Acidic Skin Care Promotes Cutaneous Microbiome Recovery and Skin Physiology in an Acute Stratum Corneum Stress Model

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Keywords
Microbiome · Skin physiology · Acidic skin care

Abstract
Introduction: Skin microbiome and skin physiology are important indicators of the epidermal homeostasis status. Stress models can reveal pathological conditions and modulating effects. Here we investigated the cutaneous microbiome in relation to skin physiology after mild tape stripping (TS) without treatment compared to two cosmetic leave-on lotions (pH 5.5 vs. pH 9.3) in 25 healthy volunteers.

Methods: The microbiome was analyzed by 16S-rRNA-gene amplicon sequencing and put in relation to the following skin physiology parameter: epidermal barrier function (TEWA-Meter TM300), stratum corneum hydration (Corneometer CM 825), surface pH (pH-Meter), and skin erythema (Mexameter).

Results: TS reduced the alpha diversity with a recovery over 7 days without treatment. Both lotions significantly accelerated the recovery of the alpha diversity already after 2 days with a slightly higher rate for the acidic lotion. After TS, the relative abundance of Proteobacteria was increased, whereas Actinobacteria were reduced. The relative abundances of typical skin-associated genera were reduced after TS. Taxa compositions returned to normal levels after 7 days in all treatment groups. An accelerated normalization could be observed with both lotions already after 2 days. A significant difference in skin pH was observed on day 2 and day 7 with an increased pH for the alkaline lotion. Both lotions induced an increase in stratum corneum hydration.

Conclusion: The study proved the suitability of an experimental stress model in the assessment of skin surface microbiome in relation to skin physiology. Stratum corneum hydration increased significantly with both lotions already at day 2. Microbiome parameters (alpha diversity, mean relative taxa, abundance of selected genera) normalized over 2–7 days. The following mechanisms could be responsible for the accelerated normalization of the microbiome: (a) optimized hydration during the recovery phase, (b) the composition of the lotion, (c) the induced repair mechanism. Thus, the formulation has a positive effect on the stratum corneum hydration and subsequently on cutaneous microbiome and skin physiology. Furthermore, this eventually has implications on the modulation of exogenous stress-induced epidermal alterations.

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Introduction

Cutaneous microbiome and skin physiology are important indicators of the epidermal homeostasis status. The microbe biodiversity in the upper epidermis is influenced by the interaction with exogenous factors. This interaction includes environmental aspects encompassing exposure to a specific professional or leisure activity or skin care habit [1–5], e.g., microbiota from cohabiting family members are shared and also with their dogs [6]. Exogenous stressors like mechanical abrasion, chemical irritants, and ultraviolet irradiation have an impact on functional homeostasis and the microbiome [3, 7, 8].

The complex interaction and variability of exogenous factors influencing the homeostasis of an organism are summarized by the term “exposome” [9, 10]. Lifestyle factors like food with a high content of antioxidative ingredients, living with a partner or a dog, as well as smoking, hygiene procedures, prescription drugs (e.g., antibiotics and immuno-suppressants) have been shown to influence both skin physiology [11, 12] and the microbiome [4, 13, 14]. Studies with an integrated look at skin physiology and the microbiome might reveal the relation between the homeostasis of functional skin parameters and adaptation of the microbiome.

The importance of the epidermal acid mantle has been described [15–18]. The understanding of the origin of the stratum corneum (SC) acid buffer system is mainly based on phospholipid/free fatty acid, histidase, and Na+-H+ exchanger-1 (NHE1) pathways [19, 20]. Acidic skin pH resides in the upper SC and shows a gradient toward neutral values in the deeper part of the epidermis in relation to active, energy-requiring mechanisms involved in keratinocyte differentiation processes [21]. The consequences of altered epidermal functions associated with an elevated skin pH are seen in inflammatory skin diseases, under hyperhydrated as well as very dry SC and skin infections [22, 23].

An acidic pH is important in leave-on and rinse-off skin care products [24]. Acidic skin pH care exerts positive effects on skin physiology and specific microbial colonization patterns, especially in atopic dermatitis [22, 25, 26].

The skin microbiome has been characterized by specific patterns in highly hydrated areas and sebum-rich areas [27–29]. The relation of sebum and hydration levels with microbiome diversity was confirmed specifically in the facial region [30–33]. The use of an emollient in infants at risk for atopic dermatitis decreased the surface pH and subsequently increased the proportion of *Streptococcus salivarius* [34].

