Dermatology Reports
https://journals.pagepress.net/dr

eISSN 2036-7406

Please cite this article as:

Gunardi KY, Novianto E, Agustin T, et al. Effectiveness and safety of topical L-ascorbic acid 15% serum compared to retinol 0.1% serum for skin aging: a double-blind randomized controlled trial study. *Dermatol Rep 2026 [Epub Ahead of Print] doi: 10.4081/dr.2026.10293*

Received: 13 February 2025; Accepted: 16 February 2026.

Effectiveness and safety of topical L-ascorbic acid 15% serum compared to retinol 0.1% serum for skin aging: a double-blind randomized controlled trial study

Keiko Yolanda Gunardi,[1] Endi Novianto,[1] Triana Agustin,[1] Dewi Friska,[2] Githa Rahmayunitha[1]

[1]Department of Dermatology and Venereology; [2]Department of Community Medicine, Dr. Cipto Mangunkusumo National Central General Hospital, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia

Correspondence: Endi Novianto, Department of Dermatology and Venereology, Dr. Cipto Mangunkusumo National Central General Hospital, Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia. E-mail: endinoviantodr@gmail.com

Key words: skin aging; L-ascorbic acid; retinol; JANUS; DPAS.

Contributions: Keiko Yolanda Gunardi: conceptualization, methodology, formal analysis, writing initial draft; Endi Novianto, Triana Agustin, Githa Rahmayunitha: methodology, writing review editing, supervision, funding acquisition; Dewi Friska: methodology, writing review editing. All authors read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Conflict of interest: the authors declare that they have no competing interests.

Ethics approval and consent to participate: the Universitas Indonesia Institutional Review Board approved the study with protocol number KET-1590/UN2.F1/ETIK/PPM.00.02/2023. Prospective participants were provided with a detailed explanation of the study's objectives, procedures, potential benefits, and risks before signing a written informed consent form.

Availability of data and materials: the datasets generated and/or analyzed during the current study are not publicly available due to patients' privacy, but are available upon reasonable request from the corresponding author.

Funding: this research was funded by the 2023 PUTI Postgraduate Grant.

Abstract

Aging is characterized by a progressive decline in physiological functions, including skin integrity and regeneration, with visible signs of skin aging typically emerging from the fourth decade of life onward. Extrinsic factors can accelerate this process. Retinoic acid has long been used as a standard anti-aging treatment, although it is associated with various side effects. L-ascorbic acid (LAA) 15% serum has emerged as a potential alternative with minimal side effects, yet its efficacy and safety in comparison to retinol 0.1% serum remain insufficiently studied. This double-blind, split-face, randomized clinical trial aimed to evaluate the effectiveness and safety of LAA relative to retinol in treating skin aging. Using the modified Dermoscopy Photo Aging Scale (DPAS) and JANUS-III, assessments were conducted on participants' cheeks. Results indicated significant improvements in both the LAA and retinol groups at weeks 2 and 4. However, no statistically significant differences were observed between the two interventions at these time points. Both treatments demonstrated similar safety profiles, suggesting that LAA is as effective and safe as retinol for anti-aging therapy.

Introduction

Intrinsic aging, or chronological aging, occurs naturally as individuals age, resulting in pale, thinner, and more fragile skin with fine wrinkles and dermal atrophy. These changes typically become evident during the fourth decade of life. In contrast, extrinsic aging is caused by external factors such as ultraviolet (UV) radiation, pollution, and lifestyle choices, leading to premature skin aging. Signs of extrinsic aging can appear as early as 30 years of age and include structural and functional changes, such as reduced collagen and elastin synthesis, altered pigmentation, and diminished skin hydration.[1] Various strategies have been developed to prevent and address skin aging. Preventive measures include the use of sunscreens and antioxidants like vitamin C, as well as treatments like retinoic acid, hydroquinone, chemical peels, botulinum toxin injections, fillers, and laser therapy.[2] Vitamin C, particularly in its active form L-ascorbic acid (LAA), exhibits potent antioxidant properties, neutralizing free radicals and promoting collagen synthesis. It also inhibits tyrosinase activity, reducing melanin production and enhancing skin brightness. Studies have shown that topical vitamin C formulations, at concentrations of 5-20%, can effectively improve skin texture and reduce signs of aging. However, higher concentrations may increase the risk of side effects, and clinical evidence regarding its efficacy and safety in managing skin aging, especially in Indonesian populations, is limited.[3] Retinoic acid is an FDA-approved gold standard for skin aging treatment due to its ability to stimulate cell turnover and collagen production.[4,5] However, its use is often associated with adverse effects such as irritation, redness, and peeling, necessitating careful dermatological supervision. Retinol, a precursor to retinoic acid, offers a milder alternative with fewer side effects, although it

requires longer application durations to achieve comparable outcomes.

