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# An Open-Label Pilot Study Exploring Skin Quality Changes and Safety of a Day-and-Night Facial Serum Combination Containing L-Ascorbic Acid, Proteoglycans, Hyaluronic Acid, *Vigna aconitifolia* Extract, and Melatonin

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## Abstract

**Background**: A novel day–night facial serum regimen combining antioxidants, hydration-enhancing agents, and bioactive compounds has been developed to address skin aging. **Objective**: The aim is to explore changes in skin aging parameters and assess the safety and tolerability of a day-and-night facial serum combination. **Methods**: In this single-arm, non-randomized, prospective, open-label study, 30 participants aged 35–55 years applied a day facial serum (DFS) and a night facial serum (NFS) for 8 weeks. Objective assessments included skin texture and depression (Antera 3D®), elasticity and firmness (Cutometer®), hydration (Corneometer®), TEWL (Tewameter®), melanin index (Mexameter®), and brightness (Colorimeter®). Evaluations were performed at baseline, at 1 month and 2 months after treatment start, and at 1 month post-treatment. **Results**: Thirty participants (Fitzpatrick III–IV) completed the study. Significant improvements in skin texture ($p$ = 0.002) and reduction in skin depression (−22.7%, $p < 0.001$) were observed after 2 months. Skin firmness increased significantly at 1 month ($p < 0.001$) and remained elevated post-treatment ($p$ = 0.008). The melanin index decreased at 1 month ($p$ = 0.048), while hydration declined after discontinuation ($p$ = 0.016). TEWL showed a significant overall time effect; however, no Bonferroni-adjusted pairwise comparison versus baseline was significant. No significant changes were observed in elasticity or brightness. Mild transient burning was the most common adverse event. Other reported adverse events included acne, miliaria rubra, oiliness, and mild itching; all were non-serious and did not result in treatment discontinuation. **Conclusions**: The combined DFS and NFS regimen was well tolerated and was associated with favorable changes in skin texture and firmness. Transient local reactions, particularly mild burning sensation, were commonly reported but did not result in treatment discontinuation. Further controlled studies are warranted to confirm these observations.

**Keywords:** L-ascorbic acid; proteoglycans; hyaluronic acid; *Vigna aconitifolia*; melatonin; anti-aging; clinical trial; pilot study

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## 1. Introduction

The skin, our body's outermost organ, serves as a crucial interface with the environment. It plays a pivotal role in protecting the body and supporting various physiological

functions. Over time, the skin undergoes the effects of both chronological aging and cumulative damage from external factors, with UV radiation being a significant contributor. The visible signs of aging include prominent wrinkles, reduced elasticity, dryness, uneven skin tone and texture, and the development of skin pigmentation issues [1,2]. These physical changes have a well-established connection with psychosocial factors, including increased social anxiety, decreased self-esteem, isolation, and even depression [3].

The appearance and health of our skin are powerful indicators of our overall well-being and how we perceive our own health [4]. Therefore, various anti-aging strategies have been developed, and topical cosmeceuticals have emerged as an appealing approach. These products have the potential to directly target and address skin concerns, providing a non-invasive and convenient option for those seeking to improve the health and appearance of their skin [5].

To comprehensively address age-related skin concerns, a combination of anti-aging serums for morning and evening use has been formulated. The daytime facial serum (DFS) incorporates L-ascorbic acid, proteoglycans, and hyaluronic acid. L-ascorbic acid, the most biologically active form of vitamin C, is known for its potent antioxidant properties, collagen-stimulating effects, and ability to reduce melanin formation while offering photoprotection [6]. Additionally, this formulation includes proteoglycans and low-molecular-weight hyaluronic acid to provide immediate hydration, stimulate fibroblast activity, and preserve the extracellular matrix [7].

Complementing the DFS, the night facial serum (NFS) contains *Vigna aconitifolia* extract and melatonin. *Vigna aconitifolia*, also known as moth bean, hailing from arid regions of India, exhibits potent free-radical-scavenging properties due to its rich content of polyphenols, antioxidants, phytic acids, and tannins [8]. Applied to the skin, it emulates the effects of retinol, contributing to the reduction in wrinkles [9]. Melatonin, primarily produced by the pineal gland, plays a crucial role in regulating the circadian rhythm. Recent research highlights its anti-aging benefits, attributed to its direct and indirect antioxidant mechanisms. A prospective clinical trial reported improvements in periorbital wrinkles, skin tone, and hydration with the use of a topical melatonin cream [10,11].

Although the anti-aging properties of vitamin C, hyaluronic acid, proteoglycans, melatonin, and *Vigna aconitifolia* extract have been reported individually, evidence regarding the clinical efficacy of a combined daytime and nighttime skincare regimen incorporating these ingredients remains limited. Furthermore, few studies have evaluated such combination regimens using objective instrumental assessments of skin quality parameters. This study was conducted to investigate changes in skin aging parameters and to assess the safety and tolerability of daytime serum containing L-ascorbic acid, proteoglycans, and hyaluronic acid when used in conjunction with a night serum formulated with *Vigna aconitifolia* extract and melatonin based on clinical and instrumental skin assessments.

## 2. Materials and Methods

### 2.1. Study Design

This single-arm, prospective, open-label clinical study was conducted at the Siriraj Skin Laser Center in Bangkok, Thailand, between July and December 2022. It received approval from the Siriraj Institutional Review Board, Faculty of Medicine, Mahidol University (COA No. Si 490/2022) and adhered to the principles outlined in the Declaration of Helsinki. All participants provided written informed consent. This study was retrospectively registered in the Thai Clinical Trials Registry on 19 July 2022 (TCTR20220719004).

