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Research Article

In Vitro Study of Antibacterial Activity of Patindis Leaf Extract (*Urophyllum arboreum*) and Microneedle Acne Patch against *Propionibacterium acnes* and *Staphylococcus aureus*

Studi In Vitro Uji Aktivitas Antibakteri Ekstrak Daun Patindis (Urophyllum arboreum) dan Sediaan Microneedle Acne Patch terhadap Bakteri Propionibacterium acnes dan Staphylococcus aureus

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ABSTRACT

Acne vulgaris is a cutaneous disorder associated with Propionibacterium acnes and Staphylococcus aureus. This study investigated the antibacterial activity of patindis leaf extract (*Urophyllum arboreum*) and its microneedle acne patch against both bacteria. The extract was prepared from dried simplicia by maceration using 96% ethanol. Phytochemical screening was conducted using test-tube methods. Antibacterial testing included determination of inhibition zone diameter using the well-diffusion method, as well as the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC). Clindamycin 1% was used as a positive control, while 20% DMSO and microneedle patches without extract served as negative controls. The *U. arboreum* leaf extract contained flavonoids, alkaloids, saponins, condensed tannins and terpenoids. At concentrations of 1.25%, 2.5%, and 5%, the extract produced inhibition zones of 12.368, 14.693, 18.403 mm against *P. acnes* and 14.523, 17.408, 18.840 mm against *S. aureus*, respectively. The MIC and MBC values against both bacteria were 0.625%. The microneedle acne patch formulations produced inhibition zones of 9.196 mm (F1), 10.140 mm (F2), and 10.713 mm (F3) against *P. acnes*, but showed no activity against *S. aureus*. These results indicate that the microneedle acne patch containing *U. arboreum* leaf extract has potential as an alternative topical antibacterial agent.

Keywords: Difussion Well, Minimum Bactericidal Concentration, Minimum Inhibitory Concentration, Transdermal System

ABSTRAK

Acne vulgaris merupakan gangguan kulit yang melibatkan bakteri Propionibacterium acnes dan Staphylococcus aureus. Penelitian ini bertujuan untuk mengevaluasi aktivitas antibakteri ekstrak daun patindis (Urophyllum arboreum) serta sediaan microneedle acne patch terhadap P. acnes dan S. aureus. Ekstrak dibuat dari simplisia kering secara maserasi menggunakan pelarut etanol 96%. Skrining fitokimia ekstrak dilakukan dengan metode uji tabung. Uji antibakteri yang dilakukan meliputi penentuan diameter zona hambat menggunakan metode difusi sumur, serta penentuan nilai KHM dan KBM, klindamisin 1% sebagai kontrol positif, serta DMSO 20% dan microneedle patch tanpa ekstrak sebagai kontrol negatif. Ekstrak daun U. arboreum positif mengandung senyawa flavonoid, alkaloid, saponin, tanin terkondensasi, dan terpenoid. Ekstrak daun U. arboreum pada konsentrasi 1,25%; 2,5%; 5% menunjukkan diameter zona hambat sebesar 12,368 mm; 14,693 mm; 18,403 mm terhadap P. acnes, dan sebesar 14,523 mm; 17,408 mm; 18,840 mm terhadap S. aureus. Nilai KHM dan KBM ekstrak terhadap kedua bakteri pada konsentrasi 0,625%. Diameter zona hambat dari sediaan microneedle acne patch sebesar 9,196 mm (F1), 10,140 mm (F2), dan 10,713 mm (F3) terhadap P. acnes, namun tidak menunjukkan daya hambat terhadap S. aureus. Berdasarkan hasil tersebut, microneedle acne patch ekstrak daun U. arboreum berpotensi dikembangkan sebagai alternatif antibakteri topikal.

Kata Kunci: Difusi Sumuran, Konsentrasi Bunuh Minimum, Konsentrasi Hambat Minimum, Sistem Transdermal

I. INTRODUCTION

The skin functions as the body's primary protective barrier and remains vulnerable to diverse pathological conditions, such as acne vulgaris, which arises due to pore blockage and inflammation (Dambur et al., 2019; Sasebohe et al., 2023). Acne not only causes physical manifestations but also affects personal, social, and psychological aspects, including an increased risk of depression, reduced self-confidence, and fear of social interaction (Aryani & Riyaningrum, 2022). Factors contributing to acne development include increased sebum production, abnormal keratinocyte desquamation, inflammation, hormonal influences, cosmetics, diet, stress, and bacterial proliferation, with *Propionibacterium acnes* and *Staphylococcus aureus* being the predominant bacteria identified in acne lesions (Legiawati et al., 2023). Acne therapy commonly involves antibiotics such as clindamycin. However, their long-term use poses a risk of inducing bacterial resistance, which is high in Indonesia (Lutfiah et al., 2023; Sitohang et al., 2019).

These conditions highlight the need to explore natural materials as safer alternative antibacterial agents, one of which is the patindis plant (*Urophyllum arboreum*), traditionally used to treat itching and wounds (Adha & Ibrahim, 2021; Jumaryatno et al., 2022). Based on the phytochemical screening conducted by Nur (2025), the leaf extract of *U. arboreum* contains several secondary metabolites, including flavonoids, tannins, alkaloids, saponins, and triterpenoids (Nur, 2025). These compounds have been reported to possess antibacterial activity, including the ability to inhibit the growth of *P. acnes* and *S. aureus* (Nurbaya et al., 2021; Syafriana et al., 2025). Nevertheless, therapeutic effectiveness depends not only on the active compound but also on the delivery system that facilitates its penetration into the skin. Conventional dosage forms, such as creams and gels, often exhibit limited penetration into deeper skin layers and carry a risk of microbial contamination (Durairaj et al., 2023; Yulianti et al., 2021).

