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An Optimized Potent Barrier-Restoring Cream for Skin Repair: A Multicenter, Randomized, Double-Blind, Split-Face Controlled Clinical Study

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ABSTRACT

Background and Objectives: Severe sensitive skin significantly impairs patients' quality of life, and moisturizer application has become a clinical imperative in its management. This study was designed to assess the skin barrier repair efficacy of an optimized, potent cream comprising *Portulaca oleracea* extract, *Prinsepia utilis* oil, *Citrus reticulata* peel extract, and *Polygonatum kingianum* extract.

Materials and Methods: A total of 103 eligible participants with sensitive skin were randomly assigned to apply the test cream (Cream A) on one cheek (left or right) and the control cream (Cream B) on the contralateral cheek, twice daily. Transepidermal water loss (TEWL), stratum corneum hydration (SCH), and erythema index (EI) were measured on both cheeks at baseline, as well as at 7, 14, and 28 days after product application. Clinical evaluations by two dermatologists and self-reports by participants were carried out at identical time points.

Results: Both clinical evaluations and participant self-reports revealed that the application of either Cream A or Cream B significantly relieved discomfort symptoms, including erythema and burning sensations; Cream A demonstrated a faster alleviation of desquamation symptoms. Both creams significantly improved TEWL, SCH, and EI in participants with sensitive skin. Notably, compared to Cream B, Cream A achieved a significantly higher improvement rate in EI at Day 7 ($p < 0.05$) and a greater improvement rate in TEWL at Day 28 ($p < 0.05$).

Conclusion: Cream A exhibits a remarkable clinical value in rapidly alleviating erythema and desquamation, with notable advantages in restoring damaged skin barriers, serving as a novel long-term management strategy for sensitive skin.

Trial Registration: National Medical Research Registration and Filing Information System: MR-33-24-019764

1 | Introduction

Sensitive skin is a syndrome characterized by subjective and objective symptoms in response to minimal external stimuli, primarily affecting the facial region. Patients may experience subjective symptoms such as burning, stinging, pruritus, and tightness, with or without accompanying objective signs

including erythema, telangiectasia, and desquamation [1]. Although not life-threatening, these symptoms significantly impair patients' quality of life. Current evidence suggests that sensitive skin pathogenesis involves a complex interplay of cutaneous barrier dysfunction, neurovascular hyperreactivity, and innate immune-inflammatory responses [2]. Compromised skin barrier function increases epidermal permeability, facilitating the

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penetration of irritants, allergens, and microorganisms that trigger inflammatory cascades while simultaneously reducing protection of dermal nerves and vasculature, thereby promoting sensitive skin manifestations [3].

Epidemiological studies demonstrate the global prevalence of sensitive skin, with reported incidence rates exceeding 50% among women in Europe, America, Japan, and Korea. In China, the prevalence among women reaches 36.1% [4]. Given this substantial disease burden, the consistent use of barrier-repairing moisturizers—whether as standalone therapy or adjunct to pharmacological and laser treatments—has become clinically imperative. Previous investigations have established the efficacy of an Anti-Sensitive Moisturizing Tolerance-Extreme Cream (manufactured by Beitaini Bio-technological Co., Ltd., China) in improving stratum corneum hydration (SCH) and texture parameters, suggesting its potential utility in sensitive skin management [5]. However, this formulation demonstrated limited efficacy in reducing transepidermal water loss (TEWL). To address this limitation, we optimized the formulation by incorporating bioactive compounds including *Polygonatum kingianum* extract and *Citrus reticulata* peel extract. The new formula aims to achieve the goal of multidimensional repair of the skin barrier function by strengthening the repair of the lipid barrier, increasing the repair of tight junctions, and improving moisturizing ability. A preliminary clinical study involving 33 volunteers with sensitive skin found that twice-daily application of this optimized cream for 4 weeks improved SCH, TEWL, and erythema area proportion, with no reported adverse reactions. To further rigorously evaluate the efficacy and safety of this optimized potent barrier-restoring cream, this study proposes a multicenter, randomized, double-blind, and split-face-controlled trial, aiming to provide a more robust evidence-based foundation for the long-term management of sensitive skin.

2 | Materials and Methods

2.1 | Study Design

This is a multicenter, randomized, double-blind, semi-face-controlled clinical trial. It has been approved by the Ethics Committee of Hangzhou Third People's Hospital (Approval No.: 2024KA070) and registered with the National Medical Research Registration and Filing Information System. The research protocol has been reviewed and approved by the ethics committees of all participating research centers. All participants signed a written informed consent form after being fully informed. This study strictly adheres to the ethical guidelines of the Declaration of Helsinki to ensure that all research procedures involving human participants comply with international medical ethical norms.

2.2 | Participants

The inclusion criteria included (a) age between 18 and 55 years; (b) visible and persistent facial erythema, as well as subjective symptoms such as burning, stinging, itching, and tightness following minor external stimuli; (c) scored ≥ 3 points on the lactic acid test and/or ≥ 3 points on the capsaicin test; and (d) absence of any local facial treatments (including but not limited to topical medications, chemical peels, and laser therapies) for at least 28 days prior to enrollment. The exclusion criteria included (a)

volunteers with systemic diseases, tumors, or immunodeficiency disorders; (b) pregnant or lactating women; (c) participants who are currently using or have taken (orally or topically) prohibited study drugs (such as glucocorticoids, immunosuppressants, antiallergic drugs, and photosensitizing drugs) within 14 days prior to the start of the trial; and (d) individuals known to be allergic to the test substances [6].

