

ORIGINAL ARTICLE OPEN ACCESS

Short-Term Topical Retinol Use Is Associated With Improved Pore-Related Parameters and Shifts in the Facial Skin Microbiome

Hye Rim Do¹ | Suyeon Kim² | Hye Lim Keum¹ | Hye-Jin Kim¹ | Taehun Park² | Sue Im Jang² | Susun An² | Jaeil Han² | Woo Jun Sul¹ 

¹Department of Systems Biotechnology, Chung-Ang University, Anseong, Republic of Korea | ²Amorepacific Corporation, R&I Center, Yongin, Republic of Korea

Correspondence: Woo Jun Sul (sulwj@cau.ac.kr)

Received: 28 November 2025 | **Revised:** 10 April 2026 | **Accepted:** 13 May 2026

Keywords: acne vulgaris | cosmetics | retinol | skin health | skin microbiome

ABSTRACT

Background: Retinol is widely used for acne-prone skin and is known to affect keratinization and sebum-related processes. However, longitudinal human data on how topical retinol use relates to changes in the facial skin microbiome remain limited.

Aims: To evaluate temporal changes in facial pore-related parameters and the skin microbiome during short-term use of a retinol-containing product in individuals with acne-prone skin, and to explore whether the addition of a low-dose polylysine altered the overall response pattern.

Methods: Forty-three Korean women with acne-prone skin used a retinol-containing product for 4 weeks. Skin parameters and facial skin microbiome profiles, assessed by 16S rRNA gene sequencing, were evaluated at baseline (week 0), week 1, and week 4. Participants used either 0.03% retinol alone or 0.03% retinol plus 0.0002% polylysine. As no broad between-formulation differences in community structure were detected, the primary longitudinal microbiome analyses were performed in the pooled cohort.

Results: Acne lesion counts, including whiteheads, blackheads, and inflammatory papules, decreased at week 4 compared with baseline. Selected skin physiological parameters also improved, with reductions in transepidermal water loss and sebum level at week 4. Pore-related parameters, including total pore volume, maximum pore depth, pore count, and pore area, were also reduced at week 4 compared with baseline. Microbiome analyses demonstrated significant temporal shifts in community composition across visits, along with significant changes in alpha diversity over time.

Conclusions: In this exploratory study, short-term topical retinol use was associated with improvements in multiple acne- and pore-related skin parameters, together with concurrent temporal shifts in the facial skin microbiome. Larger studies with longer follow-up and mechanistic endpoints are needed to clarify the clinical relevance and underlying biological pathways.

1 | Introduction

The skin microbiome comprises diverse and dynamic communities of microorganisms, including bacteria, fungi, viruses, and mites, that inhabit the skin surface and appendages [1, 2]. These

communities contribute to skin homeostasis by supporting barrier integrity, modulating immune responses, and providing colonization resistance against potential pathogens. Disruption of this balanced ecosystem (dysbiosis) has been associated with inflammatory skin disorders and altered skin physiology [3, 4].

Hye Rim Do and Suyeon Kim contributed equally to this study.

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This microbial ecosystem maintains a close, bidirectional relationship with host physiology. Microbial metabolites and structural components can influence keratinocyte differentiation, tight-junction formation, and local immune signaling. Conversely, host factors such as sebum composition, lipid availability, pH, and hydration shape microbial niche availability, particularly on sebaceous facial skin [5, 6]. Accordingly, changes in the cutaneous environment may drive structural and functional shifts in resident microbiota.

Facial pores, the visible openings of pilosebaceous follicles, are central to sebum secretion and moisture regulation. When pores become obstructed with excess sebum and cellular debris, they contribute to comedone formation and acne pathogenesis [7, 8]. Because sebaceous glands and follicular environments provide key niches for specific commensals, follicular morphology is intrinsically linked to the skin microbiome [9]. In acne-prone skin, microbial imbalance, often characterized by changes in *Cutibacterium* spp. (including *Cutibacterium acnes*), has been associated with follicular inflammation and lesion development [10, 11].

Retinol, a precursor to retinoic acid, is widely used to support skin health and improve acne-prone skin [12–15]. It modulates keratinocyte turnover and follicular keratinization and can influence sebaceous gland activity, thereby improving acne lesions and skin texture [16, 17]. By altering the cutaneous microenvironment through changes in desquamation, follicular patency, and lipid availability for lipophilic commensals, retinol may also reshape host–microbe interactions [18, 19]. However, longitudinal human data characterizing how topical retinol use relates to temporal changes in the facial skin microbiome remain limited.

To optimize acne management, retinoids are sometimes combined with antimicrobial agents to more directly address dysbiosis-related features [20]. Polylysine is a cationic polymer with broad-spectrum antimicrobial activity, primarily mediated by disruption of bacterial membranes [21–23]. In the present study, polylysine was included at a low concentration to explore whether its addition altered the clinical or microbiome response observed with retinol alone.

In this exploratory study, we investigated temporal dynamics of facial pore-related parameters and the skin microbiome during 4 weeks of topical retinol use in acne-prone individuals. The comparison between the two formulations was exploratory and was intended to assess whether the addition of low-dose polylysine substantially altered the overall response pattern. Our primary aim was to characterize short-term, retinol-associated temporal changes in clinical and microbiome features, while interpreting microbiome findings as descriptive and hypothesis-generating rather than mechanistic proof.

