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Antibacterial Activity Test of Transdermal Patch Formulation of Methanolic Extract of Moringa (*Moringa oleifera* Lam.) Stem Bark Against *Staphylococcus aureus*

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ABSTRACT

Staphylococcus aureus is an opportunistic pathogen that causes skin and systemic infections, which can lead to serious complications. Resistance to conventional antibiotics poses a major challenge in treating these infections. This study aims to determine the antibacterial activity of a transdermal patch containing methanol extract of *Moringa oleifera* Lam. bark against *Staphylococcus aureus*. The study design is experimental, using a transdermal patch formulation containing the extract in three different concentrations (4%, 8%, and 12%). The evaluation was conducted on the physical properties of the patch, including organoleptic properties, pH, weight uniformity, thickness, fold resistance, and stability test. The preference test and antibacterial activity test were conducted using the well diffusion method. The results showed that all patch formulations met the requirements for good physical characteristics. Antibacterial activity increased with increasing extract concentration, with the highest inhibition zone (21.06 mm) observed at 12% extract concentration. The acceptability test showed that the patch formulation was well accepted by the respondents. Thus, the transdermal patch formulation of methanolic extract of moringa bark has the potential as an alternative treatment for skin infections caused by Staphylococcus aureus.

INTRODUCTION

Staphylococcus aureus is an opportunistic pathogen that constitutes a major cause of both skin and systemic infections in humans, potentially resulting in a wide range of serious complications (Guo *et al.*, 2020). Infections caused by *S. aureus* may include boils, impetigo, acne, wound ulcers, pneumonia, and various skin infections characterized by redness, abscess formation and pus discharge (Deny *et al.,* 2020). This bacterium is a Gram-positive coccus that forming grape – like clusters and is frequently associated with skin infections.

The use of antibiotics represents one of the primary approaches for managing bacterial infections; however the increasing resistance to conventional antibiotics has emerged as a major concern in the healthcare field (Levy & Bonnie, 2014). In recent years, cases of antibiotic resistance have continued to rise globally (Zhao *et al.*, 2019). According to the World Health Organization (WHO), antibacterial resistance has become a major threat to global health and contributed to approximately 4.9 million deaths across 204 countries in 2019. The increasing prevalence of resistant strains has reduced the effectiveness of conventional therapies, highlighting the urgent need for alternative antibacterial agents derived from natural sources (Primadiamanti *et al.*, 2018).

Moringa (Moringa oleifera Lam.) is recognized as a multipurpose plant possessing various health benefits and notable antimicrobial activities (Bukar *et al.*, 2010). The methanolic extract of Moringa oleifera stem bark

is known to contain bioactive compounds such as tannins, alkaloids, flavonoids, and steroids, which exhibit antibacterial activity against pathogenic bacteria in polar, semi-polar, and non-polar fractions, as well as anti-inflammatory and antioxidant properties (Zaffer *et al.*, 2014). Previous studies have demonstrated that the stem bark extract of Moringa oleifera is capable of inhibiting the growth of Staphylococcus aureus, producing inhibition zones of 10.08 mm, 11.8 mm, 15.00 mm, and 17.02 mm at concentrations of 1%, 2%, 3%, and 4%, respectively (Cholifah *et al*., 2020).

However, most natural-based topical antibacterial formulations are still limited to conventional dosage forms such as ointments or creams, which may cause skin irritation and have a relatively short contact time (Tilarso *et al*., 2021). Despite the established antibacterial potential of *Moringa Oleifera* Lam., its application in advanced drug delivery systems, particularly transdermal patches using stem bark extract, remains limited and has not been widely explored. In additions, the relationship between extract concertration and antibacterial activity within a transdermal patch system has not been clearly established.

To overcome these limitations, the transdermal patch drug delivery system offers several advantages, including controlled drug release, enhanced patient comfort, and reduced dosing frequency (Jadhav et al., 2009; Yati & Pamungkas, 2018). A transdermal patch consists of a polymeric layer that enables the gradual and stable release of the active compound (Chourisa *et al.*, 2019; Hanbali, 2019).

These characteristics are particulary beneifial for plant-based extracts, which may exhibit limited stability and inconsistent bioavailability in conventional topical formulations. Furthermore, the selection of extract concentrations (4%, 8%, and 12%) in this study was based on previous findings demonstrating antibacterial activity at lower concentration (1-4%) (Cholifah et al., 2020), with the aim of evaluating a concentration-dependent effect and optimizing antibacterial efficacy within the transdermal system.