2.3 | Test Cream

The test cream (Cream A) employed in this study was the Barrier Multi-Effect Extra Care Cream (Beitaini Bio-Technological Co., China). This cream was formulated with a blend of active ingredients, including *Portulaca oleracea* extract, *Prinsepia utilis* oil, *Citrus reticulata* peel extract, *Polygonatum kingianum* extract and sodium hyaluronate, among others. In contrast, the control cream (Cream B) utilized was the Anti-Sensitive Moisturizing Tolerance-Extreme Cream, also produced by Beitaini Bio-Technological Co., China. The primary components of this control cream were relatively simple, consisting of *Portulaca oleracea* extract, *Prinsepia utilis* oil, β -glucan, and sodium hyaluronate (as detailed in Table 1).

2.4 | Randomization and Treatment

This study employed a block randomization method, with the randomization sequence generated using SAS 9.4 software (SAS Institute Inc., Cary, NC). Randomization and allocation were implemented through an interactive web response system (IWRS).

At baseline, eligible participants were randomly assigned to apply Cream A on either the left or right facial cheek, with Cream B being applied to the contralateral side. During the trial period, product usage logs were distributed, and participants were required to record their daily usage. At each follow-up visit, the consumed weights of the two types of creams were measured and recorded. Both creams were applied according to a standardized protocol: twice daily, with each application consisting of two pumps, and evenly spread on the designated side of the face (after randomization, different colored labels were affixed to the packaging to indicate the corresponding side of the face for application, with instructions for participants to apply the cream on the left face using the left hand and on the right face using the right hand). Throughout the trial period, participants were prohibited from using any facial skincare products other than those provided in this study.

2.5 | Clinical Assessment and Measurements

Clinical evaluations were independently conducted by two dermatologists with extensive clinical experience at four time points: baseline (Day 0, D0), Day 7 (D7), Day 14 (D14), and Day 28 (D28) post-treatment. The assessment indicators included erythema, dryness, skin roughness, and desquamation. Each indicator was quantitatively scored using a 5-point scale (0–4 points), with the specific scoring criteria as follows: 0 = none; 1 = slight; 2 = mild; 3 = moderate; 4 = severe [5]. In cases of inter-rater discrepancy (score difference ≥ 1 point) between the two physicians, a third senior dermatologist conducted a review, and the reassessment result was adopted as the final score.

TABLE 1 | Active ingredients of two creams and their bioactivity.

Test cream (Cream A)	Control cream (Cream B)	Bioactivities
<i>Portulaca oleracea</i> extract	<i>Portulaca oleracea</i> extract	Anti-inflammation; antiallergy [7, 8]
<i>Prinsepia utilis</i> oil	<i>Prinsepia utilis</i> oil	Improves barrier function and increase SCH [9]
Ceramide	—	Repairs the skin barrier to reduce TEWL
Cholesterol	—	Repairs the skin barrier to reduce TEWL
<i>Citrus reticulata</i> peel extract	—	Anti-inflammation; improves skin hydration and barrier function [10, 11]
β -glucan	β -glucan	Restores the damaged epidermal barrier [12]
<i>Polygonatum kingianum</i> extract	—	Anti-inflammatory, antioxidant, and maintains skin microecological balance [13]
Sodium hyaluronate	Sodium hyaluronate	Moisturizing
<i>Lithothamnion calcareum</i> extract	—	Enhances the skin's moisture retention capacity
Squalane	—	Moisturizing

On the identical schedule, participants completed self-reports. They rated the severity of five symptoms on their bilateral cheeks: redness, tightness, itching, burning, and tingling, using a 0–3 point scale (0 = none; 1 = mild; 2 = moderate; 3 = severe).

Measurements of skin physiological function were carried out at the same time points. The erythema index (EI) was measured using a Mexameter MX18 (Courage & Khazaka, Germany), while TEWL and SCH were assessed using a Tewameter TM 300 and Corneometer CM 825 (Courage & Khazaka, Germany), respectively. At D0, 3 fixed sites were picked on one cheek of each subject, where TEWL, SCH, and EI were measured respectively. Another three fixed sites at symmetrical positions on the contralateral cheek were selected for the same measurements. During follow-up visits at D7, D14, and D28, with reference to the positioning photos taken at baseline, the measurements of the above-mentioned indicators were repeated at the same sites. For each indicator at every measurement site, three repeated measurements were conducted, and the mean of the three readings was taken as the final data for subsequent statistical analysis. All measurements were performed in a standardized environment with controlled ambient conditions (22°C–24°C, 50%–60% relative humidity) and no daylight exposure. Prior to testing, participants were instructed to cleanse their faces and rest for 20 min in the controlled environment to ensure stable skin conditions.

