



Optimization and evaluation of skin cream from *Perilla frutescens* (L.) Britton and *Aloe vera* (L.) Burm.f. extracts with antioxidant activity

[Optimización y evaluación de cremas para la piel a base de extractos de *Perilla frutescens* (L.) Britton y *Aloe vera* (L.) Burm.f. con actividad antioxidante]

Nguyen Thi Linh Tuyen^{1*}, Lam Ngoc Yen¹, Huynh Kim Ngoc¹, Doan Khanh Linh¹, Huynh Boi Ngoc¹,
Do Chau Minh Vinh Tho¹, Do Quang Duong²

¹Department of Pharmacognosy, Faculty of Pharmacy, Can Tho University of Medicine and Pharmacy, 179 Nguyen Van Cu Street, Can Tho City, Vietnam.

²Department of Pharmaceutical Information Technology, Faculty of Pharmacy, University of Medicine and Pharmacy at Ho Chi Minh City, 41 Dinh Tien Hoang Street, District 1, Ho Chi Minh City, Vietnam.

*E-mail: ntlhtuyen@ctump.edu.vn

Abstract

Context: Skin aging is driven by factors such as prolonged sun exposure, pollution, poor sleep, and unhealthy lifestyle, which motivate the demand for antioxidant-rich herbal creams.

Aims: To investigate the effects of various factors, optimize, and evaluate a skin cream formulated with *Perilla frutescens* and *Aloe vera* extracts for their antioxidant activity.

Methods: Nineteen cream formulations were prepared using a D-optimal experimental design to optimize the cream composition. Three independent variables were selected for evaluation: *Perilla frutescens* extract (X_1) at concentrations of 4%, 6%, and 8%; cetyl alcohol (X_2) at 1.5%, 2%, and 2.5%; and lanolin (X_3) at 1%, 1.5%, and 2%. These variables were chosen to maximize spreadability and antioxidant activity.

Results: The optimized formulation (7.5% *P. frutescens* extract, 1.5% cetyl alcohol, and 1% lanolin) met the quality criteria. The observed spreadability ($54.84 \pm 0.91 \text{ cm}^2$) and antioxidant activity ($43.16 \pm 1.13\%$) showed no significant difference from the predicted values ($p > 0.05$), as confirmed by a one-sample t-test. The cream demonstrated strong antioxidant activity in the ABTS and FRAP assays, showing $85.70 \pm 0.45\%$ radical inhibition ($IC_{50} = 23.64 \pm 0.78 \text{ mg/mL}$) and a Trolox equivalent antioxidant capacity of $19.62 \pm 0.35 \text{ } \mu\text{mol Trolox/g}$, respectively.

Conclusions: A natural skincare cream containing *P. frutescens* and *A. vera* extracts, with good spreadability and antioxidant activity, was successfully developed.

Keywords: *Aloe vera*; antioxidant activity; *Perilla frutescens*; skin cream; spreadability.

Resumen

Contexto: El envejecimiento de la piel está impulsado por factores como la exposición prolongada al sol, la contaminación, la falta de sueño y un estilo de vida poco saludable, que motivan la demanda de cremas herbales ricas en antioxidantes.

Objetivos: Investigar los efectos de varios factores, optimizar y evaluar una crema para la piel formulada con extractos de *Perilla frutescens* y *Aloe vera* por su actividad antioxidante.

Métodos: Se prepararon diecinueve formulaciones de crema mediante un diseño experimental D-óptimo para optimizar su composición. Se seleccionaron tres variables independientes para la evaluación: extracto de *Perilla frutescens* (X_1) en concentraciones del 4%, 6% y 8%; alcohol cetílico (X_2) al 1,5%, 2% y 2,5%; y lanolina (X_3) al 1%, 1,5% y 2%. Estas variables se seleccionaron para maximizar la untabilidad y la actividad antioxidante.

Resultados: La formulación optimizada (7,5% de extracto de perilla, 1,5% de alcohol cetílico y 1% de lanolina) cumplió con los criterios de calidad. La untabilidad ($54,84 \pm 0,91 \text{ cm}^2$) y la actividad antioxidante ($43,16 \pm 1,13\%$) observadas no mostraron diferencias significativas con respecto a los valores previstos ($p > 0,05$), como lo confirmó una prueba t de una muestra. La crema demostró una fuerte actividad antioxidante en los ensayos ABTS y FRAP, con una inhibición de radicales del $85,70 \pm 0,45\%$ ($CI_{50} = 23,64 \pm 0,78 \text{ mg/mL}$) y una capacidad antioxidante equivalente a Trolox de $19,62 \pm 0,35 \text{ } \mu\text{mol Trolox/g}$, respectivamente.

Conclusiones: Se desarrolló con éxito una crema natural para el cuidado de la piel que contiene extractos de *Perilla frutescens* y *Aloe vera*, con buena capacidad de extensión y actividad antioxidante.

Palabras Clave: actividad antioxidante; *Aloe vera*; crema para la piel; *Perilla frutescens*; untabilidad.

