IFSCC 2025 full paper (IFSCC2025-1314)

Novel cosmetic for infraorbital dark circles: clinical efficacy and skin tolerance of a formulation containing vectorized caffeine, matrikines, chrysin and tranexamic acid

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1. Introduction

Infraorbital dark circles are a common cosmetic complaint, associated with the deposition of melanin or the pooling of blood in the periorbital area. Factors contributing to dark circles include genetics, thin skin, vascular leakage, dermal atrophy, and lifestyle habits such as lack of sleep or sun exposure [1,2].

From a histopathological standpoint, dark circles can arise from dermal melanin deposition (pigmentary dark circles) or increased visibility of subcutaneous vessels due to thinning skin (vascular dark circles) [3,4]. Regardless of etiology, they are perceived as signs of fatigue and aging, motivating consumers to seek effective cosmetic interventions.

The investigational cosmetic product used in this study combined key active ingredients that target the most critical biological mechanisms involved in dark circle formation since Caffeine has vasoconstrictive effects that promote microcirculation and reduce vascular stasis [5]. Its vectorization with bioavailable silicium enhances skin penetration and bioavailability, which may explain the significant reduction in vascular dark circles observed in this study.

Matrikines (Pal-GHK and Pal-GQPR) are peptides which stimulate the regeneration of the extracellular matrix, increasing collagen and elastin synthesis, thus improving dermal density [6]. Reinforcing the dermal matrix reduces the visibility of underlying vasculature, a key factor in vascular dark circles.

Chrysin enhances bilirubin degradation, and NHS facilitates its elimination, targeting the accumulation of pigmented hemoglobin by-products that contribute to the purplish hue of dark circles [7]. This combined action likely contributed to the improvements observed in redness scores and overall skin tone.

Tranexamic Acid is an emerging agent in the treatment of hyperpigmentation because it inhibits plasminogen activation, reducing melanocyte activation and melanin

synthesis [8]. Its presence in the formulation explains the significant improvement in pigmentation scores in the pigmented dark circle group.

In this context, the objective of this study was to evaluate the skin and ocular tolerability and clinical efficacy of a cosmetic formulation containing vectorized caffeine, matrikines, NHS, chrysin, and tranexamic acid in reducing the appearance of infraorbital dark circles over 90 days of regular use.

2. Materials and Methods

Study Design

A prospective, monocentric, open-label clinical trial was conducted between October 2024 and January 2025 at an independent research institute, adhering to ethical guidelines (CAAE: 82158724.9.0000.5533).

Study Participants

Fifty women aged between 18 and 60 years, presenting infraorbital dark circles with a minimum score of 3 on a modified Griffiths clinical scale, were enrolled. Participants were distributed into two groups based on dark circle type: pigmentary (n=20) and vascular (n=23). Seven participants were excluded due to protocol deviations, yielding 43 valid cases.

Inclusion criteria included good general health, consent to refrain from other cosmetic treatments, and regular use of the investigational product. Exclusion criteria included pregnancy, dermatological conditions interfering with evaluations, or hypersensitivity to cosmetic ingredients.

Studied Formulation

The cosmetic serum containing 5% vectorized caffeine (bioavailable silicium and caffeine), 2% Pal-GHK and Pal-GQPR combined with NHS and chrysin, 1% tranexamic acid was developed.

Clinical Evaluation

The formulation was applied twice daily to the infraorbital region over cleansed skin.

Skin color in the infraorbital region was graded using a modified Griffiths 10-point clinical scale.

Instrumental Analysis

Skin assessments were performed with ANTERA 3D® (Miravex, Dublin, Ireland), measuring:

- Pigmentation score
- Redness score
- Volume elevation

Subjective Evaluation

Participants completed a self-assessment questionnaire at D30, D60, and D90.

Safety and Tolerability

Cutaneous and ophthalmological tolerability were evaluated by dermatologists and ophthalmologists at each visit.

Statistical Analysis

Normality was assessed using the Shapiro-Wilk test. Depending on data distribution, comparisons between timepoints were analyzed using paired Student's t-test or Wilcoxon signed-rank test. Statistical significance was set at $p<0.05$.

3. Results

Panel Characteristics

The final study population included 43 women with an average age of 40.4 years. Participants covered a range of Fitzpatrick phototypes (I to VI), with the majority classified as phototype IV. No significant demographic differences were noted between the pigmentary and vascular groups at baseline.

