

## **DISERTASI**

# **EKSPLORASI JAMUR ENDOFITIK TANAMAN CIPLUKAN *(Physalis angulata L.) YANG BERPOTENSI SEBAGAI SUMBER ANTIOKSIDAN DAN ANTIBAKTERI***

**Diajukan untuk memenuhi salah satu syarat memperoleh gelar  
Doktor pada Program Studi Doktor Ilmu MIPA Fakultas MIPA**

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2025**

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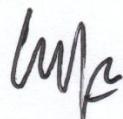
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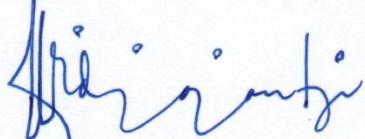
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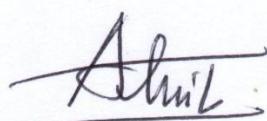
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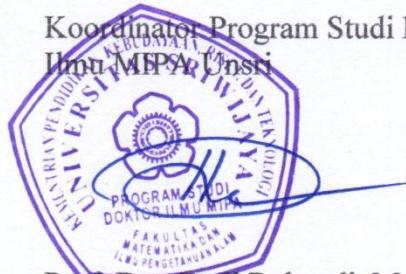
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## **HALAMAN PERSEMBAHAN**

**ومن لم يذق مر التعلم ساعة، تجرع ذل الجهل طول حياته**

“Barang siapa yang tidak merasakan pahitnya belajar sesaat, maka dia akan merasakan hinanya kebodohan seumur hidupnya”

(Muhammad bin Idris Asy-Syafi'i)

Disertasi ini ku persembahkan untuk:

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Palembang, 15 September 2025  
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## RINGKASAN

EKSPLORASI JAMUR ENDOFITIK TANAMAN CIPLUKAN (*Physalis angulata* L.) YANG BERPOTENSI SEBAGAI SUMBER ANTIOKSIDAN DAN ANTIBAKTERI

Karya Tulis Ilmiah berupa Disertasi, September 2025

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viii, 252 halaman, 70 gambar, 29 tabel, 4 lampiran

Tanaman ciplukan (*Physalis angulata* L.) telah dimanfaatkan oleh masyarakat Indonesia dan dunia sebagai obat tradisional untuk mengatasi diabetes, gusi berdarah, hipertensi, bisul, atau luka infeksi, karena efek farmakologi yang kuat sebagai antioksidan, antibakteri, hepatoprotektor, antifibrotik dan antidiare. Senyawa bioaktif tanaman ciplukan dapat diperoleh melalui jamur endofitik dengan keuntungan budidaya yang lebih singkat dan kemampuan jamur dalam menghasilkan metabolit sekunder yang mirip atau lebih baik dari inangnya. Penelitian ini bertujuan untuk menganalisis karakter fenotip dan mengidentifikasi jamur endofitik, menganalisis aktivitas antioksidan dan antibakteri ekstrak jamur endofitik, menganalisis karakterisasi dan menentukan struktur senyawa murni serta bioaktivitas dari senyawa murni tersebut. Isolasi, kultivasi dan ekstraksi jamur endofitik dilakukan untuk mengidentifikasi jenis jamur endofitik dan memperoleh ekstrak jamur endofitik. Jamur endofitik terpilih diidentifikasi secara molekuler, kemudian dianalisis menggunakan BLAST NCBI dan disusun pohon filogenetiknya menggunakan BioEdit 2.2, MEGA 11 dan iTOL. Uji aktivitas antioksidan menggunakan metode DPPH untuk ekstrak jamur endofitik dan senyawa murni. Uji aktivitas antibakteri menggunakan metode difusi *Kirby-Bauer* untuk ekstrak jamur endofitik dan senyawa murni. Senyawa murni di analisis menggunakan spektroskopi NMR dan LCMS/MS, dan penentuan struktur menggunakan ChemDraw. Berdasarkan hasil penelitian, diperoleh 47 jamur endofitik yang diisolasi dari akar (CA1-CA10), batang (CB1-CB5), daun (CD1-CD9), tangkai buah (CT1-CT6), kelopak buah (EP1-EP8) dan perikarp buah (CH1-CH2, BP1-BP7) yang terbagi menjadi 21 genera yaitu *Aspergillus*, *Bispora*, *Cladorrhinum*, *Cylindrocarpon*, *Diaporthe*, *Fusarium*, *Helicocephalum*, *Hyalodendron*, *Lasiodiplodia*, *Mortierella*, *Mucor*, *Nigrospora*, *Paecilomyces*, *Papulaspora*, *Penicillium*, *Periconia*, *Phialophora*, *Pythium*, *Trichocladium*, *Trichoderma* dan *Verticillium*. Isolasi senyawa murni dari ekstrak jamur endofitik menggunakan kromatografi kolom pada 6 isolat dengan aktivitas antioksidan dan antibakteri yang potensial. Karakterisasi senyawa menggunakan spektroskopi <sup>1</sup>H-NMR, <sup>13</sup>C-NMR, HSQC, HMBC dan LCMS/MS. Diperoleh senyawa murni *10-hydroxy-benzoisochromen-1-one* yang berasal dari isolat CA3 dan CB1. Senyawa

