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Longitudinal Changes in Facial Bacterial Communities, Co-Occurrence Networks and Skin Barrier Function During Matrinium Salicylate-Based Skincare Intervention in Acne

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Abstract

Acne vulgaris frequently co-occurs with compromised epidermal barrier integrity and microbial dysbiosis, posing therapeutic challenges, particularly in individuals with sensitive skin. In an 8-week, two-center, open-label, randomized, parallel-group study, 131 adults with mild-to-moderate acne were evaluated across four arms: negative control (NC), matrinium salicylate ([Mat][Sal])-containing sheet mask (G1), essence (G2), and their combination (G3). Longitudinal clinical lesions and standardized physiological barrier parameters were recorded. Cutaneous bacterial community dynamics and genus-level co-occurrence networks were profiled via 16S rRNA gene sequencing at the baseline, week 4, and week 8. All [Mat][Sal] regimens induced sustained reductions in inflammatory and noninflammatory lesions. Compared with single-product regimens, the combination regimen (G3) produced greater improvements in stratum corneum hydration, transepidermal water loss, and the erythema index. Alpha diversity remained stable across visits, indicating preserved ecological richness. Community shifts were modest but significant (PERMANOVA $R^2 = 0.013–0.042$). Crucially, G3 showed key taxonomic shifts, manifesting as a significant reduction in the relative abundance of the dominant *Cutibacterium*, accompanied by an increase in the relative abundance of *Staphylococcus*. Overall, [Mat][Sal]-containing regimens provide simultaneous reductions in acne lesions and improvements in epidermal barrier function, with no significant changes in microbial alpha diversity, offering a well-tolerated, barrier-protective skincare approach.

Keywords: acne vulgaris; facial microbiome; microbial community; skin barrier; co-occurrence network; matrinium salicylate

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1. Introduction

Acne vulgaris is a chronic inflammatory dermatosis of the pilosebaceous unit, characterized by comedones, papules, and pustules, frequently culminating in postinflammatory erythema, hyperpigmentation, or scarring [1]. Global epidemiological data indicate a continuous increase in age-standardized acne incidence over recent decades [2]. Although

classically associated with adolescence, acne exhibits substantial persistence into adulthood, affecting nearly 20% of adults aged 25–39 years [3,4].

The pathogenesis of acne involves interconnected perturbations, including follicular hyperkeratinization, excess sebum production, *Cutibacterium acnes* colonization, localized inflammation, and epidermal barrier impairment [5,6]. Barrier disruption increases transepidermal water loss (TEWL) and alters cutaneous lipid and protein expression [7,8], whereas barrier integrity has been associated with both microbiome diversity and community composition in acne-affected skin [6]. These findings indicate that barrier dysfunction and microbial-community alterations are related components of the cutaneous microenvironment rather than isolated disease features. Changes in sebum production, hydration, and barrier integrity can modify microbial niches, whereas the microbial-community composition is closely linked to local inflammatory activity [5,6]. Clinical lesion counts alone therefore do not capture the full spectrum of treatment-related changes. An integrated assessment of lesion outcomes, physiological barrier parameters, and microbial-community characteristics can more fully describe changes in acne-prone skin during dermocosmetic intervention.

Dermocosmetics are increasingly integrated into acne management as monotherapy for mild cases or as adjunctive maintenance to prescription therapies. They aim to reduce lesion counts while mitigating barrier impairment and treatment-induced irritation [9]. Salicylic acid remains a standard keratolytic agent in such formulations [10,11]; nevertheless, its clinical application is occasionally limited by limited aqueous solubility and cutaneous irritation potential [12]. Matrinium salicylate ([Mat][Sal]), a supramolecular ionic salt synthesized from matrine and salicylic acid, exhibits improved water solubility, transdermal delivery, and bioactivity compared with salicylic acid [12].

Despite promising in vitro and mechanistic data, robust clinical validation of [Mat][Sal]-based dermocosmetics in human subjects remains limited. Consequently, it remains unclear whether visible clinical improvement during the use of [Mat][Sal]-containing products occurs alongside changes in barrier function and facial bacterial communities. Furthermore, whether combining different topical delivery formats, such as sheet masks and topical essences, offers broader physiological and microbiological benefits than monotherapy has not been systematically investigated. Given the involvement of microbial-community composition and interspecies relationships in acne-associated inflammation [13,14], characterizing taxonomic shifts and network co-occurrence dynamics alongside clinical and physiological outcomes provides a broader framework for interpreting treatment responses.

This study aimed to assess clinical, skin physiological and facial bacterial community changes during eight weeks of [Mat][Sal]-containing mask, essence and combined skincare regimens, with a negative control for comparison. Co-occurrence networks were examined as an exploratory description of bacterial association patterns.

2. Materials and Methods

2.1. Subjects

Healthy Chinese adults (aged 18–35 years) with mild-to-moderate facial acne were recruited. The inclusion criteria required a Huaxi sensitive skin questionnaire (SS-14) score ≥ 18 to identify participants with self-reported sensitive skin at screening [15] and ≥10 combined facial comedones and papules at the baseline. The sensitivity criterion was included to assess local tolerability alongside efficacy in participants with both acne and self-reported skin sensitivity. The exclusion criteria were: (i) pregnancy or lactation; (ii) recent use (within 4 weeks) of topical/systemic anti-acne therapeutics (including corticosteroids, antibiotics, anti-inflammatory agents and retinoids) or cosmetic procedures; (iii) known hypersensitivity to study ingredients; (iv) confounding facial dermatoses; and (v) active participation in concurrent clinical trials (Supplementary Table S1).

The study was conducted in accordance with the Declaration of Helsinki and approved by the Shanghai Ethics Committee for Clinical Research (approval No. SECCR2025-202-01; approval date: 30 September 2025). Written informed consent was obtained from all participants before enrollment.

