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Effect of Solvents on the Antibacterial Activity of *Premna serratifolia* L. Leaf Extracts Against *Propionibacterium acnes* and *Staphylococcus aureus*

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Abstract

Acne vulgaris is a common skin disorder associated with the colonization of *Propionibacterium acnes* and *Staphylococcus aureus*, highlighting the need for alternative treatments derived from natural products, such as *buas-buas* leaves (*Premna serratifolia* L.). The present study aimed to evaluate and compare the influence of ethanol and honey solvents on the Total Phenolic Content (TPC) and Total Flavonoid Content (TFC), and the antibacterial inhibition zones against *P. acnes* and *S. aureus* of *buas-buas* leaf extracts. Extraction was performed using the Microwave-Assisted Extraction method. TPC and TFC were determined by UV–Vis spectrophotometry, and antibacterial activity was evaluated using the disc diffusion method at concentrations of 25%, 50%, and 100%. The use of ethanol and honey as extraction solvents significantly affected TPC and TFC values, with ethanol producing higher levels than honey. The ethanol extract exhibited weak antibacterial activity against *P. acnes*, with inhibition zones of 2,62 ± 0,72 mm and 3,77 ± 0,70 mm at concentrations of 50% and 100%, respectively. Against *S. aureus*, the ethanol extract produced an inhibition zone of 3,60 ± 0,56 mm at a concentration of 100%. In contrast, the honey extract of *buas-buas* leaves showed no antibacterial activity against either test bacterium at any of the concentrations evaluated.

Keywords: Ethanol 96%; Honey; *Premna serratifolia*; *Propionibacterium acnes*; *Staphylococcus aureus*.

INTRODUCTION

Acne vulgaris is recognized as a common dermatological disorder, particularly among adolescents, with a prevalence exceeding 85% in individuals aged 12–25 years and ranging from 40–80% in Southeast Asia (Fadilah, 2021). The development of acne is associated with multiple factors, including excessive sebum production, follicular hyperkeratinization, inflammation, and bacterial colonization. Among the bacteria involved, *Propionibacterium acnes* plays a major role in triggering inflammatory responses within obstructed follicles (Teresa, 2020). In addition, *Staphylococcus aureus* may aggravate acne lesions through tissue damage and abscess formation (Salim et al., 2023). The increasing incidence of antibiotic resistance has encouraged the exploration of natural products as alternative antibacterial agents for acne management.

Premna serratifolia L. (*buas-buas*) has been used as a medicinal plant for treating various ailments, including the treatment of skin disorders. Previous studies have reported that its leaves contain phenolic and flavonoid compounds with antibacterial properties (Arung et al., 2017; Supriningrum et al., 2017). Due to their polar characteristics, these compounds necessitate the use of suitable solvents for effective extraction. Therefore, the selection of extraction solvents is a critical factor that affects both the recovery of bioactive compounds and their biological activities (Nawaz et al., 2020).

Ethanol is commonly employed as a conventional extraction solvent for phenolic and flavonoid compounds due to its suitable polarity, high extraction efficiency, and compatibility with various bioactive metabolites (Isnindar et al., 2025; Yee et al., 2021). Growing concerns about environmental impact and the safety of conventional extraction solvents have encouraged the exploration of environmentally friendly extraction approaches (García-Roldán et al., 2023). Natural deep eutectic solvents (NADES) constitute a promising alternative to conventional solvents, offering high biodegradability, low environmental risk, and enhanced extraction efficiency for polar phytochemical constituents (Kolayli, 2023). Recently, honey has been identified as a naturally occurring eutectic system predominantly consisting of sugars and water, allowing it to serve as a green solvent for the extraction and dissolution of polar constituents. (Phaisan et al., 2020; Sitthisak et al., 2025).

