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ORIGINAL ARTICLE

Double-blind, vehicle-controlled clinical investigation of peptide OS-01 for skin rejuvenation

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Abstract

Introduction: Senescent cells contribute to age-related tissue deterioration, including the skin, which plays important roles in overall health and social interactions. This study aimed to assess the effects of the senotherapeutic peptide, OS-01 (a.k.a. Pep 14), on skin.

Methods: A 12-week split-face, double-blinded, vehicle-controlled study involving 22 participants was conducted. The OS-01-containing formulation was applied to one side of the face, while the other side received an identical control formulation lacking the peptide. Skin characteristics were assessed using instrumental measurements, expert clinical grading, and subjective questionnaires.

Results: Results showed that the OS-01 formulation significantly improved one aspect of skin barrier function, as evidenced by reduced trans-epidermal water loss compared to both baseline and vehicle control. Expert grading and Antera 3D image analysis revealed a reduction in wrinkle appearance and indentation in the periorbital area, and improved skin texture and radiance on both sides of the face, with the OS-01-containing formulation demonstrating superior results. Participants also perceived improvements in skin hydration, smoothness, radiance, and overall appearance.

Conclusion: The findings suggest that the OS-01 formulation promotes skin health by strengthening the skin barrier, protecting against dehydration, reducing the appearance of wrinkles, and improving skin texture and radiance. These effects are likely attributed to the senotherapeutic properties of OS-01 in reducing cellular senescence and its associated detrimental effects.

KEYWORDS
cellular senescence, clinical study, peptides, skin health, wrinkles

1 | INTRODUCTION

Senescent cells are defined as cells that present stable arrest of the cell cycle, typical inflammatory senescence-associated secretory phenotypes (SASP), as well as transcriptional, epigenetic, metabolic, and morphological changes.[1,2] As stated by Munhoz et al., while necessary for proper embryonic development and tissue regeneration, senescent cells contribute to the age-associated deterioration of tissue function when accumulated.[3] As such, research has shown that the selective elimination of senescent cells, termed senolysis, results in biological tissue rejuvenation.[4,5]

Often overlooked in relation to senescence and longevity research is the body's largest organ, the skin, which may be linked to senescence-associated disease pathogenesis. Age-related changes in skin function are associated with a compromised skin barrier, which has been shown to engender altered circulating inflammatory cytokine levels.[6,7] Furthermore, the accumulation of senescent cells in the skin correlates with organismal biological aging.[8] Senescent cells accumulate in the different layers of the skin throughout aging,[9–11], and are significantly associated with facial wrinkles and perceived age.[12] The role that senescent cells play in molecular, cellular, structural, and visual skin aging, is an active area of research.

To date, few studies have described the effects of cellular senescence reduction in the skin. In mice, treatment with the senolytic ABT-737 was shown to benefit the skin by rescuing epidermal atrophy, increasing hair follicle stem cell proliferation, and reducing melanocyte senescence levels[13,14]; also, the reduction of mTOR signaling due to senolysis was shown to reduce skin infections throughout aging.[15] In humans, the senolytic cocktail of Dasatinib and Quercetin (D + Q) was first shown to cause mild to moderate skin-related adverse effects in idiopathic pulmonary fibrosis patients.[16] Later on, the same drug cocktail was reported to promote decreased SASP signatures in skin samples of systemic sclerosis patients.[17] Additionally, D + Q was shown to reduce cellular senescence levels in the skin of diabetic kidney disease patients.[18]

The first report that assessed the effects of a senotherapeutic compound topically applied on human skin was in 2019 by Chung et al.[19] The authors showed that an 8-month-long rapamycin treatment promoted a significant increase in Collagen VII, a marker of skin health and barrier function, in the basement membrane of treated skin. Furthermore, macroscopically, the treatment promoted a significant reduction in skin wrinkling and dyspigmentation, according to expert grading.[19]

OS-01 (a.k.a. Peptide 14) is the main ingredient of the first topical product developed by a longevity company, focusing on promoting skin health and preventing the accumulation of senescent cells in the skin.[20] Recently, our group has shown that the OS-01 peptide reduces cellular senescence burden both in 3D human skin equivalents and ex vivo skin samples, promoting health markers and, importantly, reducing the skin's biological age.[21] Besides the OS-01 peptide, this formula contains other ingredients known to be moisturizing, anti-inflammatory, and have antioxidant properties such as Pracaxi Oil, Andiroba Oil, Oleic Pau Mulato Extract, Niacinamide, Allantoin, and Hyaluronic Acid. In this manuscript, we present the results of a 12 week-long, split-face, double-blinded, vehicle-controlled, clinical study involving 22 participants, in which the effects of the OS-01 peptide-containing formulation in the skin are compared with the performance of an identical control formulation lacking the peptide.