2.6 | Statistical Analysis

All statistical analyses were performed using SPSS 26 (IBM Corp., Armonk, NY, USA). Unless otherwise specified, two-tailed tests were applied, and a p value < 0.05 was considered statistically significant. Normality of continuous variables was assessed using both the Shapiro–Wilk test and visual inspection of Q–Q plots. For the primary outcome (two groups across four time points), if normality and sphericity assumptions were met, a two-way repeated-measures ANOVA was employed; otherwise, non-parametric methods were applied. All post hoc pairwise comparisons were adjusted using the Bonferroni correction. For non-normally distributed data, the Mann–Whitney U test (between groups) or the Wilcoxon signed-rank test (within groups) was applied. For ordinal data, comparisons were performed using the chi-squared test or Friedman two-way ANOVA by ranks, as appropriate.

3 | Results

3.1 | Participants

From June 2024 to December 2024, a total of 111 participants were screened and enrolled by five research institutions. Of these, 103 participants ultimately completed this trial, and there were no protocol deviations. The average age of the participants was 30.6 ± 6.8 years old (ranging from 21 to 53 years old), with a predominance of female participants (89.3% [$n = 92$]) compared to males (10.7% [$n = 11$]).

3.2 | Clinical Results

The results of clinical evaluation demonstrated that with the gradual extension of the treatment cycle, both creams exhibited significant efficacy in improving skin symptoms on participants' faces, including erythema, dryness, roughness

TABLE 2 | Clinical evaluations of symptoms on both cheeks of participants *n* (%).

Symptoms	Group	Time	None	Slight	Mild	Moderate	Severe	<i>p</i>
Erythema	Cream A (<i>n</i> = 103)	0 d	2 (1.9)	33 (32.0)	35 (34.0)	30 (29.1)	3 (2.9)	/
		7 d	4 (3.9)	44 (42.7)	36 (35.0)	17 (16.5)	2 (1.9)	0.084
		14 d	13 (12.6)	41 (39.8)	36 (35.0)	11 (10.7)	2 (1.9)	< 0.001**
		28 d	17 (16.5)	46 (44.7)	28 (27.2)	11 (10.7)	1 (1.0)	< 0.001**
	Cream B (<i>n</i> = 103)	0 d	2 (1.9)	31 (30.1)	34 (33.0)	33 (32.0)	3 (2.9)	/
		7 d	4 (3.9)	41 (39.8)	32 (31.1)	24 (23.3)	2 (1.9)	0.242
		14 d	8 (7.8)	45 (43.7)	33 (32.0)	15 (14.6)	2 (1.9)	< 0.001**
		28 d	21 (20.4)	36 (35.0)	33 (32.0)	12 (11.7)	1 (1.0)	< 0.001**
Dryness	Cream A (<i>n</i> = 103)	0 d	14 (13.6)	35 (34.0)	37 (35.9)	16 (15.5)	1 (1.0)	/
		7 d	29 (28.2)	46 (44.7)	22 (21.4)	6 (5.8)	0 (0)	< 0.001**
		14 d	30 (29.1)	53 (51.5)	17 (16.5)	3 (2.9)	0 (0)	< 0.001**
		28 d	48 (46.6)	41 (39.8)	13 (12.6)	1 (1.0)	0 (0)	< 0.001**
	Cream B (<i>n</i> = 103)	0 d	11 (10.7)	39 (37.9)	38 (36.9)	14 (13.6)	1 (1.0)	/
		7 d	28 (27.2)	44 (42.7)	26 (25.2)	5 (4.9)	0 (0)	< 0.001**
		14 d	28 (27.2)	51 (49.5)	19 (18.4)	5 (4.9)	0 (0)	< 0.001**
		28 d	38 (36.9)	48 (46.6)	16 (15.5)	1 (1.0)	0 (0)	< 0.001**
Roughness	Cream A (<i>n</i> = 103)	0 d	17 (16.5)	43 (41.7)	33 (32.0)	8 (7.8)	2 (1.9)	/
		7 d	31 (30.1)	43 (41.7)	25 (24.3)	3 (2.9)	1 (1.0)	0.011*
		14 d	36 (35.0)	50 (48.5)	13 (12.6)	4 (3.9)	0 (0)	< 0.001**
		28 d	49 (47.6)	45 (43.7)	9 (8.7)	0 (0)	0 (0)	< 0.001**
	Cream B (<i>n</i> = 103)	0 d	16 (15.5)	41 (39.8)	35 (34.0)	9 (8.7)	2 (1.9)	/
		7 d	29 (28.2)	43 (41.7)	27 (26.2)	3 (2.9)	1 (1.0)	0.018*
		14 d	34 (33.0)	46 (44.7)	20 (19.4)	3 (2.9)	0 (0)	< 0.001**
		28 d	45 (43.7)	43 (41.7)	15 (14.6)	0 (0)	0 (0)	< 0.001**
Desquamation	Cream A (<i>n</i> = 103)	0 d	39 (37.9)	30 (29.1)	28 (27.2)	6 (5.8)	0 (0)	/
		7 d	56 (54.4)	35 (34.0)	11 (10.7)	1 (1.0)	0 (0)	0.014*
		14 d	72 (69.6)	25 (24.3)	6 (5.8)	0 (0)	0 (0)	< 0.001**
		28 d	75 (72.8)	28 (27.2)	0 (0)	0 (0)	0 (0)	< 0.001**
	Cream B (<i>n</i> = 103)	0 d	40 (38.8)	33 (32.0)	24 (23.3)	5 (4.9)	1 (1.0)	/
		7 d	52 (50.5)	37 (35.9)	13 (12.6)	1 (1.0)	0 (0)	0.098
		14 d	68 (66.0)	26 (25.2)	9 (8.7)	0 (0)	0 (0)	< 0.001**
		28 d	68 (66.0)	30 (29.1)	5 (4.9)	0 (0)	0 (0)	< 0.001**

p* < 0.05.*p* < 0.001.

