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OPTIMIZATION OF ANTI-BACTERIAL GEL FROM ETHYL ACETATE FRACTION OF PURPLE SWEET POTATO LEAVES (*Ipomoea batatas* L.) USING HYDROXY PROPYL METHYL CELLULOSE (HPMC) AND TESTING ITS ACTIVITY AGAINST *STAPHYLOCOCCUS EPIDERMIDIS* BACTERIA

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ABSTRACT
Bacterial infections are a significant global health challenge because they can attack various body tissues and cause illnesses ranging from mild to severe. *Staphylococcus epidermidis* is a bacterium that often causes various infections. Infection by *Staphylococcus epidermidis* can slow down the wound healing process and carry the risk of serious complications if not properly managed. This study aims to formulate and optimise an antibacterial gel from the ethyl acetate fraction of purple sweet potato leaves (*Ipomoea batatas* L.) as a natural alternative for treating skin infections caused by the bacterium *Staphylococcus epidermidis*. Using the I-optimal mixture design method in Design-Expert software, the optimization analysis was performed by evaluating several responses, including pH, viscosity, spreadability, and adhesion of the gel formulation. The experimental data were fitted to an appropriate polynomial model and analyzed using ANOVA to determine the significance of the model and mixture components. Numerical optimization was then carried out by setting the desired criteria for each response to obtain the optimum formulation. The optimal formulation consisted of 2% HPMC and 13% propylene glycol, with a desirability value of 0.964. The results showed that this formulation met all the criteria for a good and stable gel, including organoleptic properties (semi-solid, brownish-green, characteristic odour, homogeneous), pH (5.81), viscosity (2316.52 cPs), spreadability (6.4 cm), and adhesion time (2.18 seconds). The optimal formulation for an antibacterial gel containing the ethyl acetate fraction of purple sweet potato leaves (*Ipomoea batatas* L.) was achieved using a 2% HPMC concentration and 13% propylene glycol, with a desirability value of 0.964, , this gel formulation is also effective and falls into the category of being highly potent in inhibiting the growth of Staphylococcus epidermidis, as evidenced by the formation of an inhibition zone of 23 mm.

Keywords: antibacterial gel; formulation optimization; HPMC; ipomoea batatas l.; staphylococcus epidermidis

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INTRODUCTION

Bacterial infections are a significant global health challenge because they can attack various body tissues and cause illnesses ranging from mild to severe. According to a WHO report (WHO, 2024), bacterial infections are responsible for more than 7 million deaths each year, driven by increasing antimicrobial resistance. Pathogenic bacteria such as Staphylococcus aureus, Staphylococcus epidermidis, Pseudomonas aeruginosa, Klebsiella pneumoniae, and Escherichia coli are often the main causes of infections in the skin, wounds, respiratory tract, and urinary tract (Pieniążek et al., 2024). Inappropriate and excessive use of antibiotics reduces their effectiveness in treatment and leads to the emergence of resistant bacterial strains (Septiana et al., 2024).

Staphylococcus epidermidis is a bacterium that often causes various infections. This bacterium is part of the normal flora on human skin, but it is opportunistic, meaning it can cause infection when there is a wound or a disruption in the body's defence system. S. epidermidis is known to cause infections in the skin, post-operative wounds, medical device infections (such as catheters and

implants), and chronic wounds such as diabetic ulcers, with a prevalence of around 22.5% (Zuliana et al., 2023). Infection by S. epidermidis can slow down the wound healing process and carry the risk of serious complications if not properly managed. Therefore, there is a need for effective, safe, and non-resistant antibacterial agents to inhibit the growth of this bacterium. To treat these infections, the use of natural ingredients as antibacterial agents is becoming increasingly popular. One plant with antibacterial potential is purple sweet potato (*Ipomoea batatas* L.). Phytochemical test results show that the leaves of this plant contain active compounds such as alkaloids, flavonoids, tannins, and saponins. These compounds have various mechanisms of action, such as saponins that damage bacterial cell membranes, tannins that inhibit bacterial cell wall formation and inactivate enzymes, and flavonoids that disrupt bacterial membrane function and energy metabolism (Susanto et al., 2019).

Pratama and Nur (Pratama & Nur, 2024) reported that the ethyl acetate fraction was more effective in inhibiting bacteria than the n-hexane and ethanol fractions. The results of the minimum inhibitory concentration (MIC) test showed that all fractions could inhibit bacteria, and the ethyl acetate fraction had optimal potential when compared to other fractions (Ningsih et al., 2025). In an effort to maximise the use of the ethyl acetate fraction (Ipomoea batatas L.), formulations can be developed to produce preparations, in this case for topical use, such as gels, ointments, or creams. Saputri (Saputri, 2024) reported that several topical preparations using ethyl acetate fractions from purple sweet potato leaves (Ipomoea batatas L.), such as 5% hair tonic, 5% gel, and 5% lotion, exhibited inhibitory activity against Staphylococcus aureus. Additionally, topical formulations based on ethosomes, such as ethosome hair tonic, ethosome gel, and ethosome lotion, demonstrated very strong inhibitory activity against Staphylococcus aureus, with zone sizes exceeding 20 mm. The use of topical gels to deliver antibacterial substances offers various advantages, including good adhesive properties, the ability to absorb fluid from wounds, no interference with skin respiration, and ease of cleaning. In gel preparation, the selection of a thickening agent is a very important factor. One of the gel ingredients that is often used is Hydroxypropyl Methylcellulose (HPMC), which can form a stable, clear gel matrix that is resistant to pH changes and stable for long-term storage (Eka Valentina & Saryanti, 2023).

In determining the formula, the use of excipients certainly plays a very important role in producing a quality formula. Therefore, researchers utilise the Design-Expert software application in determining the optimal formula. According to (Hidayat et al., 2021), the use of Design-Expert software greatly supports the formulation process by making it easier for formulators to determine the most suitable formula. This software can be used to evaluate the influence of various formulation variables on each preparation through various methods. Based on the above background, this study aimed to develop a topical gel formulation with ethyl acetate fraction from purple sweet potato leaves (*Ipomoea batatas* L.), using HPMC as the gel base, and testing its antibacterial activity against Staphylococcus epidermidis.