Stress models are used in assessing barrier-related parameters to reveal pathological mechanisms and modulating effects during the recovery phase [35–37]. This so-called “epidermal treadmill stress model” reveals underlying pathophysiological mechanisms of skin diseases with altered epidermal functions [38]. The tape stripping (TS) stress model was adapted to microbiome research: microbiome changes in the epidermis upon an acute barrier disruption by sequential TS have been characterized in humans [39]. Regeneration of the diversity after acute removal from superficial parts of the SC induces active repair processes. Bacterial deoxyribonucleic acid (DNA) was evidenced using independent detection techniques down to the dermis and the dermal adipose tissue of normal human skin [40].

In the present study, we studied the short-term and mid-term recovery of skin physiology in relation to the microbiome changes after TS. Then modulation of recovery was studied in untreated areas compared to two cosmetic leave-on lotions with different pH (pH 5.5 vs. pH 9.3). We hypothesized that (i) barrier disruption with a mild acute stress model would induce significant changes in skin physiology, (ii) the stress model would lead to an immediate decrease in the diversity of the microbiome, (iii) the recovery of both skin physiology and microbiome alteration could be accelerated with leave-on skin care, (iv) an acidic pH of the leave-on lotion would be favorable for the recovery of skin physiology and the microbiome.

Material and Methods

Study Population

The study was approved by the Ethical Committee of the Euroderma Clinic in Sofia on July 9, 2020, with protocol number 2/July 9, 2020. The 25 healthy volunteers gave their written informed consent prior to the start of the study. The statistical analysis was performed with Prism 6. The male-female ratio was 10:15; mean age 30.7 years (standard error of the mean 2.1), body mass index 21.7 (standard error of the mean 0.8), smoker: nonsmoker ratio 12:13. The mean room temperature was 19.7–20.2°C and relative humidity 44.1–46.7% as recommended [41, 42]. All treatments, measurements, and microbiome assessments were performed on the volar forearm during the late morning and the early afternoon hours.

Design of the Study

Baseline values on SC hydration (SCH), surface pH, skin color, barrier function, and microbiome analysis were assessed. TS was performed with 5 sequential stripplings with Corneofix® applied with standardized pressure (with the help of stamp with a built-in spring exerting pressure of 225 g/cm2) for 5 s [43, 44]. Three different areas on the volar forearms received TS and one remained unstripped. Skin color, barrier function, pH, SCH, and microbi-
ome swabs were obtained before, immediately after TS, 2 h after TS, after 2 days and 7 days.

**Skin Physiology Parameters**

Epidermal barrier function was measured with a Tewameter TM300 (g/m² h). SCH was assessed with Corneometer CM 825 (arbitrary units). Surface pH was quantified with the pH-Meter (pH-units). Skin color was measured with the Mexameter MX 18 (erythema and melanin index; both arbitrary units). All instruments are manufactured by Courage&Khazaka electronics (Cologne, Germany).

**Test Formulations**

Lotion A with a pH of 5.5 and lotion B of the same composition with a pH of 9.3 (adjusted and buffered by the addition of bicarbonate and sodium hydrogencarbonate) were compared. The pH 9.3 was selected for formulation reasons and to have a clear difference in applied pH. The International Nomenclature Cosmetic Ingredients list of lotion ingredients was as follows: aqua, glycerin, cetetharyl alcohol, sorbitol, heptyldecanol, heptyldecyllaurate, Chamomilla recutita flower extract, allantoin, sodium cetetharyl sulfate, citric acid, sodium hydroxide, sodium ascorbate, xanthan gum, dimethicone, parfum, alcohol, phenoxyethanol, sodium benzoate, benzyl alcohol. Each volunteer had all four treatment areas (lotion A, lotion B, TS untreated and nonstripped and untreated) and served as his own control on both volar forearms. The assignment to the different treatment modalities was selected according to a randomization list for each volunteer. A fingertip unit of both lotions was applied twice daily for 6 consecutive days.

**Microbiome Sequencing**

DNA was extracted and purified into 50 µL elution buffer using the DNeasy PowerSoil Pro-Kit (Qiagen). Empty cremes were analyzed as controls. 2.6 pg of DNA from Salinibacter ruber (DSM 13855) was added as an internal spike-in control. Amplification of the V3-V4 region of the 16S-rRNA gene was done with the ultraclean production multiplex polymerase chain reaction (PCR) master mix (Qiagen) from 5 µL DNA using the primers CCTACGGGNGCGWWGGCAG (forward) and GACTACHVGGGTATC- TAAATCC (reverse) following the Illumina 16S library preparation protocol (https://support.illumina.com/documents/documentation/chemistry_documentation/16s/16s-metagenomic-library-prep-guide-15044223-b.pdf). Sequencing was done on an Illumina MiSeq (v2 reagents) with 2 × 250 bp paired-end reads.

