

Efficacy of a botanical-based Nutricosmetic ingredient on skin aging-related markers in adult women

Abstract

Background: Recent research highlights the strong link between nutrition and skin health. Nutricosmetics, which are ingestible actives that exert an effect on the skin's appearance, have emerged as a complement to topical cosmetics, targeting systemic drivers of skin aging (e.g., oxidative stress, inflammation, glycation).

Objective: To evaluate the efficacy and safety of a standardized four-botanical nutricosmetic ingredient, on facial skin, primarily the forehead, with a special focus on wrinkles.

Materials and methods: A 12-week randomized, double-blind, placebo-controlled study was carried out in women (age 30–66 years) with visible signs of skin aging. Participants were randomized to receive the nutricosmetic ingredient Eternalyoung® (225 mg/day) or placebo capsules. Assessments were performed at baseline and at 2, 4, 8, and 12 weeks. Measurements include: forehead wrinkle volume and count (AEVA-HE 3D), gloss (Glossymeter), moisturization (Corneometer), melanin index (Mexameter) and transepidermal water loss (TEWL, Tewameter).

Results: Participants consuming the nutricosmetic exhibited sustained improvements in several endpoints. Forehead wrinkle volume decreased from baseline and reached –23.3% at week 12, compared to +13.6% observed in the placebo group. Also, wrinkle count was reduced by –24% at week 12. A significant and progressive increase in forehead skin gloss was observed from week 4 (+14.6%, $p = 0.008$) to week 12 (+20.2%, $p = 0.008$), while the placebo group remained unchanged. Among participants with a more affected optical/structural baseline profile the daily intake of the botanical blend produced a significantly larger increase in gloss than placebo at week 12 ($p = 0.021$). Melanin levels significantly decreased in the experimental group with a 13.9% decrease at week 12, compared to –7.3% in the placebo group. Significant between-group differences were observed at weeks 2, 8, and 12. Overall TEWL and hydration showed no between-group differences, but participants with impaired baseline values (TEWL >15 and hydration <40 a.u.) improved significantly in the experimental group. The product was well tolerated, with no adverse events.

Conclusion: The study supports previous clinical evidence of a botanical-based nutricosmetic ingredient, demonstrating consistent and measurable benefits on wrinkles, dullness, and hyperpigmentation, with a favorable safety profile.

Keywords: antiaging, clinical trial, nutricosmetic, forehead wrinkles, gloss, pigmentation

Volume 9 Issue 4 - 2025

Pau Navarro, Adrián García, Jonathan Jones,
Nuria Caturla

Research and Development Department, Monteloeder SL, Spain

Correspondence: Nuria Caturla, Monteloeder SL, Miguel
Servet 16, 03203 Elche, Alicante, Spain, Tel +34 965 685 275

Received: October 13, 2025 | **Published:** October 31, 2025

Introduction

From around the age of 25 the first signs of aging start to become apparent on the surface of the skin.¹ People often feel younger than their biological age leading them to seek solutions for maintaining good-looking skin.² Skin aging is a progressive process characterized by the gradual loss of key structural and functional properties, resulting in dryness, wrinkles, laxity, and unaesthetic pigmentation. This complex process is influenced by genetic, environmental factors such as ultraviolet (UV) radiation and pollution exposure, and lifestyle-related factors including diet, habits and stress.^{1–3} Therefore, a holistic approach to skin care, including a healthy diet and lifestyle, is essential for achieving effective and long-lasting results.

In recent years, the relationship between nutrition and skin health has gained increasing attention. Scientific evidence reveals that dietary components can modulate cutaneous physiology, providing antioxidant, anti-inflammatory, and photoprotective effects that help maintain skin integrity and appearance.^{4,5} This understanding has raised the development and sales growth of nutricosmetics, which

are oral supplements designed to enhance skin appearance that complement topical formulations.^{6,7} As the nutricosmetic market grows, demonstrating efficacy through clinical research is crucial for building consumer trust and credibility. Thus, it is central that novel and innovative ingredients entering the market support their claimed benefits through robust scientific evidence.⁸

Common active ingredients in nutricosmetics include plant polyphenols, carotenoids, vitamins, and other phytochemicals with recognized systemic bioactivity.^{9–11} Polyphenol-rich botanicals are prominent candidates in this space due to their antioxidant, anti-inflammatory and matrix-protective actions relevant to skin aging pathways.^{10,12} In principle, a varied antioxidant profile appears superior to large amounts of one antioxidant, indicating potential complementarity or synergy.¹³ Therefore, food supplements containing a diverse phenolic profile are an effective way to prevent and reduce the signs of skin aging.

Specifically, previous preclinical and clinical studies supported the skin antiaging potential of a proprietary nutricosmetic ingredient comprised of 4 standardized botanical extracts: pomegranate (*Punica*

granatum), sweet orange (*Citrus sinensis*), desert ginseng (*Cistanche sp.*), and gotu kola (*Centella asiatica*). In vitro studies in human dermal fibroblasts exposed to UV radiation showed that this botanical blend counteracted key mechanisms of skin aging, including reducing telomere shortening, preventing loss of proliferative capacity, lowering intracellular radical oxygen species (ROS), and decreasing advanced glycation end products (AGEs), thereby supporting dermal structural protein synthesis.¹⁴ Furthermore, in a randomized, double-blind, placebo-controlled trial, subjects showed improvements in various skin conditions, including hydration, trans-epidermal water loss (TEWL), elasticity, crow's feet wrinkles, and skin thickness.¹⁵ While these findings are promising, further confirmatory trials with broader endpoints are necessary to reinforce the evidence base for oral anti-aging interventions.