METHOD

The materials used in this experiment included purple sweet potato leaves (*Ipomoea batatas* L.), ethanol, ethyl acetate, distilled water, HPMC, propylene glycol, phenoxyethanol, DMDM hydantoin, Nutrient Agar (NA), *Staphylococcus epidermidis*, Gentamicin ointment, aluminium foil, plastic wrap, spirit, and blue and yellow tips. A sample of 5 kg of purple sweet potato leaves was obtained from Wataliku Village, Kabangka Subdistrict, Muna Regency, Southeast Sulawesi Province. The purple sweet potato leaves (*I. batatas* L.) were collected, wet sorted, separated from the stems, washed with running water, then cut into smaller pieces, dried in the sun covered with black cloth. After drying, dry sorting was carried out and then ground into simplisia powder. The extraction method used was maceration. 50 grams of purple sweet potato leaf powder was placed in a sealed container and soaked in ethanol solvent for 3 x 24 hours. Every 24 hours, filtration and replacement of the solvent was carried out to obtain filtrates I, II, and III. The filtrates were collected and concentrated by rotary evaporation using a rotary vacuum evaporator at a temperature of 50ºC until a thick extract was obtained, which was then weighed to determine its weight.

The fractionation process was carried out according to the Can-ake (2004) method, which is a partition process using 96% ethanol-water (2:3) and ethyl acetate solvents. Four grams of ethanol extract was dissolved in 20 mL of ethanol-water (2:3) mixture, then partitioned with 20 mL of ethyl acetate solvent in a separating funnel six times. The ethyl acetate fraction was then evaporated using a rotary evaporator to obtain a concentrated ethyl acetate fraction (Suhaenah et al., 2021). The formulation design was carried out using the I-optimal method with Design Expert version 13 software. HPMC was used as a thickening agent for topical applications with an upper and lower limit of 2 to 5, whilst propylene glycol, as a humectant, had a value of approximately 15 (Rowe et al., 2009). Based on the analysis using Design Expert, the designed experiments comprised 7 formulations shown in Table 1. The ratio of the two components in each formulation was 100 grams of gel preparation.

Table 1.
Formulation Results According to Design Expert Software Version 13 Using the I-Optimal Method

Formula	Run	HPMC (%)	Propylene glycol
I	1	4	11
II	2	5	10
	3	5	10
	12	5	10
III	4	2	13
	9	2	13
	13	2	13
IV	5	3,5	11,5
	6	3,5	11,5
	7	3,5	11,5
V	8	4,25	10,75
VI	10	3	12
VII	11	2,75	12,25

The preparation of the gel formulation in accordance with Table 2 began with the first stage, namely the swelling of HPMC using hot water, followed by the addition of propylene glycol. The mixture was then stirred until homogeneous, a preservative was added, and it was stirred again until homogeneous. Next, add the ethyl acetate fraction from purple sweet potato leaves (*Ipomoea batatas* L.), and stirred until homogeneous. The final stage involves the addition of distilled water to reach a volume of 100 mL.

Table 2.
Formulation of an Ethyl Acetate Fraction Gel Preparation from Purple Sweet Potato Leaves (*Ipomoea batatas* L.)

Material	Formula						
	I	II	III	IV	V	VI	VII
Ethyl acetate fraction of *Ipomoea batatas* L.	7	7	7	7	7	7	7
HPMC	4	5	2	3,5	4,25	3	2,75
Propylene glycol	11	10	13	11,5	10,75	12	12,25
Phenoxyethanol	1	1	1	1	1	1	1
DMDM Hydantoin	0,2	0,2	0,2	0,2	0,2	0,2	0,2
Purified water	100	100	100	100	100	100	100

The preparations under observation were examined for changes in shape, the presence or absence of odour, the occurrence or absence of phase separation, and changes in colour (Hidayat Rifky et al., 2021). pH measurement was carried out using a pH meter, whereby the cathode of the pH meter was immersed in the gel and the measured pH value could then be read on the display. The pH range corresponding to skin pH is 4.5–6.5 (Yusuf et al., 2022). Gel viscosity is assessed using a viscometer by inserting a spindle into the gel sample, followed by observation and calculation of the viscosity value. The optimal viscosity range for gel formulations is 2000–4000 (Thomas et al., 2023). The spreadability test is performed by placing 0.5 g of gel on a 7 cm diameter glass plate, covering it with another glass plate, and observing for 1 minute without any additional load. After measuring the initial diameter, the load is gradually increased (50 g, 100 g, 150 g, 200 g) at 1-

minute intervals to obtain a constant spread diameter. A good spreadability parameter for gel formulations is between 5 and 7 cm (Thomas et al., 2023).

The adhesion test was conducted by placing 0.5 grams of gel on a glass slide, covering it with another glass slide, and applying a 1 kg load for 3 minutes. Adhesion was determined by the time taken for the two glass slides to separate. The criterion for the adhesion test is that it must take more than 1 second (Thomas et al., 2023). The homogeneity test aims to ensure that the active substance and the materials used are well mixed (homogeneous), i.e. the preparation must exhibit a homogeneous composition with no visible coarse particles. In this case, the materials used in the gel manufacturing process have been mixed homogeneously (Thomas et al., 2023). The cyclic testing was carried out by storing the gel formulation at a low temperature of 4°C for 24 hours, after which it was transferred to an oven at 40°C for 24 hours. This procedure was repeated for 6 cycles to observe the changes more clearly. Evaluation of the physical changes in the gel preparation was carried out at the start and end of the cycle, covering organoleptic parameters and homogeneity (Yusuf et al., 2022). The instruments were sterilised using an autoclave. They were wrapped in paper and then placed in the autoclave at a temperature of 121°C and a pressure of 15 atm for 15 minutes. Meanwhile, the other instruments were sterilised using 70% alcohol for 20 minutes (Maulana et al., 2020).