**Sequence Analysis**

After sequencing, the standard UPARSE 16S protocol was used to merge the paired reads by their 3’-ends, filter reads to a minimum length of 100 bp, followed by clustering unique reads into operational taxonomic units (OTUs) using a 97% identity threshold and quantifying OTU abundances by mapping reads to the OTU sequences [45]. OTUs with a relative abundance of less than 0.01% were discarded. Each OTU sequence was searched in the NCBI Targeted Loci 16S database (NCBI accession PRJNA33175) using NCBI BLAST [46] with an identity cut-off of 97% and E-value cut-off of 0.01, and assigned to the annotated species. If no match was found, the sequence was also searched in the NCBI Nucleotide database using the same cut-offs but also excluding unclassified species or environmental sequences (based on the taxon names in the NCBI taxonomy). If no match was found in either database, the OTU was labeled as unclassified. OTUs with multiple best matches were assigned to the least common ancestor of all alignments with the same BLAST bit score. OTUs assigned to the Salinibacter ruber spike-in were discarded.

Alpha diversity is measured as the number of OTUs in each sample. Alpha diversity is a parameter in microbiome research that represents the diversity/heterogeneity in a single microbiome sample of a specific environment. Here we define alpha diversity as the number of OTUs in each sample. Relative abundances for species were calculated from classified OTUs and summarized on taxonomic ranks from species to phylum. Visualization of microbiome data was done using ggplot2 [47].

**Statistical Analysis**

Biophysical analysis

One-way ANOVA analysis within time groups was calculated followed by Sidak’s multiple comparisons test with a significance level of $p < 0.05$.

**Microbiome**

Comparison of diversity between treatment groups was performed with the Durbin-Conover test and Holm multiple testing correction using ggstatsplot [48], also using a significance level of $p < 0.05$.

**Results**

**Validity of the Epidermal Barrier Stress Model**

Transsepidermal water loss (TEWL) and erythema index were assessed immediately after and 120 min post-TS procedure to evaluate the validity of epidermal barrier disruption (Fig. 1a). A significant increase immediately after ($p < 0.001$) and 120 min ($p < 0.01$) after TS was observed, confirming the validity of the stress model of skin barrier disruption. No variations were noted for melanin and erythema index (online suppl. Fig. S4; see www.karger.com/doi/10.1159/000526228 for all online suppl. material), indicating that the stress model was of mild intensity.

**Skin Physiology Dynamics following Product Application**

A significant increase in SCH was observed on day 2 and day 7 in comparison to untreated skin sites for both lotions ($p < 0.001$). The change in SCH upon product application is shown in Figure 1c. Lotion A showed slightly higher values compared to lotion B without reaching statistical significance.

A clear difference in skin surface pH was observed at day 2 and day 7 (Fig. 1d). Lotion B application resulted in a significant increase in pH ($p < 0.001$) both at day 2 and day 7 in comparison to lotion A and untreated TS area. Skin surface pH did not differ between lotion A
and the untreated TS site. However, the values of all groups increased slightly (nonsignificant) compared to baseline, which is within normal variations with a 1-week study.

No significant difference between sites in TEWL values (Fig. 1b), erythema and melanin index (online suppl. Fig. S1) could be revealed at day 2 and 7, indicating no relevant induction of irritation (increased erythema index) or desquamation (decrease of melanin index).

Microbiome Analysis

Data from 24 out of the 25 individuals were analyzed (one individual was excluded because of missing samples). The number of sequencing reads per sample ranged from 1,117 to 168,807 (mean 207,764, median 11,356) and was on average higher in the treated samples and lowest in untreated samples after TS (online suppl. Fig. S2). A comparison between the fraction of numbers of OTUs that are classified to a taxon and the fraction of reads belonging to classified OTUs shows that on average 83% of OTUs are classified, but they comprise on average 95% of
**Fig. 2.** Distribution of alpha diversity, measured by the number of OTUs between treatment areas. Statistically significant differences are highlighted by $p$ values. The box plot shows median, 25% and 75% percentile; the red dot indicates the mean of each group. 

**a** Shows the control area over the 7 days without any treatment. No difference was detected in the untreated area. 

**b** Shows the tape-stripped area without treatment compared to control (untreated non-tape stripped). The initially reduced alpha diversity (T0) increased after 2 days (n.s.) and was significantly increased after 7 days ($p < 0.001$ compared to TS 0 h; $p < 0.001$ compared to TS 2 h). 

