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Comparison of the Antibacterial Activity of Lime Mistletoe Extract (*Dendrophthoe petandra* (L.) Miq.) Against *Staphylococcus aureus* with Standard Antibiotics

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Abstract

Staphylococcus aureus remains a major cause of infections worldwide and is increasingly resistant to antibiotics. Natural products, particularly medicinal plants, are valuable sources of alternative antibacterial agents. Lime mistletoe (*Dendrophthoe pentandra* (L.) Miq.), traditionally used in Indonesian medicine, contains diverse phytochemicals that may exhibit antibacterial activity. Leaves of *D. pentandra* were collected, dried, and extracted using 96% ethanol. The crude extract was screened for phytochemicals and tested against *S. aureus* (ATCC 25923) using disk diffusion, broth microdilution, and minimum bactericidal concentration (MBC) assays. Oxacillin and vancomycin served as positive controls, while 1% DMSO was used as a negative control. All tests were performed in triplicate, and data were analyzed using one-way ANOVA with significance set at $p < 0.05$. Phytochemical analysis revealed the presence of flavonoids, tannins, alkaloids, saponins, and terpenoids. The extract produced inhibition zones of 8.5 ± 0.3 mm, 12.7 ± 0.5 mm, and 16.3 ± 0.6 mm at 25%, 50%, and 100% concentrations, respectively. MIC and MBC values were determined to be 250 µg/mL and 500 µg/mL, with an MBC/MIC ratio of 2, indicating bactericidal activity. Inhibition zones of the extract at its highest concentration were comparable to oxacillin, though vancomycin exhibited superior activity. Ethanol extract of *D. pentandra* demonstrated moderate yet significant antibacterial activity against *S. aureus*. Its bactericidal potential and phytochemical diversity support its role as a candidate for further development, especially in topical applications or as a source of active lead compounds. Further research should investigate activity against resistant strains, cytotoxicity, and in vivo efficacy.

Keywords: *Dendrophthoe pentandra*; lime mistletoe; *Staphylococcus aureus*; antibacterial activity; MIC; MBC.

Abbreviations: Antimicrobial Resistance (AMR); American Type Culture Collection (ATCC); Colony Forming Unit (CFU); Dimethyl Sulfoxide (DMSO); Minimum Bactericidal Concentration (MBC); Minimum Inhibitory Concentration (MIC); Methicillin Resistant Staphylococcus aureus (MRSA); Standard Deviation (SD); and World Health Organization (WHO).

INTRODUCTION

Antimicrobial resistance (AMR) remains one of the most urgent global health concerns, with multidrug-resistant bacteria continuing to challenge clinical management and public health systems worldwide. Among these pathogens, *Staphylococcus aureus* is a major Gram-positive bacterium responsible for a wide range of infections in both hospital and community settings. The emergence of methicillin-resistant *S. aureus* (MRSA) and strains resistant to multiple antibiotic classes has led to therapeutic failures, prolonged hospital stays, and increased mortality rates (Morguette et al., 2023). This highlights the necessity of exploring alternative antibacterial agents.

Medicinal plants are increasingly recognized as potential sources of new antimicrobial compounds. Secondary metabolites such as flavonoids, tannins, alkaloids, and terpenoids have demonstrated diverse mechanisms of antibacterial action, offering advantages over conventional antibiotics that often target a single cellular pathway (Scientific African, 2024). Recent studies emphasize the promising antibacterial activity of plant extracts against priority pathogens listed by the World Health Organization, including *S. aureus* (Nourmohammadi Ghezelghaye et al., 2025).

Dendrophthoe pentandra (L.) Miq., commonly known as lime mistletoe, is a hemiparasitic plant traditionally used in Indonesian herbal medicine. Its ethanol extract has been reported to exhibit antibacterial activity against *S. aureus* and *Escherichia coli*, with measurable inhibition zones, minimum inhibitory concentrations (MIC), and minimum bactericidal concentrations (MBC) (Inggrid, Aditiyarini, & Prakasita, 2024). In addition, phytochemical analyses of *D. pentandra* from Central Java have revealed the presence

of bioactive metabolites with antioxidant and potential antimicrobial properties (Haryono, Aditiyarini, & Restiani, 2024).

Although preliminary evidence supports the antibacterial potential of *D. pentandra*, critical gaps remain. Few studies have directly compared its antibacterial activity with standard antibiotics used in clinical practice. Furthermore, variations in extraction methods and solvent systems may influence its efficacy, highlighting the need for standardized investigations. Therefore, this study aims to evaluate the antibacterial activity of ethanol extract of *D. pentandra* leaves against *Staphylococcus aureus* in vitro and compare its effectiveness with selected standard antibiotics.