2 | Materials and Methods

2.1 | Study Participants and Collection of Skin Microbiota

To evaluate temporal changes in facial skin parameters and the acne-prone skin microbiome during topical retinol use,

Korean female participants aged 20–39 years with ≥ 10 facial acne lesions were recruited in a single-center study conducted from June to August 2021. Exclusion criteria included pregnancy or breastfeeding; dermatologic disorders other than acne; use of systemic or topical antibiotics or acne treatments within the previous 4 weeks; use of functional anti-acne cosmetics within the previous week; or retinoid- or laser-based procedures within the previous 6 months. Enrollment was restricted to females to reduce biological heterogeneity related to sex-associated differences in sebum production, hormonal milieu, and skincare practices that may confound pore-related and microbiome endpoints. This design improved cohort homogeneity for the present exploratory study, although it limits generalizability to broader populations.

A total of 43 participants (mean age, 27.93 ± 4.80 years) were enrolled and allocated to two product groups: Group A ($n = 21$), which used a cream containing 0.03% retinol, and Group B ($n = 22$), which used the same formulation with the addition of 0.0002% polylysine. Participants were instructed to apply the assigned product twice daily (morning and evening) for 4 weeks. To standardize background skincare, all participants received standardized basic skincare products (skin softener and lotion) prepared by the manufacturer and were instructed to maintain a consistent routine throughout the study. Participants were also instructed not to initiate or change other topical or systemic acne-related treatments during the study period, including topical antibiotics, benzoyl peroxide, salicylic acid or other exfoliating acids, corticosteroids, and additional retinoids. Protocol adherence and adverse events were reviewed at each visit.

Clinical assessments and sample collection were performed at three time points: week 0 (baseline), week 1, and week 4. At each visit, participants acclimatized in a climate-controlled room ($22^{\circ}\text{C} \pm 2^{\circ}\text{C}$ and $50\% \pm 5\%$ relative humidity) for at least 15 min before visual assessment. For microbiome sampling, a 4 cm^2 area of one cheek was swabbed using a sterile dry rayon swab (108C, COPAN) for at least 1 min; swabs were used dry to preserve the native skin surface condition. After microbiome sampling, participants washed their faces and underwent a second 20-min acclimatization under the same environmental conditions, after which instrumental biophysical measurements were performed on the contralateral cheek to minimize potential interference from the prior swab procedure. After collection, samples were stored at -80°C until DNA extraction. The study protocol was approved by the Institutional Review Board, and all procedures were conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent.

2.2 | Measurement of Skin Parameters

Skin parameters including acne severity, transepidermal water loss (TEWL), hydration, sebum, and pore-related indices were assessed at week 0, week 1, and week 4.

Acne severity was evaluated by counting lesions on the entire face excluding the nose. Non-inflammatory lesions (open and closed comedones) and inflammatory lesions (papules, pustules,

and nodules) were counted independently by two investigators. Inter-rater reliability was assessed using the intraclass correlation coefficient (ICC); when ICC exceeded 0.8, the mean of the two assessments was used for analysis.

TEWL on the cheek was measured using the Vapometer SML-4001 (Delfin, Finland). Skin hydration was measured three times on the cheek using the Corneometer CM 825 (C + K, Germany), and the mean value was recorded. Sebum level was measured on the forehead using the Sebumeter SM810 (C + K, Germany). For sebum area measurements, UV frontal images acquired using VISIA CR (Canfield, USA) were analyzed with Image-Pro Plus (Media Cybernetics, USA). Pore-related parameters (total pore volume, maximum pore depth, pore count, and pore area) were measured on the cheek using ANTERA 3D CS (Miravex Limited, Ireland). Instrument-based measurements were conducted using standardized procedures at consistent facial sites across visits.

2.3 | DNA Extraction and 16S rRNA Gene Sequencing

Bacterial genomic DNA was extracted from skin swabs using the Invitrogen PureLink Genomic DNA Mini Kit (Life Technologies) with bead-beating (5 mm stainless steel beads; Bead Beater 16, Bio Spec Products Inc.) during Proteinase K processing. The Gram-Positive Bacterial Cell Lysate procedure was performed according to the manufacturer's instructions. After extraction, gDNA quantity and purity (A260/A280) were measured using NanoDrop 2000 (Thermo Fisher Scientific Inc.). For 16S rRNA gene amplification, extracted DNA was used as the PCR template with a standardized setup using a fixed input volume of 2.5 μ L per sample, corresponding to an average DNA input of approximately 2.5 ng based on the mean extracted DNA concentration.

The V4–V5 hypervariable region of the 16S rRNA gene was amplified using primers 16S 518F (TCG TCG GCA GCG TCA GAT GTG TAT AAG AGA CAG CCA GCA GCY GCG GTA AN) and 16S 926R (GTC TCG TGG GCT CGG AGA TGT GTA TAA GAG ACA GCC GTC AAT TCN TTT RAG T). PCR conditions were initial denaturation at 95°C for 3 min; 33 cycles of 95°C for 30 s, 55°C for 30 s, and 72°C for 30 s; and final extension at 72°C for 5 min [24]. Purified amplicons were sequenced on the Illumina MiSeq platform.