2 | METHODS

2.1 | Clinical study design overview

This was a 12-week, double-blinded, split-face, proof-of-concept study that evaluated the performance of the OS-01 formulation versus the vehicle formulation. The INCI list of each formula is presented in Table S1.

Participants applied the peptide-containing formula on the left side and the control formulation on the right side of the face. The side of the face that received each treatment was withheld from participants and researchers to ensure a double-blinded study regarding peptide treatment. Institutional Review Board approval was obtained prior to study initiation (Allendale IRB, 4336OST1010 version 2.0). The study was conducted by a contract research organization according to international standards of Good Clinical Practice (FDA and ICH guidelines) and applicable government regulations. Informed consent was obtained for all participants.

Study participants who met the inclusion criteria (detailed in Table S2) were instructed to use the complete formulation on one half of their face twice a day for 12 weeks, while the other half of their face was equally treated with an identical formulation lacking OS-01. Cleanser (Cetaphil Gentle Cleanser) and sunscreen (Neutrogena Oil-free moisture SPF 35) were also provided for participants to use on both sides of their faces throughout the study period.

Product efficacy was determined from analysis of results from instrumental assessments, group-blinded expert clinical grading, and image analysis executed at baseline, 6, and 12 weeks of treatment. Subjective questionnaires were also used to evaluate user perception of product performance.

2.2 | Study methods

Subjects underwent assessments at the specified time points described below. Each assessment was graded on the left and right sides of the face separately.

2.2.1 | Clinical grading for efficacy

Visual and tactile assessments were performed using 10 cm Visual Analog Scales (VAS) bilaterally at Baseline, Week 6, and Week 12. The following parameters were evaluated: fine lines/wrinkles, skin tone

(color evenness), texture/smoothness (visual), firmness (visual), elasticity (tactile), skin pores, radiance/luminosity, and overall appearance.

2.2.2 | VapoMeter

The VapoMeter (Delfin Technologies Ltd., Finland) measures the trans-epidermal water loss (TEWL) of the skin with a closed cylindrical chamber that contains sensors for relative humidity and temperature. Changes in TEWL rates provide a measure of barrier disruption or integrity, thereby providing an indication of product performance. All subjects had VapoMeter measurements taken in duplicate and averaged on the bilateral face at Baseline, Week 6, and Week 12. Assessment location was recorded on a body map for each subject.

2.2.3 | VISIA-CR

Photo documentation was carried out using the VISIA-CR imaging system (Canfield Scientific, USA), which captures high-resolution images in multiple lighting modes. Photographs were captured in Standard 1, and parallel polarized light of the center, right, and left view at Baseline, Week 6, and Week 12. In addition to being used for photo documentation, the images were analyzed according to skin radiance by calculating the participant's individual typology angle using the equipment's analysis software.

2.2.4 | Antera 3D®

The Antera 3D® (Miravex, Ireland) is an instrument combining skin profilometry, multi-spectral analysis, and colorimetry to provide a reconstruction of the skin surface in three dimensions and subsequent image analysis. Images were captured on the crow's feet area on the left and right in all subjects at Baseline, Week 6, and Week 12. The same location was measured at each time-point and recorded using a face map. Images were analyzed for texture and indentation of lines/wrinkles.

2.2.5 | Consumer perception

Subjective questionnaires were used to Gauge the subject's perception of the products after the use of the test product at Weeks 6 and 12. The question was: in your opinion, in what manner has the tested product improved the following skin parameters? The parameters were skin hydration, skin firmness/elasticity, skin radiance, skin roughness (tone and texture), eye bags, lightening of hyperpigmentation, and general appearance. Participants' overall satisfaction was evaluated using a 5-point scale, with scores of 1 (insufficient), 2 (poor), 3 (sufficient), 4 (good) and 5 (excellent).

2.3 | Statistical analysis

Expert grading, instrumentation, and images were analyzed using descriptive statistics (mean and standard deviation); paired *t*-test, monadic, mean percent improvement from baseline, percent of subject improving for changes from baseline assessment, and unpaired *t*-test for treatment comparison. Subjective questionnaires were analyzed using frequency (number and percent), percent of positive response (where applicable), and Wilcoxon test for treatment comparison. *p*-value <0.05 was considered to be statistically significant.

3 | RESULTS

Twenty-five females were recruited to the study and were instructed to apply the control and OS-01 formulation on specific sides of their face (Table 1). Throughout the study, three mild adverse events were reported, and two participants discontinued their participation prior to study completion. One participant had bronchitis, which was not related to the treatment, but had to discontinue the study. Another

TABLE 1 Participant demographics.