**c** Shows all 4 treatment areas after 2 days. Both lotions (red dots, 3rd violin lotion A; blue dots, 4th lotion B) induced a significant increase of alpha diversity compared to the control non-tape stripped (gray dots) and TS area (green dots), ($p < 0.001$ and lower) for all comparisons. Lotion A shows a slightly higher alpha diversity than lotion B without reaching the statistical significance. 

**d** Shows all 4 different treatment areas after 7 days. TS, lotion A and lotion B are slightly higher than the untreated non-tape stripped control (C) area without reaching statistical significance.
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the reads, i.e., most unclassified OTUs are of low abundance (online suppl. Fig. S3). The rarefaction analysis (online suppl. Fig. S4) shows the number of OTUs for the 11 samples per individual after subsampling to half read depth, one-fourth read depth, and further dilutions down to 1/1,024. Rarefaction curves reached a plateau in all samples, with at least 95% of OTUs present at half read depth.

The alpha diversity was unchanged during the 7 days of the study in the nonstripped and nontreated control areas (Fig. 2a), with mean values from 183 to 204. TS significantly reduced the alpha diversity to 125. The values increased in the untreated areas to 177 after 2 days and 228 after 7 days (Fig. 2b). Both lotions significantly accelerated the re-population regarding the alpha diversity already at 2 days compared with the untreated areas to a mean of 281 for lotion A and 272 for lotion B (Fig. 2c). After 7 days, no significant differences between the groups were found, but we observe a decrease of alpha diversity compared with the measurements from 2 days after TS in both lotions to levels compared to untreated areas (Fig. 2d).

The distribution of phyla (Fig. 3a) was unchanged in the control area over the 7 days of the study. After TS, the relative abundance of Proteobacteria was increased, whereas Actinobacteria abundances decreased. This shift from Actinobacteria toward Proteobacteria recovered partially after 2 days and normalized almost completely at day 7. Treatment with lotion A and lotion B accelerated the normalization: already after 2 days, the distribution was comparable to the baseline nonstripped area and remained similar on day 7. Examination of the most abundant orders revealed an increase of Burkholderiales after TS as well as a reduction, in particular, of the lower abundant orders like Corynebacteriales, Micrococcales, Propionibacteriales, and Lactobacillales, with the exception of Xanthomonadales, where the relative abundance increased (Fig. 3b). Abundances of Bacillales and Pseudomonadales remained largely unchanged.

**Fig. 3.** Distribution of the most abundant phyla (a) and orders (b) for each individual, grouped into the different treatment areas at different time points.
Fig. 4. Mean relative abundances of the 20 most abundant genera within the different treatment areas. The first row shows the control areas at baseline, after 2 days and after 7 days. The second row depicts the TS areas immediately after TS, 2 days, and 7 days after TS without treatment (the 2 h time point is shown in row 3). The third and fourth rows show lotion A and B after 2 days and 7 days, respectively.
The mean relative abundances of the 20 most abundant genera in each group are shown in Figure 4. The first row shows control areas, the second row the TS/untreated area, and the third and fourth row show lotions A and B, respectively. The control group showed a stable genus composition over the whole period, with *Staphylococcus* as the dominant genus. TS induced a relative increase of *Brevibacillus* and a reduction of *Staphylococci* and *Corynebacteria*. After 7 days, the genus composition was similar to control areas. Treatment with both lotions resulted in normalization of the genus distribution already at day 2.

Noteworthy is a major reduction of the four typical skin-associated genera *Corynebacterium*, *Cutibacterium*, *Staphylococcus*, and *Streptococcus* within the different treatment areas. Combined relative abundance of these 4 genera in relation to alpha diversity split into control, untreated, and treated areas. Controls (gray dots): no major change in the relative abundance/alpha diversity ratio was detected over time in the control area. Tape-striped areas (green dots): a slight shift of the relative abundance/alpha diversity was induced by TS with lower ratio directly after TS and an increase over time. Treated areas: (lotion A red dots; lotion B blue dots). Lotion A and B showed no major difference. Lotion treated (colored dots), at different time points: no major change in the relative abundance/alpha diversity ratio was detected over time in the control area.

**Fig. 5.**

*a* The mean relative abundance of 4 selected genera *Corynebacterium*, *Cutibacterium*, *Staphylococcus*, and *Streptococcus* within the different treatment areas. 