A microneedle patch is a dosage form that utilizes a transdermal topical drug delivery system composed of micrometersized needles. In acne therapy, microneedle formulations offer several advantages compared with other transdermal systems, including minimal pain, a faster onset of action, higher permeability, and improved therapeutic effectiveness. These advantages are attributed to the presence of microneedles that penetrate the epidermal layer without reaching the dermis, thereby avoiding damage to neural tissue (Fitriana et al., 2024; Xing et al., 2022). Microneedle patches are also selected as a dosage form for acne therapy because *P. acnes* and *S. aureus* are located within the pilosebaceous unit, allowing more effective diffusion of active compounds toward this target site (Yu & Li, 2024).

In microneedle formulations, polyvinyl alcohol (PVA) and polyvinylpyrrolidone (PVP) function as structural polymers that form the microneedle matrix. Additional components include glycerin as a humectant, dimethyl sulfoxide (DMSO) to dissolve the extract, DMDM hydantoin as a preservative, and distilled water as the primary solvent (Benson et al., 2019; Rowe et al., 2009).

. However, research examining the antibacterial effects of *U. arboreum* leaf extract on *P. acnes* and *S. aureus*, as well as the development of microneedle acne patches, remains limited. Therefore, this study aims to evaluate the antibacterial activity of *U. arboreum* leaf extract against *P. acnes* and *S. aureus* and to develop an extract-based microneedle acne patch as an alternative topical therapy.

II. METHOD

A. Instruments

The instruments used in this study included autoclave (All American®), stirring rods, bunsen burner, petri dishes, porcelain dishes, microneedle acne patch mold, cork borer, glass funnel, cotton swabs, desiccator, erlenmeyer flasks, beakers, graduated cylinder, hot plate (*Torrey Pines*®), incubator (*Memmert*®), digital vernier caliper (*Vernier Caliper*®), inoculating loop, laminar airflow cabinet (*Omega VL 120*®), watch glasses, magnetic stirrer, macerator, micropipette, analytical balance (*Ohaus*®), oven (*Memmert*®), forceps, volumetric pipette, dropper pipette, pipette filler, test tube rack, rotary evaporator, horn spoon, sonicator (*DK-009A*®), laboratory scoop, test tubes, vortex mixer, and waterbath (*Memmert*®).

B. Materials

Materials used in this study included aluminum foil, distilled water, anhydrous CH_3COOH (*Merck*®), *U. arboreum* leaves, DMDM hydantoin, DMSO (*Merck*®), 96% ethanol (technical grade), $FeCl_3$ (*Merck*®), gelatin, glycerin, HCl (*Merck*®), H_2SO_4, white cardboard paper, brown Samson paper, Whatman filter paper, clindamycin, chloroform (*technical grade*), pure culture of *P. acnes* bacteria (*ATCC*® 11827), pure culture of *S. aureus* bacteria (*ATCC*® 6538™), 0.9% NaCl solution, 0.5 McFarland standard solution, nutrient agar (NA) medium (*Merck*®), nutrient broth (NB) medium (*Merck*®), Microneedle Acne Patch Let's Glow, heat-resistant plastic, polyvinyl alcohol (PVA) (*Kuraray poval*™), polyvinylpyrrolidone (PVP) (*Fagron*®), Wagner reagent, Dragendorff reagent, magnesium powder (*Merck*®), spiritus, and yellow tips.

C. Plant Determination

U. arboreum plants were collected from Forest Area with Special Purpose of ULM, Mandiangin Timur, South Kalimantan, and plant identification was conducted at Basic Laboratory, Faculty of Mathematics and Natural Sciences, Universitas Lambung Mangkurat. Identification was performed by comparing morphological characteristics of *U. arboreum* plants with relevant literature. This process was carried out to ensure accuracy of patindis plant identity used in this study and to prevent errors in material collection (Klau & Hesturini, 2021).

D. Preparation of Simplicia and Extraction

U. arboreum leaf samples used in this study met the criteria of green colour, intact structure, and absence of fungal or mould contamination. A total of 1,000 g of U. arboreum leaves were washed water,

sliced, and dried at 55°C for 16 hours in a drying cabinet to minimise moisture and mould risk. The simplicia were then ground using a blender to obtain powdered *U. arboreum* leaf simplicia (Dima et al., 2016).

Extraction of the simplicia powder was performed by maceration with 96% ethanol. Simplicia powder (180 g) was macerated in 1,800 mL of 96% ethanol for 3 × 24 hours, with routine stirring every 8 hours and solvent replacement every 24 hours. Filtration of the macerate was performed with Whatman filter paper, followed by concentration at 50°C using a rotary evaporator. The concentrate was further thickened in a water bath at 50°C until a viscous extract with constant weight was obtained (Falestin et al., 2024; Wiritania et al., 2024).

E. Phytochemical Analysis of the Extracts

Phytochemical screening is an initial step for qualitatively identifying groups of secondary metabolites present in plants. The results provide an overview of the types of chemical compounds that may possess biological activity (Septiningrum *et al*., 2024). In this study, phytochemical screening was conducted using the test tube method, which allows rapid detection of secondary metabolites through colour changes, precipitate formation, or foam formation resulting from specific reactions between reagents and compounds in the sample (Fikayuniar et al., 2023). The procedures for phytochemical screening applied in this study are presented in Table I.

