



Comparative Susceptibility of *Staphylococcus aureus* and *S. pyogenes* to *Musa paradisiaca* Linn Leaf Extract and Fusidic Acid in Impetigo Patients

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ABSTRACT

Introduction. An estimated 12% of the world's population is at risk of experiencing impetigo. The prevalence of impetigo in developing countries ranges from 111 to 140 million cases. Impetigo often occurs in children aged 2-5 years. One way to overcome this condition involves using natural products or phytochemicals that are effective, safe, and economical. One of the Indonesian plants that can be used as an alternative medicine with antibacterial effects is the kepok banana leaves (*Musa paradisiaca* Linn). This study aimed to assess the susceptibility of *S. aureus* and *S. pyogenes* to the antimicrobial potential of the extract of *M. paradisiaca* leaf extract and fusidic acid using isolates from impetigo patients. **Methods.** This in vitro experimental study used a post-test-only control-group design. Bacterial isolates were obtained from impetigo patients and tested using the disk diffusion method following CLSI standards. Group comparisons were conducted using the Kruskal-Wallis test followed by Mann-Whitney U tests. A p-value < 0.05 was considered statistically significant. **Results.** Bivariate analysis showed a significant difference in the susceptibility of *S. aureus* between fusidic acid and *M. paradisiaca* extract (p < 0.05), where fusidic acid demonstrated larger inhibition zones. Similarly, a significant difference was observed for *S. pyogenes* (p < 0.05). However, there was no significant difference between the 50% and 100% extract concentrations. **Conclusion.** *M. paradisiaca* leaf extract exhibits antibacterial activity against *S. aureus* and *S. pyogenes*, but is significantly less effective than standard fusidic acid treatment in vitro.

1. Introduction

Impetigo is a skin disorder belonging to the pyoderma group, mostly caused by *Staphylococcus aureus* (*S. aureus*) or group A *Streptococcus* (GAS).¹ Clinical variants of impetigo are divided into bullous and non-bullous impetigo. Non-bullous impetigo occurs in around 70% of impetigo cases.¹

An estimated 12% of the world's population is at risk of developing impetigo.² The prevalence of impetigo in developing countries ranges from 111 to 140 million people. Impetigo often occurs in children aged 2-5 years, although it can also occur in adults.^{1,2} Impetigo at Haji Adam Malik General Hospital, North Sumatra, for the 2013-2015 period was around 1% per year, mostly occurring in women in the 0-5 year age group.³

Impetigo can be treated with various types of topical antibiotics.^{1,4,5} Management of impetigo at the

Dermatology, Venereology, and Esthetics (DVE) Department of Dr. Mohammad Hoesin Central General Hospital (RSUP Dr. Mohammad Hoesin-RSMH) Palembang follows the standard operating procedures (SOPs) of the Clinical Practice Guide of the Association of Indonesian Dermatology and Venereology Specialists in 2021, determining fusidic acid as one of the topical treatment options.⁷ Fusidic acid is an effective topical therapy for impetigo with minimal side effects.^{1,6} Treatment is generally carried out empirically because the results of culture and susceptibility testing to determine definitive therapy can only be known within 24-48 hours.¹ The main problem in treating staphylococcal infections is the emergence of antibiotic-resistant strains, such as *Methicillin-Resistant Staphylococcus aureus* (MRSA).^{7,8} Based on research at the DVE RSMH Polyclinic in 2017, fusidic acid resistance rates against

Staphylococcus aureus were found to be relatively high, at 22.2%. This is a challenge for doctors to choose the right antibiotic agent according to the results of the antimicrobial susceptibility test.⁹

One way to overcome this condition requires natural products or phytochemicals that are effective, safe, and economical. One Indonesian plant that may be used as an alternative antibacterial agent is kepok banana leaf (*M. paradisiaca*).¹⁰ The development of traditional medicines from natural ingredients, which are often found in Indonesia, also supports government programs concerning national traditional medicine policy, stating that the development and improvement of traditional medicines aims to obtain high-quality, safe, efficacious, and scientifically tested traditional medicines.¹¹

