

ORIGINAL ARTICLE

A new dexpanthenol-containing liquid cleanser for atopic-prone skin: Results from two prospective clinical studies evaluating cutaneous tolerability, moisturization potential, and effects on barrier function

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Abstract

Background: Gentle cleansing of the skin without further compromising its barrier function and moisture content and being simultaneously devoid of adverse effects on the skin microbiome are important features of body cleansers for atopic-prone skin sufferers. For this population, a new dexpanthenol-containing liquid cleanser (DCLC) was developed.

Methods: Two prospective 4-week studies have been conducted. Study 1 investigated the effect of once-daily DCLC on *stratum corneum* (SC) hydration, transepidermal water loss (TEWL), skin pH, and skin microbiome (all on the volar forearm) in adult subjects with dry skin (N = 44). Study 2 explored the cutaneous tolerability of DCLC and its effect on the microbiome biodiversity of the volar forearm skin in infants/children with atopic-prone skin (N = 33, aged 6 months to 6 years). In the latter study, DCLC was applied 2–3 days/week in combination with an emollient applied at least twice daily.

Results: In Study 1, on Day 29, the mean change in skin surface capacitance from baseline was significantly greater in the forearm test area treated with DCLC than in the contralateral test area (control) treated with water only (5.16 vs. 3.65 a.u.; $p = 0.011$), suggesting long-term SC hydration. DCLC use was not associated with changes in TEWL, skin pH, or microbiome biodiversity if compared to control. In Study 2, the 4-week use of DCLC in combination with an emollient was well tolerated according to pediatrician skin assessment, and no flare-ups were recorded. The microbiome biodiversity did not shift during the study.

Conclusion: These findings support the use of DCLC in subjects with atopic-prone skin.

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KEYWORDS

atopic-prone skin, dexpanthenol, dry skin, liquid cleanser, moisturization, skin microbiome

1 | INTRODUCTION

Atopic dermatitis (AD) is an inflammatory, pruritic, chronic, or chronically relapsing skin disorder which frequently starts in infancy. In most countries in the world, up to 20% of children and 2%–8% of adults are affected.¹ Typically, AD evolves with periods of acute flares alternating with periods of improvement. Subjects with AD-prone (atopic-prone) skin often belong to families with other atopic diseases (e.g., bronchial asthma or allergic rhinoconjunctivitis).¹

Dry skin is one of the main clinical symptoms of AD and is the result of skin barrier dysfunction. The latter leads to enhanced transepidermal water loss (TEWL) and decreased hydration of the stratum corneum (SC).^{1,2} The impaired barrier function is associated with SC peculiarities, such as an altered lipid organization/composition and content, as well as impaired corneocyte differentiation.³ Consequently, basic management of atopic-prone skin includes the daily application of emollients to hydrate the SC and improve skin barrier function, with the goal of relieving symptoms (e.g., itching and scratching) and lengthening time between flare-ups.^{1,4} Another essential part of managing atopic-prone skin is the regular use of cleansers to remove crusts and, in the case of bacterial superinfection, to mechanically eliminate bacterial contamination.^{1,5} However, harsh cleansing can exacerbate the already existing skin barrier dysfunction and decreased skin hydration. Gentle cleansing of the skin without further harming its barrier function and moisture content is therefore an important feature of body cleansers to be used regularly by atopic-prone skin sufferers; soap (ionic)-based cleansing products should be avoided for this purpose.^{1,6} In addition, cleansers may unfavorably influence skin health via alterations of the skin microbiome.⁷ Since the human skin microbiome contributes to maintaining the overall integrity of the skin barrier,^{8,9} this outermost functional level of the skin consisting of living microbial communities should not be affected. A product compliant with modern cleanser technology should be devoid of this property.