and desquamation. Specifically, in the assessment of skin dryness and roughness, both cheeks of the participants showed statistically significant improvement ($p < 0.05$) as early as the 7th day of treatment with the respective creams. Regarding desquamation, the desquamation score on the cheek treated with Cream A significantly decreased ($p < 0.05$) on the 7th day of treatment, while the desquamation score on the cheek treated with Cream B did not show a significant downward trend until the 14th day ($p < 0.01$). In terms of erythema improvement, obvious symptom alleviation ($p < 0.001$) was observed on both cheeks of the participants on the 14th day of treatment (Table 2).

The participant self-report results indicated that there was no significant difference between the two face creams in alleviating participants' subjective discomfort symptoms. Over the 28-day treatment period, a dynamic improvement trend was observed in the skin condition of both sides of the participants' faces. Specifically, on the 14th day of treatment, the redness and burning sensation on both cheeks were significantly relieved ($p < 0.01$). By the 28th day, the tightness, itching, and stinging

sensations of the facial skin were also notably reduced ($p < 0.05$) (Table 3).

Figure 1 demonstrates that no significant differences were observed in SCH, TEWL, or EI between the bilateral cheeks at baseline (all $p > 0.05$). With prolonged use, both creams significantly improved SCH compared to baseline at all follow-up time points (D7, D14, and D28; all $p < 0.01$), but no intergroup differences detected (all $p > 0.05$), indicating comparable efficacy in enhancing skin hydration in sensitive skin (Figures 1(a) and 1(b)).

Regarding TEWL (Figures 1(c) and 1(d)), both groups exhibited a sustained downward trend (all time points vs. baseline, $p < 0.01$). However, at D28, TEWL on the Cream A-treated cheek decreased from 22.45 ± 5.69 to 16.18 ± 3.43 , representing a 25.78% improvement, whereas the Cream B-treated cheek showed a reduction from 21.96 ± 5.80 to 17.45 ± 3.90 (16.49% improvement). The intergroup difference in TEWL improvement rates was statistically significant ($p = 0.020$), suggesting superior long-term barrier repair efficacy with cream A.

TABLE 3 | Self-reports of symptoms on both cheeks of participants *n* (%).

Symptoms	Group	Time	None	Mild	Moderate	Severe	<i>p</i>
Erythema	Cream A (<i>n</i> = 103)	0 d	22 (21.4)	34 (33.0)	35 (34.0)	12 (11.7)	/
		7 d	28 (27.2)	44 (42.7)	23 (22.3)	8 (7.8)	0.151
		14 d	31 (30.1)	51 (49.5)	16 (15.5)	5 (4.9)	0.003*
		28 d	42 (40.8)	48 (46.6)	9 (8.7)	4 (3.9)	< 0.001**
	Cream B (<i>n</i> = 103)	0 d	21 (20.4)	33 (32.0)	33 (32.0)	16 (15.5)	/
		7 d	25 (24.3)	39 (37.9)	29 (28.2)	10 (9.7)	0.332
		14 d	28 (27.2)	46 (44.7)	23 (22.3)	6 (5.8)	0.009*
		28 d	40 (38.8)	51 (49.5)	7 (6.8)	5 (4.9)	< 0.001**
Tightness	Cream A (<i>n</i> = 103)	0 d	32 (31.1)	58 (56.3)	11 (10.7)	2 (1.9)	/
		7 d	48 (46.6)	43 (41.7)	12 (11.7)	0 (0)	0.535
		14 d	42 (40.8)	56 (54.4)	4 (3.9)	1 (1.0)	0.705
		28 d	63 (61.2)	37 (35.9)	2 (1.9)	1 (1.0)	< 0.001**
	Cream B (<i>n</i> = 103)	0 d	32 (31.1)	55 (53.4)	13 (12.6)	3 (2.9)	/
		7 d	47 (45.6)	48 (46.6)	8 (7.8)	0 (0)	0.185
		14 d	42 (40.8)	55 (53.4)	5 (4.9)	1 (1.0)	0.505
		28 d	57 (55.3)	42 (40.8)	2 (1.9)	2 (1.9)	0.003*
Itching	Cream A (<i>n</i> = 103)	0 d	39 (37.9)	53 (51.5)	11 (10.7)	0 (0)	/
		7 d	50 (48.5)	43 (41.7)	10 (9.7)	0 (0)	1
		14 d	65 (63.1)	26 (25.2)	11 (10.7)	1 (1.0)	0.099
		28 d	63 (61.2)	34 (33.0)	6 (6.8)	0 (0)	0.013*
	Cream B (<i>n</i> = 103)	0 d	44 (42.7)	43 (41.7)	15 (14.6)	1 (1.0)	/
		7 d	50 (48.5)	45 (43.7)	8 (7.8)	0 (0)	0.774
		14 d	64 (62.1)	32 (31.1)	6 (5.8)	1 (1.0)	0.131
		28 d	56 (54.4)	40 (38.8)	7 (6.8)	0 (0)	0.025*
Burning	Cream A (<i>n</i> = 103)	0 d	50 (48.5)	38 (36.9)	15 (14.6)	0 (0)	/
		7 d	61 (59.2)	32 (31.1)	10 (9.7)	0 (0)	0.963
		14 d	80 (77.7)	17 (16.5)	6 (5.8)	0 (0)	0.002*
		28 d	75 (72.8)	25 (24.3)	3 (2.9)	0 (0)	0.007*
	Cream B (<i>n</i> = 103)	0 d	50 (48.5)	37 (35.9)	16 (15.5)	0 (0)	/
		7 d	64 (62.1)	28 (27.2)	11 (10.7)	0 (0)	0.376
		14 d	82 (79.6)	17 (6.5)	4 (3.9)	0 (0)	< 0.001**
		28 d	77 (74.8)	24 (23.3)	2 (1.9)	0 (0)	0.001*
Tingling	Cream A (<i>n</i> = 103)	0 d	63 (61.2)	36 (35.0)	4 (3.9)	0 (0)	/
		7 d	75 (72.8)	27 (26.2)	1 (1.0)	0 (0)	0.827
		14 d	86 (83.5)	15 (14.6)	2 (1.9)	0 (0)	0.105
		28 d	89 (86.4)	13 (12.6)	1 (1.0)	0 (0)	0.02*
	Cream B (<i>n</i> = 103)	0 d	65 (63.1)	32 (31.1)	6 (5.8)	0 (0)	/
		7 d	71 (68.9)	31 (30.1)	1 (1.0)	0 (0)	1
		14 d	83 (80.6)	17 (16.5)	3 (2.9)	0 (0)	0.275
		28 d	87 (84.5)	15 (14.6)	1 (1.0)	0 (0)	0.042*