Despite the availability of topical vitamin C products for anti-aging, clinical trials comparing their effectiveness to other standard treatments are scarce. This is the first study that compares the effectiveness and safety of LAA 15% serum with retinol 0.1% serum in improving skin aging parameters.

Materials and Methods

Study design

This randomized, double-blind, split-face clinical trial was designed to evaluate the effectiveness and safety of LAA 15% serum compared to retinol 0.1% serum for improving skin aging parameters.

Interventions

The test products included a vitamin C serum containing LAA 15% and retinol 0.1% serum. Both products were prepared by a pharmaceutical manufacturing company and underwent 30 days of stability testing for organoleptic properties. The serums were packaged identically in colorless bottles with pipettes to ensure blinding.

Patient selection

A total of 30 subjects aged 35-65 came to Dr. Cipto Mangunkusumo Hospital, the top referral hospital in Jakarta, Indonesia. Patients who consented to participate were included. Subjects with inflammatory, infectious, or open lesions on the face; use of topical facial therapies within the previous two weeks; hypersensitivity to vitamin C, retinol, or retinoids; and those pregnant or planning pregnancy were excluded. Those who were non-compliant with the study protocol, failed to attend follow-up visits within two weeks, or experienced severe side effects requiring discontinuation were dropped out.

Randomization and treatment allocation

Randomization was conducted by an individual who was not involved in the sample collection process for this study, using simple randomization to allocate interventions to the right or left face. Subjects received two interventions for each side of the face (split-face), assigned to either the LAA 15% serum or the retinol 0.1% serum. Each bottle was labeled with a code indicating subject number and side of application (left or right face). Blinding was maintained throughout the study, with only the pharmacy team and biostatistics supervisor aware of the allocation. The randomization table was sealed and only opened after data collection was complete.

Outcome measurement and evaluation

Skin aging measurements were conducted using the modified Dermoscopy Photo Aging Scale (DPAS) and the JANUS-III skin analysis system (PIE Co, Ltd), capturing parameters such as wrinkles, pores, elasticity, pigmentation, UV-induced pigmentation, tone, sebum, and hydration. Baseline measurements were obtained and assessed on both cheeks, and the DPAS score was calculated based on 11 criteria, including pigmentation changes, wrinkles, and skin texture. Follow-up evaluations (DPAS and JANUS-III) were conducted at weeks 2 and 4, and side effects were recorded through subjective and objective assessments.

Statistical analysis

Statistical analyses were conducted using SPSS® version 21. Categorical data are displayed as frequencies and percentages, numerical data are reported as means and standard deviations when normally distributed, while non-normally distributed data are presented as medians and interquartile ranges. Bivariate associations were analyzed to compare the effectiveness of 15% LAA serum and 0.1% retinol serum using independent *t*-tests or Mann-Whitney tests for numerical outcomes, and chi-square or Fisher's exact tests for categorical outcomes, as appropriate. Changes in skin aging scores before and after the intervention were analyzed using the chi-square test or assessed by DPAS and JANUS using a paired t-test or the Wilcoxon signed-rank test. A p-value <0.05 was considered statistically significant.

Results

Thirty participants were enrolled employing a split-face intervention where the right and left sides of the face received different treatments, randomized to LAA (15%) or retinol (0.1%), resulting in 60 data units. From the initial group, three participants withdrew due to adverse effects or a lack of willingness to proceed, resulting in 27 participants being included in the final analysis. Most participants were female (86.7%), with the largest age group being 41-45 years (36.7%), followed by 35-40 years and 46-50 years (23.3% each). Statistical analysis was conducted per protocol (Figure 1).

Baseline characteristics

Baseline DPAS and JANUS-III parameters were similar between the LAA and retinol groups (Table 1). The most prevalent DPAS scores were for white lines, hypo-hyperpigmented macules, and superficial wrinkles. Notably, no patients presented with yellowish discoloration, yellowish papules, or criss-cross wrinkles.

