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ORIGINAL RESEARCH

Efficacy Evaluation of a Cosmetic Product for the Periocular Area in Caucasian Women Aged Over 40 Years Old

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Purpose: The present study was aimed at evaluating the efficacy of a cosmetic product in improving the appearance of periocular skin.

Patients and Methods: An open-label study on 40 female subjects showing clinical signs of skin aging in the periocular area (including bags under the eye and dark circles) was conducted. At day 0 and day 28 the bags under eye volume, dark circles color, skin texture, skin moisturization, skin elasticity, and skin radiance were measured. The instrumental measurements were integrated by clinical analysis carried out by a board-certified dermatologist and by a self-assessment questionnaire carried out by each subject participating in the study.

Results: After 28 days of product use the volume of the bags under the eye was decreased by 6.8% (p = 0.005), the dark circle color red and blue component improved by 7.1% (p = 0.001) and 4.0% (p = 0.001), respectively, wrinkle depth and skin roughness decreased by 15.8% (p = 0.001) and 6.3% (p = 0.011), respectively, skin moisturization increased by 11.7% (p = 0.000), the skin distensibility decreased by 8.9% (p = 0.000), the overall skin elasticity increased by 10.4% (p = 0.000), and the skin radiance increased by 16.3% (p = 0.000). The instrumental measured effects were also confirmed by the clinical analysis of the dermatologist and the self-assessment questionnaire output.

Conclusion: Conclusions: our results suggest that the test product is effective for periocular skin aesthetics (reduction of imperfections undermining the periocular area) and wellness.

Keywords: bags under the eye, dark circles, periocular aging, cosmetic product, skin moisturization, skin elasticity

Introduction

Eyes, eye gaze, and periocular area appearance are of high importance in social relationship. The expression "eyes are the window to the soul" is a testimony in the common parlance of the psychological but also of the aesthetic importance of the eyes (including the periocular area). The eyes have their own non-verbal language; while the "eye contact" during conversation helps the other participants feel you are engaged and interested in the discussion. It is then clear why the appearance of periocular area is of importance in the cosmetic field.

The periocular area appearance is undermined by a series of imperfections related to both fatigue and aging. Among them: under-eye bags,[1] dark circles,[2] and general aging sign[3] (ie, loss of elasticity, dehydration, etc.) are a frequent complaint among patients who no longer feel youthful. The nature of these imperfections is multifactorial and is exacerbated by aging.[4,5]

Due to the multifactorial nature of the imperfections, cosmetic practitioners, and dermatologists have plenty of potential treatment options to propose to their patients, including botulinum toxin,[6] hyaluronic acid fillers,[7,8] wavelength tunable laser devices, and fractionated laser therapy.[4]

Even if effective, these treatments are costly, invasive and may have side effects. Furthermore, people can be reluctant/intimidated by these treatment approaches. Thus, a topical effective cosmetic treatment could be more acceptable to patients.

The present clinical/instrumental study evaluated the efficacy and confirmed the tolerability of a cosmetic product (Nutrakos Eye Contour Gel, Professional Dietetics S.p.A., Milano, Italy) developed to target bags under the eyes, dark circles and having anti-aging properties.

Materials and Methods
Subjects, Settings, and Locations
In this monocentric, open-label study, 40 (N = 40) healthy Caucasian female were included by a board-certified dermatologist. All the study procedures were carried out according to the World Medical Association's (WMA) Helsinki Declaration and its amendments (Ethical Principles for Medical research Involving Human Subjects, adopted by the 18th WMA General Assembly Helsinki, Finland, June 1964, and amendments). All subjects signed informed consent form and consent release form for the publication of photographs before any study-related procedure took place. As recommended by Colipa (now Cosmetics Europe) guidelines, all ethical rules were respected, and the test product was assessed for its safety of use before the study took place.[9] According to EU cosmetic Regulation no. 1223/2009, a cosmetic product must not cause damage to human health when applied under normal or reasonably foreseeable conditions of use and must be assessed for its safety of use before human subjects are exposed to it, and as such, further ethical approval is not required.

