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Formulation Development and Quality Evaluation of a Topical Cream Containing a Polyphenol-Rich Extract from *Spilanthes acmella* Murr.

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ABSTRACT

This study aimed to develop and evaluate a stable oil-in-water (O/W) topical cream incorporating a polyphenol-rich extract from *Spilanthes acmella* Murr. (*S. acmella*), a plant recognized for its antioxidant potential. The extract, obtained via reflux extraction with 80% ethanol, demonstrated notable free radical scavenging activity in the DPPH (2,2-diphenyl-1-picrylhydrazyl) assay, exhibiting an IC_{50} (Inhibitory concentration 50) value of 563.26 µg/mL. The cream was prepared using the hot emulsification method. Formulation variables, including oil phase concentration and composition (olive oil and cetyl alcohol), the emulsifier system (Tween 80/Span 80 blend), stirring duration, and humectant type, were systematically optimized to achieve the desired physicochemical stability and aesthetic properties. The optimized formulation contained 10% *S. acmella* extract, a 15% oil phase, a 10% emulsifier mix, and 10% glycerin. Three pilot batches were produced, all yielding a smooth, homogeneous, grayish-green cream with a pH of 5.69 ± 0.20, which is consistent with the physiological pH of human skin. The cream demonstrated good stability under stress conditions, excellent spreadability (29.87 ± 0.33 cm²), and a consistent total polyphenol content of 56.82 ± 0.69 mg gallic acid equivalents per gram. Microbial limit tests confirmed the product's microbiological safety, and *in vivo* dermal irritation tests in rabbits (ISO 10993-10) showed no signs of skin irritation. Overall, the formulated cream was found to be stable, safe, and rich in antioxidant compounds, suggesting its potential as a promising dermo-cosmetic product.

Keywords: *Spilanthes acmella*, Topical cream, Antioxidant, Formulation, Quality control, Polyphenols.

Introduction

In recent years, the global cosmetics landscape has seen a clear shift toward natural ingredients, as consumers increasingly look for products that are not only effective but also safe and derived from sustainable sources.[1] Vietnam has a wealth of medicinal plants that could fit this niche perfectly, yet many remain underexplored for skincare applications.[2] One great example is *Spilanthes acmella* Murr. (*S. acmella*), also known as paracress, which has been used in traditional medicine for ages to treat ailments ranging from toothaches to swelling.[3] Modern research is beginning to confirm what traditional use long suggested, particularly its anti-inflammatory and antioxidant properties.[4,5] The plant's pharmacological potential arises from a rich mix of compounds. While its N-isobutylamides, such as spilanthol, often take the spotlight, *S. acmella* is also rich in phenolic compounds such as vanillic and trans-ferulic acids.[6,7] These phenolics are believed to play a major role in neutralizing free radicals, making the extract a promising candidate for skincare products aimed at protecting the skin from oxidative stress and delaying signs of aging.[8]

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This project builds on our lab's previous work, where we developed a reliable extraction process for *S. acmella*, yielding an ethanolic extract with a high total polyphenol content (33.11 ± 0.19 mg GAE/g) and established basic quality standards.[9] The next logical step was to determine whether this extract could be formulated into a stable and effective topical cream. Therefore, this study aimed to develop and evaluate a stable oil-in-water (O/W) topical cream containing a polyphenol-rich extract of *S. acmella*. The specific objectives were to: (i) determine the optimal concentration of the extract, (ii) optimize key formulation variables—including the oil phase, emulsifiers, and humectants—to achieve desirable texture and stability, and (iii) establish quality control parameters for the final product.

The novelty of this research lies in formulating and standardizing, for the first time, a natural antioxidant topical cream derived from *S. acmella*, combining traditional medicinal knowledge with modern formulation science. The selected formulation and analytical methods were chosen for their relevance, scientific validity, and reproducibility in dermo-cosmetic product development.

