

Secondary Metabolite of Endophytic Fungi *Daldinia eschscholtzii* from The Leaves of *Syzygium polyanthum*

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Abstract

Salam (*Syzygium polyanthum*) is a plant that is often used by Indonesian people as traditional medicine. The leaves are consumed to treat various diseases. This study reports the endophytic fungi found from *S. polyanthum* leaves and its secondary metabolites. Endophytic fungi species were determined through morphological and molecular identification. The extraction process used ethyl acetate as a solvent and potato dextrose broth medium for growing. Antioxidant tests were carried out by using the DPPH method. Secondary metabolites were isolated using chromatographic methods, and the chemical makeup was determined through spectroscopic analysis. The sample was identified as *Daldinia eschscholtzii* by the findings of the morphological and molecular analyses. The secondary metabolite obtained from this endophytic fungi was identified as fonsecinone A with good antioxidant activity. The secondary metabolite has the potential to become a source of antioxidants through further research.

Keywords

Antioxidant, *Daldinia eschscholtzii*, Endophytic Fungi, Secondary Metabolite, *Syzygium polyanthum*

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1. INTRODUCTION

Salam (*Syzygium polyanthum*) has been utilized by the community as a traditional medicine to address conditions linked to oxidative stress, inflammation, and degenerative disorders (Aditya et al., 2022; Amir Rawa et al., 2022; Sabandar et al., 2022). The leaves have historically been used to cure ailments including diabetic mellitus, hypertension, ulcers, gastritis, high cholesterol, and skin conditions (Uddin et al., 2022; Widyawati et al., 2022). The results of the phytochemical screening described that bay leaf extract contains alkaloids, tannins, steroids, triterpenoids, phenols, essential oils, sesquiterpenes, and flavonoids (Rival et al., 2019; Stan et al., 2021). These ingredients have activity in medicine and physiological activity which indicates a potential source for useful drugs, especially being capable to counteract body's presence of free radicals (Elshafie et al., 2023; Nwozo et al., 2023; Ullah et al., 2020).

Free radicals are compounds that are produced in situ by normal cell metabolism or from external sources such as smoking, prolonged sun exposure, psychological or emotional stress,

unhealthy eating habits. Free radicals and oxidants can cause a phenomenon known as oxidative stress, or the emergence of chronic and degenerative disease processes such as cancer, hypertension, diabetes, cataracts, aging, autoimmune diseases, rheumatoid arthritis, cardiovascular and neurodegenerative disorder (Alzheimer's and Parkinson's disease) (Martemucci et al., 2022; Moazzen et al., 2022). Antioxidants are one of the strategies in dealing with free radicals, namely by breaking the chain or preventing the occurrence of free radicals. Antioxidant compounds are used by several industries, such as the food, pharmaceutical, and agricultural sectors, to treat health issues caused by oxidative stress, and numerous studies have demonstrated the antioxidant activity of bioactive substances like phenolic acids, phenylpropanoids, flavonoids, lignins, and tannins (Ayoka et al., 2022; Flieger et al., 2021; Veljković et al., 2022). Currently, there is a strong trend to look for large, to replace synthetic antioxidants with easily available and effective natural sources and decrease cell damage (López-Pedrouso et al., 2022; Parcheta et al., 2021; Samodien et al., 2019). In terms of productivity, Indonesian medicinal plant agriculture still confronts several challenges such as organizing medicinal

plant cultivation activities and maintaining their quality. To overcome this, endophytic fungi are the focus of research to find new compounds (Khalil et al., 2021; Rodrigo et al., 2021).

One of the key factors influencing development of novel drugs is natural compounds produced by endophytic fungus (Ahmed et al., 2023; Elawady et al., 2023; Elfita et al., 2022a; Hapida et al., 2022; Stelmasiewicz et al., 2023; Tammam et al., 2023; Zhu et al., 2023). The bulk of secondary metabolites generated by endophytic fungus have a different chemical structure, according to various studies (Li et al., 2023; Liu et al., 2023; Oktiansyah et al., 2023c; Rodrigo et al., 2021; Song et al., 2023; Stelmasiewicz et al., 2023). Bioactive compounds are abundant in endophytic fungus that may be exploited in the pharmaceutical, agricultural, and food sectors. These compounds include antibacterial, antifungal, immunosuppressive, antiviral, antioxidant, anti-inflammatory, and anticancer properties. Alkaloids, terpenoids, steroids, lactones, quinones, flavonoids, phenols, indole derivatives, anthraquinones, xanthenes, phenylpropanoids, phenolic acids, and peptides are some of these substances (Amr et al., 2023; Elfita et al., 2022b; Gu et al., 2022; Kour et al., 2022). *Daldinia eschscholtzii* is one of several types of endophytic fungi which are reported to have various secondary metabolites (Chutulo and Chalannavar, 2020; Liu et al., 2019).

