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# A Randomized, Double-Blind, Placebo-Controlled Clinical Study to Evaluate the Efficacy and Safety of the "Noemi: Under Eye Cream" in Reducing the Appearance of Dark Circles, Puffiness, Fine Lines, Crow's Feet, Pigmentation, and Senescence

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**Abstract**

**Background**: Under eye concerns like dark circles, puffiness, fine lines, crow's feet and hyperpigmentation arise from factors such as genetics, aging, lack of sleep, dehydration, and environmental pollutants. Various treatments are available, including creams, serums, and surgeries, but their effectiveness and risks differ. Continued research is necessary to identify safe and effective solutions for these concerns. The objective of the study is to assess the efficacy and safety of 'Noemi: Under Eye Cream' in reducing the appearance of dark circles, puffiness, fine lines, crow's feet, pigmentation, and senescence. **Material & Methods:** Digital image analysis was used to measure dark circles, puffiness, fine lines, crow's feet, and pigmentation. The 6-point Fitzpatrick scale assessed darkness in the periorbital area. Improvement in overall skin senescence assessed by the Modified Fitzpatrick Wrinkle and Elastosis Scale. Safety assessment included monitoring of AEs and SAEs. **Results:** Significant reductions in dark circles, puffiness, fine lines, crow's feet, and pigmentation were observed in the test group compared to the control group. Results showed superior efficacy of the test product over the placebo including dark circles (96% Test vs. 20% Placebo), puffiness (88% Test vs. 16% Placebo), fine lines (92% Test vs. 28% Placebo), crow's feet (84% Test vs. 24% Placebo), and pigmentation (96% Test vs. 16% Placebo). No AE/SAEs were reported during the study. **Conclusion:** Study concluded that the Test product (Noemi under eye dark circle cream) showed better efficacy results with no linked AEs as compared to placebo group.

**Keywords**:- Dark Circles, Puffiness, Pigmentation and Fine lines.

## INTRODUCTION

Throughout cultures, societal perceptions are similar, in that periorbital dark circles contribute to a tired, aged and even sad appearance. On an average, a woman in the United States spends $15,000 (USD) in her lifetime on cosmeceuticals and makeup, a large percentage of which is spent on under-eye concealers.[1] This expenditure phenomenon is worldwide, as the global beauty industry has been projected to be valued at $390.07 billion (USD) by 2020, and the skin care segment is anticipated to be the fastest growing subcategory.[2] In view of the increasing importance ascribed to physical appearance in today's world, POH exerts a significant psychological impact on a person's quality of