Materials and Methods

Plant Material and Extraction

We used whole *S. acmella* plants, which were collected in Ba Ria – Vung Tau Province, Vietnam, in March 2022 (Latitude: 10.5494727° N; Longitude: 107.48407° E). The plants were botanically authenticated at the Faculty of Pharmacy, Hong Bang International University. A voucher specimen (Voucher no.: SA-03-2022) has been deposited at the Department of Pharmaceutics and Physical Chemistry, Faculty of Pharmacy, Hong Bang International University, Ho Chi Minh City, Vietnam, for future reference. To prepare the extract, we followed a reflux extraction process that our team had previously established.[9]

Briefly, dried plant powder was repeatedly extracted with 80% ethanol at 70 °C under reflux. The combined liquid extracts were then filtered and concentrated under reduced pressure to yield a crude, dark-green ethanolic extract ready for formulation.

Chemicals and Equipment

All chemicals and reagents were of analytical grade. Key formulation components included olive oil (Calofic, Italy), cetyl alcohol (Oxy Chemical, Thailand), cetostearyl alcohol (Gemar, Thailand), Olivem 1000 (Aromazone, France), Span 80 (Shanghai Zhanyun, Taiwan), Tween 80 (Xilong, Taiwan), glycerin, and propylene glycol, which were sourced from local suppliers in Ho Chi Minh City, Vietnam. Analytical reagents and standards included gallic acid (Bio Basic, Canada), Folin–Ciocalteu reagent (Sigma-Aldrich, USA), and DPPH (2,2-diphenyl-1-picrylhydrazyl; Sigma-Aldrich, USA).

The main instruments used included a Shimadzu UV–Vis Spectrophotometer V630 (Japan), an IKA RW28 Digital Overhead Stirrer (Germany), a VELP Scientifica Heated Magnetic Stirrer (Italy), a Memmert WB14 Thermostatic Water Bath (Germany), an Elma Elmasonic S100H Ultrasonic Cleaner (Germany), a Mettler Toledo SevenDirect SD20 pH meter (USA), a Precisa XB220A Analytical Balance (Switzerland), a Shimadzu BL-620S Electronic Balance (Japan), and a DLAB 1000 µL Micropipette (USA).

Evaluation of antioxidant activity and optimization of extract concentration in the cream formulation

The antioxidant potential of the *S. acmella* extract and its incorporation concentration in the topical cream were investigated to confirm that the formulated product would exhibit effective radical scavenging capacity. The DPPH free radical scavenging assay was performed according to the method described by Gulçin and Alwasel with minor modifications.[10] A 0.6 mM methanolic DPPH solution was mixed with various concentrations of the extract prepared in methanol. After incubation in the dark for 30 minutes at room temperature (25–30 °C), the absorbance was measured at 517 nm using a Shimadzu UV–Vis spectrophotometer V630 (Shimadzu, Japan). Ascorbic acid (GHtech, China) was used as a positive control. All experiments were conducted in triplicate (n = 3), and data were expressed as mean ± SD. Statistical analysis was performed using Microsoft Excel 2010 (Microsoft Corp., USA). The percentage of DPPH inhibition was plotted against sample concentrations, and the IC_{50} value was obtained from the linear regression equation. This value was applied to estimate the theoretical minimum extract concentration required to produce an observable antioxidant effect in the cream formulation.

However, since the diffusion and activity of antioxidant compounds can be reduced in a semisolid base, a range of higher extract concentrations was investigated to ensure adequate radical scavenging potential in the finished product. Accordingly, cream formulations containing increasing extract levels (2–14% w/w) were prepared using the hot emulsification method and evaluated for solubility, uniformity, and dispersion behavior. The starting concentration of 2% was selected based on previous *S. acmella*-based emulgel studies focusing mainly on antimicrobial properties.[11,12] In this study, higher concentrations were systematically examined to determine whether an increase in extract content could enhance the antioxidant capability of the cream while maintaining acceptable formulation stability.

Formulation of the topical cream

An oil-in-water (O/W) emulsion was selected and prepared by the hot emulsification method.[13] The process was conducted in two distinct phases:

Aqueous Phase: The selected concentration of *S. acmella* extract, preservatives (nipagin M), humectants (glycerin), and the hydrophilic emulsifier (Tween 80) were dispersed in purified water and heated to approximately 75 °C using a VELP Scientifica magnetic stirrer (VELP, Italy).