p* < 0.05.*p* < 0.001.

For EI reduction (Figures 1(e) and 1(f)), Cream A demonstrated rapid effects: by D7, EI on the Cream A-treated cheek significantly decreased from 303.41 ± 67.02 to 282.93 ± 66.51 ($p < 0.001$), with a 6.07% improvement. In contrast, the Cream B-treated cheek showed only a marginal reduction from 303.22 ± 71.26 to 296.64 ± 71.08 ($p = 0.083$; 1.48% improvement), and the improvement rate was significantly lower than that of Cream A ($p = 0.022$). A significant downward trend in EI for Cream B-treated cheek was not observed until D14. Although both creams significantly reduced EI compared to baseline at D14 and D28 (all $p < 0.05$), no intergroup differences were observed ($p > 0.05$), highlighting Cream A's

advantage in providing earlier erythema relief. Figure 2 presents a representative case from this clinical trial. For the left cheek administered Cream A, a notable reduction in erythema, accompanied by a visible regression of redness, was observed as early as Day 7. This improvement persisted and further progressed throughout the entire observation period. In contrast, the right cheek treated with Cream B showed noticeable improvement only by Day 14. By the end of the 28-day observation period, both cheeks exhibited significant clinical improvement in erythema. Both creams were well tolerated, with no adverse reactions reported during the study period.

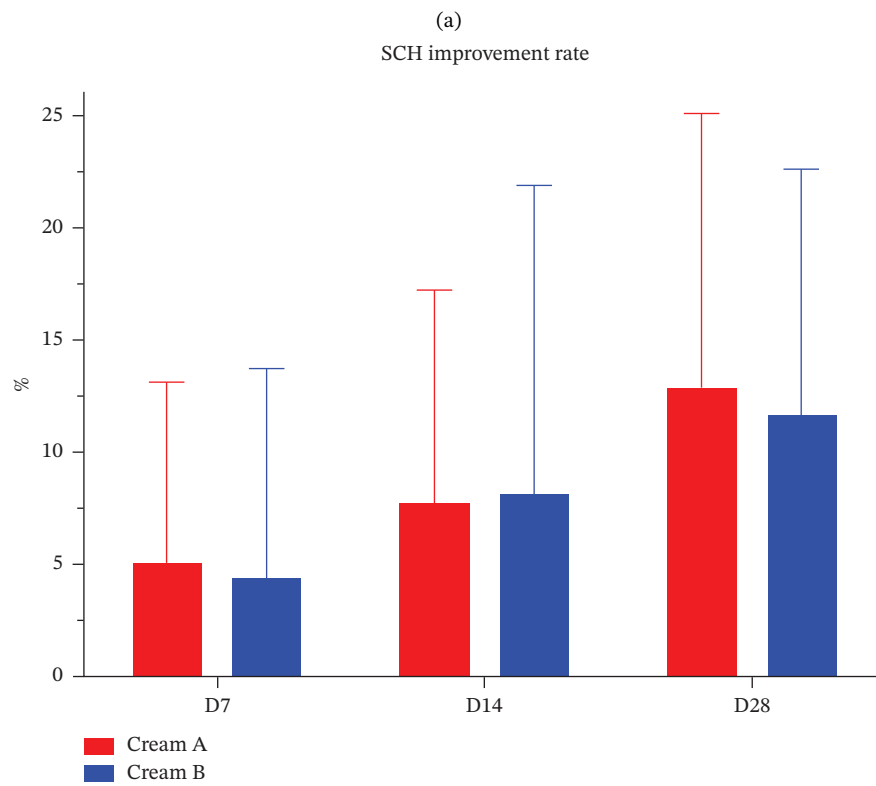
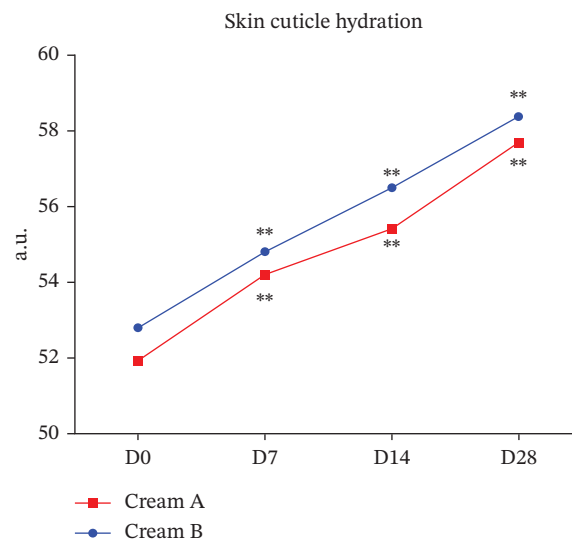