These aspects triggered the development of a new dexpanthenol-containing liquid cleanser (DCLC, Bepanthen® SensiControl Daily Gentle Body Wash) for subjects with atopic-prone skin. The composition of DCLC was primarily driven by the objective to offer a well-tolerated product to atopic-prone skin sufferers that effectively and gently cleanses the body. DCLC is a fragrance-free body wash gel and contains non-ionic-based surfactants (i.e., capryl/capramidopropyl betaine, disodium cocoyl glutamate, and lauryl glucoside) that provide foaming and gentle cleansing. Other key ingredients of DCLC are humectants (glycerin, saccharide isomerate), an anti-pruritic/soothing agent (niacinamide), and a multifunctional agent (dexpanthenol) to support the skin barrier and skin moisture content.³ For protection of the skin microbiome, the pH was adjusted at its physiologic value (5.5) and a prebiotic known to have a selective

prebiotic effect, α -glucan oligosaccharide,¹⁰ was added to DCLC. Recent *in vitro* investigations, conducted in parallel, showed that α -glucan oligosaccharide stimulates the growth of desired bacterial strains (i.e., *Staphylococcus epidermis*) present in the skin microbiome (unpublished). By selecting these key ingredients, that belong to the key components of an ideal emollient and AD care product,^{3,8} the aforementioned goal was to be achieved.

Two prospective studies, each lasting 4 weeks, were conducted to explore the cutaneous tolerability, acceptability, moisturization potential and effects on barrier function of DCLC. One study was performed in healthy adult subjects with dry skin, which allowed repeated measurements with non-invasive methods in the absence of any additional skin care. Another study was conducted in infants and children with atopic-prone skin (i.e., with a history of AD). In this study, according to EU guidelines recommendations,¹ the infants/children received continued at least twice-daily skin care with an established dexpanthenol-containing emollient as basic treatment,¹¹ while DCLC was applied once daily on 2 to 3 days a week.

2 | METHODS

The two studies were conducted at proderm GmbH, Schenefeld/Hamburg, Germany between August and November 2021, under supervision of a dermatologist (adult study) or a pediatrician (pediatric study). Both trials were performed in accordance with the principles of the Declaration of Helsinki with all its revisions. In the study in healthy adults with dry skin, subjects provided written informed consent after being informed of the trial procedures, while in the study in infants and children with atopic-prone skin, written informed consent was obtained from the parents or legal guardians of the minors prior to study enrollment. The Institutional Ethics Committee/Institution Review Board (IEC/IRB) of proderm, Schenefeld/Hamburg, Germany reviewed and approved both study protocols (approval dates: July 28, 2021, and September 22, 2021; approval numbers: 2021/027 and 2021/032). The new liquid cleanser (Bepanthen® SensiControl Daily Gentle Body Wash) was used in both trials. In the pediatric study, an established emollient (Bepanthen® SensiControl Daily Emollient)¹¹ was additionally applied on an at least twice-daily regimen as base skin care of the atopic-prone skin. Bayer Consumer Care AG (Basel, Switzerland) provided both the new liquid cleanser and the emollient.

No formal sample size calculations were performed given the exploratory nature of our studies. No primary/secondary variables were defined for the same reason. However, previous experience with similar studies demonstrated that scientifically sound results can be obtained with the selected sample sizes.^{12–14}

2.1 | Study 1: Adult study

2.1.1 | Study design

Study 1 was an exploratory, open, randomized, intra-individual comparison study in healthy adult subjects with dry skin. Visits at the trial center were scheduled for Day 1 (baseline), Day 2, and Day 29 of the study. On these days, study participants arrived at the study center without having applied DCLC before.

