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An Innovative Cream Improves Signs and Symptoms of Dermatoporosis in Patients Aged 65 and Over

Alan Widgerow MBBcH MMed,[a] Mathieu Grivet-Seyve PhD,[b] Sarah Anjuwon MS,[b] Christine Emesiani PharmD,[c] Matthew Meckfessel PhD[c]

[a]Galderma R&D, Carlsbad, CA
[b]Galderma R&D, LLC, Dallas, TX
[c]Galderma Laboratories LLP, Dallas, TX

ABSTRACT

Background: There is increasing recognition of dermatoporosis — a condition of chronic cutaneous fragility of aging skin seen primarily in older adults. Dermatoporosis can be characterized by white pseudo scars, purpura/bruising, skin thinning, and loss of volume. This study evaluated a novel cream with microdoses of mandelic acid and *Centella asiatica* that was formulated to target physiologic processes involved in dermatoporosis.

Methods: A 12-week, proof-of-concept study of participants aged 65 years and older (n=54) with sensitive skin and dermatoporosis managed with twice-daily application of the cream on both forearms and 1 leg (randomly selected, with the other leg serving as control). Key assessments included transepidermal water loss (TEWL), skin thickness measurement by ultrasound, clinical scoring for dryness and roughness, a participant questionnaire, and standard safety assessments.

Results: Twice-daily use of the novel cream resulted in an ongoing consistent positive increase in skin thickness of 5% ($P<0.05$), with improvements primarily in the dermis and epidermis but also notable in the subdermal layer. Significant improvements in hydration were observed starting from day 7 and observed through day 84 (or end of study) ($P<0.05$). Changes in TEWL showed a 20% improvement in barrier function that also was apparent early (day 7) and sustained through the study (40% improvement at day 84, $P<0.05$). The cream demonstrated excellent safety with no adverse reactions and no worsening in tolerability parameters.

Conclusions: This cream, containing microdoses of mandelic acid and *Centella asiatica*, safely and effectively improved skin thickness, firmness, and resiliency, and had high acceptability with study participants.

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INTRODUCTION

Dermatoporosis describes thin, aged, and excessively fragile skin resulting from loss of the skin's protective mechanical function.[1] Other signs and symptoms include skin atrophy, purpura, pseudoscars, skin lacerations, and dissecting hematomas.[2] Progressive weakening of the skin barrier can lead to severe morbidity with clinical manifestations that may require hospitalization.[3] Dermatoporosis is often seen on forearms, hands, presternal area, the pretibial area, and scalp.[4] It accompanies skin aging and can be accelerated by factors such as photodamage, use of medications such as corticosteroids, and genetic susceptibility.[5] These factors can trigger fibroblast senescence, which in turn leads to decreased production of elastin and collagen (with resultant negative effects on the extracellular matrix) and a reduction in hyaluronic acid in the skin.[3,4] The reduction in these extracellular matrix components results in a lack of support for cutaneous vessels rendering them susceptible to damage.[4,5] Symptoms of dermatoporosis can occur as early as 40 years old, but manifests fully between the ages of 70 and 90 years.[4]

Interventions for dermatoporosis should work holistically to repair and rebuild skin with a goal of preventing progression and improving skin integrity.[2] Optimally, they should provide support to fibroblasts and components of the extracellular matrix (collagen, elastin).[4,6] Consistent skincare regimens can help reduce the impact of aging by maintaining skin hydration, supporting a healthy skin barrier, preserving skin quality, and enhancing elasticity and smoothness.[7]

Recently, a new over-the-counter cream has been formulated with microdoses of mandelic acid and *Centella asiatica*.[4] Mandelic acid is a gentle alpha hydroxy acid exfoliant that normalizes skin pH, supports the skin's lipid bilayer and

cornedesmosome integrity, while promoting desquamation and enhancing keratinocyte turnover. *Centella asiatica* is a soothing agent that enhances skin delivery, slows degradation of hyaluronic acid in the skin, and reduces inflammation. Unexpectedly, a synergistic effect has been reported between microdoses of mandelic acid and *Centella asiatica*, increasing the anticipated anti-inflammatory and anti-senescence effects and optimizing the targeting of dermatoporosis.[4] We report here a study designed to test the cream under normal conditions in adults with sensitive skin and dermatoporosis after daily use for 12 weeks.

