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Effect of a novel "emollient plus" formulation on mild-to-severe atopic dermatitis and other dry skin-related diseases as monotherapy or adjunctive therapy: an observational study on efficacy, tolerance and quality of life in adult patients

Background: Atopic dermatitis (AD), psoriasis and senile xerosis comprise common chronic and relapsing inflammatory skin disorders with clinical symptoms such as lichenification, pruritus and inflammatory lesions that affect the quality of life of patients. *Objectives*: In this study, we aimed to evaluate the efficacy of a novel "emollient plus" formulation (Lipikar baume AP+M), containing non-living lysates of non-pathogenic *Vitreoscilla Filiformis* bacteria from LaRoche-Posay Thermal Spring water, in improving quality of life, alleviating skin pain, and managing symptoms of mild-to-severe AD or skin disorders associated with dryness or severe xerosis in adults. *Materials & Methods*: The study included 1,399 adult patients, who participated in a two-month observational study over two visits, conducted at dermatologists' practices. Visits included clinical assessment of skin disease before and after administration of the product as well as completion of the 10-question Dermatology Life Quality Index. Questionnaires were used to evaluate efficacy, safety, satisfaction and tolerance of the product both by the dermatologists and patients, as well as assess quality of life of patients. *Results*: Statistically significant improvement ($p<0.001$) by at least one grade was observed by more than 90% based on patients' evaluation of efficacy regarding intensity of the skin disease, skin dryness, surface affected by inflammatory lesions, pruritus, quality of sleep, daily discomfort, dryness and desquamation. Quality of life after two months improved by 82.6%. *Conclusion*: This study demonstrated significant reduction in symptoms of mild-to-severe skin dryness after application of the "emollient plus" formulation over two months, either alone or as adjunctive therapy.

Key words: atopic dermatitis, emollient, quality of life, skin dryness, sleep quality, xerosis

Patients suffering from dermatological conditions such as atopic dermatitis (AD) or eczema, psoriasis, senile xerosis and severe xerosis demonstrate dry skin symptoms, such as pruritus, pain, discomfort, erythema (redness), oedema, and desquamation [1-4] that can adversely affect their quality of life (QoL).

AD, also known as atopic eczema, is a common chronic and relapsing inflammatory skin disorder with a global prevalence of 2-10% in adults and 15-30% in children [5]. Psoriasis constitutes a chronic immune-mediated disease that affects 3.0% of the US adult population [3], while xerosis represents a common condition in elderly patients, affecting more than 50% of individuals above 65 years old [6].

AD and psoriasis constitute multifactorial skin disorders associated with environmental and genetic factors, as well as impaired immune responses. Environmental factors include exposure to irritants, allergens, hard water, stress or pathogenic bacteria [7, 8]. Metagenomics from sampling the cutaneous microbiome in AD patients [9, 10] revealed increased predominance of *Staphylococci* during flares, especially *Staphylococcus aureus* [9, 11] with increased colonization of the skin. A strong genetic risk factor for AD involves mutational impairments in filaggrin protein and disruption of the skin barrier [12]. *S. aureus* penetrates the dermis, producing changes in the protein and lipid content, and stimulates overexpression of proinflammatory T-helper type 2 (Th2) cytokines [13, 14], such as interleukin (IL)-4, IL-10, IL-13, and IL-31 [15]. The impaired immune responses enhance *S. aureus* proliferation, further compromising skin barrier function [16, 17], thus leading to loss of microbial diversity and skin dysbiosis.

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Due to the multifactorial pathogenesis of AD, psoriasis and xerosis [3, 4, 18], treatment can be chronic and challenging. Management depends on the severity and aims to prevent the onset of flare-ups or otherwise treat it [12]. A basic therapeutic approach [19] for AD prevention includes the use of emollients or skin moisturizers to reduce dryness of the skin, while also involves proactive anti-inflammatory therapy with topical co-administration of low-to-mid-potency corticosteroid and calcineurin inhibitor (tacrolimus and pimecrolimus) creams [12, 20]. In severe acute or chronic cases, systemic immunosuppressants or phototherapy (UV light) may be necessary [12]. Emollients and topical calcineurin inhibitors are often preferred over topical anti-inflammatory treatments, due to dermatological and non-dermatological side effects [21] as well as systemic adverse reactions [22].
Emollients are also the primary treatment for xerosis and associated pruritus in elderly patients [4, 23]. They hydrate the stratum corneum and restore epidermal differentiation, thus improving the integrity and function of the skin barrier, reducing trans epidermal water loss (TEWL) [24, 25], inflammation and pruritus [21, 26].
The goal of the present study was to assess the impact of monotherapy or adjunctive therapy (with topical or systemic corticosteroids, calcineurin inhibitors and/or antihistamines) using a new topical "emollient plus" formulation, containing putative active ingredients [19], including Aqua Posae Filiformis (APF), microresyl, shea butter and niacinamide, on symptoms and QoL of adults with mild-to-severe AD and other dermatological conditions with skin dryness or severe xerosis in adults.

Materials and methods

Design of the study

The overall design of the study is summarized in *table 1*.
The study was performed over two visits and included 16-year-old or older patients, with mild-to-severe AD, psoriasis, severe skin dryness other than AD, senile xerosis or other similar conditions. Patients with severe to very severe AD were excluded.
The initial visit included a clinical assessment of the disease by the dermatologist, a self-assessment of pain and discomfort and an evaluation of QoL by the patient, based on the 10-question Dermatology Life Quality Index (DLQI), as well as the prescription plan. The final visit, conducted after approximately two months (average time between visits: 60.5 ± 16.0 days), included the same assessments, along with an evaluation of the degree of product satisfaction and tolerance, by both dermatologists and patients.

Assessment methods

Dermatologists' evaluation
The severity grade of AD and other dry skin-related diseases was assessed based on a 5-point scale (0=absent, 1=mild, 2=moderate, 3=severe, 4=very severe*)* using the parameters: intensity of skin condition, inflammatory lesions, pruritus, impact on quality of sleep and daily discomfort. Skin dryness (xerosis) and desquamation were evaluated using a numerical scale from 0 (no symptom) to 10 (very severe symptomatology). The degree of satisfaction and tolerance of the product was assessed based on a 3-point scale (neither satisfied nor unsatisfied, satisfied, very satisfied) and a 4-point scale (low, average, high, excellent), respectively.