The endophytic fungus *D. eschscholtzii* is a fungus that is often encountered in tropical climates (Ng et al., 2016; Wutthiwong et al., 2021). Studies report that this fungus damages wood which is characterized by white to gray colonies and attaches to decaying wood substrates. However, this new study revealed that the endophytic fungus *D. eschscholtzii* is found in various plant tissues, from leaves, stems, to roots (Adedayo and Babalola, 2023; Khruengsai et al., 2021). The compounds of endophytic fungi also vary, such as polyketide and terpenoid groups, which have excellent bioactivity. Based on the above literature studies, the bioactivity and secondary metabolites of the endophytic fungus *D. eschscholtzii* are still very limited and are still a concern for exploration to uncover their benefits, so further research is carried out to produce or prove antioxidant compounds from endophytic fungi isolated from *S. polyanthum* leaves.

2. EXPERIMENTAL SECTION

2.1 Plant Materials

Lahat City in South Sumatra was where *Syzygium polyanthum* was found. The Plant Systematics Laboratory of Sriwijaya University has identified this plant. Endophytic fungi were isolated from healthy and new plant tissues.

2.2 Chemical and Instrumentation

The materials to conduct this study were Potato Dextrose Agar (PDA), Potato Dextrose Broth (PDB) from Oxoid, alcohol 70%, NaOCl solution from Onemed, TLC Si Gel plates (Merck kieselgel 60 GF254, 0.25 mm, 20 x 20 cm, column chromatography using Merck Si Gel 60 (70–230 mesh). The organic solvents used are n-hexane, ethyl acetate, and methanol

of technical grade and distilled before use, aquabidest, 2,2-diphenyl-1-picrylhydrazyl (D9182 Sigma-Aldrich). The characterization of chemical compounds using a NMR spectrum on JEOL JNM-ECZ500R/S1 500 MHz (1H); 125 MHz (13C).

2.3 Sample Preparation and Isolation of Endophytic Fungi
the third place (counting up from the branch's base). *Syzygium polyanthum* leaves were thoroughly cleaned for 5 minutes under running water. By submerging the sample surface in 70% alcohol for about a minute and washing it with sterile distilled water for about a minute, you may sterilize it. The sample was then soaked with sodium hypochloride (NaOCl) for \pm 30 seconds, rinsed again with 70% alcohol for \pm 30 seconds, and sterile distilled water for \pm 1 minute. Sterile samples were crushed aseptically using a mortar and pestle in Laminar Air Flow. Samples were deeply inoculated on PDA medium in a petri dish, 3–7 days were spent incubating at ambient temperature. Every day, observations were made. Then, fungus colonies on PDA media with various morphological traits (shape, color, and size) were purified. Purification was accomplished by moving colonies to fresh PDA media and incubating them there for two consecutive days at room temperature. Pure colonies were transferred to culture media for observation of macroscopic and microscopic characters (Oktiansyah et al., 2023b).

2.4 Characterization and Identification of Endophytic Fungi Morphologically

When the colonies of fungi endophyte were between three and seven days old, they were observed for their color, texture (cotton, grain, powder, slimy), exudate droplet presence, radial lines, and concentric circles. The Henrici's method of slide culture was used to prepare microscope preparations in order to study microscopic properties. The spores' morphology and the existence or lack of divisions on the hyphae are examples of microscopic observations (Walsh et al., 2018). Based on newly developing macroscopic and microscopic traits and literature, identification was done (Walsh et al., 2018; Watanabe, 2002).

2.5 Endophytic Fungi Molecular Identification

The identification of the most likely endophytic fungi was done after testing their bioactivity. Internal Transcribed Spacer (ITS) DNA (rDNA)-based identification. The amplification procedure made use of the ITS1 and ITS4 primers. The Bioedit application was used to build the forward and reverse primer DNA sequence assembly and remove extraneous sequences. Accessible at <http://blast.ncbi.nlm.nih.gov/Blast.cgi>, BLAST, is then used to match up the sequences. The MEGA11 program was then used to align sample sequences with databases using the CLUSTAL W technique, and phylogenetic trees were created using the Neighbor-joining tree technique with a 1000-coefficient bootstrap (Tamura et al., 2021).