ARTICLE INFO

Received: November 2, 2024.

Accepted: July 10, 2025.

Available Online: August 10, 2025.

AUTHOR INFO

ORCID:

[0000-0003-0120-6206](https://orcid.org/0000-0003-0120-6206) (NTLT)

[0009-0007-9081-1075](https://orcid.org/0009-0007-9081-1075) (LNY)

[0009-0002-4880-123X](https://orcid.org/0009-0002-4880-123X) (HKN)

[0009-0008-1644-9984](https://orcid.org/0009-0008-1644-9984) (DKL)

[0009-0008-1688-5831](https://orcid.org/0009-0008-1688-5831) (HBN)

INTRODUCTION

Skin aging is one of the most visible and widespread manifestations of the aging process, drawing increasing attention due to its impact on appearance and quality of life. It is primarily driven by prolonged exposure to ultraviolet radiation and pollutants. Additionally, internal and lifestyle-related factors, including poor sleep, unhealthy habits, and inadequate skincare routines, also contribute significantly to the aging process (Mungmai et al., 2020). These extrinsic and intrinsic factors accelerate skin deterioration, leading to visible signs such as wrinkles, hyperpigmentation, and loss of elasticity (Lee and Cho, 2021). As a result, many individuals seek effective skincare solutions to mitigate these effects.

Among the various approaches, antioxidant-based skincare products have gained popularity for their ability to combat oxidative stress and improve skin health (Mohiuddin, 2019). Herbal skincare products with antioxidant properties have gained popularity due to consumer preference for natural ingredients over synthetic chemicals. Common botanical extracts such as *Perilla frutescens*, *Aloe vera*, and *Curcuma longa* offer antioxidant protection while nourishing the skin (Amer et al., 2022; Baik et al., 2021). These ingredients provide dual benefits by shielding the skin from free radical damage and promoting overall skin health (Dunaway et al., 2018).

Perilla frutescens (L.) Britton (family *Lamiaceae*) contains several bioactive compounds, including rosmarinic acid, flavonoids, omega-3 fatty acids, and vitamin E, all of which are known to support skin health. These constituents protect against free radical damage, brighten the skin, and reduce inflammation (Anh et al., 2024; Jiao et al., 2023; Meng et al., 2009). Similarly, *Aloe vera* (L.) Burm.f. (family *Asphodelaceae*) contains aloin, emodin, and vitamins A, C, and E, which have potent antioxidant properties. These compounds protect the skin from aging, improve elasticity, and promote skin cell regeneration (Heś et al., 2019; Kaporakou et al., 2021).

This study aims to investigate the effects of various factors, optimize the formulation, and assess the quality of a skin cream formulated with *P. frutescens* and *A. vera* for their antioxidant activity. We hypothesize that the optimized formulation of these extracts maximize spreadability and antioxidant activity. To our knowledge, there are currently no published studies reporting the development of a cream that integrates both of these botanicals, indicating a significant opportunity for further research and product innovation.

MATERIAL AND METHODS

Materials

P. frutescens leaves (moisture content of 12%) were acquired from Le Hoang Medicinal (Ho Chi Minh City, Vietnam), and *A. vera* leaves were purchased at Coop Mart supermarket (Can Tho City, Vietnam). The *P. frutescens* material was submitted to the Department of Pharmacognosy for authentication and quality evaluation in accordance with the Vietnamese Pharmacopoeia V (Ministry of Health, 2017). Specifically, macroscopic and microscopic identification, powder microscopy, moisture content determination, and qualitative chemical analysis were conducted to verify the identity and quality of the plant material. Following this, the dried *P. frutescens* leaves were ground through a 1.0mm sieve, then stored in sealed nylon bags at 24-26°C at the Department of Pharmacognosy, Faculty of Pharmacy, Can Tho University of Medicine and Pharmacy (code H102023).

Chemicals and solvents: 1,1-diphenyl-2-picrylhydrazyl (DPPH, 97% purity, batch number E240965), 2,2'-azino bis (3-ethylbenzothiazoline-6-sulfonic acid) (ABTS, 98% purity, batch number M20L005), 2,4,6-tris(2-pyridyl)-s-triazine (TPTZ, 99% purity, batch number BCCM4034), Trolox (98.6% purity, batch number 648471), and ferric chloride hexahydrate ($\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$, 97% purity, batch number MKCW1451). Olive oil, cetyl alcohol, stearic acid, lanolin, polyethylene glycol-40 (PEG-40), glycerin, and niacinamide were obtained from Thanh Dat Company (Vietnam).

Equipment: Kern electronic balance (Germany); Memmert water bath (Germany); IKA magnetic stirrer (Germany); Consort pH meter (Belgium); Centrifio centrifuge (China); Jasco UV-Vis spectrophotometer (Japan).

Process of extraction

P. frutescens extract was done by the heat-reflux method. 100 g of *P. frutescens* leaves were refluxed twice for 60 minutes each in 20% ethanol at $60 \pm 2^\circ\text{C}$, with a plant-to-solvent ratio of 1:14. The combined extracts were concentrated to a soft extract (Chemat et al., 2020; Tuyen et al., 2024; Zhang et al., 2022).

