

Original article

Antibacterial Activity of Miswak Wood (*Salvadora persica*) Extracted Using Various Solvents

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Abstract

Nosocomial infections induced by medical interventions and pathogens such as *Staphylococcus aureus* and *Escherichia coli* represent a substantial public health challenge in Indonesia. Miswak wood is used traditionally as a dental cleanser and its effect on various bacterial needs requires further exploration. This investigation assessed the antibacterial efficacy of Miswak Wood (*Salvadora persica*) extracted using various solvents (ethyl acetate, n-butanol, and methanol) through maceration extraction techniques. This research constituted an in vitro experimental design that evaluated the inhibition zones produced by ethyl acetate, n-butanol, and methanol extracts from miswak wood (*Salvadora persica*) at a concentration of 500 mg/ml against *Staphylococcus aureus* and *Escherichia coli*. The extraction process employed a kinetic maceration technique utilizing ethyl acetate, n-butanol, and methanol as solvents. The assessment of antibacterial activity was conducted using the disc diffusion methodology as established by Kirby and Bauer. The Mann-Whitney test was employed to determine significant differences between the bacteria. Subsequently Wilcoxon post-hoc pairwise tests were utilized to assess the significant effect of different solvents on each bacterium. A significance threshold of $p < 0,05$ was set for all analyses. The inhibition zone observed for *Staphylococcus aureus* with ethyl acetate solvent measured 11.85 ± 0.92 mm; with n-butanol it was 9.07 ± 1.07 mm; and with methanol it was 7.98 ± 1.15 mm; conversely, for *Escherichia coli*, the results were 9.11 ± 0.81 mm with ethyl acetate solvent; 0.00 ± 0.00 mm with n-butanol; and 3.89 ± 3.70 mm with methanol. The inhibition zone generated from the ethyl acetate extract exhibited the most pronounced antibacterial activity against both *Staphylococcus aureus* and *Escherichia coli*.

Keywords: antibacterial, ethyl acetate, methanol, n-butanol, *Salvadora persica*

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Introduction

Nosocomial infections, defined as diseases contracted during medical treatment within hospital settings, represent a significant public health concern in Indonesia, exhibiting an incidence rate of 15.74%, starkly contrasting with the lower rates observed in developed nations, typically ranging from 4% to 8% (Rohima et al., 2023). The etiology of these infections is frequently associated with medical interventions, the deployment of invasive instruments, and interactions with healthcare personnel or other patients (Sardi, 2021), with predominant pathogens classified within the ESKAPE (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Enterobacter spp*) group, including *Staphylococcus aureus* and *Escherichia coli* (Khan et al., 2017; Lugito et al., 2023). Both of these bacterial species can induce systemic complications, such as sepsis, through inflammatory mechanisms, which may extend the duration of hospitalization, antibiotic resistance, and elevate mortality risk (Khan et al., 2017). This research seeks to identify solutions derived from natural substances to mitigate the escalating issue of antimicrobial resistance.

Staphylococcus aureus, a Gram-positive microorganism frequently found in human skin flora, is acknowl-

edged as a primary pathogen implicated in nosocomial infections, including ventilator-associated pneumonia, with documented prevalence rates in Indonesia attaining 17.5% in 2021 (Andayani et al., 2023). This microorganism harbors numerous virulence factors, including antiphagocytic microcapsules and protein A, obstructing the host's immune mechanisms, potentially resulting in severe conditions such as bacteremia and endocarditis (Afdhila et al., 2021). In contrast, *Escherichia coli*, although a critical constituent of the normal gastrointestinal microbiota, may act as an opportunistic pathogen associated with urinary tract infections and diarrhea, significantly contributing to approximately 1 million instances of diarrhea in Indonesia in 2018 (Basavaraju & Gunashree, 2023; RISKESDAS, 2018). The ability of *Escherichia coli* to produce the enzyme β -lactamase augments its resistance to antimicrobial agents, thereby complicating clinical management approaches (Mills et al., 2022).