*b* Combined relative abundance of these 4 genera in relation to alpha diversity split into control, untreated, and treated areas. Controls (gray dots): no major change in the relative abundance/alpha diversity ratio was detected over time in the control area. Tape-stripped areas (green dots): a slight shift of the relative abundance/alpha diversity was induced by TS with lower ratio directly after TS and an increase over time. Treated areas: (lotion A red dots; lotion B blue dots). Lotion A and B showed no major difference. Lotion treated (colored dots), at different time points: no major change in the relative abundance/alpha diversity ratio was detected over time in the control area.
Staphylococcus, and Streptococcus after TS (Fig. 5a). Both lotions accelerated their recovery to normal and even elevated levels compared with control and untreated groups. When plotting the combined relative abundance of these four genera against the alpha diversity in each sample (Fig. 5b), we observe no change over time in control areas, but a shift toward low abundance and low alpha diversity in the TS areas. The groups of both lotions show a similar distribution as in the control group and no relevant shift of both variables between the two time points, indicating that lotion-treated skin areas returned to almost normal skin flora composition already after 2 days.

Figure 6 shows the mean relative abundance of the OTUs that are assigned to different Staphylococcus species (S. aureus/S. simiae, S. capitis/S. caprae, S. capitis/S. caprae/S. epidermidis, as well as summarized other Staphylococcus spp.) and the number of samples in which they were observed. TS induced a similar reduction in all Staphylococcus OTUs. This reduction returned to almost normal levels after 2 days but only after 7 days showed comparable abundances to untreated areas.

**Discussion**

Exogenous environmental influences alter skin physiology and microbiome parameters in humans [2, 3, 7]. We hypothesized that an acute epidermal stress model would be suitable to study the effects of acidic skin care on recovery dynamics both of skin physiology and epidermal microbiome diversity and other microbiome parameters. The TS stress model is an established model to reveal subtle differences in pathological states and to study treatment responses [49, 50]. TS was also described to serve as a model in studying skin microbiome [39, 51]. We selected a mild TS model in healthy volunteers which
showed to be correctly executed with mild barrier disruption and no measurable irritation.

The recovery of skin physiology was accelerated by skin care, however, not in a significant pH-dependent manner. Both lotions (only differing in the pH-related buffer substances) revealed a positive effect on barrier-related parameters. Only for skin surface pH, a significant difference was observed at day 2 and day 7 with an increased pH induced by basic/alkaline pH of lotion B. No significant differences between sites were detectable in barrier function and irritation at day 2 and day 7.

TS significantly reduced the alpha diversity, followed by a recovery over 7 days without treatment. Thus, our assumption of TS being a relevant model for studying the dynamics of microbial recovery after superficial removal of SC was confirmed. The re-population of the stripped skin section is coming both from lateral ingrowth and from preserved, deeper parts of the skin and hair follicles [39].

Both lotions accelerated the recovery of the microbiome, showing a significantly higher alpha diversity already after 2 days, with a slightly higher induction rate for lotion A (lower pH). The alpha diversity after 7 days of treatment is lower than after 2 days of treatment. There was significant increase of alpha diversity at day 2 induced by TS seen as an acceleration of the repopulation process. This process was still ongoing at day 7 but less pronounced comparing lotion A and B to untreated tape-stripped area. This suggests that the repopulation of stripped area started with an initial overcompensation caused by a replacement flora that rapidly fills the empty niche. After a few days, the normal flora replaces this transitional microbiome. Since the pH was identified as not significantly relevant for the accelerated re-population after TS, we assume that the ingredients of both formulations are the major drivers. In vivo studies are not designed to identify the role of specific ingredients. After TS, the abundance of Burkholderiales increased, whereas abundances of several other genera decreased. In particular, the abundance of the common skin-associated genera Staphylococcus, Corynebacterium, Streptococcus, and Cutibacterium was reduced after TS. Similar to the alpha diversity, the shift in the microbiome composition returned to a normal state over the course of 7 days in untreated areas. Topical treatment with lotions accelerated the normalization of the taxa distribution, and already after 2 days, the distribution was comparable to the control non-stripped areas and remained similar on day 7.

The inter-individual differences in species distribution between the volunteers (baseline levels) represent a limiting factor when interpreting microbiome data. The high variation makes it challenging to identify significant and relevant effects induced by pH changes since they might be masked by the inter-individual variation in the present cohort size.