Eligible participants were all adult (>40 years old) Caucasian female subjects showing the clinical signs of bags under the eye and wrinkles in the periocular area (n = 20, 50% of the panelist), or dark circles and wrinkles in the periocular area (n = 20, 50% of the panelist). The subjects were of good general health, without any active skin disease in the test area or known history of atopic dermatitis and/or skin elastosis in the skin of the face.

Exclusion criteria were pregnancy or intention to become pregnant, breastfeeding, allergy/sensitivity to cosmetics, sunscreen or topical medications, unwillingness, or inability to comply with the requirement and constraints of the study protocol, dermatological problems in the test area, and history of hypersensitive skin.

Throughout the study period, subjects were asked to avoid both natural and artificial UV exposure. Subjects attended clinic visit at baseline and after 28 days of product use.

The study took place at Complife Italia Srl dermatological facility in San Martino Siccomario, Pavia, Italy, from June to November 2021. Complife Italia is an independent testing laboratory working with the University of Pavia, which specializes in in vitro and in vivo safety and efficacy assessment of cosmetics, food supplements, and medical devices.

Intervention
The tested product was an eye contour cream (Nutrakos Eye Contour Gel, Professional Dietetics S.p.A., Milano, Italy) containing AQUA, GLYCERIN, GLYCINE, SODIUM POLYACRYLATE, PROLINE, ALANINE, PEG-40 HYDROGENATED CASTOR OIL, PHENOXY-ETHANOL, VALINE, PEG/PPG-20/6 DIMETHICONE, CITRONELLYL METHYLC ROTONATE, PRO-PYLENE GLYCOL, SODIUM HYALURONATE, PPG-26-BUTETH-26, AMMONIUM ACRYLO-YLDIMETHYLTAURATE/VP COPOLYMER, POLYGLYCERYL-10 EICOSANEDI-OATE/TETRADECANEDIOATE, CAPRYLYL GLYCOL, 1,2-HEXANEDIOL, LEUCINE, ALBIZIA JULIBRISSIN BARK EXTRACT, LYSINE HCI, DISODIUM EDTA, PARFUM, DARUTOSIDE (SIEG-ESBECKIA ORIENTALIS EXTRACT).

Subjects were asked to apply the product in the eye contour area twice daily (morning and evening) after cleansing. A gentle massage was used to favor complete absorption.

Primary and Secondary Endpoints/Outcomes
The primary efficacy endpoint was the evaluation of the product in decreasing the appearance of both the bags under the eye and the dark circles. The primary outcomes were the measurement of the volume of the bags under the eye and the color of the dark circles.

The secondary efficacy endpoint was the evaluation of the product in improving skin texture (wrinkle depth and skin smoothness), skin moisturization, skin radiance, and skin elasticity. The secondary outcomes included the measurement of the following parameters: wrinkle depth, skin smoothness, skin moisturization, skin radiance, and skin elasticity. The instrumental measurements were integrated by both the clinical analysis of the dermatologist and the self-assessment questionnaire.

All the measurements were carried out, on naked skin, under temperature (21± 1∘C) and humidity (50 ± 10%) controlled conditions. Subjects were left to acclimate to the room conditions for 15 to 20 min before the beginning of the visit.

Volume of the Bags Under the Eye, Skin Texture Properties and Dark Circles Color

The volume of the bags under the eye, the skin smoothness (Sa parameter), and the wrinkle maximum depth were measured using a real 3D camera (Primos[CR] SF, Canfield Scientific, NJ, USA). The device allows to measure skin structure volume and surface properties based on structured light projection. The skin smoothness and the wrinkle maximum depth parameters were measured in the periocular area ("crow's feet" area).

Dark circles color was measured in the CIELab chromatic space using a spectrophotometer/colorimeter CM-700D (Konica-Minolta, Japan).[10] The a* (red) and b* (blue) component of the dark circles color were measured.

Skin Moisturization

The superficial (10–20 mm) skin moisturization was measured using a Corneometer[®] CM 825 (Courage + Khazaka, electronic GmbH, Cologne, Germany).[11] The instrument allows to measure the variation in the skin capacitance based on the skin moisture content.