### 2.2. Participants

This study included thirty male and female participants aged 35–55 who had consistently applied sunscreen for at least one month prior to the trial. Exclusion criteria encompassed pregnancy, breastfeeding, active skin diseases or dermatitis in the treatment area, recent use of topical whitening agents or laser treatment, oral antioxidant intake, known hypersensitivity to the study's active components, immunocompromised status, history of herpes simplex, smoking, or alcohol consumption. No formal sample size calculation was performed due to the pilot nature of the study. Consequently, the study may have been underpowered to detect small treatment effects, and non-significant findings should be interpreted with caution. The results should therefore be considered preliminary and require confirmation in larger, adequately powered studies.

### 2.3. Interventions

The investigational products included a DFS and an NFS marketed as Flavo-C Ultraglican and Flavo-C Melatonin, respectively (ISDIN SA, Barcelona, Spain). The DFS ingredients consisted of propylene glycol, aqua, ascorbic acid, bis-hydroxyethoxypropyl dimethicone, glycerin, ppg-26-buteth-26, tocopherol, peg-40 hydrogenated castor oil, fragrance, sodium benzoate, hydrogenated soybean oil, butylene glycol, potassium sorbate, hydrolyzed hyaluronic acid, sodium hydroxide, tetradecyl aminobutyroylvalylaminobutyric urea trifluoroacetate, phenoxyethanol, soluble proteoglycan, magnesium chloride, and ergothioneine. The NFS ingredients comprised aqua, glycereth-26, glycerin, propanediol, 3-o-ethyl ascorbic acid (vitamin C derivative), butylene glycol, denatured alcohol, citric acid, sodium benzoate, *Vigna aconitifolia* seed extract (Vit ATECH), 1,2-hexanediol, caprylyl glycol, ppg-26-buteth-26, peg-40 hydrogenated castor oil, maltodextrin, disodium EDTA, melatonin, parfum (fragrance), and xanthan gum.

Each participant was provided with 30 ampoules of DFS and 30 ampoules of NFS and was instructed to apply half an ampoule to the entire face in the morning and at bedtime. The serums were applied to clean, dry skin and gently massaged until fully absorbed, over eight consecutive weeks. To standardize daily photoprotection, all participants were provided with the same broad-spectrum sunscreen (Foto Ultra 100 ISDIN Spot Prevent Fusion Fluid SPF 50+, ISDIN SA, Barcelona, Spain) and were instructed to apply it every morning throughout the three-month study period with the recommended amount of two finger-tip units for the entire face. Participants were instructed to refrain from using any other sunscreen products during the study. Once opened, the day-and-night facial serums were stored in a light-protected environment at room temperature and hermetically sealed using the plastic cap provided, ensuring consumption within 48 h. Participants refrained from using moisturizers, other serums, and whitening agents, both oral and topical, for the duration of the study. The use of cosmetics regularly used before the study commenced was allowed.

Standardized photographic documentation was conducted from five views (front, 45° and 90°, on both the left and right sides) using the Canon PowerShot G9 (OMNIA® Imaging System, Canfield Scientific, Inc., Parsippany, NJ, USA) at baseline, at 1 month and 2 months after treatment start, and at the 1-month post-treatment follow-up.

### 2.4. Outcome

The primary outcomes of interest were changes in skin texture and depression measured using the Antera 3D® (Miravex, Dublin, Ireland). Objective assessments also included measuring skin elasticity and firmness using the Cutometer® MPA580, assessing moisture levels with the Corneometer® CM825, evaluating transepidermal water loss (TEWL) using the Tewameter®, determining the melanin index with the Mexameter® MX18, and

measuring brightness with the Colorimeter® CL400, all of which are devices by Courage + Khazaka Electronic GmbH in Cologne, Germany. To ensure consistency, investigators marked two areas on both upper cheeks of each subject using a transparent film during their initial visit, providing a reference for subsequent assessments. Each measurement was averaged across the left and right sides of the face.

For subjective evaluation, all participants were requested to evaluate their overall clinical improvement using a 6-point scale, where 4 indicated "most improvement," 3 represented "much improvement," 2 denoted "moderate improvement," 1 signified "some improvement," 0 indicated "no change," and −1 was assigned to "worsening."

### 2.5. Safety Outcomes and Assessments

Adverse reactions throughout the protocol were documented and managed accordingly. All objective and subjective assessments were conducted at baseline, at 1 and 2 months of serum usage, and one month after discontinuation.

### 2.6. Statistical Analysis

All data were analyzed using SPSS version 29.0 (IBM Corp., Armonk, NY, USA) and GraphPad Prism version 11.0 (GraphPad Software, San Diego, CA, USA). Descriptive analysis was used for demographic data, and quantitative data were presented as median, mean, percent change, interquartile range (IQR), and standard deviation (SD). Normality was assessed using the Shapiro–Wilk test. Repeated-measures ANOVA was used for normally distributed data, while Friedman's test was applied for non-normally distributed data to compare means and medians at each follow-up visit. For repeated-measures ANOVA, Greenhouse–Geisser-corrected degrees of freedom were reported when the sphericity assumption was violated. Results are reported as test statistics, degrees of freedom (df), $p$-values, and effect sizes ($\eta p^2$ or Kendall's W). Pairwise comparisons with baseline were performed using Bonferroni adjustment. A two-sided $p$-value $< 0.05$ was considered statistically significant.

## 3. Results

The study cohort consisted of 27 females and 3 males, with a mean age of 42 ± 5.72 years. The majority of participants had Fitzpatrick skin type IV (28/30, 93.3%), while the remaining individuals had Fitzpatrick skin type III (2/30, 6.7%) (Table 1). The participant flow diagram is shown in Figure 1.

