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ANTIBACTERIAL n-HEXANE EXTRACT OF *Uncaria Gambir* Roxb FROM PONTIANAK

ANTIBAKTERI EKSTRAK n-HEXANE *Uncaria Gambir* Roxb DARI PONTIANAK

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Abstract

Staphylococcus aureus is a Gram-positive bacterium that can act as both a commensal and an opportunistic pathogen, causing a range of infections from superficial skin conditions to life-threatening illnesses. The emergence of antibiotic-resistant strains, such as MRSA, highlights the need for alternative or complementary natural antibacterials. This study aimed to evaluate the antibacterial potential of n-hexane extract of *Uncaria gambir* Roxb (UGR) leaves against *S. aureus* through both in silico prediction and in vitro testing. The compounds present in the leaves were identified using the Knapsack family database and analyzed for antibacterial activity using PASS Online, while solubility was predicted with SwissADME. In vitro antibacterial activity was determined using the agar diffusion method at six extract concentrations (5–40%), with 10% Chloramphenicol as a positive control and sterile distilled water as a negative control. Results indicated that metabolites such as Gallic acid, Cinchonain Ia, and Procyanidins B1 and B3 exhibited the highest predicted antibacterial probabilities, with solubility patterns suggesting better extraction in nonpolar solvents. The inhibition zone diameter generally increased with extract concentration, reaching a maximum of 10.76 ± 1.58 mm at 40%, confirming a concentration-dependent effect. However, the extract's activity remained lower than that of Chloramphenicol (20.47 mm). Factors such as low compound concentration, limited solubility, chemical properties, and bacterial defense mechanisms likely contributed to the moderate inhibitory activity of the compound. Overall, the n-hexane extract of *Uncaria gambir* leaves demonstrates measurable antibacterial potential against *S. aureus*, supporting its traditional use and indicating its promise for further study as a natural antibacterial agent.

Keywords: *Uncaria gambir* Roxb, *Staphylococcus aureus*, n-hexane extract, antibacterial

Abstrak

Staphylococcus aureus adalah bakteri Gram-positif yang dapat berperan sebagai komensal maupun patogen oportunistik, menyebabkan berbagai infeksi mulai dari kondisi kulit ringan hingga penyakit yang mengancam jiwa. Munculnya strain resisten antibiotik, seperti MRSA, menekankan perlunya antibakteri alami sebagai alternatif atau pelengkap. Penelitian ini bertujuan mengevaluasi potensi antibakteri ekstrak n-heksana daun *Uncaria gambir* Roxb terhadap *S. aureus* melalui prediksi in silico dan uji in vitro. Senyawa yang terkandung dalam daun diidentifikasi menggunakan basis data

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Knapsackfamily dan dianalisis probabilitas antibakterinya dengan PASS Online, sementara kelarutan diprediksi menggunakan SwissADME. Aktivitas antibakteri in vitro ditentukan menggunakan metode difusi agar dengan enam konsentrasi ekstrak (5–40%), dengan 10% Chloramphenicol sebagai kontrol positif dan aquadest steril sebagai kontrol negatif. Hasil menunjukkan bahwa metabolit seperti Asam Galat, Cinchonain Ia, dan Procyanidin B1 serta B3 memiliki probabilitas antibakteri tertinggi, dengan pola kelarutan yang menunjukkan ekstraksi lebih efektif dalam pelarut nonpolar. Diameter zona hambat umumnya meningkat seiring konsentrasi ekstrak, mencapai maksimum 10,76 ± 1,58 mm pada 40%, menunjukkan efek bergantung konsentrasi. Namun, aktivitas ekstrak tetap lebih rendah dibandingkan Chloramphenicol (20,47 mm). Faktor-faktor seperti konsentrasi senyawa yang rendah, kelarutan terbatas, sifat kimia, dan mekanisme pertahanan bakteri kemungkinan berkontribusi terhadap aktivitas hambat yang moderat. Secara keseluruhan, ekstrak n-heksana daun *Uncaria gambir* menunjukkan potensi antibakteri terhadap *S. aureus*, mendukung penggunaan tradisionalnya dan menunjukkan prospek untuk penelitian lebih lanjut sebagai antibakteri alami.

