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Revolutionizing Holistic Beauty Care with the Super-Metabiotics Platform

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1. Introduction

Recent advancements in microbiome science have significantly transformed the development of functional ingredients for skincare and overall health [1,2]. These developments highlight the intricate relationship between the skin's neuro-immuno-cutaneous (NIC) system and systemic well-being. Therapeutic modulation of the microbiome has emerged as a promising strategy to address long-standing clinical challenges. In particular, microbiome-derived metabolites provide an effective dual approach by directly influencing host physiological pathways and promoting microbiome balance. This strategy addresses key limitations associated with conventional prebiotics and probiotics, including colonization resistance, inter-individual variability, and the generalized "one-size-fits-all" model [3].

Super-Metabiotics (SM) represent an innovative platform based on a patented multi-strain co-culture fermentation technology [4]. This method integrates biomimetic fermentation with a proprietary vibrational aging process to generate a reproducible and diverse spectrum of bioactive metabolites. These compounds exhibit synergistic effects that are particularly effective in managing complex skin microecological conditions, such as sensitivity, acne [5], and age-related changes [6].

The SM fermentation process simulates human digestive conditions, supporting the growth of a diverse consortium of lactic acid bacteria under optimized parameters. Unique to this method is the inclusion of vibrational stimulation during fermentation, which enhances microbial metabolism and metabolite diversity. The resulting product—referred to as Super-Metabiotics—is rich in bioavailable and stable compounds, including amino acids, short-chain fatty acids, bioactive peptides, and flavonoids. These metabolites collectively contribute to skin microbiome regulation, barrier reinforcement, and mitigation of sensitivity-related symptoms.

The efficacy of SM in sensitive skin applications is attributed to its multi-dimensional action on the NIC system [6]. By simultaneously modulating neural, immune, and cutaneous repair pathways, SM addresses the underlying causes of skin sensitivity, inflammation, and barrier dysfunction.

Beyond dermatological applications, SM has demonstrated significant potential in oral care, vaginal microbiome health, and nutritional support via modulation of the gut–skin axis [7]. Its ability to restore microbial balance across mucosal surfaces reinforces its potential as a

comprehensive, multi-domain therapeutic ingredient. Furthermore, preliminary evidence of efficacy in pet microbiome regulation supports the concept of SM as a universal microbiome-modulating and soothing agent.

2. Materials and Methods

The SM fermentation platform ferments organic grown black soybeans (*Glycine max L.* Merrill) with a team of multiple strains of lactic acid bacteria (LAB) under biomimetic "gut like" conditions (37℃, 120 hours). Musical vibration treatment during fermentation and aging increases metabolites production. This process optimizes microbial metabolism at each growth phase, lowering the lactic acid content to enable the production of up to 500 beneficial bioactive metabolites at peak levels, including short chain fatty acids (CFAs), amino acid metabolites polyamines, and neuroactive compounds, with enhanced bioavailability and stability. We analyzed the components of SM using CE-TOFMS and LC-TOFMS techniques, and evaluated the efficacy of SM on the skin*, gut-skin axis* and its mechanism of action from the perspective of the NIC system through in vitro and in vivo studies.

3. Results

3.1 Phytochemical ingredients analysis

The Super-Metabiotics platform can be obtained both liquid (SM-L) and solid (SM-P) products through fermentation and purification technology, containing up to 511 active metabolites. Automated amino acid analysis method and HPLC method are utilized to analyze each batch of the SM series products, ensuring batch-to-batch consistency and stability.The phytochemical ingredients of Super-Metabiotics (SM) are identified through CE-TOFMS and LC-TOFMS method presented in table 1.

Table 1. Comparison of Metabolome Profiles Between Super-Metabiotics Liquid and Powder

Metabolome Profiles	Super-Metabiotics Liquid (SM-L)	Super-Metabiotics Powder (SM-P)
Identified Metabolites Number	314	511
Main Categories of Active Components	Organic acids, amino acids and their derivatives, short peptides, cyclic peptides, flavonoids and isoflavonoids, neurotransmitters and their precursors	Organic acids, amino acids and their derivatives, short peptides, flavonoids and isoflavonoids, lipids, vitamins and related compounds

3.2 Mechanistic Validation in Vitro

The Neuro-Immuno-Cutaneous (NIC) system represents the interconnected network between the nervous system, immune system, and skin barrier. This system maintains skin homeostasis, regulates responses to external stimuli, and promotes repair. Dysregulation of the NIC system contributes to inflammation, sensitivity, and skin barrier dysfunction, highlighting its importance in skin health and treatment strategies.