**Table 1.** Participants' characteristics.

| Characteristics | Total (n = 30) |
|---|---|
| Age (years) | |
| Mean ± SD | 42 ± 5.72 |
| Range | 35–55 |
| Gender (%) | |
| Female | 27 (90) |
| Male | 3 (10) |
| Fitzpatrick Skin Type (%) | |
| IV | 28 (93.33) |
| III | 2 (6.67) |

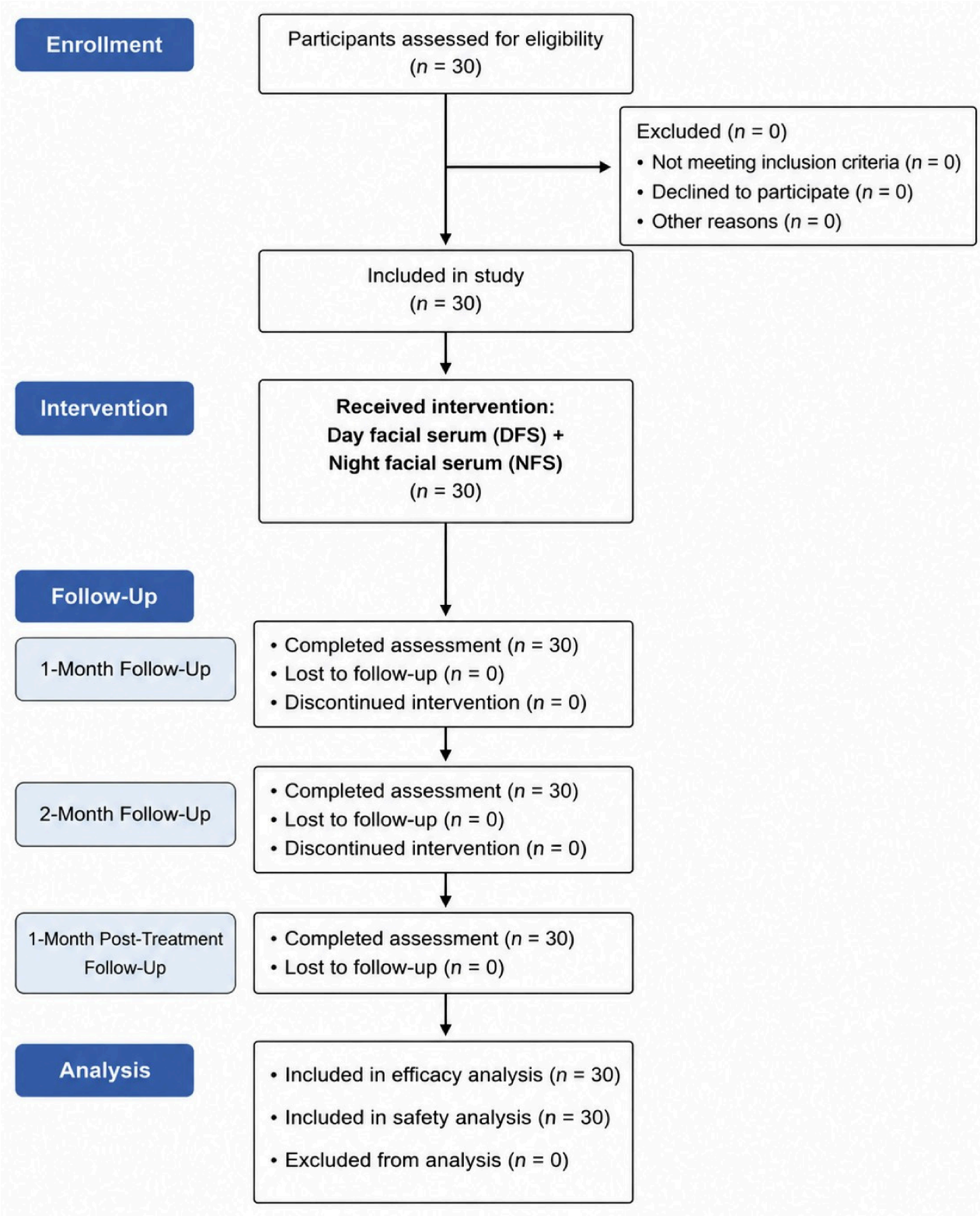



**Figure 1.** Participant flow diagram.

Favorable changes in skin texture were observed following the two-month regimen of the DFS and NFS combination ($p = 0.002$). This coincided with a marked 22.7% reduction ($p < 0.001$) in average skin depression during the same period (Figure 2).

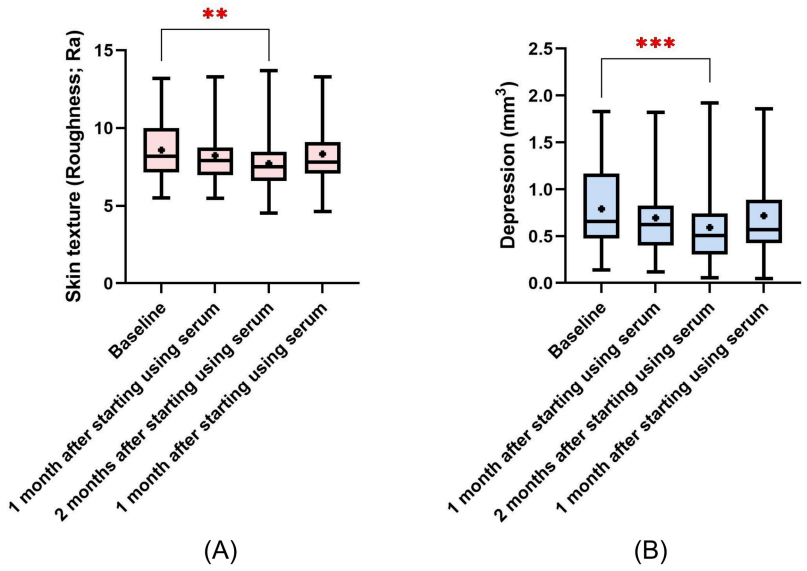



**Figure 2.** Changes in skin surface roughness and depression volume. (**A**) Skin texture/roughness, expressed as Ra, and (**B**) depression volume, expressed in $mm^3$, were measured using Antera 3D®. Data are presented as box-and-whisker plots. Boxes show medians and IQRs; whiskers show minimum–maximum values; "+" indicates mean. *p*-Values compared with baseline. n = 30. ** $p < 0.01$; *** $p < 0.001$.