2.4 | Analysis of Bacterial Communities

Microbial community analysis was performed using QIIME 2 [25]. Sequence reads underwent primer sequence removal from both forward and reverse sequences using the cutadapt plugin [26]. Paired-end sequence reads were merged, and sequences were denoised using the DADA2 plugin to ensure high-quality data for subsequent analyses [27]. Amplicon sequence variants (ASVs) were generated, and a feature table was created for all samples. Taxonomy assignment for each ASV was conducted using the feature-classifier classify-sklearn plugin with the Greengenes database [28]. Additionally, chloroplast and mitochondrial sequences from the host were excluded from both the feature table and the FASTA file. The resulting 6399 ASVs were

aligned using phylogeny align-to-tree-mafft-fasttree. Alpha diversity indices (Shannon and Faith's phylogenetic diversity) and beta diversity (unweighted UniFrac distance) were calculated using diversity core-metrics-phylogenetic with a sampling depth of 6300 reads [29, 30].

2.5 | Statistical Analysis

All statistical analyses and visualizations were performed in R [31]. Clinical data on skin parameters were presented as mean values with standard deviations. As most clinical parameters did not meet the assumption of normality, non-parametric tests were employed. For longitudinal comparisons across the three time points (week 0, week 1, and week 4), overall differences were assessed using the Friedman test. When the Friedman test indicated significant differences ($p < 0.05$), post hoc pairwise comparisons between time points were performed using the paired Wilcoxon signed-rank test.

Because the comparison between the two formulations was exploratory, the primary inferential analyses focused on longitudinal changes across visits. Overall differences in community composition between formulations were examined using unweighted UniFrac-based ANOSIM. In the absence of a significant formulation-specific effect on broad community structure, the two groups were pooled for the primary longitudinal microbiome analyses.

Alpha diversity was quantified using the Shannon index, observed ASVs, Faith's phylogenetic diversity (Faith PD), and Pielou's evenness. Differences in skin microbiome composition over time following retinol use were evaluated by principal coordinate analysis (PCoA) based on unweighted UniFrac distances, and the ANOSIM method was used to compare microbial community shifts across different time points. To explore inferred ecological associations and network structures, microbial association networks were inferred at each sampling point (weeks 0, 1, and 4). The ASV table at each time point was normalized to the total read count per sample to obtain relative abundances. Microbial networks were built using the SParse Inverse Covariance Estimation for Ecological Association Inference (SpiecEasi) method implemented in the R package SpiecEasi [32]. Network visualization and analysis, including the calculation of clustering coefficients and graph density, were performed using the igraph package in R. Specific microbial features at different time points were identified using linear discriminant analysis effect size (LEfSe) [33].

3 | Results

3.1 | Temporal Changes in Skin Parameters During Use of Retinol-Containing Products

Thirteen skin parameters were measured to evaluate changes in skin status during use of the retinol-containing products (Table 1), including non-inflammatory lesions (closed and open comedones), inflammatory lesions (papules, pustules, and nodules), skin physiological parameters (TEWL, hydration, sebum level, and U-zone sebum area), and pore-related indices (total pore volume, maximum pore depth, pore count, and pore area).

For acne lesions, whitehead counts showed a significant time effect ($p < 0.0001$), with significant reductions at week 1 and week 4 relative to baseline ($p = 0.0004$ and $p < 0.0001$, respectively), as well as a further reduction from week 1 to week 4 ($p = 0.0011$). Blackhead counts also showed a significant time effect ($p = 0.0002$) and were reduced at week 4 compared with baseline ($p = 0.002$). Inflammatory papule counts showed a significant time effect ($p = 0.0223$) and were likewise reduced at week 4 versus baseline ($p = 0.006$).

All pore-related parameters showed significant time effects, including total pore volume ($p < 0.0001$), maximum pore depth ($p = 0.0053$), pore count ($p < 0.0001$), and pore area ($p = 0.0421$). Each parameter decreased at week 4 compared with baseline ($p < 0.0001$, $p = 0.0006$, $p < 0.0001$, and $p = 0.0331$, respectively). Skin physiological parameters also improved, with significant time effects for TEWL ($p = 0.0189$) and sebum level ($p = 0.0061$) and reductions at week 4 versus baseline ($p = 0.0134$ and $p = 0.0006$, respectively). Hydration level and U-zone sebum area showed descriptive changes but did not reach statistical significance ($p = 0.2778$ and $p = 0.4863$, respectively).

Representative VISIA CR and ANTERA 3D CS images at week 0, week 1, and week 4 are provided as visual examples of the temporal changes observed in the quantitative findings (Figure 1).

3.2 | Comparison of Skin Bacterial Communities Between Retinol and Retinol-Polylysine Formulations

In total, 129 samples from 43 participants were collected for 16S rRNA gene sequencing (V4–V5 region). Across all samples, 9885946 paired-end reads were generated and merged into 7746543 high-quality reads, yielding an average of approximately 60050 merged reads per sample. All libraries passed quality control and provided sufficient sequencing depth for downstream 16S rRNA gene profiling.

To assess whether the addition of polylysine altered the overall response pattern, we first compared Group A and Group B (Figure 2A). No significant between-formulation difference in overall bacterial community composition was detected by unweighted UniFrac-based ANOSIM ($p > 0.05$), and the measured clinical outcomes showed comparable temporal patterns between the two groups. Because the between-formulation comparison was exploratory and no broad formulation-specific effect was detected, the two groups were pooled for the primary longitudinal analyses across visits (weeks 0, 1, and 4).