SM targets the Neuro-Immuno-Cutaneous (NIC) system, addressing the root causes of skin sensitivity. Its efficacy has been validated across multiple dimensions, including neurocalming effects and skin immunomodulation.

3.2.1 Neurosoothing Effects

3.2.1.1. Histamine-induced Ca^{2+} concentration in neuronal cells

Ca^{2+} influx plays an important role in the perception of pain, itch and heat, mainly through a class of ion channel receptors.Integral optical density (IOD), which reflected the Ca^{2+} concentration. HT22 cells were used as the cellular model to evaluate calcium ion influx. Histamine was applied to induce calcium ion influx, followed by co-incubation with different test groups: blank control(BC), negative control(NC), positive control (PC, trans-4-tert-butylcyclohexanol2), and 0.05% SM-L. Calcium ion levels were then measured using fluorescence labeling.

Based on neuronal cells, compared with the control group, the results showed that the Ca2+ concentration in sample group SM-L decreased significantly at the concentration of 0.05%, with the inhibition rate of 50.70%. It was considered that the sample got the neurosoothing efficacy by decreasing the Ca2+ concentration at this concentration (Figure1 and Table 2)

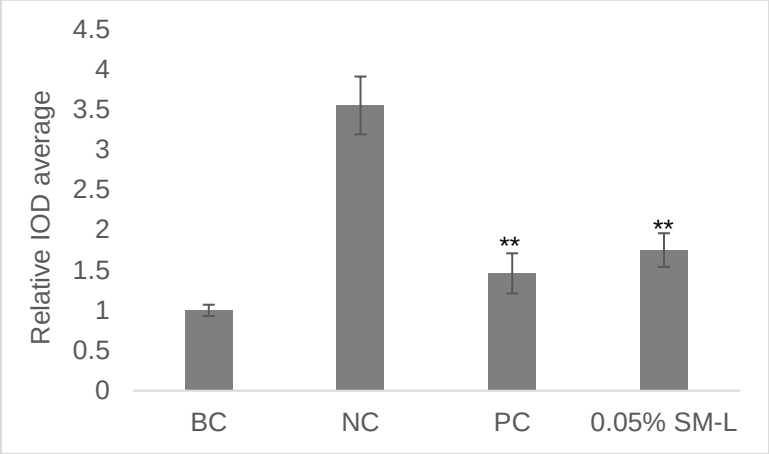
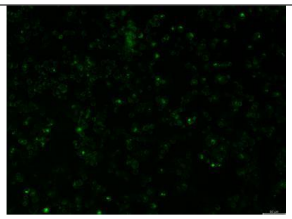
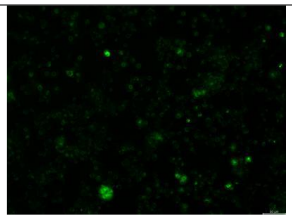
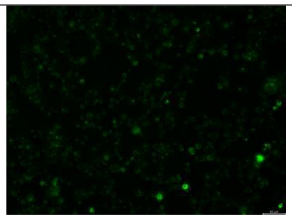
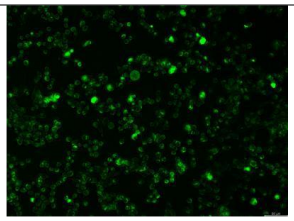
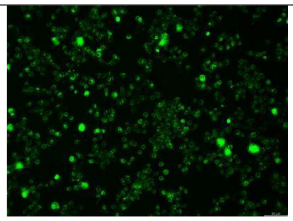
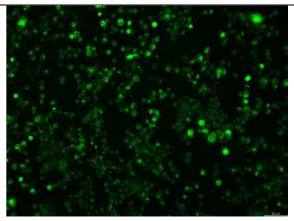
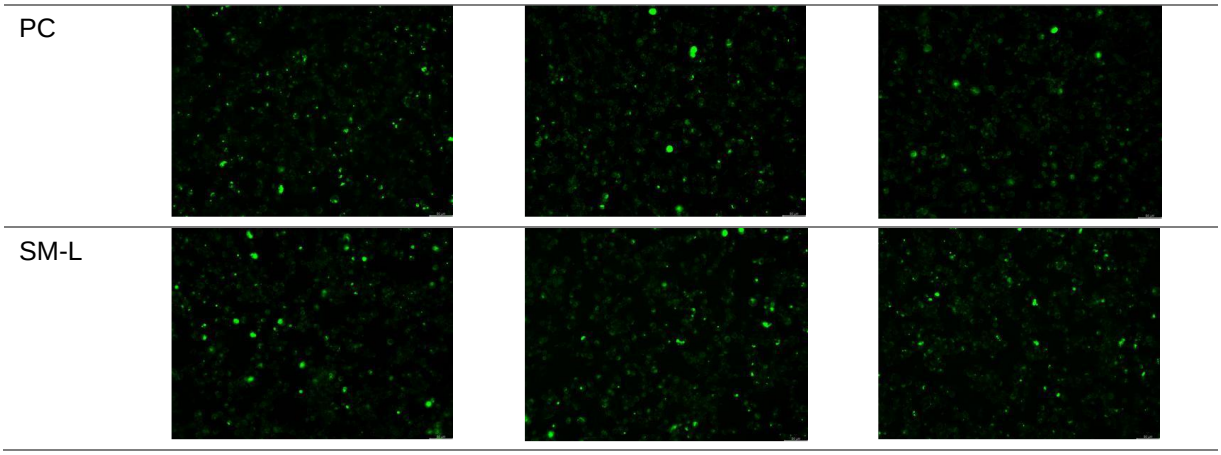