A slight reduction in gross elasticity (R2) was noted, although it was statistically insignificant (Figure 3A). However, a substantial 21% increase in skin firmness was observed after the first month of serum application ($p < 0.001$). Firmness continued to improve, with this increase reaching up to 25% in the second month, and this effect was sustained during the follow-up period ($p = 0.008$). Figure 3B illustrates a progressive reduction in R0 over the course of the study. As R0 reflects the skin's distensibility under suction, lower values indicate greater skin firmness [12].

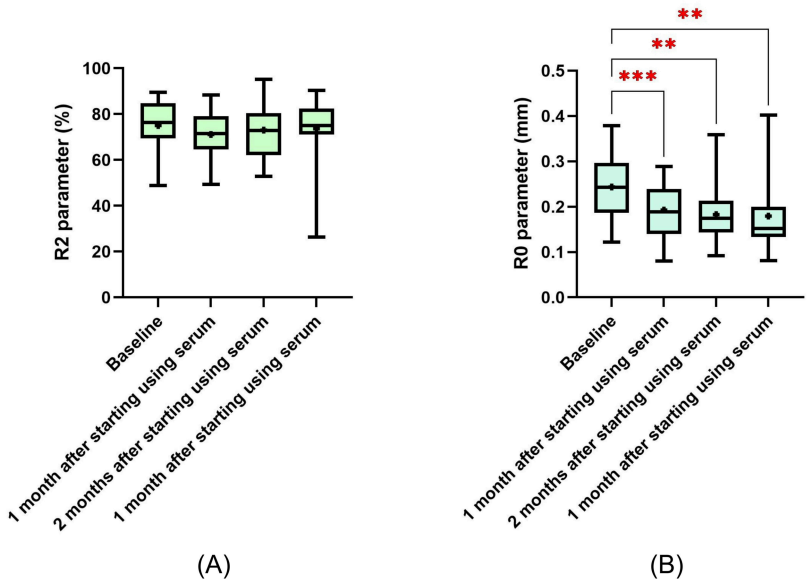



**Figure 3.** Changes in R2 and R0 parameters. (**A**) Gross elasticity, expressed as R2 parameter (%), and (**B**) R0 parameter, expressed in mm, were measured using Cutometer®. Lower R0 values indicate greater skin firmness. Data are presented as box-and-whisker plots. Boxes show medians and IQRs; whiskers show minimum–maximum values; "+" indicates mean. *p*-Values compared with baseline. n = 30. ** $p < 0.01$; *** $p < 0.001$.

During the two-month product-use period, a slight reduction in skin hydration was observed; however, one month after discontinuation of serum application, a statistically significant decrease in skin moisture from baseline was observed (Figure 4). In contrast, no significant changes in transepidermal water loss were observed throughout the study (Figure 5). TEWL showed a significant overall time effect; however, no Bonferroni-adjusted comparison versus baseline was significant, and values remained within or close to the physiological reference range (15–25 g/m$^2$/h) [13].

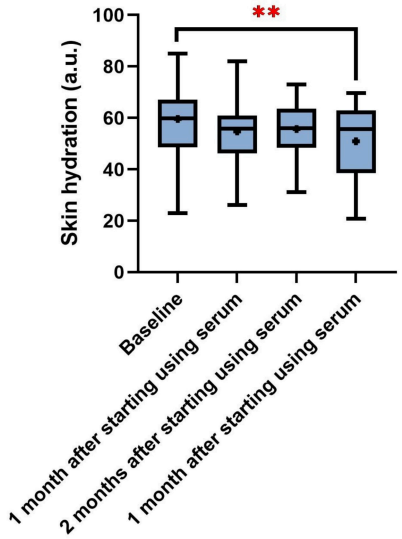



**Figure 4.** Changes in skin hydration. Skin hydration was measured using Corneometer® and is expressed in arbitrary units (a.u.). Data are presented as box-and-whisker plots. Boxes show medians and IQRs; whiskers show minimum–maximum values; "+" indicates mean. *p*-Values compared with baseline. n = 30. ** $p < 0.01$.

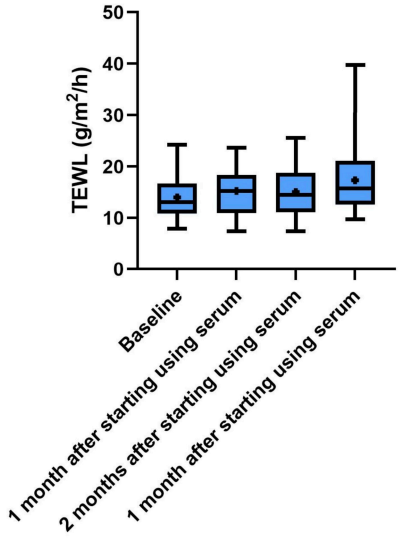



**Figure 5.** Changes in transepidermal water loss. Transepidermal water loss (TEWL) was measured using Tewameter® and is expressed as g/m$^2$/h. Data are presented as box-and-whisker plots. Boxes show medians and IQRs; whiskers show minimum–maximum values; "+" indicates mean. *p*-Values compared with baseline. n = 30.

A significant decrease in the average melanin index was noted after 1 month of using the DFS and the NFS, after which it approached baseline levels (Figure 6). No significant difference in skin lightness was measured by the Colorimeter® (Figure 7). Longitudinal changes across all outcome measures with pairwise comparisons and overall time-effect

statistics are summarized in Supplementary Table S1. Overall test statistics, degrees of freedom, and effect sizes are summarized in Supplementary Table S2.