Oil Phase: Lipophilic components, including cetyl alcohol, olive oil, and lipophilic emulsifier (Span 80) were combined and heated to approximately 70 °C using a Memmert WB14 Thermostatic Water Bath (Germany).

The hot oil phase was slowly added to the aqueous phase under constant homogenization at 1500 rpm using an IKA RW28 digital overhead stirrer (IKA, Germany). The emulsion was allowed to cool to room temperature while being gently stirred. When the temperature dropped below 40 °C, rose essential oil was added as fragrance.

Systematic formulation optimization

The final formulation was achieved through a systematic, one-variable-at-a-time optimization process. Each iteration was evaluated for its key sensory and physical properties, including appearance, feel, and initial stability, to guide subsequent adjustments. Our investigation began with the concentration of the *S. acmella* extract. A theoretically effective minimum concentration was calculated based on the extract's IC_{50} value, a common approach in early-stage formulation.[13] Guided by the work of Nipate et al (2020)[14] and Afzal et al (2023),[11,12] we selected a practical starting concentration of 2% for our subsequent solubility and formulation tests to ensure complete dispersion. Next, we optimized the oil phase, investigating total concentrations from 5% to 20% and adjusting the internal ratios of its excipients to achieve the desired viscosity. A stable emulsion was ensured by optimizing the emulsifier system. This focused on both the total concentration and the Tween 80/Span 80 ratio to achieve the required Hydrophile-Lipophile Balance (HLB) for a stable oil-in-water cream.[13] Finally, process parameters such as stirring duration were assessed, and different humectants (glycerin versus PEG 400 at 5% and 10%) were compared to finalize the formulation's aesthetic properties and skin feel.

Quality evaluation of the optimized cream

Following formulation optimization, three independent pilot batches of *S. acmella* cream were prepared to confirm reproducibility and define its quality standards, a crucial step in topical product development.[13] All experiments were conducted in triplicate (n = 3), and data were expressed as mean. Statistical analysis was performed using Microsoft Excel 2010 (Microsoft Corporation, USA).

Physicochemical and sensory evaluation

The optimized formulations were assessed for key sensory and physical attributes to ensure product stability and user acceptability. Sensory properties were visually evaluated for smooth, homogeneous texture, absence of air bubbles, pleasant herbal odor, and non-separation at ambient temperature. Phase stability was examined by centrifuging 2–5 g of cream at 3000 rpm for 30 min at 30 °C using a Electronic centrifuge 80-2 (Zhengji, China); formulations showing no phase separation were considered stable.[15] Homogeneity was evaluated according to Appendix 1.12 of the Vietnamese Pharmacopoeia V by spreading ~0.03 g between two glass slides; at least three of four samples had to be particle-free.[16] Spreadability was determined by placing 1 g of cream between glass plates with a 250 g load for one minute; the mean spread area ($S = \pi d^2/4$) was calculated and considered acceptable between 25–35 cm^2.[13] pH was measured for a 10% (w/v) cream dispersion using a Mettler Toledo Seven Direct SD20 pH meter (USA), ensuring values within 4.5–6.0.[17] Washability was examined manually with running water, confirming non-greasy removal. The reference product was Laco anti-dark spot cream of Laco International Joint Stock Company.

Phytochemical, stability and safety evaluation

To confirm that our active components were consistently present after the manufacturing process, the total polyphenol content (TPC) was quantified. This was achieved using the established Folin-Ciocalteu spectrophotometric method on a Shimadzu UV–Vis V630 spectrophotometer (Japan) at 765 nm. Calibration was performed with gallic acid, and results were expressed as mg GAE/g cream.[18]

Stability was then investigated through both short-term and long-term studies. An accelerated physical stability test was conducted by centrifuging samples at 3000 rpm, which helps predict tendencies for phase separation. Concurrently, long-term stability was monitored over

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three months at both ambient (30 ± 2°C) and accelerated (45 ± 2°C) conditions, in line with ICH guidelines.[19]
For safety evaluation, microbiological purity was a primary checkpoint. The cream was tested for total aerobic microbial count (TAMC) and total yeast and mold count (TYMC) according to the Vietnamese Pharmacopoeia V, ensuring it was free from harmful contamination.[16] Finally, a primary skin irritation assessment was performed on healthy rabbits following the ISO 10993-10 guidelines,[20] where a small amount of cream was applied to shaved skin and the site was monitored for erythema or edema over a 72 hours.