F. Antibacterial Activity Test of U. arboreum Leaf Extract

The antibacterial activity of *U. arboreum* leaf extract against *P. acnes* and *S. aureus* was evaluated using the agar well diffusion method. The bacterial strains used were accompanied by a Certificate of Analysis (CoA) verifying their identities, namely *P. acnes* with the product name *C. acnes* ATCC 11827 PK/5 and *S. aureus* with the product name *Staphylococcus aureus* subsp. *aureus* ATCCR 6538 TM. The test began with preparing samples and controls. Clindamycin 1% served as the positive control, and 20% DMSO as the negative control. Antibacterial activity test samples were prepared by diluting *U. arboreum* leaf extract with 20% DMSO to concentrations of 1.25%, 2.5%, and 5% (Liling et al., 2020)

The bacterial cell suspensions were calibrated to 0.5 McFarland turbidity equivalent (~1.5×10^8 CFU/mL). A volume of 0.1 mL of *P. acnes* and *S. aureus* suspensions was inoculated on the nutrient agar (NA) medium previously poured into Petri dishes. The Petri dishes were gently

rotated in a figure-eight (8) pattern to ensure uniform distribution of the bacterial suspension over the agar surface, and then allowed to solidify for approximately 15 minutes. The solidified NA medium was then perforated with a 6 mm cork borer. *U. arboreum* leaf extract, positive control, and negative control were each introduced into wells at a volume of 50 µL using a micropipette. The Petri dishes were incubated at 37°C for 24 hours. The test was perfomed in triplicate (Rahayu *et al*., 2022).

G. Minimum Inhibitory Concentration (MIC) Determination of U. arboreum Leaf Extract

The MIC test of *U. arboreum* leaf extract against *P. acnes* and *S. aureus* was performed using the broth dilution method. A volume of 2 mL of nutrient broth (NB) medium was transferred into test tubes, followed by addition of 1 mL of test solution at concentrations of 5%, 2.5%, 1.25%, 0.625%, 0.3125%, 0.15625%, and 0.078125%. Subsequently, 1 mL of bacterial culture was added into each test tube. The positive control was prepared by mixing 2 mL of NB medium, 1 mL of 1% clindamycin antibiotic, and 1 mL of bacterial culture. Meanwhile, the negative control was prepared by adding 2 mL of bacterial culture into a mixture of 2 mL of NB medium and 20% DMSO. Following 24 hour incubation at 37°C, turbidity was assessed in all test tubes. The MIC test was perfomed in triplicate (Yustian et al., 2025).

H. Minimum Bactericidal Concentration (MBC) Determination of U. arboreum Leaf Extract

The minimum bactericidal concentration (MBC) test in this study was conducted following the MIC test. The volume of 1 mL from each solution obtained in the MIC test was spread evenly onto nutrient agar (NA) using an L-spreader. The media were incubated at 37°C for 24 hours, after which bacterial colony growth was observed. The MBC test was perfomed in triplicate (Yustian et al., 2025).

I. Preparation of Microneedle Patch

The microneedle patch was prepared in four formulation variations, as presented in Table II. These formulations were based on the study by Fitriana et al. (2024), with modifications in the type of extract and polymer concentrations used. Preparation of the formulation began by dissolving *U. arboreum* leaf extract in 1 mL of 20% DMSO (first mixture). PVA and PVP were each dissolved in hot distilled water on a hot plate and then combined until homogeneous (second mixture). DMDM hydantoin was mixed with glycerin

(third mixture). The third mixture was then added to the first mixture and stirred until homogeneous, then added to the second mixture and further stirred until a homogeneous solution was obtained on the hot plate (Sarwo et al., 2025).

The same procedure was applied to each formulation. The resulting formulation solutions were subsequently sonicated for 60–120 minutes to remove air bubbles. Each formulation solution was then poured into moulds and dried in an oven at 50°C for 10 hours. The microneedle patches were removed from the moulds and placed in a desiccator for 20 hours, after which the formulations were stored in sealed containers to maintain their integrity and prevent exposure to moisture or environmental contaminants (Sarwo et al., 2025).

J. Antibacterial Activity Test of the Microneedle Patch

Antibacterial activity was assessed using the well-diffusion method. A volume of 0.1 mL of *P. acnes* bacterial suspension was inoculated onto NA medium in Petri dishes. The Petri dishes were gently rotated in a figure-eight (8) pattern, and the medium was allowed to stand for 15 minutes until solidified. Wells were then created in the solidified NA medium using a 6 mm cork borer. Positive and negative controls, and microneedle patch samples that had not undergone oven-drying, were each introduced into the respective wells at 50 µL. The petri dishes were maintained at 37°C for 24 hours of incubation (Nurpriatna et al., 2024).