Revitalization of *Staphylococcus epidermidis* Bacteria

Staphylococcus epidermidis bacteria were cultured in Nutrient Agar (NA) medium, 0.4 grams of which was weighed and dissolved in 20 mL of distilled water in an Erlenmeyer flask. The preparation process continued by heating the agar solution until clear, stirring occasionally. The solution was then covered with cotton wool wrapped in gauze and sterilised in an autoclave at 121°C for 15 minutes, before being transferred to 10 mL calibrated test tubes. The NA medium was placed in a laminar air flow hood and tilted to allow the medium to solidify. Staphylococcus epidermidis bacteria were collected using a sterilised inoculation loop, then streaked in a zig-zag pattern onto the medium. Subsequently, the medium was incubated in an incubator for 24 hours at 37°C (Arfiandi et al., 2025).

Preparation of a Bacterial Suspension

One loopful of rejuvenated Staphylococcus epidermidis bacteria was taken and suspended in a test tube containing 5 mL of 0.9% NaCl solution, which was homogenised using a vortex mixer. It was then incubated for 30 minutes. The results were then compared with the McFarland 0.5% turbidity scale (Arfiandi et al., 2025).

Antibacterial Testing Using the Well Method

Place 30 mL of sterilised Nutrient Agar (NA) medium into a Petri dish. Once the NA medium has solidified, mix 20 mL of NA medium with 1 mL of Staphylococcus epidermidis bacterial suspension in the Petri dish containing the NA medium. Next, create wells with a diameter of approximately ±6 mm using a well-making mould. Each well was filled with the ethyl acetate fraction gel from the extract of purple sweet potato leaves (Ipomoea batatas L.) at varying concentrations, with each well containing 100 µL of the ethyl acetate fraction gel from the extract of purple sweet potato leaves (Ipomoea batatas L.). The plates were then incubated for 24 hours at 37°C, after which observations were made and the diameter of the inhibition zones formed was measured using a Vernier caliper. Gentamicin was used as the positive control and gel base as the negative control (Kartini et al., 2024).

RESULT

Extraction and Fractionation

In this study, the extract was subsequently dried further in an oven at 50°C to remove residual ethanol, yielding 285.35 grams of concentrated purple sweet potato leaf ethanol extract from 950 grams of crude drug, with a yield of 30.03%. This extraction yield indicates the percentage by weight of the extract obtained compared to the dry weight of the crude drug used. The final yield of

the ethyl acetate fraction obtained from purple sweet potato leaves was 115.83 grams, with a yield of 40.59%. The yield of this fraction reflects the percentage of the fraction's weight relative to the weight of the initial extract used in the fractionation process. It is expected that this ethyl acetate fraction contains a higher concentration of semi-polar compounds, thereby having the potential to exhibit more optimal antibacterial activity compared to the ethanol extract prior to fractionation.

Optimization Using the Design Expert Software with the I-Optimal Mixture Method

Based on the results of formulation experiments conducted using the mixture design method with Design-Expert, 13 formula combinations were obtained, varying in their concentrations of HPMC (A) and propylene glycol (B). Each formula was subsequently tested against several response parameters, namely pH, viscosity, spreadability and adhesion, as shown in Table 3.

Table 3.
Results from the Formula Design Expert

Run	Component		Responses			
	HPMC (%)	Propylene glycol (%)	pH	Viscosity (cPs)	Spreadability (cm)	Adhesion (second)
1	4	11	5,43	3353,11	5	3,21
2	5	10	4,41	3950,1	4,5	4,3
3	5	10	4,4	3350,23	4,4	4,01
4	2	13	5,82	2315,57	6,4	2,01
5	3,5	11,5	5,49	3126,68	5,9	2,93
6	3,5	11,5	5,48	3126,8	5,8	3,34
7	3,5	11,5	5,48	3126,25	5,9	3,04
8	4,25	10,75	5,38	3581,86	4,8	3,87
9	2	13	5,81	2313,49	6,6	2,18
10	3	12	5,64	2881,86	6	3,77
11	2,75	12,25	5,72	2491,02	6,2	2,21
12	5	10	4,45	3350,11	4,4	4,96
13	2	13	5,82	2310,36	6,4	2,37

The independent variables used in this study included HPMC (2–5%) and propylene glycol (10–15%), each of which was entered into the software along with their upper and lower limits. Test results showed that the pH of the preparations ranged from 4.4 to 5.82. Viscosity values ranged from 2310.36 to 3950.1 cPs, indicating variations in viscosity due to differences in ingredient composition. The spreadability was within the range of 4.3 cm to 6.6 cm, whilst the adhesion time ranged from 2.01 seconds to 4.96 seconds, as presented in table 4.

Table 4.
Composition Constraints and Response Targets in the I-Optimal Mixture Design

	Experimental Variables	Constrains		Target
		Lower Limit	Upper Limit	
Independent Variables	HPMC	2	5	In Range
	Propylene glycol	10	15	In Range
Dependent Variables	pH	4.4	5.82	Maximize
	Viscosity	2310.36	3950.1	Minimize
	Spreadability	4.3	6.6	Maximize
	Adhesion	2.01	4.96	Minimize

Evaluation of pH response

Optimisation of the pH response of the gel formulation was carried out using an I-Optimal mixture design involving two components, namely HPMC and propylene glycol, as shown in Figure 1. Based on the Fit Summary and Sequential Model Sum of Squares analyses, a quartic model was recommended by Design-Expert as the most suitable model for the pH response. The selection of the quartic model was based on a non-significant lack of fit value ($p = 0.5420 > 0.05$), indicating that the model represents the data well and that there is no significant discrepancy between the model and the actual data.