To this end, a randomized, double-blind, placebo-controlled study was conducted to independently assess the efficacy and safety of the above-mentioned botanical blend in healthy women with visible signs of skin aging, over 12 weeks using validated instrumental endpoints. The study aimed to confirm and expand previous clinical evidence by incorporating three-dimensional (3D) wrinkle analysis, optical assessments of gloss and pigmentation, and the analysis of additional facial regions, with a specific focus on the forehead as a key area for detecting both structural and perceptual changes. Furthermore, the trial enrolled a diverse population, including Latin, Caucasian, and Asian ethnicity, covering Fitzpatrick skin phototypes II to V.

Materials and methods

Study design

A randomized, double-blind, placebo-controlled clinical trial was conducted to evaluate the efficacy and safety of a botanical-based nutricosmetic ingredient (commercially available as Eternalyoung®; see Materials and Methods: Intervention) using validated instrumental endpoints.

The study was conducted at Centro Médico Complutense (Spain) in accordance with the Declaration of Helsinki, and EU GDPR. The protocol and test conditions were approved by Research Ethics Committee of the Hospital Universitario Príncipe de Asturias (Spain), with internal code: CEIm HUPA OE 29/2024. All participants provided written informed consent before any procedure.

Study population

A total of 71 healthy women, age 30–66 years old, with visible signs of skin aging, were enrolled in the study. Participants were instructed to: (i) take one capsule daily of the assigned product (nutricosmetic or placebo) for 12 weeks; (ii) refrain from using new anti-aging products during the study; (iii) avoid intentional tanning or phototherapy; and (iv) maintain their usual daily skincare and outdoor routines.

The main exclusion criteria were: (i) pregnancy, lactation, or unreliable contraception; (ii) lesions or infections on the study areas; (iii) clinically relevant dermatoses (eczema, psoriasis, dermatitis); (iv) allergy or hypersensitivity to any product component; (v) high skin reactivity or history of cosmetic intolerance; (vi) recent dermatological procedures, botulinum toxin or hyaluronic acid injections within 6 months; (vii) oncologic disease; (viii) recent or ongoing treatments interfering with skin function (e.g., corticosteroids, retinoids, antibiotics, antihistamines, anti-acne therapies); (ix) use of any anti-aging/anti-blemish cosmetic or dietary supplement during the study; (x) intentional sun exposure/UVA lamps; and (xi) participation in another similar study.

Intervention

The experimental product was Eternalyoung®, a commercially available dietary supplement ingredient supplied by Monteloeder by Suannutra (Miguel Servet 16, Elche, Alicante, Spain). Eternalyoung® is a blend of four standardized botanical extracts: *Centella asiatica* leaf, *Punica granatum* (pomegranate) fruit, *Citrus sinensis* (sweet orange) fruit, and *Cistanche* herba stem. The blend is characterized by a minimum content of 2.5% verbascoside, 12.5% hesperidin, 3% punicalagins, and 7% asiaticosides, as verified by HPLC-DAD analysis using authentic standards for retention time and UV spectra identification as previously described.¹⁴

In the experimental arm, each soft gelatin capsule contained 225 mg of Eternalyoung®, plus excipients (245 mg microcrystalline cellulose, 10 mg magnesium salts and 5 mg silicon dioxide) for a total weight of 580 mg. The placebo capsules were identical in appearance and composition, except that 225 mg maltodextrin replaced the active blend. Both products were opaque, identical in appearance, pre-packed in blisters, and consecutively numbered according to the randomization list.

Participants were instructed to take one capsule per day of the assigned product for 12 consecutive weeks, about 30 minutes before or after meals.

Randomization, blinding

Participants were randomized 1:1 to Eternalyoung® or matched placebo capsules, administered once daily for 12 weeks. Participants, study staff, and analysts were blinded to assignments.

Outcomes and assessment schedule

The endpoints included instrumental assessments of: (i) forehead gloss (Glossymeter® GL-200, Courage+Khazaka electronic GmbH), (ii) forehead hydration (Corneometer® CM825, Courage+Khazaka electronic GmbH), (iii) forehead wrinkle topography (AEVA^{3D}-HE, Eotech, France), (iv) transepidermal water loss (Tewameter® TM 300, Courage+Khazaka electronic GmbH) on the left cheek and (v) skin color indices (Mexameter® MX18 Courage+Khazaka electronic GmbH), measured on the malar region for all subjects and on a representative lesion in those presenting hyperpigmentation.

Clinic visits occurred at baseline (T0) and after approximately 2, 4, 8, and 12 weeks of intake (T2W, T4W, T8W, T12W). Endpoints analyzed in this manuscript were measured at all points unless specified.