Results and Discussion

Evaluation of antioxidant activity and optimization of extract concentration in cream formulation
The ethanolic extract of *S. acmella* exhibited notable, concentration-dependent antioxidant activity in the DPPH assay, as indicated by a progressive decrease in absorbance at 517 nm with increasing concentrations. The extract showed an IC_{50} value of 563.26 µg/mL, compared with 2.04 µg/mL for ascorbic acid, confirming that the extract—though less potent than a pure antioxidant—possesses substantial radical scavenging capacity attributable to its polyphenol-rich composition. This finding is consistent with previous reports highlighting the strong antioxidant and skin-protective properties of S. acmella extracts.[4,5,7,21] Based on the regression model obtained, the theoretical minimum concentration required to achieve observable antioxidant activity in the cream was estimated to be 0.06% (w/w).
Building on this, a solubility and dispersion assessment of the *S. acmella* extract was conducted to determine the highest concentration that could be incorporated while maintaining formulation quality. Extract solutions ranging from 2–14% (w/w) were prepared in distilled water and subjected to 15 minutes of ultrasonication, followed by visual inspection and filtration to evaluate residue formation. As shown in *Figure 1*, complete dissolution was achieved up to 10% (w/w) beyond which visible precipitation occurred. Therefore, 10% was selected as the optimal concentration, representing the highest soluble level capable of ensuring both homogeneity and enhanced antioxidant efficacy in the topical cream balancing potential efficacy with formulation stability.
Integrating these findings, the study demonstrated that increasing the extract concentration beyond the commonly reported 2% used in antimicrobial emulgel studies can meaningfully enhance antioxidant performance in a semisolid system.[11,12] Because diffusion and antioxidant activity may be attenuated within emulsions, higher extract levels are often required to achieve comparable radical-scavenging effects. The successful incorporation of 10% extract while maintaining physicochemical stability highlights the feasibility and added functional benefit of a higher loading. These results align with recent evidence emphasizing the strong dermal antioxidant potential of *S. acmella* and supporting its application in modern skin-protection formulations.[4,5,7,22]

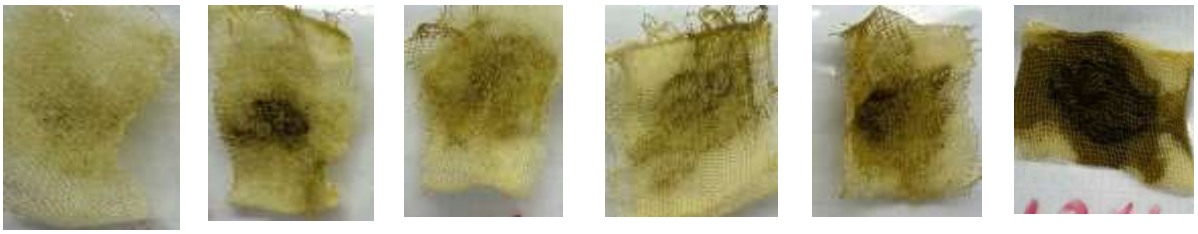

Figure 1: Solubility study image of *S. acmella* extract filtered through gauze

Formulation optimization
Formulation development was conducted by systematic screening of (1) total oil-phase percentage, (2) composition of the oil phase, (3) total emulsifier concentration, (4) ratio of Tween 80 : Span 80 (i.e, effective HLB), (5) mixing time (homogenisation), and (6) type / level of humectant. For all screening experiments, the extract concentration was fixed at 10% (w/w), and other fixed components were: propylene glycol 10%, preservative (nipagin M) 0.1%, and antioxidant (BHT) 0.02%. Assessment criteria included: organoleptic appearance, phase robustness (centrifuge test), short-term stability (visual), homogeneity (presence of particles), washability, and spreadability (cm^2). The desired target for spreadability was set at 25–35 cm^2.