Using the pooled dataset, community composition shifted significantly across sampling points (ANOSIM, $p = 0.001$) (Figure 2B), indicating time-dependent changes in the facial skin microbiome during product use. Alpha diversity was

TABLE 1 | Changes in skin parameters over time during product use.

Subject information		Total		
Subject (<i>n</i>)		43		
Age, year (range)		27.9 (20–39)		
Non-inflammatory symptom (Mean, SD)		0 Week	1 Week	4 Week
Whitehead, <i>n</i>	33.64 (17.72)	29.76 (17.06)	25.67 (14.49)	
Blackhead, <i>n</i>	8.21 (8.56)	5.97 (6.36)	5.57 (4.82)	
Inflammatory symptom (Mean, SD)		0 Week	1 Week	4 Week
Papule, <i>n</i>	17.62 (10.88)	14.26 (9.83)	14.01 (6.72)	
Pustule, <i>n</i>	8.08 (6.36)	5.74 (5.09)	6.36 (4.81)	
Nodules, <i>n</i>	0.26 (0.73)	0.16 (0.37)	0.14 (0.41)	
Skin condition measurement (Mean, SD)		0 Week	1 Week	4 Week
TEWL, g/m ² /h	17.11 (4.92)	15.86 (3.90)	16.03 (3.73)	
Hydration, %	59.56 (11.00)	60.01 (9.37)	61.93 (9.98)	
Sebum, µg/cm ²	60.49 (23.39)	53.98 (23.29)	52.81 (25.18)	
Sebum (U-zone), mm ²	6816.35 (6086.47)	5384.86 (4732.5)	5594.44 (4376.91)	
Pore-related parameter (Mean, SD)		0 Week	1 Week	4 Week
Pore total volume, µm ³	0.49 (0.27)	0.40 (0.30)	0.35 (0.21)	
Pore maximum depth, µm	0.029 (0.005)	0.027 (0.006)	0.026 (0.005)	
Pore count, <i>n</i>	222.09 (85)	188.42 (81.79)	168.35 (78.81)	
Pore area, µm ²	0.15 (0.03)	0.14 (0.04)	0.14 (0.03)	

Note: Values are presented as mean (SD). Bold text indicates a significant time effect ($p < 0.05$).