Figure 1. Histogram of the detection results of Ca2+ concentration (Compared with BC group, P-value<0.05*, P-value<0.01**; Compared with NC group, P-value<0.05*, P-value<0.01**)

Table 2. Summary table of results of fluorescence result of Ca^{2+} concentration

Groups	Rep1	Rep2	Rep3
BC			
NC			



3.2.1.2. Capsaicin-induced CGRP release in neuronal cells

Calcitonin gene-related peptide (CGRP) is a neuropeptide secreted by sensory neurons that plays a role in pain signaling, vasodilation, and the regulation of inflammatory responses.

DRG cells were used as the cellular model to evaluate CGRP release. Capsaicin was applied to induce CGRP release, followed by co-incubation with different test groups: blank control(BC), negative control(NC), 0.05% SM-L and 0.1% SM-L. CGRP levels were then measured using ELISA kit.

Based on neuronal cells, compared with the control group, the CGRP release in sample group SM-L decreased significantly at the concentration of 0.05% and 0.1%, with the inhibition rate of 46.08% and 63.04% respectively. It was concentration-dependent. It was considered that the sample got the neurosoothing efficacy by decreasing the CGRP at these concentration (Figure 2).

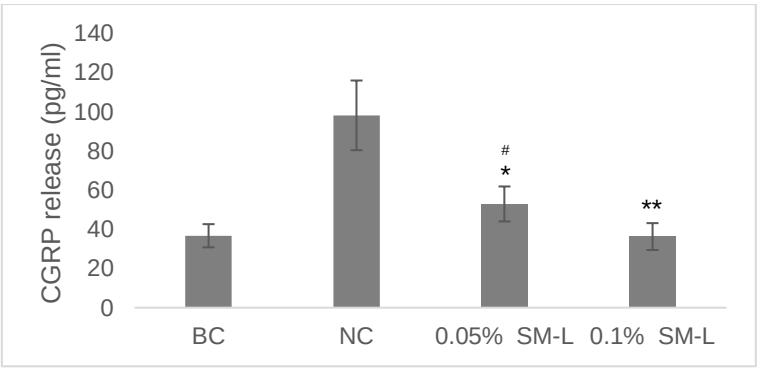


Figure 2. Histogram of the detection results of CGRP release. Compared with BC group, P-value<0.05#, P-value<0.01##; Compared with NC group, P-value<0.05*, P-value<0.01**