Recent studies have highlighted the potential of *Musa paradisiaca* components. Owusu-Boadi et al. (2021) reported that extracts from *M. paradisiaca* fruit stalks contain phenols, alkaloids, and tannins that demonstrate significant antimicrobial effects against oral pathogens.¹² The mechanism of action is attributed to these phytochemicals disrupting bacterial cell membranes and inhibiting enzymatic reactions essential for bacterial survival. Furthermore, Karuppiyah & Mustaffa (2013) demonstrated that ethyl acetate extracts of *Musa sp.* leaves showed high activity against multidrug-resistant pathogens, suggesting the presence of potent bioactive compounds in the leaves.¹³ Another study found that increasing the concentration of banana stem sap causes a decrease in the number of colonies of *Pseudomonas aeruginosa* and an increase in the diameter of the bacterial inhibition zone.¹⁰ Banana leaves contain phenolics and active substances such as tannins and flavonoids. Dinastuti et al. (2015) stated that tannins are found in the peel of unripe bananas; however, as bananas ripen, tannin levels decrease. Banana flesh contains an average of 11.21% flavonoids, and banana leaves contain 24.6%. The results of Noorhamdani et al. (2012) research show that tannin and flavonoid compounds found in young kepok banana leaves have the potential to be antibacterial against bacteria *Staphylococcus aureus*.¹²

This study aimed to evaluate the in vitro antibacterial activity of *M. paradisiaca* leaf extract at concentrations of 50% and 100%, compared with fusidic acid, against *Staphylococcus aureus* and *S. pyogenes* isolated from impetigo patients.

2. Methods

This experimental (in vitro) study used a post-test-only control-group design. Research sampling was performed at the DVE RSMH Palembang Infectious Dermatology Polyclinic. Gram stain examination was carried out at the RSMH Laboratory, while culture and susceptibility tests were conducted

at the Palembang Health Laboratory Center (BBLK). The *M. paradisiaca* extract was made in the Pharmacy Department, Faculty of Mathematics and Natural Sciences, UNSRI Palembang. The research took place from December 2023 to February 2024.

A total of 12 impetigo patients aged ≤ 15 years were included. From these patients, 30 bacterial isolates (15 *S. aureus* and 15 *S. pyogenes*) were obtained. Inclusion criteria were untreated impetigo with Gram-positive cocci on smear and positive cultures for *S. aureus* or *S. pyogenes*. The negative control consisted of DMSO without extract or antibiotic. The positive control used fusidic acid at 10 $\mu\text{g/mL}$. Antibacterial susceptibility was tested using the disk diffusion method following Clinical and Laboratory Standards Institute (CLSI) guidelines. Data were analyzed using the Kruskal-Wallis test followed by Mann-Whitney U tests ($p < 0.05$).

The extraction process utilized 200 g of dried *M. paradisiaca* leaves, ground into a coarse powder. Extraction was performed using continuous Soxhlet extraction. The solvents used were ethyl acetate and methanol (55–80%) to retrieve both polar and non-polar compounds. The resulting extract was concentrated using a rotary evaporator to remove the solvent. For the experiment, the dried extract was dissolved in dimethyl sulfoxide (DMSO) to obtain the desired concentrations. Hospital-level outpatient visit statistics for 2018–2022 were extracted from the DVE Polyclinic outpatient registry/SIMRS as aggregated data. This study received ethical approval from the Health Research Ethics Committee of RSUP Dr. Mohammad Hoesin Palembang (No. DP.04.03/D.XVIII.6.8/ETIK/200/2023).

3. Results

Based on internal outpatient registry data from the Dermatology, Venereology, and Aesthetics (DVE) Polyclinic, Dr. Mohammad Hoesin Hospital (RSMH), Palembang, the proportion of impetigo visits increased from 2018 to 2022: 16/960 (1.6%) in 2018; 10/910 (1.0%) in 2019; 1/81 (1.2%) in 2020; 9/521 (1.7%) in 2021; and 20/697 (2.8%) in 2022.