*7-hydroxy-benzochromen-6-one* dari isolat CA3, CA7 dan CB1. Senyawa *4,5,6-trihydroxy-2',3',5',6-tetramethyl-[3,4'-bipyranylidene]-2-one* dari isolat CB5 dan CH1. Senyawa *2-hydroxy-5-((6-methylheptyl)oxy)phenyl)(phenyl)methanone* dari isolat CD1. Senyawa tersebut diuji aktivitas antioksidan, secara berurutan menunjukkan IC<sub>50</sub>, dimulai dari senyawa *10-hydroxy-benzoisochromen-1-one* (IC<sub>50</sub> 262,68 dan 264,09 µg/mL), *7-hydroxy-benzochromen-6-one* (IC<sub>50</sub> 259,11 µg/mL, 256,13 µg/mL dan 258,20 µg/mL), *4,5,6-trihydroxy-2',3',5',6-tetramethyl-[3,4'-bipyranylidene]-2-one* (IC<sub>50</sub> 23,82 µg/mL dan 24,40 µg/mL), dan senyawa murni *2-hydroxy-5-((6-methylheptyl)oxy)phenyl)(phenyl)methanone* (IC<sub>50</sub> 137,07 µg/mL). Uji aktivitas antibakteri senyawa murni *10-hydroxy-benzoisochromen-1-one*, *7-hydroxy-benzochromen-6-one* dan *4,5,6-trihydroxy-2',3',5',6-tetramethyl-[3,4'-bipyranylidene]-2-one*, menunjukkan nilai KHM ≤64 µg/mL (kuat) pada semua bakteri uji. Selanjutnya senyawa murni *2-hydroxy-5-((6-methylheptyl)oxy)phenyl)(phenyl)methanone*, menunjukkan nilai KHM 125 µg/mL (sedang) pada bakteri *S. typhi* dan 250 µg/mL (lemah) pada bakteri uji lainnya. Berdasarkan struktur penyusunnya, semua senyawa murni tersebut merupakan golongan senyawa fenolat, kecuali senyawa dari isolat CB5 dan CH1 yang merupakan golongan bipyranylidene. Uji molekuler dari jamur endofit dengan aktivitas antioksidan dan antibakteri potensial terhadap 8 isolat, teridentifikasi spesies *Trichoderma virens* (CA3), *Papulaspora equi* (CA9), *Paecilomyces variotii* (CB5), *Lasiodiplodia theobromae* (CD1), *Fusarium equiseti* (CD8), *Diaporthe eucalyptorum* (CT5), *Penicillium citrinum* (EP6) dan *Penicillium chermesinum* (BP2). Hasil penelitian ini menunjukkan bahwa jamur endofitik yang diisolasi dari berbagai organ tanaman ciplukan memiliki potensi untuk dikembangkan menjadi antioksidan dan antibakteri alami.

Kata kunci : antibakteri, antioksidan, jamur endofitik, *Physalis angulata* L.  
Kepustakaan : 500 (2019-2025)

## SUMMARY

EXPLORATION OF ENDOPHYTIC FUNGI FROM CIPLUKAN (*Physalis angulata* L.) WITH POTENTIAL AS A SOURCE OF ANTIOXIDANTS AND ANTIBACTERIAL AGENTS

Doctoral Dissertation, September 2025

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viii, 250 pages, 70 figures, 29 tables, 4 appendices

*Physalis angulata* L. (commonly known as ciplukan) has been traditionally utilized in Indonesia and several other countries as a medicinal plant for the treatment of diabetes, bleeding gums, hypertension, boils, and infected wounds, owing to its strong pharmacological properties as an antioxidant, antibacterial, hepatoprotective, antifibrotic, and antidiarrheal agent. The bioactive compounds of *P. angulata* can also be obtained from endophytic fungi, which provide advantages such as shorter cultivation periods and the ability to produce secondary metabolites similar to, or even more potent than, those of the host plant. This study aimed to analyze the phenotypic characteristics and identify endophytic fungi, evaluate the antioxidant and antibacterial activities of their extracts, characterize and elucidate the structure of purified compounds, and assess their bioactivities. Isolation, cultivation, and extraction of endophytic fungi were conducted to identify fungal species and obtain crude extracts. Selected endophytic fungi were identified molecularly, analyzed using NCBI BLAST, and their phylogenetic relationships reconstructed with BioEdit 2.2, MEGA 11, and iTOL. Antioxidant activity was evaluated using the DPPH method, while antibacterial activity was tested by the Kirby–Bauer diffusion method, for both crude extracts and purified compounds. Purified compounds were analyzed by NMR spectroscopy and LCMS/MS, and their structures determined using ChemDraw. A total of 47 endophytic fungi were isolated from different organs of *P. angulata*, including roots (CA1–CA10), stems (CB1–CB5), leaves (CD1–CD9), fruit stalks (CT1–CT6), calyces (EP1–EP8), and pericarps (CH1–CH2, BP1–BP7). These isolates were assigned to 21 genera: *Aspergillus*, *Bispora*, *Cladorrhinum*, *Cylindrocarpon*, *Diaporthe*, *Fusarium*, *Helicocephalum*, *Hyalodendron*, *Lasiodiplodia*, *Mortierella*, *Mucor*, *Nigrospora*, *Paecilomyces*, *Papulaspora*, *Penicillium*, *Periconia*, *Phialophora*, *Pythium*, *Trichocladium*, *Trichoderma*, and *Verticillium*. Purification of bioactive compounds from six isolates with promising antioxidant and antibacterial potential was performed using column chromatography. Structural characterization was carried out by <sup>1</sup>H-NMR, <sup>13</sup>C-NMR, HSQC, HMBC and LCMS/MS analysis. The purified compounds obtained were *10-hydroxy-benzoisochromen-1-one* from isolates CA3 and CB1. *7-hydroxy-benzochromen-6-one* from isolates CA3, CA7,