Based on the aforementioned background, this study was conducted to develop and evaluate a transdermal patch formulation containing methanolic extract of Moringa oleifera Lam. stem bark at concentrations of 4%, 8%, and 12%, and to assess its antibacterial activity against Staphylococcus aureus using the well diffusion method. This study also aims to elucidate the relationship between extract concentration and antibacterial effectiveness within the formulated patch system, thereby contributing to the development of herbal topical formulations with potential as alternative treatments for skin infections caused by *Staphylococcus aureus.*

METHODS

Research Design

This study is an experimental laboratory research aimed at formulating and evaluating the antibacterial activity of transdermal patch formulations containing the methanolic extract of Moringa oleifera Lam. stem bark against Staphylococcus aureus. The research activities include extract preparation, patch formulation, evaluation of physical properties, stability testing, hedonic (preference) testing, and antibacterial activity assessment using the well diffusion method. The study was conducted from November 2024 to July 2025 at the Biology and Pharmaceutical Chemistry Laboratories of Harapan Bangsa University, in collaboration with the Biology Laboratories of Jenderal Soedirman University and Muhammadiyah University of Purwokerto.

Research Materials

The primary test material was the stem bark of Moringa oleifera Lam., obtained from the Sumampir area, North Purwokerto, Banyumas Regency, Central Java. Plant identification was carried out at the Biology Laboratory, Faculty of Applied Science and Technology, Jenderal Soedirman University, to verify the authenticity of the plant species used.

Other chemicals used in this study included methanol, 95% ethanol, hydroxypropyl methylcellulose (HPMC), polyvinylpyrrolidone K-25 (PVP K-25), propylene glycol, dimethyl sulfoxide (DMSO), distilled water, Nutrient Agar (NA), and a bacterial culture of Staphylococcus aureus. The positive control used was an Oxy patch containing chlorhexidine diacetate, while the negative control consisted of a patch without any active ingredient.

Research Ethics Approval

The ethical approval for this health-related research was submitted to the Health Research Ethics Committee of Harapan Bangsa University.

Plant Identification

The identification of the Moringa oleifera Lam. stem was carried out to verify the authenticity of the plant material used. The identification process was conducted at the Biology Laboratory, Faculty of Applied Science and Technology, Jenderal Soedirman University

Sample Preparation

Plant Material Preparation

The Moringa oleifera stem bark samples were obtained from the Sumampir area, North Purwokerto, Banyumas Regency, Central Java. The samples were thoroughly washed, cut into small pieces, and dried using a drying cabinet at a temperature of 70°C. Once dried, the samples were ground into a fine and uniform powder, then stored in a sealed container (Cholifah *et al*., 2020).

Extraction Process

The extraction was carried out using the maceration method. A total of 100 grams of Moringa oleifera stem bark powder was macerated in 500 mL of methanol for three days, with stirring every 24 hours at room temperature and protected from direct sunlight (Cholifah *et al*., 2020). The maceration filtrate was then filtered and concentrated using a rotary evaporator at 60°C, followed by evaporation in a water bath at 70°C until a thick extract was obtained. The extract yield was calculated using the following formula (Dewatisari et al., 2018; A. S. Wahyuni et al., 2024).

Phytochemical Screening

Flavonoid Test

A total of 1 gram of the extract was mixed with concentrated hydrochloric acid (HCl) in a test tube and heated for 15 minutes in a water bath. The appearance of a red or yellow coloration indicated a positive result for the presence of flavonoid compounds such as flavones, chalcones, and aurones (Muthmainnah, 2017).

Alkaloid Test

A total of 2 grams of the extract was mixed with 5 mL of 2N HCl, heated, then cooled, and divided into three test tubes containing 1 mL each. Different reagents were added to each tube: a positive result for alkaloids was indicated by the formation of a white or yellow precipitate with Mayer's reagent, a brown precipitate with Wagner's reagent, and an orange precipitate with Dragendorff's reagent (Muthmainnah, 2017).

Terpenoid and Steroid Test

A total of 2 grams of the extract was mixed with 2 mL of ethyl acetate in a test tube and shaken. The ethyl acetate layer was separated, dropped onto a spot plate, and allowed to dry. Subsequently, two drops of acetic anhydride and one drop of concentrated sulfuric acid were added. A positive result for terpenoids was indicated by the appearance of a red or yellow color, while a green coloration indicated the presence of steroids (Muthmainnah, 2017).