Screening of the total oil phase percentage
Four oil phase levels (5, 10, 15, 20% w/w; F1–F4) were evaluated (T*able 1)*. Formulations with 5% and 10% oil (F1, F2) produced low viscosity creams, with F1 showing phase separation under centrifugation. At 20% oil (F4), the cream became excessively viscous and greasy with reduced washability and spreadability. In contrast, the 15% oil formulation (F3) exhibited smooth texture, acceptable stability, and the highest spreadability (23.83 cm^2). Based on these outcomes, a total oil phase of 15% was selected for subsequent studies.

Table 1: Results of the investigation on oil phase ratio

Variable factor (oil phase)	F1 (5%)	F2 (10%)	*F3 (15%)*	F4 (20%)
Fixed factors	**10% *S. acmella* extract, 5% emulsifier, 5% glycerin, 10% propylene glycol, 0.1% nipagin M, 0.02% BHT**			
Sensory properties	Dark olive green, liquid	Olive green, slightly viscous	Olive green, viscous (smooth)	Pale olive, very viscous
Phase robustness	--	-	-	--
Homogeneity	-	+	+	-
Washability	+	+	+	+
Spreadability (cm^2)	19.22	20.34	23.83	13.17

Footnotes:
Phase robustness: No separation (+), Minor separation (-), Major separation (--).
Homogeneity: No particles (+), Few particles (-), Many particles (--).
Washability: Washes off cleanly (+), Does not wash off cleanly (-).

Optimization of oil phase composition
With the oil phase fixed at 15%, six ratios of olive oil, cetyl alcohol, cetostearyl alcohol, and Olivem 1000 were evaluated *(F5–F9*, Table 2). Formulations F5 and F6 exhibited poor phase robustness, whereas F8 and F9 showed less favorable washability and excessive spreadability. In contrast, the 4:1:2:3 ratio (F3) yielded uniform appearance, satisfactory stability, and spreadability close to the target range. Accordingly, this composition was selected for emulsifier optimization.

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Table 2: Results of the investigation on oil phase composition

Variable factor (olive : cetyl : cetostearyl : Olivem 1000)	**F5 1:1:2:6 HLB=10.75**	**F6 2:1:2:5 HLB=10.55**	**F7 3:1:2:4 HLB=10.35**	***F3* *4:1:2:3* HLB=10.15**	**F8 5:1:2:2 HLB=9.95**	**F9 6:1:2:1 HLB=9.75**
Fixed factors	**10% *S. acmella* extract, 5% emulsifier, 5% glycerin, 10% propylene glycol, 0.1% nipagin M, 0.02% BHT**					
Sensory properties	Green, very viscous	Green, viscous	Green, viscous	Green, viscous	Green, viscous	Green, slightly viscous
Phase robustness	--	--	-	-	-	--
Homogeneity	--	+	+	+	+	-
Washability	+	+	+	+	-	-
Spreadability (cm²)	19.23	20.82	22.23	23.83	25.82	27.26

Footnotes:
HLB: Hydrophile-Lipophile Balance
Phase robustness: No separation (+), Minor separation (-), Major separation (--).
Homogeneity: No particles (+), Few particles (-), Many particles (--).
Washability: Washes off cleanly (+), Does not wash off cleanly (-).

Screening of total emulsifier concentration
Emulsifier concentrations of 2.5, 5, 7.5, and 10% (F10, F3, F11, F12) were investigated while keeping the optimized oil-phase composition constant (Table 3). Formulations containing 5% or more emulsifier produced homogeneous and stable creams under normal conditions, but only the 10% level (F12) maintained phase integrity under centrifugation stress and achieved spreadability (25.79 cm²) within the desirable range. Therefore, 10% was identified as the optimal emulsifier concentration.