2.6 Endophytic Fungi Extraction and Cultivation

In order to grow the endophytic fungus that was isolated from the sungkai stem bark, 15 bottles of culture medium containing

300 ml of Potato Dextrose Agar (PDB) were filled with 5 blocks (5 mm in diameter) of pure culture agar. The cultures were kept in a static environment for 30 days at room temperature. After the incubation time, filter paper was used to separate the mycelia from the medium. Furthermore, the medium was extracted after being diluted with ethyl acetate (1:1). A rotary evaporator was used to separate the ethyl acetate extract from the liquid culture to be evaporated, and a 45°C oven was used to concentrate the extract. The concentrated extract is then weighed.

2.7 Antioxidant Activity Test

Antioxidant activity as measured by DPPH. Three times, methanol was used to dissolve the different endophytic fungi's ethyl acetate extracts at concentrations of 1000, 500, 250, 125, 62.5, 31.25, and 15.625 µg/mL. A 0.5 mM DPPH solution 3.8 mL in volume was added to each concentration (0.2 mL). After being homogenized, the liquid was kept in a tube of darkness for 30 minutes. utilizing a UVVis spectrophotometer with a maximum 517 nm wavelength, the absorbance value was determined (Oktiansyah et al., 2023a). In this experiment, the common antioxidant was ascorbic acid. Antioxidant activity was estimated using the IC₅₀ value and the percentage of DPPH absorption inhibition (Abbas et al., 2021).

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

A_k = Absorbance of control

A_s = Absorbance of samples

2.8 Isolation of Secondary Metabolites

Thin layer chromatography (TLC) was used to examine the amount of secondary metabolites in an ethyl acetate extract of endophytic fungus (MID9) and to determine the best eluent for the first step of separation. As much as 2 g of ethyl acetate extract was then dissolved using ethyl acetate solvent and then impregnated with silica gel 60 (70-230 mesh) with a ratio of 1:2. Separation was carried out by column chromatography (CC). The preparation of the CC was carried out by condensing a quantity of silica gel 60 (70-230 mesh) on the column with a ratio of 1:20. A higher-polarity eluent was used to elute the impregnated material after it had been introduced to the CC. The eluate was collected in vials, evaporated with an evaporator to examine the stain pattern, and then joined with other eluate with the same stain pattern to make one fraction, resulting in the production of numerous fractions.

MID9 ethyl acetate extract (2 g) was preabsorbed with 2 g silica gel 60 (70-230 mesh) and separated by column chromatography (CC) using an eluent with increased polarity, namely n-hexane:EtOAc (10:0 → 0:10) and EtOAc :methanol (10:0 → 0:10). The eluate was collected in 53 vials with a volume of 10 mL and then evaporated and TLC analysis was

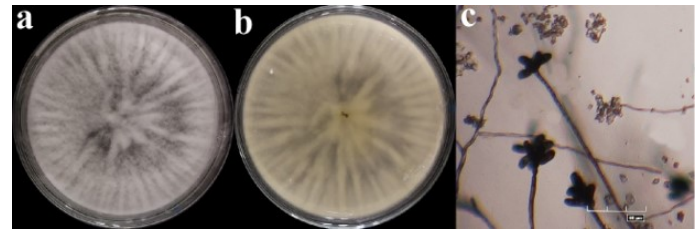


Figure 1. Colony Characteristics of the Endophytic Fungus Isolate MID9 Isolated from *S. polyanthum* Leaves (a: Front View; b: Reverse View; c: Microscopic Character)

carried out to see the stain pattern. Then, eluate with identical stain patterns were blended to create a single fraction., so that four fractions were obtained, namely F1-F4. The F3 fraction was rinsed with a solvent mixture, namely hn-hexane:EtOAc (3:7) to obtain compound 1 in the form of a yellow solid of 32.2 mg.

3. RESULTS AND DISCUSSION

3.1 Identification Morphologically

The endophytic fungus isolated in this study is a continuation of research by re-isolating the endophytic fungus isolate (MID9) from bay leaves at third position (from the base of the branch). Identification of MID9 isolates was carried out morphologically and molecularly. MID9 isolates showed macroscopic characteristics with white color (surface and reverse), cottony, rugose, and radiate while microscopic characteristics showed conidial spores, subglobose, and septate hyphae (Figure 1).