Salvadora persica is acknowledged for its effectiveness as a natural dental cleanser within the Indonesian society, demonstrating significant antibacterial properties attributed to its diverse range of secondary metabolites, including flavonoids, tannins, terpenoids, and alkaloids (Adigun et al., 2023). Despite extensive documentation of *Salvadora persica*'s antibacterial efficacy, a systematic comparative evaluation of its extracts, differentiated by various solvent polarities, remains significantly under-explored. This study, therefore, aims to identify the optimal antibacterial potential among *Salvadora persica* extracts obtained through maceration with ethyl acetate, n-butanol, and methanol. These solvents are selected

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based on solubility principles to isolate relevant bioactive compounds, which will subsequently undergo comparative evaluation against *Staphylococcus aureus* and *Escherichia coli* using a disc diffusion assay, thereby providing a more comprehensive understanding of the most promising extract.

The current study assessed the impact of solvent variation on the antibacterial efficacy of *Salvadora persica* extracts, hypothesizing that different solvents would result in different levels of effectiveness. The maceration technique was chosen for its ability to extract thermolabile compounds (Abubakar & Haque, 2020). The findings from this study are expected to provide a new perspective in optimizing the extraction of bioactive compounds from natural sources to combat nosocomial infections, especially those caused by resistant bacterial strains. By utilizing the inherent potential of *Salvadora persica*, this study supports the advancement of alternative antimicrobial therapies based on natural materials, thereby reducing dependence on synthetic antibiotics.

Methods

Study design, time and place of research

The laboratory experimental investigation employed a comparative in vitro study design to evaluate and contrast the antibacterial efficacy of *Salvadora persica* extracts obtained through maceration with ethyl acetate, n-butanol, and methanol. For this purpose, the Zone of Inhibition (ZOI) was measured using the disc diffusion assay. Specifically, each *Salvadora persica* extract (ethyl acetate, n-butanol, and methanol) was tested at a single concentration of 500 mg/mL. The bacterial strains examined in this study were clinical isolates of *Staphylococcus aureus* subsp. *aureus* WDCM 00032 Vitroids™ and *Escherichia coli* WDCM 00012 Vitroid. This research was conducted at the Integrated Laboratory of FK UNISMA during the period of January to February in the year 2025.

Plant determination

The objective of this phase is to authenticate the identity and taxonomic classification of the plant specimens utilized. The process of sample identification was executed at the UPT Herbal Laboratory Materia Medica in Batu, as documented under letter number 000.9.3/326/102.20/2025. The findings from the identification confirm that the plant in question belongs to the Salvadoraceae family and is scientifically classified as *Salvadora persica*.

Method of extraction of plant material

The methodology for extracting *Salvadora persica* was primarily adopted from established protocols by (Afdhila et al., 2021) and (Maulidina et al., 2021). This process was executed at the Islamic University of Malang Laboratory, utilizing ethyl acetate, n-butanol, and methanol as extraction solvents. For each solvent, a precise mass of 300 grams of *Salvadora persica* simplisia was accurately weighed and subsequently

introduced into an Erlenmeyer flask to undergo a maceration process for a period of 24 hours. The ratio of the simplisia mass to the solvent volume utilized was maintained at 1:5 (w/v). The maceration procedure was facilitated mechanically using a water bath shaker operating at a rotation speed of 120 rpm to enhance the extraction efficiency. Upon conclusion of the maceration phase, the extract was filtered through filter paper to separate the solid residues, which were subsequently discarded. The resultant filtrate was then subjected to evaporation via a vacuum rotary evaporator, maintained at a temperature range of 60-70°C and a rotation speed of 50 rpm for 60 minutes, yielding a viscous extract. The concentrated extract underwent a final drying process in an oven at 50°C until a completely desiccated state was attained. Finally, for the antibacterial assays, 500 mg of the dried extract was weighed and dissolved in 1 mL of 1% Tween solution.