Skin Elasticity

The skin elasticity was measured using a Cutometer[®] MPA 580 (Courage + Khazaka, electronic GmbH, Cologne, Germany).[12] The R0 (skin firmness) and R2 (skin gross elasticity) parameters were measured (Figure 1).

Skin Radiance

The skin radiance (or skin brightness) was measured using a spectrophotometer/colorimeter CM-700D (Konica-Minolta, Japan). The measured parameter was the 8° gloss parameter.

Clinical Analysis

Decrease in skin wrinkledness in the periocular area and appearance of bags under the eye and dark circles were scored by dermatologist according to a clinical scoring system reported in Table 1.

Self-Assessment Questionnaire

At the end of the study, subjects are asked to express their opinion on tested product by answering a self-assessment questionnaire. The questionnaire items were as follows: 1) the product reduces eyebag puffiness, 2) the product reduces dark circles color, 3) the product reduces fine lines/wrinkles visibility, 4) the product improves skin brightness, 5) the
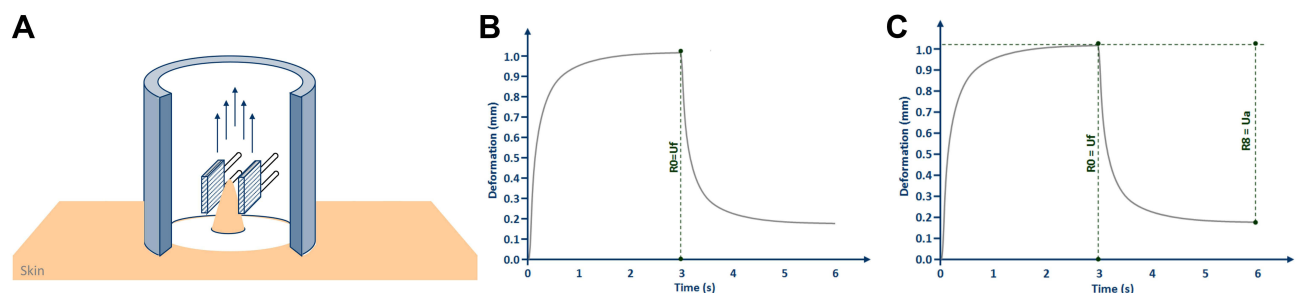

Figure 1 (**A**) Skin elasticity measurement process. (**B**) R0 (skin distensibility) represents the passive behavior of the skin to force (ie, gravity). Conceptually R0 parameter is correlated to skin firmness. (**C**) R2 (Ua/Uf, gross elasticity or overall elasticity) represents the ability of the skin to return to its basal state.

Table 1 Clinical Scoring System

	Classification at D0*	Score	Classification at D28**	Score
Skin wrinkledness	**No wrinkle**. No visible wrinkles; Continuous skin line.	0	No variation	1
	Very shallow yet visible wrinkles.	0.5	Mild improvement	2
	Fine wrinkle. Visible wrinkles and slight Indentation.	1.0	Moderate improvement	3
	Visible wrinkles and clear indentation.	1.5	Remarkable improvement	4
	Moderate wrinkles. Clearly visible wrinkles.	2		
	Prominent and visible wrinkles.	2.5		
	Deep wrinkles. Deep wrinkles and furrows.	3		
Bags under the eye	Under eye bags are very swollen		No variation	1
	Under eye bags are slightly swollen		Mild improvement	2
	Under eye bags are not swollen		Moderate improvement	3
			Remarkable improvement	4
Dark circles	Dark circles are very dark		No variation	1
	Dark circles are slightly dark		Mild improvement	2
	The palpebral skin color is normal		Moderate improvement	3
			Remarkable improvement	4

Note: *Basal visit, **Follow-up visit after 28 days of product use.

product improves skin firmness, 6) the product improves skin moisturization, 7) the product has a smoothing effect, 8) the product reduces signs of fatigue, 9) the product has a pleasant texture, 10) the product is quickly absorbed, 11) the product is easy to apply, 12) are you satisfied with the product?, 13) Would you buy the product?, 14) Is the product well tolerated?. Items from 1 to 11 are scored as follows: "Completely agree", "Agree", "Disagree", and "Completely agree"; while items from 12 to 14 as follows: "Yes" and "No".