Table 1.

Study location and duration
• The study was carried out at dermatologists' practices and lasted approximately two months for each patient
Population
• Patients of at least 16 years old of age with mild-to-severe AD and other skin diseases with dryness or severe xerosis
Products
• **Novel 'emollient plus' formulation** applied once or twice a day as prescribed by the dermatologist
Study period
• December 2019 - December 2020
Inclusion criteria
- 16 years old or older - mild-to-severe skin conditions with dryness or severe xerosis (AD, psoriasis, severe dry skin other than AD, senile xerosis or other similar conditions)
Exclusion criteria
• Severe to very severe AD

Patients' self-evaluation
Severity levels of subjective symptoms, *i.e.*, skin pain, discomfort/burning, tingling, numbness, and itching, were evaluated on a numerical scale from 0 (no sensation) to 10 (very severe sensation) while sleep quality was evaluated on a scale from 0 (no sleeplessness) to 10 (very severe sleeplessness). Quality of life was based on the 10-question Dermatology Life Quality Index, DLQI (*see supplementary table 1*). Satisfaction and tolerance were assessed as mentioned above.

Results

Patient disposition and characteristics

The study included 1,339 patients (mean age ± SD: 44.9 ± 20.8 years, 58.2% female). At baseline, most patients suffered from AD (37.6%) and severe xerosis (23.1%), with 16.2% and 15.6% suffering from senile xerosis and psoriasis, respectively (*table 2*).
At baseline, 34% of patients were not receiving any medication to manage their AD symptoms. The majority of patients (66%) were administered the novel "emollient plus" formulation in combination with other therapies, while 34% of patients were receiving monotherapy. Most

Table 2. Baseline patient characteristics.

Characteristics	Patients *n* (%)	Distribution (Years old)
Gender (*n*=1339)		
Male	560 (41.8%)	
Female	779 (58.2%)	
Age (*n*=1227)		
Min		16
Max		97
Mean (SD)		44.9 ± 20.8
Duration of the disease (*n*=1237)		
Min		0
Max		52
Mean (SD)		6.3 [± 7.8]
Phototype (*n*=1236)		
I	53 (4.3%)	
II	391 (31.6%)	
III	601 (48.6%)	
IV	172 (13.9%)	
V	19 (1.5%)	
Skin disease (*n*=1336)		
Atopic dermatitis	502 (37.6%)	
Severe xerosis (other than	308 (23.1%)	
atopic dermatitis)	216 (16.2%)	
Senile xerosis	209 (15.6%)	
Psoriasis	101 (7.6%)	
Other		
Living environment (*n*=1334)		
Urban zone	1193	
Rural zone	(89.4%)	
	141 (10.6%)	
Occupation (*n*=1332)		
In a professional activity	645 (48.4%)	
Student	224 (16.8%)	
Retired	220 (16.5%)	
Without professional activity	201 (15.1%)	
Looking for a professional activity	42 (3.2%)	

Table 3. Prescription plan at baseline.

Prescription plan (*n*=1339)	Patients *n* (%)
Novel "emollient plus" formulation therapeutic schema (*n*=1339)	
As adjunctive therapy	884 (66.0%)
As monotherapy	455 (34.0%)
Treatments combined with the "emollient plus" formulation (*n*=1139)	
No drug	455 (34.0%)
Topical corticosteroids	337 (25.2%)
Topical corticosteroids with antihistamines	284 (21.2%)
Other drug (including calcineurin inhibitors and calcipotriol)	87 (6.5%)
Antihistamines	84 (6.3%)
Other combination	77 (5.8%)
Systemic corticosteroids	15 (1.1%)
Novel "emollient plus" formulation for therapeutic schema	884 (66.0%)
As adjunctive therapy	455 (34.0%)
As monotherapy	
Novel "emollient plus" formulation dose (*n*=1336)	987 (73.9%)
Morning & evening	283 (21.2%)
Evening	66 (4.9%)
Morning	

of the participants (73.9%) applied the product twice daily (*table 3*).

Evaluation of efficacy by dermatologists

At the final visit, there was a statistically significant improvement ($p<0.001$) in efficacy regarding the clinical condition of patients for all examined parameters (intensity of the skin condition, skin dryness, surface affected by inflammatory lesions, pruritus, quality of sleep, daily discomfort, dryness and desquamation) based on evaluation by dermatologists, compared to baseline.

Specifically, for 85.6% of patients with at least mild intensity at baseline, the intensity of dry skin symptoms improved by at least one grade of disease severity. The significant mean reduction in skin disease intensity for moderate and severe grades matched the increase in mild and no grade at the final visit compared to baseline (*figure. 1*).

Similarly, for 91.4% of patients with skin dryness, an improvement was observed by at least one grade in disease severity following application of the product for two months. The significant mean reduction in skin dryness shown for moderate and severe grades matched the increase in mild and no grade at the final visit compared to baseline (*figure. 2*).

After two months of using the product, an improvement by at least one grade in disease severity was observed for 91.5% of patients with pruritus. The significant mean reduction in moderate to very severe grades matched the increase in mild and no grade at the final visit compared to baseline (*figure. 3*).

For 87.3% of the patients, after two months of product use, an improvement in inflammatory skin lesions by at least one grade was found. The percentage of patients reporting no inflammatory lesions at the follow-up visit was almost three times higher compared to baseline, and a significant percentage of patients also noticed a significant mean reduction of surface affected by skin lesions by 10% and 30% (*figure. 4*).

Similarly, 94% of patients with daily discomfort exhibited an improvement by at least one grade after two months of using the product. The significant mean reduction of mild to very severe grades matched the increase in absence of symptoms during the final visit compared to baseline (*figure 5*).

Regarding quality of sleep, there was an improvement by at least one grade for 93.5% of the patients. The significant mean reduction of mildly to very severely affected sleep quality matched the increase in no effect on sleep quality at the final visit compared to baseline (*figure 6*).

Finally, skin dryness and desquamation, after two months of applying the novel formulation, were reduced by at least 71%. Both parameters were significantly decreased by more than three times at the final visit compared to baseline (*figure 7*).