Evaluation of viscosity response

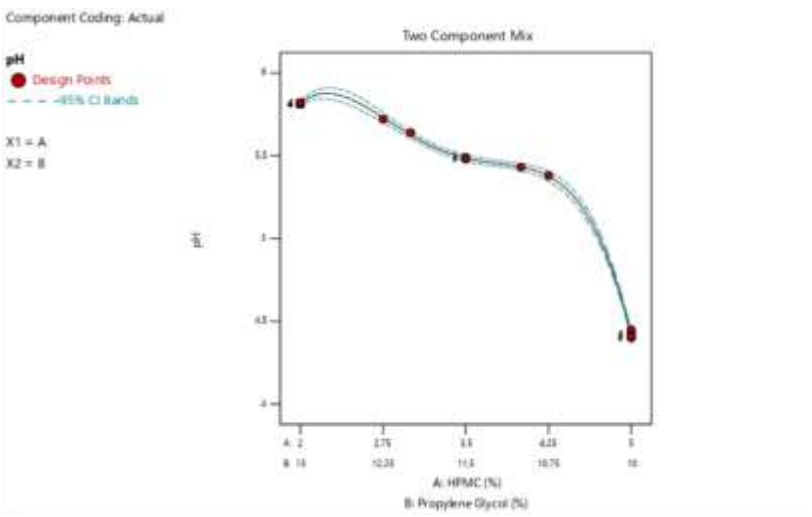


Figure 1. pH test graphic

Based on the analysis of the Fit Summary and Sequential Model Sum of Squares, Design-Expert recommends the linear model as the most appropriate model for the viscosity response. This linear model was selected because it showed a non-significant lack of fit ($p = 0.4806 > 0.05$), indicating that the model successfully describes the relationship between the components and the viscosity response without any significant misfit, as shown in Figure 2.

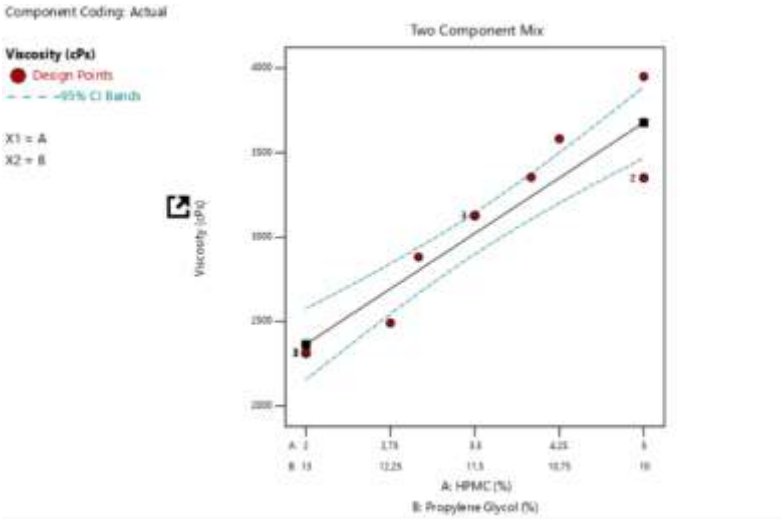


Figure 2. Viscosity Test Graphics

Evaluation of the spread response

Based on the analysis of the Fit Summary and Sequential Model Sum of Squares, Design-Expert recommends a quartic model as the most optimal model for the spread response, as shown in Figure 3. The selection of the quartic model is based on a non-significant lack of fit value ($p = 0.1 > 0.05$), indicating that the model successfully represents the data well without any significant discrepancy between the model and the actual data.

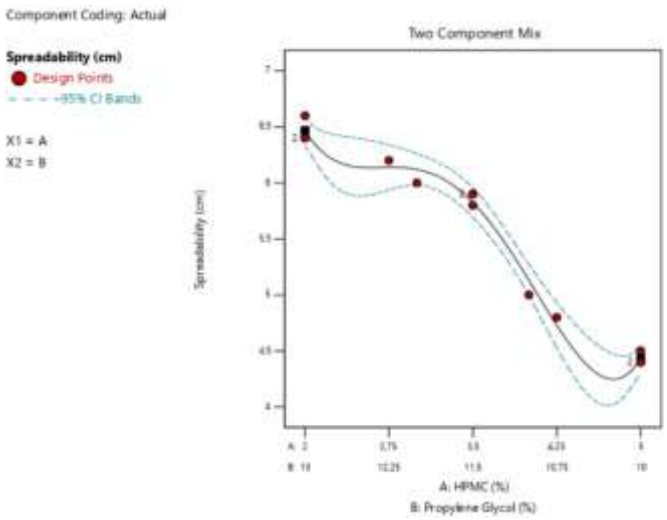
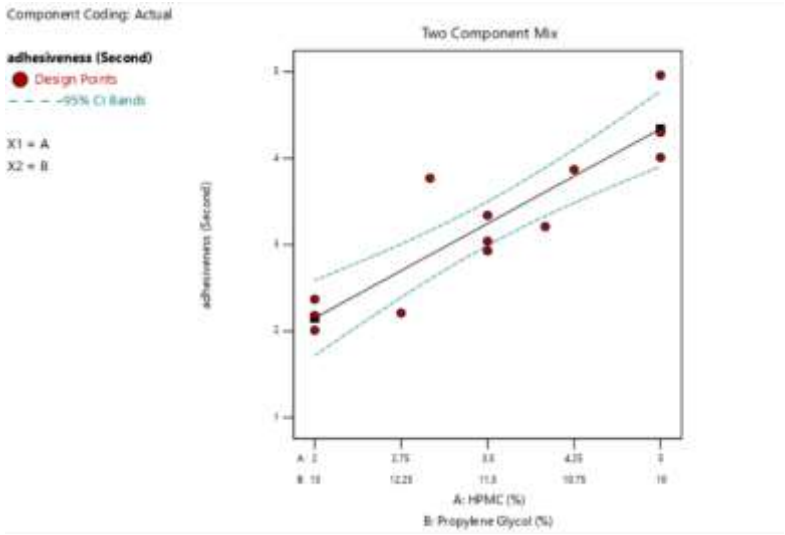


Figure 3. Dispersion Test Graphics

Evaluation of Adhesion Response

Based on the analysis of the Fit Summary and Sequential Model Sum of Squares, Design-Expert recommends the linear model as the most appropriate model for the adhesive strength response, as shown in Figure 4. This linear model was selected because it showed a non-significant lack of fit value ($p = 0.1536 > 0.05$), indicating that the model successfully describes the relationship between the components and the adhesive strength response without any significant misfit.