Statistics
The statistical analyses were performed using a Microsoft® Excel® worksheet (Microsoft 365 Apps for enterprise, version 2202, build 14931.20132) running on Microsoft® Windows® 11 Pro 64-bit edition (version 10.0.22000, build 22000). Statistical analysis was carried out by two-way t test of Student. A $p < 0.05$ was considered to be statistically significant. Statistical analysis output was reported as follows: *$p < 0.05$, **$p < 0.01$, and ***$p < 0.001$.

Results
Participants and Product Skin Tolerability
A total of 40 (N = 40) female subjects were enrolled in the study. Subjects attended clinic visits at the baseline (D0) and after 28 days (D28) of product use. All the enrolled subjects (n = 20 in the bags under the eye and wrinkles in the periocular area group and n = 20 in the dark circles and wrinkles in the periocular area) completed the study. There were no dropouts or missing results. Subjects' baseline demographics and clinical characteristics are reported in Table 2.

The product was well tolerated. No local tolerance reactions, neither physical (objective reaction) nor functional (subjective reaction), were reported by the ophthalmologist or by the subject, respectively.

Primary Endpoints: Bags Under the Eye Volume and Dark Circles Color
The primary endpoints as related to efficacy were measured by means of image analysis on real 3D pictures and colorimetry, respectively. Data are reported in Figure 2.

Eyebags volume was significantly lower (p<0.01) after 28 days of product use (Figure 2A) with a mean decrease by 6.8% (min +6.1%; max −25.9%). This instrumentally measured datum was also seen by the dermatologist in most of the subjects (60%) participating in the study (Figure 3B).

Table 2 Subjects' Baseline Demographic and Clinical Characteristics

Baseline Characteristic	Value	Units
Sex	40 (100%)	N (%)
Age	54.9 ± 1.0	Years
Subjects with bags under the eye and wrinkles	20 (50%)	n (%)
Subjects with dark circles and wrinkles	20 (50%)	n (%)
Bags under the eye volume	19.51 ± 1.48	mm^3
Dark circles color		
Red component (a*)	14.749 ± 0.739	Arbitrary units
Blue component (b*)	−21.158 ± 0.748	Arbitrary units
Wrinkle depth	344.6 ± 25.9	mm
Skin smoothness (Sa)	38.2 ± 1.6	mm
Skin moisturization	59.4 ± 1.3	Corneometric units
Skin elasticity		
R0 (skin distensibility)	0.2916 ± 0.091	mm
R2 (overall elasticity)	0.4957 ± 0.0146	%
Skin radiance	11.4 ± 0.6	Arbitrary units

The a* (red) and b* (blue) components of the typical purplish color of dark circles were measured by colorimetry. The red (a*) component was significantly lower (p<0.01) after 28 days of product use (Figure 2B) with a mean decrease by 7.1% (min −20.7%; max 7.7%). As expected, the blue (b*) component was significantly higher (p<0.01) after 28 days of product use (Figure 2C) with a mean increase by 4.0% (min −4.9%; max 12.2%). The decrease of the a* (primary color) parameter together with an increase of the b* (primary color) parameter means a decrease of the purplish (secondary color given by mixing red and blue) color of dark circles. This instrumentally measured datum was also seen by the dermatologist in most of the subjects (55%) participating in the study (Figure 3C).

Secondary Endpoints
Wrinkle Depth and Skin Smoothness
Wrinkle depth and skin smoothness were measured by structured light projection using a real 3D camera (PrimosCR, Canfield Scientific). Data are reported in Table 3.