The validity of this model has been proven as shown in Figure 1. This model was used to evaluate the effect of skin care with different pH buffering of a marketed cosmetic product on the microbiome and skin physiology parameters. No significant change in TEWL at day 2 and day 7 was registered. A probable limitation is the spontaneous barrier recovery within 2 days after TS, reflected by the nonsignificant difference between untreated TS and untreated unstripped area already at day 2. Our mild stress model only induced a mild barrier damage with a relatively fast barrier recovery [38]. A more pronounced increase in TEWL or repetitive damage would have caused more severe disturbances, with a longer regeneration phase. The chosen mild barrier disturbance corresponds to the everyday situations.

SCH increased significantly under both treatments already at day 2 and was still higher at day 7 in comparison to untreated sites. Micro-morphological changes were detectable in a multiethnic study population treated for 14 days with an acidic lotion by optical coherence tomography and reflectance confocal microscopy [52]. Changes in hygiene routines have only limited effects on the microbiome and only detectable after usage of an antiperspirant and foot powder; yet no changes were observed after usage of lotions [14, 53].

Our findings provide evidence that a mild stress model (TS) in the assessment of skin surface microbiome homeostasis in relation to skin physiology is an applicable model. SCH increased significantly after treatment with both lotions already at day 2 and was still higher at day 7 compared to untreated sites. The process of normalization of the stressed microbiome parameters (including alpha diversity, mean relative taxa distribution on the phylum-level, abundance of selected genera) was started already after 2 h. and the parameters returned to normal distribution after 7 days.

Our hypothesis could be answered as follows: (i) that barrier disruption with a mild acute stress model induced significant changes in skin physiology, measured as TEWL without leading to a relevant inflammation, (ii) the stress model lead to an immediate decrease in the diversity of the microbiome, (iii) the recovery of both skin physiology and microbiome alteration was accelerated by leave-on skin care, (iv) a significant superiority of the acidic pH lotion compared to the basic/alkaline pH lotion...
could not be shown during the recovery of skin physiology and the microbiome parameters in this model, but indications for faster microbial rebalancing at pH 5.5 should be analyzed in further studies. In future studies, higher buffer capacities and eventually even using lotions with a pH lower than 5.5 might elucidate the modulating role of pH on microbiome parameters.

The potential mechanisms for the accelerated microbiome normalization could be (a) the composition of the lotion, (b) optimized hydration during the recovery phase, (c) the induced repair mechanism. The formulation might have a positive effect on the SCH and subsequently on cutaneous microbiome and skin physiology. Furthermore, this eventually has an implication in the modulation of exogenous stress-induced epidermal alterations. Further studies would elucidate the role of prolonged application of the acidic skin care in different stress.

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Statement of Ethics

The study was approved by the Institutional Ethics Board of the Euroderma Clinic in Sofia from July 9, 2020 with protocol number 2/July 9, 2020. All volunteers signed a written informed consent.

References

1. Flandroy L, Pouyahidis T, Berg G, Clarke G, Do MC, Deaestecker E, et al. The impact of human activities and lifestyles on the interlinked microbiota and health of humans and of ecosystems. Sci Total Environ. 2018 Jun 15; 627:1018–38.
2. Khaladze I, Leonardi M, Fabre S, Messaraa C, Mouv A. The skin interactome: a holistic “genome-microbiome-exposome” approach to understand and modulate skin health and aging. Clin Cosmet Investig Dermatol. 2020; 13:1021–40.
3. Boxberger M, Cenizo V, Cassir N, La Scola B. Challenges in exploring and manipulating the human skin microbiome. Microbiome. 2021 May 30;9(1):125.
4. Moutinho-Silva L, Boraczynski N, Emmert H, Baurecht H, Szmyczak S, Schulz H, et al. Host traits, lifestyle and environment are associated with human skin bacteria. Br J Dermatol. 2021 Sep;185(3):573–84.
5. Gueniche A, Valois A, Salomao Calixto L, Sanchez Hevia O, Labatut F, Kerob D, et al. A dermocosmetic formulation containing Viteoscilla filiformis extract, niacinamide, hyaluronic acid, and vitamin E regenerates and repairs acutely stressed skin. J Eur Acad Dermatol Venereol. 2022 Jan;36(Suppl 2):26–34.
6. Stoj M, Lauber C, Costello D, Lanozena P, Gerken G, Berg-Lyons D, et al. Co-habiting family members share microbiota with one another and with their dogs. Elife. 2013 Apr 16;2:e00458.
7. Srír R, Claypool J. Microbial reference frames reveal distinct shifts in the skin microbiota after cleansing. Microorganisms. 2020 Oct 23;8(11):1E1634.
8. Schneider AM, Nelson AM. Food for thought: does host diet affect skin microbes? Br J Dermatol. 2021 Sep;185(3):481–3.
9. Wild CP. Complementing the genome with an “exposome”: the outstanding challenge of environmental exposure measurement in molecular epidemiology. Cancer Epidemiol Biomarkers Prev. 2005 Aug;14(8):1847–50.
10. Passeron T, Zouboulis CC, Tan J, Andersen ML, Katta R, Lyu X, et al. Adult skin acute stress responses to short-term environmental and internal aggression from exposome factors. J Eur Acad Dermatol Venereol. 2021 Oct;35(10):1963–75.
11. Percoco G, Patatian A, Eudier F, Grisel M, Bader T, Lati E, et al. Impact of cigarette smoke on physical-chemical and molecular proprieties of human skin in an ex vivo model. Exp Dermatol. 2020 Sep;29(9):1610–8.
12. Barresi R, Chen E, Liao IC, Liu X, Baalbaki N, Lynch S, et al. ARTICLE: alteration to the skin barrier integrity following broad-spectrum UV exposure in an ex vivo tissue model. J Drugs Dermatol. 2021 Apr 1;20(4):23s–28s.