Tabel I. Phytochemical screening of the extracts

Test	Reagen
Alkaloid	2 mL 1% HCl + 1 mL Wagner reagent
	2 mL 1% HCl + 1 mL Dragendorff reagent
Flavonoid	2 mL Concentrated HCl + Mg powder
Saponin	1 drop 0.1 N HCl
Tannin	1 mL 1% Gelatin
	2-3 drop 0,1% FeCl
Terpenoid and Steroid	0.5 mL Chloroform + 0.5 mL CH_3COOH + 2 mL concentrated H_2SO_4

(Putria et al., 2022; Dubale et al., 2023; Takaeb & Leo, 2023; Awusi & Ganang, 2025)

Table II. Formulation of *U. arboreum* leaf extract microneedle acne patch

Materials	F0 (b/b%)	F1 (b/b%)	F2 (b/b%)	F3 (b/b%)	Function
U. arboreum extract	0	1,25	2,5	5	Active ingredient
DMSO	0	1	1	1	Extract solvent
PVA	5.576	5.576	5.576	5.576	Polymer
PVP	9.424	9.424	9.424	9.424	Polymer

Materials	F0 (b/b%)	F1 (b/b%)	F2 (b/b%)	F3 (b/b%)	Function
DMDM hydantoin	0.4	0.4	0.4	0.4	Plasticizer dan preservative
Glycerin	5	5	5	5	Penetration enhancer
Aquadest	*ad* 100	*ad* 100	*ad* 100	*ad* 100	Solvent

K. Observation of Inhibition Zone Diameter

Post-incubation observations were conducted after 24 hours. The presence of a clear zone surrounding the test sample area indicated bacterial inhibition against the tested antibacterial agent. The inhibition zone diameters were quantified vertically and horizontally with vernier callipers and reported in millimetres (mm) (Sarwo et al., 2025). The inhibition zone diameter (Rahayu et al., 2022) was determined using Equation 1 and classified according to the categories listed in Table III.

$$\text{Inhibiton Zone Diameter} = \frac{(a-c)+(b-c)}{2} \quad \textbf{(1)}$$

Notes:
a = Horizontal diameter
b = Vertical diameter
c = Well diameter

Table III. Classification of antibacterial effectiveness (Sarwo et al., 2025)

Inhibition zone diameter (mm)	Inhibitory response
<5	Weak
5–10	Moderate
>10–20	Strong
>20	Very strong

L. Data Analysis

Data were analyzed using descriptive and statistical approaches. Descriptive analysis evaluated antibacterial activity based on the inhibition zone diameters of U. arboreum leaf extract and microneedle acne patch formulations. Statistical analysis was performed using SPSS version 27, including the Shapiro Wilk test for normality and Levene's test for homogeneity of variances. Data meeting the assumptions of normality and homogeneity were analyzed using One Way ANOVA, whereas non-normally distributed data were analyzed using the Kruskal Wallis test. When variances were not homogeneous, post hoc analysis was conducted using the Games Howell test, while homogeneous variances were analyzed using the Bonferroni test (Wanakusuma & Widiyanti, 2023).

III. RESULTS AND DISCUSSION

A. Plant Determination

Plant determination was conducted at the Basic Laboratory of the FMIPA, ULM, under determination number 115b/LB.LABDASAR/VI/2025. The determination was performed to confirm the specific identity of the plant species

(Listiana et al., 2022). The examined plant specimen was determined to be *Urophyllum arboreum*.

B. Preparation of Simplicia and Extraction

The simplicia powder obtained weighed 409 g, was green, and had a characteristic clove-like aroma. The simplicia powder was extracted using the maceration method with 96% ethanol as the solvent for 3 × 24 hours, yielding an extract percentage of 33.417%. The extract obtained was characterised as a thick, dark brown to blackish extract with a distinctive clove-like odour. The yield percentage obtained in this study met the criteria for a good extraction yield, namely greater than 10% (Sa'adah et al., 2025). In addition, the yield percentage in this study was higher than that reported in a previous study by Jumaryatno et al. (2022), which reported an extraction yield of *U. arboreum* leaf extract of 26.2057% (Jumaryatno et al., 2022). Differences in extraction yield percentage may be influenced by several factors, including the type of solvent used, temperature, extraction duration, particle size of the simplicia, sample-to-solvent ratio, and variations in the plant's growing location (Purwanti, 2024).

C. Phytochemical Screening of the Extract

Phytochemical examination is an initial step used to qualitatively identify groups of secondary metabolites present in plants. The results provide a general overview of chemical compounds with potential biological activity (Septiningrum et al., 2024). The phytochemical screening results in this study showed that the U. arboreum leaf extract contains alkaloids, flavonoids, saponins, tannins, and terpenoids. These findings are consistent with the study conducted by Nur (2025), which also reported that U. arboreum leaf extract contains alkaloids, flavonoids, saponins, tannins, and terpenoids. The test results are presented in Table IV.

Table IV. Phytochemical screening results of *U. arboreum* leaf extract

Test	Result	Information
Alkaloid	(+) Alkaloid	Brown precipitate
	(+) Alkaloid	Orange precipitate
Flavonoid	(+) Flavonoid	Reddish-orange solution
Saponin	(+) Saponin	Stable foam for approximately 10 minutes
Tannin	(+) Tannin	White precipitate
	(+) Condensed Tannin	Greenish-black solution
Terpenoid and Steroid	(+) Terpenoid	Brownish or violet ring

(Putria et al., 2022; Dubale et al., 2023; Takaeb & Leo, 2023; Awusi & Ganang, 2025)

D. Antibacterial Activity Test of U. arboreum Leaf Extract

The antibacterial inhibitory test of *U. arboreum* leaf extract was conducted to assess its inhibitory potential on *P. acnes* and *S. aureus* growth, which contribute to acne pathogenesis (Zahrah *et al*., 2018). The results of the inhibitory activity test of *U. arboreum* leaf extract on *P. acnes* and *S. aureus* are presented in Table V.