Aloe vera extract: 100 g of *A. vera* was separated from the leaf rind, diced, and soaked in a 1% saline solution to remove residual yellow latex. It was then blended with 500 mL of distilled water and filtered to obtain the *A. vera* extract (Wu et al., 2022).

Formulation of skin cream

Table 1 lists the ingredients for the emulsified skin cream formulation, where X_1 , X_2 , and X_3 represent *P. frutescens* extract, cetyl alcohol, and lanolin, respectively, as the independent variables in the formulation.

Table 1. Formula for skin cream.

No.	Ingredients	Rate (% w/w)
1	<i>Perilla frutescens</i> extract	Variable (X_1)
2	<i>Aloe vera</i> extract	5
3	Olive oil	4
4	Cetyl alcohol	Variable (X_2)
5	Acid stearic	3
6	Lanolin	Variable (X_3)
7	PEG 40	1
8	Triethanolamine	0.5
9	Glycerin	3
10	Phenoxyethanol	0.2
11	Niacinamide	2
12	Sodium benzoate	0.2
13	Distilled water quantity sufficient	100

The water phase (solution 1) was prepared by heating *P. frutescens* extract, *A. vera* extract, glycerin, triethanolamine, PEG-40, niacinamide, phenoxyethanol, sodium benzoate, and distilled water to 70°C. The oil phase (solution 2) consisted of stearic acid, lanolin, and cetyl alcohol, which were heated to melt, then olive oil was added at 65°C. Solution 2 was then slowly added to solution 1 while homogenizing at 950rpm for 5 min to form the final cream (Modi et al., 2024; Tadić et al., 2021).

The parameters for the independent and dependent variables were outlined in Table 2.

Effects of variables on spreadability (Y_1): 0.5 g of cream was placed at the center of a glass plate, and another glass plate was placed on top. A weight of 250 g was applied to the upper plate for 1 minute. The resulting spread diameter of the cream was recorded. Spreadability was calculated as $S = \pi d^2/4$, where d is the spread diameter (cm), and S is expressed in cm^2 .

Effects of variables on antioxidant activity (Y_2): The antioxidant activity of the skin cream was assessed using a modified method based on Brand-Williams et al. (1995) and da Silva Borges et al. (2019). A DPPH stock solution was prepared by dissolving 24 mg of DPPH in methanol in a 100 mL volumetric flask. Then, 10 mL of this solution was transferred to a 50

mL volumetric flask and diluted with methanol to obtain the working DPPH solution. The test sample was prepared by dissolving 1 g of the cream in 10 mL of methanol. Subsequently, 1 mL of the test solution was mixed with 3 mL of the DPPH working solution and incubated in the dark for 30 minutes. The absorbance was measured at 515 nm using a UV-Vis spectrophotometer. Antioxidant activity was expressed as the percentage of DPPH radical inhibition (Brand-Williams et al., 1995; da Silva Borges et al., 2019).

Optimizing the cream formulation

Nineteen experiments (F1–F19) were designed according to the D-optimal model utilizing Design Expert software (version 6.0.6, Stat-Ease Inc.). Data analysis and formulation optimization were performed using BCPharSoft, a software tool for optimization.

Determination of the antioxidant activity of cream

ABTS radical scavenging activity: The antioxidant activity of the samples was determined using the ABTS radical cation decolorization assay, as described by Nenadis et al. (2004), with slight modifications. ABTS⁺ radical cation was prepared by mixing 7 mM ABTS stock solution with 2.45 mM potassium persulfate in distilled water. The mixture was incubated in the dark at room temperature for 12-16 hours before use. For the assay, 50 μL of the sample was mixed with 950 μL of the ABTS solution and incubated at room temperature for 5 minutes. The absorbance was subsequently measured at 734 nm using a UV-Vis spectrophotometer. A blank was prepared using 950 μL of distilled water instead of the sample. Trolox (3.1–400 μM) was used as the standard antioxidant.

Ferric reducing antioxidant power (FRAP): The antioxidant activity of the samples was assessed using the FRAP assay, following the method described by Benzie and Strain with slight modifications. This assay determines the ability of antioxidants in the sample to reduce ferric ions (Fe^{3+}) to ferrous ions (Fe^{2+}) at pH 3.6. The FRAP reagent was prepared by mixing 300 mM acetate buffer (pH 3.6), 10 mM TPTZ in 40 mM HCl, and 20 mM $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ in a volume ratio of 10:1:1 (v/v/v). For the assay, 150 μL of each sample solution was mixed with 850 μL of the FRAP reagent in a test tube. A blank solution was prepared by replacing the sample with an equal volume of acetate buffer. The mixtures were incubated at room temperature for 10 minutes, and the absorbance was then measured at 593 nm using a UV-Vis spectrophotometer. Trolox (3.1–400 μM) was used as the standard antioxidant (Benzie and Strain, 1996).

Table 2. Variables in experimental design.