Table 3: Results of the investigation on the emulsifier ratio

Variable factor (total emulsifier)	**F10 (2.5%)**	**F3 (5%)**	**F11 (7.5%)**	***F12 (10%)***
Fixed factors	**10% *S. acmella* extract, 15% oil phase (4:1:2:3 ratio), 5% glycerin, 10% propylene glycol, 0.1% nipagin M, 0.02% BHT**			
Sensory properties	Green, non-homogeneous	Green, viscous	Light green, viscous	Grayish-green, viscous
Phase robustness	--	-	-	+
Homogeneity	--	+	+	+
Spreadability (cm²)	22.10	23.17	25.32	25.79

Footnotes:
Phase robustness: No separation (+), Minor separation (-), Major separation (--).
Homogeneity: No particles (+), Few particles (-), Many particles (--).

Optimization of Tween 80 : Span 80 ratio
To optimize the emulsifier system, Tween 80 and Span 80 ratios were adjusted to yield effective HLB values from 8.15 to 12.15 while keeping the total emulsifier at 10% (Table 4*)*. Low HLB formulations (F13, F14) showed poor phase robustness, whereas higher HLB values improved stability. Among them, F15 (HLB = 11.15; Tween 80 : Span 80 = 6.4 : 3.6) demonstrated the most favorable combination of stability, homogeneity, washability, and spreadability (27.32 cm²), and was therefore selected for further development. This result was consistent with fundamental emulsion theory, where appropriate phase ratios and emulsifier balance were essential for droplet stabilization and long-term product integrity.

Effect of mixing time
Mixing times of 4, 5 and 6 minutes at 1500 rpm were assessed using the optimized oil and emulsifier system (Table 5). All batches showed satisfactory appearance, stability, and homogeneity, with spreadability increasing slightly as mixing time increased. While 6 minutes produced the highest spreadability (30.65 cm²), the 5-minute condition (29.46 cm²) offered a favorable balance between product performance and processing efficiency, and was therefore selected as optimal.

Evaluation of humectant type and concentration
The impact of humectant type and concentration was examined by adding glycerin (5% and 10%) or PEG 400 (5% and 10%) to the optimized formulation *(*Table 6). PEG-based creams showed lower viscosity, poor washability, and foaming on application, whereas glycerin provided smooth texture, good washability, and higher spreadability. The 10% glycerin formulation (F17) achieved the most favorable balance of properties (30.21 cm² spreadability) and was selected for the final cream.

Formula and process of preparing skin cream containing extract
From the stepwise screening described above, the final optimized formula was laid out in Table 7
The preparation process was carried out by the emulsification method, as shown in Figure 2, including the following steps:

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Table 4: Results of the investigation on emulsifier composition (Tween 80 : Span 80 ratio)

Variable factor (total emulsifier) (HLB)	**F13 (8.15)**	**F14 (9.15)**	**F12 (10.15)**	***F15 (11.15)***	**F16 (12.15)**
Fixed factors	**10% *S. acmella* extract, 15% oil phase (4:1:2:3 ratio), 10% total emulsifier, 5% glycerin, 10% propylene glycol, 0.1% nipagin M, 0.02% BHT.**				
Sensory properties	Light green, viscous	Light green, viscous, smooth	Grayish-green, viscous, smooth	Grayish-green, viscous, smooth	Grayish-green, viscous, smooth
Phase robustness	--	-	+	+	+
Homogeneity	-	+	+	+	+
Spreadability (cm²)	26.27	31.17	25.79	27.32	27.79

Footnotes:
Phase robustness: No separation (+), Minor separation (-), Major separation (--).
Homogeneity: No particles (+), Few particles (-), Many particles (--).

Table 5: Results of the investigation on stirring time (fixed: F15 composition; 1,500 rpm)

Variable factor (mixing time)	**F15a (4 min)**	***F15b (5 min)***	**F15c (6 min)**
Sensory properties	Grayish-green, soft, smooth	Grayish-green, soft, smooth	Grayish-green, soft, smooth
Phase robustness	+	+	+
Homogeneity	+	+	+
Spreadability (cm²)	27.32	29.46	30.65

Footnotes:
Phase robustness: No separation (+), Minor separation (-), Major separation (--).
Homogeneity: No particles (+), Few particles (-), Many particles (--).