and CB1. *4,5,6-trihydroxy-2',3',5',6-tetramethyl-[3,4'-bipyranylidene]-2-one* from isolates CB5 and CH1. *2-hydroxy-5-((6-methylheptyl)oxy)phenyl)(phenyl)methanone* from isolate CD1. The antioxidant activities of the isolated compounds were evaluated based on their IC<sub>50</sub> values. The results, in order, were as follows: *10-hydroxy-benzoisochromen-1-one* (IC<sub>50</sub> 262.68 and 264.09 µg/mL), *7-hydroxy-benzochromen-6-one* (IC<sub>50</sub> 259.11, 256.13, and 258.20 µg/mL), *4,5,6-trihydroxy-2',3',5',6-tetramethyl-[3,4'-bipyranylidene]-2-one* (IC<sub>50</sub> 23.82 and 24.40 µg/mL), and *2-hydroxy-5-((6-methylheptyl)oxy)phenyl)(phenyl)methanone* (IC<sub>50</sub> 137.07 µg/mL). Antibacterial assays showed that *10-hydroxy-benzoisochromen-1-one*, *7-hydroxy-benzochromen-6-one*, and *4,5,6-trihydroxy-2',3',5',6-tetramethyl-[3,4'-bipyranylidene]-2-one* exhibited strong inhibitory effects against all tested bacteria, with minimum inhibitory concentration (MIC) values ≤64 µg/mL. In contrast, *2-hydroxy-5-((6-methylheptyl)oxy)phenyl)(phenyl)methanone* displayed moderate antibacterial activity against *S. typhi* (MIC = 125 µg/mL) and weak activity against the other tested bacteria (MIC = 250 µg/mL). Structurally, all purified compounds belonged to the phenolic class, except those isolated from CB5 and CH1, which were classified as bipyranylidene derivatives. Molecular identification of eight bioactive isolates revealed them as *Trichoderma virens* (CA3), *Papulaspora equi* (CA9), *Paecilomyces variotii* (CB5), *Lasiodiplodia theobromae* (CD1), *Fusarium equiseti* (CD8), *Diaporthe eucalyptorum* (CT5), *Penicillium citrinum* (EP6), and *Penicillium chermesinum* (BP2). The findings of this study demonstrate that endophytic fungi isolated from different organs of *P. angulata* have significant potential to be developed as natural sources of antioxidant and antibacterial agents.

Keywords : antibacterial, antioxidant, endophytic fungi, *Physalis angulata* L.  
Citation : 500 (2019-2025)

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# BAB 1

## PENDAHULUAN

### 1.1 Latar Belakang

Penyakit degeneratif dan infeksi bakteri termasuk jenis penyakit yang umum diderita oleh masyarakat, baik di Indonesia maupun di dunia, serta sering menjadi fokus kajian ilmiah dalam bidang kedokteran dan farmasi. Penyakit degeneratif seperti *diabetes mellitus* (DM) dan infeksi bakteri seperti diare merupakan penyakit dengan prevalensi kematian tinggi di dunia. Data GBD (*Global Burden of Disease Study*) tahun 2021 menunjukkan, kematian akibat DM pada semua umur meningkat dari 238.100 kasus menjadi 723.700 kasus dari seluruh negara, atau naik 203,9% sejak tahun 1990. Kemudian, data jumlah DALY (*Disability Adjusted Life Years*) terkait DM pada semua umur juga meningkat dari 10,4 juta menjadi 39,3 juta, atau meningkat 276,7% dari tahun 1990. Kasus tersebut diperkirakan dapat mencapai 1,3 juta kasus kematian dan 85,5 juta untuk jumlah DALY pada semua umur di tahun 2045. Prevalensi global memperkirakan pada tahun 2030, kasus kematian mencapai 7.079 kasus dari setiap 100 ribu penduduk dunia (Huang *et al.*, 2025; Khan *et al.*, 2020). Data GBD tahun 2019 menunjukkan kematian akibat infeksi bakteri pathogen mencapai 7,7 juta dari total 13,7 juta kasus kematian dunia. Dari keseluruhan data, sebanyak 54,9% kasus infeksi disebabkan oleh bakteri jenis *Staphylococcus aureus*, *Escherichia coli*, *Streptococcus pneumoniae*, *Klebsiella pneumoniae* dan *Pseudomonas aeruginosa*. Selebihnya disebabkan oleh bakteri jenis lain (GBD, 2022; Vaart *et al.*, 2022). Penyakit DM, disebabkan oleh resistensi insulin (T2DM) atau kerusakan sel beta pankreas (T1DM). Resistensi insulin atau apoptosis sel  $\beta$ -pankreas dapat diinduksi oleh stress oksidatif akibat tingginya konsentrasi radikal bebas di dalam tubuh (Masenga *et al.*, 2023; Yavuz *et al.*, 2024). Radikal bebas dinetralisir dengan antioksidan untuk mengurangi stres oksidatif, menurunkan kerusakan sel dan menginisiasi regenerasi sel yang rusak (Chaudhary *et al.*, 2023). Kemudian, penyakit diare terjadi akibat infeksi bakteri di dalam tubuh melalui saluran cerna atau luka, ketika imun tubuh mengalami penurunan akibat jumlah atau fungsi neutrofil terlalu rendah (Nemeth & Pfleghaar, 2025). Bakteri penyebab diare seperti *Escherichia coli*, *Shigella*

*dysentriae* atau *Salmonella typhi* dapat ditemukan pada air tercemar atau makanan mentah (Teshome *et al.*, 2019). Untuk mengobati penyakit akibat radikal bebas dan infeksi bakteri diperlukan antioksidan dan antibakteri.