Two skin test areas (approximately 16 cm² each) were defined and marked on each volar forearm. At one area on each arm, instrumental measurements were conducted, while the remaining two areas were used for microbiome analysis. Within a given subject, DCLC was always applied on the whole volar forearm. The contralateral arm was treated with water only and served as control. For each study participant, the volar forearm to be treated with DCLC was selected based on a balanced randomization scheme. For each application, approximately 2 g of DCLC (corresponding to one push of the pump container) was distributed on the assigned volar forearm. Subjects were instructed to wet the forearm in lukewarm water, apply DCLC evenly over the assigned volar forearm and gently massage the study product, then rinse and gently wipe the arm dry. For the control side, subjects were told to wet the forearm in lukewarm water, gently massage the water over the assigned volar forearm, apply again lukewarm water, and then gently wipe dry. The control side was always treated first. DCLC and water applications took place on a once-daily schedule. The subjects were instructed to use DCLC on the whole body for routine showering, thereby avoiding any contact of DCLC with both volar forearms. The quantity needed for the whole body varied from 6 g (3 pushes of the pump container) to 10 g (5 pushes). Compliance with DCLC use was confirmed by weighing each pump container with the body wash gel (400 ml) before and after the 4-week study period.

2.1.2 | Subjects and assessments

Healthy male and nonpregnant female subjects with dry skin and aged between 18 and 70 years were eligible for study enrolment. A corneometer value of ≤ 35 arbitrary units (a.u.) at the volar forearms corresponded to the protocol definition of dry skin. Female subjects of childbearing potential had to use reliable methods of contraception during the entire duration of the study.

Subjects were excluded if they presented with any skin condition at the test areas that might influence the interpretation of study results; a condition necessitating the use of drugs interfering with study data within 1 week (antihistamines, immunosuppressive drugs) or within 3 days (any topical medication at the test areas, anti-phlogistics, analgesic agents except paracetamol and acetylsalicylic acid) prior to or during the trial; or suffered from allergies to cosmetic products or ingredients thereof. Subjects were also excluded if they had infectious hepatitis, human immunodeficiency virus infection,

received cancer treatment within the last 2 years, or were addicted to alcohol or drugs.

Study participants were not allowed to undergo intensive exposure of the test areas to UV-therapy, artificial tanning, and/or sun within 4 weeks before and during the trial, or to apply any detergents or leave-on cosmetics on the test areas from 3 days before until cessation of the study. Furthermore, study participants were not permitted to change their lifestyle habits or to engage in sweaty, strenuous physical activities over the study course. On days of visits at the study center, subjects were asked not to consume any caffeinated beverages or to smoke within 2 h before instrumental measurements. Similarly, any contact of the volar arms with water was to be avoided within 24 h before assessments on Day 1 (baseline) and Day 29 (study end), and within 2 h before instrumental measurements on Day 2.

The measurement of SC hydration was performed by the electrical capacitance method using the corneometer (Corneometer® CM825, Courage & Khazaka, Cologne, Germany). Electrical capacitance of the skin surface is a function of SC hydration (i.e., the better the skin hydration the higher the electrical capacitance).¹⁵ Electrical capacitance was determined in both assigned skin areas on Day 2 (i.e., 24 h after first application of DCLC), and on Day 29 (i.e., 1 day after the last application of DCLC). There were 5 measurements per test area and assessment time point. Following exclusion of the lowest and highest reading, the other three measurements were averaged to receive the final value to be used for further analysis.

To quantify skin barrier function, TEWL measurements (Tewameter® TM 300, Courage & Khazaka, Cologne, Germany) took place on each of the two allocated test areas at baseline and on Day 29. There was one measurement per test area per assessment time. Each measurement lasted for 30 s, with one reading collected per second. The average of the final 10 readings represented the TEWL value, which was included in the analysis.

The skin surface pH was determined on both pre-specified test areas using the Skin-pH-Meter PH 900 PC (Courage & Khazaka, Cologne, Germany). Two measurements were performed (and averaged) per test area at baseline and on Day 29.