Saponin Test

A total of 1 gram of the extract was mixed with 10 mL of hot water in a test tube, then cooled and vigorously shaken for 10 seconds. The formation of a stable froth measuring 1–10 cm in height that persisted for more than 10 minutes and did not disappear after the addition of one drop of 2N HCl indicated a positive result for saponins (Muthmainnah, 2017).

Tannin Test

A total of 1 gram of the extract was mixed with 10 mL of hot water in a test tube and boiled for 5 minutes. The resulting filtrate was then added with 3–4 drops of $FeCl_3$ solution. The appearance of a bluish-green or dark green coloration indicated the presence of catechol-type tannins, while a dark blue coloration suggested the presence of pyrogallol-type tannins (Muthmainnah, 2017).

Formulation of the Transdermal Patch

The transdermal patch formulations were prepared at three different extract concentrations: 4%, 8%, and 12% (Kalsum et al., 2023).

Tabel 1. Components of the Transdermal Patch Formulation

Components	F0	F1	F2	F3	Function
Methanolic extract of Moringa oleifera stem bark (%)	–	4	8	12	Active ingredient
HPMC (%)	3	3	3	3	Film-forming polymer
PVP K-25 (%)	1	1	1	1	Hydrophilic polymer
Propilen glikol (mL)	0.5	0.5	0.5	0.5	Plasticizer
DMSO (mL)	0.1	0.1	0.1	0.1	Penetration enhancer
Etanol 95% ad (mL)	10	10	10	10	Solvent

HPMC was dissolved in hot distilled water and allowed to stand for 15 minutes until fully swollen. PVP K-25 was dissolved separately in hot distilled water, and the two solutions were then combined and stirred until homogeneous. The Moringa oleifera stem bark extract was dissolved in 95% ethanol, followed by the addition of propylene glycol and DMSO. Both mixtures were combined, thoroughly mixed, and the total volume was adjusted to 30 mL. The mixture was poured into silicone molds with a diameter of 2.5 cm, dried at 40°C for 10 hours, and stored in a desiccator for 20 hours (Kalsum *et al.*, 2023).

Evaluation of Physical Properties of the Patch

Organoleptic Test

This test was conducted visually to assess the shape, color, odor, and texture of the patch formulation (Gunarti *et al.*, 2024).

Weight Uniformity Test

Three patches were randomly selected from each formulation and weighed. The patches were considered uniform if the coefficient of variation (CV) was less than 5% (Wardani & Saryanti, 2021).

Thickness Test

The thickness of the patch was measured using a screw micrometer at three different points. An acceptable patch thickness should not exceed 1 mm (Balaji *et al*., 2012).

Folding Endurance Test

The patch was repeatedly folded at the same position until it broke. A satisfactory folding endurance is indicated by more than 200 folds (Jadhav et al., 2009).

pH Test

The patch was immersed in 2 mL of distilled water for two hours at room temperature, after which the pH was measured using a pH meter. A safe pH range for topical formulations is between 4.5 and 6.5 (Mariadi & Bernardi, 2023).

Cycling Test

This test was conducted to evaluate the physical stability of the transdermal patch containing Moringa oleifera stem bark methanolic extract by storing the formulation at 50°C for 12 hours, followed by 35°C for 12 hours, repeated for 6 cycles. Observations indicated no physical changes in the shape, odor, color, thickness, or weight uniformity of the patch (Nurmesa *et al.*, 2019).

Hedonic (Preference) Test

A total of 20 panelists evaluated the color, aroma, and skin sensation of the patch using a 5-point scale (1 = dislike, 5 = like very much)(Dira *et al.*, 2022).

Antibacterial Activity Test

The antibacterial activity was evaluated using the well diffusion method. The well diffusion method was selected due to its suitability for evaluating antibacterial activity of extract-based and semi-solid formulations, allowing diffusion of active compounds into the agar medium. A total of 25 mL of Nutrient Agar (NA) was mixed with 25 µL of Staphylococcus aureus suspension, homogenized, and poured into sterile Petri dishes to solidify. The bacterial suspension was standardized to 0.5 McFarland turbidity prior to use. Wells with a diameter of approximately 6 mm were created to accommodate the samples: positive control (Oxy patch), negative control (patch without active ingredient), and transdermal patches containing methanolic extract of *Moringa oleifera* stem bark at concentrations of 4%, 8%, and 12% (Cholifah *et al*., 2020). Each sample was tested in triplicate (n=3) in three independent experiments. The plates were incubated for 24 hours at 37°C

(Trista hapsari & Samodra, 2022). The diameter of the inhibition zones was measured in milimeters using a caliper and expressed as mean ± standard deviation (Aprilia *et al.*, 2017).