Antioksidan meredam radikal bebas dengan cara mendonorkan atom H dari gugus hidroksilnya (Moussa & Al-Mamary, 2021). Antioksidan sangat diperlukan tubuh, baik untuk pencegahan penyakit maupun pengobatan. Semakin beragam senyawa antioksidan, maka semakin banyak jenis radikal bebas yang dapat dinetralkan (Zehiroglu & Ozturk Sarikaya, 2019). Selanjutnya, antibakteri membunuh bakteri dengan cara membentuk ikatan dengan membran maupun merusak sel bakteri dengan mengikat DNA polymerase. Senyawa antibakteri, yang dalam penggunaan sehari-hari dikenal sebagai antibiotik, suatu metabolit yang dihasilkan oleh mikroorganisme, yang dapat membunuh atau menghambat pertumbuhan mikroorganisme lain (Byrne *et al.*, 2019). Antioksidan sintetik dan antibiotik tersedia banyak dalam berbagai produk yang sudah terstandar.

Penggunaan antioksidan sintetik dan antibiotik memberikan efek yang cepat dan konsisten. Namun, penggunaan yang tidak sesuai dosis dan dalam jangka waktu yang lama, berpotensi menimbulkan efek samping yang membahayakan. Antioksidan *Butylated Hydroxytoluene* (BHT) memiliki efek toksik pada sel Leydig (penghasil testosterone) tikus melalui induksi disregulasi kalsium dan disfungsi retikulum endoplasma-mitokondria (Ham *et al.*, 2020). Selanjutnya penggunaan antibiotik secara terus menerus menyebabkan bakteri resisten, seperti bakteri *Staphylococcus aureus* yang resisten terhadap antibiotik penicillin dengan tingkat resistensi 93,1% (Gizaw *et al.*, 2023). Bakteri *E. coli* resisten terhadap antibiotik sulfonamide dan trimethoprim (Mulder *et al.*, 2019). Bakteri *S. typhi* resisten terhadap antibiotik *sulfamethoxazole* dengan daya resistensi diatas 50% (Rahman, 2019). Bakteri *B. subtilis* juga resisten terhadap chloramphenicol (95,2%), erythromycin (85,7%) dan gentamicin (42,9%) (X. Jin *et al.*, 2024). Beberapa fakta tersebut mengindikasikan pentingnya eksplorasi senyawa antioksidan dan antibakteri dari bahan alam yang lebih aman dengan efek samping yang relatif kecil. Bahan alam dapat berasal dari akar, rimpang, batang, kulit batang, daun, bunga, buah atau biji. Diantara bahan alam yang berpotensi, tanaman ciplukan telah dikenal sebagai obat alami.

Tanaman ciplukan dimanfaatkan sebagai obat tradisional untuk mengatasi diabetes, gusi berdarah, hipertensi, bisul, tukak lambung, demam, atau mengobati penyakit yang terkait dengan sistem saraf pusat dan sindrom metabolik (Vargas-Arana *et al.*, 2025; Fadhillah *et al.*, 2020). Metabolit sekunder yang terdapat pada tanaman ciplukan diantaranya alkaloid, physalin, withanolides, saponin, steroid, flavonoid dan triterpenoid (Wang *et al.*, 2023a; Odusina & and Onocha, 2022) Berdasarkan penelitian, tanaman ciplukan memiliki efek farmakologi seperti antioksidan, antibakteri, antiradang, hepatoprotektor, antifibrotik dan antidiare (Pillai *et al.*, 2022; Lin *et al.*, 2020; Liu *et al.*, 2022). Tanaman obat lain yang masih satu familia (Solanaceae) memiliki potensi mirip dengan ciplukan diantaranya *Capsicum spp.*, *Solanum nigrum*, *Datura metel*, *Nicotiana tabacum*, *Withania somnifera* dan *Lycium barbarum*. Beberapa tanaman ini memiliki aktivitas antioksidan yang kuat terhadap DPPH dan antibakteri terhadap *S. aureus*, *E. coli*, *Salmonella*, *Helicobacter pylori* dan *P. aeruginosa* (Zhang *et al.*, 2025; Zhang *et al.*, 2024b; Islam *et al.*, 2023; Mikulska *et al.*, 2023; Shailabi *et al.*, 2025; Periferakis *et al.*, 2023; Romero-Luna *et al.*, 2023). Keunggulan tanaman ciplukan dibanding beberapa tanaman tersebut karena komposisi bioaktif yang kuat. Ciplukan mengandung *physalins*, *withanolides*, *polifenol* dan *flavonoid*, kombinasi yang memberikan mekanisme ganda: pemerangkap radikal bebas (antioksidan) dan gangguan dinding/virulensi bakteri (antibakteri) (Vargas-Arana *et al.*, 2025; Liang *et al.*, 2024). Fakta tersebut mendukung tanaman ciplukan untuk dipilih sebagai sampel pada penelitian ini.