FIGURE 1 | (Continued)

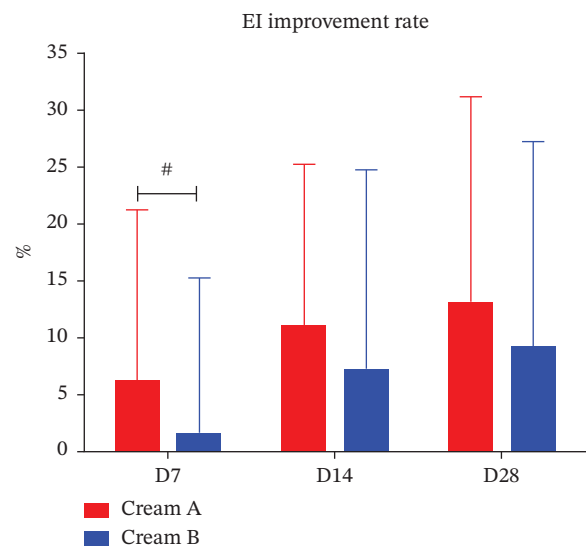
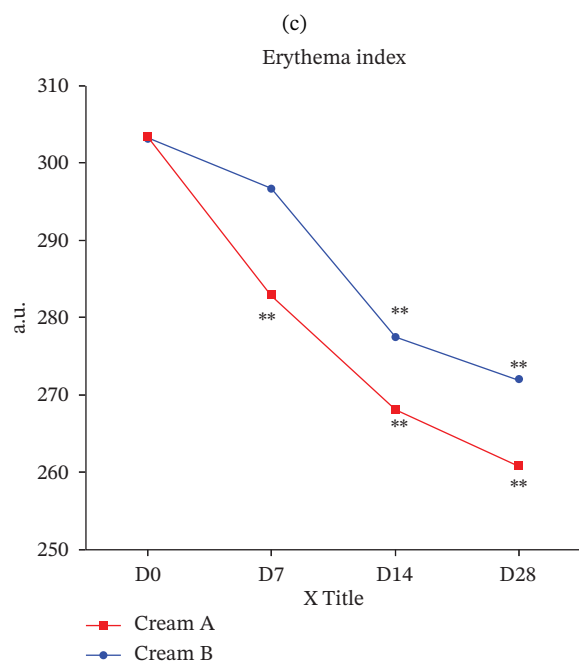
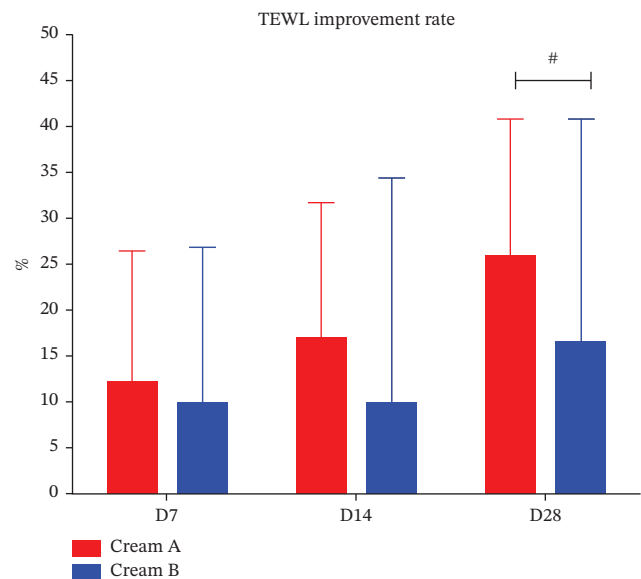
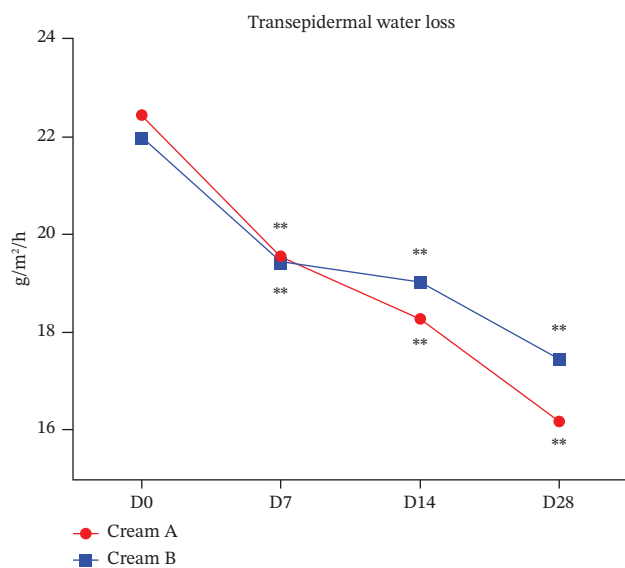