Variations in solvent characteristics may have a significant impact on the extraction yield and recovery efficiency of phenolic and flavonoid compounds, which in turn affect antibacterial activity. Earlier studies have reported that higher concentrations of phenolic and flavonoid compounds are often associated with stronger antibacterial effects (Hastuti & Mulangsri, 2021; Ramayani et al., 2021). Although the antibacterial activity of *P. serratifolia* leaf extracts has been investigated using conventional solvents, studies evaluating honey-based solvents for the extraction of bioactive compounds from this plant remain limited. Furthermore, comparative information regarding the effects of ethanol and honey solvents on Total Phenolic Content (TPC), Total Flavonoid Content (TFC), and antibacterial activity against *P. acnes* and *S. aureus* is still scarce. This study was conducted to investigate the influence of ethanol and honey as extraction solvents on the total phenolic content (TPC), total flavonoid content (TFC), and antibacterial properties of *P. serratifolia* leaf extracts against *P. acnes* and *S. aureus*. The results are anticipated to contribute to a better understanding of honey's suitability as a green extraction solvent and its role in enhancing the recovery of antibacterial bioactive compounds from *P. serratifolia* leaves.

MATERIALS AND METHODS

Materials

The materials used were *Premna serratifolia* L. leaves, honey, technical ethanol, ethanol p.a., methanol p.a., distilled water, dimethyl sulfoxide (DMSO), Folin–Ciocalteu reagent, gallic acid, aluminum chloride ($AlCl_3$), sodium carbonate (Na_2CO_3), sodium acetate, sodium chloride (NaCl 0.9%), Mueller–Hinton Agar (Thermo Fisher Scientific®), paper discs (Macherey-Nagel®), clindamycin discs (Oxoid®), sterile cotton (Innova Husada®), *Proionibacterium acnes* ATCC 6919 and *Staphylococcus aureus* ATCC 25923 (Thermo Fisher Scientific®). The equipment used in this study included glassware (Iwaki®, Pyrex®), an autoclave (Hiclave HVE-50®), blender (Miyako®), bunsen burner, cotton swabs, desiccator, incubator (Memmert®), caliper, inoculating loop (Biologix®), laminar airflow cabinet (Andaru®), micropipettes (Dragon Lab®), microwave-assisted extraction system (Sharp®), oven (Memmert®), forceps, UV-Vis spectrophotometer (Shimadzu®), and digital balances (Shimadzu AUY220® and Ohaus®).

Methods

Plant material

Leaves of *Premna serratifolia* L. were collected from Pontianak, West Kalimantan, Indonesia. The plant material was authenticated at the Biology Laboratory, Faculty of Mathematics and Natural Sciences, Universitas Tanjungpura. The leaves were washed, sorted, dried, pulverized, and sieved to obtain a homogeneous powdered sample. The leaves were subjected to wet sorting, washed under running water, air-dried, and sliced into small pieces. The material was then dried in an oven at 50°C for 10 h, followed by grinding and sieving through a 60-mesh sieve to produce simplicia powder (Supriningrum et al., 2018).

Preparation of Honey Solvent

The honey-based natural deep eutectic solvent (NADES) was prepared by mixing honey and distilled water at a ratio of 80:20 (v/v). The mixture was stirred until a homogeneous solution was obtained before being used as the extraction solvent (Bragagnolo et al., 2025).

Extraction

Powdered leaves were extracted separately using ethanol and honey solvent at a sample-to-solvent ratio of 1:10 (w/v). Extraction was carried out using Microwave-Assisted Extraction (MAE) at 225 W for 7 min. The extracts were filtered and stored for further analysis (Herman et al., 2021; Isnindar et al., 2025).

Determination of Total Phenolic Content (TPC)

The total phenolic content was quantified using the Folin–Ciocalteu assay. An aliquot of 0.5 mL extract was combined with 2.5 mL of 10% Folin–Ciocalteu reagent and incubated for 5 min, followed by the addition of 2 mL of 7.5% sodium carbonate. After standing for 30 min at room temperature, the absorbance was recorded using a UV–Vis spectrophotometer at the optimized wavelength. Gallic acid was used as the standard, and the results were reported as mg GAE/g extract (Andriani & Murtisiwi, 2018).