Perkembangan ilmu pengetahuan dan teknologi menunjukkan metabolit sekunder yang dihasilkan tanaman ciplukan dapat diperoleh melalui jamur endofitik dalam tanaman. Jamur endofitik dapat ditemukan pada akar batang, daun, bunga dan buah yang menghabiskan setengah atau seluruh siklus hidupnya di dalam jaringan tumbuhan yang sehat, baik intraseluler maupun interseluler. Jamur endofitik memiliki kemampuan untuk meniru metabolit sekunder dari inang dan menunjukkan aktivitas farmakologis yang mirip (Wen *et al.*, 2022; Alam *et al.*, 2021). Jamur endofitik yang diisolasi dari tanaman ciplukan diantaranya *Penicillium* sp., *Hyphomycetes* sp. dan *Fusarium* sp. Jamur *Penicillium* sp, memiliki aktivitas antibakteri dengan diameter hambat sebesar 7,6 mm pada *S.*

*aureus* dan 6,4 mm pada *E. coli*. Jamur *Hypomyctes* sp., menunjukkan aktivitas antioksidan paling baik dengan nilai IC<sub>50</sub> 52,43 µg/mL (Mahardhika *et al.*, 2021). Aktivitas antibakteri dari kedua jamur tersebut terhadap bakteri *S. aureus* dan *E. coli*, memiliki nilai KHM 8 - 64 µg/mL (Palupi *et al.*, 2021). Penelitian tersebut menunjukkan jamur endofitik pada tanaman ciplukan berkhasiat sebagai antioksidan dan antibakteri, mirip seperti inangnya.

Berdasarkan keadaan global tentang bahaya penyakit degeneratif dan infeksi bakteri yang dapat menyebabkan kematian serta efek samping obat sintetik, diperlukan solusi dari bahan alam seperti tanaman ciplukan dengan potensi kuat sebagai obat alami. Khasiat obat alami tanaman ini dapat diperoleh melalui jamur endofitik. Selanjutnya karena kemampuan jamur endofitik dalam meniru metabolism sekunder inang, waktu kultivasi yang singkat dan aktivitasnya yang kuat, perlu adanya eksplorasi lebih lanjut terhadap jamur endofit yang ada pada tanaman ciplukan. Eksplorasi ini bertujuan untuk mengidentifikasi jamur endofit dari akar, batang, daun dan buah tanaman ciplukan, menguji bioaktivitas ekstrak jamur endofitik dan mengisolasi senyawa murni dari jamur tersebut dengan aktivitas paling kuat.

Penelitian ini dimulai dengan mengisolasi jamur endofitik dari organ akar, batang, daun dan buah ciplukan. Isolat jamur dipisahkan dari jamur lain untuk memperoleh isolat jamur murni yang akan digunakan pada proses karakterisasi dan kultivasi. Hasil karakterisasi akan digunakan untuk proses identifikasi fenotip, sementara untuk identifikasi molekuler akan dilakukan terhadap jamur endofitik dengan bioaktivitas paling kuat. Jamur endofitik murni dikultivasi, dipartisi dengan etil asetat kemudian diuapkan hingga diperoleh ekstrak pekat. Ekstrak yang diperoleh akan digunakan untuk uji aktivitas antioksidan dan antibakteri secara invitro. Ekstrak jamur endofitik dengan bioaktivitas paling kuat akan diisolasi senyawa murninya menggunakan kromatografi kolom gravitasi. Senyawa murni yang diperoleh akan digunakan pada uji antioksidan untuk memperoleh IC<sub>50</sub> dan uji antibakteri untuk memperoleh konsentrasi hambat minimum (KHM).

Eksplorasi jamur endofitik yang akan dilakukan pada penelitian ini bertujuan untuk mengisolasi senyawa murni berkhasiat yang dihasilkan oleh jamur endofitik, karena secara umum penelitian yang dilakukan terhadap jamur endofitik

dari tanaman ini terbatas pada bioaktivitas ekstrak jamur endofitik, bukan pada senyawa murni. Selanjutnya, senyawa murni tersebut akan dibandingkan dengan senyawa yang dihasilkan oleh inang, untuk mengetahui kemiripan struktur atau bioaktivitasnya. Senyawa murni yang dihasilkan sangat diperlukan dalam pembuatan antioksidan dan antibakteri untuk mengatasi penyakit akibat radikal bebas dan infeksi bakteri. Senyawa murni ini dapat memberikan pilihan bahan obat yang berkhasiat untuk dikembangkan pada industri farmasi.

Penelitian ini diharapkan dapat memberikan pengetahuan kepada masyarakat, akademisi, peneliti maupun praktisi kesehatan tentang jamur endofitik potensial dari tanaman obat ciplukan dan aktivitas farmakologinya. Diharapkan informasi ini mampu membangkitkan kreativitas masyarakat dalam memanfaatkan jamur endofitik secara lebih sederhana tanpa harus mengisolasi senyawa murninya, sehingga manfaat jamur endofit dari tanaman ciplukan dapat dirasakan oleh semua lapisan masyarakat.

## 1.2 Rumusan Masalah

Penyakit degeneratif dan infeksi bakteri memiliki tingkat bahaya tinggi hingga kematian. Untuk mengatasi kedua penyakit tersebut digunakan obat sintetik dengan efek yang cepat, terukur dan konsisten. Namun karena penggunaan yang tidak disiplin, timbul efek samping yang justru berbahaya. Selain itu, perubahan struktur sel pada mikroorganisme karena proses adaptasi menimbulkan resistensi obat. Keadaan ini mendorong para ilmuwan atau praktisi kesehatan untuk menemukan agen antioksidan atau antibakteri baru dari bahan alam yang sudah dikenal berkhasiat sebagai obat seperti tanaman ciplukan. Efek penyembuhan dari bahan alam relatif lebih lambat, namun efek samping atau potensi resistensi dari bahan alam relatif lebih kecil. Khasiat tanaman ciplukan tidak selalu menggunakan tanaman inang, melainkan dapat diperoleh melalui jamur endofitik. Diduga jamur endofitik memiliki bioaktivitas yang lebih kuat dibandingkan inang. Pemilihan jamur endofitik juga dikarenakan kultivasi yang singkat dan tidak memerlukan tempat yang luas. Pemanfaatan ekstrak jamur endofitik sebagai obat akan lebih kuat bioaktivitasnya menggunakan senyawa murni yang terbukti efektif sebagai antioksidan dan antibakteri. Senyawa murni diisolasi dari ekstrak jamur endofitik setelah kultivasi. Kultivasi jamur endofitik hanya menggunakan kultur murni jamur