Clinical Evaluation

Clinical grading of infraorbital dark circles demonstrated statistically significant improvement over time (table 1).

Table 1. Clinical score changes over time (mean ± standard deviation)

Group	D0	D30	D60	D90	% Change D90 vs D0	p-value
Total Population (n=43)	5.30 ± 1.03	5.06 ± 1.08	4.56 ± 1.11	3.80 ± 1.12	-28.4%	<0.001
Pigmented Dark Circles (n=20)	5.30 ± 0.92	5.22 ± 1.04	4.63 ± 1.06	4.03 ± 1.01	-23.9%	<0.001
Vascular Dark Circles (n=23)	5.30 ± 1.13	4.91 ± 1.10	4.48 ± 1.16	3.57 ± 1.19	-32.7%	<0.001

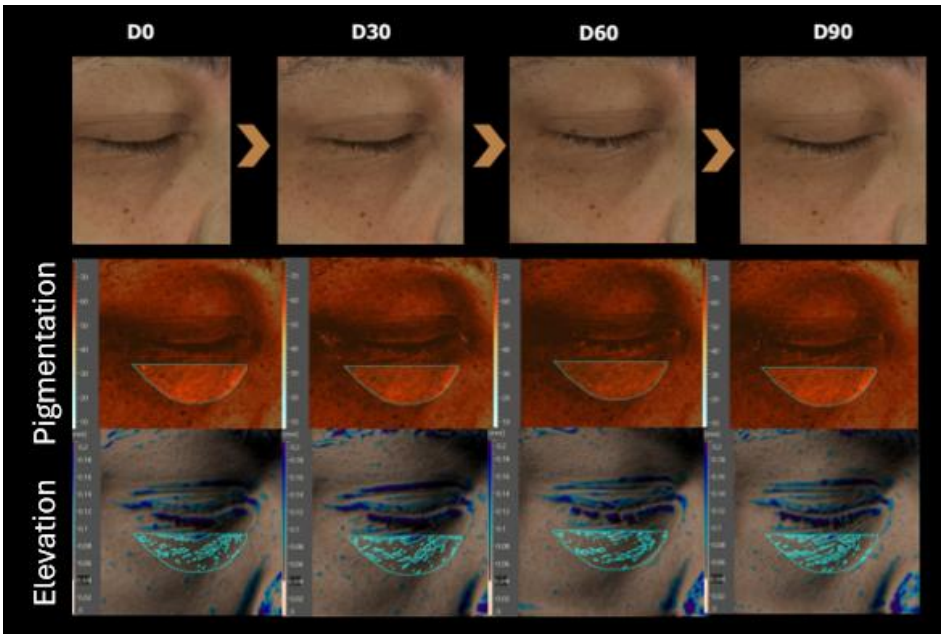
Significant reductions were already observed at D30 for vascular dark circles (-6,2%, $p=0.0391$) and at D60 for both groups (-14%, $p<0.001$). Improvement continued consistently through D90.

Instrumental Evaluation

Pigmentation Score (Pigmented Dark Circles)

Using ANTERA 3D®, a significant reduction in pigmentation was recorded at D30 compared to baseline (-7.17%, $p<0.05$). This reduction was maintained throughout D90, indicating the sustained effect of the formulation (figure 1).