The occurrence of adverse events (AEs) was monitored throughout the study by the investigators and based on subjects' diary entries. Investigators rated the observed and reported AEs as being either severe or non-severe based upon their potential relationship to study treatment. Participants had a contact number to report any issue.

Statistics

Data analysis was performed using Jamovi software (version 2.6.22). Student's t-test was used to compare outcomes. Data normality was checked using Shapiro–Wilk normality test and data shape. Both intergroup statistical analysis was carried out, using Student's t-test.

For between-group analysis, the independent samples Student's t-test was used to compare the experimental and placebo groups at each time point. A two-tailed hypothesis (Group 1 ≠ Group 2) was stated to account for differences in either direction. For within-group analysis, the paired samples Student's t-test was used to evaluate

longitudinal changes within each group over the study period, specifically comparing each time point vs start of the study (Week 0). All statistical analyses were performed with a confidence level of 0.05 and a 95% confidence interval.

Before any type of analysis, an identification of outliers was conducted to determine whether they should be excluded from the analysis. When missing values (due to patient dropout, instrumental errors, not measured at some of the visits), protocol violations, and/or outliers the volunteer was excluded from the study to maintain the same sample size at each experimental time point and thus avoid noise in our analysis. Missing or excluded volunteers are indicated in the introduction of each parameter analyzed.

Results

A total of 71 women were randomized in a 1:1 ratio to receive either Eternalyoung® (n=36) or a placebo (n=35). During the follow-up period, five participants in the treatment group either dropped out of the study or had protocol deviations, and two had incomplete outcome measurements. In the placebo group, four participants dropped out, while one had incomplete outcome measurements.

The population were female subjects, 30-66 years of age. Demographics and baseline characteristics were similar across the treatment arms (Table 1).

Table 1 Baseline demographic characteristics of participants in the active treatment group (Eternalyoung®) and in the placebo group

Characteristic	Eternalyoung	Placebo
n	36	35
Age, years (mean ± SD)	49.06 ± 9.76	48.14 ± 8.58
Age range, years	31 – 66	32 – 66
Ethnicity — Latin, Caucasian, Asian (%)	55.6%, 38.9%, 5.6%	42.9%, 48.6%, 8.6%
Phototype (%)		
I	0	0
II	19.4	34.1
III	63.9	55.3
IV	5.6	5.7
V	11.1	4.9

Safety

No serious adverse events occurred, and no discontinuations were due to safety. Only one participant reported persistent mild flatulence throughout the treatment period in the active group.

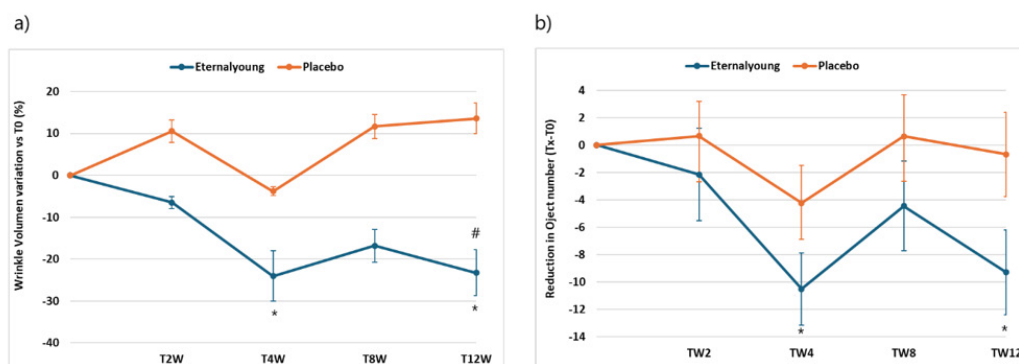
Wrinkles

Wrinkle-reduction efficacy was assessed using a three-dimensional scanning sensor that measured skin topography based on fringe-projection technology combined with active stereometry. In this study, the primary objective was to evaluate wrinkle volume in the forehead, since volume changes reflect not only the depth but also the extension of wrinkles across the skin surface. The volunteers that were not measured at all-time points and those who started with a volume of 0 were excluded from the statistical analysis. Thus, the final sample size was 28 in the treatment group and 30 in the placebo.

The AEVA-HE 3D analysis revealed that in the active treatment arm, the baseline wrinkle volume ($3.87 \pm 0.63 \text{ mm}^3$) in the forehead was significantly reduced as early as week 4 compared to the start of the study, which was maintained and further reinforced up to week 12 (-23.3% vs. baseline). In contrast, the placebo group, with baseline wrinkle volume of $2.65 \pm 0.46 \text{ mm}^3$, did not present any statistically significant improvement at any time point. In fact, wrinkle volume increased by $+13.6\%$ in week 12. The wrinkle volume variation observed in the dietary supplement group was statistically significant when compared to the placebo group at the end of the study (Figure 1a). Also, 83% of volunteers in the treatment group exhibited positive changes, with maximum reductions of 93.8% at the end of the study.