yang sudah diidentifikasi fenotip. Karena itu, diperlukan adanya eksplorasi dan identifikasi fenotip jamur endofitik yang tumbuh dan berkembang di dalam organ tanaman ciplukan. Berdasarkan alasan tersebut, rumusan masalah dalam penelitian ini sebagai berikut.

1. Bagaimana keanekaragaman jamur endofitik yang diisolasi dari akar, batang, daun dan buah tanaman ciplukan yang dianalisis berdasarkan karakter fenotipiknya?
2. Apakah ekstrak jamur endofitik yang diisolasi dari tanaman ciplukan menunjukkan aktivitas antioksidan dan antibakteri?
3. Apakah ekstrak dan senyawa murni dari jamur endofitik yang diisolasi dari tanaman ciplukan menunjukkan aktivitas atau struktur yang mirip dengan inangnya?

### **1.3 Hipotesis**

- H1 : Jamur endofitik yang ditemukan pada tanaman ciplukan menunjukkan keanekaragaman yang tinggi berdasarkan karakter fenotipnya
- H2 : Ekstrak jamur endofitik yang diisolasi dari tanaman ciplukan menunjukkan aktivitas antioksidan dan antibakteri
- H3 : Ekstrak dan senyawa murni dari jamur endofitik tanaman ciplukan menunjukkan aktivitas dan struktur yang mirip dengan inangnya

### **1.4 Tujuan Penelitian**

Tujuan penelitian ini adalah:

1. Menganalisis karakter fenotip dan mengidentifikasi jenis jamur endofitik dari akar, batang, daun dan buah tanaman ciplukan untuk menentukan keanekaragaman jamur endofitik
2. Menganalisis aktivitas antioksidan dan antibakteri ekstrak jamur endofitik yang diisolasi dari tanaman ciplukan
3. Menganalisis karakterisasi dan menentukan struktur senyawa murni dari jamur endofitik, membandingkan struktur senyawa murni yang berasal dari jamur endofitik dengan inang, dan menganalisis aktivitas antioksidan dan antibakteri senyawa murni dari jamur endofitik