Figure 4. Adhesion test graphic



Determination of the Optimal Formula Based on Desirability

The results of the optimisation process show that the most optimal formulation was achieved with a composition of 2% HPMC and 13% propylene glycol, with a desirability value of 0.964, as shown in Figure 5. This desirability value, which is close to 1, indicates that the formula can imultaneously meet all the established response criteria, including pH, viscosity, spreadability, and adhesion.

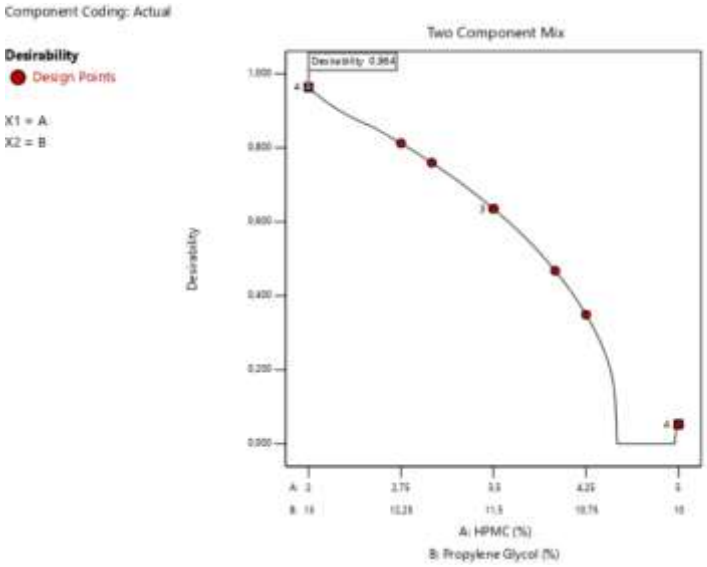


Figure 5. Optimized Formula Prediction Results Graphics

Verification of the optimal formulation was carried out through three replicates (runs = 3) in gel preparation at the selected composition (2% HPMC, 13% propylene glycol). The average results show a pH value of 5.94; viscosity of 2327.91 cP; spreadability of 6.47 cm; and an adhesion time of 2.19 seconds, as shown in Table 5.

Table 5.
Results of the Verification of the Optimum Formula

Response	Predicted Mean	Data Mean (Observed)	95% Lower Confidence	95% Upper Confidence	Notes
pH	5,81645	5,81667	5,78758	5,84531	Predicted
Viscosity	2364,78	2316,52	2034,19	2695,38	Predicted
Spreadability	6,46741	6,46667	6,27203	6,66279	Predicted
Adhesion	2,15227	2,18667	1,4658	2,83796	Predicted

Formulation of an Antibacterial Gel from Purple Sweet Potato Leaves (*I. batatas* L.)

The chosen gel formulation, based on the results of Design Expert optimization: 100 grams of gel were prepared using the formulation shown in Table 6.

Table 6.
Gel Formulation Based on the Results of Design Expert Optimization

Ingredient	Concentration (%)
Ethyl acetate fraction of *Ipomoea batatas* L.	7
HPMC	2
Propylene Glycol	13
Phenoxyethanol	1
DMDM Hydantoin	0,2
Purified water	100

Analysis Characteristics and Stability of an Antibacterial Gel from Purple Sweet Potato Leaves (*Ipomoea batatas* L.)

The evaluation of the characteristics and stability of the antibacterial gel derived from purple sweet potato leaves (*Ipomoea batatas* L.) was carried out in two stages: before and after the cycling test. In each stage, observations were made regarding organoleptic properties, homogeneity, pH, viscosity, spreadability and finally, adhesion evaluation.

Table 7.
Evaluation the characteristics and stability of antibacterial gels

Parmeters		Before Cycling Test	After Cycling Test
Organoleptic	Form	Semi-Solid	Semi-Solid
	Colour	Brownish Green	Brownish Green
	Odour	Distinctive	Distinctive
Homogenity		Homogeneous	Homogeneous
pH		5,81	5,64
Viscosity		2316,52	2253,9
Spreadability		6,4	6,5
Adhesion		2,18	2,04

Antibacterial Activity of the Ethyl Acetate Fraction of Purple Sweet Potato Leaves (I. batatas L.) Against Staphylococcus epidermidis

The antibacterial activity of the ethyl acetate fraction gel derived from purple sweet potato leaves was tested using the diffusion method, with the measurement parameter being the diameter of the inhibition zone formed around the wells or discs against the test bacterium Staphylococcus epidermidis. This bacterium is a Gram-positive bacterium that is naturally present as part of the normal skin flora, but can act opportunistically and contribute to various skin infections.Based on the results of three replicates (Figure 6 and Table 8), a significant difference was observed between the negative control (F0), the positive control (K+), and the test formulation (F1).

A B C

Figure 6 Results of the antibacterial activity test of the ethyl acetate fraction gel of purple sweet potato leaves (Ipomoea batatas L.) against Staphylococcus epidermidis. Legend: A. Replication 1; B. Replication 2; C. Replication 3; F0. Negative control; F1. Test formulation ; K+. Positive control.

Table 8.
Results of Inhibitory Zone Diameter Measurements (mm) in the Antibacterial Activity Test of Purple Sweet Potato Leaf Extract Gel (Ipomoea batatas L.) against Staphylococcus epidermidis.

