

# Effectiveness of Secang Wood Isolate in Combination with Amoxicillin Against MRSA

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**Abstract:** Bacterial resistance to antibiotics is a global health threat, with Methicillin-Resistant *Staphylococcus aureus* (MRSA) as one of the most deadly pathogens. MRSA is resistant to methicillin and other  $\beta$ -lactam antibiotics, causing therapy failure and increased mortality up to 64% higher than non-resistant bacterial infections. This condition urges the development of new therapeutic strategies. This study focuses on sappan wood (*Caesalpinia sappan* L.), which is rich in compounds such as brazilin (the main component), flavonoids, and tannins, which have been reported to have significant antibacterial activity against various Gram-positive and Gram-negative pathogenic bacteria, including *Staphylococcus aureus*. Brazilin, a flavonoid, specifically exhibits inhibitory activity against MRSA. Based on the urgency of MRSA resistance and the pharmacological potential of sappan wood, this study aims to test the effectiveness of sappan wood isolation combined with amoxicillin against MRSA. The research method is a laboratory study that focuses on extract preparation, compound isolation, and in vitro antibacterial activity testing. The core results of the study showed that sappan wood extract (*Caesalpinia sappan* L.), which was identified to contain active compounds such as brazilin, was successfully extracted with a yield of 10.15%. Most importantly, the combination of sappanwood extract with amoxicillin showed a strong synergistic effect, as evidenced by the large inhibition zone diameter (up to  $30.40 \pm 0.75$  mm) against MRSA bacteria.

**Keywords:** Amoxicillin; MRSA; Secang wood extract; Synergy

## Introduction

Bacterial resistance to antibiotics is a condition in which the bacteria causing the infection are no longer affected by antibiotics that were previously able to kill or inhibit their growth (Uddin et al., 2021); (Muteeb et al., 2023). MRSA is a bacterium that is highly resistant to methicillin and other  $\beta$ -lactam antibiotics, resulting in the failure of medical therapies that rely on the use of these antibiotics. According to the World Health Organization (WHO), it is estimated that patients infected with methicillin-resistant *Staphylococcus aureus* have a 64% higher risk of death compared to those infected with bacteria that are not resistant to the

same antibiotic (Budianu et al., 2025); (MacPherson et al., 2018). As the number of pathogenic bacteria exhibiting antibiotic resistance increases, various studies have focused on utilizing bioactive compounds from plants that have the potential to provide synergistic effects in increasing antibiotic effectiveness (Sartini et al., 2020); (Abullais Saquib et al., 2021). Developing new drugs or therapeutic strategies against MRSA is urgently needed. Growing evidence suggests that herbal extracts and antibiotics can have a synergistic effect against MRSA (He et al., 2024); (Jeong et al., 2023).

This study focuses on commonly used antibiotics combined with herbal extracts against MRSA and their corresponding mechanisms (Bao et al., 2020). Previous

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research has demonstrated the synergistic effect of antibiotics and herbal extracts against MRSA (Kuok et al., 2017); (Hartman et al., 2025); (Atta et al., 2023). The combination of antibiotics and herbal extracts has proven to be a promising approach to combating MRSA by not only restoring antibiotic sensitivity, reducing dosages, and mitigating toxic side effects, but also reversing MRSA resistance (Hajhamed et al., 2025); (Khan et al., 2024). One plant with antibacterial activity is the sappan wood (*Caesalpinia sappan* L.). Secang wood contains chemical compounds such as flavonoids, brazilin, tannins, saponins, brazilein, and sappanchalcone, and exhibits antioxidant, anti-inflammatory, and antibacterial activity (Lakbar et al., 2021). Secang wood extract has potential as an antibacterial against several types of Gram-positive and Gram-negative pathogenic bacteria.

Sappan wood extract inhibits the growth of *Bacillus subtilis*, *Staphylococcus aureus*, *Escherichia coli* (Aba et al., 2021) and *Vibrio cholerae* (Sazali et al., 2024). Triterpenoids, flavonoids, and heterocyclic oxygen compounds were identified in isolated components of sappanwood, and brazilin was identified as the main component in sappanwood, which is thought to play a key role in its pharmacological effects (Asevedo et al., 2025); (Vij et al., 2023). Brazilin has pharmacological activities such as anti-inflammatory, antimicrobial, antioxidant, antiviral, and anticomplementary properties. This compound is the main and characteristic component of sappanwood. Several previous studies have also shown that brazilin, a flavonoid, has inhibitory activity against MRSA. Based on the above data, the purpose of this study was to test the effectiveness of sappanwood isolates combined with amoxicillin against MRSA.