## 1.5 Kebaruan Penelitian

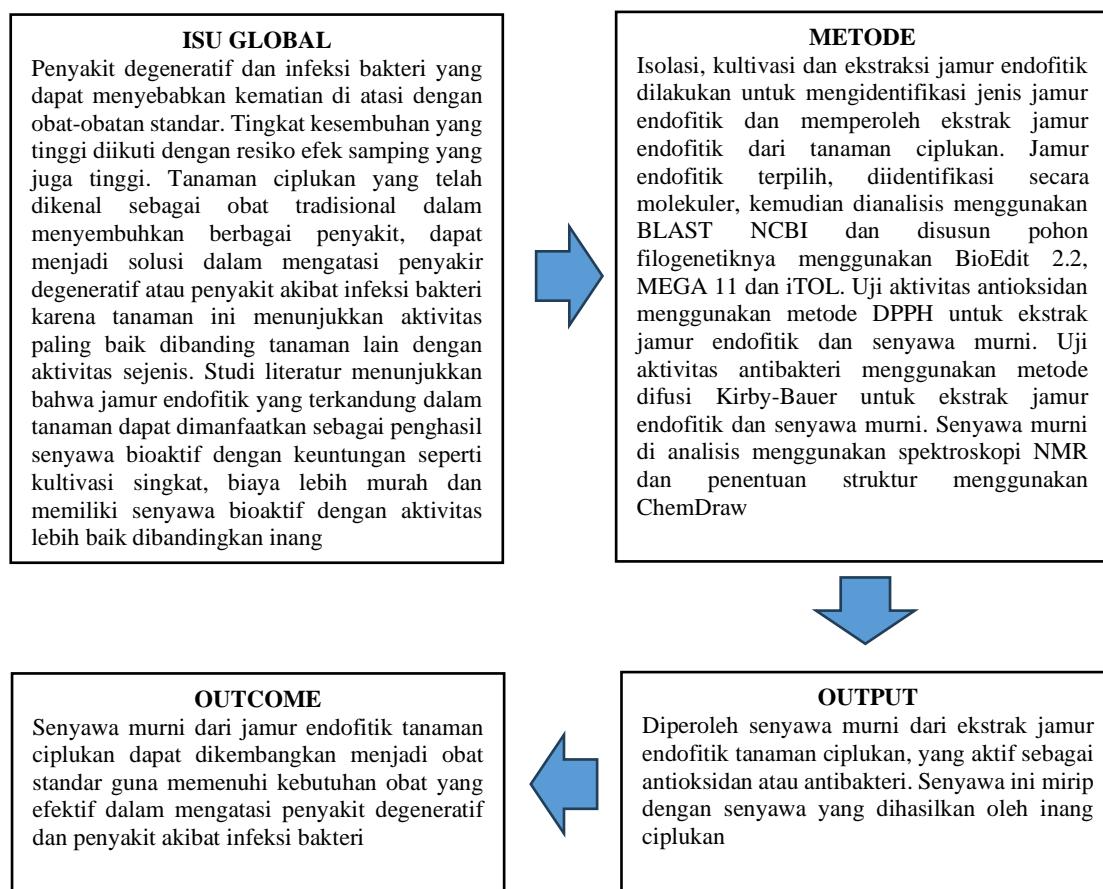
Jamur endofitik yang berhasil diisolasi dari akar, batang, daun dan buah (tangkai, kelopak, perikarp) tanaman ciplukan, diidentifikasi berdasarkan karakter fenotip. Genera jamur endofitik ini belum pernah ditemukan sebelumnya pada tanaman ciplukan yaitu *Bispora*, *Cladorrhinum*, *Cylindrocarpon*, *Diaporthe*, *Helicocephalum*, *Lasiodiplodia*, *Mortierella*, *Mucor*, *Nigrospora*, *Paecilomyces*, *Papulaspora*, *Periconia*, *Phialophora*, *Pythium*, *Trichocladium*, dan *Verticillium*. Analisis molekuler terhadap jamur endofitik terpilih menunjukkan spesies yang baru ditemukan pada ciplukan yaitu *Trichoderma virens* (CA3/akar), *Papulaspora equi* (CA9/akar), *Paecilomyces variotii* (CB5/batang), *Lasiodiplodia theobromae* (CD1/daun), *Fusarium equiseti* (CD8/daun), *Diaporthe eucalyptorum* (CT5/tangkai), *Penicillium citrinum* (EP6/kelopak) dan *Penicillium chermesinum* (BP2/perikarp). Jamur endofitik menunjukkan aktivitas antioksidan tertinggi pada isolat CT5 (tangkai buah) dengan nilai IC<sub>50</sub> 14,11 µg/mL dan antibakteri tertinggi pada isolat CA3 (akar) dengan presentase hambat 73,91%-96,15%. Aktivitas ini lebih kuat dari penelitian terdahulu (IC<sub>50</sub> 52,43 µg/mL dan diameter hambat 7,6 mm). **Kebaruan** pada penelitian ini adalah senyawa murni yang berhasil diisolasi menunjukkan struktur yang berbeda dari inang. Senyawa tersebut antara lain *10-hydroxy-benzoisochromen-1-one* dihasilkan oleh isolat CA3 (*Trichoderma virens*) dan CB1 (*Papulaspora*). Senyawa *7-hydroxy-benzochromen-6-one* dihasilkan oleh isolat CA3 (*Trichoderma virens*), isolat CA7 (*Verticillium*) dan CB1 (*Papulaspora*). Senyawa *4,5,6-trihydroxy- 2',3',5',6' -tetramethyl- [3,4'-bipyrranylidene]-2-one* dihasilkan oleh isolat CB5 (*Paecilomyces variotii*) dan CH1 (*Fusarium*). Senyawa *2-hydroxy-5- ((6-methylheptyl) oxy) phenyl (phenyl) methanone* dihasilkan oleh isolat CD1 (*Lasiodiplodia theobromae*). Uji aktivitas antioksidan senyawa murni ditunjukkan dengan nilai IC<sub>50</sub> yaitu *10-hydroxy-benzoisochromen-1-one* (IC<sub>50</sub> 262,68 dan 264,09 µg/mL) *7-hydroxy-benzochromen-6-one* (IC<sub>50</sub> 259,11 µg/mL, 256,13 µg/mL dan 258,20 µg/mL), *4,5,6-trihydroxy- 2',3',5',6' -tetramethyl-[3,4'-bipyrranylidene]-2-one* (IC<sub>50</sub> 23,82 µg/mL dan 24,40 µg/mL), dan senyawa murni *2-hydroxy-5-((6-methylheptyl) oxy)phenyl (phenyl) methanone* (IC<sub>50</sub> 137,07 µg/mL). Uji aktivitas antibakteri senyawa murni dengan nilai KHM ≤64 µg/mL (kuat) pada senyawa *10-hydroxy-*

*benzoisochromen-1-one, 7-hydroxy-benzochromen -6-one dan 4,5,6- trihydroxy -2',3',5',6 -tetramethyl -[3,4'-bipyrranylidene]-2-one.* Selanjutnya nilai KHM  $\geq 65 \mu\text{g/mL}$  (sedang dan lemah) pada senyawa *2-hydroxy-5-((6-methylheptyl)oxy)phenyl)(phenyl) methanone*.

## 1.6 Manfaat Penelitian

Penelitian ini diharapkan dapat memberikan pengetahuan kepada masyarakat, akademisi, peneliti maupun praktisi kesehatan tentang keanekaragaman jamur endofitik dari tanaman ciplukan, bioaktivitas ekstrak jamur endofitik, spesies jamur endofitik potensial, dan senyawa murni dari ekstrak jamur endofitik potensial. Selain itu, senyawa murni jamur endofitik yang berhasil diisolasi dapat bermanfaat untuk dikembangkan menjadi obat standar dalam mengobati penyakit degeneratif atau penyakit akibat infeksi bakteri.