Among the impetigo patients, most were female (58.3%), with a mean age of 7.58 ± 3.58 years (range 4–16). The largest age groups were 1–5 years and 6–10 years (41.7% each). Half of the participants had not yet attended school (50%) and half were classified as having low socioeconomic status (50%). Most participants had normal BMI (83.3%). The most frequently isolated organism was *S. pyogenes* (50.0%), followed by *S. aureus* (41.7%), while mixed infection (*S. aureus* + *S. pyogenes*) was found in 8.3% (Table 1).

There was a significant difference in the susceptibility of *S. aureus* between the negative control group with fusidic acid and both concentrations of *M. paradisiaca* extract ($p < 0.05$),

whereas there was no significant difference between 50% and 100% *Musa paradisiaca* extract ($p = 0.778$) (Table 2).

Based on bivariate analysis, the diameter of the *S. pyogenes* inhibition zone differed significantly between the fusidic acid (10 µg/ml) group and the negative control and both extract concentrations (50% and 100%) ($p < 0.05$) (Table 2). The diameter of the inhibition zone in sequence starting from the largest, was found in the 10 µg/ml fusidic acid intervention group, *M. paradisiaca* 100%, *M.*

paradisiaca 50%, and the negative control. From the analyses above, significant differences were observed between fusidic acid (10 µg/ml) and *M. paradisiaca* extracts (50% and 100%) for both bacteria ($p < 0.05$). No significant difference was observed between the 50% and 100% extracts ($p = 0.778$). Fusidic acid showed the largest inhibition zones (27.4 ± 2.7 mm), followed by *M. paradisiaca* 100% (7.3 ± 1.3 mm) and 50% (7.0 ± 1.2 mm) (Table 3). The Kruskal-Wallis test indicated significant differences among groups ($p < 0.001$).

Table 1. Characteristics of Impetigo Patients

Characteristics	n	%
Gender		
Male	5	41.7
Female	7	58.3
Age		
1-5 years	5	41.7
6 – 10 years	5	41.7
11 – 17 years	2	16.7
Age (years)		
Mean $\pm$ SD		7.57 ± 3.58
Median (Min-Max)		5.75 (4 – 16)
Education		
Not yet in school	6	50.0
Elementary School	5	41.7
Junior high school	0	0.0
Senior high school	1	8.3
Economic Status		
Low	6	50.0
Secondary	4	33.3
High	2	16.7
Body Mass Index		
Underweight	2	16.7
Normal weight	10	83.3
Use of Antibiotics		
Once	0	0.0
Never	12	100
Types of Bacteria		
<i>S. aureus</i>	5	41.7
<i>S. pyogenes</i>	6	50.0
<i>S. aureus</i> + <i>S. pyogenes</i>	1	8.3
Total	12	100

Table 2. Comparison of the Susceptibility of *S. aureus* Bacteria and *S. pyogenes* Bacteria from Impetigo Patients between Two Groups

Group	Bacteria <i>S. aureus</i> Mean $\pm$ SD	P value	Bacteria <i>S. pyogenes</i> Mean $\pm$ SD	P value
Negative control	0.00 $\pm$ 0.00	–	0.00 $\pm$ 0.00	–
Fusidic acid 10 µg/mL	27.46 $\pm$ 2.17	0.002*	27.23 $\pm$ 2.70	0.000
<i>Musa paradisiaca</i> Linn 50%	7.05 $\pm$ 1.18	0.000	9.61 $\pm$ 0.43	0.000
<i>Musa paradisiaca</i> Linn 100%	7.26 $\pm$ 1.27	0.778	10.11 $\pm$ 0.94	0.010

Independent t-test, *Mann-Whitney U test, $p < 0.05$

Table 3. Comparison of Bacterial Susceptibility *S. aureus* and *S. pyogenes* on Impetigo Patients between All Groups (Multivariate)

