* 15, p.1395658.
Ozimek, E., Hanaka, A. 2021. Mortierella species as the plant growth-promoting fungi present in the agricultural soils. *Agriculture (Switzerland)*, *11*(1), pp.1–18.
Ozyigit, I.I., Dogan, I., Hocaoglu-Ozyigit, A., Yalcin, B., Erdogan, A., Yalcin, I.E., Cabi, E., Kaya, Y. 2023. Production of secondary metabolites using tissue culture-based biotechnological applications. *Frontiers in Plant Science*, *14*(June), pp.1–28.
Paller, C.J., Wang, L., Fu, W., Kumar, R., Durham, J.N., Azad, N.S., Laheru, D.A., Browner, I., Kachhap, S.K., Boyapati, K., Odeny, T., Armstrong, D.K., Meyer, C.F., Gaillard, S., Brahmer, J. R., Page, I., Wang, H., Diaz, L.A. 2023. Phase I Trial of Intravenous Mistletoe Extract in Advanced Cancer. *Cancer Research Communications*, *3*(2), pp.338–346.
Pelzer, F., Loef, M., Martin, D.D., Baumgartner, S. 2022. Cancer-related fatigue in patients treated with mistletoe extracts: a systematic review and meta-analysis. *Supportive Care in Cancer*, *30*(8), pp.6405–6418.
Peng, X., Wu, B., Zhang, S., Li, M., Jiang, X. 2021. Transcriptome Dynamics Underlying Chlamydospore Formation in *Trichoderma virens* GV29-8. *Frontiers in Microbiology*, *12*(June), pp.1–23.
Pietrzak, W., Nowak, R. 2021. Impact of harvest conditions and host tree species on chemical composition and antioxidant activity of extracts from *Viscum album* l. *Molecules*, *26*(12). https://doi.org/10.3390/molecules26123741
Probst, M., Telagathoti, A., Mandolini, E., Peintner, U. 2024. Fungal and bacterial communities and their associations in snow-free and snow covered (sub-)alpine Pinus cembra forest soils. *Environmental Microbiome*, *19*(1), pp.1–23.

Qiu, S., Cai, Y., Yao, H., Lin, C., Xie, Y., Tang, S., Zhang, A. 2023. Small molecule metabolites: discovery of biomarkers and therapeutic targets. *Signal Transduction and Targeted Therapy*, *8*(1), pp.1–37.

Rojas, P., Jung-Cook, H., Ruiz-Sánchez, E., Rojas-Tomé, I.S., Rojas, C., López-Ramírez, A.M., Reséndiz-Albor, A.A. 2022. Historical Aspects of Herbal Use and Comparison of Current Regulations of Herbal Products between Mexico, Canada and the United States of America. *International Journal of Environmental Research and Public Health*, *19*(23). https://doi.org/10.3390/ijerph192315690

Roy, S., Sarkar, T., Chakraborty, R. 2024. Enhancing nutritional profile, antioxidant capacity, sensory characteristics, and shelf life of coconut snowball (Naru) through *Borassus flabellifer* endosperm substitution. *Discover Food*, *4*(1). https://doi.org/10.1007/s44187-024-00098-4

Sakyiamah, M. M., Gordon, P. K., Bolah, P., Baffour, P. K., Ehun, E., Quasie, O., Kumadoh, D., Archer, M.A., Mintah, S.O., Appiah, A.A. 2023. Assessment of the phytochemical composition and antimicrobial properties of *Tapinanthus bangwensis* leaves hosted by the branches of *Persea americana*. *BMC Complementary Medicine and Therapies*, *23*(1), pp.1–10.

Samadlouie, H.R., Hamidi-Esfahani, Z., Alavi, S.M., Varastegani, B. 2014. Expression analysis for genes involved in arachidonic acid biosynthesis in *Mortierella alpina* CBS 754.68. *Brazilian Journal of Microbiology*, *45*(2), pp.439–445.

Santra, H.K., Banerjee, D. 2022. Bioactivity study and metabolic profiling of *Colletotrichum alatae* LCS1, an endophyte of club moss Lycopodium clavatum L. *PLoS ONE*, *17*(4 April), pp.1–29.

Shen, N., Chen, Z., Cheng, G., Lin, W., Qin, Y., Xiao, Y., Chen, H., Tang, Z., Li, Q., Yuan, M., Bu, T. 2023. Diversity, chemical constituents and biological activities of endophytic fungi from *Alisma orientale* (Sam.) Juzep. *Frontiers in Microbiology*, *14*(June), pp.1–16.