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life, especially among young women, who might be perceived as sad, tired, or stressed due to dark circles. Hence, most people are willing to incur a substantial cost burden to conceal and manage POH.[3,4] The objective of this overview to get focus on cream used in under Eye Dark Circles, Puffiness, Fine Lines, Crow's Feet and Hyper Pigmentation by Noemi as unique C.A.K.E. which stand for vitamins, Vitamins : C as AA2G, A as Retinol, K as Menadione, E as Tocopherol, Coenzyme Q10, Astaxanthin, Hyaluronic Acid, Collagen 3 Peptides, L Carnosine. Vitamin C is effective in treating pigmentation as it contains ascorbic acid one of the potent ingredients to help reduce dark circles.[5] AA-2G has certain prospects to substitute L-AA for even wider application in food, medical care, cosmetic, etc. due to its superior properties as ascorbic acid derivatives. The strong resistance to light, heat and acid of AA-2G allows it to be less restricted in food processing. The stronger free radical scavenging ability in the long run allows AA-2G to show better antioxidant properties in the cosmetics field. The property of easy to release L-AA in vivo makes AA-2G a better choice in the healthcare field.[6] ALISTIN (of Exsymol, Monaco), and L-Carnosine help to clear cellular debris, due to glycation and oxidation, which helps to delay cellular senescence. AA2G significantly decreases the activity of senescence associated-β-galactosidase more effectively than L-AA,[6] also protects cells from UVB radiation by acting as a radical scavenger to reduce initial DNA damage,[7] it limits melanogenesis & is effective in the treatment of hyperpigmentation, melasmas and sunspots.[8] Coenzyme Q (10) (CoQ(10)) is a well-known antioxidant and has been used in many skincare products for anti-ageing purpose. However, the molecular mechanisms of CoQ(10) function in skin cells are not fully understood,[9] Coenzyme Q10 enhances dermal elastin expression and inhibits melanin synthesis,[9] a cutaneous antioxidant, with 10 fold higher levels in epidermis,[10] it topically prevents photoaging by reducing UV oxidation and wrinkle depth.[10] But Ascorbic Acid 2 Glucoside has outstanding thermal stability and releases Vitamin C in vivo. AA2G is resistant to oxidation, more effective and acts longer than plain Vitamin C. AA 2G is natural vitamin C stabilized with glucose, and was originally developed for use in cosmetic compounds. AA2G remains in the body longer than AA and showed evidence for less toxicity at high doses.[11,12,13] In Vitamin K decreases melanin synthesis through ERK activation Extracellular-signal-regulated kinase (ERK) and Retinol, an Anti-Wrinkle agent, is among the most effective Anti-Aging substances.[14,15] The knowledge about vitamin E effects is essential to guide its use in dermatological treatments, Vitamin E has antioxidant, photoprotective, moisturizing and anti-aging properties. It decreases expression lines, wrinkles, freckles and smoothens the skin.[16] The association of vitamin E and its derivatives with other ingredients increased the effectiveness of different dermocosmetic treatments.[17] Reduces Under Eye Puffiness: Topical Astaxanthin showed significant reduction of wrinkles and puffiness on the lower eye & cheeks (in 2 weeks).[17] Anti-wrinkle properties of retinoid[14] Promotes keratinocytes proliferation Reduces trans-epidermal water loss (TEWL) Protects collagen against degradation Inhibits metallo-proteinases (MMPs). There are number of methods both natural and medically prescribed that people use to get rid of, or lessen the appearance of, dark circles under their eyes.

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Although not all of these treatments are permanent, with maintenance and consistency they will help reduce the appearance of dark circles but here are some major actives reduce or cover the appearance of dark circles, puffiness, fine lines, Crow's Feet and Hyper Pigmentation under the eyes are Coenzyme Q10, Vitamin K, Astaxanthin, Retinol, Vitamin E, Ascorbic Acid 2 Glucoside, Sodium Hyaluronate, Peptide Collagen Type 3, L- Carnosine. This cream is free from Sulphates, Parabens, Phthalates, Alcohol, and Synthetic Colours & Fragrances.

## MATERIAL AND METHODS

This was a randomized, double-blind, placebo-controlled clinical study to assess the efficacy and safety of the dark circle cream in reducing the appearance of dark circles, puffiness, fine lines, crow's feet, pigmentation, and senescence in adult subjects, as well as to evaluate the safety of the cream in the study population. The study population was randomized in two groups. 1. Test group and 2. control group (placebo cream was given) and it was conducted by qualified Investigator at single centre in India and it was approved by the local Ethics Committee and written informed consent was obtained from all adult participants. The study was conducted in accordance with the Declaration of Helsinki. This study was consisted of 50 subjects, out of 50, 32 female and 18 male subjects aged 25-65 years with visible signs of dark circles, puffiness, fine lines, crow's feet, pigmentation, and senescence around the eyes. The potential subjects were screened as per the inclusion and exclusion criteria only after obtaining written informed consent from the subjects.

All 50 enrolled subjects were prescribed and allotted test product on baseline visit and subjects were instructed to apply the cream from day 01 to end of visit. Subjects were instructed to apply approximately 0.5 g of cream around the eyes, twice daily (morning and evening), and using gentle circular motions until the cream fully absorbed. Subjects were followed up on visit 3, 4 and 5. A complete physical examination was performed at screening visit. At subsequent visits, only partial physical examination was done. There were total of 5 visits in this study - Visit 01: Screening Visit (Within 30 Days Prior to Day 1), Visit 02: Baseline (Day 01), Visit 03: Evaluation Phase 1 (Day 30 ± 2 Days), Visit 04: Evaluation Phase 2 (Day 60 ± 2 Days), Visit 05: Evaluation Phase 3 and End of Study (Day 90 ± 2 Days). Each evaluation phase consisted physical examination of the participants and capturing digital images.