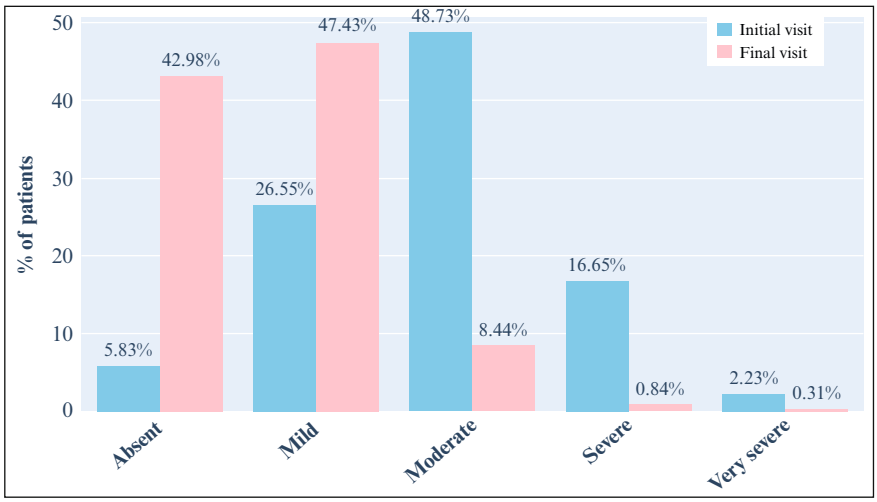

Figure 1. Percentage of patients as per dermatologists' assessments of the intensity of skin disease (n=1303) based on a 5-point scale at the initial and final visits (p<0.001).

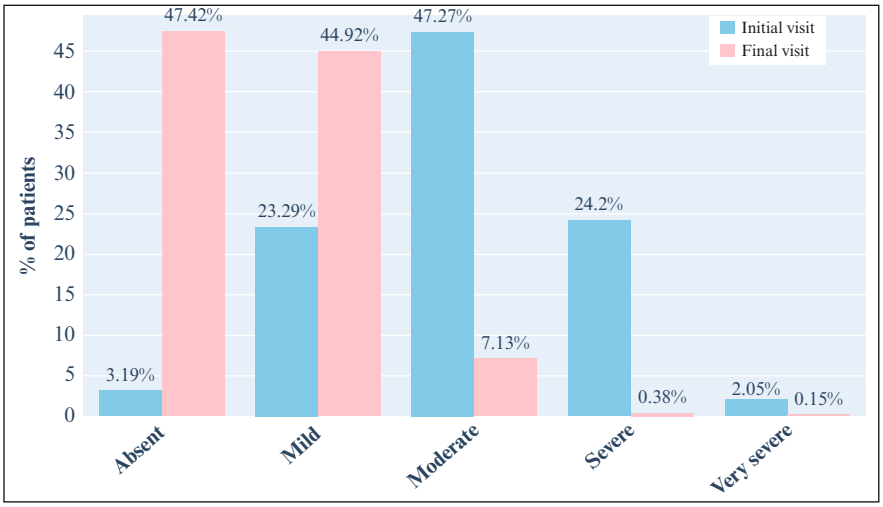

Figure 2. Percentage of patients as per dermatologists' assessments of skin dryness (n=1318) based on a 5-point scale, at the initial and final visits (p<0.001).

Satisfaction and evaluation of tolerance by dermatologists

Overall satisfaction and tolerance rate for the product, as assessed by the dermatologists, was 98.8% and 97.7%, respectively, with 82.16% and 73.71% reporting "very satisfied" and "excellent tolerance rate", accordingly (*figures 8, 9*).

Patient self-assessment

After application of the product, a significant improvement was found in the mean intensities of all the evaluated parameters for skin discomfort (skin pain, sleep quality and sensation of itching, numbness, tingling and burning), with a mean reduction by more than 80% compared to baseline. More specifically, the mean reduction in skin pain and sleep quality was 87.0% and 87.7%, respectively, compared to baseline. Similarly, skin sensations, such as burning, tingling, numbness and itching, were significantly reduced by 86.4%, 88.6%, 84.6% and 81.1%, respectively, compared to baseline (*figure 10*).

Patients' evaluation of QoL

Ten questions of the dermatology life quality index (DLQI) (*see supplementary table 1*), evaluating QoL, were answered by the patients. Overall, the QoL of patients with mild to severe AD and other dry skin-related diseases improved, as reflected by the mean DLQI total score which was reduced by 82.6%, changing on average from moderate to no impact (*figure 11*).

Patients' satisfaction and evaluation of tolerance

Overall, patients' satisfaction and tolerance rate for the product was 97% and 96%, respectively, with 76.31%

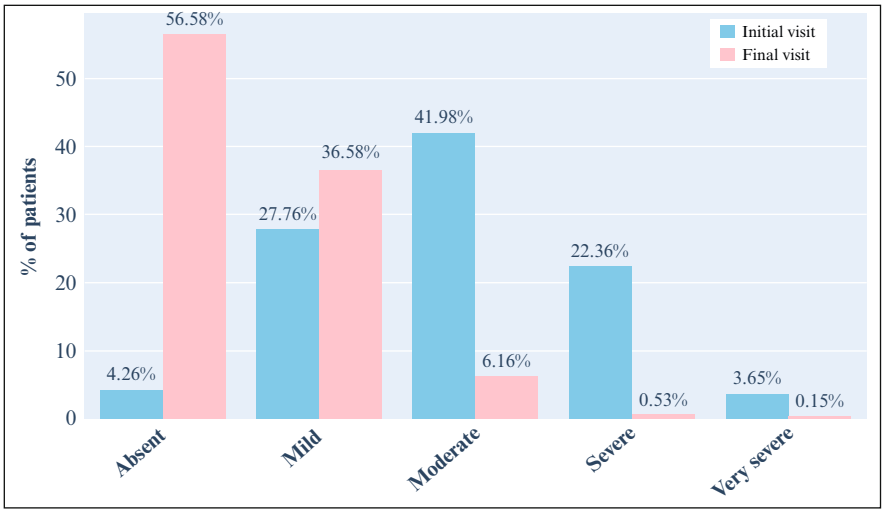

Figure 3. Percentage of patients as per dermatologists' assessments of pruritus (n=1315) based on a 5-point scale, at the initial and final visits (p<0.001).