Code	Sample	Resistive diameter (mm) (mean ± SD, n=3)	Interpretation
F0	Negative control (No active ingredient)	0.0 ± 0.0	None
F1	Formula 1 (7% ethyl acetate fraction)	23.0 ± 1.6	Very strong
K+	Positive control (Gentamicin)	22.0 ± 0.5	Very strong

DISCUSSION

Extraction and Fractionation

Purple sweet potato leaves were extracted using the maceration method, a cold extraction technique involving the soaking of the material in a suitable solvent to extract active compounds without the use of high heat, thereby minimising the risk of degradation of bioactive compounds (Hayati et al.,

2019). In this study, the solvent used was ethanol. Ethanol was selected due to its relatively safe nature, low toxicity, and polar properties, making it effective in extracting various active compounds, particularly polar compounds such as flavonoids, phenolics, and glycosides, which are believed to be present in purple sweet potato leaves (Sernita et al., 2024).

The fractionation process was carried out using a liquid-liquid partition method employing ethyl acetate as the solvent, with the aim of increasing the content of semi-polar compounds in the extract. The choice of ethyl acetate as a solvent is based on its ability to selectively extract semi-polar compounds, such as flavonoids and certain phenolic compounds, so that the resulting fractions are expected to have more specific and higher biological activity compared to the crude extract. Furthermore, this fractionation process also serves to reduce the content of impurities or compounds that do not contribute to the activity, thereby improving the effectiveness and consistency of the test results (Miranti et al., 2025). Next, ethyl acetate solvent is added and the mixture is shaken gently, occasionally opening the tap to release the pressure. The mixture is then left to stand until two distinct phases form: the aqueous phase at the bottom and the ethyl acetate phase at the top. The ethyl acetate fraction is separated and the partitioning process is repeated several times with the addition of fresh ethyl acetate solvent to ensure that the semi-polar compounds are extracted to the maximum extent. This is repeated until the ethyl acetate phase appears clear, indicating that the compounds soluble in this solvent have been optimally extracted. All the ethyl acetate fractions obtained are then combined. The combined ethyl acetate fraction is then evaporated using a rotary vacuum evaporator at a temperature of approximately 50°C to remove the solvent, yielding a concentrated ethyl acetate fraction. This concentrated fraction is then further dried in an oven at the same temperature to ensure the absence of any residual solvent.

Optimization Using the Design Expert Software with the I-Optimal Mixture Method

According in the result, the independent variables used in this study included HPMC (2–5%) and propylene glycol (10–15%), each of which was entered into the software along with their upper and lower limits. Test results showed that the pH of the preparations ranged from 4.4 to 5.82. Viscosity values ranged from 2310.36 to 3950.1 cPs, indicating variations in viscosity due to differences in ingredient composition. The spreadability was within the range of 4.3 cm to 6.6 cm, whilst the adhesion time ranged from 2.01 seconds to 4.96 seconds, as presented in Table 2. In general, variations in the concentrations of HPMC and propylene glycol affect all the observed responses. An increase in HPMC concentration tends to increase viscosity and adhesion, but reduces spreadability. On the other hand, propylene glycol serves to improve spreadability and influences other physical characteristics of the formulation. The data from these formulation runs were then used as the basis for an analysis using the Design of Experiment method to determine a mathematical model, the influence of each component, and the optimisation of the formulation to produce the desired formulation characteristics.

Evaluation of pH response

The results of the analysis of variance (ANOVA) indicate that the quartic model for the pH response is significant, with an F-value of 3749.34 and a p-value < 0.0001, meaning that there is a highly significant effect of the combination of HPMC and propylene glycol on the pH of the gel formulation. All model terms, including the linear component (Linear Mixture), the AB interaction, the quadratic interaction AB(A-B), and the quartic interaction AB(A-B)², all made a significant contribution ($p < 0.0001$) to the pH response. The Adequate Precision value of 146.846 far exceeds the minimum required value of 4, indicating that the model has an excellent signal-to-noise ratio and can therefore be used for design space exploration. The coefficient of variation (CV) value of 0.2875%, which is very small, indicates that the data has low variability and the experimental results are highly reproducible (Beg, 2021).

As shown in Figure 1, it can be seen that the pH of the gel formulation undergoes significant changes in line with variations in the proportions of HPMC and propylene glycol. At a low HPMC concentration (2%) with a high propylene glycol concentration (13%), the pH value was recorded in

the range of 5.8–5.9. As the HPMC concentration increased and the propylene glycol concentration decreased, the pH value tended to stabilise within the range of 5.4–5.7; however, a drastic drop occurred when the HPMC concentration reached 5% with 10% propylene glycol, at which point the pH fell to 4.4. The decrease in pH at high HPMC concentrations is thought to be related to the weak acidic nature of the HPMC polymer in aqueous solution. All design points fall within the 95% confidence interval, confirming the model's reliability in predicting pH responses across the entire design space. The pH values obtained from all formulations ranged from 4.4 to 5.82, the majority of which remained within the physiological pH range of normal skin, i.e. 4.5–6.5 (Yusuf et al., 2022), meaning that the resulting gel preparations are safe and do not have the potential to irritate the skin.

Evaluation of viscosity response

The results of the analysis of variance (ANOVA) indicate that the linear model for viscosity response is significant, with a calculated F-value of 71.8 and a p-value of < 0.0001. The Adequate Precision value of 16.66 far exceeds the minimum required value of 4, indicating that the model has an adequate signal-to-noise ratio for use in design space navigation. The coefficient of variation (CV) value of 6.65% indicates that the data variability remains within acceptable limits. Based on the Component Effects (Cox) analysis, HPMC has a gradient in reals value of +6,544.30 with a component effect of +6,565.57 ($p < 0.0001$), whilst propylene glycol has a gradient in reals of −6.544,30 with a component effect of −6565,57 ($p < 0.0001$). This indicates that HPMC and propylene glycol exert opposite but equally significant effects on the viscosity of the gel formulation. As shown in Figure 2, there is a positive linear relationship between HPMC concentration and the viscosity of the gel formulation. At a low HPMC concentration (2%) and a high propylene glycol concentration (13%), the viscosity ranges from 2310.36 to 2315.57 Cp, whilst at high HPMC concentrations (5%) with low propylene glycol (10%), viscosity increased to reach 3,350–3,950 Cp. This linear pattern confirms the dominant influence of HPMC on gel structure formation. The viscosity of a good topical gel formulation is generally within the range of 2,000–4,000 Cp (Thomas et al., 2023), so all formulations in this study met the requirements for good gel viscosity and are suitable for application to the skin.