2.2. Study Design

This 8-week, two-center, open-label, randomized, parallel-group trial was conducted across two certified testing facilities (Beijing and Hangzhou EWISH Testing Technology Co., Ltd., Beijing and Hangzhou, China). Participants were randomly assigned (1:1:1:1) to receive either the negative control (NC), the facial mask alone (G1), the essence alone (G2), or the combined regimen (G3; application protocols in Supplementary Table S2). The sample size was guided by relevant Chinese standards, including the Safety and Technical Standards for Cosmetics (2015 Edition) and Test methods for anti-acne efficacy of cosmetic products (T/CAFFCI 67-2023), with a target of at least 30 evaluable participants per group [16,17]. Additional participants were recruited to account for potential withdrawals. Participants were asked to maintain their usual diet and mild cleansing routine; they could continue using their usual non-efficacy moisturizers, sunscreens, and makeup. Other efficacy-targeted facial skincare products, including exfoliants, and cosmetic or aesthetic procedures, including light-based treatments and chemical peeling, were prohibited throughout the study.

The primary efficacy assessment focused on changes in acne volume, affected area and lesion counts from BL to W8. Efficacy, skin physiological parameters, facial imaging, and safety endpoints were evaluated at the baseline (BL), week 1 (W1), week 2 (W2), week 4 (W4), and week 8 (W8). Swab sampling for 16S rRNA sequencing was performed at BL, W4, and W8. Prior to all noninvasive evaluations, the subjects underwent facial cleansing and acclimatized for 30 min in a climate-controlled room (21 ± 1 °C; 50 ± 10% relative humidity). The overall study flow is depicted in Figure 1.

2.3. Test Products

The investigational formulations were the FUERJIA ACNE CLEANSING REPAIR MASK 2.0 (Harbin Fuerjia Technology Co., Ltd., Harbin, China) and FUERJIA ACNE CLEANSING REPAIR ESSENCE 2.0 (Guangdong Luowei Cosmetics Co., Ltd., Guangzhou, China). Both formulations contained [Mat][Sal], Punica granatum peel extract, Leptospermum scoparium extract, and asiaticoside II as core functional agents. The mask additionally contained citrus fruit extract, panthenol, and sodium hyaluronate, whereas the essence additionally contained *Saccharomyces/Laminaria* saccharide ferment and niacinamide. The NC vehicle essence was supplied by Harbin Fuerjia Technology Co., Ltd. (Harbin, China) and contained water, butylene glycol, 1,2-pentanediol and glycereth-26, without the functional agents included in the test products. Further product details are provided in Supplementary Table S2.

2.4. Clinical Assessments and Skin Physiological Measurements

At each visit, trained dermatological assessors quantified facial comedones, papules, and pustules to calculate total lesion counts. Acne severity was graded according to the Chinese Guidelines for the Management of Acne Vulgaris (2019 revision) [18]. Lesion volume and affected surface area were determined using an AEVA-HE 3D imaging system (AEVA-V4 software, version 20.03.01.05; EO-TECH, Marcoussis, France).

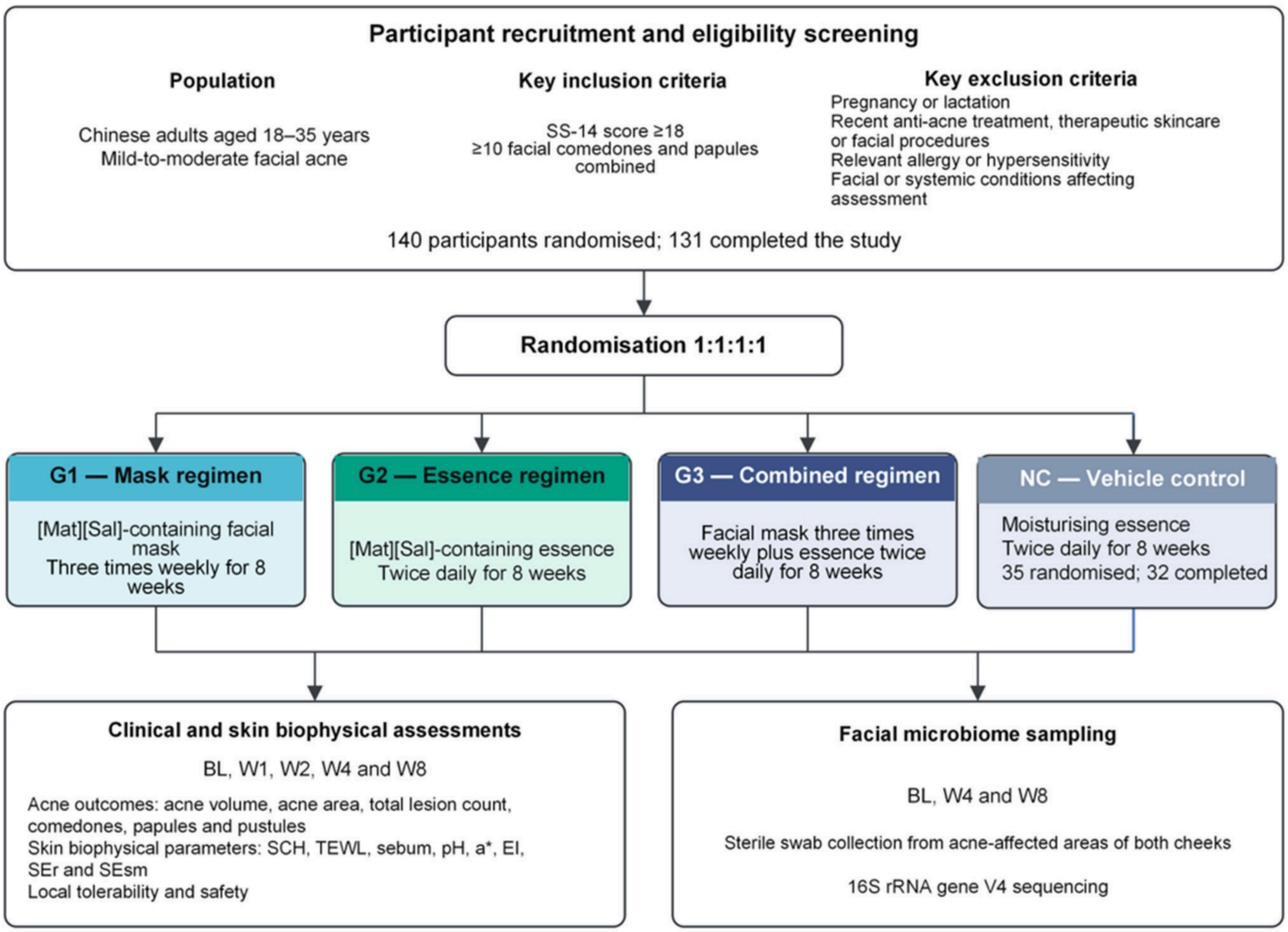


Figure 1. Study design and assessment schedule. [Mat][Sal], matrinium salicylate; BL, baseline; W, week; SCH, stratum corneum hydration; TEWL, transepidermal water loss; a*, red–green coordinate in the CIELAB color space; EI, erythema index; SEr, skin roughness; SEsm, skin smoothness.