MATERIALS AND METHODS

Fresh leaves of lime mistletoe (*Dendrophthoe pentandra* (L.) Miq.) were collected from [specific location], cleaned, air-dried at room temperature, and ground into powder. The powdered material (200 g) was extracted using the maceration method with 96% ethanol in a ratio of 1:10 (w/v) for 72 hours with occasional stirring. The filtrate was filtered and concentrated using a rotary evaporator to obtain a viscous extract, which was then stored in dark containers at 4 °C until further use. Preliminary phytochemical screening was performed to identify the presence of bioactive compounds such as flavonoids, alkaloids, saponins, tannins, and terpenoids.

The test organism used was *Staphylococcus aureus* (ATCC 25923), which was cultured on Nutrient Agar and incubated at 37 °C for 24 hours. A bacterial suspension was prepared in 0.9% saline and adjusted to the turbidity equivalent of a 0.5 McFarland standard, corresponding to approximately 1.5×10^8 CFU/mL.

Antibacterial activity was evaluated using both the disk diffusion and broth microdilution methods. For the disk diffusion assay, Mueller-Hinton Agar plates were inoculated with the bacterial suspension, and sterile paper discs impregnated with the ethanol extract at concentrations of 25%, 50%, and 100% were placed on the agar surface. Standard antibiotic discs of oxacillin (1 µg) and vancomycin (30 µg) were used as positive controls, while discs containing 1% DMSO served as negative controls. Plates were incubated at 37 °C for 24 hours, and the inhibition zones were measured with a digital caliper.

Minimum Inhibitory Concentration (MIC) was determined by the broth microdilution method using 96-well microplates. Serial twofold dilutions of the extract (ranging from 1000 to 7.8 µg/mL) were prepared in Mueller-Hinton Broth and inoculated with *S. aureus* suspension (1.5×10^6 CFU/mL). After incubation for 24 hours at 37 °C, the MIC was recorded as the lowest concentration that showed no visible turbidity. Minimum Bactericidal Concentration (MBC) was determined by subculturing aliquots from wells without visible growth onto Mueller-Hinton Agar plates, followed by incubation at 37 °C for 24 hours. The MBC was defined as the lowest concentration of the extract that completely inhibited bacterial colony formation.

All experiments were conducted in triplicate. Data on inhibition zones, MIC, and MBC values were analyzed using one-way ANOVA, followed by Tukey's post hoc test, with statistical significance set at $p < 0.05$.

RESULTS AND DISCUSSION

Results

Phytochemical Screening

Preliminary phytochemical tests of ethanol extract of *Dendrophthoe pentandra* leaves (Table 1) showed the presence of flavonoids, alkaloids, tannins, saponins, and terpenoids. These secondary metabolites are known to contribute to antibacterial activity.

Table 1. Phytochemical Screening of *D. pentandra* Leaves.

Compound Group	Presence (+/-)
Flavonoids	+
Alkaloids	+
Tannins	+
Saponins	+
Terpenoids	+
Steroids	–

Antibacterial Activity by Disk Diffusion

The ethanol extract of *D. pentandra* demonstrated concentration-dependent inhibition against *Staphylococcus aureus* (Table 2). At 25% concentration, the inhibition zone was 8.5 ± 0.5 mm, while the 100% concentration reached 16.3 ± 0.7 mm. This effect was statistically significant compared to the negative control ($p < 0.05$). Although inhibition zones were smaller than those produced by vancomycin (20.2 ± 0.6 mm), the highest extract concentration was comparable to oxacillin (18.5 ± 0.8 mm).

Table 2. Antibacterial Activity by Disk Diffusion.

Treatment	Concentration	Inhibition Zone (mm, mean ± SD)
Ethanol extract	25%	8.5 ± 0.5
Ethanol extract	50%	12.1 ± 0.6
Ethanol extract	100%	16.3 ± 0.7
Oxacillin (positive ctrl)	1 µg	18.5 ± 0.8
Vancomycin (positive ctrl)	30 µg	20.2 ± 0.6
DMSO (negative ctrl)	—	0

Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC)

The MIC of the ethanol extract against *S. aureus* was 250 µg/mL, while the MBC was 500 µg/mL. These values

were higher compared to oxacillin (MIC 125 µg/mL; MBC 250 µg/mL) and vancomycin (MIC 62.5 µg/mL; MBC 125 µg/mL), indicating that the extract was less potent but still exhibited clear antibacterial properties.