Modified DPAS measurement

At week 2, there was a significant improvement in both groups, LAA (p=0.005) and retinol (p=0.022). At week 4, there was also a significant improvement in both interventions, LAA (p=0.002) and retinol (p=0.04). The DPAS scores, measured at weeks 0, 2, and 4, showed no significant difference between the retinol and LAA groups (Figure 2, Table 2).

JANUS-III measurement

After 4 weeks of intervention, JANUS-III parameters improved on several components in both LAA and retinol groups. In the LAA group, an increase in pigmentation (p=0.004), UV pigmentation (p=0.000), and sebum (p=0.005) significantly differed in week 4 compared to the baseline. Meanwhile, in the retinol group, an increase in pigmentation (p=0.009), UV pigmentation (p=0.000), and sebum (p=0.001) and porphyrin (p=0.025) significantly differed at week 4 compared to baseline. However, no differences within any JANUS-III parameters between retinol and LAA groups were noted (Figure 3, Table 3).

Adverse effects

Five out of twenty-seven participants experienced mild side effects. Two participants in the LAA group reported a stinging sensation, and two others reported mild itching, which did not interfere with daily activities. One participant in the retinol group experienced mild burning. All side effects were minimal, resolved without treatment, and disappeared within 24 hours.

Discussion

This study is a randomized double-blind controlled trial with a split-face method used, allowing both groups to be assessed within the same patient. As a result, changes observed during follow-up were attributed to the interventions rather than differences in baseline conditions. The DPAS assessment revealed that the most common skin conditions were hypo-hyperpigmented macules and superficial wrinkles, while conditions like yellowish discoloration and papules were not found, differing from a previous study by Respati *et al.*,[6] which reported more cases of yellowish discoloration in patients living near the coast. This discrepancy could be attributed to regional differences and inclusion criteria, as this study involved patients from all over Indonesia, while Respati *et al.*'s study focused on coastal residents with more sun exposure and younger patients.[6]

Similarly, the JANUS-III assessment, a quantitative tool for evaluating skin characteristics, showed no significant baseline differences between groups. It provides a score for each skin parameter, where

higher scores indicate worse skin conditions for certain parameters (*e.g.*, pores, wrinkles, pigmentation, sebum) and better conditions for others (*e.g.*, elasticity, skin tone, moisture). The JANUS-III tool was effective in reducing bias, providing more objective measurements compared to subjective dermatological assessments. The use of JANUS-III reduced bias compared to subjective dermatologist assessments.

Our findings show that LAA and retinol were effective in improving skin conditions, particularly in reducing white lines, with no significant differences between groups. Significant improvements in the DPAS scores were observed at week 2 and 4 for both groups. These results align with the theory that both LAA (vitamin C) and retinol have anti-aging effects. LAA neutralizes reactive oxygen species, reduces oxidative stress, and supports collagen stability. Retinol, a commonly used topical anti-aging treatment, regulates epidermal cell proliferation, stimulates collagen production, and prevents collagen degradation. The anti-aging effects of LAA in this study were comparable to those of retinol. Previous studies, including a double-blind trial by Humbert *et al.*,[7] found significant improvement in skin conditions with LAA after 3-6 months of use. Similarly, a study by Pratiwi *et al.*[8] demonstrated improved skin conditions with LAA compared to placebo in microneedling therapy for photoaging signs.

The JANUS-III assessment revealed no significant differences in efficacy between LAA and retinol at both 2-week and 4-week follow-ups. However, JANUS-III revealed specific changes in skin parameters for both groups. Hyperpigmentation, a key indicator of skin aging, worsened in both groups for pigmentation, UV pigmentation, and sebum production. This contradicts previous studies where retinol is shown to protect against hyperpigmentation. Retinol is known to reduce hyperpigmentation by inhibiting tyrosinase, inducing desquamation, and promoting epidermal turnover.[9,10] LAA also inhibits pigmentation by reducing melanin production through tyrosinase inhibition,[11,12] aligning with previous studies showing its brightening effects.[13]

The findings may be due to reduced sunscreen use among participants during the study, leading to increased sun exposure and worsening pigmentation. However, based on participants' feedback, the skin appeared lighter and brighter. Given that this study was conducted over a duration of only 4 weeks, it is recommended that the follow-up period be extended in future research.