For microbiome analysis, skin bacteria were collected from the respective test areas at baseline and on Day 29 (without previous cleaning) using the swabbing method as described previously.^{16,17} In brief, the designated area was rubbed back and forth applying firm pressure under slow rotation about 50 times with a sterile cotton swab that was pre-moistened in molecular grade DNA-free water. Subsequently, the swab head was aseptically cut, put in a sterile microcentrifuge tube without buffer, and stored at -80°C until skin microbiome analysis by Microbiome Insights Inc., Vancouver, Canada. For assessment of α -diversity, as a measure for microbial richness and evenness, the Shannon Index was calculated. A high Shannon Index represents high and even microbial richness.¹⁸

Instrumental measurements (corneometry, TEWL, skin pH) were conducted in an air-conditioned room ($22 \pm 2^{\circ}\text{C}$, $50 \pm 7.5\%$ relative humidity), after the study participants had spent ≥ 30 min in this climatic environment. Adverse events (AE) occurring during the study

were to be recorded in a diary. Skin tolerability of DCLC was assessed by objective and subjective dermatological evaluations conducted at baseline and on Day 29.

2.1.3 | Statistical evaluation

Statistical evaluations were performed using SAS® 9.4 for Windows (IT@Cornell, Ithaca, NY, USA). For the DCLC-treated and control site, mean change in skin surface capacitance from baseline at each post-application assessment time was calculated. Differences in the mean change in skin surface capacitance from baseline between the DCLC-treated and control site were statistically analyzed using the paired *t*-test. For each site (DCLC-treated and water-treated), it was also determined whether mean absolute values for skin capacitance statistically differed between baseline and post-application assessment times using the paired *t*-test. For statistical analyses of results from TEWL and skin pH measurements, the same approach was used. Linear mixed model was applied to determine significant differences in the Shannon Index. The level of significance was set at 0.05. AE frequencies and results from cutaneous tolerability assessments were evaluated descriptively.

2.2 | Study 2: Pediatric study

2.2.1 | Study design

Study 2 was an exploratory, open, non-comparative study in infants and children with atopic-prone skin. Visits at the study center took place on Day 1 (baseline) and Day 29 (study end). DCLC was applied by the parents at home until Day 28. For microbiome analysis, one skin area (approximately 16 cm²) was marked on the right or left volar forearm in a balanced fashion. Parents were instructed by a technician to apply approximately 5 g of DCLC to the whole body (including the face) once daily on 2–3 days per week. After the cleansing procedure, DCLC should be rinsed off and the skin gently dried. In addition, all infants/children received an established dexpanthenol-containing emollient as base skin care. The emollient was spread on the body and face at least twice daily (about 5 g per application). On days of concomitant use, the emollient was to be applied immediately after using DCLC. Neither the emollient nor DCLC should have been used in the 24 h prior to the scheduled visit on Day 29. Compliance was verified by weighing the containers of DCLC and emollient at the end of the study.

2.2.2 | Subjects and assessments

Male and female infants/children between 6 months and 6 years of age with a Fitzpatrick skin type of I–IV and a history of mild to moderate AD were to be enrolled. Study participants were required to have had no AD symptoms for at least 30 days and to have received no AD therapy in the same time period. Exclusion criteria and study restrictions were largely the same as those of Study 1.

Swabs for microbiome analysis were collected from the test area at baseline and on Day 29, thereby following the same procedure as described for Study 1. Evaluation of cutaneous tolerability was performed by a pediatrician before first application of DCLC and at the end of the 4-week usage period. The entire skin was investigated for the presence of erythema, dryness, scaling, fissures, papules, pustules, edema, vesicles, and weeping. The degree of dry skin was assessed by a combination of visual parameters (scaling, whiteness) and tactile (roughness) examination of the skin. Each item was rated on a 5-point scale, with a score of 0 (none) reflecting the most favorable condition and 4 (strong) the worst. Any AEs occurring during the study were to be recorded by the parents in a diary. Acceptability of DCLC was assessed using a validated questionnaire that included 25 positive statements about the product's features. The parents had to complete the questionnaire at the study center on Day 29. All statements had predefined identical options that were to be checked off: –3 = strongly disagree, –2 = moderately disagree, –1 = slightly disagree, 0 = neither agree nor disagree, 1 = slightly agree, 2 = moderately agree, 3 = strongly agree.