The periocular wrinkle ("crow's feet" wrinkle) depth, measured in point of its maximum depth, was significantly lower (p<0.01) after 28 days of product use with a mean decrease by 15.8% (min +8.1%; max −38.9%). This
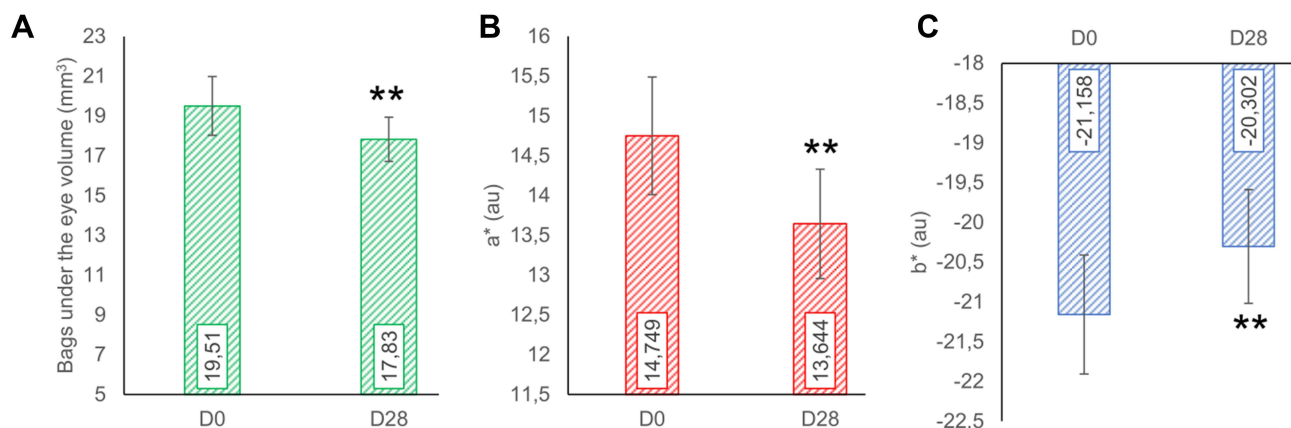

Figure 2 (**A**) Bags under the eye volume results. (**B**) Dark circles color results (a*, red component). (**C**) Dark circles color results (b*, blue component). Data are average (± standard error). The statistical analysis (D28 vs D0) is reported above the bar as follows: ** p<0.01. au arbitrary units. D0 baseline. D28 follow-up visit after 28 days of product use.

Figure 3 (**A**) Periocular wrinkles (standard general white lighting). (**B**) Bags under the eye volume results (standard general white lighting). (**C**) Dark circles color (cross-polarized filter).

instrumentally measured datum was scored as a "mild improvement" by the dermatologist in most of the subjects (70%) participating in the study (Figure 3A).

The skin smoothness in the periocular area was quantified by Sa parameter analysis. Sa is an extension of Ra (arithmetical mean height of a line) to a surface. Sa is the average of profile height deviation from the mean surface and is used to measure the roughness of a surface. Sa parameter was significantly lower ($p<0.05$) after 28 days of product use

Table 3 Secondary Endpoint Results

Parameter	D0	D28	Units	% Variation
Wrinkle depth	344.6 ± 25.9	284.7 ± 20.1 **	mm	−15.8%
Skin smoothness, Sa	38.2 ± 1.6	35.7 ± 1.7 *	mm	−6.3%
Skin moisturization	59.4 ± 1.3	66.1 ± 1.1 ***	cu	+11.7%
Skin elasticity				
R0 (skin distensibility)	0.2916 ± 0.091	0.2661 ± 0.0100 ***	mm	−8.9%
R2 (overall elasticity)	0.4957 ± 0.0146	0.5466 ± 0.0165 ***	%	+10.4%
Skin radiance	11.4 ± 0.6	13.0 ± 0.3 ***	au	+16.3%

Notes: Data are average (± standard error). The statistical analysis (D28 vs D0) is reported as follows: * $p<0.05$, ** $p<0.01$, and *** $p<0.005$. D0 baseline. D28 follow-up visit after 28 days of product use. au arbitrary units. cu corneometric units.

with a mean decrease by 6.3% (min +11.5%; max −25.6%). The decrease of Sa can be translated into absolute value as an improvement of the skin smoothness due to anti-aging and/or antiwrinkle properties of the test product.

Skin Moisturization

The skin moisture content (Table 2) was significantly higher (p<0.001) after 28 days of product use with a mean increase by 11.7% (min −4.0%; max +26.0%).

Skin Elasticity

The skin elasticity was measured by means of both the evaluation of its maximum distensibility (R0 parameter, skin distensibility) and the evaluation of the ratio between the maximum skin deformation and the return to the baseline condition (R2, overall elasticity). Data are reported in Table 2.