Variable	*n*	Mean ± SD	Min	Max
Age (years)	22	59.36 ± 5.37	47	65
Height (inches)	22	63.79 ± 2.63	59	69
Weight (pounds)	22	144.50 ± 33.57	107	230
			n	%
Ethnicity	22	Not Hispanic or Latino	22	100
Race	22	White	22	100
Sex	22	Female	22	100
Fitzpatrick skin type	22	Skin type II	12	54.5
		Skin type III	10	45.5
Facial skin type	22	Combination	5	22.7
		Dry	5	22.7
		Normal	12	54.5

participant experienced mild dryness and a rash on the cheek that lasted for 26 days, which was likely due to the treatment, and resolved after discontinuing its use. This participant was also required to discontinue the study. The third participant experienced mild irritation on the cheek that lasted for only 5 min after applying the product. This participant completed the study (Table S3).

3.1 | OS-01 formulation strengthens the skin barrier and protects the skin from dehydration

Skin barrier was assessed using a vapometer, which assesses skin barrier function by measuring TEWL (where a lower number represents a stronger barrier). Skin treated with the OS-01-containing formulation presented a 14%–18% lower TEWL ($p < 0.001$ at 6 weeks and $p = 0.011$ at 12 weeks vs. baseline; Table 2), while the vehicle control demonstrated a TEWL similar to baseline throughout the 12 weeks of the study. Direct comparisons of TEWL between the formulations, normalized to baseline, revealed significant improvements in the OS-01-treated side at both 6 and 12 weeks ($p < 0.001$; Table 2), denoting an improved skin barrier with the addition of the peptide.

Corroborating such observations, 86.4% of users reported positive effects of the tested formulations (both with and without OS-01) on skin hydration at 12 weeks, and all the participants affirmed that they noticed improvements in skin hydration after using both vehicle and OS-01-containing formulations before the first month of use (when responding the questionnaire at the 6-week timepoint; Figure 1).

3.2 | OS-01 formulation decreases wrinkle indentation and improves skin texture/smoothness

3.2.1 | Wrinkle indentation and skin texture (roughness)

Using the Antera 3D equipment to analyze wrinkle appearance, as measured by indentation and skin roughness, we highlighted that treatment with the OS-01 formulation promoted wrinkle appearance reduction, as shown by a mean reduced wrinkle indentation at both Week 6 and 12 of 3.71% ($p = 0.055$ vs. baseline) and 6.6% ($p = 0.065$ vs. baseline), respectively (Table 2). Meanwhile, the formulation lacking the peptide promoted a less intense reduction in skin wrinkle indentation ($p = 0.44$ and $p = 0.68$ vs. baseline at 6 and 12 weeks, respectively). Moreover, the formula containing OS-01 promoted a marked improvement at 12 weeks of use ($p = 0.07$) when directly compared to the vehicle control (Table 2). Representative images obtained from two participants exemplifying the superior beneficial effects of the OS-01-containing formulation in wrinkle appearance are demonstrated in Figure 2.

A mean improvement in skin texture (roughness) of 5.05% was experienced by the participants in the OS-01-treated side ($p = 0.024$ vs. baseline), which was not observed in the vehicle formulation side (Table 2). Representative images used for skin texture analysis are shown in Figure 3. The instrumental analysis results were corroborated by group-blinded expert analysis (Table S4), which pointed to a progressive reduction of lines/wrinkles appearance ($p < 0.001$ vs. baseline at 12 weeks) in both experimental groups.

Skin smoothness, assessed by expert grading (Table S4), presented a similar progressive improvement between baseline, 6, and 12 weeks of treatment ($p < 0.001$ vs. baseline) for both sides of the face of all participants at Week 12. The benefits in skin smoothness/roughness were noticed on both sides of the face by 81.8% of participants, according to subjective questionnaires (Figure 1). Finally, according to expert grading, participants presented a significant improvement in skin pores on both sides of the face with both formulas (Table S4).

3.2.2 | Skin radiance

Using the VISIA-CR imaging system, we determined the radiance/luminosity aspect of the participant's skin. After 12 weeks of use, the formulation with OS-01 peptide significantly improved radiance by approximately 16% ($p = 0.018$ vs. baseline), while the vehicle formulation demonstrated a nonsignificant trend toward improved radiance ($p = 0.593$ vs. baseline) (Table 2). Representative images (Figure 4) are shown highlighting the beneficial effects of the OS-01 formulation on skin radiance. Blinded expert grading (Table S4) supported these findings and observed significant improvements in skin radiance on both sides of the participant's face. Skin evenness was also significantly improved for both OS-01 and vehicle formulation-treated sides of the face (Table S4). The improvement of skin radiance was reported by 77.3% and 86.3% of participants, when asked to assess skin radiance after treatment with OS-01 formula or vehicle formulation, respectively (Figure 1).