3.2 Molecular Identification

MID9 isolate molecular test showed 100% similarity with *Daldinia eschscholtzii*. Figure 2 displayed the phylogenetic tree, which had the following order: TAGGGGAAGCGGAGGACATTACTGAGTTATCTAAACTCCAACCCTATGTGAACTTACCGCCGTTGCCTCGGCCGGCCGCGTTCGCCCTGTAGTTTACTACCTGGCGGCGCGCTACAGGCCCGCCGGTGGACTGCTAAACTCTGTTATATATACGTATCTCTGAATGCTTCAACTTAATAAGTTAAACTTTCAACAA CGGATCTCTTGGTTCTGGCATCGATGAAGAACGCAGCGAAATGCCGATAAGTAATGTGAATTGCAGAATTCAGTGAATCATCGAATCTTTGAACGCACATTGCGCCCAT TAGTATTCTAGTGGGCATGCCTGTTCCGAGCGTCATT TCAACCCTTAAGCCCCCTGTTGCTTAGCGTTGGGAATCTAGGTCTCCAGGGCCTAGTTCCCCAAAGTCATCGGCGGAGTCGGAGCGTACTCTCAGCGTAGTAATACCAT TCTCGCTTTTGCAGTAGCCCCGGCGGCTTGCCGTAA AACCCTATATCTTTAGTGGTTGACCTCGAATCAGGTAGGAATACCCGCTGAACCTTAAGCATATCATAAGACGGGAGAGAAAA

The genus *Daldinia* belongs to the Ascomycota and is known as a pathogenic endophytic or latent organism. This genus is usually found in decaying wood and has been found to be non-pathogenic in humans (Chutulo and Chalannavar, 2020; Ng

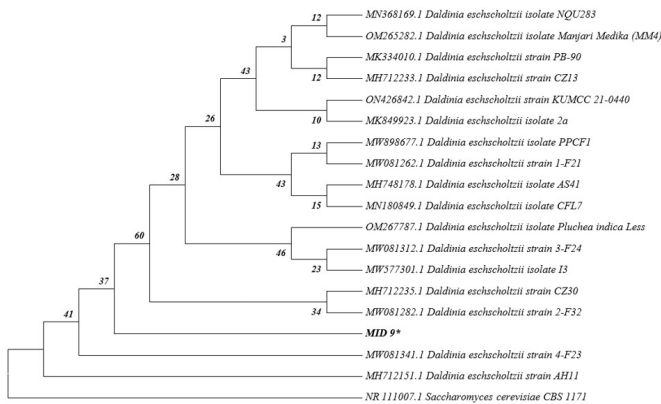


Figure 2. Phylogenetic Tree of MID9* Isolates (*Daldinia eschscholtzii*)

et al., 2016). This study found that the endophytic fungus *Daldinia eschscholtzii* was also present in plant tissues, particularly in the leaves of *S. polyanthum*. There have also been reports of this fungus in plant roots (Liao et al., 2019a; Suebrasri et al., 2020; Syamsia et al., 2021). This finding indicates that *D. eschscholtzii* is endophytic not only in stem parts, but also in other plant tissues, such as leaves and roots. Fungi that are endophytic in medicinal plants usually have the same bioactivity as their host plants (Chen et al., 2023; Khorasani et al., 2023; Mulyani et al., 2023; Wen et al., 2022). Its ability to produce secondary metabolites is very useful for host plants for defense so that the relationship between endophytic fungus and the plants they live on is mutually beneficial. This species has been reported to contain secondary metabolites with good bioactivity (Chigozie et al., 2020; Chutululo and Chalannavar, 2020; Liao et al., 2019b).

3.3 Bioactivity of Endophytic Fungi

The DPPH technique yielded an IC_{50} value of 19.9 $\mu\text{g}/\text{mL}$ in the strong category for the MID9 ethyl acetate extract's antioxidant activity. MID9 had excellent potential to be developed into a novel antioxidant material when compared to the IC_{50} value of the benchmark antioxidant ascorbic acid, which was 10.1 $\mu\text{g}/\text{mL}$.