Data Analysis

The data from the physical evaluations were analyzed using SPSS software. All antibacterial activity data were expressed as mean ± standard deviation from triplicate measurements. Normality was assessed using the Shapiro–Wilk test, and homogeneity was tested with Levene's test. If the data were normally distributed and homogeneous, analysis was performed using One-Way ANOVA; otherwise, the non-parametric Friedman test was applied. Results were presented as mean ± standard deviation with a 99% confidence level.

RESULT AND DISCUSSION

Research Ethics Approval Results

This study was an experimental laboratory investigation assessing the sensory acceptance of transdermal patches containing methanolic extract of Moringa oleifera stem bark through a hedonic test by panelists. As it involved human subjects, ethical approval was obtained from the Health Research Ethics Committee of Harapan Bangsa University (No. B.LPPM-UHB/558/06/2025), valid from June 3, 2025, to July 3, 2026. The ethical process adhered to the seven WHO standards, CIOMS Guidelines, and the principles of respect for persons, beneficence, and justice from The Belmont Report to ensure participant rights and safety (Throne, 2024). Additionally, the study emphasized social value and fairness, as highlighted by Van Delden and Van Der Graaf (2017). With this ethical approval, the research was deemed appropriate, scientific, and responsibly conducted.

Plant Identification Results

The plant material used was the stem bark of Moringa oleifera Lam. Prior to use, identification was conducted at the Environmental Laboratory, Faculty of Biology, Jenderal Soedirman University to verify the authenticity and identity of the plant. The results confirmed that the sample was indeed Moringa oleifera Lam.

Preparation Results of Methanolic Extract of *Moringa oleifera* Stem Bark

The methanolic extract of Moringa oleifera stem bark was obtained as a viscous extract with a greenish-brown color, a characteristic odor, and a bitter taste. Based on Figure 1 From 1,200 grams of powdered sample, 30.364 grams of concentrated extract were obtained, yielding 25.30%. This yield was higher than those reported by Nugrahani and Ayuwardani (2023) at 2.188% and Ariyanti et al., (2019) at 18.96%, which may be influenced by factors such as particle size, moisture content, and maceration duration.

Figure 1. Methanolic Extract of Moringa oleifera Stem Bark

The yield of 25.30% complies with the standard specified in the *Indonesian Herbal Pharmacopoeia* which requires a minimum yield of 9.2% for bark samples.

Phytochemical Screening Test Results

Based on **Table 2**, the results of the phytochemical screening revealed that the methanolic extract of *Moringa oleifera* Lam. stem bark contains various secondary metabolites. The alkaloid test showed a positive result, indicated by the formation of a brown precipitate after the addition of Wagner's reagent. Both terpenoid and steroid tests were positive, as evidenced by the appearance of yellow and green colors, respectively. The addition of concentrated HCl in the flavonoid test produced a red coloration, confirming the presence of flavonoids. The saponin test showed the formation of a stable foam layer approximately 2.5 cm high after the addition of 2N HCl, while the tannin test yielded a dark green color following $FeCl_3$ addition. These findings confirm that the extract contains alkaloids, flavonoids, terpenoids, steroids, saponins, and tannins.

Table 2. Results of Phytochemical Screening

Test Parameter	Result	Reference Description
Alkaloids	+	Formation of a brown precipitate with Wagner's reagent indicates the presence of alkaloids (Muthmainnah, 2017).
Terpenoids	+	Formation of a yellow color indicates the presence of terpenoids (Muthmainnah, 2017).
Steroids	+	Formation of a green color indicates the presence of steroids (Muthmainnah, 2017).
Flavonoids	+	Formation of a red or orange-yellow color indicates the presence of flavonoids(Muthmainnah, 2017).
Tanins	+	Formation of a greenish-black color indicates the presence of tannins (Muthmainnah, 2017).