The following noninvasive skin physiological parameters were measured under climate-controlled conditions: stratum corneum hydration (SCH), TEWL, sebum surface output, skin-surface pH, CIELAB a* value, erythema index (EI), skin roughness (SEr), and skin smoothness (SEsm). The detailed instruments and measurement procedures are provided in Supplementary Table S3. Participant-reported tolerability symptoms (itching, stinging, and burning) and assessor-evaluated signs (redness, dryness, and flushing) were recorded under standardized lighting. Adverse reactions were graded according to T/CNMIA 0015-2020 (Clinical Test Assessment of Cosmetics for Sensitive Skin) [19], and objective skin reactions were additionally scored on a 0–4 scale according to GB 17149.2-1997 [20].

2.5. Facial Microbiome Sampling and Sequencing

Facial microbial sampling was performed after a 24-h washout of facial cleansers and topical products on the sampling day. Four sterile swabs moistened with 0.9% sodium chloride containing 0.1% Tween-20 were rubbed firmly over the lesioned cheek areas for 1 min in a spiral motion. The swabs were snap-frozen in liquid nitrogen and stored at −80 °C. All samples were collected by trained personnel wearing sterile gloves, which were changed between participants to minimize cross-contamination.

The hypervariable V4 region of the bacterial 16S rRNA gene was amplified using 515F/806R primers and sequenced on an Illumina NovaSeq 6000 platform (Novogene Co., Ltd., Beijing, China). Paired-end reads were merged using FLASH v1.2.11, quality-

filtered using fastp v0.23.1, and screened for chimeric sequences using UCHIME [21,22]. Amplicon sequence variants (ASVs) were delineated using DADA2 in QIIME 2 (v2022.2) and annotated against the SILVA 138.1 database [23,24]. Sequencing depth was normalized by rarefaction prior to downstream ecological analyses.

2.6. Bioinformatic and Network Analyses

Alpha diversity was estimated using the Shannon and Chao1 indices. Beta diversity was visualized via principal coordinates analysis (PCoA) based on Bray–Curtis distances. Community dissimilarity across time points was tested using PERMANOVA (999 permutations restricted within participants to account for repeated measurements). The homogeneity of multivariate dispersion was assessed using PERMDISP. Pairwise p values were adjusted using the Holm method. Longitudinal shifts in alpha diversity and the relative abundance of key genera were tested using Wilcoxon signed-rank tests with Benjamini–Hochberg correction.

For each group, networks at BL, W4 and W8 were constructed from the same participants with sequencing samples available at all three visits. Strictly assigned bacterial genera were filtered independently within each group and visit using identical criteria: a mean relative abundance $\geq 0.1\%$ and a prevalence $\geq 30\%$. All retained genera were included as nodes, including those without inferred edges, allowing the node set to vary across visits. Edges were defined by Spearman correlations ($|r| \geq 0.60$, Benjamini–Hochberg-adjusted $p < 0.05$). Edge count, mean degree and density were calculated. Sensitivity analyses varied the mean-abundance and correlation thresholds and compared the Spearman with CLR–Pearson correlations.

2.7. Statistical Analysis

Efficacy analyses were based on the 131 participants who completed the study; the nine participants withdrew and were excluded. Data analysis was conducted using Python (v3.12) and R (v4.6.0). Continuous variables are expressed as the mean ± standard deviation (SD) or median with interquartile range (IQR). Normality was assessed using the Shapiro–Wilk test. Group comparisons at the baseline were performed utilizing one-way ANOVA. Repeated measures were analyzed using participant-clustered Gaussian GEE with group × time interactions. Acne outcomes were analyzed using Gaussian GEE on the $\log(1 + \text{raw value})$ scale; physiological outcomes were analyzed on their original or standardized scales, as appropriate (Supplementary Table S4). Longitudinal within-group changes were assessed using paired t tests or Wilcoxon signed-rank tests. Between-group differences in changes from BL, including G3 versus each single-product group, were estimated from the GEE models and reported with 95% confidence intervals (CIs). Percentage change was calculated as $(\text{follow-up} - \text{BL})/\text{BL} \times 100\%$; observations with a baseline value of zero were excluded from the corresponding percentage-change analysis. Multiple comparisons for clinical and physiological outcomes were adjusted using Holm's method. All tests were two-sided, and adjusted p values < 0.05 were considered to indicate statistical significance.

3. Results

3.1. Subject Baseline Characteristics

Of the 140 randomized subjects, 131 completed the 8-week protocol (NC: 32; G1–G3: 33 each; 9 withdrew because of nonstudy-related personal reasons). Withdrawal details are provided in Supplementary Table S5. Baseline lesion counts, sebum excretion, and SS-14 scores were well-balanced across the four groups (all $p > 0.05$). Although age differed statistically among the groups ($p = 0.004$), the group means ranged narrowly between

24.6 and 28.8 years (Table 1). This difference was deemed clinically inconsequential, as all participants were young adults within a homogeneous postadolescent age band.

Table 1. Baseline characteristics of the final analysis population.

Characteristic	NC (n = 32)	G1 (n = 33)	G2 (n = 33)	G3 (n = 33)	Total (n = 131)	p Value
Age (years)	28.8 ± 5.0	26.4 ± 4.7	24.8 ± 5.8	24.6 ± 4.7	26.1 ± 5.3	0.004
Forehead sebum (μg/cm^2)	148.8 ± 25.9	165.6 ± 30.5	161.7 ± 30.0	157.5 ± 33.0	158.5 ± 30.3	0.140
Facial comedone and papule count	26.7 ± 17.9	37.1 ± 32.9	36.8 ± 28.6	37.1 ± 22.3	34.5 ± 26.2	0.291
SS-14 score	25.2 ± 5.5	25.4 ± 3.1	26.0 ± 3.6	25.3 ± 4.2	25.5 ± 4.2	0.870

The data are presented as the mean ± SD. p values were calculated using one-way ANOVA.