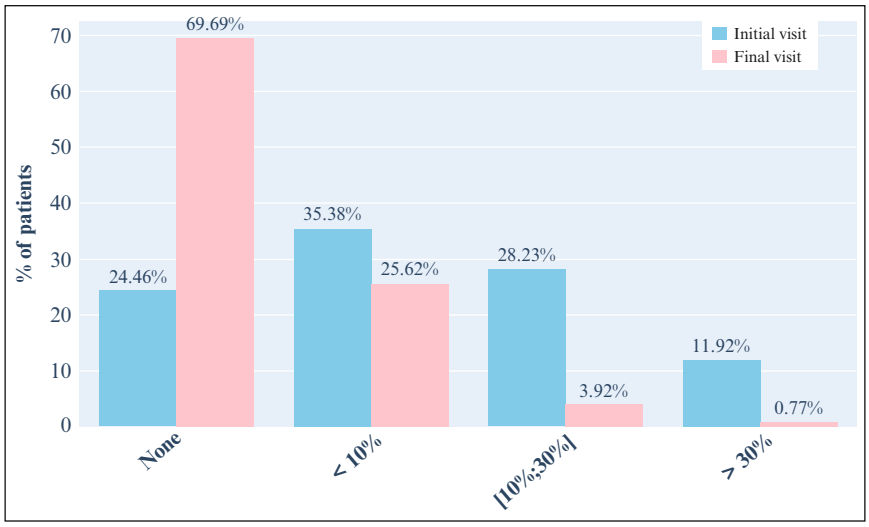

Figure 4. Percentage of patients as per dermatologists' assessment of surface affected by inflammatory lesions (n=1300) based on a 4-point scale of skin lesion coverage, at the initial and final visits (p<0.001).

and 70.23% reporting "very satisfied" and "excellent tolerance rate", accordingly (*figure 12, 13*).

Discussion

AD, psoriasis and senile and severe xerosis are characterized by a chronic and recurrent flaring nature with symptoms that can have a negative impact on patient's QoL. The combination of skin barrier dysfunction, microbial dysbiosis and immune dysregulation are the leading causes of the pathogenesis of AD and other skin diseases associated with dryness or severe xerosis [3, 6, 25, 27]. A number of studies have demonstrated the benefits and safety of emollients in different age groups of patients with AD [28] or associated skin disorders with dryness or severe xerosis in adults.

In this study, a new "emollient plus" formulation was evaluated on its efficacy in improving symptoms and QoL after an average use of two months, either alone or as an adjuvant therapy, in adults with mild-to-severe AD or other dry skin-related diseases.

The product contains APF, and together with the novel patented ingredient microresyl, comprise the prebiotic source of the novel AP+M formulation. APF is comprised of non-living lysates, originating from Gram-negative non-pathogenic bacteria, *Vitreoscilla Filiformis (Vf)*, which are naturally cultured in Thermal Spring water of La Roche Posay ([LRP]-TSW) [29, 30], attributing the "emollient plus" characteristic to the product, according to the relevant European guideline

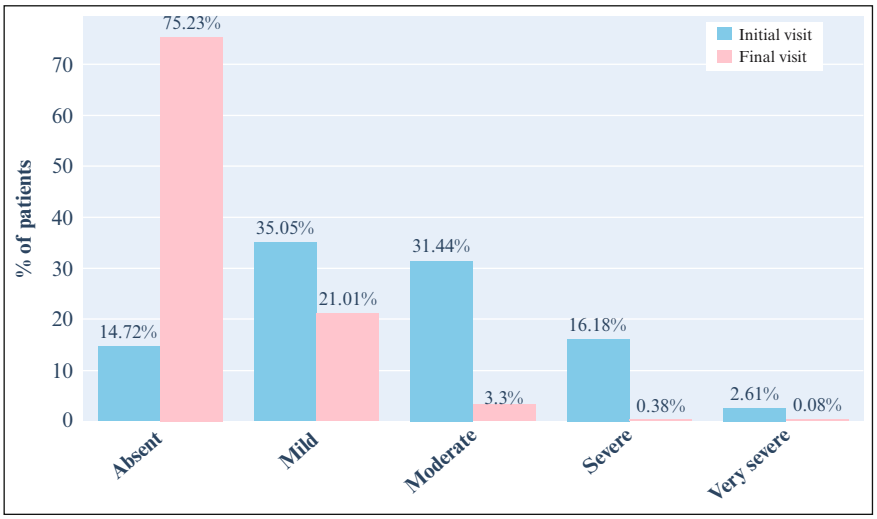

Figure 5. Percentage of patients as per dermatologists' assessment of daily discomfort (n=1304) based on a 5-point scale, at the initial and final visits (p<0.001).

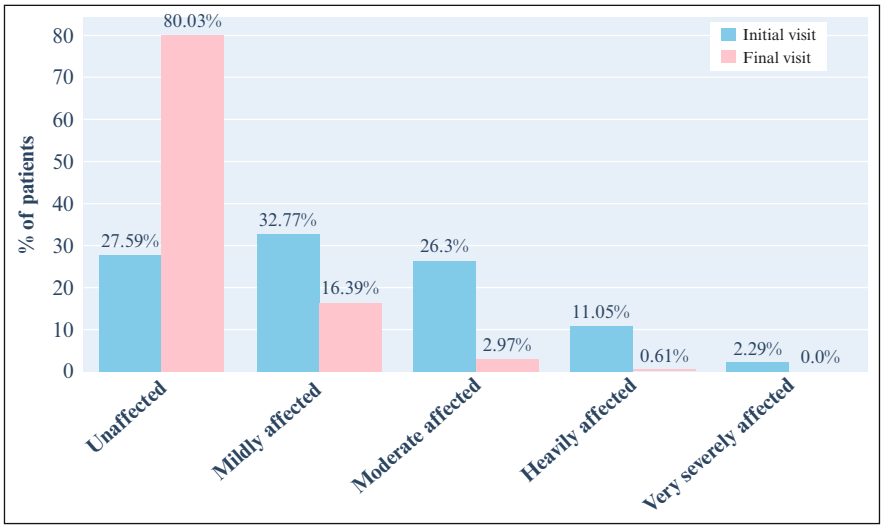

Figure 6. Percentage of patients as per dermatologists' assessment of the degree of affected sleep quality (n=1312) based on a 5-point at the initial and final visits (p<0.001).