Finally, according to group-blinded expert analysis, the overall appearance of the skin was improved in all participants after treatment, regardless of the side of the face (Table S4). The benefits were also perceived on both sides of the face by over 60% of participants at 6 weeks and over 80% of participants at 12 weeks of study (Figure 1).

4 | DISCUSSION

As the largest and most accessible organ, the skin plays a crucial role in protection from external hazards that may be biological, chemical, or radiological. Moreover, the skin is heavily involved in social interactions with a potential perception of status, health, and age. Cellular senescence has been highlighted as a key pathway in a host of diseases, in particular age-related diseases, such as cancer,[22] as well as playing a role in skin aging and the associated effects.[23] OS-01 is a unique senotherapeutic peptide, shown to be safe[24] and to reduce cellular senescence burden and, consequently, reduce the

TABLE 2 Instrumental evaluation.

			OS-01 formulation					Control formulation				
			Left side					Right side				P_T-value
Assessment	Time point	*n*	Mean ± SD	Mean percent improvement *from BL mean*	Percent of subjects showing improvement *from BL*	*p*-value *TX* versus *BL*	*n*	Mean ± SD	Mean percent improvement *from BL mean*	Percent of subjects showing improvement *from BL*	*p*-value *TX* versus *BL*	*L* versus *R*
TEWL (Vapometer)	Baseline	21^	14.85 ± 2.94				21^	13.12 ± 3.08				
	Week 6	20^	11.86 ± 2.45	18.89%	80.0%	<0.001*	20^	12.42 ± 3.61	5.00%	70.0%	0.218	0.012[L]
	Week 12	21^	12.37 ± 3.16	14.19%	81.0%	0.011*	21^	12.94 ± 3.02	1.20%	61.9%	0.808	0.055
Texture (Antera 3D)												
Roughness	Baseline	22	18.22 ± 5.43				22	15.57 ± 4.69				
	Week 6	22	16.89 ± 4.08	4.87%	68.2%	0.029*	22	15.19 ± 3.18	NI	45.5%	0.505	0.245
	Week 12	22	16.93 ± 4.26	5.05%	72.7%	0.024*	22	15.74 ± 4.50	NI	54.5%	0.659	0.030[L]
Wrinkles (Antera 3D)												
Indentation	Baseline	22	17.13 ± 4.54				22	14.81 ± 3.88				
	Week 6	22	16.12 ± 3.41	3.71%	63.6%	0.055	22	14.45 ± 2.71	0.37%	50.0%	0.445	0.358
	Week 12	22	16.19 ± 3.65	6.62%	68.2%	0.065	22	14.95 ± 3.71	NI	54.5%	0.684	0.072
Radiance/Luminosity (VISIA-CR)												
ITA	Baseline	22	21.34 ± 8.85				22	22.37 ± 9.17				
	Week 12	22	23.70 ± 9.16	16.63%	72.7%	0.018*	22	22.94 ± 9.05	7.11%	59.1%	0.593	0.208

Note: * indicates a statistically significant improvement compared to baseline, $p < 0.05$. L indicates Left Side statistically significantly outperformed the Right Side, $p < 0.05$. ^ indicates One subject (#22) did not have Baseline Vapometer data and one subject (#13) had invalid data at Week 6 and was not used for analysis (21 subjects analyzed at Baseline and Week 12 and 20 subjects analyzed at Week 6).