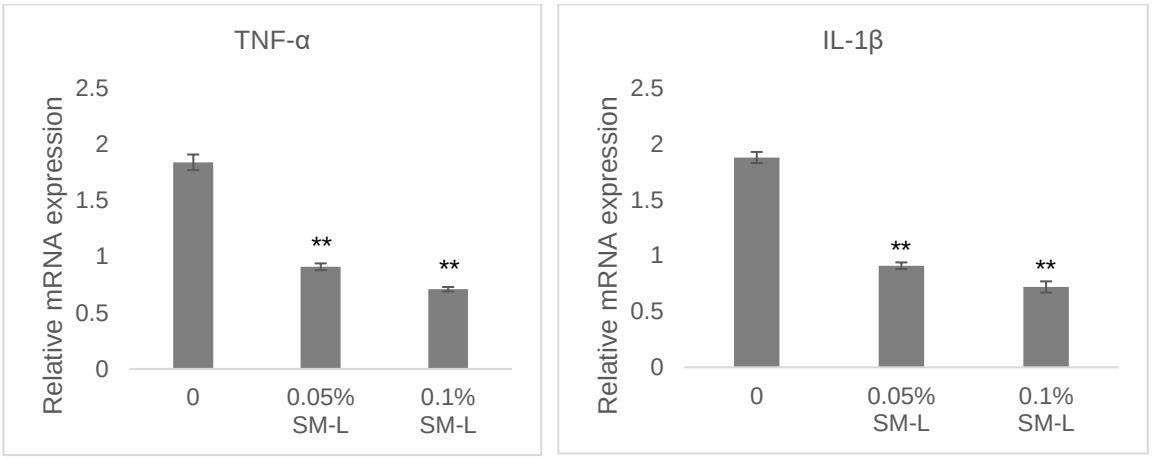
3.2.2 Immunomodulation

3.2.2.1. The three stages of inflammation (initiation, amplification, and execution)

We evaluate the immunomodulatory efficacy of SM-L across the three key stages of inflammatory amplification: initiation, amplification, and execution.Inflammatory amplification refers to the process where an initial immune response triggers a cascade of signals, causing inflammation to extend beyond its intended scope. While this amplification is essential for pathogen defense and tissue repair, excessive amplification can lead to tissue damage, chronic inflammation, autoimmune diseases, and skin sensitivity.

In the immune initiation stage, LPS-induced upstream pro-inflammatory cytokines (IL-1β, TNF-α) mRNA expression by qPCR.

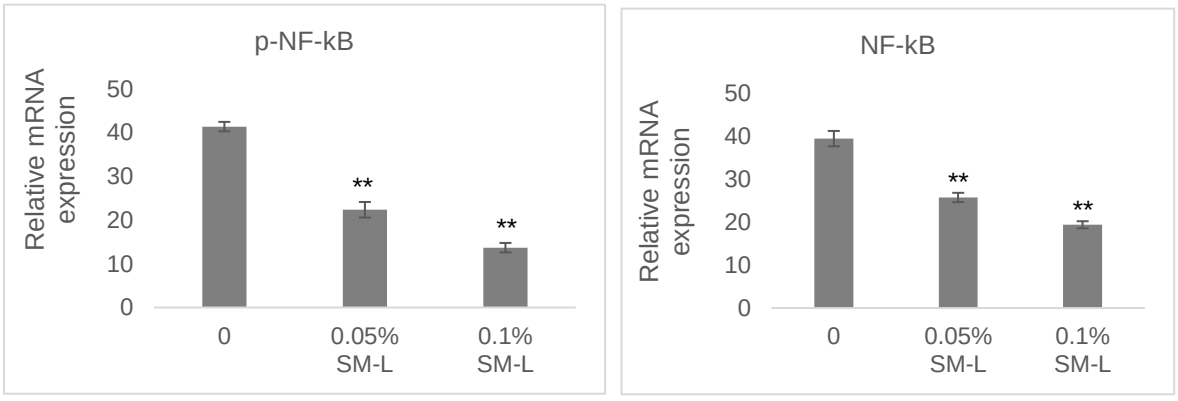
Based on human epidermal cells, compared with the control group, the TNF-α (Figure 3a) and IL-1β (Figure 3b) concentration in sample group SM-L decreased significantly at the concentration of 0.05% and 0.1%. It was concentration-dependent. It was considered that the sample may block inflammation by reducing upstream pro-inflammatory cytokines (TNF-α, IL-1β) at this concentration, thereby exerting an immunomodulatory effect.



(a) (b)

Figure 3. Relative mRNA expression of TNF-α and IL-1β in HaCaT cells pretreated with, followed by LPS stimulation. Values are presented as mean ± SD (n=3). *P < 0.05, **P < 0.01 compared to LPS-stimulated untreated cells.

In the immune amplification stage, LPS-induced key transcription factor NF-κB and p-NF-κB mRNA expression by Western Blot. Based on human epidermal cells, compared with the control group, the p-NF-κB (Figure 4a) and NF-κB (Figure 4b) concentration in sample group SM-L decreased significantly at the concentration of 0.05% and 0.1%. It was concentration-dependent. It was considered that the sample may block inflammation by reducing key transcription factor NF-κB and p-NF-κB at this concentration, thereby exerting an immunomodulatory effect.