3.2. Clinical Lesion Efficacy

All three regimens resulted in reductions in acne volume, affected area, and total lesion count, with significant differences versus NC at selected time points (Figure 2a–c). Specific subgroup counts of noninflammatory (comedones) and inflammatory lesions (papules and pustules) similarly decreased progressively through W8 (Figure 2d–f). Compared with G1 and G2, G3 showed greater reductions in acne area at W4 and W8 and in total lesion count than G1 at W4 (Supplementary Table S6, Panel B).

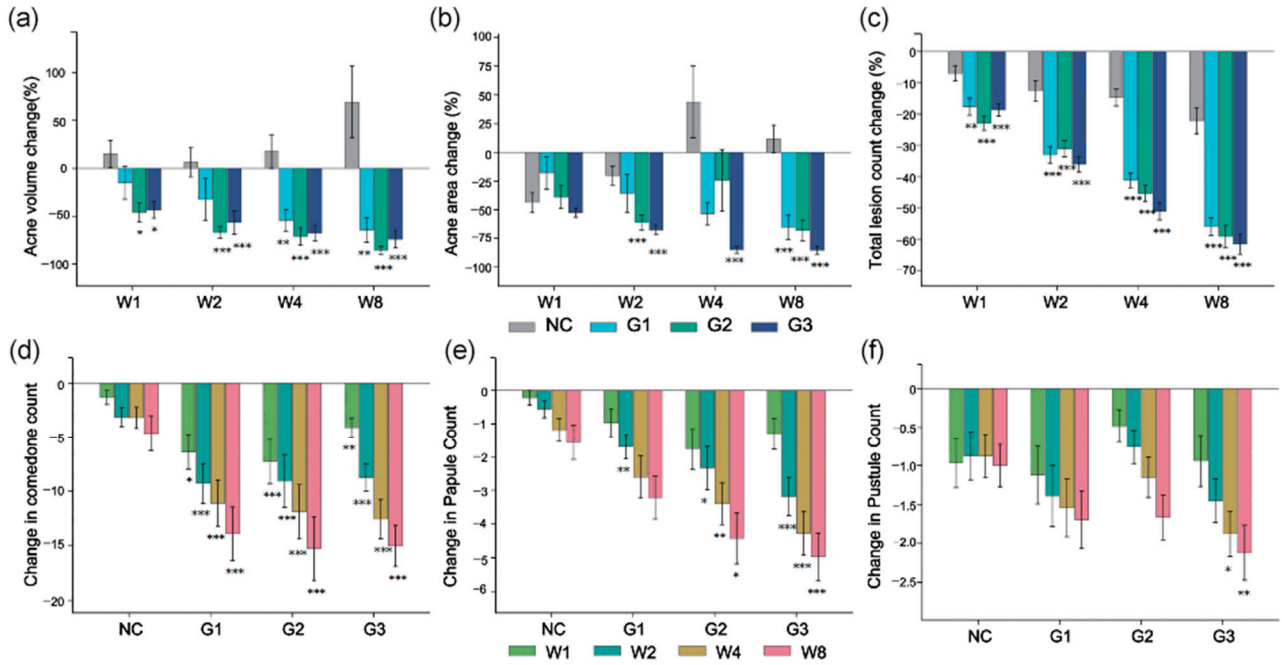


Figure 2. Changes in acne-related clinical parameters during the 8-week intervention. (**a**–**c**) Percentage changes in acne volume, acne area and total lesion count from BL at W1, W2, W4, and W8 in NC, G1, G2 and G3. (**d**–**f**) Absolute changes from BL in comedone, papule and pustule counts. The data are presented as the mean ± SEM. Asterisks indicate differences in changes from BL between each intervention group and the NC (GEE, Holm-adjusted p values): * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$.

3.3. Skin Physiological and Barrier Responses

Standardized physiological scores revealed improvements in several skin parameters in the intervention groups by W4 and W8 (Figure 3a). Compared with the NC, all three regimens showed significantly greater improvements in SCH, TEWL and a* at W4 and W8 (Figure 3b). Notably, compared with NC, G3 showed significant improvements in SCH and reductions in TEWL, a* and EI at all follow-up visits. Greater improvements in SEr were

also observed in G3 at W2, W4 and W8, and in SEsm at W2 and W8. Absolute SCH and TEWL values and W8 GEE estimates are provided in Supplementary Table S6, Panel A.