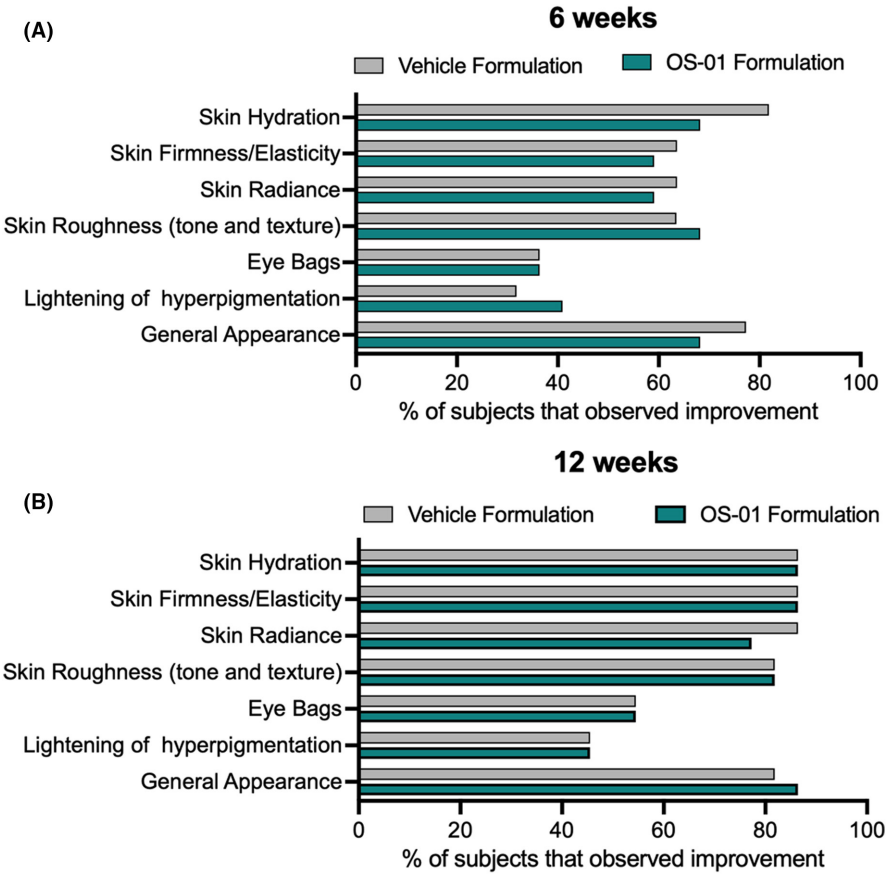

FIGURE 1 Subjective questionnaire results for 6 weeks (A) and 12 weeks (B) of study.

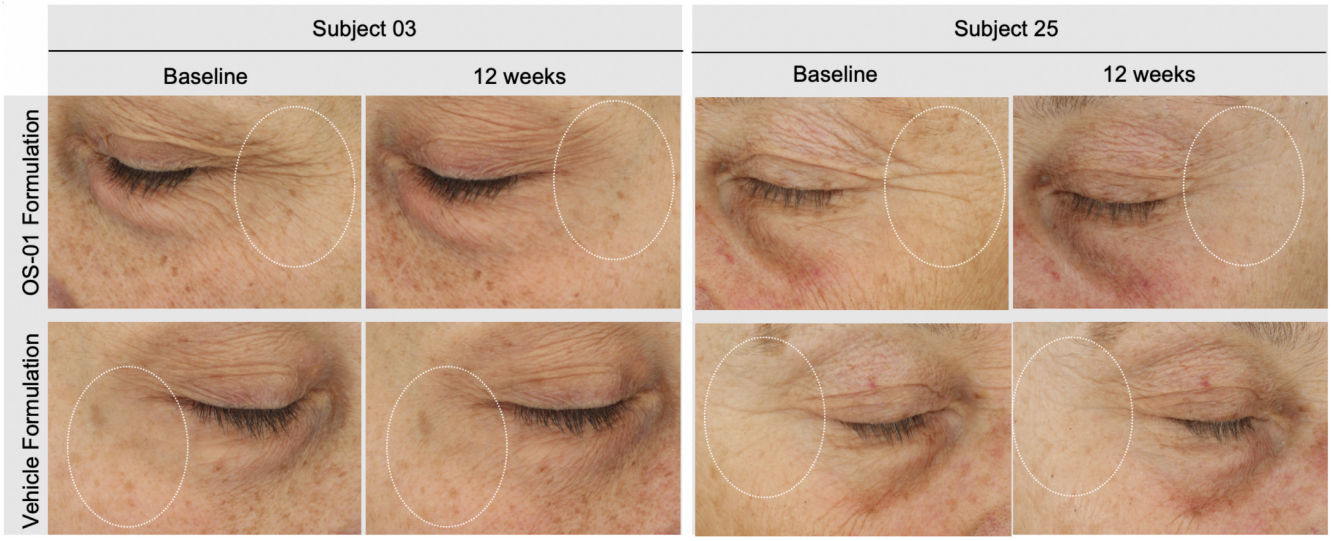

FIGURE 2 Representative images highlighting skin wrinkles in two subjects (03 and 25) after 12 weeks of OS-01 or vehicle formulation treatment.

skin biological age in vitro and ex vivo.[21] While the importance of these previous studies demonstrates the peptide's safety, efficacy, and underlying mechanisms as an active ingredient used in topical formulations, it is important to assess the effects of the peptide formulation in vivo. The randomized, split-face study presented above demonstrates the efficacy and benefits of a face moisturizer containing the OS-01 peptide.