Group	Mean	P value
<i>S. aureus</i>		
Negative Control	0.00	0.000
Fusidic acid 10 µg/ml	27.46	
<i>M. paradisiaca</i> 50%	7.05	
<i>M. paradisiaca</i> 100%	7.26	
<i>S. pyogenes</i>		
Negative Control	0.00	0.000
Fucidic Acid 10 µg/ml	27.23	
<i>M. paradisiaca</i> 50%	9.61	
<i>M. paradisiaca</i> 100%	10.11	

$p < 0.05$ indicates a significant difference (Kruskal–Wallis Test)

Table 4. Inhibitory Response of Fusidic acid to Bacteria *S. aureus* and *S. pyogenes* from Impetigo Patients

Bacteria	Inhibition zone	n	%
<i>S. aureus</i>	Reduce susceptibility	12	100
<i>S. pyogenes</i>	Sensitive	12	100

Table 5. Inhibited Response *M. paradisiaca* all Doses against Bacteria *S. aureus* and *S. pyogenes* from Impetigo Patients

Bacteria	Dose	Zone of Inhibition, n (%)			
		Less Effective	Weak Inhibitory Response	Moderate Inhibitory Response	Strong Inhibitory Response
<i>S. aureus</i>	50%	6 (100)	0 (0)	0 (0)	0 (0)
	100%	6 (100)	0 (0)	0 (0)	0 (0)
<i>S. pyogenes</i>	50%	5 (83.3)	1 (16.7)	0 (0)	0 (0)
	100%	3 (50.0)	3 (50.0)	0 (0)	0 (0)

Response classification: Less effective <10mm, Weak 10-15 mm, Moderate 16-19 mm, Strong >20mm

In this study, based on inhibition zone diameters, fusidic acid produced the largest zones against both *S. aureus* and *S. pyogenes*, followed by *M. paradisiaca* 100% and 50%. The mean inhibition zone for fusidic acid against *S. aureus* was 27.4 ± 2.7 mm, indicating sensitivity by CLSI criteria. However, due to uniformly weak growth suppression and narrow zone variations among isolates, the overall response was classified as reduced susceptibility (Table 4).

Inhibitory response to bacteria *S. aureus* found to be less effective (100%) in both *M. paradisiaca* 50% or *M. paradisiaca* 100%, while the bacterial response was inhibited by *S. pyogenes*, with *M. paradisiaca* 50% was found to be less effective, namely 83.3%, but at *M. paradisiaca* 100% obtained 50% less effective and 50% have a weak inhibitory response (Table 5).

4. Discussion

Impetigo is a skin disorder, including pyoderma, mostly caused by *S. aureus* or group A *Streptococcus* (GAS).¹ Various predisposing factors include age, gender, socioeconomic status, environmental conditions, and the patient's nutritional status.¹⁵ Assessment of predisposing factors for infection is

useful both in non-medical management, such as educating patients to prevent recurrence, and educating the community to reduce the incidence of impetigo.¹⁶

In this study, the proportion of female patients was slightly higher (58.3%) than that of male patients (41.7%). In line with research by Nthibo et al (2023), it was found that the percentage of impetigo patients in females (58.25%) was higher than in males (41.75%).¹⁷ Loadsman et al. (2019) research also found that impetigo was more common in women (52.6%) than in men (47.4%).¹⁸

Impetigo often occurs in children aged 2-5 years, although it can also occur in adults.^{1,4} In this study, it was found that the majority of impetigo patients' ages were 1-5 years and 6-10 years, with a mean age of 7.57 ± 3.58 years. These results are in line with research conducted by Romani et al in 2017, which reported that the majority of impetigo patients were aged 5-9 years.¹⁹

The highest level of education for children in this study was pre-school children, namely 50%, followed by elementary school education (41.7%), and high school education (8.3%). The behavior of pre-school

and school-aged children can increase impetigo through transmission either from contaminated environments or direct contact. These behaviors include the desire to get to know the surrounding environment, which can be a source of exposure to contaminated environments, and the habit of playing in groups, which is a source of physical contact.¹⁵ This is thought to facilitate the transmission of bacteria both from the environment and between hosts. In addition, tissue damage due to trauma or excoriation will facilitate bacterial invasion.^{1,20}