Kata Kunci: *Uncaria gambir* Roxb, *Staphylococcus aureus*, ekstrak n-heksana, antibakteri

INTRODUCTION

Staphylococcus aureus is a versatile Gram-positive spherical bacterium (coccus), capable of surviving both aerobic and facultative anaerobic conditions. (Bashabsheh *et al*., 2024). It plays a dual role as both a commensal and an opportunistic pathogen, causing a variety of diseases in humans. As one of the most clinically significant bacterial pathogens, *S. aureus* is responsible for infections ranging from minor superficial skin infections to severe, life-threatening illnesses, including pneumonia, endocarditis, osteomyelitis, septic arthritis, and bacteremia. (Yamazaki *et al*., 2024). Although it commonly colonizes the anterior nasal passages, skin, and mucosal surfaces in approximately 30% of healthy individuals, *S. aureus* can exploit gaps in the host defenses or compromised immune systems to cause invasive infections, demonstrating its adaptability and resilience. (Touaitia *et al*., 2025). Considering the ability of *S. aureus* to exploit host vulnerabilities and develop resistance, natural antibacterials represent a promising complementary or alternative approach to addressing this issue.

Natural antibacterials are very necessary, and some of the reasons are pretty strong, namely, Antibiotic resistance - Excessive use of synthetic antibiotics has triggered the emergence of resistant bacteria (such as MRSA from Staphylococcus aureus) *(Ali Alghamdi et al*., 2023). Natural antibacterials can be an alternative or complement to reduce dependence on chemical antibiotics (Gupta & Sharma, 2022). Fewer side effects – Many natural antibacterial compounds (e.g., flavonoids, tannins, terpenoids, essential oils) are derived from plants, so they tend to be safer than synthetic antibiotics, which can cause digestive problems or organ damage when used long-term (Stan *et al*., 2021). Abundant resources – Medicinal plants, spices, and natural products (such as honey, propolis, and herbal extracts) are widely available, making them a more affordable and accessible solution (Refaey *et al*., 2024). Diverse mechanisms of action – Natural antibacterials often work with multiple targets (e.g., damaging cell membranes, inhibiting enzymes, disrupting bacterial cell communication), thereby reducing the risk of rapid emergence of resistance (Belay *et al*., 2024). Supporting holistic health – In addition to their antibacterial properties, many natural compounds also exhibit antioxidant, anti-inflammatory,

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or immunomodulatory effects, providing further health benefits (Dongho Dongmo *et al*., 2025). Natural antibacterials are very important as an alternative, complement, or source of inspiration for the development of new drugs in the era of antibiotic resistance (Muteeb *et al*., 2023). Antibacterial studies of n-hexane extract of UGR leaves against S. aureus have been carried out. *Uncaria gambir* Roxb. was chosen because many people claim that this plant is traditionally used as an antibacterial (Dewi *et al*., 2023). However, no one has yet conducted an antibacterial study on the n-hexane leaf extract of this plant in Pontianak.

RESEARCH METHODS

UGR Leaf Extraction

The dried UGR leaves were ground and weighed to 50 grams, then immersed in n-hexane for three days. Afterward, the mixture was filtered and concentrated with a rotary evaporator to produce a dry extract.

Determination of UGR Antibacterial Probability in Silico

The term "*Uncaria gambir*" was entered into the "Knapsackfamily" database, and the last updated data was on 2024/12/24 (Wijaya *et al*., 2016; Kusumawati *et al*., 2025), obtaining the names of compounds and SMILES codes contained in the UGR plant (Ratnawati *et al*., 2018; Mswahili & Jeong, 2024). The SMILES codes were then analyzed using Pass Online to determine their antibacterial probabilities. (Desai & Joshi, 2019; Amrilah & Hilman, 2024).

In Silico Solubility Test of Each Compound

Determining the solubility class in water is performed using the SMILES code for analysis with SwissADME. The results yield three Log S values: Log S (ESOL), Log S (Ali), and Log S (SILICOS-IT). These three values are averaged. (Daina *et al*., 2017; *Majumdar et al*., 2023).