Table V. Results of the inhibitory activity test of *U. arboreum* leaf extract against *P. acnes* and *S. aureus*.

Sample	***P. acnes*** **(mm)**	**Mean ± SD (mm)**	**Category**	***S. aureus*** **(mm)**	**Mean ± SD (mm)**	**Category**
1.25%	11.905	12.368 ± 0.412[a]	Strong	14.775	14.523 ± 0.197[a]	Strong
	12.505			14.420		
	12.695			14.375		
2.5%	18.050	14.693 ± 0.747[a]	Strong	17.410	17.408 ± 0.197[b]	Strong
	18.085			17.605		
	19.075			17.210		
5%	18.050	18.403 ± 0.581[b]	Strong	19.095	18.840 ± 0.223[c]	Strong
	18.085			18.675		
	19.075			18.750		
K (+)	56.375	55.690 ± 0.598[c]	Very strong	40.670	41.500 ± 1.057[d]	Very strong
	55.430			42.690		
	55.265			41.140		
K (-)	0.000	0.000 ± 0.000[d]	No inhibitory activity	0.000	0.000 ± 0.000[e]	No inhibitory activity
	0.000			0.000		
	0.000			0.000		

Notes:
Positive control = clindamycin 1%
Negative control = 20% DMSO
Values with the same letter are not significantly different (p value > 0.05)
Values marked with different letters differ significantly (p value < 0.05)

Based on Table V, *U. arboreum* leaf extract at concentrations of 1.25%, 2.5%, and 5% exhibited strong inhibition against both *P. acnes* and *S. aureus*. An increase in extract concentration led to a larger inhibition zone diameter, indicating a greater amount of antibacterial compounds in the extract, consistent with findings reported by Husnia et al. (2022). Clindamycin 1% showed very strong inhibitory activity, whereas DMSO 20% did not produce an inhibition zone. This finding indicates that the solvent did not influence the antibacterial activity of the treatment groups and that the activity originated from the active compounds in the extract (Ulfah et al., 2019).

Antibacterial activity of U. arboreum leaf extract is attributed to flavonoids, alkaloids, saponins, condensed

tannins, and terpenoids. Alkaloids inhibit peptidoglycan synthesis and disrupt membrane permeability, causing leakage of intracellular components. Flavonoids interfere with membrane integrity and inhibit enzymes involved in cell wall synthesis, weakening bacterial walls. Saponins interact with membrane lipids, increasing permeability, while condensed tannins damage membranes and cause leakage of essential ions and metabolites. Terpenoids disrupt membrane lipid biosynthesis and permeability balance, impairing bacterial function and survival (Samaniyah et al., 2025).

Studies on the antibacterial activity of *U. arboreum* leaf extract against *P. acnes* remain limited; therefore, a comparison was conducted with studies on plants from the same family (Rubiaceae). Wulandari et al. (2023) reported that ethanol extract of gambir (*Uncaria gambir*) leaves at concentrations of 12.5%, 25%, and 50% produced zone of inhibition of 14.57 mm, 18.00 mm, and 23.67 mm against *P. acnes*, respectively (Wulandari et al., 2023). In the present study, *U. arboreum* leaf extract exhibited comparable activity at lower concentrations, with a 5% concentration producing an inhibition zone of 18.403 mm, comparable to gambir leaf extract at 25%. In addition, at a concentration of 2.5%, *U. arboreum* leaf extract produced an inhibition zone of 14.693 mm, which was relatively comparable to the activity of gambir leaf extract at 12.5%. These results indicate that *U. arboreum* leaf extract has higher antibacterial potential than gambir leaf extract.

Studies on the antibacterial activity of *U. arboreum* leaf extract against *S. aureus* are also limited; therefore, comparisons were made with previous studies on plants from the same family, Rubiaceae. Afiff and Amilah (2017) reported that noni (*Morinda citrifolia* L.) leaf extract at concentrations of 40%, 60%, and 80% produced zones of inhibition of 0.45 mm, 0.54 mm, and 0.7 mm against *S. aureus*, respectively (Afiff & Amilah, 2017). In the present study, *U. arboreum* leaf extract showed higher antibacterial activity than *M. citrifolia* leaf extract. This finding indicates that *U. arboreum* leaf extract has greater antibacterial potential. Differences in plant variety, environmental growing conditions, and bacterial test strains can influence variations in antibacterial activity, affecting active compound content and bacterial sensitivity to antibacterial compounds (Geofani et al., 2022).

Results of the Shapiro–Wilk test for extract activity against *P. acnes* showed p-value> 0.05, indicating normal data distribution. Further testing using the Levene Statistic yielded p p-value < 0.05, indicating non-homogeneous variance.

Analysis was continued using One-Way ANOVA, since the data were normally distributed and ANOVA is robust to violations of the homogeneity of variances assumption. One-way ANOVA results showed p-value < 0.05, indicating significant differences among treatment groups, followed by the Post Hoc Games–Howell test. Analysis showed that the antibacterial activity of *U. arboreum* leaf extract at 1.25% and 2.5% did not differ significantly, whereas 5% did. Antibacterial activity of the extract groups differed significantly from the positive and negative controls, indicating that the antibacterial activity of *U. arboreum* leaf extract was lower than that of clindamycin 1% (positive control) but higher than that of DMSO 20% (negative control), and demonstrating potential as an antibacterial agent against *P. acnes*.