3.4 Isolation and Identification of Secondary Metabolite

The $^1\text{H-NMR}$ (500 MHz, CDCl_3) spectrum (Figure 3) revealed that 12 proton signals were present consisting of six methyl signals with singlet multiplicity, four aromatic proton signals and two vinylic proton signals. The six methyl compounds were identified as four methoxyl groups at δ_{H} 3.95 (3H, s); 3.78 (3H, s); 3.58 (3H, s); and 3.45 ppm (3H, s), and two methyl groups, namely at δ_{H} 2.43 (3H, s) and 2.14 ppm (3H, s). The four aromatic proton signals identified two aromatic protons bound to different rings, each at δ_{H} 7.34 (1H, s); 7.24 and (1H, s) and two meta-position aromatic protons at δ_{H} 6.49 (1H, d, $J = 2$); 6.22 ppm (1H, d, $J = 2$). Two vinylic

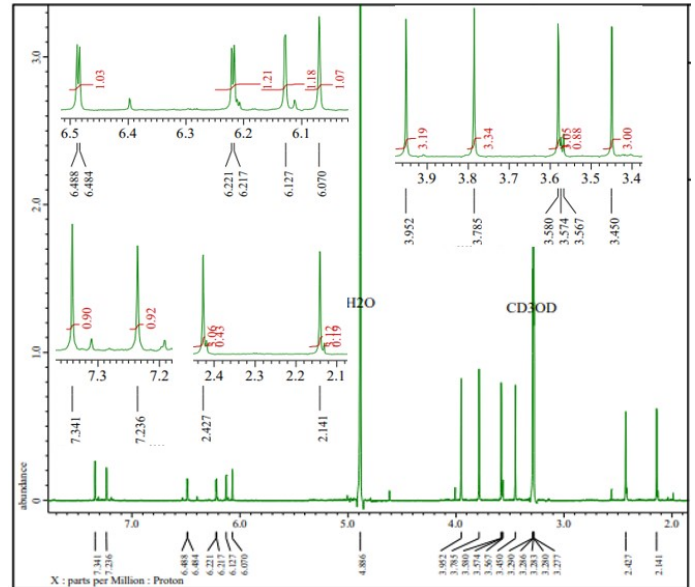


Figure 3. The $^1\text{H-NMR}$ Spectral of Compound 1

protons with singlet multiplicity appear at δ_{H} 6.13 (1H, s) and 6.07 ppm (1H, s), respectively.

The $^{13}\text{C-NMR}$ spectrum (Figure 4) shows the existence of 32 carbons with 6 carbons in the aliphatic region at $\delta_{\text{C}} < 100$ ppm and 26 carbons in the $\delta_{\text{C}} > 100$ ppm region as sp^2 carbons. The carbon signal at δ_{C} 55.2 ppm has 2x intensity compared to the other two oxy-methoxy carbon signals, namely at δ_{C} 61.2 and 54.3 ppm. This indicates the presence of an equivalent oxy-methoxy carbon. In the aromatic region, there are four signals of methine carbon with higher intensity, namely at δ_{C} 101.8; 101.7; 96.9; and 96.0. Signals with δ_{C} values of 184.8 and 184.7 ppm are typical signals of ketone carbonyl carbon. Oxy-aryl carbon and oxy-vinyl carbon signals were found on nine carbons with δ_{C} values of 169.3; 168.9; 162.0; 161.9; 161.7; 161.5; 160.9; 160.1; 157.8 ppm. Quaternary methine carbon sp^2 signals were found in eight other signals. Based on the information obtained from the $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$ spectrum, it strengthens the possibility that the structure of the isolated compounds has aromatic groups, hydroxyl groups, methoxyl, ketone carbonyl groups, and aliphatic groups in their structure.

The HMQC spectrum (Figure 5) shows the presence of 12 signal protons bonded directly to the carbon atom. The spectrum shows a correlation between the four methoxyl protons with a δ_{H} value of 3.95 (3H, s); 3.78 (3H, s); 3.58 (3H, s); 3.45 ppm (3H, s) bonded directly to the respective sp^3 carbons at δ_{C} 55.2; 55.2; 54.3; and 61.2 ppm. The two methyl protons at δ_{H} 2.43 (3H, s) and 2.14 ppm (3H, s) bind directly to δ_{C} 19.3 and 19.1 ppm, respectively. The HMQC spectrum also showed a correlation of four aromatic protons in the δ_{H} region of 6.22-7.34 ppm, and a correlation of two vinylic protons at δ_{H} 6.07 (1H, s) and 6.13 ppm (1H, s) with sp^2 carbon at δ_{C}