This study aimed to assess the clinical effects of OS-01 peptide when added to a base formula that was designed to support overall skin health. Many ingredients present in the vehicle formulation, such as Pracaxi (Pentaclethra macroloba) oil, Andiroba (*Carapa guianensis Aubl.*) oil, Niacinamide, Pau mulato (*Calycophyllum spruceanum*) Oleic Extract, Allantoin, and Hyaluronic Acid can be considered as bioactive compounds, which exert moisturizing,

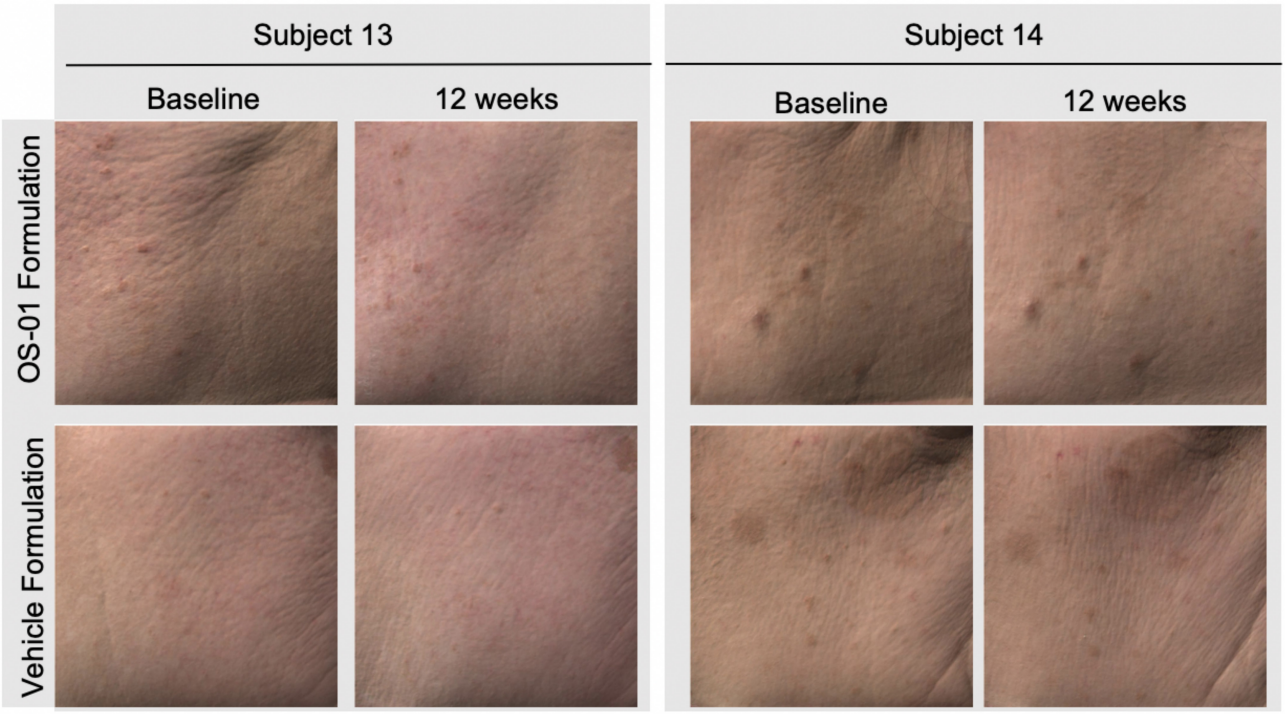

FIGURE 3 Representative images highlighting skin texture in two subjects (13 and 14) after 12 weeks of OS-01 or vehicle formulation treatment.

hydrating, antioxidant, anti-inflammatory and regenerative effects on skin.[25–31] Nevertheless, the clinical results observed in the present study highlight the benefits brought by the inclusion of the senotherapeutic OS-01 peptide in the tested topical formulation.