Results of the Shapiro–Wilk test for extract activity against *S. aureus* showed p-value> 0.05, indicating normal data distribution. Variance homogeneity testing using the Levene Statistic yielded p p-value < 0.05, indicating non-homogeneous variance. Nevertheless, analysis continued using One-Way ANOVA, which showed a p-value < 0.05. These results indicate significant differences among the treatment groups; therefore, a Post Hoc Games–Howell test was conducted, which showed that all treatment groups exhibited significant differences in antibacterial activity. The antibacterial activity of *U. arboreum* leaf extract at various concentrations differed significantly from each other and from the positive and negative controls. Based on these results, the antibacterial activity of *U. arboreum* leaf extract against *S. aureus* was lower than that of clindamycin 1% (positive control) but higher than of DMSO 20% (negative control), indicating its potential as a natural antibacterial agent against *S. aureus*.

E. Minimum Inhibitory Concentration (MIC) Determination of *U. arboreum* Leaf Extract

The MIC value was determined to identify the lowest concentration of the sample that still inhibited bacterial growth in liquid medium after 24 hours of incubation (Fitriani et al., 2024). The test results showed that in the test tubes containing the extract at concentrations of 0.625%, 1.25%, 2.5%, and 5%, no growth of *P. acnes* and *S. aureus* was observed, as indicated by the medium remaining clear. Similar results were also observed in the tube containing the positive control of 1% clindamycin, which showed no bacterial growth. In contrast, bacterial growth of *P. acnes* and *S. aureus* was observed in the tube containing the negative control, indicated by turbidity in the medium

(Yustian et al., 2025). Based on these results, the MIC value obtained in this test was 0.625%. Results of MIC testing of *U. arboreum* leaf extract are presented in Table VI.

F. Minimum Bactericidal Concentration (MBC) Determination of U. arboreum Leaf Extract

The MBC was determined by inoculating the solution from the MIC test into agar media (Nurbaeti et al., 2024). This method assessed the bactericidal effect of the extract by observing bacterial growth on the agar surface. The results showed that at extract concentrations of 0.625%, 1.25%, 2.5%, and 5%, no bacterial growth was observed. This indicates that the extract at concentrations of 0.625%, 1.25%, 2.5%, and 5% exhibited bactericidal activity against *P. acnes* and *S. aureus*. Similar bactericidal activity was also observed in the positive control, which was able to kill both bacteria. In contrast, the negative control did not demonstrate the ability to kill either of the tested bacteria (Yustian et al., 2025). Based on these results, the MBC value obtained in this test was 0.625%. The results of the MBC testing of *U. arboreum* leaf extract are presented in Table VII.

Table VI. Results of minimum inhibitory concentration (MIC) of *U. arboreum* leaf extract against *P. acnes* and *S. aureus*

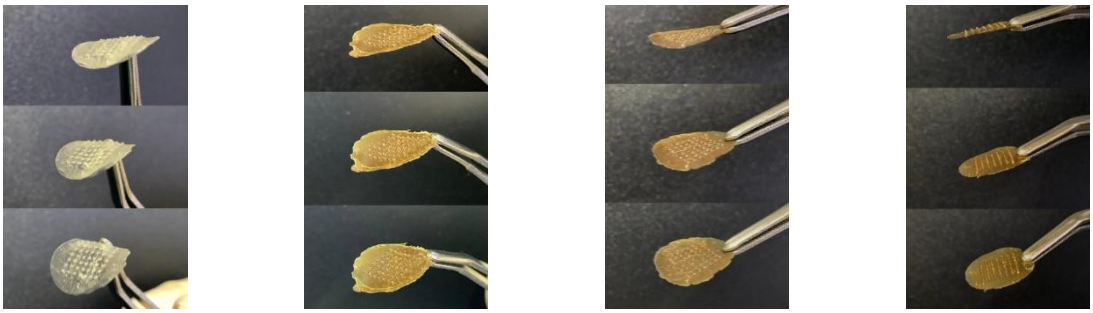
Bacteria	Concentration (%)	Result	Remarks
P. acnes	5	Clear	No bacterial growth
	2.5	Clear	No bacterial growth
	1.25	Clear	No bacterial growth
	0.625*	Clear	No bacterial growth
	0.3125	Turbid	Bacterial growth observed
	0.15625	Turbid	Bacterial growth observed
	0.078125	Turbid	Bacterial growth observed
	Positive control	Clear	No bacterial growth
	Negative control	Turbid	Bacterial growth observed
S. aureus	5	Clear	No bacterial growth
	2.5	Clear	No bacterial growth
	1.25	Clear	No bacterial growth
	0.625*	Clear	No bacterial growth
	0.3125	Turbid	Bacterial growth observed
	0.15625	Turbid	Bacterial growth observed
	0.078125	Turbid	Bacterial growth observed
	Positive control	Clear	No bacterial growth
	Negative control	Turbid	Bacterial growth observed

Notes:
(*) indicates the MIC value
Positive control = clindamycin 1%
Negative control = 20% DMSO

Table VII. Results of minimum bactericidal concentration (MBC) of *U. arboreum* leaf extract against *P. acnes* and *S. aureus*