Bacterial inoculation and zone of inhibition test procedure

The test bacteria were prepared for the antibacterial activity assay by diluting bacterial colonies in 10 mL of normal saline. The turbidity of the resultant bacterial suspension was meticulously adjusted to meet the 0.5 McFarland standard. This standardized suspension was then inoculated onto Mueller Hinton Agar (MHA) medium using a sterile cotton swab, streaking in a zigzag pattern to ensure even bacterial distribution, following standard microbiological practices (Afdhila et al., 2021). Subsequently, the antimicrobial activity of the *Salvadora persica* extracts (ethyl acetate, n-butanol, and methanol) was evaluated using the disc diffusion assay. The extracts, prepared at a 500 mg/mL concentration, were dissolved in 1% Tween 80 before being uniformly applied to sterile blank discs. These extract-loaded discs were carefully placed onto the MHA medium pre-inoculated with the respective test bacteria. After incubation at 37°C for 24 hours, the diameter of the Zone of Inhibition (ZOI) around each disc was measured in millimeters (mm) using a caliper.

Statistic data analysis

The ZOI data were analyzed using IBM SPSS Statistic 30 Software to calculate the mean value and standard deviation. Since the data were not normally distributed, the analysis proceeded with the *Kruskal-Wallis non-parametric* test to evaluate differences between groups. Then, a *posthoc pairwise Wilcoxon* test was performed to identify significant differences between pairs of groups.

Results

Results of zone of inhibition against *Staphylococcus aureus*

The Zone of Inhibition (ZOI) test for *Staphylococcus aureus* was conducted with nine repetitions using a concentration of 500 mg/ml of *Salvadora persica* extract prepared in ethyl acetate, n-butanol, and methanol solvents. The diameter of the clear zone around the discs

was measured using a caliper and documented in millimeters, as depicted in Figure 1 and Table 1.

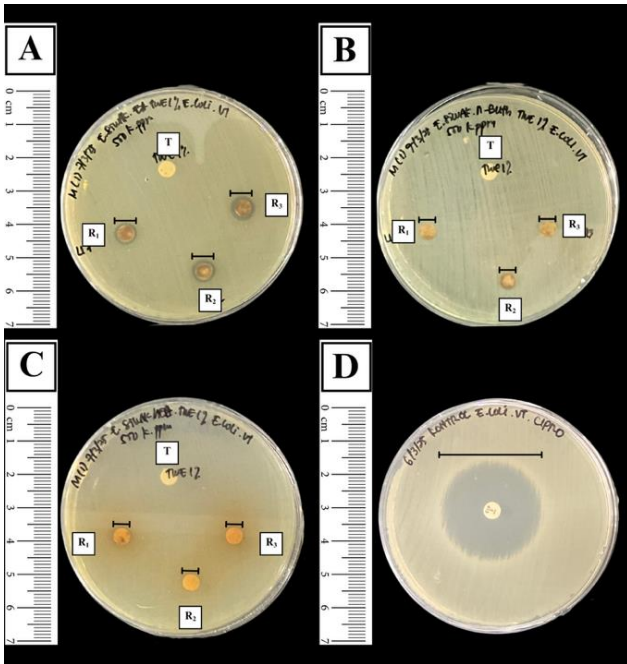


Figure 1. Clear zone diameter from *Staphylococcus aureus* plates after administration of discs containing *Salvadora persica* extracted using (A) Ethyl acetate, (B) n-Butanol, and (C) Methanol, each demonstrating a zone of inhibition. Each plate was given a tween 1% control exhibiting no inhibition. Plate (D) was used as an antibiotic control

Results of zone of inhibition against *Escherichia coli*

The zone of Inhibition (ZOI) of *Escherichia coli* bacteria was carried out nine times using a dose of 500 mg/ml on *Salvadora persica* extract using ethyl acetate, butanol, and methanol solvents. The inhibition zone was measured using a caliper, noting the diameter of the clear zone formed around the disc, recorded in millimeters, as shown in Figure 2 and Table 1.