MATERIALS AND METHODS

In a 12-week proof of concept clinical study, the investigational cream was used under normal conditions of use by participants aged 65 years or older with self-reported sensitive skin and dermatoporosis. The investigational product was applied twice daily for 84 days on both arms and one leg, with one calf randomly excluded as a control. The clinical study was conducted in agreement with the most recent Helsinki Declaration and general principle of Good Clinical Practice, and all patients provided written informed consent and a HIPAA form. Study protocol was submitted to an Institutional Review Board before participant inclusion.

Participants were aged 65 years and older, and gender, race/ethnicity, and Fitzpatrick skin phototype were unrestricted. They had visibly aged skin on their extremities and evidence of dermatoporosis (skin atrophy and pigmentary changes) as well as sensitive skin per a screening questionnaire. Furthermore, their baseline health status was generally good, and participants agreed to discontinue their current body personal care products (cleansers, serums, sunscreens) for the duration of the study. They also agreed to not sunbathe/tan and avoid sun/ultraviolet exposure as much as possible during the study. Participants were excluded if they were taking any medications that could mask or interfere with test results at the time of the study start (corticosteroids, nonsteroidal anti-inflammatory drugs, antihistamines, and immunosuppressive medications). Those with an active (flaring) disease that would interfere with study evaluations or recently treated skin cancer were also excluded, as were those with damaged skin at or in proximity to test sites (dermal irritation, active lesions, excessive hyperpigmentation or moles, tattoos, or other abnormalities).

Assessments included skin hydration (Corneometer CM 825, Courage and Khazaka), skin barrier transepidermal water loss (TEWL, Dermalab Evaporimeter, Cortex Technology), skin thickness measured by ultrasound (Dermalab USB ultrasound 20 mHz, Cortex Technology), cutaneous tolerability evaluated by a dermatologist (0=none to 3=severe), clinical scoring of roughness (0=very soft skin to 9=not soft skin, very rough texture) and dryness (10-point visual analog scale), and a self-evaluation questionnaire to be answered by the participants.

Descriptive statistics were collected and reported. Changes from baseline in tolerability, clinical scoring, ultrasound, corneometer, and TEWL results were analyzed by paired *t*-test. If normality failed, Wilcoxon signed-rank test was used to assess differences. Binomial law test was used on percentages of participants with favorable responses from the questionnaire. For n=50, the minimum percentage of favorable responses for statistical significance was calculated at 69.3%. Statistical significance for all evaluations was declared if the 2-tailed *P* value was 0.05.

RESULTS

A total of 54 participants with self-perceived sensitive skin and dermatoporosis aged 65 years to 82 years participated, with demographics as shown in Table 1.

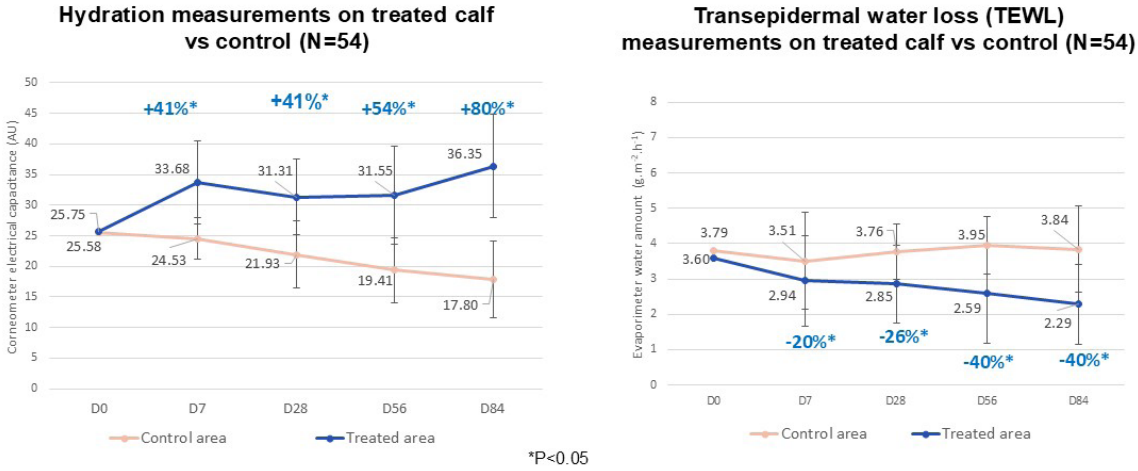
As expected, hydration and TEWL values were improved from baseline with the cream vs control ($P<0.05$ from day 7 to week 12, Figure 1). In a separate study, hydration occurred rapidly, with observable increases as early as 1 hour after a single application. In addition, the cream reduced water loss compared to the untreated control area.