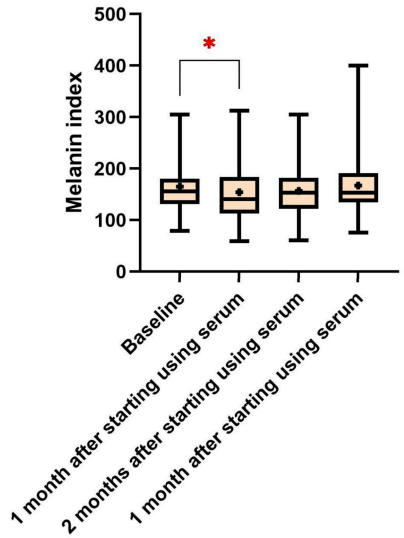



**Figure 6.** Changes in melanin index. Melanin index was measured using Mexameter®. Data are presented as box-and-whisker plots. Boxes show medians and IQRs; whiskers show minimum–maximum values; "+" indicates mean. *p*-Values compared with baseline. n = 30. * $p < 0.05$.

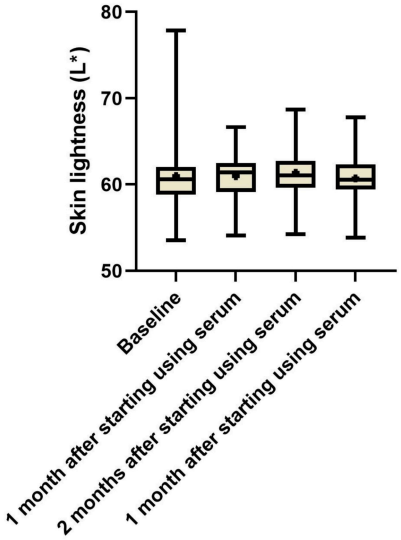



**Figure 7.** Changes in skin lightness. Skin lightness was measured using Colorimeter® and expressed as L*. Data are presented as box-and-whisker plots. Boxes show medians and IQRs; whiskers show minimum–maximum values; "+" indicates mean. *p*-Values compared with baseline. n = 30.

Based on participants' clinical self-assessments, the majority observed significant improvement in overall skin quality throughout the study. In the first month, 50% of the subjects already reported significant improvement in their skin, followed by 30% who rated moderate improvement and 13% who saw some improvement. In the following month, there was a noted increase in the number of subjects who observed significant improvement from 50% to 67%. Two (7%) noted the most improvement at this time. After one month of discontinuing the serums, more than half of the participants (57%) still reported significant improvement in their skin, followed by 17% of volunteers who saw some improvement. Four respondents reported no improvement compared with baseline at the one-month follow-up. None of the participants reported a worsening of their skin condition throughout the study (Figures 8 and 9).

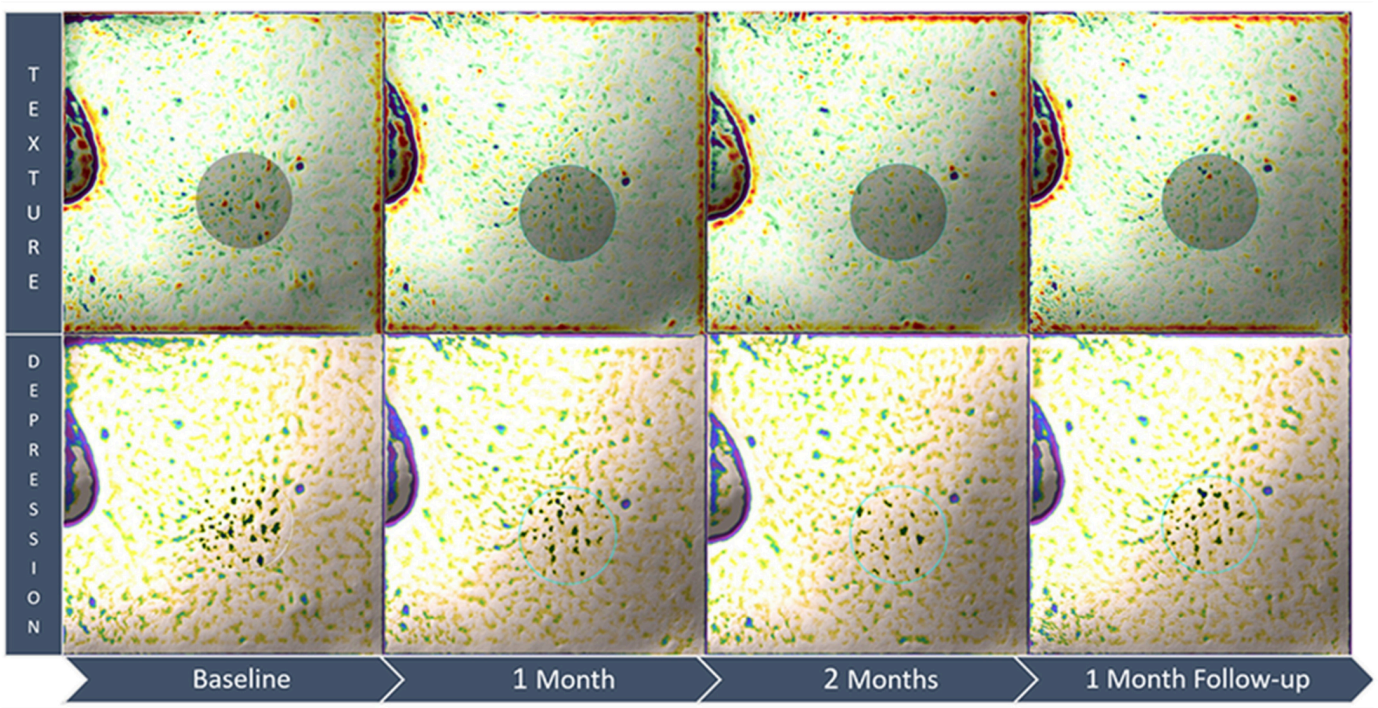



**Figure 8.** Representative Antera 3D® images demonstrating improvement in skin texture and depression. Improvement in overall skin texture and depression in a representative case, showing progress from baseline to 1 and 2 months of continuous combination serum application to 1 month after discontinuation of the serum regimen.