Bacteria	Concentration (%)	Remarks
P. acnes	5	No bacterial growth
	2.5	No bacterial growth
	1.25	No bacterial growth
	0.625*	No bacterial growth
	0.3125	Bacterial growth observed
	0.15625	Bacterial growth observed
	0.078125	Bacterial growth observed
	Positive control	No bacterial growth
	Negative control	Bacterial growth observed
S. aureus	5	No bacterial growth
	2.5	No bacterial growth
	1.25	No bacterial growth
	0.625*	No bacterial growth
	0.3125	Bacterial growth observed
	0.15625	Bacterial growth observed
	0.078125	Bacterial growth observed
	Positive control	No bacterial growth
	Negative control	Bacterial growth observed

Notes:
(*) indicates the MBC value
Positive control = clindamycin 1%
Negative control = 20% DMSO



(a) (b) (c) (d)

Figure 1. Microneedle acne patch preparations: (a) Formula 0; (b) Formula 1; (c) Formula 2; (d) Formula 3 (Personal documentation, 2025)

The MIC and MBC values obtained indicate that the leaf extract of *U. arboreum* possesses antibacterial activity with bactericidal properties against acne-causing bacteria. The MBC value being equal to the MIC value suggests that the extract is not only capable of inhibiting bacterial growth but can also directly kill the bacteria. The bactericidal activity of *U. arboreum* leaf extract provides advantages in acne therapy, as it can significantly reduce the bacterial population in the pilosebaceous unit, which is the primary site of colonization by *P. acnes* and *S. aureus*. The

reduction in bacterial population may help decrease inflammatory in the pilosebaceous follicle, thereby accelerating the healing of acne lesions and reducing the risk of recurrence (Fitriani, 2024; Yu & Li, 2024).

G. Microneedle Patch Preparation

The microneedle patches in this study were prepared in four concentrations of *U. arboreum* leaf extract: 0%, 0.625%, 1.25%, and 2.5%. Each formulation weighed approximately 0.07 g and had a needle height of 0.63 mm. Visual observation of the physical condition of the formulation indicated that the needles were formed properly and that the extract was homogeneously distributed. Increasing the amount of extract in the microneedle patch resulted in a darker color of the formulation. Formula 0 appeared transparent, Formula 1 was yellow, Formula 2 was slightly brownish-yellow, and Formula 3 exhibited a brownish-yellow color. The resulting microneedle patches are shown in Figure 1.

H. Antibacterial Activity Test of the Microneedle Patch

The antibacterial efficacy assessment of the formulation was performed to evaluate the ability of the formulation containing *U. arboreum* leaf extract to inhibit the growth of *P. acnes*. The antibacterial activity in this study was evaluated using the agar diffusion method as an initial step to identify the antibacterial potential of the microneedle patch formulation. This method can provide a preliminary indication of a substance's ability to inhibit bacterial growth through the observation of inhibition zones on agar media. However, microneedle systems are fundamentally designed to penetrate the skin and release active compounds in a controlled manner at the target tissue. Therefore, the agar diffusion method in this study was used to provide an initial overview of the antibacterial activity of the extract formulated within the microneedle patch system.

Table VIII. Results of antibacterial inhibitory activity of microneedle acne patch formulation against *P. acnes*

Sample	*P. acnes* (mm)	Mean ± SD (mm)	Category	*S. aureus* (mm)	Mean ± SD (mm)	Category
F1	9.310	9.196 ± 0.098[a]	Moderate	0.000	0.000 ± 0.000[e]	No inhibitory activity
	9.130			0.000		
	9.150			0.000		
F2	10.160	10.140 ± 0.043[b]	Strong	0.000	0.000 ± 0.000[e]	No inhibitory activity
	10.090			0.000		
	10.170			0.000		
F3	10.640	10.713 ± 0.087[b]	Strong	0.000	0.000 ± 0.000[e]	No inhibitory
	10.810			0.000		

	10.690			0.000		activity
PC1	58.920	58.930 ± 0.425[d]	Very strong	0.000	0.000 ± 0.000[e]	No inhibitory activity
	58.510			0.000		
	59.360			0.000		
KpK	0.000	0.000 ± 0.000[e]	No inhibitory activity	0.000	0.000 ± 0.000[e]	No inhibitory activity
	0.000			0.000		
	0.000			0.000		
NC1	0.000	0.000 ± 0.000[e]	No inhibitory activity	0.000	0.000 ± 0.000[e]	No inhibitory activity
	0.000			0.000		
	0.000			0.000		
NC2	0.000	0.000 ± 0.000[e]	No inhibitory activity	0.000	0.000 ± 0.000[e]	No inhibitory activity
	0.000			0.000		
	0.000			0.000		

Notes:
Positive control-1 (PC1) = clindamycin 1%
KpK = commercial comparator microneedle patch
Negative control-1 (NC1) = 20% DMSO
Negative control-2 (NC2) = microneedle patch formulation without extract
Values with the same letter are not significantly different (p value > 0.05)
Values marked with different letters differ significantly (p value < 0.05)

The *U. arboreum* leaf extract microneedle acne patch formulations were prepared in four concentration variations, namely 0%, 0.625%, 1.25%, and 2.5%, to assess the effect of extract concentration on the inhibitory activity of bioactive constituents against bacterial growth (Putri et al., 2024). The results of the antibacterial inhibitory activity of *U. arboreum* leaf extract microneedle acne patches *P. acnes* and *S. aureus* are presented in Table VIII.