Based on Table 3, the organoleptic evaluation showed that increasing the extract concentration intensified the color from greenish-brown to dark brown and enhanced the characteristic odor of *Moringa oleifera.* The color change was associated with the presence of flavonoids and tannins, which are major polyphenolic compounds in the methanolic stem bark extract (Gunarti, *et al.*, 2024). Despite these changes, all formulations remained homogenous and physically stable, indicating uniform distribution of the active ingredients within the polymer matrix. Similar observations have been reported by Kalsum *et al.*, (2023) who found that higher concentration of plant extracts increased color intensity without compromising formulation stability.

The weight uniformity test demonstrated that all formulations complied with the acceptance criterion (CV ≤ 5%) (Kristianti *et al.*, 2024). Although formula F1 exhibited a slightly higher CV value, all formulations remained within the acceptable range. Variations in patch weight may be influenced by formulation homogeneity, viscosity, drying conditions, and cutting precision (Pratiwi *et al.*, 2020). In addition, polymer composition contributes to weight consistency, with PVP tending to increase variability and HPMC improving uniformity (Shah *et al.*, 2011). Statistical analysis revealed a significant effect of extract concentration on patch weight ($p = 0.003$; $p < 0.05$), althought the differences were not substantial enough to affect overall product uniformity.

Patch thickness increased proportionally with extract concentration, ranging from 0.25 mm in F0 to 0.77 mm in F3, while remaining within the acceptable specification (Balaji et al., 2012). This trend may be attributed to increased film density and viscosity caused by the higher extract content (Fakruddin et al., 2019). similar findings were reported by Singh and Bali, (2016) who demonstrated a direct relationship between active ingredient concentration and patch thickness. While thicker films may improve mechanical strength, excessive thickness can potentially reduce drug release efficiency (Agis Wahyuni *et al*, 2023). ANOVA confirmed significant differences among formulations p-value of 0.000 ($p < 0.05$).

Based on Table 3, all formulations exhibited folding endurance values above 200, indicating adequate flexibility and resistance to mechanical stress (Jadhav et al., 2009). The observed increase in folding endurance with higher extract concentrations may be related to enhanced matrix density and the plasticizing effect of propylene glycol, which improves film elasticity (Latif et al., 2022; Singh & Bali, 2016; Wardani & Saryanti, 2021). These finding are consistent with previous studies showing that increased matrix viscosity contributes to improved mechanical performance of transdermal films. Statistical analysis showed significant differences among formulation p-value of 0.000 ($p < 0.05$).

The pH values of all formulations ranged from 4.5 to 6.20, indicating compatibility with topical application requirements (Mariadi & Bernardi, 2023). Variations in pH were likely influenced by interactions between the extract constituents and excipients, which helped maintain formulation stability (Jain et al., 2024). The slightly higher pH observed in F2 and the decrease in F3 may be associated with differences in the relative contribution of phytochemicals, including flavonoids and tannins (Yamamoto et al., 2015). similar pH behavior has been reported in herbal based transdermal systems, where excipients extract interactions play an important role in maintaining formulation stability (Jain et al.,

2024). ANOVA analysis indicated significant differences among formulations p-value of 0.000 ($p < 0.05$).

Table 3. Physical Evaluation Results Of The Transdermal Patch

Parameters	F0	F1	F2	F3
Color	Clear white	Transparent greenish-brown	Dark brown	Dark brown
Odor	Odorless	Characteristic odor of *Moringa oleifera* stem bark methanolic extract	Characteristic odor of *Moringa oleifera* stem bark methanolic extract	Characteristic odor of *Moringa oleifera* stem bark methanolic extract
Shape and Characteristics	Round, thin, smooth, and elastic	Round, thin, smooth, and elastic	Round, thin, smooth, and elastic	Round, thin, smooth, and elastic
Weight Uniformity (gram)	(0.15 ± 0.01)	(0.17 ± 0.01)	(0.18 ± 0.02)	(0.22 ± 0.01)
CV(%)	4.6	0.58	3.8	3.1
Thickness (mm)	(0.25 ±0.02)	(0.40± 0.04)	(0.54 ±0.05)	(0.77 ±0.04)
Folding Endurance (times)	(369 ± 25.05)	(474 ± 24.87)	(609 ± 32.51)	(736 ± 29.54)
pH value	(4.57 ±0.20)	(5.23 ±0.32)	(6.2 ±0.1)	(6.1±0.20)

Control Negative (F0) F1 F2 F3

Figure 2. Organoleptic Characteristics of the Transdermal Patches, including observations of color, texture, surface uniformity, and odor.