Independent variables	Level 1	Level 2	Level 3
X ₁ : <i>Perilla frutescens</i> extract (%)	4	6	8
X ₂ : Cetyl alcohol (%)	1.5	2	2.5
X ₃ : Lanolin (%)	1	1.5	2
Dependent variables	Constraints		
Y ₁ : spreadability (cm ²)	Maximum		
Y ₂ : antioxidant activity (%)	Maximum		

Evaluation of quality standards for skin cream

Standards for the quality of the cream derived from *P. frutescens* and *A. vera* were established following the technical criteria from the Vietnamese Pharmacopoeia V. These include parameters such as physical appearance, pH, homogeneity, spreadability, and antioxidant activity (Ministry of Health, 2017).

Physical appearance: the cream had a uniform, off-white color, smooth texture, and a notable herbal scent of *P. frutescens*.

pH: The pH was measured using a calibrated pH meter at 25°C after diluting 1 g of cream to a 10% (w/v) concentration with distilled water. Electrical conductivity was determined under the same conditions. Each formulation was analyzed in triplicate, and the average values were determined.

Homogeneity: four packaging units (each weighing 0.02-0.03 g) were spread on 4 glass slides. Each slide was covered with a second glass slide and pressed to form a spot approximately 2 cm in diameter. The resulting spots were observed with the naked eye (from a distance of 30 cm). In 3 out of 4 samples, no visible particles were detected. If particles were visible in the majority of samples, the test was repeated using eight units, allowing no more than two visible particles.

Spreadability and antioxidant activity, as described in the previous section.

Statistical analysis

All analyses were done in triplicate, and results were expressed as mean $\pm$ standard deviation. The statistical software SPSS 26 (SPSS, Inc., Chicago, IL, USA) was employed to compare observed and predicted data. One-sample t-test analysis indicated no significant difference between the expected and observed data ($p > 0.05$), confirming the consistency of the ideal outcomes with the results predicted by the BCPharSoft program.

RESULTS

Formulation of skin cream

The skin cream formulations were developed using Design Expert software, comprising 19 experiments. Table 3 presents the independent variable levels for each run (F1–F19) and the resulting spreadability (Y₁) and antioxidant activity (Y₂).

The data in Table 3 served as inputs for BCPharSoft to examine cause-and-effect relationships and optimize the formulation. The accuracy of the model statistics obtained from the outputs of BCPharSoft was presented in Table 4.

Table 4 demonstrated that both the R² training and R² test values exceeded 0.9, indicating a high reliability of the models. These models were suitable for multivariate optimization.

To enhance understanding of the cause-and-effect relationships between the independent and dependent variables, the three-dimensional (3D) response surface plots of the fitted models were presented. Each 3D diagram illustrated the influence of two independent variables on the dependent variable at a time while the third variable was kept constant.

Effects of variables on spreadability (Y₁) and antioxidant activity (Y₂)

Based on the optimization criteria presented in Table 2, both spreadability (Y₁) and antioxidant activity (Y₂) were set as targets for maximization. The trends observed in the response surface plots (Figs. 1 and 2) guided the selection of the optimal formulation variables: X₁ = 7.5% (*P. frutescens* extract), X₂ = 1.5% (cetyl alcohol), and X₃ = 1% (lanolin).

Optimizing the skin cream

The skin cream formula of *P. frutescens* and *A. vera* was optimized using BCPharSoft software, with variables X₁, X₂, and X₃ set at 7.50%, 1.50%, and 1.00%, respectively. To validate the results, three replicated

batches of the optimized formula were produced, as shown in the experimental results presented in Table 5.

The statistical software SPSS 26.0 (SPSS, Inc.) was utilized to compare the experimental and predicted results. As shown in Table 5, the observed values for spreadability ($54.84 \pm 0.91 \text{ cm}^2$) and antioxidant activity ($43.16 \pm 1.13\%$) closely matched the predicted values (54.73 cm^2 and 43.14% , respectively), with p-values of 0.89 and 0.95, respectively. The one-sample t-test indicated that the predicted results and the validated results were not significantly different ($p > 0.05$), confirming that the optimal formulation matched the predictions made by the BCPharSoft OPT software. Therefore, the optimized formulation

of the cream included 7.5% *P. frutescens* extract, 1.5% cetyl alcohol, and 1% lanolin.

Determination of the antioxidant activity of *P. frutescens* and *A. vera* cream

The antioxidant activity of the cream was assessed using DPPH, ABTS, and FRAP assays, and the results are summarized in Table 6.

Evaluation of quality standards for skin *P. frutescens* and *A. vera* cream

The results of the *P. frutescens* skin cream evaluation are presented in Table 7.

Table 3. The independent variables of 19 experiments (F1-F19) and their responses.