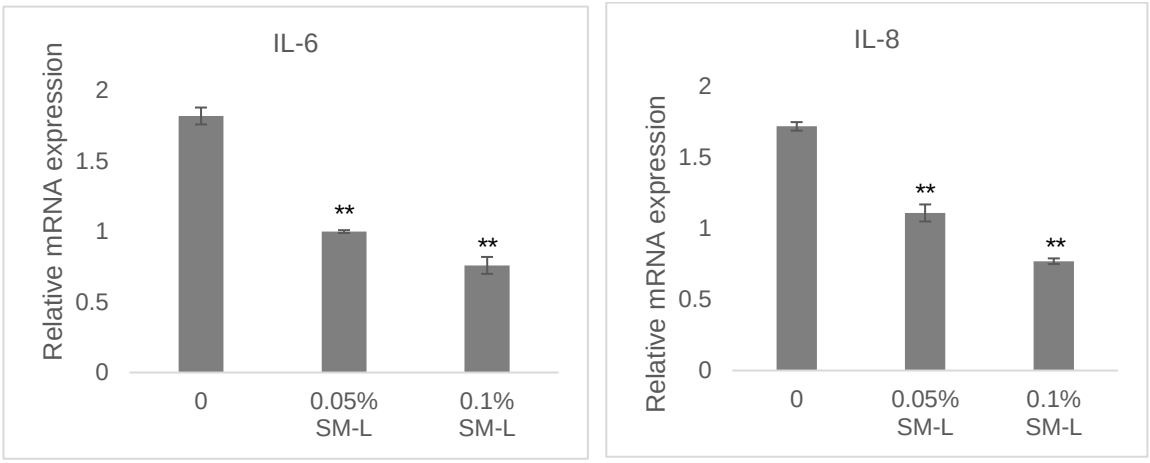


(a) (b)

Figure 4. Relative mRNA expression of NF-κB and p-NF-κB in HaCaT cells pretreated with, followed by LPS stimulation. Values are presented as mean ± SD (n=3). *P < 0.05, **P < 0.01 compared to LPS-stimulated untreated cells.

In the immune execution stage, LPS-induced downstream pro-inflammatory cytokines (IL-6, IL-8) mRNA expression by qPCR. Based on human epidermal cells, compared with the control group, the IL-6 (Figure 5a) and IL-8 (Figure 5b) concentration in sample group SM-L

decreased significantly at the concentration of 0.05% and 0.1%. It was concentration-dependent. It was considered that the sample may alleviating redness and inflammatory responses by reducing downstream pro-inflammatory cytokines (IL-6, IL-8) at this concentration, thereby exerting an immunomodulatory effect.



(a) (b)

Figure 5. Relative mRNA expression of IL-6 and IL-8 in HaCaT cells pretreated with, followed by LPS stimulation. Values are presented as mean ± SD (n=3). *P < 0.05, **P < 0.01 compared to LPS-stimulated untreated cells.

3.2.2.2. Allergic inflammation

Allergic Inflammation is an immune response triggered by allergens, involving overactivation of the immune system. It begins with allergen recognition by IgE antibodies bound to mast cells, leading to the release of histamine, cytokines, and other mediators. This causes symptoms like redness, swelling, itching, and pain.

Set the concentration gradient test group (0.005/0.01/0.02/0.03% SM-L) and control. Using human myeloma cell line U266 as a model, the concentration of IgE was detected by ELISA and microplate reader.

Compared with the control group, the IgE concentration (Figure 6) in sample group SM-L decreased significantly and shown concentration-dependent. It was considered that the sample may reduce allergic inflammation by reducing allergy-inducing factors IgE at this concentration, thereby exerting an immunomodulatory effect.

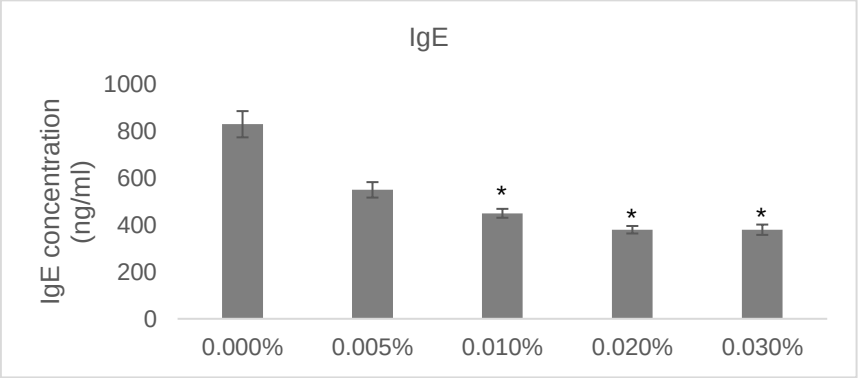


Figure 6. Histogram of the detection results of IgE release. Values are presented as mean ± SD (n=3). *P < 0.05.