## Method

The research method is a laboratory study that focuses on extract preparation, compound isolation, and in vitro antibacterial activity testing.

### *Tools and materials*

The tools used in this study were Laminar Air Flow (Enviroco®), an autoclave (All American Model 25X-2®), an oven (Ecocell®), test tubes (Pyrex®), beakers (Iwaki®), micropipettes (Dragonlab®), plastic Petri dishes (Onelab®), an incubator (Mettler®), a 96-well microplate, and a desiccator. The materials used in this study were: sappanwood extract, Amoxicillin (Supelco), NA (Nutrient Agar), NB (Nutrient Broth), 70% ethanol.

### *Simple Material Preparation*

The test material used was sappanwood obtained from the Gowa area of South Sulawesi. The sappanwood was cleaned of impurities and ground into powder.

### *Secang wood Extract Preparation*

The sappanwood extraction process was carried out using the maceration method using 70% ethanol. A total of 500 grams of sappanwood powder was placed in an Erlenmeyer flask, then 70% ethanol was added until the powder was completely submerged and a solvent layer of approximately 3 cm was formed above the surface. The container was closed, the mixture was stirred periodically, and then allowed to stand for 3 x 24 hours. Afterward, the mixture was filtered using filter paper to obtain the filtrate. The remaining residue was re-macerated until the color faded. The entire filtrate was then evaporated using a rotary evaporator to obtain a thick extract.

### *Phytochemical Screening Process of Secang Wood Extract*

The thickened ethanol extract was partitioned with distilled water and ethyl acetate in a separating funnel at a 1:1 ratio, resulting in two fractions: the water fraction and the ethyl acetate fraction. The ethyl acetate fraction was then evaporated using a rotary evaporator to obtain a thick ethyl acetate extract. This extract was then separated using TLC. To prepare the silica gel, it was first heated at 160°C for 3 hours, then cooled in a desiccator. Afterward, the silica gel was slurried and placed into a column, where it was left overnight. The thickened ethyl acetate extract was ground together with the silica gel, placed into the column, and the eluent was slowly added while the valve was open. The solvent mixtures used included: ethanol:ethyl acetate (3:2), n-hexane:ethyl acetate (2:3), butanol:acetic acid:water (4:1:5), and methanol:ethyl acetate (1:6) (Jatmiko & Mursiti, 2021).

The thick ethyl acetate extract was spotted onto a silica plate at a distance of 0.5 cm from the bottom and side edges of the plate. Afterward, the plate was air-dried, and the spotting was repeated until a sufficient sample size was achieved. Next, the plate was developed using eluents with various solvent ratios as previously mentioned. After the elution process was complete, the plate was removed from the vessel and air-dried, then observed under ultraviolet light at a wavelength of 254 nm. The spots that appeared were then analyzed by calculating the Rf value using the formula.

$$Rf = \frac{\text{Distance of Stain Movement}}{\text{Eluent Movement Distance}} \quad (1)$$

### *Antibacterial effectiveness test*

1 ml of each isolate and amoxicillin solution was placed in a test tube and homogenized. Then, 10 µL was

taken and dropped onto a blank disk. The solvent control disk was dripped with 10 µL of 70% ethanol extract solvent and 10 µL of the positive antibiotic control (Oxycycline). TSA media was inoculated with 150 µL of bacterial suspension ( $1.50 \times 10^8$  CFU/mL). The disc was placed on the media that had been planted with bacteria. The culture was then incubated at 37°C for 24 hours. The diameter of the inhibition zone around the disc was observed and measured to determine antibacterial activity.