## 1.7 Kerangka Pikir Penelitian



## 1.8 State of The Art

Tanaman ciplukan telah digunakan secara tradisional untuk mengatasi demam, infeksi, gangguan liver, diabetes, dan peradangan kronis. Penelitian telah mengkonfirmasi bahwa ekstrak dari berbagai bagian tanaman ciplukan seperti buah, daun, batang dan akar, mengandung senyawa sekunder seperti *withanolides* dan *physalins* yang menunjukkan aktivitas antimikroba, anti-inflamasi, antidiabetik, dan antioksidan yang signifikan. Studi kimia-farmakologis pada ciplukan mengungkapkan lebih dari 350 senyawa withanolide, termasuk physangulidines A–C, yang menunjukkan efek antiproliferatif terhadap sel tumor. Beberapa physalin, seperti physalin F, telah dilaporkan memiliki aktivitas imunsupresif terhadap sel mononuklear pasien dengan HTLV-1-associated myelopathy. Selain itu, aktivitas inhibisi nitric oxide oleh ekstrak tanaman ini telah menunjukkan potensi sebagai agen anti-inflamasi melalui modulasi jalur NF-κB. Secara keseluruhan, data kimia dan bioaktivitas mendukung penggunaan tradisional ciplukan sebagai sumber senyawa terapeutik alami (Vargas-Arana *et al.*, 2025; Wang *et al.*, 2021b).

Eksplorasi senyawa tidak terhenti pada inang tanaman ciplukan. Perhatian dunia juga tertuju pada mikroorganisme yang hidup simbiotik di dalam jaringan tanaman yaitu jamur endofitik. Jamur endofitik telah diakui sebagai reservoir metabolit sekunder bioaktif seperti alkaloid, polifenol, terpenoid, steroid, isokumarin, dan lain-lain yang memiliki potensi antikanker, antioksidan, antimikroba, dan antidiabetik (Ebadi & Ebadi, 2024). Studi umum menunjukkan jamur endofitik dari genus *Colletotrichum*, *Penicillium*, *Fusarium*, dan *Epicoccum* mampu menghasilkan senyawa dengan aktivitas farmakologis kuat, termasuk taxol dan emodin (Hashem *et al.*, 2023). Khusus tanaman ciplukan, terdapat 14 isolat jamur endofitik dari bunga, batang, daun, dan kelopak buah tanaman, menunjukkan aktivitas antioksidan dan antibakteri. Jamur endofitik *Hyphomycetes* (dari bunga) menunjukkan aktivitas antioksidan moderat dengan IC<sub>50</sub> 52,43 μg/mL), dan enam isolat lainnya menunjukkan aktivitas antibakteri kuat terhadap *Escherichia coli* dan *Staphylococcus aureus* dengan MIC 8–64 μg/mL. Isolat-isolat tersebut termasuk satu *Fusarium* spp. dari batang dan empat *Colletotrichum* spp. dari daun dan kelopak buah yang menunjukkan aktivitas antibakteri terbaik (Palupi *et al.*, 2021).

Penelitian lain berhasil mengidentifikasi berbagai jenis jamur endofitik dari tanaman ciplukan seperti *Penicillium verrucosum*, *Colletotrichum alienum*, *Fusarium subglutinans*, *Aspergillus nidulans*, *Mycelia sterilia*, dan *Rhizoctonia* spp. Metabolit yang dihasilkan oleh *Penicillium verrucosum* menunjukkan aktivitas antimikroba tertinggi terhadap *B. subtilis*, *E. coli*, dan *S. aureus* (Hastuti *et al.*, 2021).

Penelitian jamur endofitik pada ciplukan sampai saat ini sebagian besar hanya mencakup ekstrak kasar, profil KLT dan aktivitas bioaktif umum, tanpa isolasi dan karakterisasi sistematis senyawa bioaktif murni. Jamur endofitik *Colletotrichum* yang juga ada pada ciplukan mampu memproduksi senyawa antimikroba seperti emodin dan taxol pada inang lain (Yehia, 2023; Hashem *et al.*, 2023). Selanjutnya, banyak jamur endofitik menghasilkan berbagai jenis senyawa bioaktif seperti flavonoid, fenolik, terpenoid, isokumarin dan steroid yang belum dievaluasi dari tanaman ciplukan secara terstruktur (Anwar *et al.*, 2023; Bando *et al.*, 2024; Yu *et al.*, 2023).

Berdasarkan data hasil penelitian, terdapat gap penelitian proposisional yaitu belum ada laporan isolasi dan karakterisasi lengkap senyawa murni dari jamur endofitik yang berasal dari tanaman ciplukan, sementara jamur endofitik *Colletotrichum*, *Fusarium*, dan *Penicillium* yang terbukti aktif sebagai antioksidan atau antibakteri belum dievaluasi lebih lanjut ke arah senyawa murni. Oleh karena itu, arah penelitian ke depan sangat penting untuk fokus pada isolasi fraksi aktif dari ekstrak endofitik ciplukan dengan pendekatan kromatografi (KLT, kolom) dan karakterisasi struktural senyawa murni menggunakan spektroskopi NMR. Setiap senyawa yang diisolasi harus diuji aktivitas antioksidan, antibakteri, sitotoksitas, dan menentukan nilai IC<sub>50</sub> atau MIC. Kemudian, membandingkan sifat bioaktif senyawa murni endofit dengan senyawa yang diperoleh dari tanaman itu sendiri, seperti physalin atau withanolide, akan memberikan pemahaman lebih dalam tentang kontribusi mikroba endofitik terhadap khasiat farmakologis ciplukan tradisional. Lebih lanjut, penelitian ini dapat diarahkan untuk identifikasi genetik (DNA ITS sequencing) dari isolat jamur endofitik yang terbukti aktif sebagai antioksidan atau antibakteri.

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