Furthermore, a clinically significant reduction in the number of forehead wrinkles was observed in the experimental group. The experimental group demonstrated a significant average reduction of 9 wrinkles at the end of the study, which corresponds to a 24% decrease in the overall count of forehead wrinkles. Subjects consuming Eternalyoung® showed significant within-group reductions in wrinkle object number at W4 and W12 versus baseline, whereas those taking the placebo showed no significant change. The between-group analysis revealed an almost statistically significant difference ($p = 0.06$). Specifically, the number of wrinkles in the frontal area decreased from 36.6 ± 4.59 to 28.2 ± 4.59 over the 12-week period. In contrast, the placebo group showed no meaningful improvement, with the number of wrinkles decreasing only slightly from 29.5 ± 4.59 to 28.82 ± 3.09 (Figure 1b).

Figure 1 Reduction of forehead wrinkles in treatment group using AEVA-HE 3D analysis (a) Wrinkle volume variation vs T0 (%) and (b) reduction in wrinkle



number vs T0, from week 2 to week 12 (W2, W4, W8, W12) in the treatment (blue line) and placebo group (orange line). Data are means ± SEM and negative percentages indicate a reduction vs baseline. Statistical analysis is reported as follows: * indicates within-group significance vs T0 ($p < 0.05$). Between-group statistical significance is reported with # $p < 0.05$.

Representative images of the three-dimensional scanning sensor AEVA-HE 3D can be found in Figure 2, where a progressive reduction in wrinkle depth and surface irregularities can be observed over time.

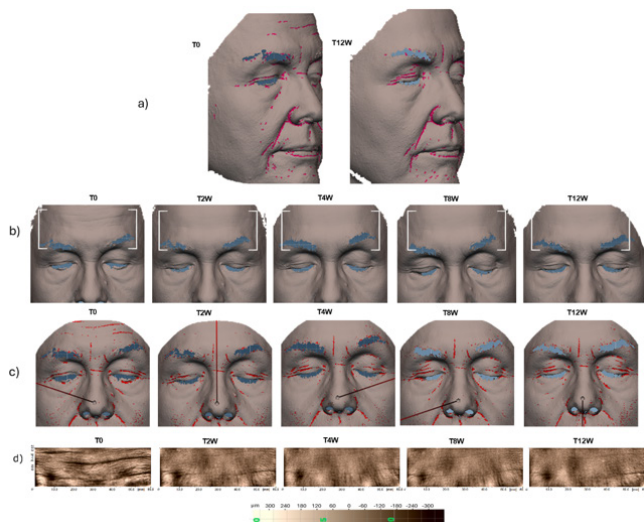


Figure 2 Representative AEVA-HE 3D images of one volunteer from the treatment group showing progressive improvement in forehead wrinkle topography over 12 weeks. a) Image of the right profile of volunteer at the start of the study (T0) and at the end (T12W) illustrating a visible reduction in wrinkles and surface irregularities. b) Evolution of wrinkles in the forehead region at each time point (T0–T12W). c) Gradual reduction of wrinkles classified as class III (>100 µm, marked in red), over time. d) Topography maps of the forehead region of the same volunteer at different time points. The maps display the depth distribution of skin microrelief and wrinkles within the defined region of interest. Color coding represents height variations in micrometers (µm), with light tones indicating elevations and darker tones representing depressions.

Skin gloss

Efficacy of Eternalyoung on improvement in skin glow was measured by Glossymeter in the forehead area. The volunteers that dropped out of the study and were not measured at all-time points were excluded from statistical analysis. Therefore, the sample size was 24 in the treatment group and 30 in the placebo.

At baseline, the mean DSC (directly reflected light) values were 6.23 ± 0.37 GU for Eternalyoung and 6.88 ± 0.61 GU for placebo. In Eternalyoung, gloss initially showed a minimal change (+0.8 %) at the first assessment, followed by a significant increase of +14.6 % at 4 weeks ($p = 0.008$), +21 % at 8 weeks ($p = 0.003$), and +20.2 % at 12 weeks ($p = 0.008$). In contrast, the placebo group remained largely unchanged throughout the 12-week period, with no significant increases observed. In fact, a slight decrease of -15.6% was detected during the first assessment (T2W), followed by modest fluctuations: +5.6%, +8.8%, and +1% at T4W, T8W, and T12W, respectively. By the end of the study, 75% of participants in the active treatment group showed positive changes, with the highest increase reaching 99.2%.

Participants were classified as having a more affected optical/structural baseline profile if they met ≥ 1 of the following: low baseline gloss on the forehead ($DSC \leq 5.30$ GU; lower tercile), presence of a hyperpigmented lesion in the predefined region, or higher forehead wrinkle volume at baseline (≥ 4.31 mm³; upper tercile). When evaluating gloss changes in this subgroup ($n = 20$ in the Eternalyoung® arm; $n = 26$ in the placebo arm), the results were even better in favor of the Eternalyoung group. While the placebo group showed no significant changes over the 12 weeks, the participants in the Eternalyoung group exhibited a progressive and significant increase

starting from 4 weeks. Also, a significant improvement was detected compared to the placebo group by the end of the study ($p = 0.021$). At the end of the study, 85% of participants in the active treatment group with compromised skin showed improvements. Details of the results can be seen in Figure 3.