Determination of Antibacterial Activity against *S. aureus*

The inhibition test was performed using the agar diffusion method with paper discs, following the Kirby-Bauer procedure. This study used six concentrations of the extract, namely 5%, 10%, 20%, 25%, 30%, and 40%, with 10% Chloramphenicol as the positive control and sterile distilled water as the negative control. The test was performed against *Staphylococcus aureus* using UGR leaf extract. The rejuvenated *S. aureus* culture was suspended in sterile distilled water and homogenized using a vortex. Nutrient Agar (NA) media was inoculated with the bacterial culture using sterile cotton swabs on the solidified agar surface. Each treatment was labeled, and then the media were incubated for 24 hours at 37°C. The inhibition zones or clear areas formed around the paper discs were measured using a caliper in millimeters. Observations were made after 24 hours of incubation, with both vertical and horizontal diameters of the inhibition zones recorded as indicators of bacterial sensitivity to the tested

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extract. The measurement of inhibition zones can be performed according to the instructions outlined in Figure 1.

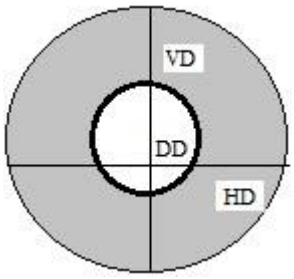

Figure 1. Instructions for Measuring the Inhibition Zone against S. aureus Bacteria.

The diameter of the inhibition zone is measured using the formula:

Diameter Inhibition = $\frac{1}{2}$ x [(VD-DD)+(HD-DD)]

with the information VD (vertical diameter), DD (disc diameter), and HD (horizontal diameter) in mm (Magvirah *et al*., 2020).

RESULTS AND DISCUSSION

Table 1. Active Probability of Compound in UGR

No	Metabolite	Antibacterial (Pa)	Log S (ESOL)	Log S (Ali)	Log S (SILICOS-IT)	average	Solubility class
1	(+)-Catechin	0.320	-2.22	-2.24	-2.14	-2.20	Soluble
2	(-)-Epicatechin	0.320	-2.22	-2.24	-2.14	-2.20	Soluble
3	(+)-Epicatechin	0.320	-2.22	-2.24	-2.14	-2.20	Soluble
4	Mitraphylline	0.185	-3.18	-2.66	-3.96	-3.27	Soluble
5	Roxburghine B	-	-5.90	-5.48	-8.02	-6.47	Poorly
6	Catechol	0.321	-1.63	-1.31	-1.18	-1.37	Very
7	Gallic acid	0.418	-1.64	-2.34	-0.04	-1.34	Very
8	Cinchonain Ia	0.335	-4.33	-5.17	-4.19	-4.56	Moderately
9	Gambiriin C	0.319	-5.28	-6.58	-4.51	-5.46	Moderately
10	Gambiriin A1	0.220	-5.16	-7.21	-3.96	-5.44	Moderately
11	Gambiriin A3	0.311	-4.5	-6.12	-3.96	-4.86	Moderately
12	Gambiriin B1	0.253	-5.69	-7.37	-4.87	-5.98	Moderately
13	Gambiriin B3	0.287	-5.69	-7.37	-4.87	-5.98	Moderately
14	Procyanidin B3	0.319	-5.14	-6.65	-3.91	-5.23	Moderately
15	Procyanidin B1	0.319	-5.14	-6.65	-3.91	-5.23	Moderately
16	Uncarine B	0.185	-3.18	-2.66	-3.96	-3.27	Soluble
17	Gambiriin A2	0.220	-5.16	-7.21	-3.96	-5.44	Moderately
18	Gambiriin B2	0.253	-5.69	-7.37	-4.87	-5.98	Moderately

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Table 2. Inhibition Zone of UGR n-Hexane Extract

Inhibition Zone (mm)		
Sample concentration (%)	Replication	**Average ± Stdev**
5	6.54	6.39±0.22
	6.23	
10	7.07	7.35±0.40
	7.63	
20	7.65	
	8.27	7.96±0.44
25	6.02	6.65±0.89
	7.28	
30	9.59	9.33±0.37
	9.06	
40	9.64	10.76±1.58
	11.87	
Chloramphenicol (10%)		20.47
Aquadest		0.00