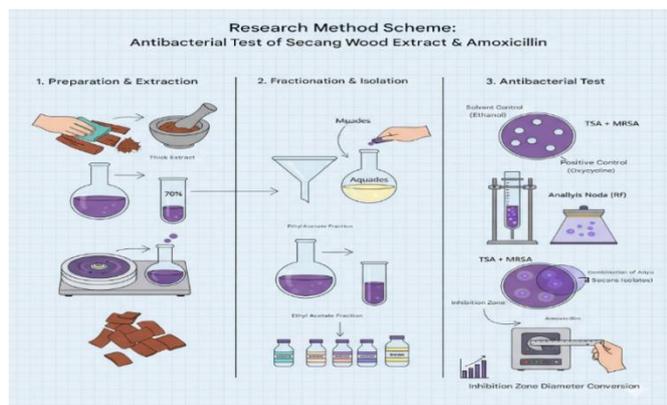


Figure 1. Research method scheme

## Result and Discussion

The maceration method for extracting sappanwood using 70% ethanol resulted in a yield of 10.15%, weighing 20.30 grams. The higher the yield, the more effective the treatment, regardless of other characteristics. Based on the yield results, it can be assumed that sappanwood contains approximately 10.15% bioactive components. A high yield indicates a high bioactive content. The resulting thick sappanwood extract is dark brown, tasteless, and has a distinctive sappanwood aroma (Ambari et al., 2020).

Table 1. Results of % Yield of Red Secang wood Extract (*Caesalpinia sappan* L.)

Sample Weight (g)	Extract weight (g)	Yield
200	20.30	10.15

### Compound separation using thin-layer chromatography (TLC)

Thin-layer chromatography was performed to identify the compounds present in the sappanwood extract. Phytochemical screening tests revealed that sappanwood contains various active compounds, including brazilein, terpenoids, triterpenoids, saponins, alkaloids, and flavonoids. The results of the phytochemical screening test for brazilein are indicated by the appearance of a red color. The presence of brazilein in a sample is indicated by a color change to

red, yellow, or orange (Artati et al., 2025); (Ngamwonglumlert et al., 2020). Based on this, it can be concluded that sappan wood extract (*Caesalpinia sappan* L.) contains brazilein. The presence of brazilein indicates that sappan wood has the potential to be used as a natural dye.

### Antibacterial Test

The results of the diffusion test showed a synergistic effect consistent with the findings of the microdilution test. Based on the results obtained, the inhibition zone and its size against MRSA bacteria by amoxicillin combined with sappan wood extract were significant. The positive control using oxycycline had greater inhibitory effect than the negative control. The observed inhibition zone diameter was  $23.00 \pm 0.42$  mm for the combination of extract with amoxicillin 1%:0.16 mg/l,  $29.00 \pm 0.77$  mm for the combination of sappanwood extract with amoxicillin 29.00 ± 0.77 and  $30.40 \pm 0.75$  for the combination of sappanwood extract with amoxicillin 3%:0.16 mg. This shows that the combination of sappanwood extract with Amoxicillin has inhibitory power against MRSA bacteria.



Figure 2. Results of phytochemical screening of sappan wood extract (*Caesalpinia sappan* L.)

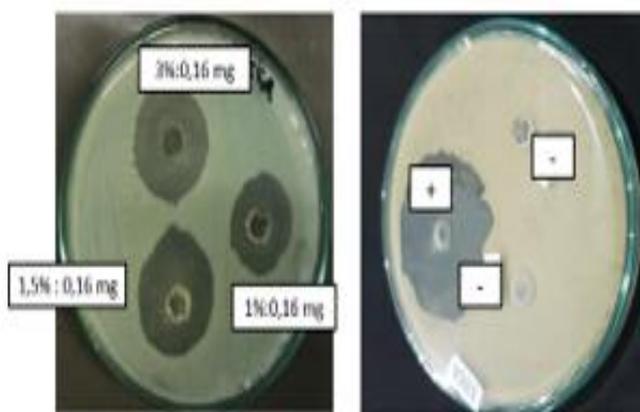


Figure 3. Results of the MRSA bacterial inhibition test

### *Extraction Effectiveness and Identification of Bioactive Compounds*

The initial process of this research focused on obtaining sappan wood (*Caesalpinia sappan* L.) extract using a maceration method with 70% ethanol. 70% ethanol was chosen based on its ability to extract polar and semipolar compounds, which include most bioactive components such as flavonoids and tannins. The extraction results showed a yield of 10.15% (20.30 grams). This relatively high yield indicates that sappan wood is rich in ethanol-extractable components, strengthening the assumption that this material contains significant levels of bioactive compounds. The resulting thick extract was dark brown, consistent with the general visual characteristics of sappan wood extracts. Compound identification was further conducted through phytochemical screening and thin-layer chromatography (TLC).