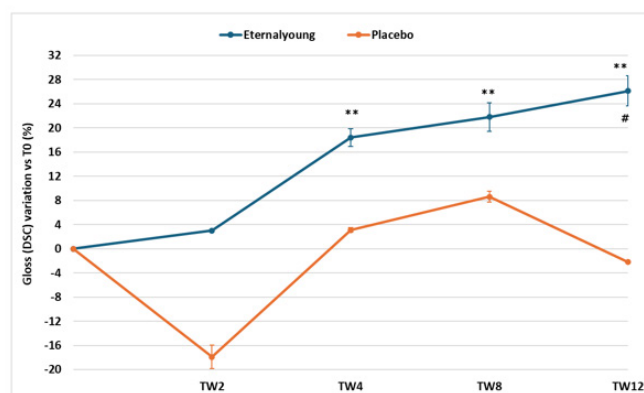


Figure 3 Changes in skin gloss during 12 weeks of Eternalyoung® supplementation. Gloss variation vs T0 (%), assessed by Glossymeter® probe, from week 2 to week 12 (W2,W4,W8,W12) in the treatment (blue line) and placebo group (orange line). Data are means \pm SEM and negative percentages indicate a reduction vs baseline. Statistical analysis is reported as follows: * indicates within-group significance vs T0; ** ($p < 0.01$). Between-group statistical significance is reported with # $p < 0.05$.

Melanin

The melanin contents were evaluated using a Mexameter®.

The volunteers that were not measured at all-time points were excluded from statistical analysis. Therefore, the sample size was 29 in the treatment group and 31 in the placebo.

In the active arm, the mean melanin index (209 ± 17 a.u.) showed a significant decrease from the first follow-up. Specifically, a 5.3% reduction at week 2, 5.7% at week 4, 9.1% at week 8, and 13.9% at week 12 were detected compared to baseline. In contrast, the placebo group, which had a baseline melanin index of 179 ± 19 a.u., experienced a slight increase of 2.2% at week 2. However, significant reductions compared to baseline were detected at week 8 (-4.5%) and week 12 (-7.3%). Between-group comparisons revealed significant differences, with improvements in the treatment group at weeks 2, 8, and 12, as illustrated in Figure 4. By the end of the study, 90% of participants in the active treatment group exhibited positive changes, with the maximum reduction reaching 32.5%.

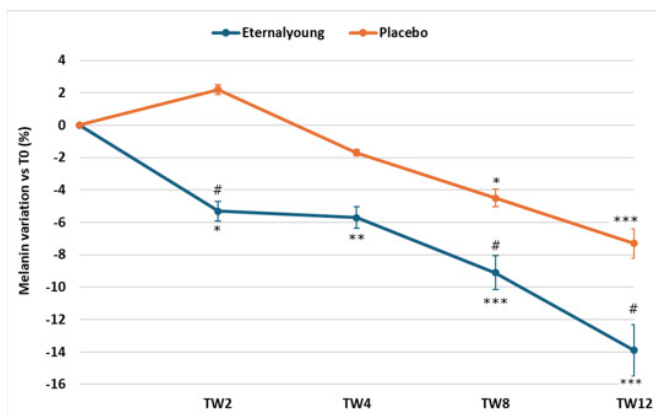


Figure 4 Changes in melanin index during 12 weeks of Eternalyoung® supplementation. Melanin Index variation vs T0 (%), assessed by Mexameter®.

probe, from week 2 to week 12 (W2, W4, W8, W12) in the treatment (blue line) and placebo group (orange line). Data are means \pm SEM and negative percentages indicate a reduction vs baseline.

Statistical analysis is reported as follows: *indicates within-group significance vs T0: *($p < 0.05$), ** ($p < 0.01$) and *** ($p < 0.001$). Between-group statistical significance is reported with # $p < 0.05$.

Also, in those volunteers with a hyperpigmented zone, the melanin evolution in the lesion area was evaluated. A total of 17 participants from the Eternalyoung group and 21 from the placebo group were included in the analysis. The results indicated significant differences between the two groups at week 2 ($p = 0.04$). The treatment group showed a reduction in the melanin index by 4.2%, while the placebo group experienced a slight increase of 0.5%. By week 4, both groups exhibited a significant decrease in melanin levels compared to baseline, but the active treatment group demonstrated a more significant decrease, achieving a total reduction of 13.5% by the end of the study. A clear visual representation of this improvement can be found in Figure 5.

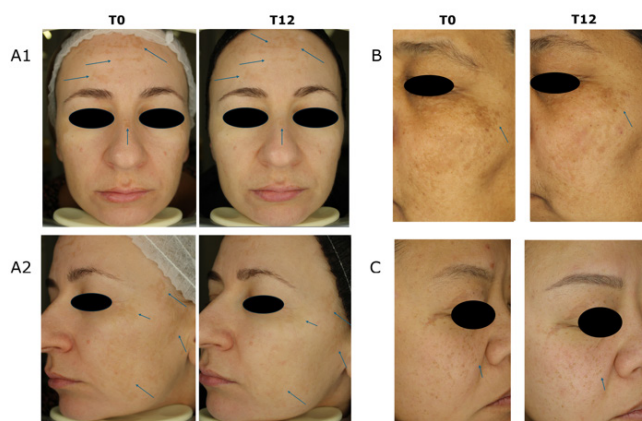


Figure 5 Representative standardized photographs, of three volunteers, showing improvement in facial pigmentation after 12 weeks (T12) of Eternalyoung® supplementation. (A) Volunteer A (Caucasian). Compared to T0, the T12 images show noticeable lightening of the mottled hyperpigmented macules on the forehead (A1) and malar region (A2), with reduced intensity, smaller area, and softer edges for a more uniform complexion. (B) Left malar region of volunteer B (Latin) with a significant reduction in mottled brown macules from T0 to T12, resulting in a more even complexion. (C) Left malar-periorbital region, of volunteer C (Asian) with mild lightening of hyperpigmented spots, leading to a more uniform skin tone by T12.