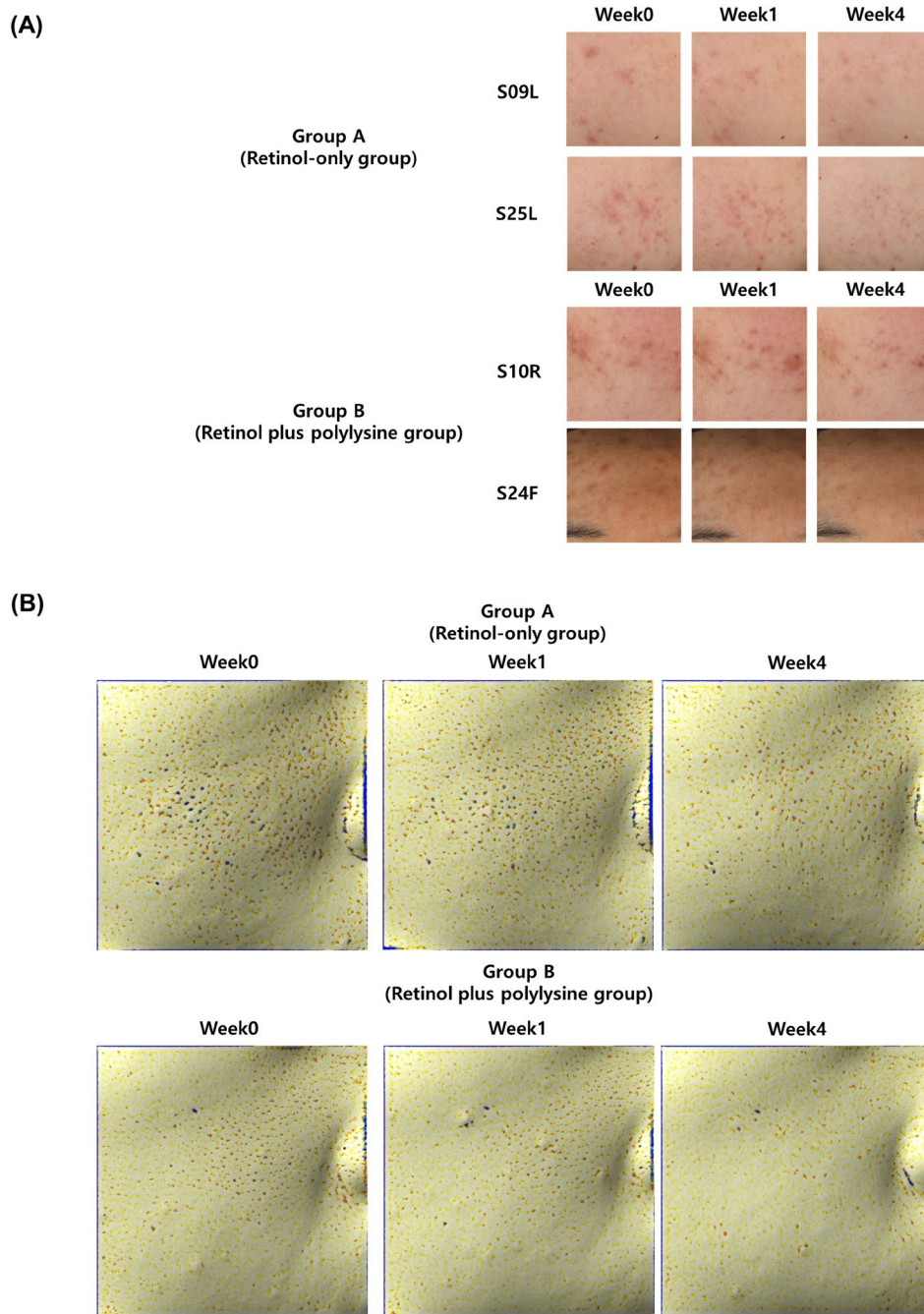


FIGURE 1 | Representative VISIA CR and ANTERA 3D CS images across three time points. (A) VISIA CR images at baseline (W0), week 1 (W1), and week 4 (W4). Regions of interest are indicated to facilitate visual comparison. (B) Corresponding ANTERA 3D CS images acquired from matched facial regions at the same time points. All images were obtained under standardized instrument settings and lighting conditions and were de-identified. L, left; R, right; F, forehead.

assessed over time using four metrics (Figure 2C). Compared with baseline, all indices except Pielou's evenness increased by week 4 ($p < 0.0001$).

3.3 | Temporal Taxonomic Shifts in Facial Skin Bacteria During Product Use

Temporal changes in bacterial composition were evaluated at the genus level using the 10 most abundant genera (Figure 3A).

Cutibacterium was dominant across all time points, followed by *Staphylococcus*; together, these genera accounted for approximately 80%–90% of the community. The relative abundance of *Cutibacterium* decreased from baseline to week 1 and returned toward baseline by week 4, whereas *Staphylococcus* showed the reciprocal pattern, increasing at week 1 and decreasing toward baseline by week 4. Additional taxa exhibited time-dependent increases by week 4, including members of the Neisseriaceae family, *Streptococcus*, and *Enhydrobacter* (Figure 3B). Compositional changes in key taxa are summarized in Supplementary Table S1.