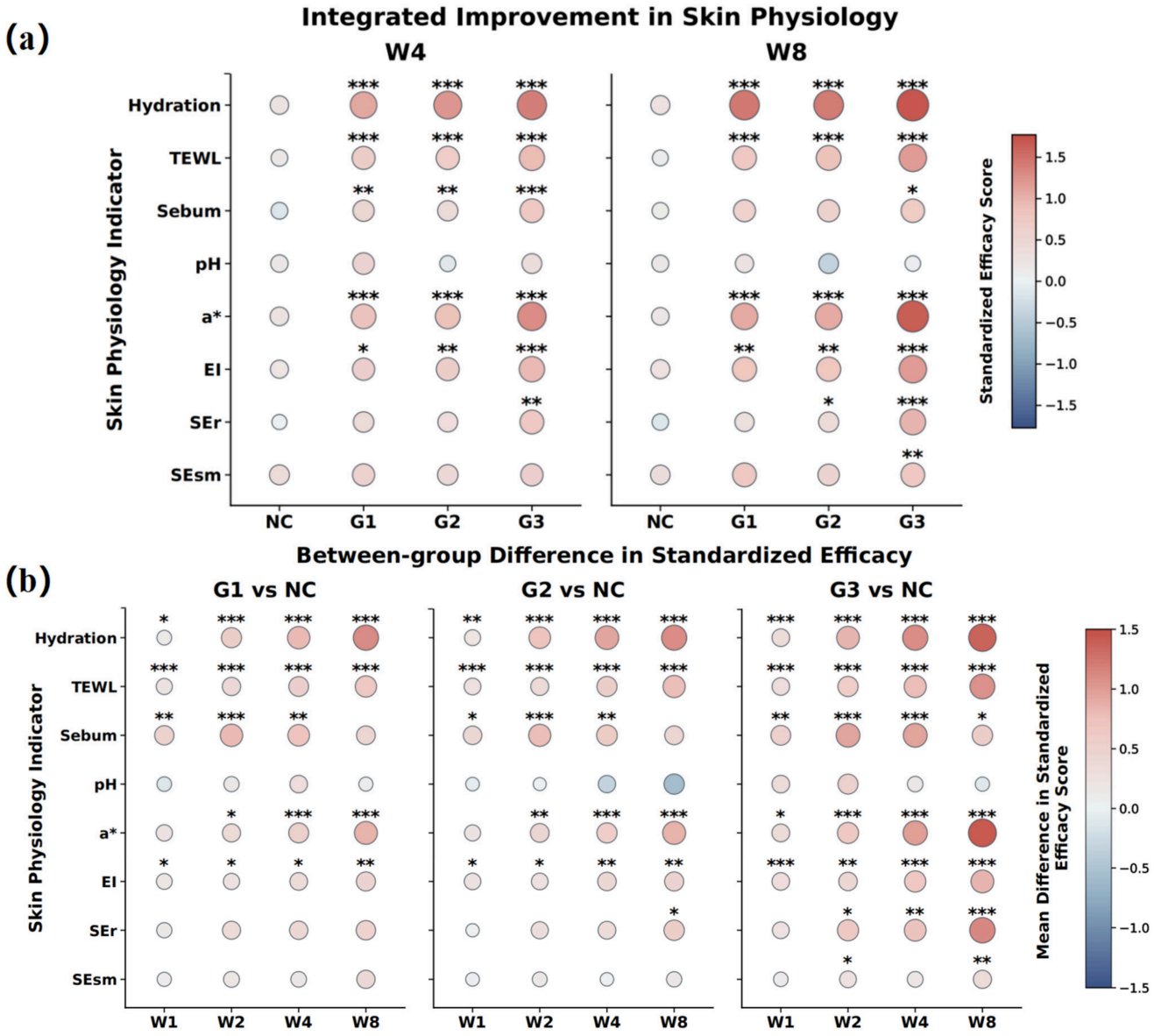


Figure 3. Integrated changes in skin physiological indicators during the 8-week intervention. (**a**) Group-mean standardized efficacy scores for SCH, TEWL, sebum, pH, a*, EI, SEr and SEsm in NC, G1, G2 and G3 at W4 and W8. (**b**) GEE-estimated differences in standardized efficacy scores for G1, G2 and G3 versus NC at W1, W2, W4 and W8. Holm-adjusted GEE p values versus NC: * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$.

3.4. Facial Microbiome Alterations

3.4.1. Diversity Metrics

Alpha diversity (Shannon index and log10-transformed Chao1 richness) exhibited no significant temporal fluctuations within G1, G2 or G3 over 8 weeks, indicating that overall microbial richness and evenness were preserved in these groups (Figure 4a). PCoA ordination based on Bray–Curtis dissimilarities revealed overlapping clusters across visits within each group (Figure 4b). Nevertheless, PERMANOVA identified statistically significant but modest longitudinal changes in all four groups (NC: $p = 0.014$; G1: $p = 0.039$; G2: $p = 0.004$;

G3: $p = 0.004$), with small explained variances ($R^2 = 0.013$–0.042). PERMDISP detected no significant differences in multivariate dispersion across visits in any group (all $p > 0.05$).

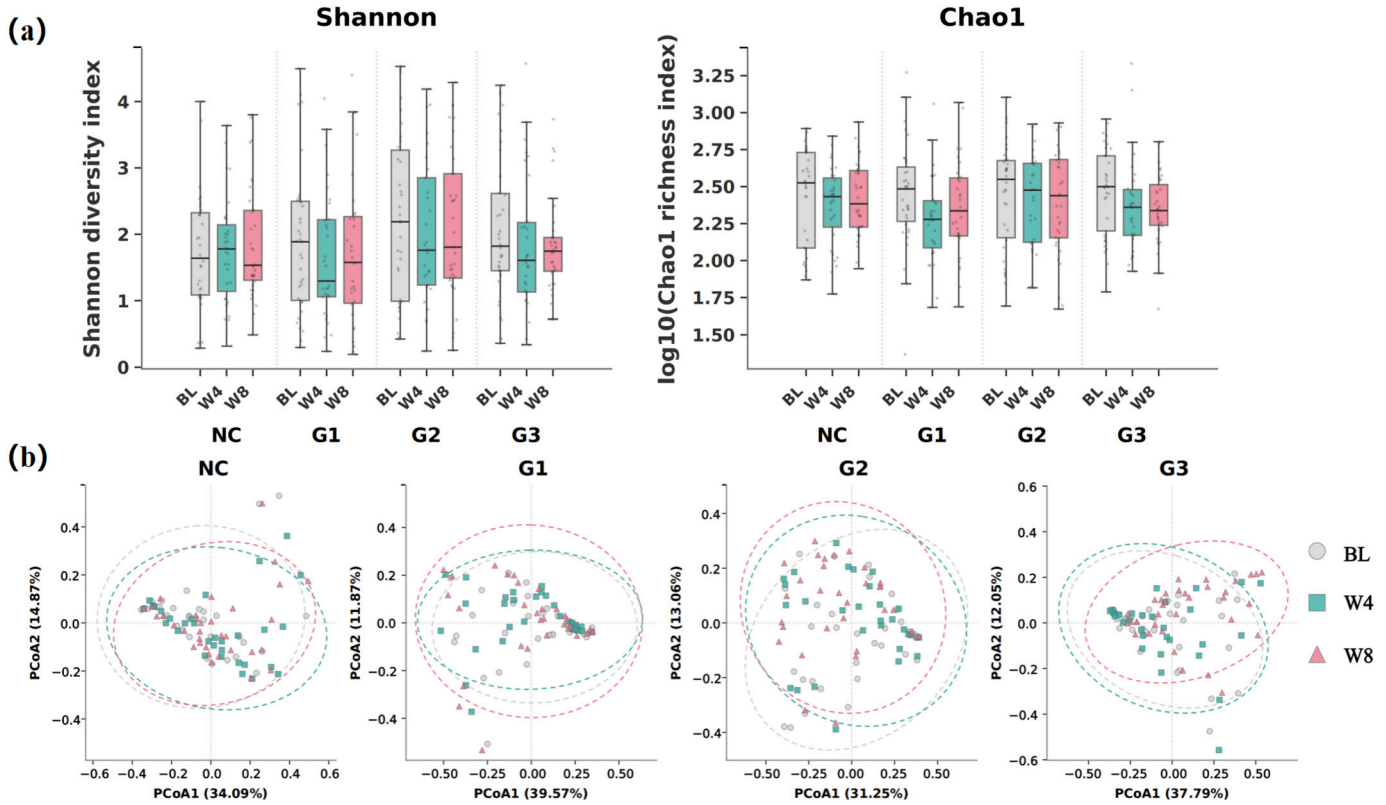


Figure 4. Changes in facial bacterial community diversity and composition during the 8-week intervention. (**a**) Shannon diversity and Chao1 richness. (**b**) Bray-Curtis PCoA ordination across time points. The gray, teal, and pink dashed ellipses show the spread of samples at baseline (BL), week 4 (W4), and week 8 (W8), respectively.