Skin barrier function. Transepidermal water loss and moisturization

Transepidermal water loss (TEWL) and stratum corneum hydration were measured with a Tewameter and Corneometer, respectively, under controlled conditions after acclimatization.

TEWL decreased in the active treatment group compared to baseline. However, this reduction did not reach statistical significance, either within the group (compared to T0) or when compared to the placebo group at any visit. It is important to note that most volunteers started with TEWL values indicative of an excellent to good barrier at the measured site, with a group mean of $13.8 \text{ g} \cdot \text{m}^{-2} \cdot \text{h}^{-1}$ at the beginning of the study. This baseline level limited the potential for further improvement. Only 10 participants in the treatment group and 11 in the placebo group had TEWL values greater than $15 \text{ g} \cdot \text{m}^{-2} \cdot \text{h}^{-1}$ at baseline, indicating a slightly altered barrier. In this subgroup, the reduction in TEWL was larger and statistically significant compared to the start of the study from week 2; however, there was still no

significant difference between the two groups at any time point. By the end of the study, the active treatment group experienced a 20.5% reduction in TEWL, while the placebo group showed an 18.4% reduction, which was not statistically significant.

Regarding the forehead moisturization in the overall population, most participants presented well-hydrated skin at baseline (Corneometer $> 40 \text{ a.u.}$), so although moisture was increased in the active treatment group during follow-up, changes were not statistically significant neither vs start of the study nor between groups at any visit. In contrast, when focusing on participants with low baseline hydration ($< 40 \text{ a.u.}$; $n=13$ per group), Eternalyoung showed significant within-group increases in hydration at all-time points, and a between-group significant difference at week 2 ($p=0.02$) where Eternalyoung increased their moisturization by $38 \pm 3.9\%$ while placebo also improved but to a lesser extent ($6.8 \pm 0.8\%$). By the end of the study, the difference between groups was reduced and no differences between groups were found, where the Eternalyoung group increased on average $30 \pm 3\%$ and the placebo increased by $22 \pm 2\%$.

Discussion

This study demonstrated that daily oral supplementation with Eternalyoung®, a standardized four-botanical blend, produced significant and clinically relevant improvements in key parameters of skin aging: reduction in the volume and number of forehead wrinkles, increased gloss, decreased melanin index (both globally and in hyperpigmented areas), and, in subgroups with compromised skin barrier or hydration, improved TEWL and moisturization. These findings further support the antiaging efficacy of the ingredient and build on existing evidence.

The magnitude of wrinkle reduction observed in the present study (-23.3% in wrinkle volume and -24% in wrinkle number) is comparable or even superior to those reported with other oral anti-aging interventions.^{16,17} Also, the effects observed here are consistent with those reported in the previous clinical study of the same formulation, where significant improvements were observed in skin elasticity, hydration, and crow's feet wrinkle.¹⁵ The present study extends those findings to a different facial region, the forehead, using 3D volumetric analysis (AEVA-HE). The forehead is one of the most expressive and exposed areas of the face, making it highly susceptible to wrinkle formation even at a relatively young age. A reduction in wrinkle volume measured reflects a meaningful improvement in skin smoothness and anti-aging efficacy. Since volume changes capture not only wrinkle depth but also their extension across the surface, this parameter was considered more sensitive than simple wrinkle count or depth alone.

On the other hand, the increase in skin gloss ($+20.2\%$) and the reduction in melanin index (-13.9%) observed in this study can be directly compared with the spectrophotometric endpoints used in the previous clinical trial,¹⁵ where facial luminosity and pigmentation was quantified spectrophotometrically by CIE L^* value and Individual Typology Angle (ITA°), respectively. In this context, gloss, indicating specular reflection and surface smoothness, aligns with a higher L^* value (greater perceived lightness/radiance) whereas a lower melanin index is expected to correspond with a higher ITA° value (lighter skin color). Therefore, the current findings reproduce and extend prior observations using different yet complementary methodologies, Glossmeter/Mexameter vs. spectrophotometric L^* and ITA° , showing that Eternalyoung® consistently enhances skin radiance and reduces pigment heterogeneity. Improvements in pigmentation and skin-tone uniformity are consistent with the documented depigmenting

and antioxidative properties of the botanical actives comprising the ingredient, such as hesperidin, punicalagins, asiaticosides, and verbascoside, as previously reported.^{18–21} The findings of the present study expand the evidence that systemic botanical supplementation can contribute to brightening and even skin tone. Similar effects have also been observed with other botanical-based oral ingredients such as hydroxytyrosol from olive, ellagic-rich pomegranate or pine bark extract,^{22–24} which supports the notion that systemic antioxidants can modulate melanogenesis and enhance optical skin appearance.