There was a gradual increase in skin thickness (Figure 2), with inner forearm thickness increasing from a mean of 907.06µm at day 0 to 950.08 µm on day 84 ($P<0.05$). The visualization shows increased lighter colors, indicating improvements primarily in the epidermis and dermis tissues but also observable in the subdermal layer (Figure 2).

TABLE 1.

Participant Demographics; All Had Sensitive Skin	
Gender	
Male	9 (17%)
Female	45 (83%)
Age, mean (range)	68 years (65-82 years)
Ethnicity	
Caucasian/White	29 (54%)
Black/African American	12 (22%)
Hispanic/Latin American	10 (18.5%)
Asian/Indian	1 (2%)
Other	2 (4%)
Phototype	
I	4 (7%)
II	24 (44%)
III	15 (28%)
IV	4 (7%)
V	3 (6%)
VI	4 (7%)

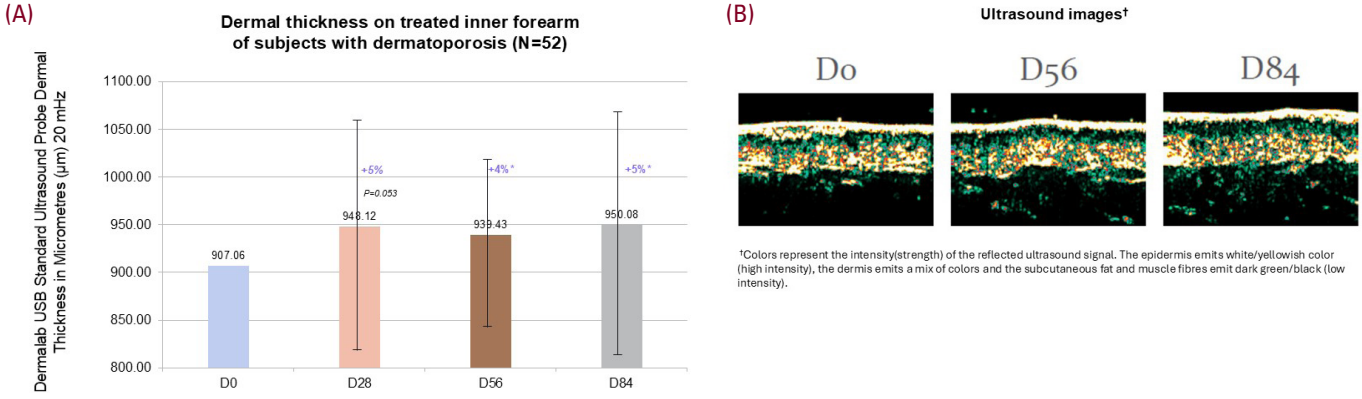
FIGURE 1. Twice-daily cream application significantly improves skin hydration and barrier function vs control at all timepoints.



*P<0.05

AU=arbitrary unit; TEWL=transepidermal water loss. *$P<0.05$.

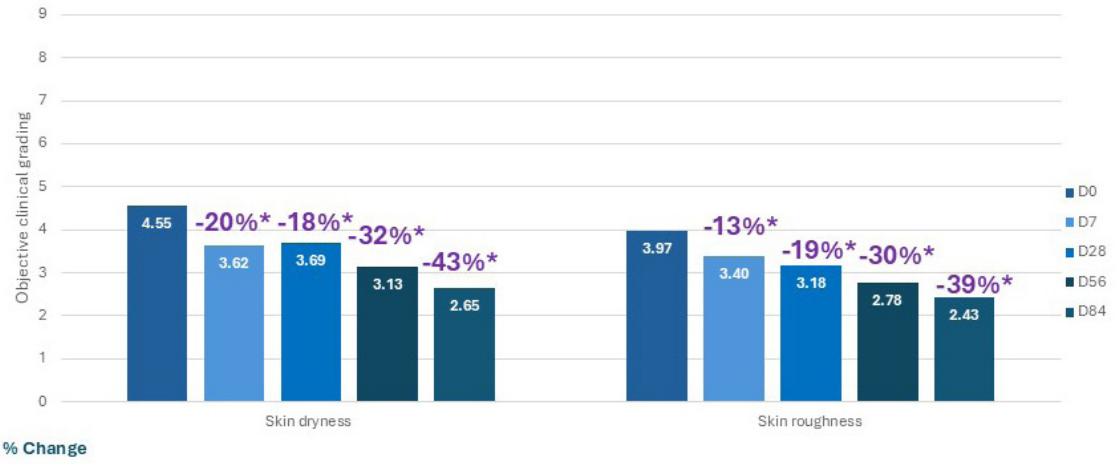
FIGURE 2. Significant increase in skin thickness on ultrasound (A) graph of mean dermal thickness and (B) ultrasound showing increase in dermal thickness from day 0 to day 84 in a representative participant. The epidermis emits white/yellowish color (high intensity), the dermis emits a mix of colors, and the subcutaneous fat and muscle fibers emit dark green/black (low intensity).