Run	X ₁ (%) <i>P. frutescens</i> extract	X ₂ (%) cetyl alcohol	X ₃ (%) lanolin	Y ₁ (cm ²) spreadability	Y ₂ (%) antioxidant activity
F1	4.00	2.00	2.00	40.70	21.61
F2	4.00	1.50	2.00	48.40	23.75
F3	6.00	2.00	1.00	53.40	25.26
F4	8.00	2.50	2.00	39.60	43.26
F5	6.00	2.00	1.50	41.80	35.52
F6	8.00	1.50	1.00	54.10	39.16
F7	6.00	1.50	1.50	50.70	36.16
F8	6.00	2.50	2.00	42.70	36.92
F9	6.00	2.50	1.00	50.20	40.78
F10	6.00	1.50	2.00	43.00	29.84
F11	8.00	2.00	1.50	51.50	38.62
F12	4.00	1.50	1.00	56.72	23.06
F13	4.00	2.50	1.50	49.00	24.12
F14	4.00	2.50	1.00	55.40	24.41
F15	4.00	2.00	1.00	47.80	21.17
F16	4.00	1.50	1.50	49.80	25.17
F17	8.00	2.00	2.00	51.50	37.83
F18	8.00	1.50	2.00	50.24	44.25
F19	8.00	2.50	1.50	50.24	44.66

Table 4. Model statistics from BCPharSoft outputs, including training and test coefficients of determination (R²).

Dependent variables	R ² test	R ² training
Y ₁ (Spreadability)	0.97	0.97
Y ₂ (Antioxidant activity)	0.97	0.99

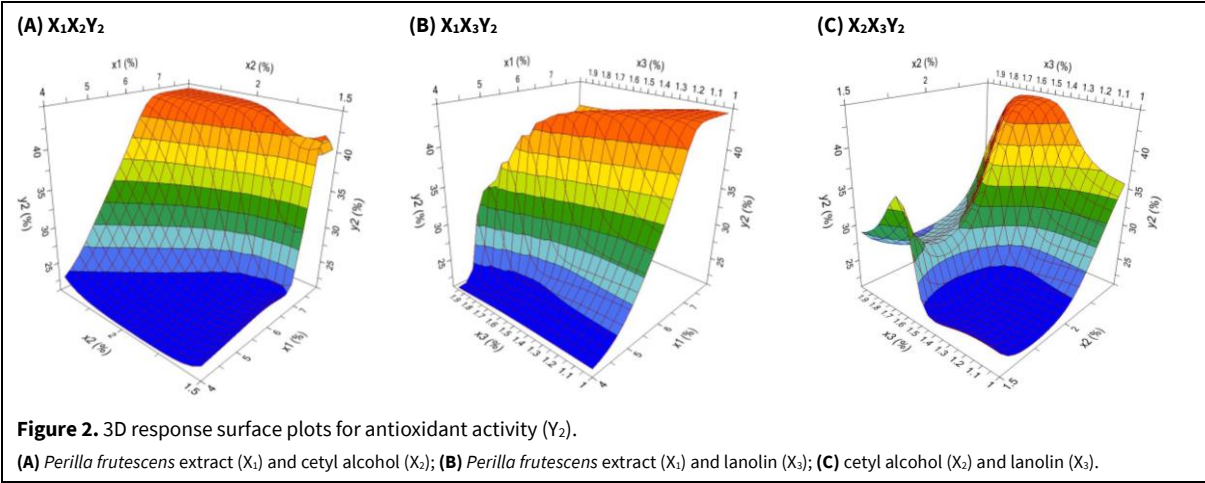
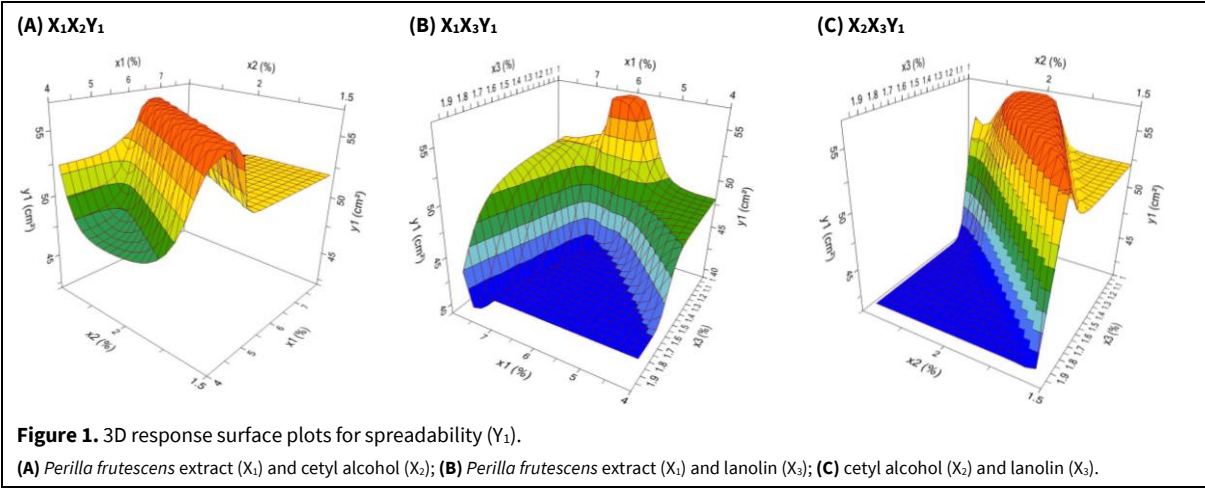


Table 5. Comparison of the predicted and observed responses for *P. frutescens* and *A. vera* cream.