Table 6: Results on the choice of humectant type and ratio

Variable factor (humectant)	**F15 (Glycerin 5%)**	***F17 (Glycerin 10%)***	**F18 (PEG 400 5%)**	**F19 (PEG 400 10%)**
Sensory properties	Grayish-green, soft, smooth	Grayish-green, soft, smooth	Grayish-green, slightly viscous	Grayish-green, slightly viscous
Washability	+	+	-	-
Spreadability (cm²)	29.46	30.21	24.71	20.43

Footnotes: Washability: Washes off cleanly (+), Does not wash off cleanly (-).

Table 7: Composition of the optimized topical cream (F17)

Ingredient	**Concentration (% w/w)**
Spilanthes acmella extract	10.0
Olive oil	6.0
Cetyl alcohol	1.5
Cetostearyl alcohol	3.0
Olivem 1000	4.5
Tween 80	6.4
Span 80	3.6
Propylene glycol	10.0
Glycerin	10.0
Nipagin M (Methylparaben)	0.1
BHT	0.02
Rose essential oil	0.1
Purified water	q.s. to 100

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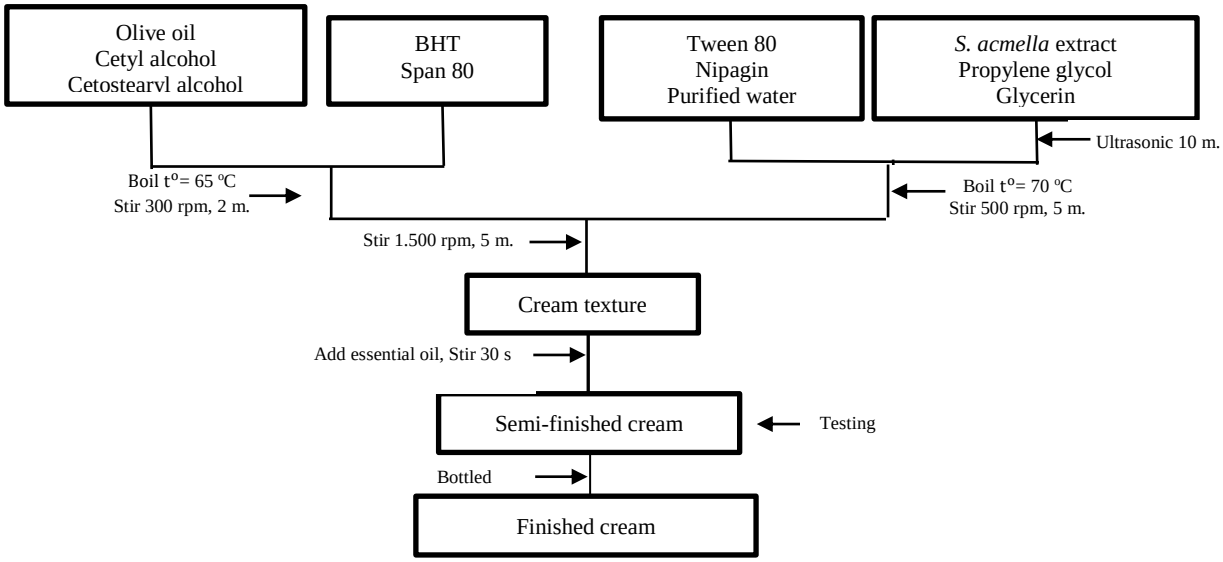

Figure 2: Flowchart of the manufacturing process for the *S. acmella* topical cream

Step 1. Preparation of the aqueous phase
Weigh the plant extract and disperse it in propylene glycol and glycerin (solution 1).
Dissolve Tween 80 and Nipagin M in purified water (solution 2).
Add solution 1 slowly into solution 2 under magnetic stirring (500 rpm) at 70 °C for 5 minutes.