†Colors represent the intensity(strength) of the reflected ultrasound signal. The epidermis emits white/yellowish color (high intensity), the dermis emits a mix of colors and the subcutaneous fat and muscle fibres emit dark green/black (low intensity).

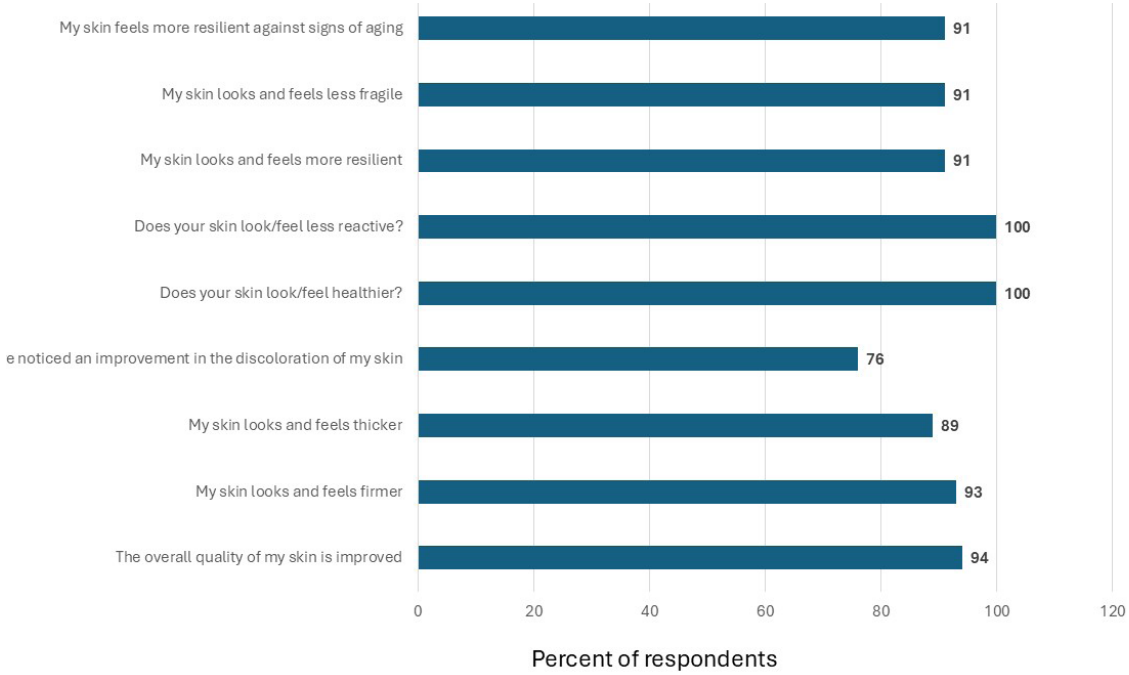
*$P<0.05$.

FIGURE 3. Investigator evaluation of improvements in skin dryness and roughness throughout the study period.



*$P<0.05$.

FIGURE 4. Results from participant questionnaire at week 12.