Responses	Y_1 (cm ²) spreadability	Y_2 (%) antioxidant activity
Predicted	54.73	43.14
Observed	54.84 ± 0.91	43.16 ± 1.13
P-values*	0.89	0.95

*One Sample t-test. Data are expressed as mean ± SD (n = 3).

Table 6. Antioxidant activity of the *P. frutescens* and *A. vera* cream was evaluated by DPPH, ABTS, and FRAP assays.

Assay	% inhibition	IC ₅₀	Trolox equivalent antioxidant capacity
DPPH	43.16 ± 1.13%	39.29 ± 1.05 µg/mL	-
ABTS	85.70 ± 0.45%	23.64 ± 0.78 mg/mL	-
FRAP	-	-	19.62 ± 0.35 µmol Trolox/g

Table 7. Final product specifications of the *P. frutescens* and *A. vera*.

Parameter	Result
Physical appearance	Uniform, off-white, smooth texture, and herbal scent of <i>P. frutescens</i>
pH	6.01 ± 0.08
Homogeneity	Complies
Spreadability	54.84 ± 0.91 cm ²
Antioxidant activity	43.16 ± 1.13% (DPPH)
	85.70 ± 0.45% (ABTS)
	19.62 ± 0.35 µmol Trolox/g (FRAP)

Data are expressed as mean ± SD (n = 3).

DISCUSSION

The optimized *P. frutescens* and *A. vera* cream demonstrated antioxidant activity while meeting essential quality specifications. These findings are consistent with previous studies reporting the antioxidant and antimicrobial properties of Perilla and Aloe extracts (Heř et al., 2019; Meng et al., 2009). This supports the growing interest in natural cosmetics. By utilizing natural antioxidants, the formulation potentially reduces dependence on synthetic compounds and their associated side effects (Gulcin, 2020), aligning with the current shift toward natural cosmeceutical products.

The combination of *P. frutescens* and *A. vera* extracts in the cream aimed to harness the antioxidant benefits of both ingredients, helping protect and soothe the skin. As shown in Fig. 2A-B, higher concentrations of *P. frutescens* extract increased antioxidant activity. This enhanced activity may contribute to skin repair and regeneration, consistent with the known role of antioxidants in protecting against oxidative stress (Munteanu and Apetrei, 2021).

Emulsifiers played a crucial role in the cream formulation by combining the oil and water phases into a homogeneous and stable mixture. Additionally, emulsifiers influenced the texture of the cream, providing a smooth feel when applied to the skin, while also ensuring that active ingredients were evenly distributed, thereby enhancing the moisturizing effect. In this study, cetyl alcohol was used as both an emulsifier and an emollient. It helped improve the skin's feel by reducing greasiness and preventing dryness and cracking. Cetyl alcohol has been recognized as safe for use in food and cosmetics by regulatory authorities. Its concentration was found to affect product characteristics: as it increased, viscosity and stability improved, but excessive amounts could lead to instability and reduced product quality (Franco-Gil et al., 2024; Sepulveda et al., 2003). Furthermore, cetyl

alcohol increased viscosity while decreasing spreadability, making the cream harder to apply evenly (Ali et al., 2022; Sepulveda et al., 2003). Therefore, optimizing its concentration in the formulation was essential to ensure a balance between stability and ease of application. These findings were consistent with our experimental results (Fig. 1A and C).

Lanolin served as a key moisturizer and emollient in the cream formulation. Due to its structural similarity to skin lipids, it supported moisture retention and nutrient absorption. It also contributed to a smooth, protective skin feel, aligning with its sensory attributes reported in previous studies (Danielle et al., 2023). As shown in Fig. 1C, low lanolin concentration improved spreadability, and Fig. 2C confirmed minimal impact on antioxidant activity. Thus, incorporating lanolin at 1% was optimal for balancing cost and product performance.

Fig. 1A–C indicates that higher concentrations of *P. frutescens* extract combined with lower levels of cetyl alcohol and lanolin optimized spreadability, while Fig. 2A–C shows that antioxidant activity increased with *P. frutescens* concentration, consistent with the findings of Meng et al. (2009).

The use of software-assisted formulation design in this study helped shorten experimental time and reduce the number of required trials. It also enabled modeling of the effects of independent variables, thereby supporting the optimization of the cream formulation. Similar optimization approaches have been successfully applied in other pharmaceutical contexts, such as the spray-drying process of herbal extracts (Tuyen et al., 2024).

CONCLUSION

A natural skincare cream containing *Perilla frutescens* and *Aloe vera* extracts, with good spreadability and antioxidant activity, was successfully developed. Future studies should evaluate accelerated, long-term

stability and skin absorption to support wider application.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ACKNOWLEDGMENTS

The authors would like to express their gratitude to Assoc. Prof. Do Quang Duong from the University of Medicine and Pharmacy at Ho Chi Minh City, Vietnam, and colleagues from the Can Tho University of Medicine and Pharmacy, Vietnam, for their support in this research.