The hydration of the skin relates to the overall health and strength of the skin barrier. Using TEWL measurement, we demonstrated that OS-01 significantly improved the skin barrier over time (18.89% and 14.19% average improvement after 6 and 12 weeks) while there was no change in the side of the face treated with the basic formula. Additionally, the benefits in skin hydration were perceived by over 85% of participants. It is important to note that the present study was conducted in a dry climate during the winter months, so a reduction of skin hydration was expected throughout the study period. Kikuchi et al.[32] concluded that skin hydration, as measured by conductance (a parameter that reflects skin hydration), presented a decrease during winter of approximately <10%. Additionally, Egawa and Tagami observed significant differences of approximately 20% in the capacitance of facial skin between summer and winter conditions, making significant improvements compared to baseline, possibly more of note.[33] Hydrated, healthy stratum corneum works more effectively as a skin barrier, preventing allergies,[34] atopic dermatitis,[35] and even decreasing organismal inflammation.[6] As such, the effects of OS-01 results in improved skin barrier and hydration, as measured both quantitatively as well as qualitatively, may have health implications beyond the appearance of the skin. Most likely, the positive results obtained in vivo regarding skin hydration and skin barrier are a reflection of the data obtained from 3D skin equivalents and skin biopsies tested with OS-01 peptide in vitro, which presents an increase in the epidermal thickness following peptide treatment, as well as increased mRNA expression of Hyaluronan Synthase 2, an enzyme that synthesizes hyaluronic acid in the skin, promoting water retention.[21] The improvement in the skin barrier function was not observed in the vehicle formula, suggesting that it is directly associated with the presence of the peptide. Based on our previously published investigations into the mechanisms of OS-01, we posit that the improved skin barrier is due to OS-01 targeting and reducing senescent cells, as well as promoting cellular proliferation, as assessed by Ki67 staining in vitro.[21] The results presented here suggest that such mechanisms were effective in enhancing the health of the skin, measured by assessing the impact of a formulation containing the OS-01 peptide on improving the skin barrier function, compared to the vehicle formulation only. Nevertheless, it is important to highlight that while TEWL has proven to be a valuable metric in assessing skin barrier function, relying solely on this measurement presents certain limitations in capturing the comprehensive dynamics of skin barrier integrity. TEWL primarily reflects the water vapor diffusion across the stratum corneum, offering insights into epidermal permeability. However, it overlooks other crucial aspects of barrier function, such as lipid composition, intercellular cohesion, and the overall structural integrity of the skin. Future assessments are required for a more nuanced and accurate evaluation of skin barrier function.

Previously published studies correlate cellular senescence to perceived age, which is heavily influenced by skin wrinkles.[12] Wrinkle formation depends on epidermal, dermal, and hypodermal mechanical properties of the skin, of which senescent cells alter by modulating cellular function, tissue inflammation, and extracellular

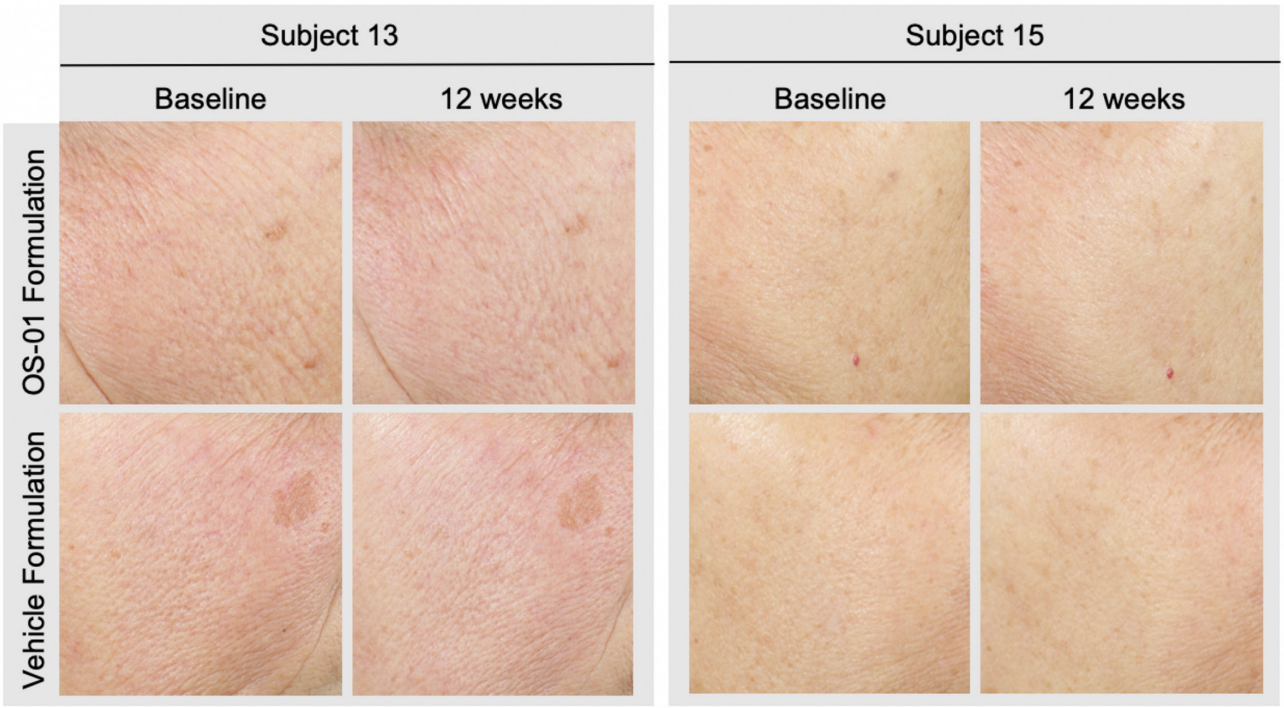

FIGURE 4 Representative images highlighting skin radiance in two subjects (13 and 15) after 12 weeks of OS-01 or vehicle formulation treatment.