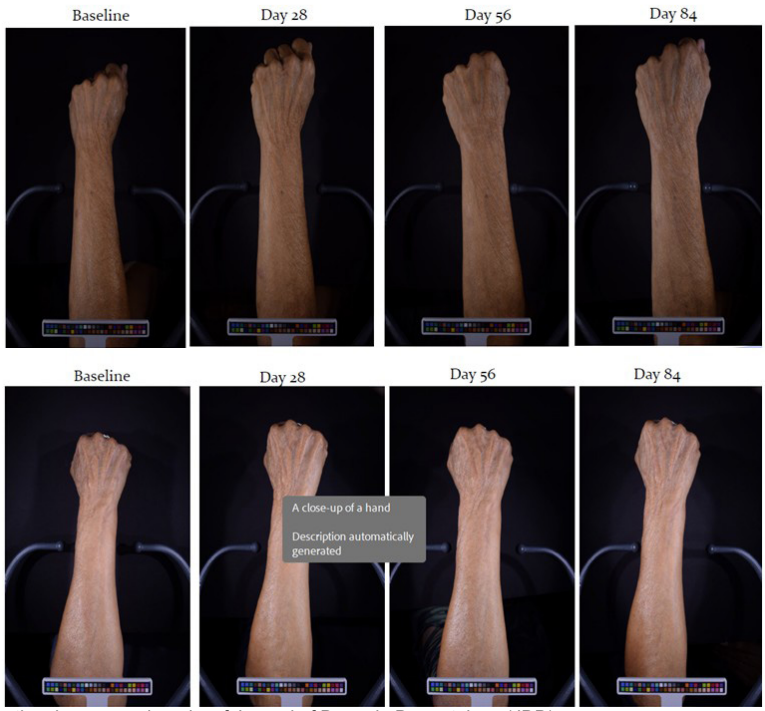


Four-point scale, answers given from "likely agree" to "strongly agree."

The cream visibly improved skin dryness and tactile roughness on treated areas of skin in participants with dermatoporosis (Figure 3). Further, participants reported that their skin felt soothed from dryness as early as 1 week of twice-daily use. As shown in Figure 3, clinical grading showed a mean decrease of 1.9 points compared to baseline and a decrease of 1.5 in skin roughness at day 84.

Questionnaire results and correlation with improvements in clinical grading. At week 1, participants reported skin smoothness was improved (94%), skin quality was better (93%), their skin felt more hydrated (93%), and they noticed an overall improvement in skin (89%). Further, they reported the cream had good cosmetic qualities and they perceived their skin to look/feel healthier (96%) and less reactive (93%). At 4 weeks, >90%

FIGURE 5. Clinical photos of participants treated with the cream.



of participants reported improvements in overall appearance, skin quality, hydration and smoothness, firmness of skin, youthful appearance, and better skin tautness. Results on the questionnaire consistently improved, and Figure 4 shows the excellent participant satisfaction reported in the questionnaire at week 12.

Safety

The cream was found to have good tolerability with no related adverse events and no significant changes in cutaneous tolerability (erythema, edema, dryness, scaling, and peeling). Additionally, no potential for dermal irritation or allergic contact sensitization was observed.

DISCUSSION

Dermatoporosis is an increasingly recognized condition of chronic fragility of aging skin due to impairment of the skin's protective mechanical function.[3,5] Consistent skin care can help to address dermatoporosis by supporting a healthy epidermal barrier and preserving skin integrity. This support may be particularly important for individuals with sensitive skin (an estimated 26% to 54% of studied populations in various countries), who often have stinging, burning, and itching that can be triggered by a number of environmental factors.[8] Understanding key signs of aging/dermatoporosis skin can be used to tailor skincare solutions for patients; for skin atrophy, clinicians can target non-functioning senescent cells resulting in increased collagen production and promoting cellular turnover and proliferation, and for skin dryness, increasing skin surface hydration and decreasing TEWL.[9-11] Improvements in skin barrier function and exfoliation to allow product penetration can also ameliorate skin dryness, and increased collagen and elastin production translates to better skin elasticity.[9-11]

In this proof-of-concept study with individuals presenting a variety of skin types and sensitive dermatoporotic skin, this novel cream improved and maintained skin thickness after 8 and 12 weeks of twice-daily use and was associated with an excellent level of participant satisfaction and overall local tolerability. This shows that an intervention with a consistent supportive skincare regimen can help prevent progression of dermatoporosis and sustain skin integrity.

Improvements in understanding the physiologic processes involved in dermatoporosis have been translated to new technology in moisturizing formulations. This study shows that novel ingredients such as microdosed mandelic acid and *Centella asiatica* formulated in a cream adapted to sensitive skin, can provide a gentle yet clinically effective solution for dermatoporosis-prone skin. It demonstrates the importance of skin care in protecting aging skin and supporting healthy skin function and the likelihood of better outcomes with increased awareness and early recognition.

CONCLUSION

A novel formulation adapted to sensitive skin and including 2 dedicated ingredients to address early "dermatoporotic" skin signs has shown to have a rapid onset and to be very efficient and well-tolerated. This product will bring a new cosmetic solution specifically adapted for aging patients with early "dermatoporotic" skin.

DISCLOSURES

All authors are employees of Galderma.

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AUTHOR CORRESPONDENCE

Christine Emesiani PharmD

E-mail:..... Christine.emesiani@galderma.com