Determination of Total Flavonoid Content (TFC)

Total flavonoid content was determined using the aluminum chloride colorimetric method. An aliquot of extract solution The determination of total flavonoid content was performed by the aluminum chloride colorimetric method. The extract solution was mixed with aluminum chloride and sodium acetate reagents, followed by incubation under predetermined optimal conditions. Absorbance measurements were carried out using a UV–Vis spectrophotometer at the optimized wavelength. Quantification was based on a quercetin calibration curve, and the flavonoid content was reported as milligrams of quercetin equivalents per gram of extract (mg QE/g extract) (Suharyanto & Hayati, 2021).

Antibacterial Activity Assay

The antibacterial activity of the extracts was assessed against *Propionibacterium acnes* ATCC 6919 and *Staphylococcus aureus* ATCC 25923 using the disc diffusion assay. Bacterial inocula were prepared in 0.9% NaCl and standardized to the turbidity of a 0.5 McFarland standard. The bacterial suspensions were uniformly spread onto Mueller–Hinton Agar (MHA)

plates using sterile cotton swabs. Sterile paper discs containing extract solutions at concentrations of 25%, 50%, and 100% were then applied to the agar surface. Clindamycin discs served as positive controls, whereas the respective extraction solvents were used as negative controls. Following incubation at 37°C for 24 h, the diameters of the inhibition zones were measured with a caliper. Each treatment was conducted in triplicate. (Isnindar et al., 2023).

RESULTS AND DISCUSSION

Preparation of Simplisia, Honey Solvent, and Extracts of *Premna serratifolia* Leaves

Fresh leaves of *Premna serratifolia* L. were collected from West Pontianak, West Kalimantan, Indonesia. The leaves were cleaned through wet sorting and washing with running water before being oven-dried at 50°C for 10 h. The dried leaves were then ground and sieved through a 60-mesh sieve to obtain a homogeneous simplisia powder suitable for extraction.

The honey solvent used in this study was prepared by mixing honey and distilled water at a ratio of 80:20. The addition of water was intended to reduce the viscosity of honey and facilitate extraction while maintaining the hydrogen-bonding interactions characteristic of NADES systems. The resulting solvent appeared homogeneous and was used directly for extraction (Bragagnolo et al., 2025).

Extraction of *buas-buas* leaf powder was performed using the Microwave-Assisted Extraction (MAE) method at 225 W for 7 min (Ahmad et al., 2020). Two extraction solvents were used, namely 96% ethanol and honey solvent, with a sample-to-solvent ratio of 1:10 for both extraction systems (Isnindar et al., 2025). The ethanol extract obtained was subsequently concentrated at 50°C to remove the solvent and produce a more concentrated extract. In contrast, the extract obtained using the honey solvent was not subjected to a concentration process because honey-based solvents possess low volatility and high viscosity, making solvent evaporation difficult (Schuh et al., 2023). Consequently, the resulting extracts exhibited different physical characteristics, with the ethanol extract being concentrated after solvent removal, whereas the honey extract remained in liquid form.

Total Phenolic Content and Total Flavonoid Content of *Premna serratifolia* Leaf Extracts

The Total Phenolic Content (TPC) and Total Flavonoid Content (TFC) values of ethanol and honey extracts of *Premna serratifolia* leaves (Table 1). Statistical analysis using the Independent Samples *t*-test showed a significant difference between the two extracts ($p < 0.05$). The ethanol extract exhibited a higher TPC and TFC value than the honey extract.

Table 1. Total Phenolic Content (TPC) and Total Flavonoid Content (TFC) of Ethanol and Honey Extracts of *Premna serratifolia* Leaves.