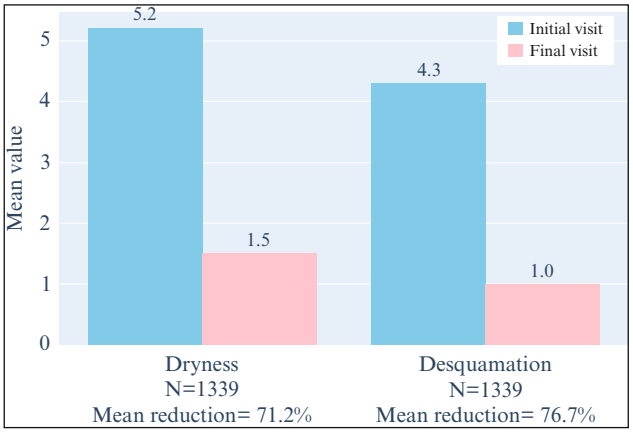

Figure 7. Mean values of intensity of dryness and desquamation, as per dermatologists' assessment (n=1339) at the initial and final visits (p<0.001).

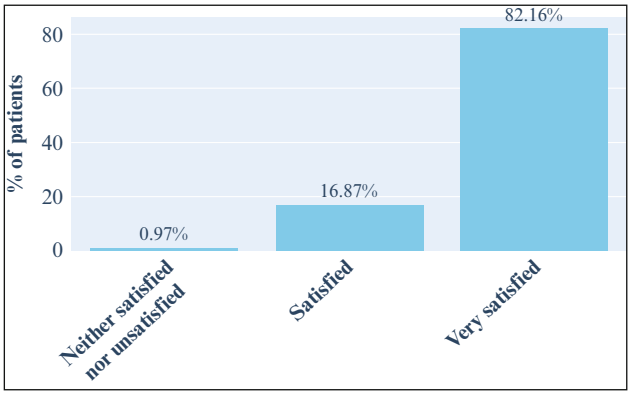

Figure 8. Satisfaction rate as per dermatologists' assessment (n=1334) of the novel formulation after two months of application by the patients based on a 3-point scale ("neither satisfied nor unsatisfied, satisfied, very satisfied").

[19]. The mixture is known for its antioxidant properties to improve skin dryness and pruritus [29], and can be used as a prebiotic source to selectively modulate the activity and growth of probiotics and commensal skin bacteria and the function of the skin barrier, and thus rebalance the skin microbiome [17, 25].

LRP-TSW maintains a diverse skin microbiome and deters dysbiosis of commensal microbes by stimulating the growth of commensal bacteria beneficial for skin homeostasis, thus restoring barrier function in the stratum corneum [17, 29-31]. Specifically, LRP-TSW is rich in selenium and strontium [30] which have been shown to reduce *Staphylococci* bacteria with an increase in *Xanthomonas* genus bacteria [29]. Its antioxidant properties have been shown to provide significant improvement in pruritus, skin dryness and pain in patients with AD or other skin diseases associated with dryness or severe xerosis, as well as an overall positive impact on their QoL [32]. A double-blind, randomized study, which included AD patients with moderate disease, treated for one month with topical application of emollients supplemented with *Vf* grown in LRP-TSW, revealed a significant reduction in the *Staphylococcus* genus and a simultaneous increase in the *Xanthomonas* genus in the skin microbiome [33]. These differences were more evident during relapse [33], indicating that application of *Vf* in LRP-TSW medium onto the skin tends to reduce the number and severity of flare-ups, and thus normalizes the diversity of the skin microbiome.

Additionally, previous *in vitro* and *in vivo* data, as well as clinical studies have shown the benefits of *Vf* use on the skin microbiome. *Vf* in LRP-TSW resulted in increased antimicrobial mRNA and peptide expression in reconstructed *in vitro* skin epidermal cells through the action of a Toll-like receptor 2 (TLR2) signal transduction pathway by modulating the activity of the free-radical scavenger, mitochondrial superoxide dismutase 2 (SOD2), at the mRNA and protein level [30, 34]. Similar results were observed in a mice study, in which topical application reduced AD-like inflammation by activating Toll-like receptor 2 (TLR2) and suppressing T-effector cells, while inducing interleukin (IL)-10-producing dendritic cells (DC)s [15]. In a prospective, placebo-controlled clinical study, the benefits of *Vf* extract added to AD skin care emollients revealed significant clinical efficacy in reducing pruritus, skin dryness, xerosis and daily discomfort as well as improving the quality of sleep compared to placebo [35].

Microresyl is a natural active ingredient originating from the roots of Ophiopogon japonicus which prevents the overgrowth and biofilm formation of *S. aureus*, thus rebalancing the skin microbiome. Microresyl, as a prebiotic, modulates the activity and growth of probiotics and commensal skin bacteria. This is in line with various studies demonstrating a beneficial role of prebiotics which prevent AD and other dry skin-related diseases [29, 30, 36] by rebalancing the skin microbiome and improving skin microbial diversity.

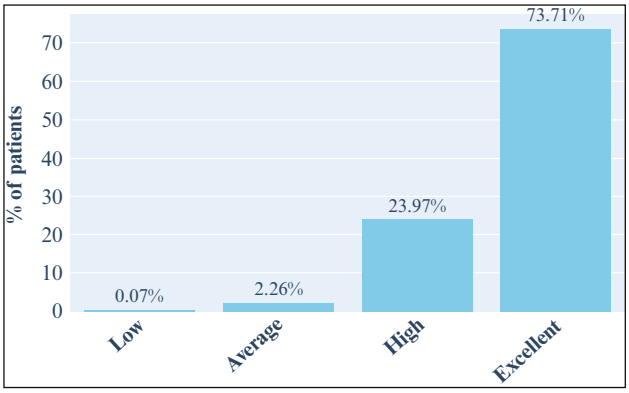

Figure 9. Tolerance rate as per dermatologists' assessment (n=1506) of the novel formulation after two months of application based on a 4-point scale ("low, average, high, excellent").