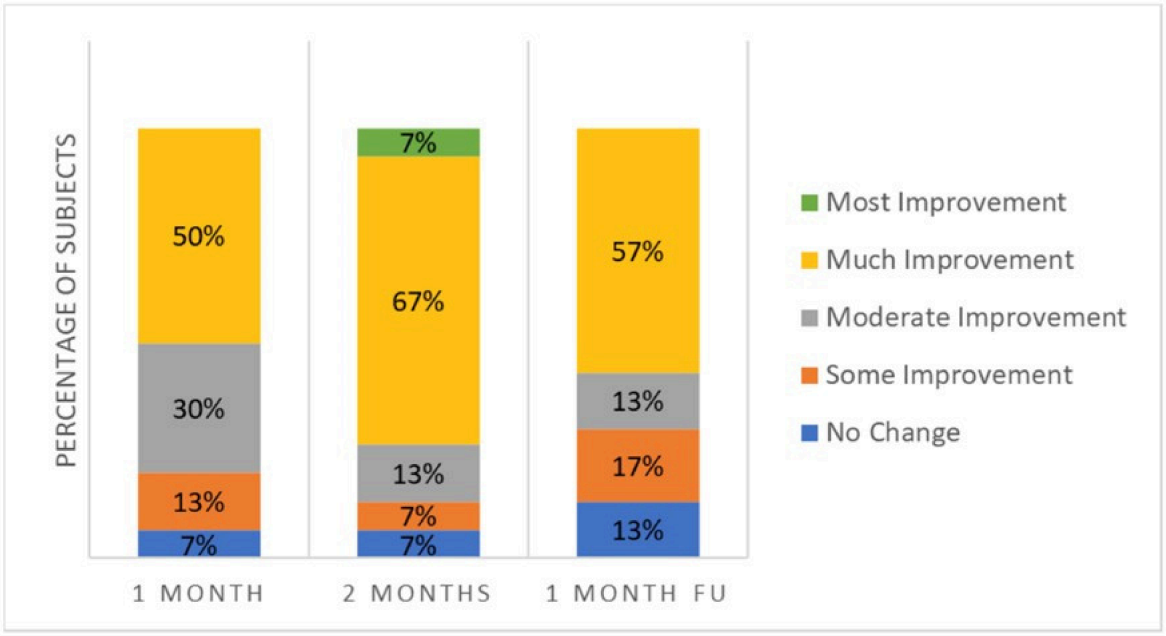



**Figure 9.** Patient-reported rating scale of improvement. Data show the percentages of participants reporting no change, some improvement, moderate improvement, much improvement, or most improvement at 1 month and 2 months and at the 1-month follow-up. n = 30.

No serious adverse events occurred. Twelve volunteers (40%) reported a slight but temporary burning sensation upon serum application, which eventually disappeared. Nine (30%) and four (13%) participants observed acne formation and miliaria rubra, respectively. Other effects noted were oiliness (13%) and mild itching (10%).

## 4. Discussion

The clinical signs of aging result from a complex interplay of various factors. Oxidative stress, characterized by the generation of reactive oxygen species (ROS), is a primary contributor to skin aging. This process degrades dermal extracellular matrix components, such as collagen and elastin, leading to wrinkles, a rough texture, and diminished elasticity [7]. Additionally, a decrease in proteoglycans and skin moisture contributes to dryness and altered skin texture. Topical antioxidant supplementation has been recognized as an effective strategy to counteract oxidative stress and neutralize free-radical damage [14,15].

Another significant factor in skin aging is the depletion of dermal proteins, which disrupts the extracellular matrix and leads to visible signs of aging. Moreover, aging skin has been associated with broader implications for overall health, including susceptibility to various diseases. Therefore, addressing skin aging is not only about aesthetics but also about maintaining overall well-being [7].

Each serum in this study was carefully formulated to maximize its effectiveness based on the time of application. The night serum, in particular, was designed to align with the body's natural production of melatonin, which peaks in the evening. Applying melatonin at bedtime may enhance the skin's repair mechanisms, mirroring its physiological effects [10,11].

The present study was associated with favorable changes in skin texture and firmness associated with the combination of a day facial serum (DFS) containing L-ascorbic acid, proteoglycans, and hyaluronic acid and a night facial serum (NFS) composed of *Vigna aconitifolia* extract and melatonin. The objective assessments revealed significant improvements in skin texture and firmness, as measured by the Antera 3D® and Cutometer®. No significant changes in skin hydration were observed during serum application, although hydration decreased at the 1-month follow-up after discontinuation. This finding may be partly explained by the study protocol, as participants were asked to avoid moisturizers, other serums, and whitening agents throughout the study; therefore, after stopping the serum, no active hydrating product was provided. The reduction may also have been influenced by uncontrolled factors such as lifestyle, humidity, and seasonal variation. Since no participants reported a worsening of skin condition, the clinical impact of this decrease may be limited. Further controlled studies with longer follow-up are needed to confirm this finding. While TEWL exhibited a significant overall time effect, the absence of significant Bonferroni-adjusted differences from baseline and the maintenance of values within or close to the physiological reference range (15–25 $g/m^2/h$) suggest that the intervention had limited effects on skin barrier integrity [13]. Additionally, a reduction in melanin levels was observed. The contribution of individual ingredients, including vitamin C, could not be determined in the present study [6]. The objective improvements in skin texture and firmness were accompanied by favorable participant self-assessments, supporting a possible clinical benefit that requires confirmation in controlled studies.