matrix (ECM) deposition.[36] Indeed, it has already been shown that senescent cells co-localize with altered ECM and that their number directly correlates with skin wrinkling in elders.[12] The analysis of the topology of the skin is a reliable method to evaluate wrinkles and can be performed using imaging systems such as the Antera 3D® system,[37] which presents higher sensitivity than the imaging system VISIA-CR® for wrinkle investigations.[38] Here, Antera 3D equipment analysis revealed that the peptide-containing formulation promoted progressive reductions in wrinkle indentation during the study period in a superior fashion to the vehicle formulation. Such measurement could also be observed in the VISIA-CR® images, obtained at baseline, as well as at 6 and 12 weeks after treatment. Here, we showed representative images of the different results achieved after treatment with the OS-01 formulation compared to the vehicle formulation. In both examples included, treatment with the peptide formulation promoted superior results, with less visual wrinkles and better skin overall appearance, compared to the vehicle formulation-treated side of the face, highlighting again the benefits of the OS-01 peptide.

In cell cultures, 3D skin equivalents, and organotypic ex vivo skin cultures, the OS-01 peptide reduced cellular senescence levels and inflammation while boosting cellular renewal, and the expression of Collagen and Hyaluronan Synthase 2.[21] Furthermore, the peptide promoted better skin structural profiles, as well as rejuvenated mRNA and DNA methylation profiles, characterizing a lower biological age of treated samples and a decreased senescence burden. We infer that such results may explain why the formula containing the peptide promoted superior results in wrinkle reduction compared to the vehicle formulation. This may also explain the improved radiance of the skin treated with the peptide-containing formulation compared to the vehicle formulation only since skin inflammation and aging are related to dyspigmentation and senescence.[39] Finally, the peptide-containing formula promoted superior skin texture compared to both baseline, and the vehicle formulation, supporting, once again, that the biological rejuvenation promoted by the peptide observed in vitro might be responsible for the significant benefits identified when adding OS-01 in a topical skin product.

Follow-up studies will aim to expand on the findings described here in a more diverse population, as well as include additional in vivo biological assays to establish the effects of the formulation on skin health. Despite some limitations of this study, the treatments highlight the ability of OS-01 to improve the skin barrier, reduce wrinkle appearance, boost skin radiance, and improve skin texture through objective instrumental measurements. Importantly, the benefits to the skin detected by instrumental analysis were also supported by both group-blinded expert analysis, as well as the personal perceptions of the participant's skin, which are less accurate and more subjective assessments but highly valuable results from a user point of view.

5 | CONCLUSIONS

Our data show that both the OS-01 and the vehicle formulations are safe and effective in treating skin changes related to aging. In this pilot study of 22 women from 47 to 65 years of age, the formulation

with and without peptide promoted increases in skin health on the face over 12 weeks of treatment. However, the OS-01 peptide formulation promoted superior clinical results compared to that without peptide. Adding the OS-01 peptide to the formula resulted in significant improvements in skin barrier function, texture, and radiance, as measured by instrument analysis. Also, it promoted improvement in wrinkle indentation compared to the vehicle formula. Therefore, this study highlights the use of the senotherapeutic peptide OS-01 as a compelling treatment to reduce the visible signs of aging.

AUTHOR CONTRIBUTIONS

Alessandra Zonari, Mariana Boroni, Carolina R. Oliveira, Lear E. Brace, and Juliana L. Carvalho designed and analyzed the research study. Juliana L. Carvalho wrote the original draft. Alessandra Zonari, Lear E. Brace, Nathaniel H. O. Harder, and Claire Harker reviewed and edited the draft. All authors have read and approved the final manuscript.

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CONFLICT OF INTEREST STATEMENT

Alessandra Zonari, Mariana Boroni, Carolina Reis de Oliveira, Lear Brace, and Juliana L. Carvalho are named as inventors of a patent directed at this invention, which is solely owned by OneSkin, Inc. Alessandra Zonari, Mariana Boroni, Carolina Reis de Oliveira, and Juliana L. Carvalho are co-founders of OneSkin Inc.

DATA AVAILABILITY STATEMENT

Research data are not shared.

ETHICS STATEMENT

Institutional Review Board approval was obtained prior to study initiation (Allendale IRB, 4336OST1010 version 2.0). The study was conducted by a contract research organization according to international standards of Good Clinical Practice (FDA and ICH guidelines) and applicable government regulations. Informed consent was obtained for all participants.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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