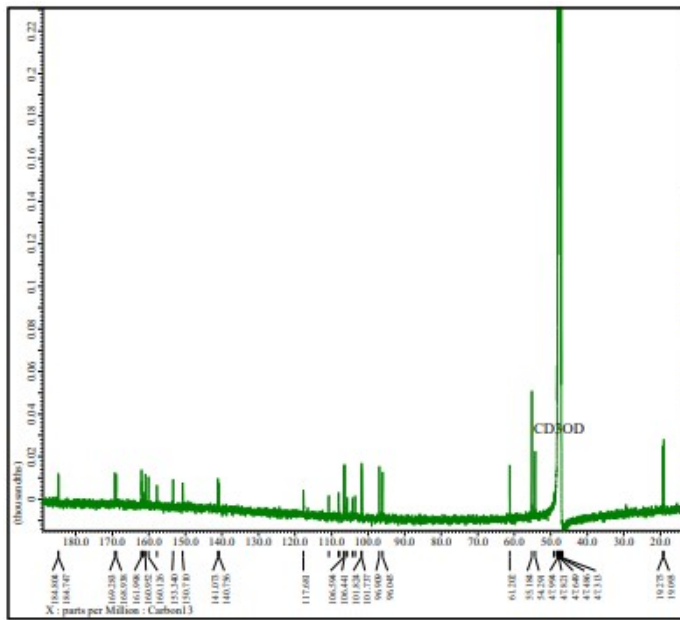


Figure 4. The ^{13}C -NMR Spectral of Compound 1

106.4 and 106.6 ppm, respectively.

The HMBC spectrum (Figure 6) displays the correlation between the four methoxyl protons at δ_{H} 3.95 (3H, s); 3.78 (3H, s); 3.58 (3H, s); and 3.45 ppm (3H, s) which correlated respectively with the oxy-methoxy carbon at δ_{C} 160.9; 160.1; 162.0; and 157.8 ppm. The four methoxyl groups are attached to two aromatic rings. This is indicated by the correlation of aromatic protons at δ_{H} 6.49 to oxy-methoxy carbon at δ_{C} 162.0 and correlation of aromatic protons at δ_{H} 7.24 ppm to oxy-methoxy carbon at δ_{C} 160.1 ppm. The methyl group proton at δ_{H} 2.43 ppm correlates with the oxy-carbon sp^2 at δ_{C} 169.3 ppm and the vinylic carbon at δ_{C} 106.6 ppm. The other methyl group proton at δ_{H} 2.14 ppm correlates with the oxy carbon sp^2 at δ_{C} 168.9 ppm and vinylic carbon at δ_{C} 106.4 ppm. This indicates that both methyl groups are attached to the aliphatic oxy-carbon sp^2 . Compound 1 has four aromatic protons of which there are two aromatic protons at the meta position. An indication of this is seen by the comparison using the aromatic proton at δ_{H} 6.49 ppm (1H, *d*, $J = 2$) to the carbon at δ_{C} 96.0; 108.0; 162.0 ppm and the correlation of an aromatic proton at δ_{H} 6.22 ppm (1H, *d*, $J = 2$) to a carbon at δ_{C} 96.9; 105.7; 108.0 ppm. The next two aromatic protons with singlet cleavage lie in different rings three bonds apart. This indication is seen by the correlation between the proton and the aromatic carbon through three bonds. Aromatic proton at δ_{H} 7.34 ppm (1H, s) to aromatic methine carbon at δ_{C} 101.7 ppm and correlation of aromatic proton at δ_{H} 7.24 ppm (1H, s) to aromatic methine carbon at δ_{C} 101.8 ppm. Table 1 displays the 1D and 2D NMR spectra data for compound 1.

Compound 1 was identified as a phenolic chemical based on data from 1D and 2D NMR spectroscopy consisting of four