Conflict of Interest Statement

Joachim W. Fluhr and Razvigor Darlenski have received consulting fees from Sebapharma. Benjamin Kaestle, Michaela Arens-Corell, and Lina Praefke are employees of Sebapharma. All other authors have no competing interests regarding the content of this article.

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Author Contributions

Conception of the study: Joachim W. Fluhr, Razvigor Darlenski, Nikolai K. Tsankov, Laurent Misery, Benjamin Kaestle, Michaela Arens-Corell, and Lina Praefke. Performing the study: Dessyslava G. Nikolaeva, Joachim W. Fluhr, and Razvigor Darlenski. Microbiome analysis: Peter Menzel and Rolf Schwarz. Data analysis: Joachim W. Fluhr, Peter Menzel, Rolf Schwarz, Dessyslava G. Nikolaeva, and Razvigor Darlenski. Interpretation of the data: all authors. Writing of the manuscript: all authors. All authors have read the manuscript, agreed on its submission, and consented to its publication.

Data Availability Statement

All data generated or analyzed during this study are included in this published article and its online supplementary material. The sequencing data for all 264 microbiome samples are available at NCBI Genbank under Bioproject accession number PRJNA713953.
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13 Nichols RG, Peters JM, Patterson AD. Interplay between the host, the human microbiome, and drug metabolism. Hum Genomics. 2019 Jun 11;13(1):27.

14 Pinto D, Ciardiello T, Franzoni M, Pasini F, Giuliani G, Rinaldi F. Effect of commonly used cosmetic preservatives on skin resident microflora dynamics. Sci Rep. 2021 Apr 22;11(1):6965.

15 Fluhr JW, Kao J, Jain M, Ahn SK, Feingold KR, Elias PM. Generation of free fatty acids from phospholipids regulates stratum corneum acidification and integrity. J Invest Dermatol. 2001 Jul;117(1):44–51.

16 Kleesz P, Darlenksi R, Fluhr JW. Full-body skin mapping for six biophysical parameters: baseline values at 16 anatomical sites in 125 human subjects. Skin Pharmacol Physiol. 2012;25(1):23–33.

17 Fluhr JW, Darlenksi R. Skin surface pH in newborns: origin and consequences. Cutr Probl Dermatol. 2018;54:26–32.

18 Novackova A, Sagrafena I, Pullmannova P, Marenus KD, Feingold KR, et al. Skin pH-dependent assembly of skin barrier lipids in vitro. J Invest Dermatol. 2021 Aug;141(8):1915–21.e4.

19 Fluhr JW, Mao-Qiang M, Brown BE, Hachem JP, Moskowitz DG, Demerjian M, et al. Functional consequences of a neutral pH in neonatal rat stratum corneum. J Invest Dermatol. 2004 Jul;123(1):140–51.

20 Fluhr JW, Elias PM, Man MQ, Hupe M, Selden C, Sundberg JP, et al. Is the filaggrin-histidine-urocanic acid pathway essential for stratum corneum acidification? J Invest Dermatol. 2010 Aug;130(8):2141–4.

21 Damen M, Wirtz L, Soroka E, Khatif H, Kukat C, Simons BD, et al. High proliferation and delamination during skin epithelial stratification. Nat Commun. 2021 May 28;12(1):3227.