Sample	Replicate	TPC (mgGAE/g)	Mean (mgGAE/g ± SD)	TFC (mg QE/g)	Mean (mgQE/g ± SD)
Ethanol extract	1	117,971	119,00±1,39	22,488	22,365±0,13
	2	118,453		22,220	
	3	120,588		22,387	
Honey Extract	1	6,923	7,01±0,08	0,988	0,977±0,01
	2	7,026		0,967	
	3	7,089		0,976	

Antibacterial Activity Against *Propionibacterium acnes* and *Staphylococcus aureus*

The antibacterial activity of ethanol and honey extracts against *Propionibacterium acnes* and *Staphylococcus aureus* (Table 2; Figure 1). Ethanol extract produced inhibition zones against both tested bacteria, whereas the honey extract did not produce any detectable inhibition zone. At concentrations of 50% and 100%, the ethanol extract produced mean inhibition zones of 2.62 mm and 3.77 mm against *P. acnes*, respectively. Against *S. aureus*, the ethanol extract at 100% concentration produced a mean inhibition zone of 3,60 mm. Based on the inhibition zone classification, these values were categorized as weak antibacterial activity. In contrast, clindamycin exhibited strong antibacterial activity, with mean inhibition zones of 14,00 mm against *P. acnes* and 13.19 mm against *S. aureus*.

Table 2. Antibacterial Activity of Ethanol and Honey Extracts of *Premna serratifolia* Leaves Against *Propionibacterium acnes* and *Staphylococcus aureus*.

Sample	Concentration	*P. acnes* (mm) Mean ± SD	*S. aureus* (mm) Mean ± SD
Ethanol extract	25%	0.00 ± 0.00	0.00 ± 0.00
	50%	2,62 ± 0,72	0.00 ± 0.00
	100%	3,77 ± 0,70	3,60 ± 0,56
Honey extract	25%	0.00 ± 0.00	0.00 ± 0.00
	50%	0.00 ± 0.00	0.00 ± 0.00
	100%	0.00 ± 0.00	0.00 ± 0.00
Honey solvent	25%	0.00 ± 0.00	0.00 ± 0.00
	50%	0.00 ± 0.00	0.00 ± 0.00
	100%	0.00 ± 0.00	0.00 ± 0.00
Positive control (Clindamycin)	2 µg	14,00 ± 0,70	13,19 ± 0,10
Negative control (DMSO)	1%	0.00 ± 0.00	0.00 ± 0.00

Discussion

Extraction efficiency was strongly influenced by the solvent used. Extracts obtained with ethanol were characterized by greater TPC and TFC values and demonstrated antibacterial effects against *Propionibacterium acnes* and *Staphylococcus aureus*. Conversely, honey-based extracts produced lower concentrations of these phytochemicals and failed to generate inhibition zones against the tested microorganisms.

The lower phenolic and flavonoid contents observed in the honey extract may be associated with the physicochemical characteristics of the honey-based solvent. Honey is a natural eutectic mixture composed mainly of fructose, glucose, and water that interact through an extensive hydrogen-bonding network. The high sugar concentration causes most water molecules to become associated with sugar molecules, reducing the amount of free water available in the system. This condition increases solvent viscosity and decreases solvent mobility during extraction. Consequently, mass transfer between the solvent and plant matrix becomes less efficient, resulting in reduced release of intracellular bioactive compounds from plant tissues. Strong hydrogen-bond interactions among honey constituents may also affect the ability of the solvent to solubilize bioactive compounds present within plant cells (Chevé-kools & Chapeland-leclerc, 2025).

Water addition in NADES systems has an optimum range of approximately 20–30%. The addition of water above 50% may gradually weaken the hydrogen bonds between hydrogen bond acceptors (HBA) and hydrogen bond donors (HBD), causing NADES dissociation and disruption of its supramolecular structure (Savi et al., 2019). Therefore, the amount of water added in this study was maintained within the recommended range. However, the viscosity of the solvent remained relatively high and may have limited solvent penetration into plant tissues, thereby reducing the extraction efficiency of phenolic and flavonoid compounds.