Short study duration and potential skin irritation could also have contributed to this outcome. Additionally, retinol was associated with increased sebum production that might possibly be due to skin barrier damage through several mechanisms.[14] Retinoids promote sebocyte differentiation and proliferation,[3,14] while LAA might increase sebum to maintain hydration, though no studies confirm this.[14] Retinol showed improvement in porphyrin levels, suggesting reduced oxidative stress and inflammation, preventing acne. Previous studies also support retinol's efficacy in reducing

porphyrins,[15] which is a benefit not seen with LAA.

Adverse effects

This study found minimal adverse effects, including stinging and itching with LAA and stinging with retinol 0.1%. These effects are consistent with previous studies; Garre *et al.*[16] reported no objective side effects from LAA serum for anti-aging, with only mild itching in a few participants. Wang *et al.*[13] showed low cytotoxicity and no allergic reactions in high-concentration vitamin C trials. In the retinol group, only one participant reported side effects. Retinol, being a weaker retinoid than tretinoin, has fewer side effects and requires longer use for results. Literature shows retinoids may cause local irritation, and while teratogenic effects exist, this study excluded pregnant participants. Studies by Kang *et al.*[17] and Fluhr *et al.*[9] indicate retinol causes less irritation and side effects compared to other retinoids. Overall, vitamin C's antioxidant properties offer an effective anti-aging treatment with minimal side effects.

Limitations

The follow-up duration was limited to a period of 4 weeks.

Conclusions

LAA was selected as an alternative to retinol due to its comparable clinical efficacy combined with broader applicability across diverse patient profiles and practical considerations. In this study, LAA 15% demonstrated similar improvements in skin aging parameters to retinol 0.1% without significant differences in DPAS or JANUS-III outcomes, confirming its effectiveness as an anti-aging agent. Importantly, LAA exhibited a more favorable tolerability profile, making it particularly suitable for patients with sensitive skin, underlying barrier dysfunction, or comorbid conditions such as rosacea or inflammatory dermatoses, in whom retinoids may exacerbate irritation. LAA is also advantageous for patients who are pregnant, planning pregnancy, or unable to tolerate retinoids, as well as for individuals requiring daytime use with antioxidant and photoprotective benefits. From a practical standpoint, LAA-based therapy may reduce the need for intensive monitoring, stepwise titration, and adjunctive barrier-repair treatments often required with retinoids, thereby improving adherence and potentially lowering overall treatment-related costs. Considering its efficacy, safety, patient acceptance, and real-world feasibility, LAA represents a rational and accessible option for both initial and maintenance anti-aging therapy.

References

1. Helfrich YR, Sachs DL, Voorhees JJ. Overview of skin aging and photoaging. Dermatol Nurs 2008;20:177-83.
2. Addor FAS. Beyond photoaging: Additional factors involved in the process of skin aging. Clin Cosmet Investig Dermatol 2018;11:437-43.
3. Baumann L, Allemann IB. Antioxidants. In: Baumann L, Saghari S, Weisberg E (eds) Cosmetic Dermatology Principles and Practice. McGraw-Hill Co; 2009, p. 298.
4. Kohl E, Steinbauer J, Landthaler M, et al. Skin ageing. J Eur Acad Dermatol Venereol 2011;25:873-84.
5. Makrantonaki E, Zouboulis CC. Characteristics and pathomechanisms of endogenously aged skin. Dermatology 2007;214:352-60.
6. Respati RA, Yusharyahya SN, Wibawa LP, et al. The Dermoscopic Features of Photoaging and Its Association with Sun Index Score in the Coastal Population at Cilincing, Jakarta: A Cross-Sectional Study. Clin Cosmet Investig Dermatol 2022;15:939-46.
7. Humbert PG, Haftek M, Creidi P, et al. Topical ascorbic acid on photoaged skin. Clinical, topographical and ultrastructural evaluation: double-blind study vs. Placebo Exp Dermatol 2003;12:237-44.
8. Pratiwi KD, Listiawan MY, Ervianti E, et al. The Efficacy of Topical Vitamin C and Microneedling for Photoaging. Berkala Ilmu Kesehatan Kulit dan Kelamin (Periodical of Dermatology and Venerology) 2021;33:55-62.
9. Fluhr JW, Vienne MP, Lauze C, et al. Tolerance profile of retinol, retinaldehyde and retinoic acid under maximized and long-term clinical conditions. Dermatology 1999;199:57-60.
10. Yin L, Morita A, Tsuji T. Evidence From Epidemiological and Molecular Studies. Photodermatol Photoimmunol Photomed 2001;17:178-83.
11. Pullar JM, Carr AC, Vissers MCM. The roles of vitamin C in skin health. Nutrients 2017;9:866.
12. Jagetia GC, Rajanikant GK, Rao SK. Evaluation of the Effect of Ascorbic Acid Treatment on Wound Healing in Mice Exposed to Different Doses of Fractionated Gamma Radiation. Radiat Res 2006;159:371-80.
13. Wang MP, Lu WW, Ge XY, et al. Study on the Efficacy of Vitamin C Lotion on Skin: Permeable and Anti-Aging. J Cosmet Dermatol Sci Appl 2022;12:67-82.
14. Shapiro SS, Saliou C. Role of vitamins in skin care. Nutrition 2001;17:839-44.
15. Draelos ZD. Modern moisturizer myths, misconceptions, and truths. Cutis 2013;91:308-14.
16. Garre A, Narda M, Valderas-Martinez P, et al. 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;11:253-63.