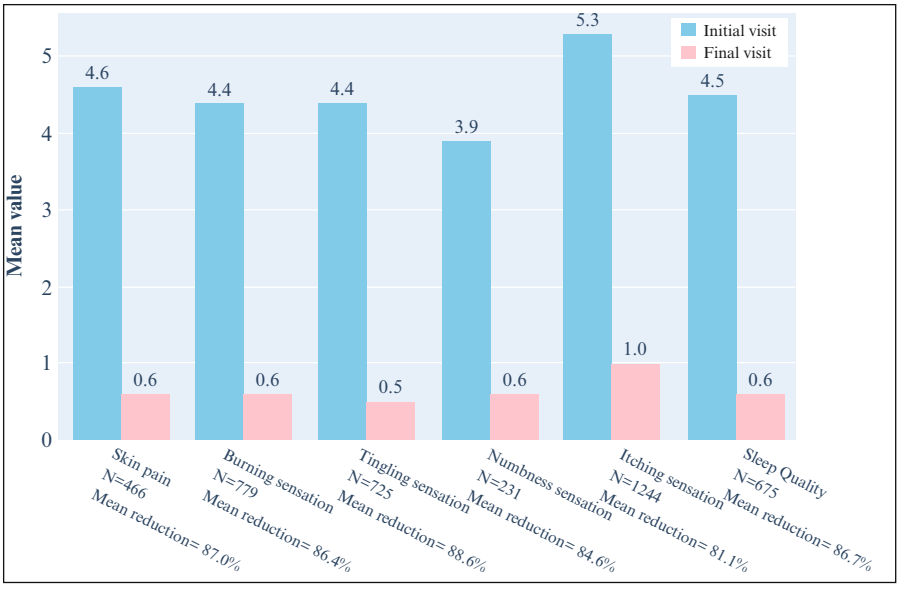

Figure 10. Mean values of skin discomfort parameters as assessed by patients, at the initial and final visits.

Shea butter, another ingredient of the product, is a plant-based moisturizer and is used as a soothing agent by increasing moisture retention and acting as a protective layer over the skin to deter water loss. Niacinamide, also known as nicotinamide or vitamin B3, is an essential dietary vitamin, which has been demonstrated to be an effective moisturizer for dry skin or severe xerosis symptom management. Studies have demonstrated that it enhances the level of ceramides in the epidermis, while strengthening the epidermal permeability barrier by decreasing the levels of TEWL and increasing stratum corneum hydration [37].

The results of the present study demonstrate a significant improvement in all parameters evaluated by dermatologists and patients. The significant mean reduction of skin pain, dryness and pruritus compared to baseline, revealed improvement of sleep quality and a positive impact on patients' overall QoL. These findings are in line with earlier evidence of the benefits of LRP-TSW, and with the results of *in vitro, in vivo* and clinical studies demonstrating the benefits of LRP-TSW together with *Vitreoscila filiformis (Vf)*.

Furthermore, a high satisfaction rate and an excellent dermatological tolerance rate was observed based on both the dermatologists' and patients' assessments, which is consistent with previous studies demonstrating high tolerance and satisfaction in both children and adults with moderate-to-severe AD or other skin diseases associated with dryness who applied emollient with LRP-TSW [31, 33].

An advantage of this study is the large number of participants, the objective (dermatologist) and subjective (patient) assessment of the disease, as well as the evaluation of a variety of parameters, some of which are not often mentioned in the literature, such as pain. A limitation of this study includes its duration. Two months is a relatively short period to prove that the product can deter flare-ups by encouraging propagation and growth of beneficial commensal bacteria, such as of the Xanthomonas genus, and maintain a balance with S. aureus. Additionally, the impact of the novel formulated cream on the outcomes of this study is unclear since the majority (66%) of patients received adjunctive therapy and 34% received the "emollient plus" formulation as monotherapy. Therefore, the degree to which any adjuvant medication (*e.g.*, topical corticosteroids, antihistamines, calcineurin inhibitors) contributed to the results of this study cannot be determined. The present study covers a wide spectrum of disease severity, thus a subgroup analysis and a corresponding comparison between patients with mild and moderate as well as moderate and severe forms would provide additional clinical information. Similarly, the study would benefit from subgroup analyses of individual skin diseases (*e.g.*, on only AD, psoriasis or senile xerosis). Of note, the evaluation of efficacy and improvement of skin parameters in this study did not include the application of tools that measure the extent and severity of eczema (EASI or SCORAD) or psoriasis (PASI calculator). Another limitation involves the lack of a control group, which is attributed to the difficulty in designing and developing placebos for cosmetic studies.

Understanding the relationship between bacteria, microbiota and disease activity will allow direct interventions on the cutaneous microbiome which will re-establish microbial diversity and lead to the development of alternative therapeutic approaches for managing the symptoms of dry skin or severe xerosis, with the goal of reducing chronic use of conventional treatments and their associated adverse reactions. Future studies could investigate the efficacy of probiotics and prebiotics in combination with LRP-TSW, and segregate trials into those focusing on remission and those focusing on flare-ups, while also increasing the study duration. This will provide useful information on understanding the mechanism(s) of action and the impact of the ingredients

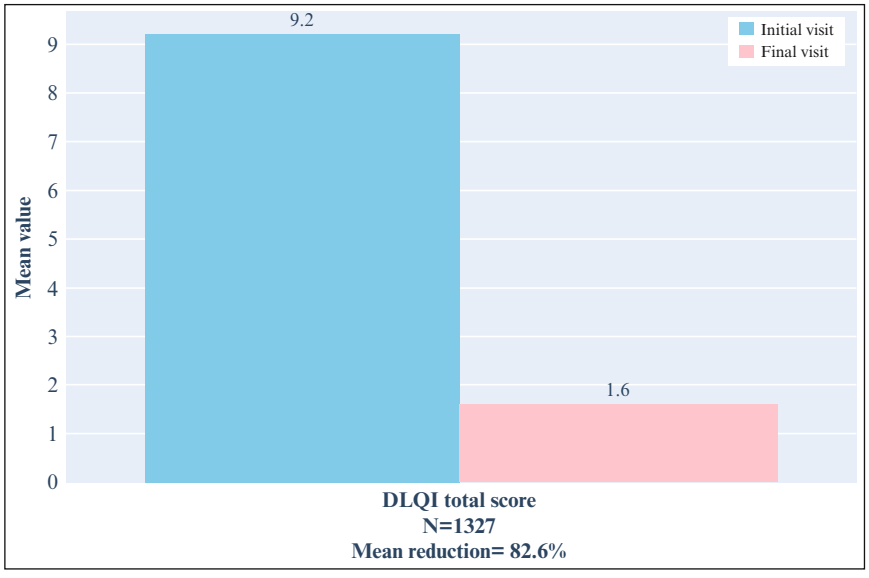

Figure 11. Patients' self-assessment based on DLQI total score after using the novel formulation for two months.