The skin distensibility was significantly lower (p<0.001) after 28 days of product use with a mean increase by 8.9% (min +5.4%; max −26.1%). A decrease of the R0 parameter implicates an increase in the skin firmness.

The skin overall elasticity was significantly higher (p<0.001) after 28 days of product use with a mean increase by 10.4% (min −2.2%; max +29.5%). An increase of the R2 parameter is related to the function of the elastic fibers of the skin.

Skin Radiance

The skin radiance (Table 2) was significantly higher (p<0.001) after 28 days of product use with a mean increase by 16.3% (min −10.1%; max +44.1%). An increase of the skin radiance can be related to both an improvement of the skin microcirculation and to an anti-aging effect.

Self-Assessment Questionnaire

The product was scored as effective and pleasant by most of the subjects participating in the study. The complete self-assessment questionnaire output is reported in Table 4.

Table 4 Self-Assessment Questionnaire Output. Data are the Percentage of Subjects Giving a Particular Answer

No.	Item	Completely Agree	Agree	Disagree	Completely Disagree	Positive Answers
01	The product reduces the bags under the eye puffiness*	15%	75%	10%	0%	90%
02	The product reduces dark circles color**	25%	70%	5%	0%	95%
03	The product reduces fine lines/wrinkles visibility	20%	70%	10%	0%	90%
04	The product improves skin brightness	35%	65%	0%	0%	100%
05	The product improves skin firmness	40%	58%	3%	0%	98%
06	The product improves skin moisturization	35%	65%	0%	0%	100%
07	The product has a smoothing effect	35%	60%	5%	0%	95%
08	The product reduces signs of fatigue	20%	73%	8%	0%	93%
09	The product has a pleasant texture	63%	35%	3%	0%	98%
10	The product is quickly absorbed	48%	50%	3%	0%	98%
11	The product is easy to apply	63%	38%	0%	0%	100%
No.	Item	Yes	No			Positive answers
12	Are you satisfied with the product?	100%	0%			100%
13	Would you buy the product?	98%	3%			98%
14	Is the product well tolerated?	100%	0%			100%

Notes: * The question was asked only to subjects showing bags under the eyes (n = 20). ** The question was asked only to subjects showing dark circles (n = 20).

Discussion

The periocular area appearance and wellness is undermined by a series of imperfections related to both fatigue and aging.[1–3] Different aesthetic treatments/procedures have been shown to have effective periocular area appearance.[4,6–8] However, subjects can be reluctant to them, due to invasiveness, side effects, and cost.

In the present study, we investigated the efficacy of a cosmetic product in improving the bags under the eye, the dark circles, and the aging signs by both an instrumental and a clinical approach.

The product was shown to be effective in improving the aesthetics of the periocular area by decreasing the appearance of both the bags under the eye and the dark circles color. The skin moisturization and the skin elasticity improvement underlie its effect in decreasing the "crow's feet" wrinkle and in improving the skin smoothness. Interestingly, these effects were not only instrumentally measured but were also visible in the clinical analysis carried out by the dermatologist.

The overall subject's satisfaction was high for all the subjects participating in the study. The perceived efficacy is of interest in evaluating the compliance of the subjects to the treatment.

Limitations. Generally, the overall positive influence of any cosmetic product on skin should be investigated for a longer period than the present study, due to the intrinsic mechanism related to skin imperfection mechanisms. The short duration of the study and of the treatment period might have limited our results, especially in terms of wrinkles and bags under the eye decrease. Anyway, the results obtained were satisfactory in the study period.

Conclusion

The use of Nutrakos Eye Contour Gel (Professional Dietetics S.p.A., Milano, Italy) for 28 days, twice a day, was effective in improving periocular area appearance and wellness. The product use was well-tolerated and ophthalmologically tested. To the best of our knowledge, this is the first study reporting the efficacy of a cosmetic product in decreasing the bags under eye volume and dark circles color and in improving aging-related signs.

Acknowledgments

The authors would like to express their gratitude to the Complife staff, who contributed to the study and recruited the subjects, for their professionalism and support during the study development.

Disclosure

The authors report no conflicts of interest in this work.

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