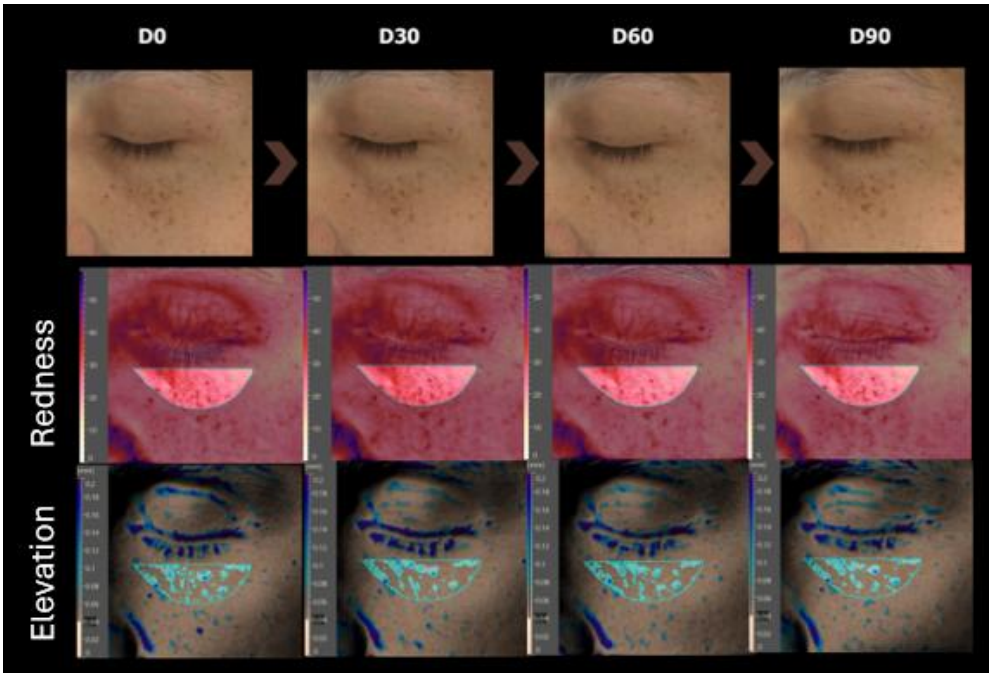
Figure 1: images of subject 031 captured using ANTERA 3D® showing the parameters evolution (pigmentation and volume/elevation) throughout 90 days of investigational product use.



Redness Score (Vascular Dark Circles)

In participants with vascular dark circles, redness score decreased significantly by D90 (-3.15%, $p<0.05$), corresponding with the clinical improvement noted (figure 2).

Figure 2: images of subject 018 captured using ANTERA 3D® showing the parameters evolution (redness and volume/elevation) throughout 90 days of investigational product use.



Volume Measurement

No significant variation in infraorbital volume (elevation) was detected during the study, suggesting that improvements were not linked to mechanical changes in skin thickness, but primarily to pigmentary and vascular improvements.

Subjective Evaluation

Self-assessment questionnaires revealed high satisfaction rates at D90:

- 93.02% of participants agreed their dark circles were less visible.
- 100% noted improved skin hydration.
- 95.35% observed healthier-looking skin.
- 79.07% noticed reduced puffiness and fine lines in the eye contour area.

Safety and Tolerability

No adverse dermatological or ocular events were reported during the study. Dermatological examinations at D30, D60, and D90 confirmed excellent tolerability. Participants reported high comfort during application with no sensations of burning, irritation, or discomfort.

4. Discussion

Infraorbital dark circles are multifactorial in origin, with dermal melanin deposition and vascular congestion being the primary etiologies [1–4]. Managing dark circles is challenging due to their varied causes and the delicate nature of periorbital skin. Therefore, effective cosmetic formulations must act on multiple pathways simultaneously.

The clinical and instrumental results of this study align with previous findings highlighting the efficacy of these actives individually [5–8], and importantly, demonstrate their enhanced effect when used synergistically in a combined formulation.

Significant improvements were observed in clinical grading scores, instrumental pigmentation and redness measurements, and participant self-assessments. These effects are attributed to the synergistic action of vectorized caffeine, matrikines, chrysin, N-hydroxysuccinimide, and tranexamic acid targeting the multiple mechanisms involved in dark circle formation.

Self-assessment results further support objective findings, with the majority of participants noting visible improvements in their dark circles, skin hydration, and overall eye contour appearance. Subjective perception is particularly important in cosmetic dermatology, where consumer satisfaction determines product success. Moreover, such satisfaction is also linked to treatment adherence, which is essential in treating aesthetic concerns such as dark circles.

In addition, excellent tolerability profile, with no adverse dermatological or ocular events reported, further supports its safe use for daily application in the periorbital area.

Finally, compared to previous clinical trials investigating topical approaches to dark circles [9,10], this study stands out by employing a multi-targeted active formulation validated by both instrumental and subjective methods over an extended period.

5. Conclusion

The developed formulation was considered safe on a daily use basis, reducing the intensity of dark and purplish infraorbital dark circles, whether of pigmentary or vascular origin, after 28 days of daily use.

In addition, the formulation showed excellent cutaneous and ocular tolerability over the 90-day period. No adverse events or irritation were reported, emphasizing its suitability for daily application on periorbital skin – which often presents a thinner stratum corneum.

In summary, these findings suggest that the investigational product represents a promising non-invasive alternative for individuals seeking to reduce the appearance of infraorbital dark circles, responding to a growing consumer demand for effective and well-tolerated skin care solutions.

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