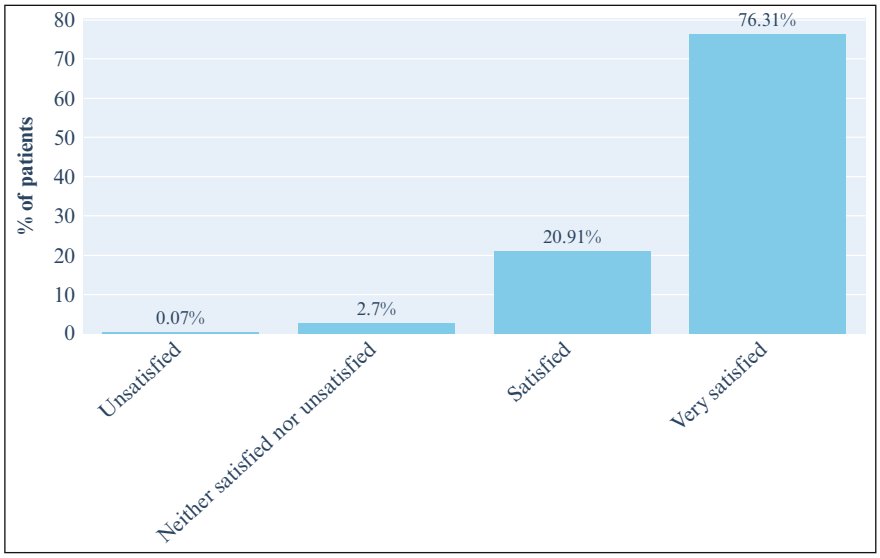

Figure 12. Rate of patients' satisfaction (n=1334) after two months of application.

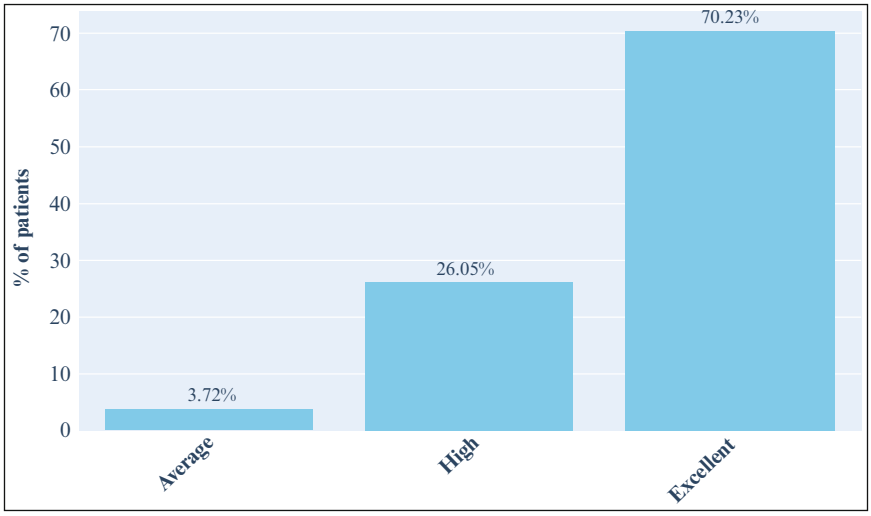

Figure 13. Rate of patients' tolerance (n=1505) after two months of application.

during remission and flare-ups, as well as on the appropriate emollient for a given patient. Rebalancing the skin microbiome through topical emollient application is the ultimate goal which can further be investigated for other chronic inflammatory skin diseases such as acne, rosacea, and psoriasis.

Conclusions

This study demonstrates a significant improvement in the symptoms of mild-to-severe AD and other dermatological conditions associated with skin dryness or severe xerosis in adults, following two months application of a novel formulated product, either alone or as adjunctive therapy (with topical or systemic corticosteroids, calcineurin inhibitors and/or antihistamines). Skin pain, pruritus, dryness, and discomfort were reduced after using the product, followed by an improvement in sleep quality and overall QoL. Therefore, the product can be used either as maintenance treatment or to prevent flares, and its inclusion in available therapeutic management has been proposed. ■

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References

1. Blome C, Radtke MA, Eissing L, Augustin M. Quality of life in patients with atopic dermatitis: disease burden, measurement, and treatment benefit. *Am J Clin Dermatol* 2016 ; 17 : 163-9.

2. Eichenfield LF, Tom WL, Berger TG, *et al.* Guidelines of care for the management of atopic dermatitis: section 2. Management and treatment of atopic dermatitis with topical therapies. *J Am Acad Dermatol* 2014 ; 71 : 116-32.

3. Armstrong AW, Read C. Pathophysiology, clinical presentation, and treatment of psoriasis. *JAMA* 2020 ; 323 : 1945.

4. White-Chu EF, Reddy M. Dry skin in the elderly: complexities of a common problem. *Clin Dermatol* 2011 ; 29 : 37-42.

5. Silverberg J. Public health burden and epidemiology of atopic dermatitis. *Dermatol Clin* 2017 ; 35 : 283-9.

6. Berger TG, Shive M, Harper GM. Pruritus in the older patient. *JAMA* 2013 ; 310 : 2443.

7. Bonamonte D, Filoni A, Vestita M, Romita P, Foti C, Angelini G. The role of the environmental risk factors in the pathogenesis and clinical outcome of atopic dermatitis. *Biomed Res Int* 2019 ; 2019 : 2450605.

8. Wollenberg A, Barbarot S, Bieber T, *et al.* Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part I. *J Eur Acad Dermatol Venereol* 2018 ; 32 : 657-82.

9. Kong HH, Oh J, Deming C, *et al.* Temporal shifts in the skin microbiome associated with disease flares and treatment in children with atopic dermatitis. *Genome Res* 2012 ; 22 : 850-9.

10. Grice E The skin microbiome: potential for novel diagnostic and therapeutic approaches to cutaneous disease. *Semin Cutan Med Surg* 2014 ; 33 : 98-103.