Cycling Test

Organoleptic Stability Test Results

Based on the results of the organoleptic evaluation, all transdermal patch formulations containing methanolic extract of *Moringa oleifera* stem bark showed no observable changes in odor, shape, or color during six stability testing cycles (Figure 2). Therefore, the formulations were considered organoleptically stable throughout the stability testing process.

Based on Table 4, the pH of the formulations decreased with increasing extract concentration, ranging from F0 (±6.3) to F3 (±4.6); however, all formulations remained within the safe range of 4.5–6.5 (Mariadi & Bernardi, 2023). This decrease was attributed to the acidic nature of the extract and chemical reactions such as hydrolysis and the formation of acidic compounds during storage (Nitiariksa & Iskandar, 2021; Sugiharta & Ningsih, 2021; Yamamoto et al., 2015). Components such as HPMC, PVP, propylene glycol, and DMSO contributed to maintaining pH stability (Kalsum *et al.*, 2023). Results from the Repeated Measures ANOVA indicated that F0–F2 remained stable ($p > 0.05$), whereas F3 ($p = 0.007$) showed a significant change due to the higher

concentration of acidic extract (Banerjee et al., 2014). The folding endurance values increased from F0 (361 ± 1) to F3 (668 ± 3.78), all exceeding the standard threshold of >200 folds, indicating good elasticity and mechanical strength of the patches (Jadhav et al., 2009). This increase corresponds to the higher extract concentration, which enhances the film structure and flexibility (Latif et al., 2022; Singh & Bali, 2016). Formula F3 demonstrated the highest folding endurance, consistent with Wardani and Saryanti, (2021) who stated that patches with folding endurance ≥200 exhibit strong and elastic matrices. The Repeated Measures ANOVA results showed p-values for F0–F3 greater than 0.05, indicating that all formulations were stable in terms of folding endurance.

Table 4. Cycling Test Results of Transdermal Patch

No	pH Stability Test	F0	F1	F2	F3
1	1	(6.3 ±0.15)	(6.0 ±0.1)	(5.5 ±0.1)	(4.7 ±0.2)
	2	(6.3 ±0.1)	(6.0 ±0.1)	(5.5±0.26)	(4.76±0.32)
	3	(6.3 ±0.1)	(5.9 ±0.1)	(5.5 ±0.2)	(4.76±0.15)
	4	(6.3 ±0.2)	(5.9 ±0.1)	(5.5 ±0.1)	(4.63 ±0.32)
	5	(6.3 ±0.26)	(5.9 ±0.2)	(5.4±0.15)	(4.6 ±0.1)
	6	(6.33±0.20)	(5.9±0.15)	(5.4±0.20)	(4.6 ±0.26)
2	Weight Uniformity Stability Test				
	1	(0.21 ± 0.02)	(0.22 ± 0.02)	(0.34 ± 0.03)	(0.36 ± 0.05)
	CV	0.05%	0.07%	0.13%	0.15%
	2	(0.21 ± 0.25)	(0.22 ± 0.23)	(0.34 ± 0.02)	(0.36 ± 0.03)
	CV	0.21%	0.06%	0.05%	0.11%
	3	(0.20 ± 0.03)	(0.22 ± 0.03)	(0.34 ± 0.01)	(0.36 ± 0.01)
	CV	0.16%	0.17%	0.035%	0.03%
	4	(0.20 ± 0.02)	(0.22 ± 0.04)	(0.33 ± 0.03)	(0.34 ± 0.04)
	CV	0.085%	0.22%	0.12%	0.14%
	5	(0.20 ± 0.02)	(0.21 ± 0.03)	(0.33 ± 0.02)	(0.34 ± 0.03)
	CV	0.10%	0.21%	0.05%	0.12%
	6	(0.20 ±0.05)	(0.21 ±0.02)	(0.32 ±0.03)	(0.34 ±0.05)
	CV	0.3%	0.18%	0.09%	0.20%
3	Folding Endurance Stability Test				
	1	(362 ± 2)	(453 ± 6.08)	(559 ± 27.4)	(668 ± 8.54)
	2	(361 ± 1.52)	(453 ± 5.68)	(559 ± 28.3)	(668 ± 3.78)
	3	(361 ± 2.64)	(454 ± 4.58)	(559 ± 17.03)	(361 ± 2.64)
	4	(361 ± 1)	(454 ± 1)	(550 ± 9.60)	(667 ± 10)
	5	(361 ± 2)	(454 ± 2)	(560 ±2)	(666 ± 11.5)
	6	(361 ± 2.51)	(454 ± 3)	(560 ± 2)	(667 ± 15.7)
4	Thickness Stability Test				
	1	(0.31 ± 0.045)	(0.42 ± 0.033)	(0.53 ± 0.030)	(0.58 ± 0.014)
	2	(0.31 ± 0.036)	(0.42 ± 0.033)	(0.53 ± 0.024)	(0.58 ± 0.024)
	3	(0.31 ± 0.022)	(0.41± 0.014)	(0.53 ± 0.017)	(0.58 ± 0.057)
	4	(0.31 ± 0.043)	(0.41 ± 0.028)	(0.53 ± 0.022)	(0.58 ± 0.053)
	5	(0.32 ± 0.024)	(0.41 ± 0.017)	(0.53 ± 0.045)	(0.58 ± 0.075)
	6	(0.31 ± 0.012)	(0.41 ± 0.015)	(0.53 ± 0.026)	(0.58 ± 0.015)