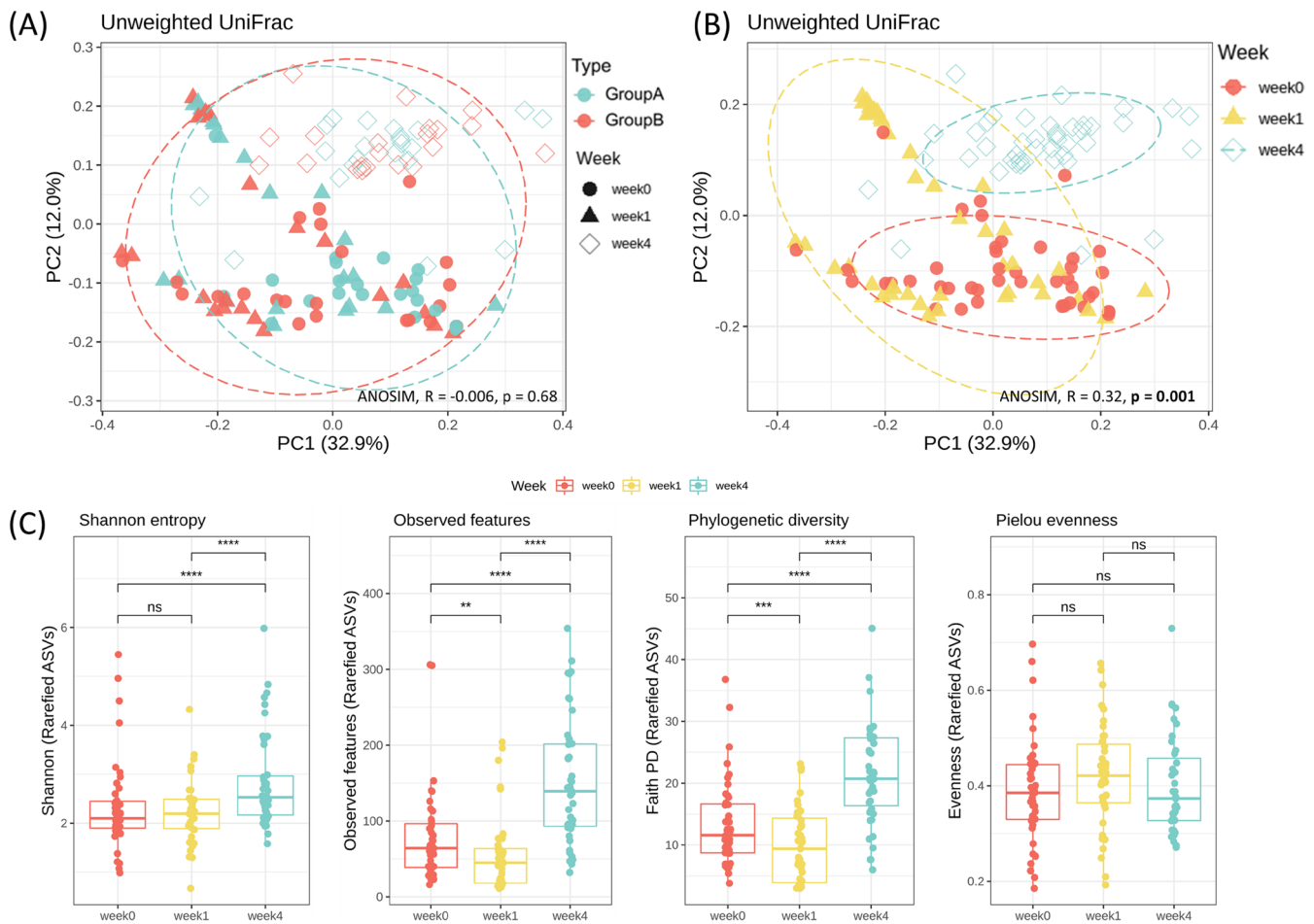


FIGURE 2 | Facial skin bacterial community structure across formulations and time points. Principal coordinates analysis (PCoA) plots based on unweighted UniFrac distances showing (A) comparison of bacterial community composition between the retinol-only and retinol-polylysine formulations and (B) temporal shifts in the pooled cohort across weeks 0, 1, and 4. No significant between-formulation difference was detected in panel A, whereas a significant temporal shift was observed across visits in panel B (ANOSIM, $p = 0.001$). (C) Alpha diversity metrics of bacterial communities across time points. Asterisks indicate significant pairwise differences calculated using the paired Wilcoxon signed-rank test (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$).

3.4 | Differentially Abundant Taxa Identified by LefSe

LefSe was used to identify taxa differing between baseline (week 0) and week 4 (Figure 4). Taxa with an LDA score ≥ 2.0 were considered discriminative. Notably, *Lactobacillus* showed higher relative abundance at week 4 compared with baseline, and this pattern remained consistent when analyses were conducted separately by product group (Supplementary Figure S1).

3.5 | Microbial Network Properties Over Time

Inferred microbial association network analysis was performed to evaluate changes in network topology during retinol use (Figure 5). In this context, network density reflects the overall extent of inferred connections among taxa, whereas transitivity reflects the tendency of connected taxa to form locally clustered groups. Network density decreased slightly from 0.0195 at week 0 to 0.0180 at week 1, suggesting lower overall connectivity early in product use. During the same period, transitivity increased from 0.163 to 0.189, indicating

greater local clustering. By week 4, network density increased to 0.0218, exceeding baseline, while transitivity decreased toward baseline (0.176). Collectively, these findings indicate time-dependent changes in microbial association network topology across the study period. Because these network metrics do not directly measure resilience, stability, or disease susceptibility, these results should be interpreted as descriptive ecological features rather than evidence of functional improvement or impairment.

4 | Discussion and Conclusion

Retinol-containing topical products are widely used to manage acne-prone skin and are known to influence keratinization and sebum-related processes [34–36]. In this study, short-term topical retinol use was associated with improvements in acne- and pore-related parameters together with time-dependent shifts in the facial skin microbiome. Given the modest sample size, single-center design, and 4-week study duration, these findings should be regarded as exploratory and hypothesis-generating. Nevertheless, they provide a structured description of concurrent