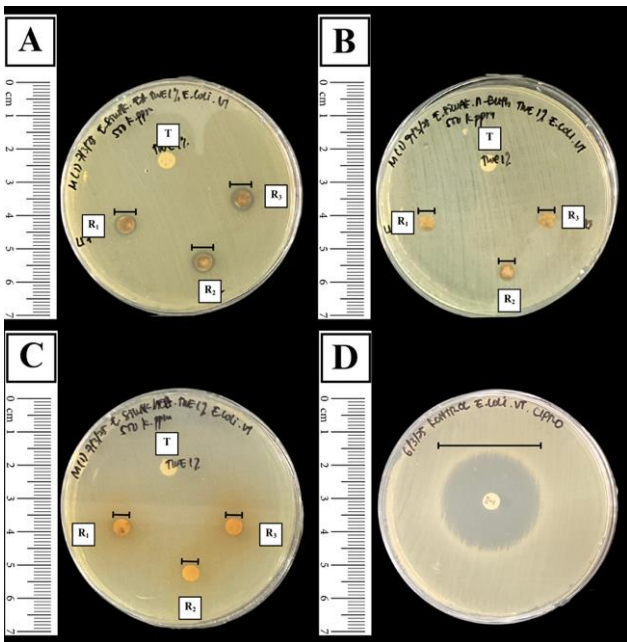


Figure 2. Clear zone diameter from *Escherichia coli* plates after administration of discs containing *Salvadora persica* extracted using (A) Ethyl acetate, (B) n-Butanol, and (C) Methanol, each demonstrating a zone of inhibition. Each plate was given a tween 1% control exhibiting no inhibition. Plate (D) was used as an antibiotic control.

Table 1. Zone of Inhibitor Diameter of *Salvadora persica* extracted using Ethyl acetate, n-butanol and methanol against bacterial

Solvent	<i>Staphylococcus aureus</i>	<i>Escherichia coli</i>
Ethyl acetate	11,85±0,92mm ^a	9,11±0,8mm ^b
n-Butanol	9,07±1,07mm ^c	00,00±0,00mm ^d
Methanol	7,98±1,15mm ^e	3,89±3,7mm ^f
Tween 1% (-ve)	00,00±0,00mm ^g	00,00±0,00mm ^g
Amoxicillin (+ve)	45,28±2,15mm	-
Ciprofloxacin (+ve)	-	41,00 ± 2,57mm

Note: Different notations indicate significant differences

The average ZOI test results against *Staphylococcus aureus* were highest in the ethyl acetate extract, averaging 11.85 ± 0.92 mm. The second highest ZOI test was n-butanol, which was 9.07 ± 1.07 mm, and the smallest was methanol, which was 7.98 ± 1.15 mm. At 1% tween, no clear zone was found on the disk. So, it can be concluded that the ethyl acetate extract has more inhibitory activity against *Staphylococcus aureus* bacteria than other extracts.

The average ZOI test results were highest in ethyl acetate extract, with an average of 9.11 ± 0.81 mm. The second highest ZOI test was methanol, which was 3.89 ± 3.70 mm, and the smallest was n-butanol, which was 0.00 ± 0.00 mm. At 1% tween, no clear zone was found on the disk. So, it can be concluded that ethyl acetate extract has more inhibitory activity against *Escherichia coli* bacteria than other extracts.

Discussion

According to the research conducted by Davis and Stout in 1971, the assessment of the inhibitory zones of ethyl acetate, n-butanol, and methanol extracts from *Salvadora persica* at a concentration of 500 mg/ml against *Staphylococcus aureus* revealed that the methanol extract (7.98±1.15 mm) and the n-butanol extract (9.07 ± 1.07 mm) are classified within the weak inhibitory category. In contrast, the ethyl acetate extract (11.85 ± 0.92 mm) falls into the intermediate category. The statistical analysis utilizing the *Kruskal-Wallis* test indicated the ranking of inhibitory efficacy from highest to lowest: ethyl acetate, n-butanol and methanol extracts. The evaluation of the inhibition zone for ethyl acetate, n-butanol, and methanol *Salvadora persica* extracts at the same concentration of 500 mg/ml against *Escherichia coli* demonstrated that the ethyl acetate extract (9.11±0.81 mm) is categorized as intermediate, while both the n-butanol extract (0.00 ± 0.00 mm) and the methanol extract (3.89 ± 3.70 mm) exhibited no discernible antibacterial activity. The *Kruskal-Wallis* statistical assessment further corroborates the ranking of inhibitory capacity from highest to lowest among the ethyl acetate, methanol, and n-butanol extracts.