Although statistically significant changes were observed in several objective parameters, the clinical significance of these changes remains uncertain because established minimal clinically important differences for instrumental measurements such as Antera 3D®, Cutometer®, Corneometer®, and Mexameter® have not been clearly defined. Nevertheless, the objective findings were accompanied by favorable participant self-assessments, suggesting that at least some of the observed changes may have been perceptible to participants. Further controlled studies are required to determine the clinical relevance and practical significance of these findings.

These findings align with previous studies by Garre and Goldberg, supporting the efficacy of topical serums containing similar active ingredients [7,16]. Garre's study demonstrated preservation of the dermal matrix and effective antioxidant protection with the use

of a vitamin C, proteoglycan, and tripeptide serum. Goldberg's study showed significant improvements in wrinkles, skin firmness, and overall skin quality with a night serum containing melatonin, bakuchiol, and ascorbyl tetraisopalmitate.

The observed changes in skin texture and firmness may be explained by mechanisms previously reported for the individual ingredients contained in the formulations. L-ascorbic acid enhances collagen synthesis by acting as a cofactor for prolyl and lysyl hydroxylase, facilitating the hydroxylation of proline and lysine residues essential to collagen stability while also inhibiting melanogenesis via tyrosinase suppression. Proteoglycans contribute to extracellular matrix organization and hydration, while low-molecular-weight hyaluronic acid enhances water retention and dermal bioavailability. Melatonin exerts both direct free-radical-scavenging activity and indirect antioxidant effects through upregulation of endogenous antioxidant enzymes. In addition, *Vigna aconitifolia* extract has been shown to exhibit retinol-like activity, promoting epidermal renewal and wrinkle reduction without the irritation commonly associated with retinoids [6,7,9]. However, because multiple active ingredients were administered concurrently and no mechanistic assessments were performed, the present study cannot determine the contribution of individual ingredients or confirm synergistic effects.

Safety and tolerability were acceptable, with no serious adverse events reported throughout the study. The most common local reaction was a slight, transient burning sensation after serum application, reported by 40% of participants, which resolved spontaneously. This temporary sensation may be related to the acidic nature of some active ingredients, particularly L-ascorbic acid, which is commonly formulated at a low pH to enhance skin penetration [17]. Other formulation components may also have contributed; however, causality cannot be confirmed from the present study. Acne formation, miliaria rubra, oiliness, and mild itching were also reported by a minority of participants. Overall, the reported adverse events were mild and self-limited, and no participant discontinued treatment because of treatment-related reactions.

Given that the majority of participants had Fitzpatrick skin type IV, these findings are particularly relevant for Asian populations, where pigmentation and barrier function responses may differ from lighter skin types. The transient reduction in the melanin index observed in this study supports the role of vitamin C in modulating melanogenesis in darker skin phototypes [6]. Daily photoprotection is an important component in the prevention and management of photoaging and may itself contribute to improvement in skin aging parameters. To reduce variability from over-the-counter sunscreen use, all participants were provided with the same sunscreen and standardized application instructions throughout the study. Nevertheless, photoprotection remains a potential confounding factor.

This study has several limitations, including its single-arm, open-label design, lack of a randomized control group, relatively small sample size, and short follow-up period, which limit causal inference. The observed improvements should be interpreted in the context of potential influences from placebo effects, environmental factors, skincare adherence, and subjective reporting. Although the known mechanisms of action of the individual ingredients provide a plausible biological rationale for the observed findings, the serum contains multiple active ingredients administered concurrently; therefore, conclusions regarding ingredient-specific effects or potential synergistic interactions remain speculative. As commercially available formulations were used, potential batch-to-batch variation and the contribution of individual active components could not be completely excluded. Further randomized controlled studies with larger populations and longer follow-up are needed to confirm these findings.

## 5. Conclusions

The use of a day-and-night facial serum combination containing L-ascorbic acid, proteoglycans, hyaluronic acid, *Vigna aconitifolia* extract, and melatonin was associated with favorable changes in skin texture and firmness in this exploratory pilot study. Participants reported improved overall skin quality, consistent with sustained improvements in objectively measured skin firmness that persisted for at least one month after serum discontinuation. Improvements in skin texture and depression were most evident after 2 months of use. The most common adverse effect was a mild, transient burning sensation, reported by 40% of participants. Other reported adverse events included acne, miliaria rubra, oiliness, and mild itching; all were non-serious and did not result in treatment discontinuation. These findings should be interpreted cautiously and require confirmation in randomized controlled studies.

**Supplementary Materials:** The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/cosmetics13030146/s1, Table S1: Longitudinal changes in skin quality, biophysical parameters, and overall time-effect statistics. Table S2: Overall time-effect test statistics and effect sizes.

**Author Contributions:** Conceptualization: R.W. Methodology: R.W., S.D.L., N.V., T.H., and T.L. Formal analysis: T.L., P.B., T.W., and S.D.L. Investigation: R.W., N.V., T.H., T.L., P.B., and T.W. Data curation: R.W., N.V., T.H., T.L., P.B., and T.W. Writing—original draft preparation: R.W., N.V., T.H., and T.L. Writing—review and editing: S.D.L., P.B., and T.W. Supervision: R.W. Project administration: R.W. Funding acquisition: R.W. All authors have read and agreed to the published version of the manuscript.

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**Institutional Review Board Statement:** This study was conducted in accordance with the principles of the Declaration of Helsinki (Fortaleza, Brazil) and its later amendments. The study protocol received its approval from the Siriraj Institutional Review Board, Faculty of Medicine, Mahidol University (COA No. Si 490/2022) and was retrospectively registered in the Thai Clinical Trials Registry with identification code TCTR20220719004 on 19 July 2022.