3.3 Clinical trials

3.3.1. Regulate skin microbiome and pH

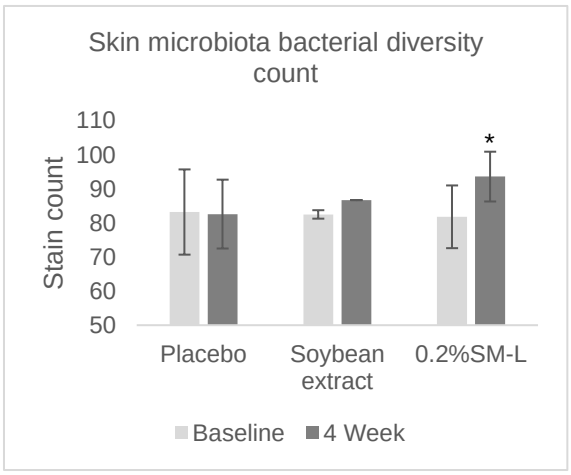
This study included 30 participants, comprising male and female subjects aged 25 to 50 years (inclusive). Participants applied a body cream containing either a placebo, 2% soybean extract, or 0.2% SM-L once daily for 4 weeks. The impact of the product on the skin microbiome was assessed across three dimensions: microbial diversity, symbiotic bacterial abundance, and skin pH levels.

The study revealed that the SM-L group significantly enhanced skin parameters. Neutral skin pH was maintained, skin moisture content increased, and skin microbiota diversity showed a notable improvement in the SM-L group compared to the placebo group after 4 weeks (Figure 7b). While the soybean extract group demonstrated moderate improvements over the placebo group, no changes in skin parameters were observed in the placebo group.

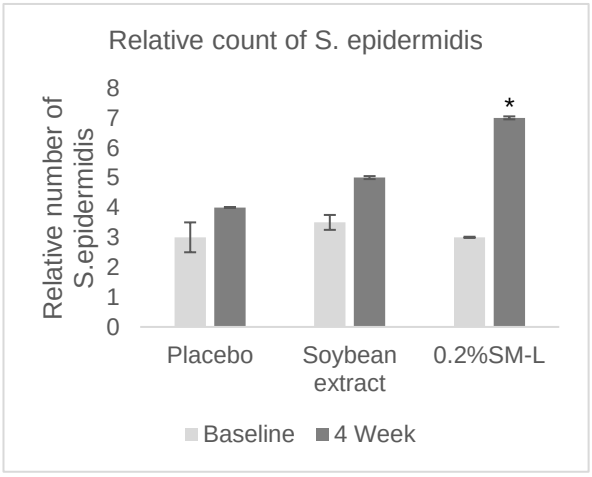
Key findings for the SM-L group:

- Skin microbiota diversity: Increased by 13.31% (Figure 7a)
- S. epidermidis count: Increased by 75% from the initial concentration (Figure 7b)
- Skin pH: Maintained at 5.5 (Figure 7c)

Furthermore, the SM-L group was well-tolerated. This study suggests that incorporating Super-Metabiotics as a nutritional supplement may enhance skin moisture content, increase the diversity of beneficial skin bacteria, and contribute to overall skin health.



(a)



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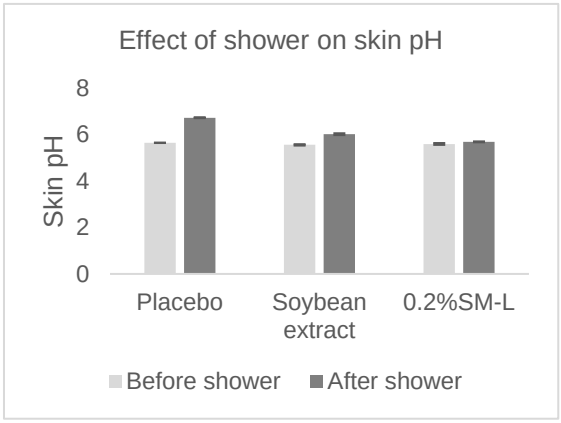


(c)

Figure 7. (a) Histogram of Skin microbiota bacterial diversity count (*P-value<0.05**), (b) Histogram of Relative count of S. epidermidis (*P-value<0.05**), (c) Histogram of skin pH change

3.3.2. Soothes skin discomfort

12 participants with healthy skin, aged 18-60 years, were included in the study. The test was conducted on facial skin using a 0.05% SM-L group versus a placebo. A 10% lactic acid solution was applied to the test area, and participants evaluated the sensation at 0, 2, 4, and 8 minutes after application. When the sensation intensity score exceeded 3, the test lotion was applied, and pain intensity was assessed at T0, T2, T4, and T8 minutes following the application of the lotion.

At 4 minutes, and 8 minutes post-application, the differences in scores and total scores between the investigation product and the control product were statistically significant ($P < 0.05$) (Figure 8). At all evaluated time points, the median scores and total scores for the group using the investigation product were lower than those of the control group, indicating that the soothing effect of the SM-L group was superior to that of the blank control.