Another factor that may have contributed to the lower TPC and TFC values was the absence of a concentration step after extraction. Unlike the ethanol extract, the honey extract remained in liquid form because the honey-based solvent possesses low volatility and high viscosity, making solvent evaporation difficult. Consequently, the extracted bioactive compounds remained dispersed within a larger solvent volume, resulting in lower concentrations of active compounds per unit volume than those in the ethanol extract. In contrast, the ethanol extract underwent a concentration process that removed most of the solvent and produced a more concentrated extract. These differences likely contributed to the lower TPC and TFC values observed in the honey extract.

The lower TPC and TFC values may also have been influenced by the extraction conditions employed in this study. According to previous studies, the high viscosity of DES and NADES systems can reduce solvent diffusivity, limit penetration into plant matrices, and hinder mass transfer during extraction. As a result, the release of intracellular bioactive compounds, including phenolics and flavonoids, becomes less efficient, leading to lower extraction yields. Furthermore, the MAE conditions applied in this study (225 W for 7 min) may not have been sufficient to completely overcome the mass-transfer limitations associated with highly viscous solvent systems. Consequently, the extraction of bioactive compounds from *P. serratifolia* leaves may not have occurred optimally (Şahin et al., 2026).

The observed antibacterial activity may be associated with differences in the levels of phenolic and flavonoid compounds. Phenolic compounds and flavonoids have been reported to exert antibacterial effects through multiple mechanisms, such as disrupting bacterial cell membranes, modifying membrane permeability, inhibiting nucleic acid synthesis, and interfering with essential metabolic activities. Consequently, lower levels of these compounds may diminish the antibacterial efficacy of the extract (Kisiriko et al., 2021; Ningsih et al., 2023).

However, antibacterial activity cannot be explained solely by TPC and TFC values. Earlier investigations have reported that alkaloids and terpenoids are present in *P. serratifolia* leaves, which may also contribute to antibacterial activity (Az-zahra et al., 2023; Sarma et al.,

2021; Supriningrum et al., 2017). In addition, not all phenolic and flavonoid compounds possess the same antibacterial potency. Therefore, higher TPC and TFC values do not necessarily correspond to proportionally greater antibacterial activity.

The absence of inhibition zones in the honey extract may also have been influenced by the antibacterial testing method. The disc diffusion assay relies on the ability of active compounds to diffuse from the paper disc into the agar medium. During testing, some metabolites may not have dissolved completely, resulting in only a limited amount of active compounds being absorbed onto the discs. Furthermore, the immersion time of the paper discs in the extract solution was approximately ±1 min, which may not have been sufficient to allow optimal absorption of active compounds (Febriyanto et al., 2022). Another study reported that paper discs should be immersed in a honey solution for 5–10 min to ensure complete absorption of bioactive compounds before being placed onto the inoculated agar medium (Ihsan et al., 2022).

The relatively high viscosity of the honey extract may have further limited the diffusion of active compounds through the agar medium. Reduced diffusion rates can result in smaller inhibition zones or even the absence of visible inhibition despite the presence of antibacterial compounds. Therefore, the absence of inhibition zones observed in the honey extract should not necessarily be interpreted as the absence of antibacterial constituents, but may also reflect limitations related to extraction efficiency, compound concentration, and diffusion behavior during disc diffusion testing.

CONCLUSIONS

The extraction solvent significantly affected the Total Phenolic Content (TPC), Total Flavonoid Content (TFC), and antibacterial activity of *Premna serratifolia* leaf extracts. Ethanol extract exhibited significantly higher TPC and TFC values than honey extract and demonstrated weak antibacterial activity against *Propionibacterium acnes* and *Staphylococcus aureus*. In contrast, the honey extract showed lower TPC and TFC values and did not produce inhibition zones against either tested bacterium. These findings indicate that ethanol was more effective than the honey-based solvent for extracting bioactive compounds and antibacterial constituents from *P. serratifolia* leaves under the extraction conditions used in this study.

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Authors' Contributions: Isnindar and Nera Umilia Purwanti were responsible for study design, data analysis, and oversight of research quality assurance. Nisrina Falayati conducted the experimental work and performed data preparation and cleaning prior to analysis.

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