**Informed Consent Statement:** Informed consent was obtained from all subjects involved in the study.

**Data Availability Statement:** All data sets generated and analyzed in this study are available from the corresponding authors upon reasonable request.

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**Conflicts of Interest:** The study products were provided by ISDIN SA. The sponsor had no role in study design, data analysis, manuscript preparation, or decision to publish. The authors declare no other conflicts of interest.

## References


1. Costello, L.; Dicolandrea, T.; Tasseff, R.; Isfort, R.; Bascom, C.; von Zglinicki, T.; Przyborski, S. Tissue engineering strategies to bioengineer the ageing skin phenotype in vitro. *Aging Cell* **2022**, *21*, e13550. [CrossRef] [PubMed]
2. Naylor, E.C.; Watson, R.E.; Sherratt, M.J. Molecular aspects of skin ageing. *Maturitas* **2011**, *69*, 249–256. [CrossRef] [PubMed]
3. Gupta, M.A.; Gilchrest, B.A. Psychosocial aspects of aging skin. *Dermatol. Clin.* **2005**, *23*, 643–648. [CrossRef] [PubMed]
4. Zouboulis, C.C.; Ganceviciene, R.; Liakou, A.I.; Theodoridis, A.; Elewa, R.; Makrantonaki, E. Aesthetic aspects of skin aging, prevention, and local treatment. *Clin. Dermatol.* **2019**, *37*, 365–372. [CrossRef] [PubMed]
5. Rattanawiwatpong, P.; Wanitphakdeedecha, R.; Bumrungpert, A.; Maiprasert, M. Anti-aging and brightening effects of a topical treatment containing vitamin C, vitamin E, and raspberry leaf cell culture extract: A split-face, randomized control trial. *J. Cosmet. Dermatol.* **2020**, *19*, 671–676. [CrossRef] [PubMed]
6. Al-Niaimi, F.; Chiang, N.Y.Z. Topical Vitamin C and the Skin: Mechanisms of Action and Clinical Applications. *J. Clin. Aesthet. Dermatol.* **2017**, *10*, 14–17. [PubMed]
7. Garre, A.; Narda, M.; Valderas-Martinez, P.; Piquero, J.; Granger, C. Antiaging effects of a novel facial serum containing L-Ascorbic acid, proteoglycans, and proteoglycan-stimulating tripeptide: Ex vivo skin explant studies and in vivo clinical studies in women. *Clin. Cosmet. Investig. Dermatol.* **2018**, *11*, 253–263. [CrossRef] [PubMed]
8. Gupta, N.; Shrivastava, N.; Singh, P.K.; Bhagyawant, S.S. Phytochemical Evaluation of Moth Bean (*Vigna aconitifolia* L.) Seeds and Their Divergence. *Biochem. Res. Int.* **2016**, *2016*, 3136043. [CrossRef] [PubMed]
9. Brown, A.; Furmanczyk, M.; Ramos, D.; Ribes, A.; Pons, L.; Bustos, J.; de Henestrosa, A.R.F.; Granger, C.; Jourdan, E. Natural Retinol Analogs Potentiate the Effects of Retinal on Aged and Photodamaged Skin: Results from In Vitro to Clinical Studies. *Dermatol. Ther.* **2023**, *13*, 2299–2317. [CrossRef] [PubMed]
10. Day, D.; Burgess, C.M.; Kircik, L.H. Assessing the Potential Role for Topical Melatonin in an Antiaging Skin Regimen. *J. Drugs Dermatol.* **2018**, *17*, 966–969. [PubMed]
11. Rusanova, I.; Martínez-Ruiz, L.; Florido, J.; Rodríguez-Santana, C.; Guerra-Librero, A.; Acuña-Castroviejo, D.; Escames, G. Protective Effects of Melatonin on the Skin: Future Perspectives. *Int. J. Mol. Sci.* **2019**, *20*, 4948. [CrossRef] [PubMed]
12. Kim, S.H.; Lee, S.J.; Kim, H.J.; Lee, J.H.; Jeong, H.S.; Suh, I.S. Aging-related changes in the mid-face skin elasticity in East Asian women. *Arch. Craniofac. Surg.* **2019**, *20*, 158–163. [CrossRef] [PubMed]
13. Gardien, K.L.; Baas, D.C.; de Vet, H.C.; Middelkoop, E. Transepidermal water loss measured with the Tewameter TM300 in burn scars. *Burns* **2016**, *42*, 1455–1462. [CrossRef] [PubMed]
14. Chen, L.; Hu, J.Y.; Wang, S.Q. The role of antioxidants in photoprotection: A critical review. *J. Am. Acad. Dermatol.* **2012**, *67*, 1013–1024. [CrossRef] [PubMed]
15. Pinnell, S.R. Cutaneous photodamage, oxidative stress, and topical antioxidant protection. *J. Am. Acad. Dermatol.* **2003**, *48*, 1–22. [CrossRef]
16. Goldberg, D.J.; Mraz-Robinson, D.; Granger, C. Efficacy and safety of a 3-in-1 antiaging night facial serum containing melatonin, bakuchiol, and ascorbyl tetraisopalmitate through clinical and histological analysis. *J. Cosmet. Dermatol.* **2020**, *19*, 884–890. [CrossRef] [PubMed]
17. Pinnell, S.R.; Yang, H.; Omar, M.; Monteiro-Riviere, N.; DeBuys, H.V.; Walker, L.C.; Wang, Y.H.; Levine, M. Topical L-ascorbic acid: Percutaneous absorption studies. *Dermatol. Surg.* **2001**, *27*, 137–142. [CrossRef] [PubMed]


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