The results showed that F1, F2, and F3 exhibited antibacterial activity against *P. acnes* but did not inhibit *S. aureus*. F1 produced a moderate inhibitory effect, whereas F2 and F3 showed strong inhibitory activity against *P. acnes*. An increase in inhibition zone diameter indicated that higher extract concentrations enhanced antibacterial effectiveness. Clindamycin 1% as the positive control exhibited very strong inhibitory activity against *P. acnes*, while the commercial comparator control, negative control DMSO 20% and microneedle patch without extract did not produce inhibition zones. The results of this negative control confirm that the observed antibacterial activity originates from the active compound and not from the extraction solvent or excipients.

The microneedle patch formulation did not exhibit inhibitory activity against *Staphylococcus aureus*. This result may be influenced by pH changes during formulation. At a concentration of 1.5%, the extract exhibited a more acidic pH (4.8) than the microneedle patch formulation

(6.2). This pH shift may affect the stability of active compounds and the sensitivity of *S. aureus* to antibacterial agents, as antibacterial activity against these bacteria has been reported to be more optimal under acidic conditions. The pH shift is associated with the presence of secondary metabolite compounds contained in *U. arboreum* leaves. One of the compounds that plays a role as an antibacterial agent is flavonoids. The antibacterial mechanism of flavonoids occurs through the formation of complexes with extracellular proteins as well as soluble proteins, which leads to damage to the bacterial cell membrane followed by the leakage of intracellular components. In addition, flavonoid compounds are known to have low stability under changes in chemical conditions, including variations in pH (Cahyani et al., 2024; Silvyana et al., 2024; Yuliani et al., 2017).

Studies on the antibacterial activity of *U. arboreum* leaf extract microneedle patch formulations against *P. acnes* remain limited; therefore, comparisons were made with previous studies using gel formulations containing active ingredients from the Rubiaceae family. Putri et al. (2024) reported that a serum gel combining ethanolic extract of Arabica coffee leaves and forest honey at concentrations of 10%, 20%, and 30% produced zones of inhibition of 8.0 mm, 16.7 mm, and 23.3 mm, respectively, against *P. acnes*. In the present study, the microneedle acne patch demonstrated higher antibacterial activity at lower active compound concentrations, as indicated by an inhibition zone diameter of 10.173 mm at 2.5%, which was greater than that observed with the serum gel at 10%. These findings suggest that the *U. arboreum* leaf extract microneedle acne patch has higher antibacterial potential against *P. acnes*. Differences in inhibition zone diameters between this study and Putri et al. (2024) may be attributed to variations in the type and concentration of active compounds, diffusion capacity in the agar medium, and the sensitivity of the test microorganisms. Bacterial cell wall structure and growth rate also influence responses to antibacterial agents and the resulting inhibition zones (Putri et al., 2024; Sartika et al., 2019).

The Shapiro–Wilk test results for the microneedle patch formulations against *P. acnes* showed $p > 0.05$, indicating normally distributed data, while the Levene test yielded $p < 0.05$, indicating non-homogeneous variances. Nevertheless, analysis continued using One-Way ANOVA because the data were normally distributed and ANOVA is robust to heteroscedasticity. The One-Way ANOVA results showed $p < 0.001$, indicating significant differences among treatment groups; therefore, Post-Hoc Games–Howell testing was performed.

The analysis revealed that formulation 3 exhibited significantly higher antibacterial activity than formulations 1 and 2, and formulation 2 showed higher activity than formulation 1. Clindamycin 1% as the positive control demonstrated the highest antibacterial activity and differed significantly from all formulation groups. However, all microneedle patch formulations exhibited significantly higher antibacterial activity than the negative controls, confirming that the antibacterial effect originated from the active ingredients and indicating their potential against *P. acnes*.

The antibacterial inhibitory activity of *U. arboreum* leaf extract in the microneedle patch formulation decreased compared with the extract prior to formulation, against both *Propionibacterium acnes* and *Staphylococcus aureus*. This reduction is presumably due physical and chemical interactions between the extract and excipients, which may affect the stability and bioavailability of the active compounds (Cahyani et al., 2024). Additionally, the PVA and PVP polymer matrices in the microneedle patch may retain active compounds within the polymer network, resulting in slower release and reduced diffusion of antibacterial agents into the surrounding environment, thereby decreasing the inhibition zone diameter (Liu et al., 2022; Yusuf et al., 2020). The absence of a drug release study and stability testing of the active compounds within the microneedle system represents a limitation of this study, as both parameters play an important role in determining the availability and effectiveness of the active compounds released from the polymer matrix. Therefore, future studies are expected to investigate the drug release profile and the stability of the active compounds to obtain a more comprehensive understanding of the therapeutic performance of the microneedle system.

IV. CONCLUSION

U. arboreum leaf extract contains bioactive secondary metabolites such as flavonoids, alkaloids, saponins, tannins, and terpenoids, which contribute to its antibacterial activity. The extract exhibited strong antibacterial activity against *P. acnes* and *S. aureus*, with inhibition zone diameters increasing in line with increasing extract concentration, as well as MIC and MBC values at 0.625%. The microneedle acne patch formulation demonstrated antibacterial activity against *P. acnes*, with greater inhibition at higher extract concentrations; however, it did not exhibit activity against *S. aureus*. Although the antibacterial effectiveness of the microneedle acne patch formulation

remained lower than that of clindamycin 1%, the findings of this study indicate that *U. arboreum* leaf extract has potential to be developed as a natural-based topical antibacterial alternative for the treatment of acne vulgaris.

CONFLICT OF INTEREST

All authors declare that there is no conflict of interest in this study.

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