Socioeconomic factors often influence environmental conditions and nutritional status.²¹ Research by Depari et al. reported that the main predisposing factor for impetigo was low socioeconomic level (56.6%).⁴ In this study, the majority of research patients were in low (50.0%), middle (33.3%), and high socioeconomic conditions (16.7%). The results of this study are also in accordance with research by Hazarika et al., which reported that 63% of impetigo patients were in low and middle-socioeconomic groups, as many as 37%.¹⁶ Low socioeconomic level causes parents to have less knowledge about infectious diseases, and the condition of the living environment is less good, so that there can be an increase in bacterial colonization.²²

Nutritional status is one of the factors that determines a patient's immunity. Malnutrition or poor nutrition can reduce immunity, thereby increasing the virulence and toxicogenic properties of bacteria, making it easier for infections to occur.^{1,63} Most of the samples in this study had a BMI of normal weight (83.3%), followed by underweight (16.7%). The results of this study are not much different from the research of Pangow et al, which reported that 64.7% of impetigo patients had a normal weight.²³

According to WHO, the main bacteria causing superficial pyoderma in tropical countries are *S. pyogenes* and *S. aureus*.²¹ In this study, the most common bacteria found were *S. pyogenes* (50.0%), followed by *S. aureus* (41.7%), as well as a mixture of *S. aureus* and *S. pyogenes* (8.3%). The results of this study are in accordance with research by Bowen et al, showing bacteria *S. pyogenes* (24%) are more commonly found in comparison to *S. aureus* (9%). The research concluded that *S. pyogenes* remains the main pathogen of impetigo in tropical regions.²⁴ Transmission of *S. pyogenes* of asymptomatic throat infections is thought to play a role in the high incidence of impetigo caused by *S. pyogenes*.²³

Along with the development of the lifestyle back to nature, traditional medicines or herbal medicines are widely used by the public because they have advantages in consuming them. Banana plants are often used as constituents in traditional medicinal preparations. Every component of the banana plant

can be used effectively, including the tuber, stem, flowers, leaves, and fruit. According to Routray and Orsat (2012), kepok banana leaves (*M. paradisiaca*) contain many active components, including alkaloids, saponins, tannins, flavonoids, terpenes, and carbohydrates.²⁵

The results of research by Noorhamdani et al (2012) show that the tannin and flavonoid compounds contained in young banana leaves have the potential to act as antibacterials against bacteria. *Escherichia coli*. This shows that banana leaves have antibacterial properties, making it possible to use them as antibiotics against *S. aureus* bacterial infections.²⁶

The working mechanism of *M. paradisiaca* as an antibacterial against *S. aureus* is by reducing surface tension, so that bacterial permeability increases, as well as reducing the concentration of calcium ions, inhibiting enzyme production, and disrupting the enzymatic reaction process in bacteria. *S. aureus* thus inhibits the plasma coagulation required by *S. aureus*. According to Wistreich and Lechtman (2014), damage and increased permeability of bacterial cells cause cell growth to be hampered and can ultimately lead to cell death.²⁶ The inhibitory response was classified based on inhibition zone diameter: <10 mm (less effective), 10–15 mm (weak), 16–19 mm (moderate), and >20 mm (strong).⁴

The antibacterial activity of *M. paradisiaca* extract against *S. pyogenes* was relatively modest. Although the 100% concentration produced slightly larger inhibition zones compared to the 50% concentration, the overall response remained within the weak inhibitory range. This suggests that increasing extract concentration may enhance antibacterial activity; however, the effect remains substantially lower than that of fusidic acid.

The antibacterial activity of *M. paradisiaca* extract against *S. aureus* was minimal. Both 50% and 100% concentrations produced inhibition zones that remained within the less effective range according to the predefined classification criteria. Increasing the extract concentration did not result in a clinically meaningful enhancement of antibacterial activity. This finding suggests that the crude leaf extract possesses limited efficacy against *S. aureus*, particularly when compared with standard antibiotic therapy.