17. Kang S, Duell EA, Fisher GJ, et al. Application of retinol to human skin in vivo induces epidermal hyperplasia and cellular retinoid binding proteins characteristic of retinoic acid but without measurable retinoic acid levels or irritation. J Invest Dermatol 1995;105:549-56.

Figure 1. Study flowchart.

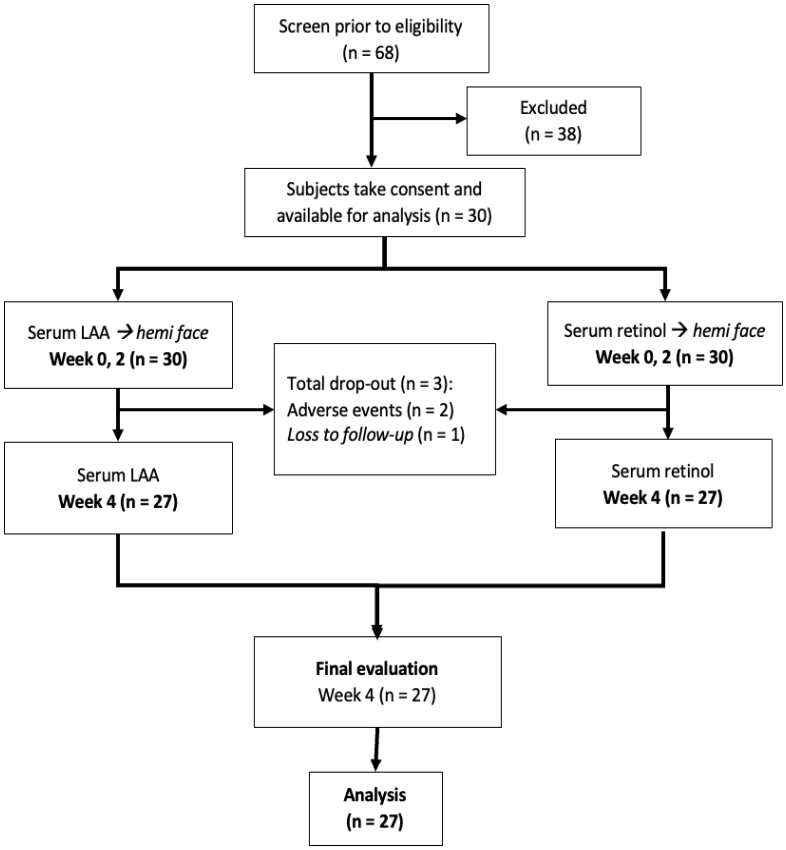

Figure 2. Before treatment with LAA on the left side and retinol on the right side.

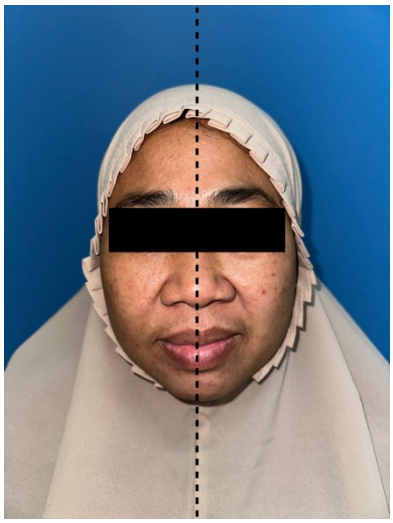

Figure 3. After treatment with LAA on the left side and retinol on the right side.