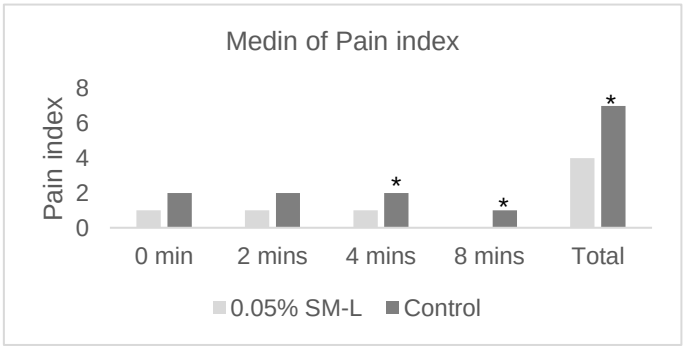
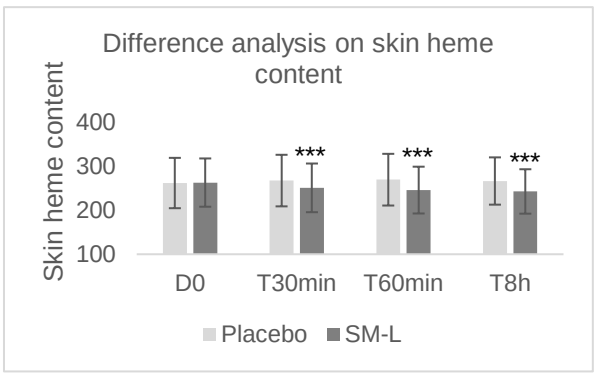


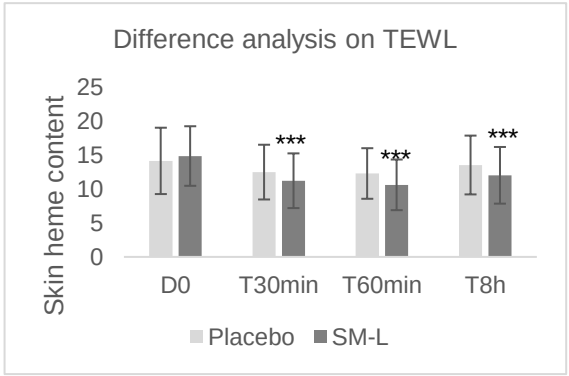
Figure 8. Histogram of Medin of pain index (*P-value<0.05**)

3.3.3. Reduces erythema and improves trans epidermal water loss

The study included 30 participants with healthy skin, aged 20-57 years. Testing was conducted on inner forearm, comparing the effects of a 0.2% SM-L solution to a placebo. A 3% SLS solution was applied to the test area, and participants evaluated skin sensations at 0, 30 minutes, 1 hour, and 8 hours post-application. Erythema and trans epidermal water loss were subsequently analyzed using relevant instruments to assess skin response.

After applying the test products, skin heme content and TEWL on the inner forearms showed a significant decreasing trend at T30min, T60min, and T8h. The changes in the test product group were greater than those in the placebo group, indicating that the test product effectively repaired the skin barrier (Figure 9b) and reduced skin heme content under the test conditions (Figure 9a).





(a) (b)

Figure 9. (a) Histogram of skin heme content (*P-value<0.001****), (b) Histogram of skin TEWL (*P-value<0.001****)