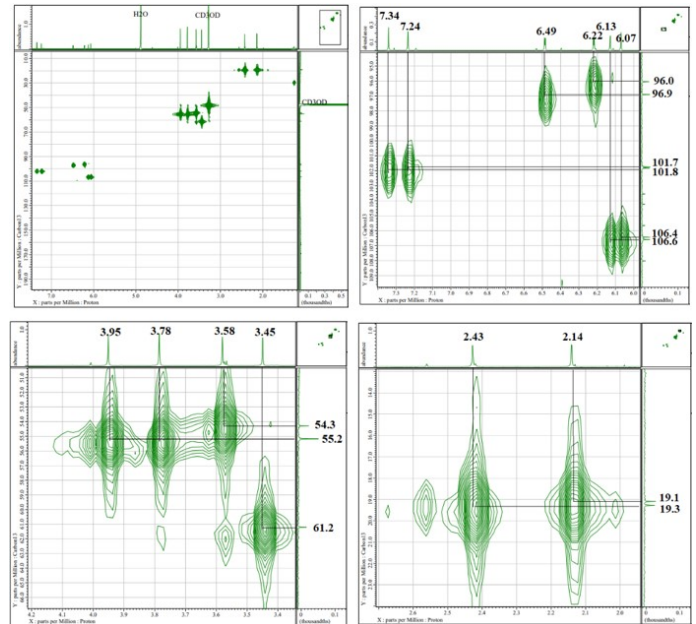


Figure 5. The HMQC Spectral of Compound 1

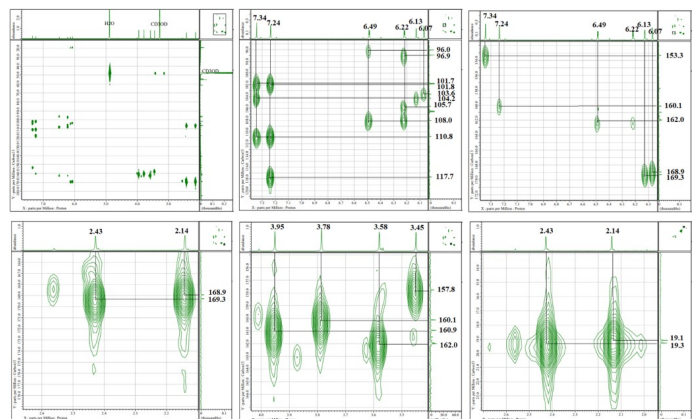


Figure 6. The HMBC Spectral of Compound 1

aromatic rings with four aromatic protons, two pyranone rings with two vinylic protons, two hydroxyl groups, four methoxyl groups, and two methyl groups. Identification of the structure of compound 1 was compared with the same compound from the literature, namely compound 1* which was isolated from the *Aspergillus aculeatus* from the leaves of *Melia azedarach* (Campos et al., 2005). So, the fonsecinone A compound's molecular structure is suggested. Figure 7 depicts the molecular structure of compound 1, including the numbering of carbon atoms, the location of the protons' and carbons' chemical shifts, and the HMBC correlation.

According to test results, compound 1's IC_{50} value for antioxidant activity was $54.3 \mu\text{g}/\text{mL}$, which was lower than the antioxidant activity value of the ethyl acetate extract. This might be due to the MID9 extract contained additional antioxidants that haven't been separated. Another hypothesis is that

Table 1. The NMR Data of Compound 1 (¹H-500 MHz, ¹³C-125 MHz in CDCl₃) and 1* (1H-400 MHz, ¹³C-100 MHz in CDCl₃)

No. C	δ _C ppm 1	δ _H ppm (σH. Multiplicity, Hz)1	HMBC 1	δ _C ppm 1*	δ _H ppm (σH. Multiplicity, Hz)1*
2	169.3			167.5	
2-CH ₃	19.3	2.43 (3H, s)	169.3 ; 106.6	20.6	2.49 (3H, s)
3	106.6	6.13 (1H, s)	19.3 ; 169.3	110.7	6.34 (1H, s)
4	184.7			183.0	
4a	110.8			109.4	
5-OH	157.8			156.7	12.85 (1H, s)
6	101.8	7.34 (1H, s)	101.7 ; 104.2 ; 110.8 ; 153.3	106.1	7.06 (1H, s)
6a	141.1			140.8	
7	101.7	7.24 (1H, s)	101.8 ; 110.8 ; 117.7 ; 160.1	101.6	6.97 (1H, s)
8	160.1			160.0	
8-OCH ₃	55.2	3.78 (3H, s)	160.1	56.0	3.79 (3H, s)
9	117.7			117.2	
10	157.8			156.9	
10-OCH ₃	61.2	3.45 (3H, s)	157.8	61.3	3.44 (3H, s)
10a	104.2			108.0	
10b	153.3			155.1	
2'	168.9			166.9	
2'-CH ₃	19.1	2.14 (3H, s)	168.9 ; 106.4	20.7	2.13 (3H, s)
3'	106.4	6.07 (1H, s)	19.1 ; 103.6 ; 168.9	107.4	6.01 (1H, s)
4'	184.8			184.6	
4'a	103.6			104.3	
5'-OH	161.9			162.8	15.27 (1H, s)
5'a	108.0			108.6	
6'	162.0			161.1	
6'-OCH ₃	54.3	3.58 (3H, s)	162.0	56.3	4.04 (3H, s)
7'	96.9	6.49 (1H, d, J = 2)	96.0 ; 108.0 ; 162.0	97.0	6.43 (1H, d, J = 2.2)
8'	160.9			161.6	
8'-OCH ₃	55.2	3.95 (3H, s)	160.9	55.2	3.63 (3H, s)
9'	96.0	6.22 (1H, d, J = 2)	96.9 ; 105.7 ; 108.0	96.3	6.19 (1H, d, J = 2.2)
9'a	140.8			140.6	
10'	105.7			105.0	
10'a	150.7			150.8	