Although no overall significant changes were observed in TEWL or hydration among all participants in the present trial, the improvements observed in subjects with impaired baseline values ($>15 \text{ g} \cdot \text{m}^{-2} \cdot \text{h}^{-1}$ TEWL or <40 a.u. hydration) indicate a homeostatic effect, favoring barrier recovery in compromised skin rather than exceeding physiological thresholds in normal skin. This adaptive response is consistent with findings from other nutricosmetic ingredients, such as wheat ceramides and krill oil, which mainly benefit individuals with lower baseline hydration or impaired barrier function.^{25,26} These results support the notion that skin barrier benefits are baseline-dependent and highlight the importance of selecting the right subpopulations when assessing the effectiveness of nutricosmetic interventions. Notably, in our previous clinical study with the same formulation, significant group-level improvements in both TEWL and hydration were observed at the cheek site in the overall population, with the largest effects in participants with drier skin and lower baseline TEWL.¹⁵ Variations in the anatomical site (hydration of the forehead in this study versus the cheek in the previous one), along with greater differences between individuals and a wider baseline distribution in this cohort, likely diluted the overall significance here.

Overall, the outcomes of this study substantiate the clinical relevance of polyphenol-based nutraceuticals in improving signs of skin aging, aligning with recent reviews and clinical research that confirm the efficacy of oral supplements containing antioxidants, polyphenols, flavonoids, terpenoids, and carotenoids in promoting skin rejuvenation and photoprotection.^{7,16,27–31}

Altogether, the current study reinforces and expands upon previous clinical evidence for Eternalyoung®,¹⁵ confirming its role as an effective oral intervention for improving multiple aspects of facial skin aging, addressing both structural aging (wrinkles, elasticity) and optical aging (dullness, uneven tone). The product's excellent safety profile, with no adverse events reported, supports its suitability for long-term use. Its efficacy across diverse ethnicities and skin phototypes (II–V) further supports its broad applicability and relevance in real-world conditions. Thus, Eternalyoung® is a promising complement to topical skincare and healthy lifestyle habits, offering an effective and safe approach to support youthful skin. Its multifunctional benefits position as an innovative tool for long-term dermal health and appearance. Future research should explore molecular biomarkers of collagen synthesis, oxidative balance, and melanogenesis to deepen understanding of the mechanisms underlying the observed clinical outcomes.

The strengths of this study include the randomized, double-blind, placebo-controlled design, validated instrumental methodology, and the inclusion of different ethnicities representing various Fitzpatrick skin phototypes. Despite these strengths, some limitations to point out: the exploratory sample size, the exclusive inclusion of female participants, and the relatively short duration of the intervention may restrict the detection of subtler or longer-term effects. Future investigations incorporating molecular biomarkers (e.g., markers of collagen synthesis or oxidative stress) and extended follow-up periods

could offer deeper insights into the biological mechanisms involved and the persistence of clinical benefits.

Conclusion

Daily supplementation with Eternalyoung®, a standardized four-botanical blend rich in polyphenols, flavonoids, and triterpenes, significantly reduced forehead wrinkle volume and count, enhanced skin gloss (radiance), decreased hyperpigmented spots (lower melanin index), and improved skin barrier function in subjects with baseline dryness or elevated water loss. These outcomes confirm and extend the findings of the previous clinical study, now using more comprehensive 3D and optical assessments, and they strongly support the initial hypothesis that a multi-component nutraceutical can produce measurable anti-aging benefits in the skin. The data presented here provide a robust clinical basis for the continued use of Eternalyoung® as a scientifically validated, multi-target oral strategy for supporting youthful, radiant, and even-toned skin.

Acknowledgments

None.

Conflict of interests

The authors declare there is no conflict of interest.

Funding

None.

References

1. Krutmann J, Bouloc A, Sore G, et al. The skin aging exposome. *J Dermatol Sci*. 2017;85(3):152–161.
2. Rubin DC, Berntsen D. People over forty feel 20% younger than their age: subjective age across the lifespan. *Psychon Bull Rev*. 2006;13(5):776–780.
3. Khavkin J, Ellis DAF. Aging skin: histology, physiology, and pathology. *Facial Plast Surg Clin N Am*. 2011;19(2):229–234.
4. Yang Q, Li H, Zhang H, et al. Effectiveness of dietary supplements for skin photoaging in healthy adults: a systematic review and meta-analysis of randomized controlled trials. *Front Med*. 2025;12:1582946.
5. Januszewski J, Forma A, Zembala J, et al. Nutritional supplements for skin health—a review of what should be chosen and why. *Medicina (Mex)*. 2024;60(1):68.
6. Dini I, Laneri S. Nutricosmetics: a brief overview. *Phytother Res PTR*. 2019;33(12):3054–3063.
7. Hernandez DF, Cervantes EL, Luna-Vital DA, et al. Food-derived bioactive compounds with anti-aging potential for nutricosmetic and cosmeceutical products. *Crit Rev Food Sci Nutr*. 2021;61(22):3740–3755.
8. *Nutricosmetics Market Share & Competitive Positioning*. Future Market Insights. 2025.
9. Giménez Martínez RJ, Rivas García F, March Cerdá JC, et al. Bioactive substances and skin health: an integrative review from a pharmacy and nutrition perspective. *Pharmaceuticals*. 2025;18(3):373.
10. Lucius K. Botanical medicine and phytochemicals in healthy aging and longevity—part 1. *Altern Complement Ther*. 2020;26(1).
11. Farjadmand F, Karimpour-Razkenari E, Nabavi SM, et al. Plant polyphenols: natural and potent UV-protective agents for the prevention and treatment of skin disorders. *Mini Rev Med Chem*. 2021;21(5):576–585.