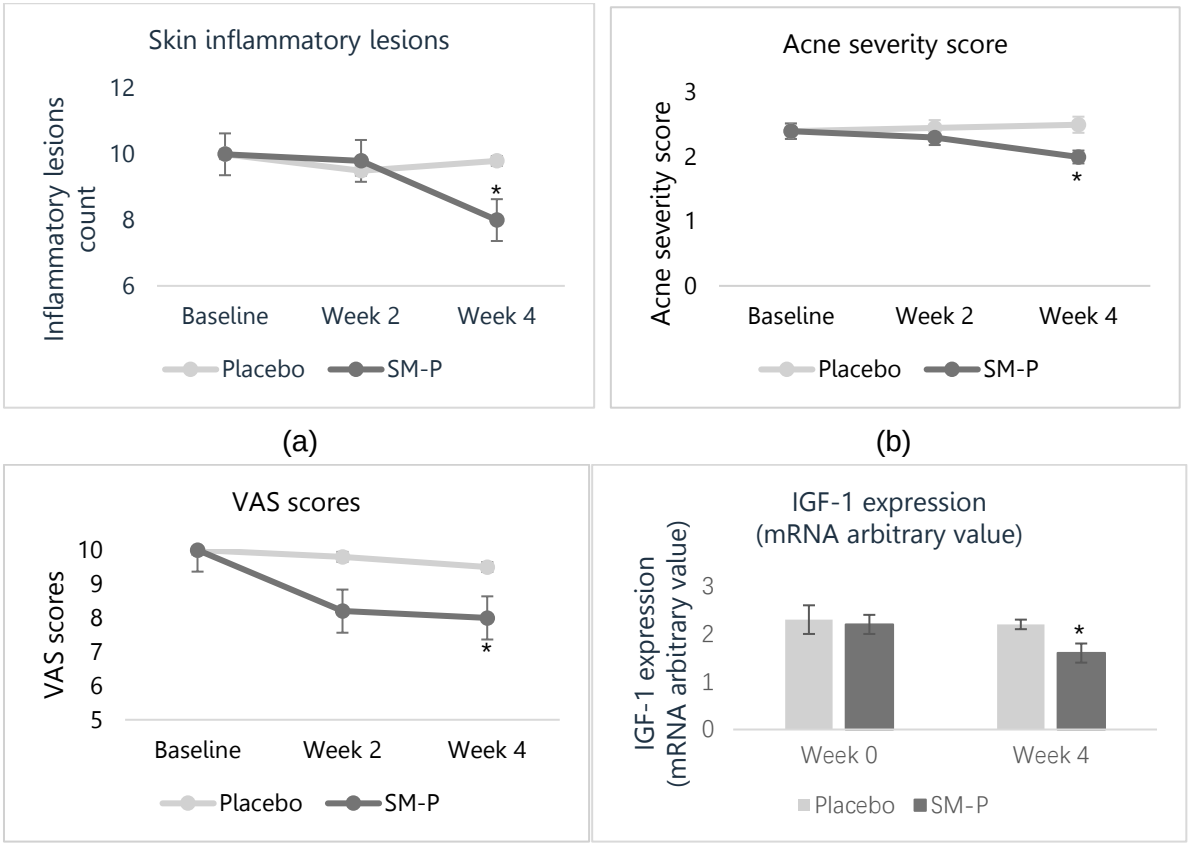
1.4 Enhance skin barrier function and reduce acne inflammation through the gut-skin axis.

The gut-skin axis highlights the connection between gut microbiota and skin health, where a balanced gut microbiome supports skin barrier integrity and reduces inflammation by modulating immune responses and producing beneficial metabolites, such as short-chain fatty acids, contributing to healthier, more resilient skin.

A prospective, randomized, double blind, two arm, parallel, placebo controlled clinical study evaluate the effectiveness of the Super-Metabiotics powder(SM-P) on acne severity and inflammation through gut-skin axis.

60 subjects were enrolled and randomly assigned in a 1:1 ratio to 2 groups: the treatment group received SM-P, while the other group received a placebo.

The results showed that taking SM-P at a dosage of 100mg/day for 4 weeks, , the degree of inflammatory lesions (Figure 10a, Figure 10d) and acne severity of facial skin (Figure 10b, Figure 10c) of the subjects were significantly reduced compared with Placebo.



(a) (b)

(c) (d)

Figure 10. Analysis of Skin inflammatory lesions (a), Acne severity (b), VAS scores (c) at the time points (Baseline, Week2, Week4). Analysis of IGF-1 expression values (d) at the time points Week 0 and Week 4. *p<0.05 vs. Baseline.

4. Discussion and Conclusion

The Super-Metabiotics multi-strain fermentation platform utilizes advanced biomimetic fermentation technology that mimics human digestive conditions to ensure the production of a stable, highly effective, and broadly adaptable portfolio of metabolites, collectively referred to as Super-Metabiotics. The Super-Metabiotics multi-strain fermentation platform represents a paradigm shift in microbiome-based skincare, leveraging cutting-edge biomimetic multi-lactic-acid bacteria strains fermentation technology to provide highly effective and versatile solutions for sensitive and damaged skin.

Super-Metabiotics' ability to holistically regulate the neuro-immune-cutaneous (NIC) system through Neurosoothing Effects / Immunomodulation / Skin repair, and the gut-skin axis makes it a transformative ingredient in dermatological innovation. Clinical and scientific evidence highlights its efficacy in enhancing microbial diversity, reducing inflammation, and strengthening the skin barrier, while its robust stability and formulation flexibility allow for seamless integration into a variety of cosmetic and health applications. As such, this heralds a huge potential for this platform technology to address challenges such as skin sensitivity, inflammation, and a damaged skin barrier.

Super-Metabiotics offers a scientifically validated, natural and sustainable approach to multi-dimensional skin health. The superior performance of these metabolite synergic combinations represents a breakthrough in skin care, providing a natural and scientifically validated solution for multi-dimensional skin health. Super-Metabiotics not only meets current market needs, but also sets a new standard for microbiome-based skin care innovation. The platform highlights the potential to unlock the next frontier in holistic beauty and wellness using advanced fermentation science.

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