Salvadora persica exhibits a greater sensitivity towards *Staphylococcus aureus* than *Escherichia coli* in this research. The structural composition of *Staphylococcus aureus* features a robust peptidoglycan cell wall devoid of an outer membrane, thereby rendering it more vulnerable to antibacterial agents capable of penetrating

or compromising the structural integrity of the cell wall. Conversely, *Escherichia coli* is safeguarded by an outer membrane enriched with lipopolysaccharides, which act as an additional defensive mechanism against hydrophilic or larger molecular entities, consequently diminishing the extract's efficacy. The Antibacterial mechanism of *Salvadora persica* extracted has been well established.

The ethyl acetate extract derived from *Salvadora persica* demonstrates considerable antibacterial efficacy against *Staphylococcus aureus*, attributable to the presence of secondary metabolites, particularly phenolic compounds such as tannins, triterpenoids, phenols, and phenylpropanoids. Research utilizing kinetic maceration extraction methods has revealed that extracts obtained with methanol, n-butanol, and ethyl acetate solvents test positive for flavonoids, alkaloids, terpenoids, phenolic compounds, and tannins. At the same time, saponins are absent in the ethyl acetate fraction. Quantitative analysis of flavonoid content indicates that the ethyl acetate extract contains the highest concentration at 99.15 ± 8.14 mgEQ/g (9,9%), followed by n-butanol at 62.08 ± 6.10 mgEQ/g (6,2%) and methanol at 13.23 ± 7.47 mgEQ/g (1,3%) (Ramadhan et al., 2025 in review; see Supp. file for detailed data). The predominant flavonoid constituents encompass *catechin*, *rutin*, *myricetin*, *quercetin*, and *kaempferol*, with *catechin* being the most abundant compound identified (EL-Hefny et al., 2017; Khanam et al., 2022). *Catechin* exhibits antibacterial properties through mechanisms that compromise the integrity of bacterial cell membranes and augment the generation of reactive oxygen species (ROS) (Veiko et al., 2023). The potency of this extract is notably amplified against Gram-positive bacteria, such as *Staphylococcus aureus*, due to the favourable interactions facilitated by the thick peptidoglycan layers. In contrast, the lipopolysaccharide membrane in Gram-negative bacteria obstructs such interactions (Donadio et al., 2021).

Another investigation concerning the ethyl acetate extract of *Salvadora persica* has identified alkaloid compounds. The presence of these alkaloid compounds is recognized as a prospective secondary metabolite exhibiting a broad-spectrum antibacterial property due to its ability to inhibit both Gram-positive and Gram-negative bacteria via several mechanisms (Yan et al., 2021). The principal mechanisms encompass the inhibition of bacterial cell wall synthesis, modification of cell membrane permeability, disruption of bacterial metabolic processes, and suppression of nucleic acid and protein synthesis. *Salvadorine*, a specific alkaloidal compound derived from *salvadora persica*, demonstrates antibacterial efficacy by interfering with the peptidoglycan structural components of bacterial cells, thereby preventing the complete formation of the cell wall and resulting in cellular lysis (Amalia et al., 2018). Furthermore, *benzeneacetonitrile*, which is present in the roots and stems of *Salvadora persica* (71.41%), exhibits antibacterial properties by compromising bacterial cell membranes through the reactivity of isothiocyanate groups ($N=C=S$), which can interact with membrane proteins (EL-Hefny et al., 2017).

Conclusion

The Diameter Zone of inhibition of *Salvadora persica* extract against *Staphylococcus aureus* and *Escherichia coli* is ranked from highest to lowest: ethyl acetate extract, n-butanol extract, and methanol extract. The antibacterial efficacy of *Salvadora persica* exhibits greater sensitivity towards *Staphylococcus aureus* than *Escherichia coli*.

Future Direction

Conduct extraction utilizing optimal temperature protocols and solvents with enhanced polarity variations to augment the concentration of bioactive compounds, particularly saponins and flavonoids, derived from Miswak Wood (*Salvadora persica*). Refine fractionation methodologies to enhance the yield and concentration of secondary metabolites, especially phenolics and alkaloids, which possess significant potential as antibacterial agents. Pursue further investigations into the antibacterial properties of Miswak Wood (*Salvadora persica*) against other pathogenic bacteria, such as *Pseudomonas aeruginosa* or *Klebsiella pneumoniae*, to assess potential applications in the treatment of bacterial infections with an extensive therapeutic spectrum.

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