2.2.3 | Statistical evaluation

Results of the dermatological examinations and the questionnaire, as well as the frequency of AEs, were evaluated using descriptive statistics. Linear mixed model was applied to determine significant differences in the Shannon Index; a significance level of 0.05 was selected.

3 | RESULTS

3.1 | Study 1: Adult study

A total of 44 subjects (43 females, 1 male; with a Fitzpatrick skin type of II (2.3%) and III (97.7%)) were included and all finished the study. The mean age was 48.7 years (range: 19–70 years).

3.1.1 | Corneometry (SC hydration)

DCLC-treated and water-treated forearm skin areas had similar corneometry values at baseline consistent with the definition of dry skin (Table 1). The application of DCLC was associated with a significantly enhanced SC hydration after the first application at 24 h and improved further as once-daily DCLC use continued (Table 1). After 4 weeks (Day 29), SC hydration had improved by 17.2% in comparison with baseline (5.16 a.u.; *p* < 0.001). There were also significant increases from baseline in the control area treated with water only. However, at the end of the treatment period (Day 29), the increase in mean skin surface capacitance was less pronounced (11.8%). This is also confirmed by evaluating bilateral differences in the mean change of SC hydration from baseline. On Day 29, the mean change in electrical capacitance of the skin from baseline (and thus the

TABLE 1 Absolute skin capacitance values and changes from baseline 24 h after the first application of DCLC and water control, and after once-daily application over 4 weeks

Time	DCLC			Water control		
	Absolute value	Change from BL	<i>p</i> -Value*	Absolute value	Change from BL	<i>p</i> -Value*
BL	30.01 ± 4.24	–	–	30.82 ± 3.83	–	–
24 h	33.11 ± 5.68	3.17 ± 3.41 [#]	<0.001	33.99 ± 4.61	3.27 ± 3.29 [#]	<0.001
Day 29	35.17 ± 5.46	5.16 ± 4.76 [§]	<0.001	34.47 ± 4.85	3.65 ± 3.97 [§]	<0.001

Note: *N* = 43–44. All data are shown as mean ± standard deviation and are presented in arbitrary units (a.u.).

Abbreviations: BL, baseline skin capacitance value; DCLC, dexpanthenol-containing liquid cleanser.

[#]*p* = 0.820 for the difference in mean change from baseline (DCLC site vs. control site), paired *t*-test.

[§]*p* = 0.011 for the difference in mean change from baseline (DCLC site vs. control site), paired *t*-test.

*For the mean change from baseline, paired *t*-test.

TABLE 2 Absolute transepidermal water loss (TEWL) values and changes from baseline following once-daily application of DCLC or water for 4 weeks

Time	DCLC			Water control		
	Absolute value	Change from BL	<i>p</i> -Value*	Absolute value	Change from BL	<i>p</i> -Value*
BL	14.1 ± 2.1	–	–	13.9 ± 2.2	–	–
Day 29	14.5 ± 2.4	0.5 ± 2.0 [#]	0.143	14.2 ± 2.1	0.3 ± 1.9 [#]	0.327

Note: *N* = 44. All data are shown as mean ± standard deviation and are presented in g/m²/h.

Abbreviations: BL, baseline TEWL value; DCLC, dexpanthenol-containing liquid cleanser.

[#]*p* = 0.636 for the difference in mean change from baseline (DCLC site vs. control site), paired *t*-test.

*For the mean change from baseline, paired *t*-test.

TABLE 3 Absolute skin pH values and changes from baseline following once-daily application of DCLC or water for 4 weeks

Time	DCLC			Water control		
	Absolute value	Change from BL	<i>p</i> -Value*	Absolute value	Change from BL	<i>p</i> -Value*
BL	5.21 ± 0.50	–	–	5.18 ± 0.47	–	–
Day 29	5.18 ± 0.45	–0.04 ± 0.53 [#]	0.621	5.22 ± 0.40	0.04 ± 0.42 [#]	0.508

Note: *N* = 44. All data are shown as mean ± standard deviation.