Based on Table 4, the six-cycle evaluation showed an increase in the mean values with increasing extract concentration, ranging from 0.21 in F0 to 0.38 in F3. All formulations

exhibited coefficient of variation (CV) values between 0.03% and 0.3%, which were well below the acceptable limit of ≤5%, indicating good weight uniformity (Novia & Noval, 2021; Wardani & Saryanti, 2021).

The low CV values demonstrate stable and homogeneous weight distribution among the patches, reflecting a consistent formulation process (Pratasik *et al.*, 2019). Results of the Repeated Measures ANOVA test showed p-values > 0.05 for all formulations (F0–F3), confirming that all transdermal patch formulations were stable in terms of weight uniformity.

All formulations exhibited a thickness of less than 1 mm, meeting the criteria for an ideal transdermal patch (Balaji et al., 2012). The mean thickness increased with extract concentration, ranging from 0.31 mm in F0 to 0.58 mm in F3, and remained stable up to the sixth cycle. The uniform thickness indicates a homogeneous formulation mixture (Pratasik *et al.*, 2019).

The increase in thickness is influenced by film density and the higher concentration of HPMC polymer (Fakruddin *et al.*, 2019; Kalsum *et al.*, 2023). Stable thickness also contributes to comfort during skin application (Wardani & Saryanti, 2021). he Repeated Measures ANOVA results showed p-values greater than 0.05 for all formulations, indicating no significant difference; thus, the patches were considered stable in terms of thickness.

This study has several limitations. The evaluation was primarily limited to the physicochemical properties, hedonic characteristics, and in vitro antibacterial activity of the transdermal patch formulations containing methanolic extract of Moringa oleifera stem bark. In addition, stability assessment was restricted to accelerated testing, while long-term stability under real-time storage conditions was not evaluated.

The antibacterial activity was assessed against only one bacterial strain, which may not fully represent the broader antimicrobial potential of the formulation. Furthermore, drug release kinetics and skin permeation profiles were not investigated, limiting the understanding of active compound delivery through the skin. Therefore, future studies should include long-term stability testing, broader-spectrum antimicrobial evaluations, and in vitro or ex vivo permeation studies to provide a more comprehensive assessment of the efficacy and therapeutic potential of the developed transdermal patch.

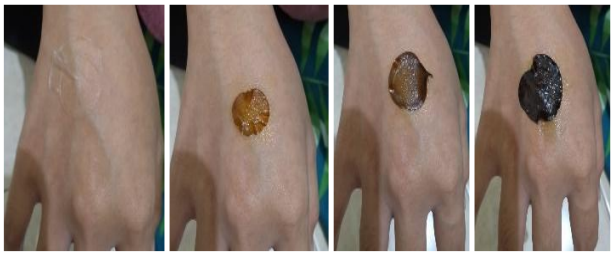
Hedonic Test

The analysis using the Friedman test revealed significant differences in color, aroma, and skin sensation (Asymp. Sig < 0.05). Formula F1 obtained the highest mean ranks for color (3.25) and skin sensation (3.63), indicating an attractive greenish-brown appearance with a smooth and elastic texture (Supit *et al.*, 2015; Qamariah *et al.*, 2022).

Formula F0 showed the highest score for aroma due to its odorless characteristic (Lamusu, 2018; Khalisa *et al.*, 2021). Overall, Formula F1 was the most preferred by the panelists and has the greatest potential to be developed as the optimal transdermal patch formulation containing the methanolic extract of *Moringa oleifera* Lam. stem bark.