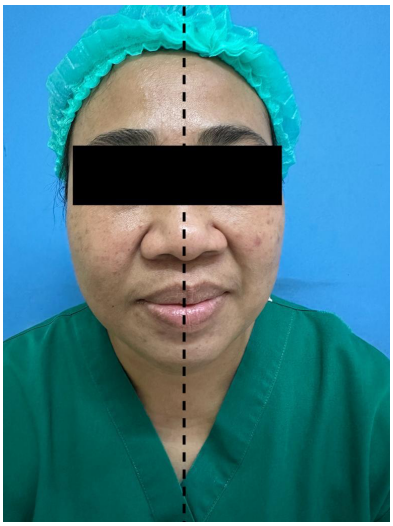

Table 1. Baseline characteristics of facial skin using DPAS.

DPAS parameter	**LAA** **n, %**	**Retinol** **n, %**
Yellowish discoloration	0 (0)	0 (0)
White line	7 (25.9)	8 (29.6)
Lentigo	1 (3.7)	0 (0)
Telangiectases	1 (3.7)	2 (7.4)
Hypo-hyperpigmented macules	22 (81.5)	22 (81.5)
Yellowish papules	0 (0)	0 (0)
Actinic keratosis	1 (3.7)	1 (3.7)
Senile comedones	2 (7.4)	3 (11.1)
Deep wrinkles	0 (0)	1 (3.7)
Superficial wrinkles	27 (100)	25 (92.6)
Criss-cross wrinkles	0 (0)	0 (0)
JANUS-III parameter	**LAA** **mean ± SD**	**Retinol** **mean ± SD**
Pores	46.40±6.11	46.61±5.11
Elasticity	57.37±16.83	62.15±17.15
Wrinkles	15.78±6.55	15.50±8.25
Pigmentation	24.48±8.07	23.96±7.33
UV Pigmentation	14.37±8.30	15.92±7.71
Skin tone	50.74±4.18	50.96±4.19
Sebum, median (IQR)	92.0 (147.0)	114.5 (136.5)
Porphyrin	30.67±10.80	33.42±11.18
Moisture, median (IQR)	27.0 (6.0)	26.5 (4.5)

DPAS, Dermoscopy Photo Aging Scale; LAA, L-ascorbic acid; SD, standard deviation; IQR, interquartile range.

Table 2. Comparison of DPAS parameters after the intervention period between the retinol and LAA groups.

DPAS	**LAA median (IQR)**	**Retinol median (IQR)**	**Retinol *vs.* LAA p-value***
Week 0	2 (1-4)	2 (1-4)	0.708
Week 2	2 (1-3)	2 (1-3)	1
Week 4	2 (1-4)	2 (1-3)	0.749

DPAS, Dermoscopy Photo Aging Scale; LAA, L-ascorbic acid; IQR, interquartile range; *Mann-Whitney test.

Table 3. Comparison of JANUS-III parameters after a 4-week intervention period between retinol and LAA groups.

JANUS-III	**LAA**	**Retinol**	**LAA *vs.* retinol p-value**
Week 2			
Pores	46.89±6.88	46.67±5.66	0.897
Elasticity	59.18±14.81	59.96±14.08	0.844
Wrinkles	16.03±7.03	15.04±6.11	0.579
Pigmentation	25.59±9.44	26.0 (7.0)	0.822*
UV pigmentation	19.30±8.90	19.74±8.97	0.856
Skin tone	50.81±3.55	52.0 (4.0)	0.619*
Sebum	291.59±204.61	354.96±237.48	0.298
Porphyrin	29.67±8.48	29.70±9.21	0.988
Moisture	26.0 (6.0)	26.0 (6.0)	0.821*
Week 4			
Pores	46.63±7.10	46.59±7.10	0.985
Elasticity	57.07±17.0	57.11±16.40	0.994
Wrinkles	16.15±6.94	14.93±6.13	0.496
Pigmentation	27.15±10.90	27.0 (10.0)	0.788*
UV pigmentation	19.44±9.74	21.26±8.40	0.467
Skin tone	50.70±3.37	51.1±3.68	0.673
Sebum	193.0 (294.0)	276.0 (416.0)	0.115*
Porphyrin	28.30±7.46	28.30±8.27	1.000
Moisture	25.67±8.09	25.52±7.27	0.944

LAA, L-ascorbic acid; data for JANUS-III are presented as median (IQR) or mean ± SD; data were analyzed using a dependent *t*-test unless otherwise specified; *Mann-Whitney test.