Abbreviations: BL, baseline pH value; DCLC, dexpanthenol-containing liquid cleanser.

[#]*p* = 0.132 for the difference in mean change from baseline (DCLC site vs. control site), paired *t*-test.

*For the mean change from baseline, paired *t*-test.

moisturizing effect) was significantly greater in the forearm test area treated with DCLC than in the contralateral test area treated with water only (5.16 vs. 3.65 a.u.; *p* = 0.011; [Table 1](#)). No significant bilateral difference in mean change from baseline was observed after the first application at 24 h.

3.1.2 | Transepidermal water loss

At baseline, mean TEWL values were comparable between DCLC-treated and water-treated forearm skin areas ([Table 2](#)). After the 4-week usage period, no significant difference in TEWL was found for either of the two treatments if compared to baseline. Similarly, the difference between the DCLC-treated and water-treated skin areas in terms of mean change of TEWL from baseline did not reach statistical significance after the 4-week application period ([Table 2](#)), indicating that DCLC did not adversely affect skin barrier function.

3.1.3 | Skin pH

Applications of DCLC or water to the test areas had no effect on skin pH. Mean skin pH values remained essentially unchanged and were within the physiological range during the study period, and showed no significant differences compared with baseline or between treatments ([Table 3](#)).

3.1.4 | Skin microbiome (Shannon Index: α -diversity)

At baseline, the Shannon Index was in accordance with healthy skin¹⁸ and comparable between DCLC-treated and water-treated skin test areas ([Table 4](#)). For both treatments, statistical comparison of the assessment time points revealed a significant difference in the Shannon Index between baseline and Day 29. The shift in α -diversity from baseline to Day 29 was similar for DCLC and water control

Time	DCLC		Water control	
	Absolute value	p-Value*	Absolute value	p-Value*
BL	2.020±0.571	-	1.988±0.544	-
Day 29	1.705±0.671 [#]	<0.001	1.788±0.630 [#]	<0.001

Note: N = 33–43. All data are shown as mean ± standard deviation.

Abbreviations: BL, baseline value; DCLC, dexpanthenol-containing liquid cleanser.

[#]p = 0.970 for the bilateral difference in absolute values (DCLC site vs. control site), Linear mixed model.

*For comparison with the baseline absolute value, Linear mixed model.

(Table 4). In fact, there was no significant difference in the mean Shannon Index between DCLC-treated and water-treated skin areas after the 4-week usage period (1.705 vs. 1.788, $p = 0.970$), indicating that the microbiome biodiversity of the volar forearm skin was not affected by DCLC use.

3.1.5 | Tolerability

Applications of DCLC were well tolerated. No subject reported a systemic or local AE considered to be related to the study product. The objective and subjective dermatological evaluations revealed no difference between DCLC-treated and water-treated skin. In particular, there were no increased cases of erythema or skin irritation upon use of DCLC.

3.2 | Study 2: Pediatric study

This study enrolled 33 infants and children (12 females, 21 males) with a Fitzpatrick skin type of II (76%), III (18%), and IV (6%). The mean age was 3.5 years (range: 6 months to 6 years). One subject prematurely discontinued the study due to AEs (erythema and itching).

3.2.1 | Skin microbiome (Shannon Index: α-diversity)

No significant change was observed upon 4-week use of DCLC in combination with an emollient. In fact, comparison of the assessment time points revealed no significant difference in the mean Shannon Index between baseline and Day 29 (3.293 ± 0.492 vs. 3.102 ± 0.681 , $p = 0.092$), indicating that the microbiome biodiversity did not change over the study course.