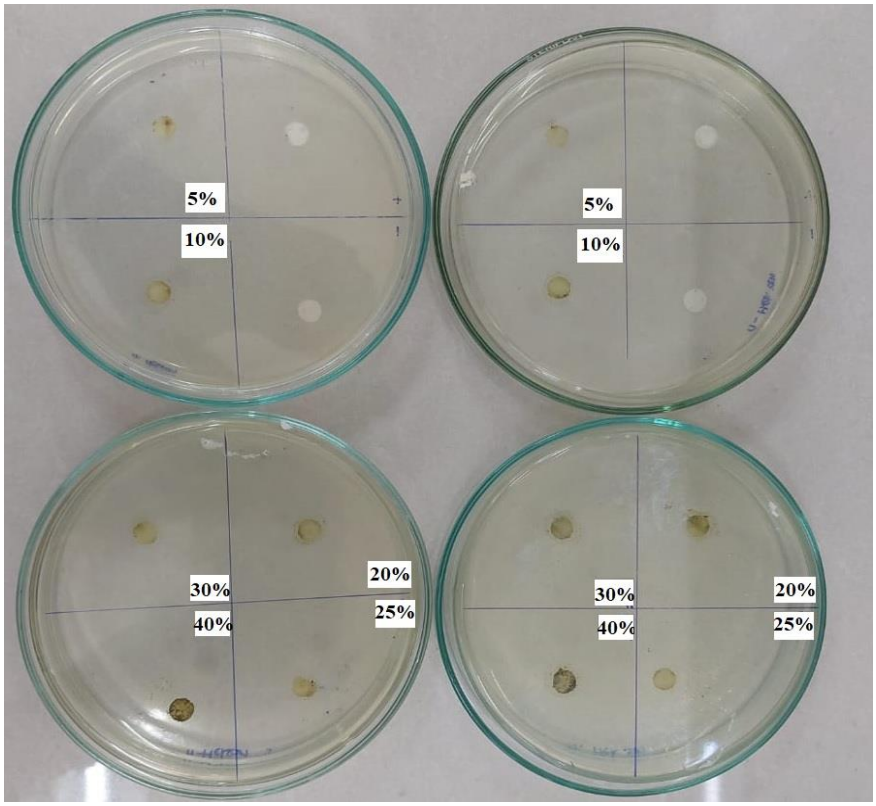

Figure 2. Inhibition Zone of UGR n-Hexane Extract

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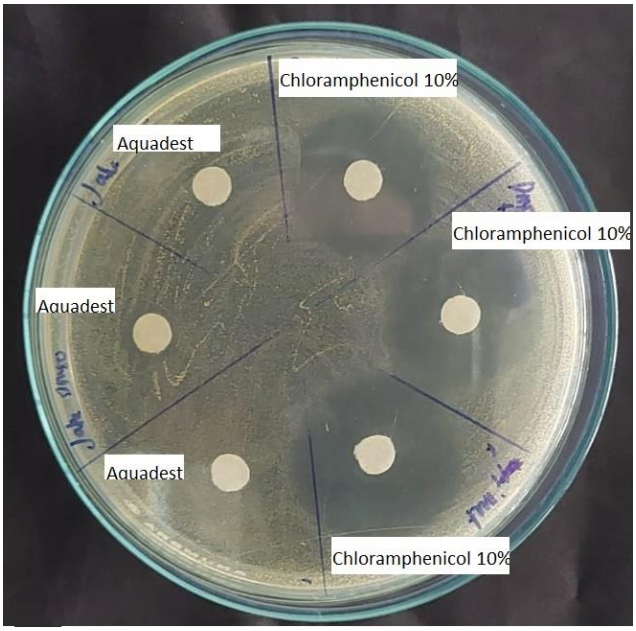