3.4.2. Taxonomic Composition and Predominant Genera

Cutibacterium and *Staphylococcus* dominated the cutaneous bacterial profiles across all four groups (Figure 5a). Over time, the relative abundance of *Cutibacterium* generally decreased, whereas that of *Staphylococcus* increased. The decline in *Cutibacterium* was most noticeable in G3 (from 50.39% at BL to 42.85% at W8; FDR-adjusted $p = 0.043$; Figure 5b). Conversely, the relative abundance of *Staphylococcus* significantly increased from the baseline to W8 in all four groups (Figure 5c), with G3 showing a greater increase in BL–W8 than NC (Holm-adjusted $p = 0.040$).

3.5. Ecological Network Topology

Exploratory genus-level networks showed different temporal patterns across the NC, G1, G2 and G3 groups (Figure 6a,b). From BL to W8, edge counts increased in all four groups, whereas density increased in NC and G3 but decreased in G1 and G2. The G2 edge counts decreased at W4 before increasing at W8 (Supplementary Table S7). Node degree did not directly mirror taxonomic abundance: despite its substantial increase in abundance, *Staphylococcus* maintained a low node degree across all groups, while *Cutibacterium* remained weakly connected in G3 (Figure 6b). The increases in edge count and average degree in G3 were consistent across the tested settings, but the changes in density were less robust (Supplementary Table S8).

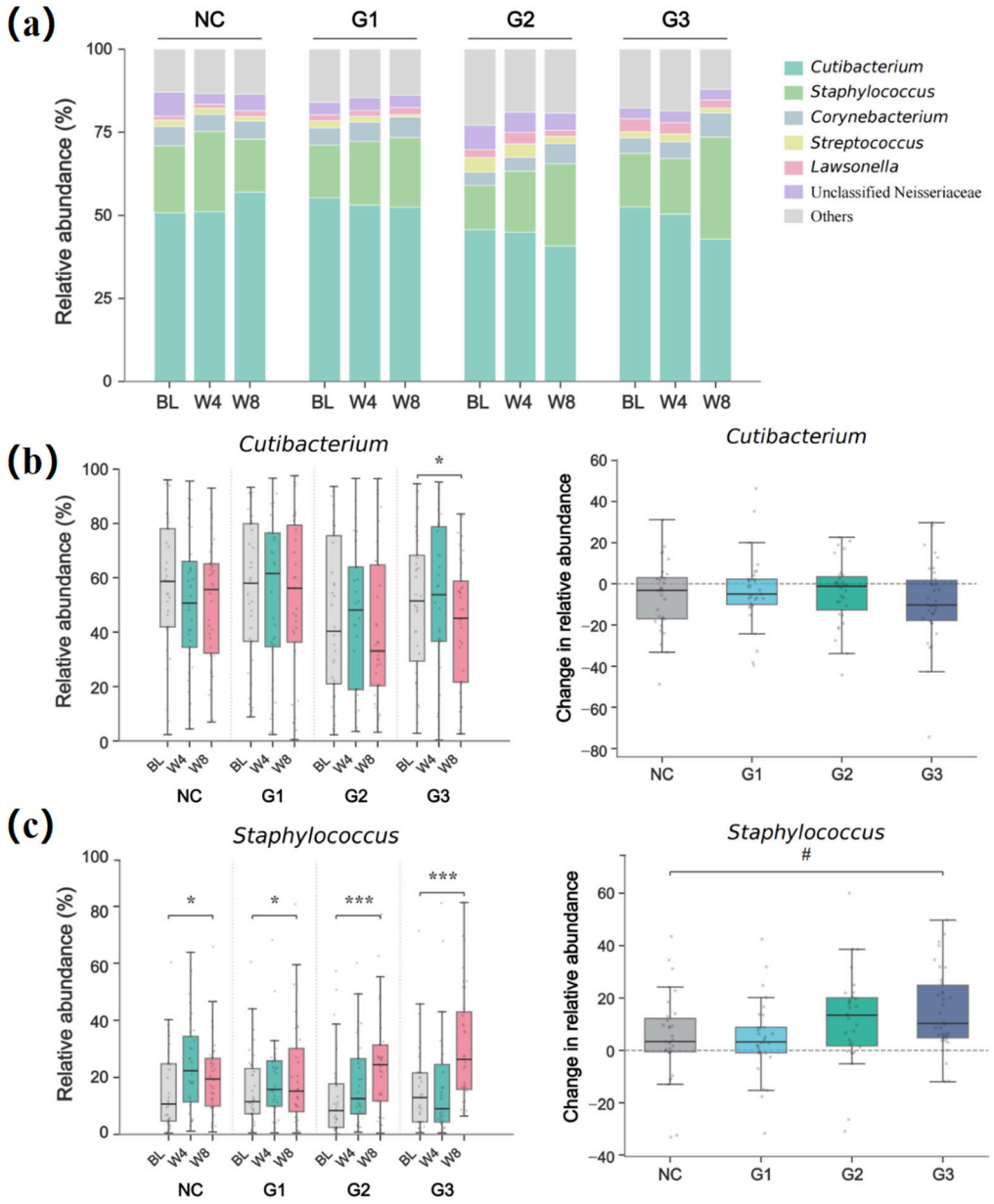


Figure 5. Genus-level composition of the facial bacterial community and changes in predominant genera during the 8-week intervention. (**a**) Relative abundances at BL, W4 and W8. (**b**,**c**) Relative abundances at BL, W4 and W8 (**left**) and BL-to-W8 changes (**right**) for *Cutibacterium* and *Staphylococcus*. Paired Wilcoxon tests (BL–W8, BH-FDR): * $p < 0.05$ and *** $p < 0.001$; Mann–Whitney U tests (BL-to-W8 changes vs. NC, Holm): # $p < 0.05$.