Step 2. Preparation of the oil phase
Mix olive oil, cetyl alcohol, cetostearyl alcohol, and Olivem 1000 in the ratio 4:1:2:3.
Heat the mixture in a water bath to 65 °C until completely liquefied.
Incorporate Span 80 and BHT, stirring at 300 rpm for 2 minutes to ensure uniform dissolution.

Step 3. Emulsification and homogenisation
Gradually add the hot oil phase into the aqueous phase.
Homogenise using a high-shear stirrer at 1500 rpm for 5 minutes.

Step 4. Cooling and finishing
Allow the emulsion to cool to 40–45 °C.
Add the flavoring agent and mix for 30 seconds.

Step 5. Filling and storage
Transfer the finished cream into clean containers.
Seal tightly and store under appropriate conditions until further testing.

Development of basic standards and evaluation of the quality of topical creams
Samples of topical creams prepared according to the final formula and process were tested for quality based on the proposed basic standards. The results of verification and evaluation according to the draft basic standards are presented in Table 8.
The optimized cream exhibited excellent physicochemical and microbiological quality across three independent batches. Its pH (5.53 – 5.91) fell within the physiological range of the skin (4.5 – 6.0), minimizing irritation risk.[17,23] Notably, the total polyphenol content remained stable (56 – 57 mg GAE/g), confirming the extract's chemical integrity after processing. Polyphenols are potent antioxidants,[10, 18] that play a vital role in neutralizing reactive oxygen species, thereby protecting against photoaging and maintaining skin elasticity.[22] Recent evidence highlights that these compounds modulate oxidative pathways involved in collagen degradation and inflammation, underscoring their crucial role in modern dermocosmetic formulations.[22] The non-irritant classification obtained under ISO 10993-10 guidelines further confirms the formulation's safety profile.[19]
Collectively, these findings highlight that the 10% *S. acmella* extract concentration not only ensures formulation stability but also maximizes antioxidant efficacy, supporting its use in antioxidant-rich dermocosmetic products. This concentration represents a meaningful advancement beyond prior *S. acmella* formulations that employed lower levels primarily for antimicrobial purposes,[11,12] demonstrating its broader therapeutic potential in skincare.

Table 8: Quality evaluation results of three batches of the final formulation (F17)

Parameter	Requirement	Result			Control
		Batch 1	Batch 2	Batch 3	
Sensory properties	Grayish-green, viscous, soft, smooth, homogeneous cream	Pass	Pass	Pass	Pass
pH	4.5 – 6.0	5.53	5.62	5.91	6.0
Stability	No change in appearance, no phase separation	Pass	Pass	Pass	Pass
Homogeneity	No particles observed in 3 of 4 slides	Pass	Pass	Pass	Pass
Spreadability (cm^2)	25 - 35	29.75	30.24	29.62	24.35
Microbial limits	Total aerobic microbial count ≤1000 CFU/g	80 CFU/g			-
Skin irritation	Non-irritant	Not significant			-
		Pass			
Qualitative analysis	Positive reactions (lactone ring, $FeCl_3$, Lieberman-Burchard, Fehling)	Pass	Pass	Pass	-
Total polyphenol content (mg GA/g)		56.07	56.66	57.73	-

Footnotes: control: Laco anti-dark spot cream of Laco International Joint Stock Company.

Conclusion

This study successfully transformed *S. acmella* extract into a stable, reproducible oil-in-water cream. The optimized formulation (15% oil phase with a 4:1:2:3 ratio of olive oil, cetyl alcohol, cetostearyl alcohol, and Olivem 1000; 10% emulsifier with Tween 80 : Span 80 = 6.4 : 3.6; 10% glycerin; and controlled homogenization) consistently produced creams with desirable sensory properties, robust physical stability, appropriate pH, uniform polyphenol content, and no skin irritation. The results confirm the feasibility of developing a safe and effective phytocosmetic product from *S. acmella*, supporting its valorization as a natural resource for dermo-cosmetic applications in Vietnam. With its demonstrated antioxidant content, favorable skin compatibility, and reproducibility, this formulation represents a promising candidate for further preclinical and consumer testing, and eventual commercialization.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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