REFERENCES

- Ali A, Skedung L, Burleigh S, Lavant E, Ringstad L, Anderson C, Wahlgren M, Engblom J (2022) Relationship between sensorial and physical characteristics of topical creams: A comparative study on effects of excipients. *Int J Pharm* 613: 121370. <https://doi.org/10.1016/j.ijpharm.2021.121370>
- Amer SA, Abdel-Wareth AAA, Gouda A, Saleh GK, Nassar AH, Sherief WRIA, Albogami S, Shalaby SI, Abdelazim AM, Abomughaid MM (2022) Impact of dietary lavender essential oil on the growth and fatty acid profile of breast muscles, antioxidant activity, and inflammatory responses in broiler chickens. *Antioxidants* 11(9): 1798. <https://doi.org/10.3390/antiox11091798>
- Anh TTH, Sil NT, Tien LTD, Tram TB, Uy NHT, Tuyen DTK, Phuc LT, Tho DCMV (2024) Development and validation of an HPLC/PDA methodology for assessing the quality of folium *Perilla frutescens* under diverse soil conditions and growth stages based on the bioactive compound rosmarinic acid. *Trop J Nat Prod Res* 8(7): 7891–7897. <https://doi.org/10.26538/tjnpr/v8i7.36>
- Baik I-H, Kim K-H, Lee K-A (2021) Antioxidant, anti-inflammatory and antithrombotic effects of ginsenoside compound K enriched extract derived from ginseng sprouts. *Molecules* 26(13): 4102. <https://doi.org/10.3390/molecules26134102>
- Benzie IF, Strain JJ (1996) The ferric reducing ability of plasma (FRAP) as a measure of “antioxidant power”: The FRAP assay. *Anal Biochem* 239(1): 70–76. <https://doi.org/10.1006/abio.1996.0292>
- Brand-Williams W, Cuvelier ME, Berset C (1995) Use of a free radical method to evaluate antioxidant activity. *LWT - Food Sci Technol* 28(1): 25–30. [https://doi.org/10.1016/S0023-6438\(95\)80008-5](https://doi.org/10.1016/S0023-6438(95)80008-5)
- Chemat F, Vian MA, Fabiano-Tixier A-S, Nutrizio M, Jambak AR, Munekata, SPE, Lorenzo JM, Barba FJ, Binelloe A, Cravotto G (2020) A review of sustainable and intensified techniques for extraction of food and natural products. *Green Chem* 22(8): 2325–2353. <https://doi.org/10.1039/C9GC03878G>
- da Silva Borges L, Lima GPP, Artes F, de Souza ME, de Souza Freitas L, de Jesus HI, Santos NFA, Melo MRS (2019) Efficiency of DPPH and FRAP assays for estimating antioxidant activity and separation of organic acids and phenolic compounds by liquid chromatography in fresh-cut nectarine. *Aust J Crop Sci* 13(7): 1053–1060. <https://doi.org/10.21475/ajcs.19.13.07.p1368>
- Danielle D, McCabe M, Bourdillon K (2023) The impact of refinement on the sensory properties of lanolin. *J Sens Stud* 38(3): e12822. <https://doi.org/10.1111/joss.12822>
- Dunaway S, Odin R, Zhou L, Ji L, Zhang Y, Kadekaro AL (2018) Natural antioxidants: multiple mechanisms to protect skin from solar radiation. *Front Pharmacol* 9: 392. <https://doi.org/10.3389/fphar.2018.00392>
- Franco-Gil ME, Graça A, Martins A, Marto J, Ribeiro HM (2024) Emollients in dermatological creams: Early evaluation for tailoring formulation and therapeutic performance. *Int J Pharm* 653: 123825. <https://doi.org/10.1016/j.ijpharm.2024.123825>
- Gulcin İ (2020) Antioxidants and antioxidant methods: An updated overview. *Arch Toxicol* 94(3): 651–715. <https://doi.org/10.1007/s00204-020-02689-3>
- Heř M, Dziedzic K, Górecka D, Jędrusek-Golińska A, Gujska E (2019) *Aloe vera* (L.) Webb.: Natural sources of antioxidants – A review. *Plant Foods Hum Nutr* 74(3): 255–265. <https://doi.org/10.1007/s11130-019-00747-5>
- Jiao P, He X, Ma S, Wang S, Niu Q (2023) Ultrasonic-assisted extraction of antioxidants from *Perilla frutescens* leaves based on tailor-made deep eutectic solvents: Optimization and antioxidant activity. *Molecules* 28(22): 7554. <https://doi.org/10.3390/molecules28227554>
- Kaparakou EH, Kanakis CD, Gerogianni M, Maniati M, Vekrellis K, Skotti E, Tarantilis PA (2021) Quantitative determination of aloein, antioxidant activity, and toxicity of leaf gel products from Greece. *J Sci Food Agric* 101(2): 414–423. <https://doi.org/10.1002/jsfa.10650>
- Lee JH, Cho Y-S (2021) Assessment of phenolic profiles from various organs in different species of perilla plant (*Perilla frutescens* (L.) Britt.) and their antioxidant and enzyme inhibitory potential. *Ind Crops Prod* 171: 113914. <https://doi.org/10.1016/j.indcrop.2021.113914>
- Meng L, Lozano YF, Gaydou EM, Li B (2009) Antioxidant activities of polyphenols extracted from *Perilla frutescens* varieties. *Molecules* 14(1): 133–140. <https://doi.org/10.3390/molecules14010133>
- Ministry of Health (2017) Vietnamese Pharmacopoeia V. Medical Publishing House, Hanoi, Vietnam.
- Modi J, Rathore S, Dwivedi S, Saraogi G (2024) Formulation and evaluation of multipurpose herbal cream. *Int J Newgen Res Pharm Healthcare* 2(1): 129–134. <https://doi.org/10.61554/ijnrph.v2i1.2024.82>
- Mohiuddin AK (2019) Skin aging & modern age anti-aging strategies. *Int J Clin Dermatol Res* 7(4): 209–240. <https://doi.org/10.19070/2332-2977-1900052>
- Munteanu IG, Apetrei C (2021) Electrochemical determination of chlorogenic acid in nutraceuticals using voltammetric sensors based on screen-printed carbon electrode modified with graphene and gold nanoparticles. *Int J Mol Sci* 22(16): 8897. <https://doi.org/10.3390/ijms22168897>
- Mungmai L, Preedalikit W, Aunsri N, Amornlerdpison D (2020) Efficacy of cosmetic formulation containing *Perilla frutescens* leaves extract for irritation and aging skin. *Biomed Pharmacol J* 13(02): 779–787. <https://dx.doi.org/10.13005/bpj/1942>
- Nenadis N, Wang LF, Tsimidou M, Zhang HY (2004) Estimation of scavenging activity of phenolic compounds using the ABTS•+ assay. *J Agric Food Chem* 52(15): 4669–4674. <https://doi.org/10.1021/jf0400056>
- Sepulveda E, Kildsig DO, Ghaly ES (2003) Relationship between internal phase volume and emulsion stability: The cetyl alcohol/stearyl alcohol system. *Pharm Dev Technol* 8(3): 263–275. <https://doi.org/10.1081/PDT-120022155>
- Tadić VM, Žugić A, Martinović M, Stanković M, Maksimović S, Frank A, Nešić I (2021) Enhanced skin performance of emulgel vs. cream as systems for topical delivery of herbal actives (immortelle extract and hemp oil). *Pharmaceutics* 13(11): 1919. <https://doi.org/10.3390/pharmaceutics13111919>
- Tuyen NTL, Linh NTT, Lien PTT, Duong DQ (2024) Optimization of spray-drying conditions and quality assessment of dry