3.6. Safety and Local Tolerability

All formulations were well-tolerated over the 8-week period. Objective irritation scores (erythema, dryness, and flushing) and subjective symptoms (stinging, burning, and itching) decreased or remained low from BL to W8 across the four groups (Supplementary Table S9). In G3, the burning and stinging scores remained at zero throughout follow-up, whereas the itching, redness, dryness and flushing scores were lower at W8 than at BL. No discontinuations occurred because of safety concerns.

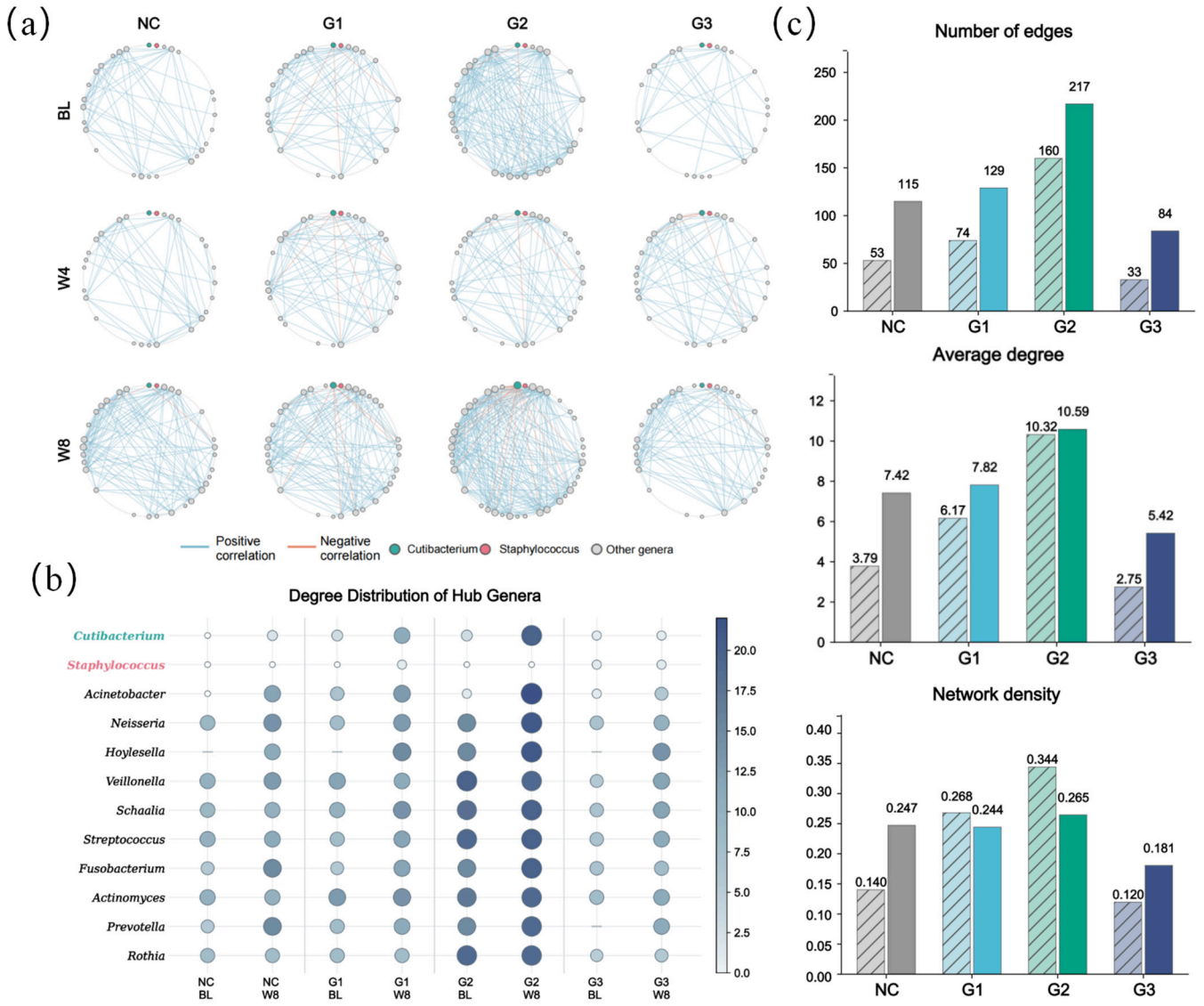


Figure 6. Exploratory genus-level co-occurrence networks in NC, G1, G2 and G3. (**a**) Co-occurrence networks constructed from genus-level relative abundance data at BL, W4 and W8. Nodes represent genera, with *Cutibacterium* and *Staphylococcus* highlighted; blue and orange edges indicate positive and negative Spearman correlations, respectively. (**b**) Degree distributions of selected genera at BL and W8 across the four groups. In panel (**b**), larger, darker circles indicate higher node degree (the number of edges connected to each genus). (**c**) Network topology characteristics at BL and W8, including the number of edges, average degree and network density. Hatched and solid bars indicate BL and W8, respectively.

4. Discussion

This eight-week study evaluated the effects of three [Mat][Sal]-containing skincare regimens in adults with mild-to-moderate facial acne. All three regimens were associated with sustained reductions in acne lesions. Compared with the use of either product alone, the combined use of the mask and essence was associated with greater reductions in acne area at W4 and W8, as well as greater improvements in selected skin physiological parameters. The clinical, physiological and microbial outcomes also followed different temporal patterns: improvements in acne lesions appeared early, whereas some physiological and microbiological changes were observed mainly later in the intervention.

Acne volume, affected area and lesion counts decreased continuously from W1 to W8, with improvements observed in both noninflammatory and inflammatory lesions (Figure 2). A recent prospective study similarly reported reductions in acne severity and sebum production following 21 days of treatment with a salicylic acid-containing gel [25]. The present study further revealed that clinical improvement was sustained through W8. Between-group comparisons showed greater reductions in affected area with G3 than with G1 or G2 at W4 and W8 (Supplementary Table S6, Panel B). The additional benefits of combined use were therefore reflected in both a greater reduction in acne area and improvements in selected skin physiological parameters. These findings may inform the selection of skincare formats for acne-prone skin, particularly when impaired hydration, barrier dysfunction, facial redness or rough skin texture accompany acne lesions.