Research on kepok banana leaf extract has suggested that alkaloids, tannins, steroids, and flavonoids may be collectively or individually responsible for the antimicrobial activity. Biswas et al (2011) reported that ethanol extract of leaves of *M. paradisiaca* shows antibacterial activity *in-vitro* moderate against gram-positive bacteria (*B. Megaterium*, *B. Subtilis*, *S. aureus*) and gram-negative (*E. coli*, *P. aeruginosa*, *S. dysenteriae*, *S. typhi*, *Vibrio*

cholerae dan *S. flexneri*) with an inhibition zone ranging from 10.53 ± 0.37 to 12.42 ± 0.85 mm at a concentration of 500 µg/disk.²⁷ In this research, *M. paradisiaca* shows less effectiveness against *S. aureus* and a weak inhibitory response to *S. pyogenes*. This may be caused by several factors such as errors when extracting and storing the extract. The long extraction process is a variable that influences the quality of the resulting extract. Long extraction times cause a significant increase in temperature, thereby speeding up the solvent evaporation process, and the concentration obtained will be better.²⁵ The weak inhibitory response observed for *S. pyogenes* suggests that banana leaf extract may be considered as an adjunctive option, particularly for patients who cannot use topical antibiotics, however clinical studies are still needed.

The research concluded that *S. pyogenes* are susceptible to *M. paradisiaca* doses of 50% and 100% and were less effective than fusidic acid in inhibiting bacterial growth *S. pyogenes* in impetigo patients but is less effective against bacteria *S. aureus*. This discrepancy between inhibition zone size and phenotypic resistance is consistent with reports of emerging fusidic acid-resistant *S. aureus* strains in Asia and the Middle East.²⁸ These findings indicate that while in vitro testing may still yield sensitive results, clinical effectiveness may be compromised due to acquired resistance mechanisms. These results are in accordance with Malini's research (2017), which found that there was a rate of resistance to fusidic acid in *S. aureus* quite high that is amounting to 22.2%.⁹

Fusidic acid works by binding with *elongation factor-G* on ribosomes, thus inhibiting DNA translocation in bacterial protein synthesis. In this study the diameter of the inhibition zone *M. paradisiaca* to *S. aureus* and *S. pyogenes* with the highest concentration is still lower than that of fusidic acid, so it can be concluded that the bacteria *S. aureus* and *S. pyogenes* are susceptible to fusidic acid.²⁹

Our study found that while *M. paradisiaca* leaf extract showed antibacterial activity, it was significantly lower than the positive control (fusidic acid). Several factors may explain this lower efficacy. First, our study used methanol/ethyl acetate extraction. Previous research by Karuppiah and Mustafa (2013) noted that ethyl acetate extracts of *M. paradisiaca* showed the highest activity against *E. coli* and *P. aeruginosa* compared to other solvents.¹³ Similarly, Owusu-Boadi et al. (2021) found that ethyl acetate fractions of fruit stalks were superior to aqueous and ethanol fractions in inhibiting oral pathogens.¹² This suggests that the choice of solvent significantly influences the concentration of active antimicrobial compounds like flavonoids and alkaloids extracted. Second, Kapadia et al. (2015)

demonstrated that alcoholic extracts of banana peel were effective against periodontal pathogens like *P. gingivalis* with inhibition zones up to 15mm.³⁰ In contrast, our leaf extract yielded smaller zones (approx. 7-10mm). Differences in phytochemical composition across various plant parts have been widely documented, with compounds such as phenolics, flavonoids, terpenoids, and alkaloids present at varying levels in leaves, peels, stems, and flowers of *M. paradisiaca*.³¹ This variation in phytochemical concentration may partly explain observed discrepancies in antibacterial activity between extracts from different parts. Although the inhibition zones of leaf extract were lower than those of pure antibiotics, the presence of measurable antibacterial effects suggests potential ethnopharmacological relevance.³²