2.1 Evaluation of the spread response

The results of the analysis of variance (ANOVA) indicate that the quartic model for the spreadability response is significant, with a calculated F-value of 185.8 and a p-value < 0.0001, meaning that there is a highly significant effect of the combination of HPMC and propylene glycol on the spreadability of the gel formulation. All model terms, including the linear component (Linear Mixture), AB interaction, cubic AB(A-B) interaction, and quartic AB(A-B)² interaction, all made a significant contribution ($p < 0.05$) to the spreadability response. The Adequate Precision value of 31.58 far exceeds the minimum required value of 4, indicating that the model has an excellent signal-to-noise ratio. The very low coefficient of variation (CV) value of 1.87% indicates that the data has low variability and the experimental results are highly reproducible. As shown in Figure 3, it can be seen that the spreading ability of the gel formulation undergoes significant changes in line with variations in the proportions of HPMC and propylene glycol, exhibiting a pattern opposite to that of the viscosity response. At a low HPMC concentration (2%) with a high propylene glycol content (13%), the spreading ability reaches its highest value of approximately 6.4–6.6 cm. As the HPMC concentration increased and the propylene glycol concentration decreased, the spreadability decreased quite sharply, reaching a range of 4.4–4.5 cm at an HPMC concentration of 5% with 10% propylene glycol. This decrease in spreadability aligns with the increase in viscosity observed in formulations with high HPMC concentrations; as the viscosity of the formulation increases, resistance to flow becomes greater, thereby reducing the formulation's ability to spread across the skin surface. All design points fall within the 95% confidence interval, confirming the model's reliability. Good spreadability for topical gels is generally within the range of 5–7 cm (Thomas et al., 2023); thus, formulations with low to moderate HPMC concentrations meet these requirements, whilst those with high HPMC concentrations require optimisation to achieve an optimal balance between viscosity and spreadability.

Evaluation of Adhesion Response

The results of the analysis of variance (ANOVA) indicate that the linear model for the adhesive strength response is significant, with a calculated F-value of 46.33 and a p-value < 0.0001, meaning that there is a highly significant effect of the combination of HPMC and propylene glycol on the adhesive strength of the gel formulation. The Adequate Precision value of 13.39 exceeds the minimum required value of 4, indicating that the model has an adequate signal-to-noise ratio for use in design space navigation. The coefficient of variation (CV) value of 12.84% indicates an acceptable level of data variability, given that the measurement of adhesive strength is relatively more variable than other physical parameters. Based on the Component Effects (Cox) analysis, HPMC has a gradient in reals of +10.94 with a component effect of +2.19 ($p < 0.0001$), whilst propylene glycol has a gradient in reals of −10.94 with a component effect of −2.19 ($p < 0.0001$). This indicates that HPMC and propylene glycol exert opposite but equally significant effects on the adhesion of the gel formulation, with HPMC increasing adhesion whilst propylene glycol reduces it.

As shown in Figure 4, there is a positive linear relationship between HPMC concentration and the adhesion time of the gel formulation. At a low HPMC concentration (2%) and a high propylene glycol concentration (13%), the adhesion time was recorded at its lowest value, namely approximately 2.01–2.37 seconds. Conversely, at a high HPMC concentration (5%) with low propylene glycol (10%), the adhesion time increased to 3.21–4.96 seconds. This linear pattern aligns with the viscosity pattern, where formulations with high viscosity also exhibit greater adhesion. Good adhesion of a topical gel formulation should not be less than 1 second (Thomas et al., 2023); therefore, all formulations in this study met this criterion and were deemed to possess good adhesion for topical use on the skin.

Determination of the Optimal Formula Based on Desirability

The optimisation results show that the most optimal formulation was obtained with a composition of 2% HPMC and 13% propylene glycol, with a desirability value of 0.964. A desirability value close to 1 indicates that the formulation can simultaneously meet all the established response criteria, including pH, viscosity, spreadability and adhesion. Figure 5 shows that the highest desirability value (0.964) was achieved at the lowest HPMC concentration (2%) and the highest Propylene Glycol concentration (13%). The desirability value shows a significant decrease as the proportion of HPMC in the formulation increases, reaching a lowest value approaching 0 at an HPMC concentration of 5% with 10% Propylene Glycol. This indicates that an excessive increase in HPMC concentration has a negative impact on the overall fulfilment of response targets, particularly regarding the viscosity and spreadability parameters. Confirmatory test results at a 95% confidence level (two-sided, confidence = 95%) show that all observed response values fall within the model's 95% Prediction Interval (PI), as shown in Table 5. This proves that the I-Optimal Mixture Design model constructed is valid and capable of accurately predicting the formula's response. Therefore, the formula with a composition of 2% HPMC and 13% propylene glycol is established as the optimal gel formula.

Formulation of an Antibacterial Gel from Purple Sweet Potato Leaves (*I. batatas* L.)

Table 6 presents the formulation composition of the gel preparation obtained based on the optimisation results using Design-Expert software. The selected formulation contains a 7% ethyl acetate fraction of Ipomoea batatas L. as the active ingredient, formulated in a gel base with a combination of excipients that has been adjusted to produce optimal physical characteristics. The gel-forming components consist of 2% HPMC as a gelling agent and 13% propylene glycol as both a humectant and a cosolvent. In addition, 1% phenoxyethanol and 0.2% DMDM hydantoin were used as preservatives to maintain the microbiological stability of the formulation, whilst distilled water was added to make up 100% as the main solvent. The primary objective of formulating this gel preparation is to produce a topical delivery system capable of ensuring optimal contact between the active ingredient and the skin surface, thereby enhancing the antibacterial efficacy of the ethyl acetate fraction of Ipomoea batatas L.. HPMC is used as a gelling agent due to its ability to produce stable viscosity, its non-irritating properties, and its good compatibility with various active

ingredients (Vlad et al., 2025). Propylene glycol acts as a humectant capable of maintaining the formulation's moisture content whilst enhancing the penetration of the active ingredient into the skin through its permeability-enhancing effect (Carrer et al., 2019). The combination of phenoxyethanol and DMDM hydantoin was selected as the preservative system due to its broad spectrum of antimicrobial activity, thereby preventing contamination during storage and use. Distilled water acts as a solvent medium that supports the homogeneity of the system and ensures the even distribution of components.