The additional effects of combined use were particularly evident in the skin physiological measurements. The increase in SCH was greater in G3 than in G1 at W1, W2 and W4, whereas the reduction in TEWL was greater in G3 than in G1 at W8 (Figure 3, Supplementary Table S6, Panel C), indicating additional benefits in selected hydration and barrier outcomes. The reduction in a* was also greater in G3 than in both single-product groups at W4 and W8, whereas decreases in EI and the later improvements in SEr reflected reduced facial redness and improved surface texture. Acne-prone skin is frequently characterized by impaired barrier function and altered inflammatory status [6–8]; these physiological changes therefore broaden the assessment of improvement beyond lesion-related outcomes. Previous studies of ceramide-containing skincare products and moisturizers used as adjuncts to acne treatment have likewise included skin barrier restoration as an important component of acne management [26,27]. Cosmetic moisturization has also been associated with concurrent changes in skin barrier properties and microbial composition [28]. Local tolerability scores remained low or decreased across the four groups, and no participants discontinued because of safety concerns (Supplementary Table S9), indicating that all three regimens were well-tolerated throughout the eight-week study.

Microbiome changes were more apparent in community composition than in alpha diversity. Neither the Shannon diversity nor the Chao1 richness changed significantly during follow-up, whereas the Bray–Curtis PERMANOVA revealed modest temporal differences in composition across all four groups (R^2 = 0.013–0.042; Figure 4). In G3, the community composition at W8 differed from that at both BL and W4. Longitudinal observations have also revealed seasonal variation in facial microbial composition and skin biophysical parameters [29]. As reductions in acne lesions were evident earlier, the bacterial community continued to change during sustained clinical improvement. Previous skincare research has also linked selected bacterial taxa with skin characteristics [30].

The most apparent taxonomic change was a shift in the relative balance between *Cutibacterium* and *Staphylococcus* (Figure 5). The abundance of *Cutibacterium* generally decreased, whereas that of *Staphylococcus* increased from BL to W8 in all four groups. Previous studies of topical retinoic acid and benzoyl peroxide have similarly reported reductions in *Cutibacterium* relative abundance and increases or upward trends in the abundance of Staphylococcus [31,32]. In G3, most of the increase in *Staphylococcus* occurred between W4 and W8, and its BL–W8 increase was greater than that in NC. This later divergence gives the community-level change a specific taxonomic context and shows that the microbial profile continued to evolve after lesion improvement began. Previous studies have demonstrated strain-dependent differences in the inflammatory properties of *C. acnes* and *S. epidermidis* [33–38], highlighting the importance of species- and strain-level characterization.

Exploratory co-occurrence networks revealed changes in genus-level association patterns across all four groups (Figure 6), an analytical perspective also adopted in recent acne skincare research [39]. From BL to W8, edge counts increased in every group, with

increases in network density in NC and G3 (Supplementary Table S7). Changes in the NC may reflect temporal variation or influences of the vehicle formulation and permitted routine skincare [28,29]. In G3, the increases in edge count and mean degree persisted across the tested analysis settings, whereas the density results were less consistent (Supplementary Table S8). The increase in the relative abundance of *Staphylococcus* was not matched by a comparable increase in node degree, indicating that abundance and association patterns captured different features of the changing community.

Several limitations of this study warrant consideration. The findings relate to adults with mild-to-moderate acne who met the questionnaire-based skin sensitivity criterion. Efficacy analyses included only study completers, and no sensitivity analysis was performed to assess the impact of withdrawals; potential attrition bias therefore cannot be excluded. Although the tested formulations showed clinical benefits, the specific contribution of [Mat][Sal] warrants further evaluation because both products contained multiple functional ingredients. The eight-week follow-up does not establish whether the clinical and physiological improvements persist after discontinuation. Permitted home skincare products and concomitant medication and supplement use were not fully standardized during follow-up, potentially contributing to variability in the observed outcomes. Microbiome analysis was based on 16S V4 sequencing and relative-abundance data; absolute bacterial abundance was not quantified, and functional differences at the species or strain level could not be resolved. Co-occurrence networks represent statistical associations, and some topology measures varied across analytical settings.

5. Conclusions

After 8 weeks, all three [Mat][Sal]-containing regimens showed sustained reductions in acne lesions and good local tolerability. Compared with single-product use, combined use of the mask and essence showed greater reductions in affected acne area and greater improvements in selected skin physiological parameters. These clinical improvements occurred without significant changes in cutaneous microbial alpha diversity. Changes in genus-level relative abundance included a significant decrease in Cutibacterium and an increase in Staphylococcus in G3, alongside changes in genus-level co-occurrence networks. Collectively, these findings support the tested [Mat][Sal]-containing formulations as a well-tolerated, barrier-protective skincare approach for acne-prone skin.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/cosmetics13060306/s1, Table S1: Complete inclusion and exclusion criteria; Table S2: Study products and application regimens; Table S3: Skin physiological and imaging assessment parameters; Table S4: Definitions and calculation of standardised improvement scores for skin physiological parameters; Table S5: Participant withdrawals by group and follow-up visit; Table S6: Clinical and skin physiological outcomes with comparisons versus NC and between skincare regimens; Table S7: Sample inclusion and main-analysis network parameters at each timepoint; Table S8: Sensitivity of BL-to-W8 network changes to mean-abundance threshold and correlation method; Table S9: Local tolerability scores in NC, G1, G2 and G3 during the 8-week intervention.

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Data Availability Statement: The raw 16S rRNA gene sequencing data generated and analysed during the current study have been deposited in the NCBI Sequence Read Archive (SRA) under BioProject accession PRJNA1514939. Additional data supporting the findings of this study are available from the corresponding author upon reasonable request, subject to applicable ethical and privacy restrictions.

Conflicts of Interest: Y.Z., L.W. and T.L. are employees of Harbin Fuerjia Technology Co., Ltd., which developed the investigational facial mask and essence evaluated in this study and manufactured the facial mask. S.C. and J.W. are employees of Beijing EWISH Testing Technology Co., Ltd. The company had no role in the design of the study; in the collection, analyses or interpretation of data; in the writing of the manuscript; or in the decision to publish the results. The remaining authors declare no conflicts of interest.

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