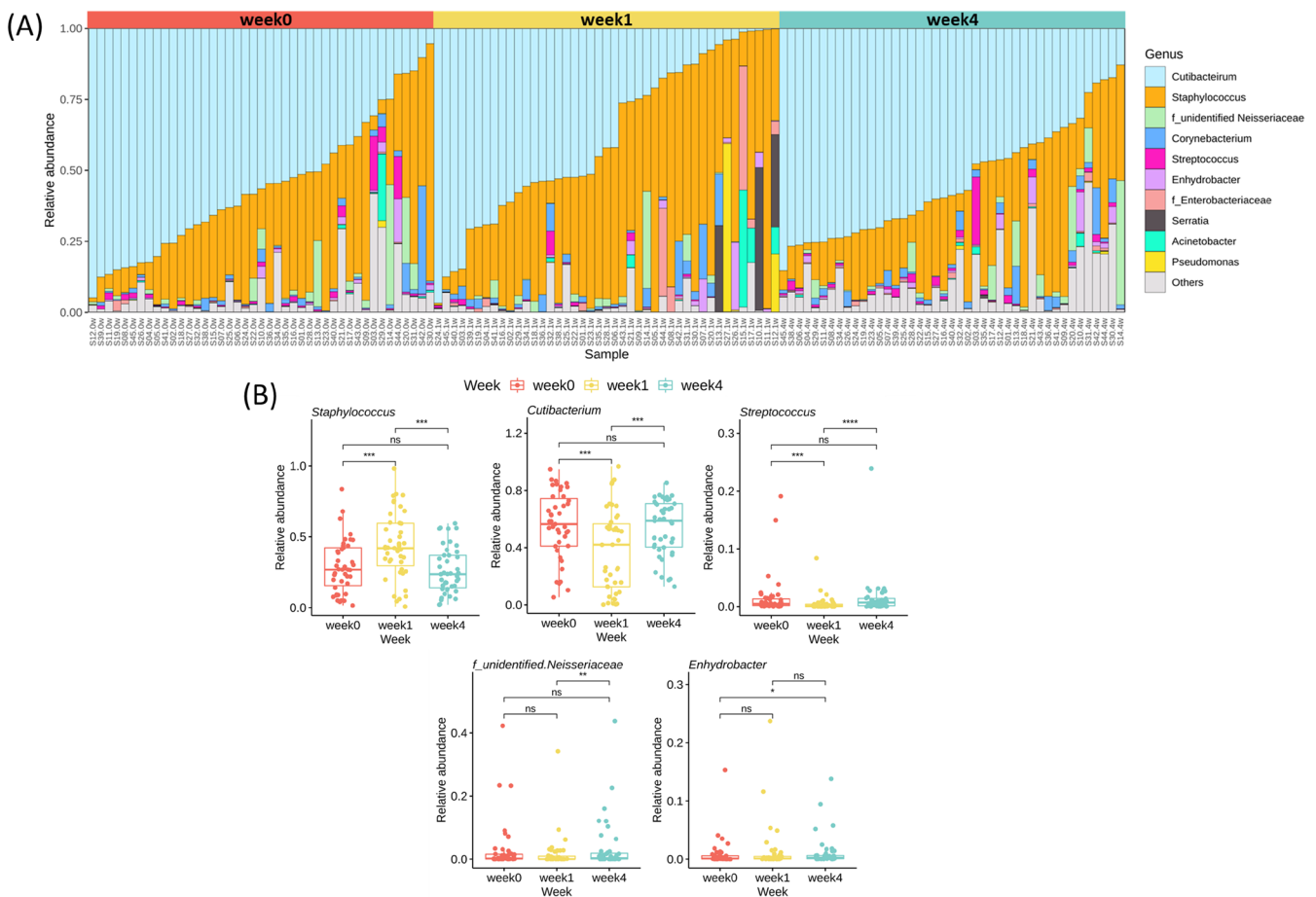


FIGURE 3 | Taxonomic composition of bacterial communities. (A) Relative abundance of the top 10 bacterial genera at weeks 0, 1, and 4. (B) Box plots showing temporal changes in the relative abundance of selected genera across time points. Statistical significance is indicated as follows: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$; ns, not significant.

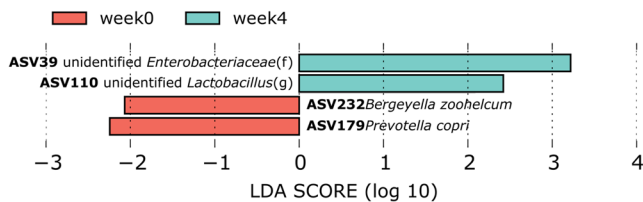


FIGURE 4 | Linear discriminant analysis (LDA) scores of differentially abundant bacterial features between baseline and week 4. LEfSe identified discriminative bacterial features between week 0 and week 4, with features showing an LDA score ≥ 2.0 considered informative. Higher LDA scores indicate greater effect sizes for the corresponding features.

clinical and microbiome changes during topical retinol use in acne-prone individuals.

The clinical and microbial findings may be biologically connected rather than solely independent observations. Retinol can alter keratinocyte turnover, follicular patency, desquamation dynamics, sebum availability, and barrier properties, each of which may reshape the local cutaneous niche and thereby influence microbial community composition over time [37, 38]. Within this framework, the observed microbiome shifts are interpreted as ecologically plausible responses to retinol-associated changes

in the skin microenvironment rather than as direct evidence of a causal microbial mechanism.

A key microbiome feature of the present study was the time-dependent pattern observed across visits. At the community level, beta diversity analyses indicated significant compositional shifts during product use. At the genus level, *Cutibacterium* and *Staphylococcus* remained dominant and showed reciprocal temporal patterns between the early and later time points [39–41]. Because V4–V5 16S rRNA profiling primarily supports genus-level resolution and does not reliably capture species or strain-level heterogeneity, these findings are described at the genus level rather than being assigned definitively to *C. acnes* [42, 43]. Species and strain-level dynamics, which may be clinically relevant in acne, merit further examination in future studies using higher-resolution taxonomic approaches [44, 45].

LEfSe identified *Lactobacillus* as enriched at week 4. Although the functional implications of this shift cannot be inferred from 16S profiling alone, prior work has suggested that certain *Lactobacillus* taxa may support skin barrier function and immune homeostasis through multiple mechanisms, including production of antimicrobial compounds, acidification via lactic acid, competitive exclusion, and modulation of inflammatory responses [46–50]. Accordingly, the enrichment of *Lactobacillus* observed in this study warrants interpretation