The study evaluated the effectiveness of the test product on various skin parameters, including puffiness, fine lines, crow's feet, pigmentation, and senescence, through digital image analysis. Images of the periorbital area were captured using a DSLR camera equipped with a macro lens and ring light under standardized lighting conditions and camera settings. The digital image analysis software quantified the degree of darkness in the periorbital area, and a trained dermatologist reviewed each image to confirm the presence or absence of dark circles.

At baseline and the end of the study period, participants were evaluated for changes in the severity of dark circles, puffiness, fine lines, crow's feet and pigmentation over the different scales like Fitzpatrick scale, Allergan fine line scale and digital image analysis. By assessing the change over these 5 parameters, trained dermatologist calculated the number of the

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participants those marked the improvement. Skin senescence was evaluated through Fitzpatrick Wrinkle and Elastosis Scale. The evaluations were performed by the same trained dermatologist who reviewed the images. The results showed a significant improvement in all parameters, indicating the effectiveness of the test product in improving skin quality. The digital image analysis proved to be a reliable and accurate method for evaluating the changes in skin parameters, making it a useful tool for future studies in the field of dermatology.

## RESULTS

A total 50 participants (25 with dark circles and 25 without) were enrolled in this study, 32 female and 18 male subjects aged 25-65 years. Participants were instructed to avoid using any topical products around the eye area for 24 hours prior to imaging with and received/apply at least one dose of study product and were included in the safety population. The images were then analysed using a digital image analysis software that quantified the degree of darkness in the periorbital area. Additionally, to ensure the accuracy of the digital image analysis, each image was reviewed by a trained dermatologist who confirmed the presence or absence of dark circles. The dermatologist was blinded to the treatment status of the participants during image review. The study was conducted as a randomized, double-blind, placebo-controlled trial. Participants with dark circles were randomly assigned to receive either the treatment cream or a placebo cream. The treatment group received the cream formulated with active ingredients, while the placebo group received a cream without active ingredients. The creams were applied to the periorbital area twice daily for 12 weeks. Participants were instructed to avoid using any other topical products in the periorbital area during the study period. Statistical analysis was performed using SPSS software.

### Efficacy Endpoints

The reduction in the appearance of dark circles was measured by digital image analysis. The degree of darkness in the periorbital area was measured using a 6-point Fitzpatrick scale by a dermatologist.

Puffiness around the eyes was measured through digital image analysis by using a software program to quantify the degree of swelling in the periorbital area.

The images were uploaded to the software program, which uses algorithms to analyze the pixel intensity and colour of the area to quantify the degree of swelling. Through these results, dermatologist assessed the reduction in puffiness. Reduction in the appearance of fine lines and crow's feet as measured by digital image analysis and dermatologist used Allergan Fine line scale to assess the reduction in the fine lines and crow’s feet.

Change in control group and test group were assessed over these parameters. Through these parameters, the number of benefitted subjects were analysed in order of visits.

[Table 1 and Figure 1], clearly represent that there was a significant reduction in dark circles, puffiness, fine lines, crow’s feet and pigmentation with respect to control group. At the end of the study visit more than 84% subject displayed reduction over each parameter in

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Test group. The results represented a visible reduction in test group with respect to the placebo over the parameter of dark circle (96% Test vs 20% Placebo), puffiness (88% Test vs 16% Placebo), Fine Lines (92% Test vs28% Placebo), Crow's Feet (84% Test vs 24% Placebo) and Pigmentation (96% Test vs 16% Placebo).

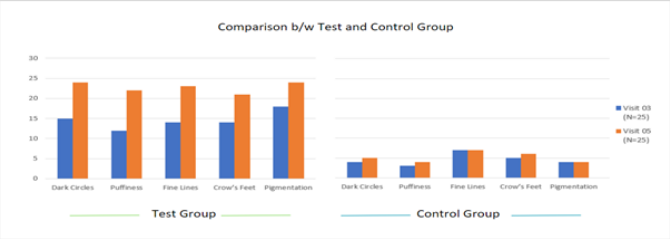


**Figure 1:** Comparison between Test and control group over different parameters.

Improvement in overall skin senescence was assessed via Fitzpatrick Wrinkle and Elastosis Scale which is a 4-point grading scale ranges from 0 to 3, with 0 indicating no wrinkles or elastosis and 3 indicating severe wrinkles and elastosis. Here, improvement in skin senescence from baseline to end of the study visit was analysed through comparing the average scale for test and placebo product.