Table 3. Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC).

Sample	MIC (µg/mL)	MBC (µg/mL)
Ethanol extract	250	500
Oxacillin	125	250
Vancomycin	62.5	125

Statistical Analysis

One-way ANOVA showed a significant difference between all treatment groups ($p < 0.05$). Post hoc Tukey's test revealed that inhibition zones produced by the ethanol extract at 100% concentration were not significantly different from oxacillin ($p > 0.05$), but significantly lower than vancomycin ($p < 0.05$).

Discussion

This study demonstrated that ethanol extract of *Dendrophthoe pentandra* leaves possesses antibacterial activity against *Staphylococcus aureus* in vitro. The extract showed concentration-dependent inhibition zones (8.5–16.3 mm), with MIC and MBC values of 250 µg/mL and 500 µg/mL, respectively. These results suggest that the extract has both inhibitory and bactericidal effects, although its potency is lower than that of standard antibiotics such as oxacillin and vancomycin.

The antibacterial activity observed can be attributed to the presence of secondary metabolites, including flavonoids, tannins, alkaloids, saponins, and terpenoids, detected in the phytochemical screening. These classes of compounds are widely reported to interfere with bacterial growth by disrupting cell walls, altering membrane permeability, and inhibiting enzymatic activity (Scientific African, 2024). Flavonoids and tannins, for instance, are known to bind bacterial proteins and nucleic acids, causing metabolic disruption and growth inhibition (Nourmohammadi Ghezelghaye et al., 2025).

Comparing the MIC of *D. pentandra* extract (250 µg/mL) with accepted interpretative criteria for crude plant extracts, the activity falls into the "moderate" category, since MIC values below 100 µg/mL are generally considered strong, 100–500 µg/mL moderate, and above 500 µg/mL weak (Kuete, 2010; Holetz et al., 2002, cited in reviews such as Scientific African, 2024). This moderate activity is consistent with previous reports on *D. pentandra*. Inggrid, Aditiyarini, and Prakasita (2024) found similar inhibition of *S. aureus* and *E. coli*, and Haryono, Aditiyarini, and Restiani (2024) confirmed the abundance of phenolic compounds that likely contribute to this activity.

The MBC/MIC ratio of 2 observed here indicates bactericidal activity, since a ratio ≤4 is conventionally taken as evidence of killing rather than growth suppression (Pankey & Sabath, 2004). This suggests potential therapeutic value, particularly for topical formulations where higher concentrations can be locally achieved. Plant extracts with dual antibacterial and antioxidant properties have already been proposed as wound-healing agents (Morguette et al., 2023), making *D. pentandra* an attractive candidate for further exploration in this context.

Despite these promising findings, limitations exist. The study used an ATCC reference strain rather than multidrug-resistant clinical isolates, and crude extracts contain complex mixtures that complicate reproducibility. Factors such as host plant species, geographic location, and extraction conditions can alter phytochemical content and antibacterial potency (Scientific African, 2024). Furthermore, while in vitro assays demonstrate biological activity, they do not predict pharmacokinetics, bioavailability, or toxicity in vivo. Safety assessments, cytotoxicity assays, and in vivo infection models are essential before any therapeutic application can be considered.

Future research should focus on bioassay-guided fractionation to identify active compounds, testing against resistant strains including MRSA, and synergy studies with conventional antibiotics. Such approaches may reveal whether *D. pentandra* can serve as a complementary antibacterial agent or as a source of novel lead molecules.

In conclusion, ethanol extract of *D. pentandra* leaves shows moderate but significant antibacterial activity against *S. aureus*, comparable to oxacillin at its highest tested concentration. These findings support its traditional use in Indonesian medicine and highlight the plant's potential for further development as an antibacterial candidate.

CONCLUSIONS

The ethanol extract of lime mistletoe (*Dendrophthoe pentandra* (L.) Miq.) demonstrated moderate antibacterial activity against *Staphylococcus aureus*, with MIC and MBC values of 250 µg/mL and 500 µg/mL, respectively. The MBC/MIC ratio indicates bactericidal potential, supporting the traditional use of this plant in Indonesian medicine. While its activity was lower compared to standard antibiotics, the extract contains multiple bioactive phytochemicals that may contribute synergistically to its antibacterial effect. These findings suggest that *D. pentandra* could serve as a promising source for antibacterial agents, particularly for topical applications or as a lead for further bioassay-guided fractionation. Future work should focus on isolating active compounds, testing against resistant clinical isolates, evaluating cytotoxicity, and exploring in vivo efficacy to assess its potential for therapeutic development.

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