Analysis Characteristics and Stability of an Antibacterial Gel from Purple Sweet Potato Leaves (*Ipomoea batatas* L.)

Based on the data presented in Table 7, the results of the tests on the characteristics of the antibacterial gel derived from purple sweet potato leaves (Ipomoea batatas L.) before and after the cycle test indicate that, overall, the preparation exhibits good physical stability. This is evidenced by relatively minor changes in the parameters, which remain within acceptable limits. Organoleptically, there were no changes in the form, colour or aroma of the preparation. The gel retained its semi-solid form with a brownish-green colour and characteristic aroma, indicating that there was no significant degradation of the active ingredients or excipients due to exposure to extreme temperatures during the cyclic testing. Similarly, regarding the homogeneity parameter, the preparation continued to show an even distribution of components without any phase separation, indicating that the gel system formed was sufficiently stable against temperature fluctuations.

The pH value decreased from 5.82 to 5.72. This decrease in pH is thought to be caused by the degradation of active compounds, particularly anthocyanins and phenolic compounds in the ethyl acetate fraction of purple sweet potato leaves, which are sensitive to changes in temperature and pH. Previous research has shown that anthocyanins undergo significant degradation under high-temperature conditions and less acidic pH, which can produce more acidic derivative compounds, thereby lowering the pH of the formulation (Fendri et al., 2018). Nevertheless, this pH value remains within the physiological pH range of the skin (4.5–6.5) (Appendix 8), making it safe for topical use. Viscosity showed a slight decrease from 2316.52 to 2253.9 cP. An increase in temperature can disrupt the gel network and reduce interactions between HPMC polymer chains, leading to a decrease in viscosity. This is consistent with studies showing that increased temperature can damage the gel network and reduce viscosity due to decreased interchain polymer bonding. Furthermore, the thermorheological properties of HPMC indicate that temperature variations play a significant role in modifying the structure and strength of the gel (Ji et al., 2022). Nevertheless, the viscosity values following cyclic testing remained within the desired range, thus not compromising the formulation's application characteristics.

In line with the decrease in viscosity, the spreadability increased from 6.4 cm to 6.7 cm. This phenomenon is consistent, as lower viscosity enhances the gel's ability to spread across the skin's surface. This increase in spreadability remains within the specified range, thereby continuing to support the ease of application of the formulation. Conversely, the adhesion time showed a slight decrease from 2.18 seconds to 2.04 seconds. This decrease also correlates with the reduction in viscosity, as a thinner gel tends to have lower adhesion properties. Nevertheless, this adhesion time remains sufficient to maintain contact between the formulation and the skin surface for a duration long enough to allow absorption of the active ingredient. Overall, the optimised gel formulation demonstrated good physical stability against the effects of cyclic testing. The changes observed in each parameter were minimal and remained within acceptable limits; it can therefore be concluded that the formulation is capable of maintaining its characteristics during storage under varying temperature conditions.

Antibacterial Activity of the Ethyl Acetate Fraction of Purple Sweet Potato Leaves (I. batatas L.) Against Staphylococcus epidermidis

The negative control (F0), which is a gel base without any active substance, showed no inhibition zone (0.0 mm) in any of the replicates. This indicates that the gel base has no antibacterial activity

against Staphylococcus epidermidis; therefore, the inhibitory effect observed in the test formula can be directly attributed to the active compounds present in the ethyl acetate fraction of purple sweet potato leaves. Consequently, the gel base can be considered inert and does not affect the growth of the test bacteria. The positive control (K+), consisting of gentamicin, showed an average inhibition zone diameter of 22.0 mm, classified as very strong activity. The inhibition zones formed appeared clear and were relatively consistent in each replication, reflecting gentamicin's high efficacy in inhibiting the growth of Staphylococcus epidermidis. This activity is related to gentamicin's mechanism of action, which inhibits bacterial protein synthesis through interaction with the 30S ribosomal subunit.

Formula F1, containing a 7% ethyl acetate fraction of purple sweet potato leaves, exhibited an average zone of inhibition diameter of 23.0 mm, which falls into the 'very strong' category and is slightly larger than that of the positive control. The high antibacterial activity of F1 against Staphylococcus epidermidis is attributed to the presence of secondary metabolites in the ethyl acetate fraction, such as flavonoids and phenolic compounds. Overall, the 7% ethyl acetate fraction of purple sweet potato leaves exhibited very strong antibacterial activity against Staphylococcus epidermidis, comparable to—and even slightly higher than—that of the gentamicin positive control. This demonstrates the great potential of the ethyl acetate fraction of purple sweet potato leaves as a natural source of antibacterial agents that could be further developed for use in topical formulations.

CONCLUSION

Based on the research findings, it can be concluded that the optimal formulation for an antibacterial gel containing the ethyl acetate fraction of purple sweet potato leaves (Ipomoea batatas L.) was achieved using a 2% HPMC concentration and 13% propylene glycol, with a desirability value of 0.964. This formulation was found to meet all the established physical quality criteria—including organoleptic testing, homogeneity, pH, viscosity, spreadability, and adhesion—and demonstrated excellent physical stability with no significant changes following a cycling test. In addition to being physically stable, this gel formulation is also effective and falls into the category of being highly potent in inhibiting the growth of Staphylococcus epidermidis, as evidenced by the formation of an inhibition zone of 23 mm. It is recommended that further in vivo testing and irritation tests be carried out to ensure the safety of the formulation. In addition, long-term stability testing and testing against various types of bacteria should be conducted to determine the spectrum of antibacterial activity.

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