It is clearly visible through figure 02 and table 02 that nominal change in the control group condition while test group condition improved from 2.4 (Moderate wrinkles and/or elastosis < 2.4 < Severe wrinkles and/or elastosis) to 1.5 (Mild wrinkles and/or elastosis < 1.5 < Moderate wrinkles and/or elastosis).

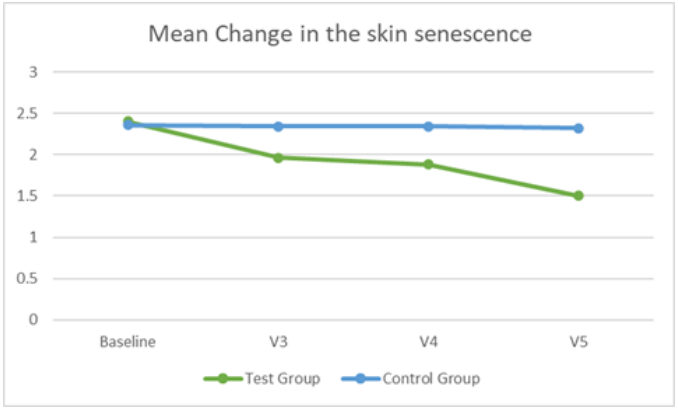


**Figure 2:** Mean change in the skin senescence over the Fitzpatrick Wrinkle and Elastosis Scale

Safety Endpoint:

There was no Adverse event reported during the study conduct. Also, No Serious adverse event/ death was reported.

**Table 1:** Comparison between Test and control group over different parameters

| | Control Group | | | Test Group | | |
|---|---|---|---|---|---|---|
| **Parameter** | **Visit 03 (N=25)** | **Visit 05 (N=25)** | **Reduction in Symptoms from baseline to EOS visit (%)** | **Visit 03 (N=25)** | **Visit 05 (N=25)** | **Reduction in Symptoms from baseline to EOS visit (%)** |
| Dark Circles | 4 | 5 | 20% | 15 | 24 | 96% |
| Puffiness | 3 | 4 | 16% | 12 | 22 | 88% |
| Fine Lines | 7 | 7 | 28% | 14 | 23 | 92% |
| Crow's Feet | 5 | 6 | 24% | 14 | 21 | 84% |
| Pigmentation | 4 | 4 | 16% | 18 | 24 | 96% |

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**Table 2:** Mean change in the skin senescence over the Fitzpatrick Wrinkle and Elastosis Scale

| | **Baseline** | **V3** | **V4** | **V5** |
|---|---|---|---|---|
| Test Group | 2.4 | 1.96 | 1.88 | 1.5 |
| Control Group | 2.36 | 2.34 | 2.34 | 2.32 |

## CONCLUSIONS & DISCUSSION

The problem of under-eye dark circles, puffiness, fine lines, crow's feet, pigmentation, and senescence is a common concern among individuals. These issues not only affect one's physical appearance but can also have a negative impact on their self-esteem and overall well-being.

Currently, there are various treatments available for these concerns, such as topical creams, fillers, lasers, and surgery. However, each of these treatments comes with its own set of limitations and potential risks. Topical creams may not provide significant improvement, fillers and surgery can be invasive and expensive, and lasers may cause skin damage.

Therefore, this study aims to evaluate the efficacy and safety of a newly developed dark circle cream that claims to address multiple under-eye concerns, including dark circles, puffiness, fine lines, crow's feet, pigmentation, and senescence. The results of the study demonstrated a statistically significant improvement in all efficacy endpoints, including dark circles, puffiness, fine lines, crow's feet, pigmentation, and senescence. Participants using the cream showed a significant reduction in the severity of dark circles and puffiness, as well as a reduction in the appearance of fine lines, crow's feet, and pigmentation with no AE and SAE. In addition, the cream was found to improve the overall appearance of skin by reducing senescence. These results suggest that the cream is a promising solution for addressing multiple signs of aging and skin discoloration.

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