3.2.2 | Tolerability and acceptability

Applications of DCLC in combination with a basic emollient treatment were associated with a good cutaneous tolerability. One subject experienced mild AEs (erythema and itching) that were

TABLE 4 Shannon Index of test sites at baseline and after once-daily application of DCLC or water for 4 weeks

considered to be related to DCLC. Following discontinuation of the study product, the conditions resolved. Otherwise, no subject experienced a local or systemic AE considered to be DCLC-related. The proportion of subjects with some degree of dry skin—as assessed by a pediatrician—decreased from 70% at baseline to 45% at study end ($p < 0.05$, Wilcoxon signed-rank test). Apart from that, the skin examinations did not show any remarkable findings or changes. No flare-ups of AD were observed in any of the subjects during the study.

The acceptability of DCLC was highly scored by the parents. For 24 out of 25 favorable statements about the product features, the rating was 3 (strongly agree), 2 (moderately agree), or 1 (slightly agree) by >70% of parents on Day 29. For instance, 97% of parents provided a scoring of 1–3 for each of the following statements: “effectively cleans without irritating my baby’s/child’s sensitive/eczema prone skin”, “wash and cream combination leave my baby’s/child’s sensitive/eczema prone skin feeling soft”, “wash and cream combination leave my baby’s/child’s sensitive/eczema prone skin feeling moisturized.”

4 | DISCUSSION

Within the framework of the development of DCLC, a new body wash gel for atopic-prone skin, two 4-week studies were performed. One study investigated DCLC’s effects on SC hydration, TEWL, skin pH, and skin microbiome in healthy adult subjects with dry skin. Another study explored the cutaneous tolerability of DCLC and its effect on the skin microbiome in infants and children with atopic-prone skin in the presence of a basic emollient skin care.

The two studies provided the following results: (1) following repeated once-daily applications of DCLC, skin surface capacitance was significantly higher compared with water-treated skin suggesting long-term SC hydration; (2) DCLC use was not associated with changes in TEWL, indicating that the product did not adversely affect skin barrier function; (3) the skin pH was not negatively influenced by DCLC applications; (4) after once-daily application of DCLC to healthy adults for 4 weeks, microbiome biodiversity of the volar forearm skin was not affected if compared to water-treated skin; (5) in infants/children with atopic-prone skin, the 4-week use of DCLC in combination with an emollient, the microbiome biodiversity of the volar forearm skin did not shift over the study course; (6) DCLC was

well tolerated in both studies and its acceptability was highly scored by the parents of infants/children with atopic-prone skin.

It can be inferred that DCLC meets the requirements of a modern body cleanser to be used by atopic skin sufferers. Our results are consistent with a previous study using emollient-enriched body/face wash gels for dry skin.¹⁴ In that study, the wash gels had a similar composition to DCLC. The products were effective, non-irritating cleansers that simultaneously exerted a moisturizing effect on the skin without impairing barrier function.

In light of recent findings, it can be assumed that the skin hydrating effect and favorable acceptability of DCLC observed in our two studies were due to the emollient ingredients present in the formulation. In addition to mild non-ionic-based surfactants, DCLC contains ingredients belonging to the key constituents of an ideal emollient and AD care product.^{3,8} Glycerin and saccharide isomerate have humectant properties and increase SC hydration.^{19,20} Apart from its antipruritic/soothing effect, niacinamide increases the synthesis of natural lipids in the SC such as ceramides.^{21,22} Dexpanthenol acts as a humectant, but also triggers protein/lipid synthesis and compensates for decreased SC hydration by reducing the increased stiffness of SC lipid lamellae and keratin filaments (i.e., it increases molecular mobility/fluidity of SC lipid lamellae and proteins) observed in dry skin conditions.^{3,23}

There is growing evidence that the cutaneous care of atopic-prone skin sufferers should start at an early age with regular use of non-alkaline cleansers and moisturizers to maintain skin barrier function.²⁴ The results of our studies suggest that DCLC is a suitable option for this recommendation. DCLC did not affect the barrier function of the skin, which distinguishes it from conventional, soap (ionic)-based cleansing products. The latter may significantly compromise the skin barrier integrity.^{1,6}