12. Peno-Mazzarino L, Radionov N, Merino M, et al. Protective potential of a botanical-based supplement ingredient against the impact of environmental pollution on cutaneous and cardiopulmonary systems: preclinical study. *Curr Issues Mol Biol.* 2024;46(2):1530–1555.
13. Williamson EM. Synergy and other interactions in phytomedicines. *Phytomedicine.* 2001;8(5):401–409.
14. Quiles J, Cabrera M, Jones J, et al. In vitro determination of the skin anti-aging potential of four-component plant-based ingredient. *Molecules.* 2022;27(22):8101.
15. Nobile V, Schiano I, Germani L, et al. Skin anti-aging efficacy of a four-botanical blend dietary ingredient: a randomized, double blind, clinical study. *Cosmetics.* 2023;10(1):16.
16. Buonocore D, Lazzeretti A, Tocabens P, et al. Resveratrol-procyanidin blend: nutraceutical and antiaging efficacy evaluated in a placebocontrolled, double-blind study. *Clin Cosmet Investig Dermatol.* 2012;5:159–165.
17. de Miranda RB, Weimer P, Rossi RC. Effects of hydrolyzed collagen supplementation on skin aging: a systematic review and meta-analysis. *Int J Dermatol.* 2021;60(12):1449–1461.
18. Kwon KJ, Bae S, Kim K, et al. Asiaticoside, a component of *Centella asiatica*, inhibits melanogenesis in B16F10 mouse melanoma. *Mol Med Rep.* 2014;10(1):503–507.
19. Yu ZY, Xu K, Wang X, et al. Punicalagin as a novel tyrosinase and melanin inhibitor: inhibitory activity and mechanism. *LWT.* 2022;161:113318.
20. Lee HJ, Lee WJ, Chang SE, et al. Hesperidin, a popular antioxidant inhibits melanogenesis via Erk1/2 mediated MITF degradation. *Int J Mol Sci.* 2015;16(8):18384–18395.
21. Son YO, Lee SA, Kim SS, et al. Acteoside inhibits melanogenesis in B16F10 cells through ERK activation and tyrosinase down-regulation. *J Pharm Pharmacol.* 2011;63(10):1309–1319.
22. Bagatin JT, Gonçalves Ma PMB, Bagatin E. A pilot clinical study to evaluate the effectiveness of olive extract containing hydroxytyrosol for oral and topical treatment of melasma. *Biomedical and Biopharmaceutical Research Journal.* 2020;17:1–15.
23. Kasai K, Yoshimura M, Koga T, et al. Effects of oral administration of ellagic acid-rich pomegranate extract on ultraviolet-induced pigmentation in the human skin. *J Nutr Sci Vitaminol (Tokyo).* 2006;52(5):383–388.
24. Ni Z, Mu Y, Gulati O. Treatment of melasma with pycnogenol. *Phytother Res.* 2002;16(6):567–571.
25. Handeland K, Wakeman M, Burri L. Krill oil supplementation improves transepidermal water loss, hydration and elasticity of the skin in healthy adults: results from two randomized, double-blind, placebo-controlled, dose-finding pilot studies. *J Cosmet Dermatol.* 2024;23(12):4285–4294.
26. Bizot V, Cestone E, Michelotti A, et al. Improving skin hydration and age-related symptoms by oral administration of wheat glucosylceramides and digalactosyl diglycerides: a human clinical study. *Cosmetics.* 2017;4(4):37.
27. Tuong W, Kuo S, Sivamani RK. Photoprotective effect of botanicals and vitamins: a systematic review of clinical trials. *J Dermatol Treat.* 2015;26(6):558–570.
28. Nobile V, Michelotti A, Cestone E, et al. Skin photoprotective and antiageing effects of a combination of rosemary (*Rosmarinus officinalis*) and grapefruit (*Citrus paradisi*) polyphenols. *Food Nutr Res.* 2016;60:31871.
29. Ren Y, Liu D, Xu B. Critical review on orally administered nutricosmetics: food-based solutions conferring skin health from the inside out. *Trends Food Sci Technol.* 2025;159:104946.
30. Nobile V, Cestone E, Ghirlanda S, et al. Skin and scalp health benefits of a specific botanical extract blend: results from a double-blind placebo-controlled study in urban outdoor workers. *Cosmetics.* 2024;11(4):139.
31. Tran JT, Diaz MJ, Rodriguez D, et al. Evidence-based utility of adjunct antioxidant supplementation for the prevention and treatment of dermatologic diseases: a comprehensive systematic review. *Antioxidants.* 2023;12(8):1503.