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Lintang Sephia Dewi, Wahyu Aristyaning Putri, S.Si., M.Sc., Ph.D. ; Prof. Rina Sri Kasiamdari, S.Si., Ph.D.
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INTISARI

Peningkatan resistensi antibiotik yang disebabkan oleh menurunnya efektivitas obat menjadi ancaman serius bagi kesehatan manusia. Eksplorasi fungi endofit dari tanaman obat sebagai sumber senyawa antimikroba baru sangat penting untuk mengatasi infeksi dan meningkatkan efektivitas pengobatan. Penelitian menunjukkan bahwa fungi endofit yang diisolasi dari tanaman kayu manis (*Cinnamomum burmannii*) menghasilkan metabolit bioaktif antibakteri. Penelitian dilakukan untuk mengetahui aktivitas anti-*multi drug resistant* dari tanaman kayu manis (*Cinnamomum burmannii*) terhadap bakteri MDR serta senyawa aktif yang berperan dalam sebagai anti-MDR. Metode yang digunakannya terdiri dari isolasi fungi endofit, identifikasi morfologi fungi endofit makroskopis dan mikroskopis, identifikasi molekuler daerah *Internal Transcribed Spacer* (ITS) ribosomal DNA fungi, fermentasi dan ekstraksi fungi endofit, uji aktivitas antibakteri, LC-HRMS, serta *molecular docking.* Hasil isolasi fungi endofit dari daun *Cinnamomum burmannii* diperoleh sebanyak 48 isolat fungi endofit. Seluruh isolat memiliki kemampuan menghambat pertumbuhan bakteri dalam kategori lemah hingga sangat kuat berkisar 0-25 mm. Isolat DS1.6, paling potensial dengan daya hambat 19 mm (*Escherichia coli* MDR), 18 mm (*Klebsiella pneumoniae* MDR), 0 mm (*Citrobacter freundii* MDR), dan 18,25 mm (MRSA). Isolat DS1.6 telah teridentifikasi termasuk dalam spesies *Colletotrichum aenigma* berdasarkan hasil analisis BLAST dengan tingkat homologi sangat tinggi, yaitu persamaan *Query cover* sebesar 100% dan *Percent Identity* mencapai 99.82%. Ekstrak fungi *Colletotrichum aenigma* pelarut etil asetat memiliki daya hambat lebih unggul yakni 25 mm (*Escherichia coli* MDR), 21 mm (*Klebsiella pneumoniae* MDR), 3 mm (*Citrobacter freundii* MDR), dan 15 mm (MRSA) dibandingkan pelarut etanol. Senyawa *Quinoline* teridentifikasi sebagai nilai PA (*Probable Activity*) > PI (*Probable Inactivity*) serta prediksi aktivitas biologis yang baik berdasar parameter PASS online. Hasil penambatan molekuler senyawa *Quinoline* terhadap protein target bakteri menunjukkan binding affinity yang baik (AcrB: -5,7 kkal/mol; PBP2a: -6,5 kkal/mol; OmpK36: -5,7 kkal/mol; β-laktamase AmpC: -6,9 kkal/mol) dengan nilai RMSD yang sangat baik (AcrB: 0,781 Å; PBP2a: 1,005 Å; OmpK36: 0,848 Å; AmpC: 0,898 Å), di mana seluruh RMSD berada di bawah 2 Å. Ikatan hidrogen terbentuk pada penambatan protein PBP2A MRSA dengan residu asam amino LEU570 dan protein Ompk36 *Klebsiella pneumoniae* dengan residu asam amino GLN61.

KATA KUNCI: *Multidrug Resistant*, tanaman kayu manis, fungi endofit

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Isolation, Identification, and Anti Multidrug Resistant (MDR) Effectivity of Endophytic Fungi from Leaves Cinnamon Plant (*Cinnamomum burmannii* (Nees & T. Nees) Blume)

By

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ABSTRACT

The increase in antibiotic resistant, caused by reduced drug efficacy, has become a serious threat to human health. The exploration of endophytic fungi from medicinal plants as a source of new antimicrobial compounds is vital for combating infections and improving the effectiveness of treatment. Research indicates that endophytic fungi isolated from the cinnamon plant (*Cinnamomum burmannii*) produce antibacterial bioactive metabolites. Research was conducted to investigate the anti multidrug resistant (MDR) activity of the cinnamon plant (*C. burmannii*) against MDR bacteria, in addition to the active compounds responsible for anti-MDR efficacy. The methods involved endophytic fungal isolation, macroscopic and microscopic morphological identification of endophytic fungi, molecular identification using the Internal Transcribed Spacer (ITS) region of fungal ribosomal DNA, fermentation and extraction of endophytic fungi, antibacterial activity testing, LC-HRMS, and molecular docking. The results showed that 48 endophytic fungal isolates were obtained from the leaves of *C. burmannii*. All isolates had the ability to inhibit bacterial growth, as indicated by the formation of clear zones around the colonies. Isolate DS1.6, the most promising, showed the greatest potential, with inhibition zones of 19 mm (MDR *Escherichia coli*), 18 mm (MDR *Klebsiella pneumoniae*), 0 mm (MDR *Citrobacter freundii*) and 18.25 mm (MRSA). Isolate DS1.6 was identified as belonging to the species *Colletotrichum aenigma* based on BLAST analysis results showing a very high level of homology, namely a Query Cover of 100% and a Percent Identity of 99.82%. The *Colletotrichum aenigma* fungi extract using ethyl acetate as a solvent showed superior inhibitory activity, with 25 mm (*E. coli* MDR), 21 mm (*K. pneumoniae* MDR), 3 mm (*C. freundii* MDR), and 15 mm (MRSA) compared to the ethanol solvent. The Quinoline compound was identified as a PA (Probable Activity) value > PI (Probable Inactivity) and good prediction of biological activity based on the PASS online parameters. Molecular docking results of the Quinoline compound against bacterial target proteins showed good binding affinity (AcrB:-5.7 kcal/mol; PBP2a:-6.5 kcal/mol; OmpK36:-5.7 kcal/mol; AmpC β-laktamase:-6.9 kcal/mol) with excellent RMSD values (AcrB: 0.781 Å; PBP2a: 1.005 Å; OmpK36: 0.848 Å; AmpC: 0.898 Å), all RMSD values were below the 2 Å threshold. Hydrogen bonds were formed at the binding site of the MRSA PBP2A protein with the amino acid residue LEU570 and the *K. pneumoniae* OmpK36 protein with the amino acid residue GLN61.

KEYWORDS: Multidrug Resistant, cinnamon plant, endophytic fungi