The phytochemical screening results confirmed the presence of various compound classes, including terpenoids, triterpenoids, saponins, alkaloids, and most crucially, flavonoids and brazilein (Mathe et al., 2024); (Hassan et al., 2020); (Jhumur et al., 2025). The presence of brazilein was specifically indicated by the appearance of a red color in the screening test. Brazilein is a marker compound and the main component of sappanwood, structurally a heterocyclic oxygen compound (Jamaddar et al., 2023). The presence of these compounds, particularly brazilein, is highly relevant because the scientific literature has extensively reported the role of flavonoids and their derivatives as antibacterial, anti-inflammatory, and antioxidant agents, providing a logical basis for further activity testing (Ullah et al., 2020); (Górniak et al., 2019); (Chagas et al., 2022).

### *Synergistic Activity of the Combination of Secang Wood Extract and Amoxicillin Against MRSA*

Antibacterial activity testing against Methicillin-Resistant *Staphylococcus aureus* (MRSA) using the disc diffusion method showed significant results, confirming a synergistic effect between sappanwood extract and amoxicillin (Chomnawang et al., 2009). Amoxicillin, as a  $\beta$ -lactam antibiotic, is generally ineffective against MRSA because this bacterium possesses resistance mechanisms against this class of bacteria (Zhang & Cheng, 2022); (Wang et al., 2024). Therefore, the ability of this combination to produce a zone of inhibition indicates that sappanwood extract successfully overcomes or reverses MRSA resistance to amoxicillin (Tayeb et al., 2025); (Stachelska et al., 2025).

Quantitative data showed an increase in the diameter of the zone of inhibition with increasing concentration of the extract combined with amoxicillin (0.16 mg/l). The diameter of the inhibition zone increased from  $23.00 \pm 0.42$  mm (for the lower extract

concentration) to a maximum value of  $30.40 \pm 0.75$  mm for the combination of 3% extract and 0.16 mg/l amoxicillin. The magnitude of this inhibition zone even approached or exceeded that of the positive control (Oxycycline), underscoring the therapeutic potential of this combination. This synergistic effect is likely due to a dual mechanism, in which brazilein or other flavonoids in the extract act through a different pathway than amoxicillin (Wrońska et al., 2022); (Lam et al., 2024); (Okoduwa et al., 2024), or even interfere with efflux pumps or MRSA cell wall components responsible for resistance, thereby restoring bacterial sensitivity to amoxicillin (Sodhi et al., 2021); (Spatz et al., 2023); (Galgano et al., 2025). This finding is crucial in efforts to develop complementary therapies to combat resistant MRSA infections.

### **Conclusion**

Conclusion of this study that sappan wood extract (*Caesalpinia sappan* L.) has antibacterial activity against MRSA. A concentration of 3% has the highest inhibitory power. It was found that the higher the concentration of the extract used, the greater the inhibitory power against MRSA bacteria. Secang wood extract (*Caesalpinia sappan* L.) contains active compounds such as brazilein and shows a strong synergistic effect when combined with amoxicillin. This combination effectively inhibits the growth of MRSA, as evidenced by an increase in the inhibition zone up to  $30.40 \pm 0.75$  mm, which indicates the potential to overcome antibiotic resistance.

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### **Author Contributions**

"Conceptualization, B.Y. and H.A.; methodology, B.Y.; software, H.R.; validation, B.Y., H.A. and H.R.; formal analysis, H.R.; investigation, H.A.; resources, B.Y.; data curation, H.R.; writing—original draft, H.A.; writing—review and editing, H.A.; visualization, B.Y.; supervision, H.R.; project administration, H.A.; funding acquisition, B.Y. All authors have read and approved the published version of the manuscript."

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### **Conflicts of Interest**

This research was conducted under the institutional mandate to improve the competence and capacity of lecturers. It is hoped that the findings of this study will have a significant

positive impact on human resource development, particularly in the academic environment, and support innovation and progress in education.

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