FIGURE 1 | (a) Changes in stratum corneum hydration (SCH) with the two creams; (b) SCH improvement rates with two creams; (c) changes in transepidermal water loss (TEWL) with the two creams; (d) TEWL improvement rates with two creams; (e) changes in erythema index (EI) with the two creams; (f) EI improvement rates with two creams. ** $p < 0.01$ vs. baseline and # $p < 0.05$ vs. Cream B.

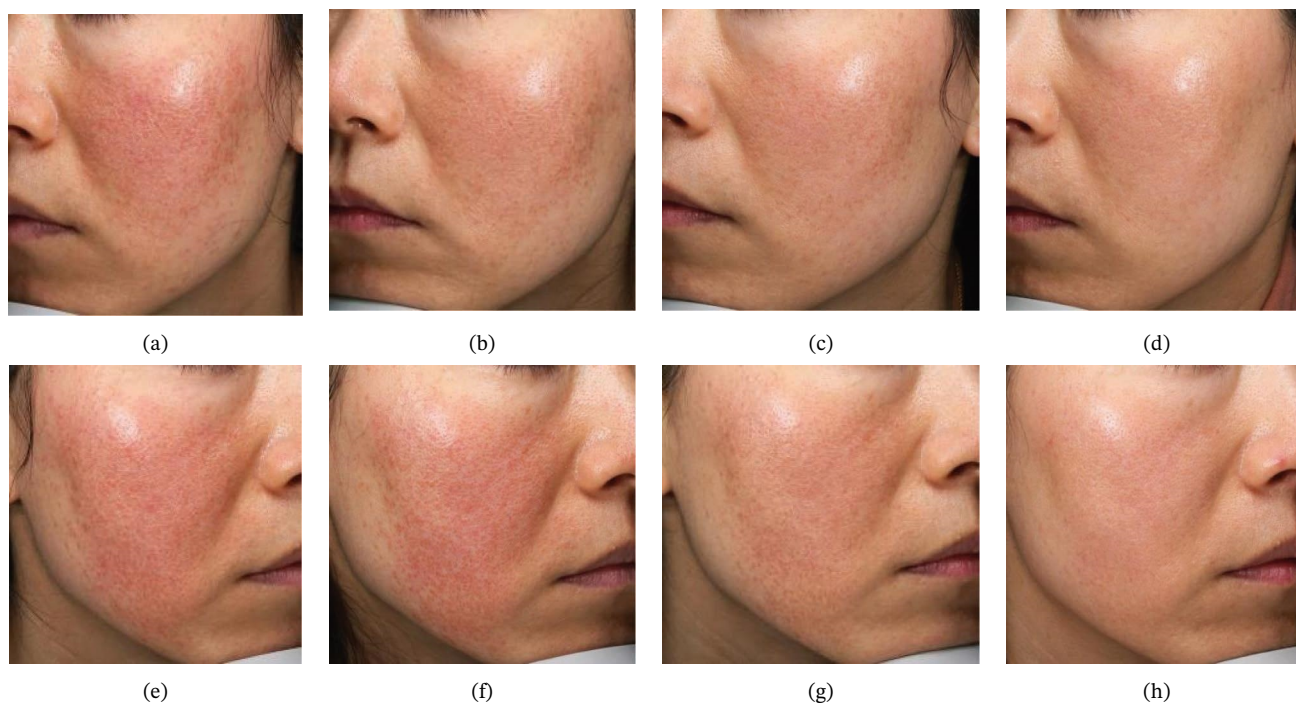


FIGURE 2 | Clinical images demonstrating the effects of creams over time. (a–d) Left cheek: baseline, 7-day, 14-day, and 28-day results after using Cream A. (e–h) Right cheek: baseline, 7-day, 14-day, and 28-day results after using Cream B.

4 | Discussion

Sensitive skin, characterized by its high susceptibility to recurrence, results from dynamic interactions between skin barrier disruption, neurovascular hypersensitivity, and innate immune-driven inflammation. Impairment of the skin barrier leads to diminished protective capacity of the TRP pathway in nerve endings [14], resulting in activation of TRP ion channels and subsequent release of vasoactive neuropeptides such as substance p (SP), calcitonin gene-related peptide, and vasoactive intestinal peptide [15]. These mediators induce cutaneous vasodilation and increased blood flow. Notably, SP further triggers mast cell degranulation, elevating proinflammatory cytokines and chemokines, which collectively contribute to inflammatory manifestations. Clinically, this cascade presents as burning sensations, stinging pain, and persistent erythema [2, 16].