11. Yamamura S, Morita Y, Hasan Q, Yokoyama K, Tamiya E. Keratin degradation: a cooperative action of two enzymes from Stenotrophomonas sp. *Biochem Biophys Res Commun* 2002 ; 294 : 1138-43.

12. Thomsen SF. Atopic dermatitis: natural history, diagnosis, and treatment. *ISRN Allergy* 2014 ; 2014 : 354250.

13. Hamid Q, Boguniewicz M, Leung DY. Differential in situ cytokine gene expression in acute versus chronic atopic dermatitis. *J Clin Invest* 1994 ; 94 : 870-6.

14. Nakatsuji T, Chen TH, Two AM, *et al.* Staphylococcus aureus exploits epidermal barrier defects in atopic dermatitis to trigger cytokine expression. *J Investig Dermatol* 2016 ; 136 : 2192-200.

15. Volz T, Skabytska Y, Guenova E, *et al.* Nonpathogenic bacteria alleviating atopic dermatitis inflammation induce IL-10-producing dendritic cells and regulatory Tr1 cells. *J Investig Dermatol* 2014 ; 134 : 96-104.

16. Ellison JA, Patel L, Kecojevic T, Foster PJ, David TJ, Clayton PE. Pattern of growth and adiposity from infancy to adulthood in atopic dermatitis. *Br J Dermatol* 2006 ; 155 : 532-8.

17. Baldwin HE, Bhatia ND, Friedman A, Eng RM, Seite S The role of cutaneous microbiota harmony in maintaining a functional skin barrier. *J Drugs Dermatol* 2017 ; 16 : 12-18.

18. Peng W, Novak N. Pathogenesis of atopic dermatitis. *Clin Exp Allergy* 2015 ; 45 : 566-74.

19. Wollenberg A, Christen-Zäch S, Taieb A, *et al.* ETFAD/EADV Eczema task force 2020 position paper on diagnosis and treatment of atopic dermatitis in adults and children. *J Eur Acad Dermatol Venereol* 2020 ; 34 : 2717-44.

20. Schmitt J, von Kobyletzki L, Svensson Å, Apfelbacher C. Efficacy and tolerability of proactive treatment with topical corticosteroids and calcineurin inhibitors for atopic eczema: systematic review and meta-analysis of randomized controlled trials. *British J Dermatol* 2011 ; 164 : 415-28.

21. Proksch E. The role of emollients in the management of diseases with chronic dry skin. *Skin Pharmacol Physiol* 2008 ; 21 : 75-80.

22. Ellison JA, Patel L, Ray DW, David TJ, Clayton PE. Hypothalamic-pituitary-adrenal function and glucocorticoid sensitivity in atopic dermatitis. *Pediatrics* 2000 ; 105 : 794-9.

23. Izumi R, Negi O, Suzuki T, *et al.* Efficacy of an emollient containing diethylene glycol/dilinoleic acid copolymer for the treatment of dry skin and pruritus in patients with senile xerosis. *J Cosmet Dermatol* 2017 ; 16 : e37-41.

24. Nygaard U, Deleuran M, Vestergaard, C. Emerging treatment options in atopic dermatitis: topical therapies. *Dermatology* 2017 ; 233 : 333-43.

25. Seite S, Bieber T. Barrier function and microbiotic dysbiosis in atopic dermatitis. *Clin Cosmet Investig Dermatol* 2015 ; 8 : 479-83.

26. Hong J, Buddenkotte J, Berger TG, Steinhoff M. Management of itch in atopic dermatitis. *Semin Cutan Med Surg* 2011 ; 30 : 71-86.

27. Magnifico I, Petronio Petronio G, Venditti N, *et al.* Atopic dermatitis as a multifactorial skin disorder. Can the analysis of pathophysiological targets represent the winning therapeutic strategy? *Pharmaceuticals* 2020 ; 13 : 411.

28. Catherine Mack Correa, M., Nebus, J. Management of patients with atopic dermatitis: the role of emollient therapy. *Dermatol Res Pract* 2012 ; 2012 : 836931.

29. Zeichner J, Seite Phd B A Mount, S., Hospital, S., York, N. & Roche-Posay, L. From Probiotic to Prebiotic Using Thermal Spring Water. *J Drugs Dermatol* 2018 ; 17.

30. Seite S. Thermal waters as cosmeceuticals: La Roche-Posay thermal spring water example. *Clin Cosmet Investig Dermatol* 2013 ; 6 : 23-8.

31. Friedman A *Emollient-Based Therapy for AD: A Potential Role for Rebalancing the Microbiome.* October 2019 supplement to *Practical Dermatology* vol. 1 (2019). [Available at: https://practicaldermatology.com/articles/2019-oct-supplement/emollient-based-therapy-for-ad-a-potential-role-for-rebalancing-the-microbiome].

32. Cacciapuoti S. Luciano MA, Megna M, *et al.* The role of thermal water in chronic skin diseases management: a review of the literature. *J Clin Med* 2020 ; 9 : 3047.

33. Seité S, Zelenkova H, Martin R. Clinical efficacy of emollients in atopic dermatitis patients - relationship with the skin microbiota modification. *Clin Cosmet Investig Dermatol* 2017 ; 10 : 25-33.

34. Mahe YF, Martin R, Aubert L, *et al.* Induction of the skin endogenous protective mitochondrial MnSOD by Vitreoscilla filiformis extract. *Int J Cosmet Sci* 2006 ; 28 : 277-87.

35. Gueniche A, Knaudt B, Schuck E, *et al.* Effects of nonpathogenic gram-negative bacterium *Vitreoscilla filiformis* lysate on atopic dermatitis: a prospective, randomized, double-blind, placebo-controlled clinical study. *Br J Dermatol* 2008 ; 159 : 1357-63.

36. Alesa D, Alshamrani HM, Alzahrani YA, Alamssi DN, Alzahrani NS, Almohammadi ME. The role of gut microbiome in the pathogenesis of psoriasis and the therapeutic effects of probiotics. *J Family Med Prim Care* 2019 ; 8 : 3496.

37. Soma Y, Kashima M, Imaizumi A, Takahama H, Kawakami T, Mizoguchi M. Moisturizing effects of topical nicotinamide on atopic dry skin. *Int J Dermatol* 2005 ; 44 : 197-202.