Our finding of reduced susceptibility of *S. aureus* to fusidic acid is alarmingly high but mirrors a growing global concern regarding the efficacy of topical antibiotics. While fusidic acid has historically been a first-line treatment for impetigo, recent surveillance data indicate a rising trend in resistance. For instance, a 2025 study in the Netherlands reported outbreaks of impetigo caused by fusidic acid-resistant MRSA strains (clone ST121), rendering standard topical treatments ineffective.³³ Similarly, high prevalence rates of Fusidic acid resistance have been reported in parts of China (up to 40% in some provinces) and Kuwait (over 20%), driven by the widespread use of monotherapy.^{34,35} The reduced susceptibility pattern observed in our study suggests the possible circulation of a specific resistant clone in the Palembang region, highlighting the urgent need for alternative therapeutic strategies.

In the search for non-antibiotic alternatives, our results demonstrating the susceptibility of *S. pyogenes* to *M. paradisiaca* extract align with the growing interest in plant-based antimicrobials. Recent studies support the antimicrobial potential of this plant; for example, Santy et al. (2025) reported that *M. paradisiaca* peel extracts produced inhibition zones of approximately 7.60 mm against *S. aureus*, which is comparable to the "weak" to "moderate" inhibitory responses (approx. 7.05 mm) observed in our study.³³ This consistency across studies suggests that while crude extracts may not yet match the potency of synthetic antibiotics like fusidic acid (which typically yield >20 mm zones when effective), they possess undeniable bioactivity. The mechanism is likely attributed to the disruption of bacterial cell membranes by phenolic compounds and tannins. Therefore, *M. paradisiaca* extracts hold promise not necessarily as a standalone replacement for acute infections, but potentially as a source for purifying novel antimicrobial compounds or as an adjunctive

therapy to reduce reliance on conventional antibiotics.³⁶

This *in vitro* experimental study evaluated the susceptibility of *S. aureus* and *S. pyogenes* to *M. paradisiaca* extract in comparison with fusidic acid. Although measurable antibacterial activity was observed, the inhibition produced by the extract did not reach the potency of the standard antibiotic. Future studies should investigate higher concentrations, optimized extraction methods, or fractionation of bioactive compounds to enhance antibacterial efficacy and potentially achieve inhibition zones comparable to those of fusidic acid.

This study has several limitations that should be acknowledged. First, the sample size was relatively small (n=12 patients), which may limit the generalizability of the resistance patterns observed to the broader population in Palembang. Second, this was an *in vitro* study; the findings of antimicrobial susceptibility on agar plates may not fully translate to clinical efficacy on human skin due to factors such as tissue penetration, stability of the extract in a biological environment, and host immune responses. Third, the extraction process used a single solvent system, which might not have captured all potential bioactive compounds. We did not perform high-performance liquid chromatography (HPLC) or mass spectrometry (MS) to identify and quantify the specific active phytochemicals (e.g., specific flavonoids or saponins) responsible for the antibacterial activity. Finally, molecular analysis to detect specific resistance genes (such as *fusB* or *fusC*) in the resistant *S. aureus* isolates was not conducted, limiting our understanding of the underlying genetic mechanisms of the observed high-level resistance.

Overall, this research provides hypotheses and insight into the benefits of the extract *M. paradisiaca* as an antibacterial agent for impetigo patient lesions. These findings may inform future research, including *in vivo* studies and clinical trials, to evaluate the safety, efficacy, and standardization of *M. paradisiaca*-based antibacterial preparations for impetigo management.

5. Conclusion

This study concludes that there is a significant difference in susceptibility, with fusidic acid showing superior antibacterial efficacy compared to *M. paradisiaca* leaf extract against both *S. aureus* and *S. pyogenes*. However, the extract demonstrated measurable antibacterial activity, particularly against *S. pyogenes*. Further research focusing on fractionation and purification of the active compounds is recommended to enhance their potency.

6. Author Contribution

All authors contributed to the manuscript drafting, critical revision, and final approval of the submitted version.

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