Table 5. Sensory Evaluation of Transdermal Patch Formulations

Parameter	Formula	Mean rank	Asymp Sig
Color	F0	2.45	0.010
	F1	3.25	
	F2	2.13	
	F3	2.17	
Aroma	F0	3.25	0.000
	F1	3.15	
	F2	2.10	
	F3	1.50	
Skin Sensation	F0	3.13	0.000
	F1	3.63	
	F2	1.58	
	F3	1.68	



F0 F1 F2 F3

Figure 3. Visual comparison applied on human skin for hedonic evaluation

Antibacterial Activity

Table 6. Antibacterial Activity of Transdermal Patch Formulations Expressed as Inhibition Zone Diameter Against Staphylococcus aureus

Sample	Inhibition Zone Diameter (mm)	Inhibition Category
F0	0.00	Weak
Positive Control	6.82	Moderate
F1	10.51	Strong
F2	16.24	Strong
F3	21.06	Very strong

Based on Table 6, the negative control showed no inhibitory activity, whereas the positive control (Oxy patch) exhibited a moderate inhibition zone of 6.82 mm (Sarwo et al., 2025). Based on Figure 4 Inhibitory effect against Staphylococcus aureus increaseswith extract concentration: F1 = 10.51 mm, F2 = 16.24 mm, dan F3 = 21.06 mm (Faradina *et al.*, 2019). The antibacterial activity is attributed to the presence of bioactive compounds such as flavonoids, tannins, alkaloids, terpenoids, and saponins, which can disrupt bacterial cell walls and inhibit metabolic processes (Paikra *et al.*, 2017; Fauzan *et al*, 2019; Maria and Nay, 2023). The increase in extract concentration (4–12%) was directly correlated with enhanced bacterial inhibition (Rompas *et al.*, 2022).

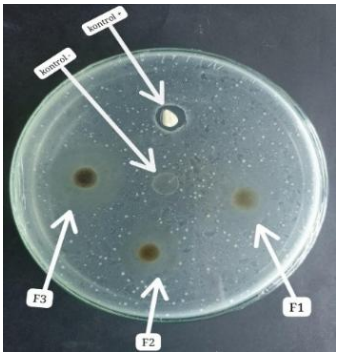


Figure 4. Antibacterial Activity of Transdermal Patch

Final Interpretation

Based on the overall results, formula F3 containing 12% extract exhibited the best physical properties, high stability, favorable acceptability, and the strongest antibacterial activity. These findings indicate that the methanolic extract of *Moringa oleifera* Lam. stem bark has promising potential to be developed as an active ingredient in transdermal patch formulations for the treatment of skin infections caused by *Staphylococcus aureus* (Bukar *et al.*, 2010; Tilarso *et al.*, 2021).

CONCLUSIONS

Based on the results of this study, the transdermal patch formulation containing methanolic extract of *Moringa Oleifera* Lam. Stem bark met the required standards for physical and stability evaluations, including organoleptic properties, weight uniformity, thickness, and folding endurance.

The antibacterial activity test against *Staphylococcus aureus* demonstrated a concentration-dependent increase in inhibitory activity, with inhibition zones of 10.51 mm, 16.24 mm, and 21.06 mm for formulas F1, F2, and F3, respectively, indicating that formula F3 exhibited the strongest antibacterial effect. However, based on the hedonic evaluation, formula F1 showed the highest level of panelist preference in terms of color, aroma, and skin sensation.

These findings indicate a trade-off between antibacterial efficacy and patient acceptability, where higher extract concentrations enhance antibacterial activity but may reduce sensory acceptance. Therefore, while formula 3 is the most effective in terms of antibacterial activity, formula 1 demonstrates greater potentialfor practical application due to its higher user acceptability. Further optimization is required to achieve a balnced formulation with both high efficacy and favorable patient compliance.

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AUTHORS' CONTRIBUTIONS

All authors contributed equally to this research.

CONFLICT OF INTERESTS

The authors have no financial, personal, or professional relationships that could inappropriately influence (or be perceived to influence) this work.

ETHICAL CONSIDERATION

The study complied with ethical standards. Human volunteers for the hedonic test provided written informed consent, and the protocol was approved by the Health Research Ethics Committee of Harapan Bangsa University, approval number B.LPPM-UHB/558/06/2025. The authors declare that all principles regarding plagiarism, data fabrication, and duplicate publication have been fully observed.

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