extract from *Perilla frutescens* (L.) Britton leaves. J Pharm Pharmacogn Res 12(6): 1056–1066.
https://doi.org/10.56499/jppres24.2009_12.6.1056

Wu J, Peng Z, Wu Q, Tang RWL, Dong T, Wang H, Tsim KWK (2022) The water extract of *Aloe vera* prevents fluoxetine-induced multiple-drug resistance of *E. coli* by inhibiting reactive oxygen species formation and membrane permeability. Phytomedicine 106: 154421.
<https://doi.org/10.1016/j.phymed.2022.154421>

Zhang X, Zhao Y, Li B, Guo M, Lv J, Wei Y (2022) Comparison of three extraction methods for anthocyanins from *Perilla frutescens* leaves. Sustain Chem Pharm 29: 100817.
<https://doi.org/10.1016/j.scp.2022.100817>

AUTHOR CONTRIBUTION:							
Contribution	Tuyen NTL	Yen LN	Ngoc HK	Linh DK	Ngoc HB	Tho DCMV	Duong DQ
Concepts or ideas	x	x	x	x	x		
Design	x	x	x	x	x	x	x
Definition of intellectual content	x						x
Literature search	x						
Experimental studies	x	x	x	x	x	x	
Data acquisition	x	x	x	x	x	x	x
Data analysis	x	x	x			x	x
Statistical analysis	x	x	x	x	x		
Manuscript preparation	x	x	x	x	x		
Manuscript editing	x						
Manuscript review	x	x	x	x	x	x	x

Citation Format: Tuyen NTL, Yen LN, Ngoc HK, Linh DK, Ngoc HB, Tho DCMV, Duong DQ (2025) Optimization and evaluation of skin cream from *Perilla frutescens* (L.) Britton and *Aloe vera* (L.) Burm.f. extracts with antioxidant activity. J Pharm Pharmacogn Res 13(6): 1629–1637.
https://doi.org/10.56499/jppres25.2275_13.6.1629

Publisher’s Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

Open Access: This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), which permits use, duplication, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license and indicate if changes were made.