Figure 3. Inhibition Zone of Chloramphenicol 10% & Aquadest

Based on Table 1, the probability of being active as an antibacterial from the highest to the lowest is Gallic acid (0.418), Cinchonain Ia (0.335), Catechol (0.321), (+)-Catechin (0.320), (-)-Epicatechin (0.320), (+)-Epicatechin (0.320), Gambiriin C (0.319), Procyanidin B3 (0.319), Procyanidin B1 (0.319), Gambiriin A3 (0.311), Gambiriin B3 (0.287), Gambiriin B1 (0.253), Gambiriin B2 (0.253), Gambiriin A1 (0.220), Gambiriin A2 (0.220), Mitraphylline (0.185), Uncarine B (0.185), and Roxburghine B (0.000). As for the metabolites that are likely not completely soluble in polar solvents such as water (moderately group, Log S -6)<Log S<-) (Odhiambo et al., 2025) There is also a possibility of being soluble in nonpolar solvents, such as n-hexane. (Plaskova & Mlcek, 2023), (Abubakar & Haque, 2020). So the metabolites that have an average solubility category of moderate are Cinchonain Ia, Gambiriin C, Gambiriin A1, Gambiriin A3, Gambiriin B1, Gambiriin B3, Procyanidin B3, Procyanidin B1, Gambiriin A2, Gambiriin B2, and Roxburghine B with log S values in sequence as follows: -4.56, -5.46, -5.44, -4.86, -5.98, -5.98, -5.23, -5.23, -5.44, -5.98, and -6.47. These predicted antibacterial probabilities and solubility characteristics provide important context for interpreting the results of actual inhibition tests, as they suggest why specific metabolites may exhibit stronger or weaker activity against S. aureus.

The antibacterial inhibition test results showed that increasing the sample concentration was generally followed by an increase in the inhibition zone diameter (Table 2, Figs. 2 and 3). At a concentration of 5%, the inhibition zone was 6.39 ± 0.22 mm, which gradually increased at 10% (7.35 ± 0.40 mm) and 20% (7.96 ± 0.44 mm). Interestingly, at 25% concentration, there was a slight decrease to 6.65 ± 0.89 mm, which may have been influenced by biological variation or technical factors during testing. Subsequently, the 30% concentration showed an increase again with an inhibition zone of 9.33 ± 0.37 mm, and the 40% concentration produced the largest inhibition zone, namely 10.76 ± 1.58 mm. Overall, these results indicate that the antibacterial activity of the extract is concentration-dependent. The comparison with controls highlights that, while the extract shows measurable activity, it remains lower than that of the

standard antibiotic Chloramphenicol (10%), which produced an inhibition zone of 20.47 mm. Meanwhile, the negative control (aquadest) did not produce any inhibition zone (0 mm), indicating that the observed antibacterial effect was solely due to the active compounds in the extract rather than the solvent.

Metabolites may exhibit low inhibitory activity against *S. aureus* due to several factors. The tested compound concentration might be too low. (Odhiambo *et al*., 2025), so the number of active molecules is insufficient to disrupt the growth of *S. aureus* (Nikolic *et al*., 2024), or the chemical properties of the metabolite, such as lipophilicity or hydrophilicity, may limit its penetration into *S. aureus* cells (Halevas *et al*., 2022). In addition, *S. aureus* possesses natural defense mechanisms, including efflux pumps. (Sinha *et al*., 2024), detoxifying enzymes, or a cell wall that prevents compound entry (Chamani *et al*., 2025), while some metabolites may also rapidly degrade or oxidize during testing (Pinu *et al*., 2017). The testing medium factors, such as nutrients, ions, or pH, can also reduce metabolite effectiveness, and not all metabolites have a broad antibacterial spectrum, resulting in low inhibitory activity against *S. aureus.* (Darbandi *et al*., 2022; Zouine *et al*., 2024).

CONCLUSION

The extract, containing various metabolites, exhibited concentration-dependent antibacterial activity against S. aureus, with the highest effectiveness observed at a concentration of 40%. Although some metabolites were predicted to have high antibacterial potential, their actual inhibitory effect was lower than that of the standard antibiotic Chloramphenicol, likely due to factors such as compound concentration, chemical properties, cell penetration ability, and the natural defense mechanisms of S. aureus. Metabolite solubility also influenced their availability to interact with bacterial targets. Overall, these findings highlight the importance of considering predicted activity, physicochemical properties, and bacterial biological mechanisms when evaluating the antibacterial potential of plant-derived metabolites.

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