The skin barrier serves as a critical defense system with dual physiological functions: the stratum corneum's "brick-and-mortar" structure physically blocks penetration of exogenous irritants, while simultaneously maintaining epidermal hydration homeostasis by preventing excessive TEWL [17–19]. Robust evidence has demonstrated significantly elevated TEWL values in patients with sensitive skin, providing an objective biomarker for impaired barrier function [20–22]. Consequently, restoration of skin barrier integrity and reduction of TEWL have emerged as cornerstone therapeutic strategies in clinical management. Long-term application of moisturizers with dual barrier-repairing and anti-inflammatory properties represents a mainstay approach for managing this condition.

A previous study demonstrated that twice-daily application of Cream B for 28 days in participants with sensitive skin significantly improved skin stratum corneum water content and roughness while effectively alleviating typical sensitive

symptoms such as itching, stinging, dryness, and tightness [5]. These improvements were attributed to the combined effects of *Prinsepia utilis* oil, β -glucan, and sodium hyaluronate in the formulation. *Portulaca oleracea* possesses anti-inflammatory and antiallergic properties, which help reduce skin irritation and enhance skin tolerance [7, 8]. *Prinsepia utilis* oil promotes the expression of key proteins involved in barrier integrity, thereby facilitating skin barrier repair [9]. β -glucan restores the damaged epidermal barrier via Dectin-1 by promoting differentiation, cell–cell junctions, and lipid synthesis [12]. However, this study did not observe a significant reduction in TEWL in participants with sensitive skin.

In our study, the reformulated Cream A contains *Polygonatum kingianum* extract, which reduces inflammatory cell infiltration and alleviates oxidative damage via the Nrf2/HO-1 signaling pathway [13]. Unpublished data from the ingredient research and development team further show that this extract significantly upregulates the expression level of the antimicrobial peptide LL-37, which helps maintain skin microecological balance and thereby synergistically repairs the skin barrier. *Citrus reticulata* peel extract inhibits the production of inflammatory mediators while promoting hyaluronic acid synthesis and the expression of key proteins such as filaggrin [10]. By strengthening intercellular tight junctions in the stratum corneum, it significantly improves skin hydration and barrier function, an effect potentially linked to increased AQP3 levels in keratinocytes and the enhanced AQP3 function [11]. A clinical observation conducted by the ingredient research and development team demonstrated that volunteers with mild atopic dermatitis and xerosis exhibited a 64% increase in SCH and a 33% decrease in TEWL following 8 weeks of treatment with 2% *Citrus reticulata* peel extract. *Prinsepia utilis* oil, ceramide, and cholesterol synergistically maintain the

structural integrity of the skin lipid layer and efficiently repair the damaged skin barrier; sodium hyaluronate, *Lithothamnion calcareum* extract, and squalane significantly enhance skin moisturizing capacity; *Portulaca oleracea* extract, *Citrus reticulata* peel extract, and *Polygonatum kingianum* extract all exhibit distinct anti-inflammatory activities. Notably, *Polygonatum kingianum* extract can maintain skin micro-ecological balance, while *Citrus reticulata* peel extract further improves skin hydration and strengthens barrier function. The scientific combination of these multiple active ingredients collectively endows Cream A with multidimensional skin barrier repair efficacy.

In this multicenter, large-scale clinical trial, we systematically compared the barrier-repairing efficacy of Cream A and Cream B by comprehensively assessing subjective facial discomfort symptoms in participants with sensitive skin and dynamically monitoring changes in physiological function indicators. Clinical evaluation and participant self-report results demonstrated that both creams showed no significant difference in alleviating common subjective discomforts such as burning, itching, and tightness in participants with sensitive skin, and both were effective in improving symptoms like dryness and desquamation. However, Cream A exhibited a more rapid improvement effect; a significant reduction in desquamation scores was observed as early as 7 days after participants started using Cream A, with a marked alleviation of desquamation symptoms. Results of physiological function tests showed that both creams improved the physiological functions of sensitive skin. After just 14 days of use, SCH values on both cheeks increased significantly ($p < 0.01$), indicating a significant enhancement of SCH capacity. Concurrently, TEWL and EI levels decreased significantly ($p < 0.01$), suggesting simultaneous skin barrier repair and inflammation reduction. However, the optimized Cream A demonstrated superior barrier-restoring effects. Specifically, EI decreased significantly after only 7 days of Cream A application, with an improvement rate of 6.1%. Its efficacy in reducing erythema was 2.6 times greater than that of Cream B, confirming its advantage in rapidly alleviating inflammation and reducing redness. By the 28-day endpoint, the improvement rate of TEWL in the Cream A group reached 25.8%, which was 56.4% higher than that in Cream B, fully highlighting its superior ability to restore skin barrier integrity. These objective improvements suggest that the optimized Cream A has significant clinical value in rapidly reducing erythema and repairing the compromised skin barrier, offering a promising long-term management strategy for sensitive skin.

5 | Conclusion

Compared with Cream B, the optimized Cream A showed a more rapid resolution of erythema and desquamation, as well as enhanced restoration of the impaired skin barrier. This suggests its potential utility as a long-term clinical management option for sensitive skin conditions.

Author Contributions

Anqi Sheng, Miaoni Zhou, Wenting Hu, and Ai'e Xu researched and/or provided data for the article. Anqi Sheng and Miaoni Zhou wrote the first

draft of the article. All authors contributed substantially to the discussion of the content and reviewed and/or edited the manuscript before submission.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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