The pH of cleansers for subjects with atopic-prone skin should be in the physiological cutaneous range of about 5.⁸ DCLC has a pH of 5.5, which explains why we observed a stable natural skin pH upon repeated use of DCLC. This is considered advantageous because an altered skin pH may affect the composition of the skin microbiome.⁸

Recently, it has been postulated that the barrier function of the epidermis can be divided into three distinct functional layers, with the skin microbiome representing the outermost layer.⁹ These functional levels (chemical, physical, and microbiome) are highly interdependent. It is therefore a noteworthy finding of our studies that DCLC did not impair the skin microbiome. One might have expected that DCLC increases the microbiome biodiversity in children/infants with a history of AD due to the presence of α -glucan oligosaccharide—a prebiotic—in the formulation. In fact, in lesional atopic skin fewer bacteria species are present compared with healthy skin due to the predominance of *Staphylococcus aureus*.⁸ However, in our pediatric study, the children/infants were in the remission phase with a Shannon Index resembling normal skin at baseline. The latter, and the fact that we did not identify bacterial species in the microbiome analysis, might have rendered invisible the beneficial effects of DCLC on the diversity of the skin microbiome.

DCLC was well tolerated and achieved a high acceptability, which is consistent with previous studies conducted with

emollient-enriched body cleansers.^{13,14} Considering the properties of DCLC we observed in the studies, the product has the potential to become a valuable body cleanser for subjects with atopic-prone skin.

A limitation of the pediatric study is that DCLC was applied in combination with an emollient as basic treatment. It was considered unethical to withhold the use of emollients for several weeks in infants and children with a history of AD. Of note, the combined use of cleanser and emollient reflects the everyday life of atopic-prone skin sufferers. Moreover, the pediatric study was open and uncontrolled. Therefore, the possibility that acceptability results were influenced by study expectations cannot be excluded. Finally, in the skin microbiome analyses, we did not identify bacterial species (just bacterial genera). Therefore, the effect of DCLC on the abundance ratio of *Staphylococcus epidermis* to *Staphylococcus aureus* in the skin microbiome could not be detected.

5 | CONCLUSIONS

Continued once-daily applications of DCLC to dry skin for 4 weeks provided a significant moisturizing effect without affecting skin pH, barrier function or the skin microbiome. In addition, DCLC applications over 4 weeks (2–3 days/week) in combination with an emollient were well tolerated by infants/children with atopic-prone skin and achieved a high acceptability; no shift in the microbiome biodiversity was observed. The results of our two studies indicate that DCLC meets the requirements of a modern body cleanser for regular use by atopic-prone skin sufferers. The concept of integrating emollient ingredients into body cleansers for atopic-prone skin is supported.

AUTHOR CONTRIBUTIONS

Erwan Peltier, Sonja Trapp, and Ana Barrionuevo-Gonzalez designed the studies. Raffaella de Salvo and Connie Sun made substantial contributions to the conduct of the trials and provided project management support. Marianne Brandt, Sabrina Laing, and Natascha Hennighausen had the study performance oversight. All authors have read and approved the final manuscript.

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Edgar A. Mueller, 3P Consulting drafted the initial version of the manuscript. The authors were responsible for critical revisions of the manuscript and provided important intellectual content.

CONFLICT OF INTEREST

Erwan Peltier, Sonja Trapp, Raffaella de Salvo, and Connie Sun are employees of Bayer Consumer Care AG, Basel, Switzerland. Ana Barrionuevo-Gonzalez is an employee of Bayer Hispania, S.L., Sant Joan Despí, Spain. The other authors report no conflicts of interest.

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DATA AVAILABILITY STATEMENT

The data presented in this paper are available from the corresponding author upon reasonable request.

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