Simamora, A.V., Hahuly, M.V., Henuk, J.B. 2021. Endophytic fungi as potential biocontrol agents of *Phytophthora palmivora* in the cocoa plant. *Biodiversitas*, *22*(5), pp.2601–2609.

Singh, H., Kumar, S., Arya, A. 2024. Evaluation of antibacterial, antioxidant, and anti-inflammatory properties of GC/MS analysis of extracts of Ajuga. integrifolia Buch.-Ham. leaves. *Scientific Reports*, *14*(1), pp.1–13.

Staupe, H., Buentzel, J., Keinki, C., Buentzel, J., Huebner, J. 2023. Systematic analysis of mistletoe prescriptions in clinical studies. *Journal of Cancer Research and Clinical Oncology*, *149*(9), pp.5559–5571.

Sukhikh, S., Babich, O., Prosekov, A., Kalashnikova, O., Noskova, S., Bakhtiyarova, A., Krol, O., Tsvetkova, E., Ivanova, S. 2023. Antidiabetic Properties of Plant Secondary Metabolites. *Metabolites*, *13*(4). https://doi.org/10.3390/metabo13040513

Syarifah, Elfita, Widjajanti, H., Setiawan, A., Kurniawati, A.R. 2021. Diversity of endophytic fungi from the root bark of Syzygium zeylanicum, and the antibacterial activity of fungal extracts, and secondary metabolite. *Biodiversitas*, *22*(10), pp.4572–4582.

Szurpnicka, A., Kowalczuk, A., Szterk, A. 2020. Biological activity of mistletoe: in vitro and in vivo studies and mechanisms of action. In *Archives of Pharmacal Research* (Vol. 43, Issue 6). Pharmaceutical Society of Korea. https://doi.org/10.1007/s12272-020-01247-w

Toppo, P., Jangir, P., Mehra, N., Kapoor, R., Mathur, P. 2024. Bioprospecting of endophytic fungi from medicinal plant *Anisomeles indica* L. for their diverse role in agricultural and industrial sectors. *Scientific Reports*, *14*(1), pp.1–18.

Walsh, T.J., Hayden, R.T., Larone, D. H. 2018. Larone's Medically Important Fungi. In *Larone's Medically Important Fungi*. https://doi.org/10.1128/9781555819880

Wang, Y., Wang, L., Suo, M., Qiu, Z., Wu, H., Zhao, M., Yang, H. 2022. Regulating Root Fungal Community Using *Mortierella alpina* for *Fusarium oxysporum* Resistance in Panax ginseng. *Frontiers in Microbiology*, *13*(May). https://doi.org/10.3389/fmicb.2022.850917

Wani, Z. A., Kumar, A., Sultan, P., Bindu, K., Riyaz-Ul-Hassan, S., Ashraf, N. 2017. *Mortierella alpina* CS10E4, an oleaginous fungal endophyte of *Crocus sativus* L. enhances apocarotenoid

biosynthesis and stress tolerance in the host plant. *Scientific Reports*, *7*(1), pp.1–11.
Watanabe, T. 2010. Pictorial Atlas of Soil and Seed Fungi. In *Pictorial Atlas of Soil and Seed Fungi*. https://doi.org/10.1201/ebk1439804193
Wijesekara, T., Xu, B. 2023. Health-Promoting Effects of Bioactive Compounds from Plant Endophytic Fungi. *Journal of Fungi*, *9*(10). https://doi.org/10.3390/jof9100997
Witoyo, J.E., Utoro, P.A.R. 2023. Phytochemicals - Bioactivity of Avicennia marina Leaves Extract, and Its Application in Food Products: A Brief Literature Review. *Rona Teknik Pertanian*, *16*(2), pp.114–127.
Yousefvand, S., Fattahi, F., Hosseini, S. M., Urech, K., Schaller, G. 2022. Viscotoxin and lectin content in foliage and fruit of *Viscum album* L. on the main host trees of Hyrcanian forests. *Scientific Reports*, *12*(1), pp,1–9.
Zhu, M., Zhou, P.P., Yu, L.J. 2002. Extraction of lipids from *Mortierella alpina* and enrichment of arachidonic acid from the fungal lipids. *Bioresource Technology*, *84*(1), pp.93–95.
Zuo, Y., He, P., Zhang, J., Li, W., Ning, D., Zeng, Y., Yang, Y., Xia, C., Zhang, H., Deng, H. 2022. Contrasting Responses of Multispatial Soil Fungal Communities of Thuja sutchuenensis Franch., an Extremely Endangered Conifer in Southwestern China. *Microbiology Spectrum*, *10*(4), pp.1–17.