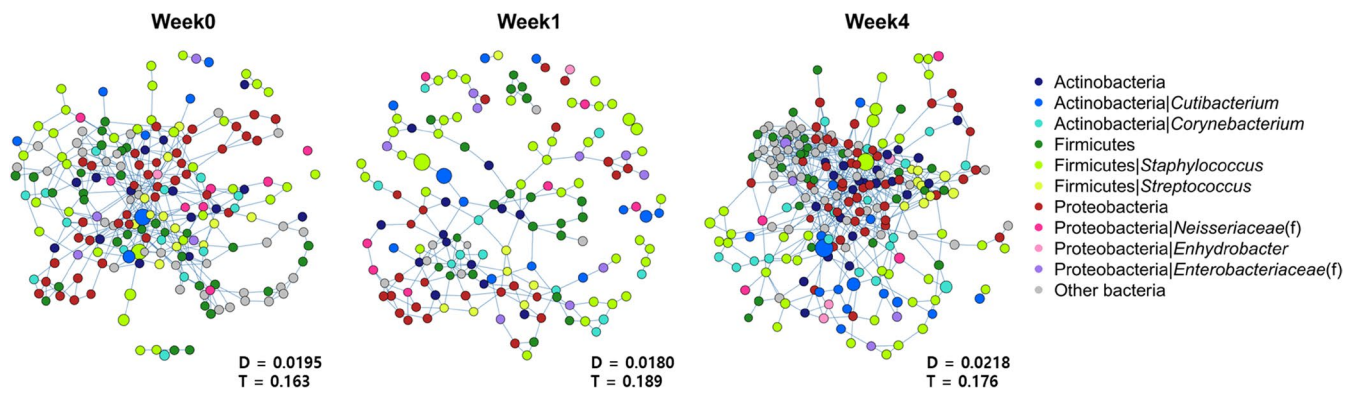


FIGURE 5 | Network analysis of bacterial amplicon sequence variants (ASVs) within the facial skin microbiome. Inferred microbial association networks are shown for each time point to illustrate changes in network topology during product use. Node colors represent dominant taxa at the genus level, and node size is scaled according to relative abundance. Insets display transitivity (T) and graph density (D) as summary network metrics.

as a descriptive ecological shift that may be compatible with a more favorable skin microenvironment, rather than as direct evidence of clinical or mechanistic benefit demonstrated in the present dataset.

Network analyses further suggested time-dependent changes in inferred community organization. Network density is interpreted as a summary of the overall extent of inferred connectivity among taxa, whereas transitivity reflects the degree of local clustering within the community [51]. The week 1 pattern of slightly lower density with higher transitivity may indicate an early reorganization toward more locally clustered associations, whereas the partial return toward baseline by week 4 is compatible with community adaptation during continued product use. Because these networks are inferential and were not linked to direct measures of function, resilience, or disease susceptibility, these findings should be interpreted as descriptive ecological features rather than evidence of improved or impaired community stability [52–54].

While the 4-week intervention was sufficient to capture short-term temporal dynamics, the study was not designed to determine whether the observed microbiome shifts represent stable remodeling or merely transient adaptation. Consequently, the week 4 pattern may reflect early reorganization rather than definitive stabilization [55]. Furthermore, because wrinkle-related parameters and aging biomarkers were not assessed, any link between the observed microbiome changes and skin aging remains speculative. Although prior literature suggests that microbial dysbiosis can influence aging-related pathways such as oxidative stress and matrix remodeling, these connections require direct validation in future studies [56–59]. Accordingly, any connection between the observed microbiome shifts and aging-related biology remains speculative and requires direct testing in dedicated studies.

Furthermore, we evaluated whether polylysine supplementation influenced the response compared with retinol alone. No significant between-formulation difference was detected at the level of broad community structure, supporting the use of pooled analyses for the primary longitudinal characterization. Nevertheless, subtle taxon-specific or functional differences between formulations cannot be excluded and should be examined in adequately powered studies.

This study has additional limitations. Sampling occurred during summer months (June–August), when heat and humidity may influence sebum secretion and other biophysical characteristics of the skin, potentially affecting the skin microbiome. Although participants were assessed under standardized temperature and humidity conditions after acclimatization and the study used a within-subject longitudinal design, these procedures reduce measurement noise rather than fully eliminate broader seasonal physiology as a source of variation. The cohort was also restricted to young Korean female participants with acne-prone skin, which improves homogeneity for exploratory analysis but limits generalizability across sexes, age groups, ethnic backgrounds, and baseline skin states. These host factors may influence sebum composition, barrier properties, inflammatory tone, and baseline microbial niche structure, and may therefore affect responsiveness to topical retinol. Finally, mechanistic endpoints such as inflammatory markers, barrier biomarkers, and microbial functional readouts were not measured; therefore, the functional relevance of taxonomic shifts cannot be established from compositional profiling alone.

In conclusion, this exploratory study suggests that short-term topical retinol use is associated with improvements in acne- and pore-related parameters together with time-dependent shifts in the facial skin microbiome in acne-prone individuals. These findings should be interpreted as descriptive and hypothesis-generating; however, they support further investigation in larger, longer, and mechanistically informed studies to clarify their durability, functional relevance, and generalizability.

Acknowledgments

This research was supported by a grant from the Chung-Ang University Graduate Research Scholarship in 2022 and by the AmorePacif Co. R&I Center.

In addition, this study was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: RS-2023-KH136575).

Funding

This work was supported by Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI),

funded by the Ministry of Health & Welfare, Republic of Korea, RS-2023-KH136575 AmorePacific Co. R&I Center Chung-Ang University Graduate Research Scholarship in 2022.

Ethics Statement

This study was approved by the Institutional Review Board of AMOREPACIFIC Co. (IRB No. 1-220777-A-N-01-DICN21115) and was conducted in accordance with the Declaration of Helsinki and institutional guidelines. All participants provided written informed consent prior to enrollment.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Figure S1:** Linear Discriminant Analysis Effect Size (LEfSe) results identifying differentially abundant taxa between baseline and week 4, stratified by product group (LDA score ≥ 2.0). **Table S1:** Summary of the relative abundance and compositional changes of key bacterial taxa across all time points.