22 Schmid-Wendtner MH, Korting HC. The pH of the skin surface and its impact on the barrier function. Skin Pharmacol Physiol. 2006;19(6):296–302.

23 Kao SH, Chen CJ, Shen CF, Cheng CM. Role of pH value in clinically relevant diagnosis. Diagnostics. 2020 Feb 16;10(2):E107.

24 Gustin J, Bohman L, Ogle J, Chaudhry T, Li L, Fadayel G, et al. Use of an emollient-containing diaper and pH-buffered wipe regimen restores skin pH and reduces residual enzymatic activity. Pediatr Dermatol. 2020 Jul;37(4):626–31.

25 Huberbin C, Tremmel K, Hammel G, Bhatia M, de Tomassi A, Nussbaumer T, et al. Skin pH-dependent Staphylococcus aureus abundance as predictor for increasing atopic dermatitis severity. Allergy. 2020 Nov;75(11):2888–98.

26 Korting HC, Lukacs A, Vogt N, Urban J, Ehret W, Ruckdeschel G. Influence of the pH-value on the growth of Staphylococcus epidermidis, Staphylococcus aureus and Propionibacterium acnes in continuous culture. Zentralbl Hyg Umweltmed. 1992 Jun;193(1):78–90.

27 Schommer NM, Gallo RL. Structure and function of the human skin microbiome. Trends Microbiol. 2013 Dec;21(12):660–8.

28 Riverain-Gillet E, Guet-Revillet H, Jais JP, Ungeheuer MN, Duchateau S, Delage M, et al. The surface microbiome of clinically unaffected skinfolds in Hidradenitis Suppurativa: a cross-sectional culture-based and 16S rRNA gene amplicon sequencing study in 60 patients. J Invest Dermatol. 2020 Sep 140(9):1847–55.e6.

29 Park J, Logjan M, Svedfelt ND, Jo JH, Zhang Z, Pillay L, Phang S, et al. Shifts in the skin bacterial and fungal communities of healthy children transitioning through puberty. J Invest Dermatol. 2022;142(1):212–9.

30 Mukherjee S, Mitra R, Maitra A, Gupta S, Kumar S, Chakrabarty A, et al. Sebum and hydration levels in specific regions of human face significantly predict the nature and diversity of facial skin microbiome. Sci Rep. 2016 Oct 27;6:36062.

31 Brandwein M, Fuls G, Israel A, Hodak E, Sabaf B, Steinberg D, et al. Biogeographical landscape of the human face skin microbiome viewed in high definition. Acta Derm Venereol. 2021 Nov 24;101(11):adv00603.

32 Kong HH, Oh J. State of residency: microbial strain diversity in the skin. J Invest Dermatol. 2022;142(5):1260–4.

33 Roux PF, Oddos T, Stamatas G. Deciphering the role of skin microbiome in skin health: an integrative multomics approach reveals three distinct metabolite-microbe clusters. J Invest Dermatol. 2022;142(2):469–79.e5.

34 Glatz M, Jo HH, Kennedy EA, Polley EC, Segre JA, Simpson EL, et al. Emollient use alters skin barrier and microbes in infants at risk for developing atopic dermatitis. PLoS One. 2018;13(2):e0192443.

35 Garg A, Chen MM, Sands LP, Matsui MS, Marenus KD, Feingold KR, et al. Psychological stress perturbs epidermal permeability barrier homeostasis and stratum corneum integrity: inhibition of epidermal lipid synthesis accounts for functional abnormalities. J Invest Dermatol. 2003 Mar;120(3):456–64.

36 Mao-Qiang M, Fowler AJ, Schmuth M, Lau P, Stenlock C, Graham KM, et al. Microbiome dynamics of furred vs. non-furred skinfolds in Hidradenitis Suppurativa: origin and consequences. Curr Opin Dermatol. 2019 Jun 11;13(1):27–38.

37 Hughes AJ, Tawfik SS, Barua HS, O’Toole EA, O’Shaughnessy RFL. Tape strips in dermatology research. Br J Dermatol. 2021 Jul;21(1):54.

38 Schmuth M, Feingold KR, Elias PM. Stress test of the skin: the cutaneous permeability barrier treadmill. Exp Dermatol. 2020 Jan;29(1):112–3.

39 Zeeuw PJLM, Boekhorst J, van den Bogaard EH, de Koning HD, van der Kerkhof PMC, Saulnier DM, et al. Microbiome dynamics of human epidermis following skin barrier disruption. Genome Biol. 2012 Nov 15;13(11):R101.