the elements in the MID9 ethyl acetate extract synergize to provide a high level of antioxidant activity.

Compounds produced by *D. eschscholtzii* from bay leaves (Figure 7) showed medium antioxidant activity (IC₅₀ < 100 µg/mL). According to studies, the antioxidant action is enhanced by hydroxyl groups at particular locations on the aromatic ring. At least, one hydroxyl group in ring A (especially at C-7) is essential for the bioactivity of flavonoids (Adamczak et al., 2019; Liu et al., 2022; Mutha et al., 2021; Thebti et al., 2023; Zulkefli et al., 2023). However, there are studies which reveal that a number of hydroxyl groups on two aromatic rings can reduce the antibacterial effect (Diksha et al., 2023; Hasan et al., 2023; Stuper Szablewska et al., 2022; Świsłocka et al., 2023). The findings of this study were consistent with the notion that the specific placement of the hydroxyl group can

modify bioactivity, and several studies have demonstrated that the hydroxyl group also significantly affects antioxidant activity. The substance's chemical makeup, including the amount of hydroxyl groups, where para is located in the aromatic ring, and how esterified it is, all have a direct bearing on its antioxidant capability. Studies explain that removing hydroxyl groups can reduce coplanarity which can diminish a substance's capacity to scavenge free radical (Lv et al., 2021; Platzer et al., 2022). The antioxidant properties of quercetin can be neutralized by substituting a methyl or glycosyl group for the group of hydroxyl at its position (C3). The same amount of aromatic rings have hydroxyl groups attached, phenolic acids' antioxidant properties do not change noticeably (Laoué et al., 2022; Šamec et al., 2021; Wang et al., 2021). The antioxidant activity of 4-hydroxy-3-methoxy benzoic acid is greater than

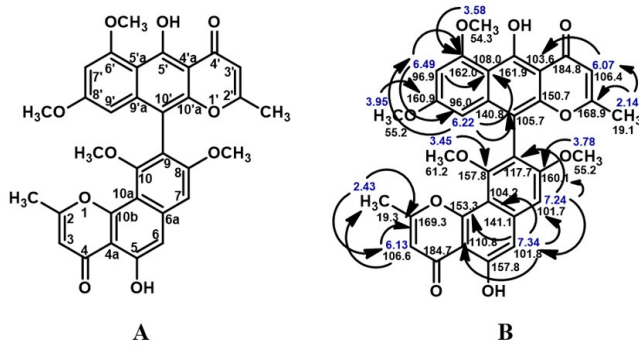


Figure 7. Structure of Compound 1, Fonsecinone A with Numbering of Carbon Atom (A), Placement of Proton Chemical Shifts, Carbons, and HMBC Correlation (B)

that of Methoxy-3-hydroxy-4-benzoic acid (Aytac et al., 2023; Dobros et al., 2022; Heryanto et al., 2023). This indicates that the position of the hydroxyl group significantly affects the antioxidant properties of a compound. In this study, compound fonsecinone A has a double bond with hydroxyl groups, causing this compound to be active as an antioxidant.

4. CONCLUSION

The pure compound found from *Daldinia eschscholtzii* found in the leaves of *S. polyanthum* was fonsecinone A. This compound has lower antioxidant activity than the ethyl acetate extract. For the development of this endophytic fungus as a source of antioxidant compounds, ethyl acetate extract was preferred. If we want to choose the fonsecinone A compound as an antioxidant material, it is necessary to carry out further research with structural modifications.

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