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## ***“Preserving and/or restoring the facial and neck beauty in aged panelists”***

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### **1. Introduction**

Two most recognizable indicators of beauty are the shape of the face and the appearance of the neck, which strongly influence perceptions of age, gender, and attractiveness [1]. In women, a well-defined oval facial contour and a smooth, wrinkle-free neck are widely regarded as signs of youth, attractiveness and beauty [2].

However, these regions undergo significant morphological changes with age, primarily due to skin laxity, loss of firmness, and structural weakening [3]. These alterations lead to a less defined jawline and increased sagging in the lower face and neck, contributing to an aged appearance. While invasive aesthetic procedures such as dermal fillers are commonly used to restore facial contours, there is growing interest in effective non-invasive alternatives [4].

In this study, we investigated the cosmetic efficacy of a topically applied miniprotein as a non-invasive strategy to preserve or restore key aesthetic features of the face and neck in an aging population. The objective was to assess its impact on facial contour and skin firmness using a comprehensive set of clinical, instrumental, and 3D imaging evaluations.

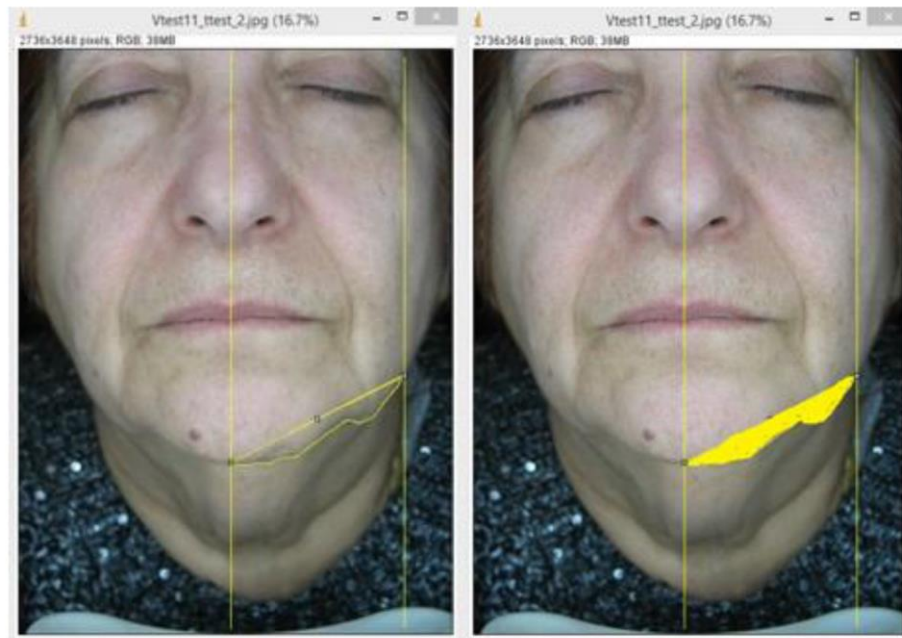
### **2. Materials and Methods**

A double-blind, randomized placebo-controlled, split-face clinical trial was conducted on 33 healthy Caucasian women aged between 49 to 71 years old (mean age 60.9 year old). The study protocol was approved by an independent Ethics Committee. Prior written informed consent was obtained from all subjects, and the study was performed following the Declaration of Helsinki (1964) and its subsequent amendments and the COLIPA Guidelines for the Evaluation of the Efficacy of Cosmetic Products. The study was conducted according to Good Clinical Practice Guidelines and general principles of Law 46/2004 of August 19.

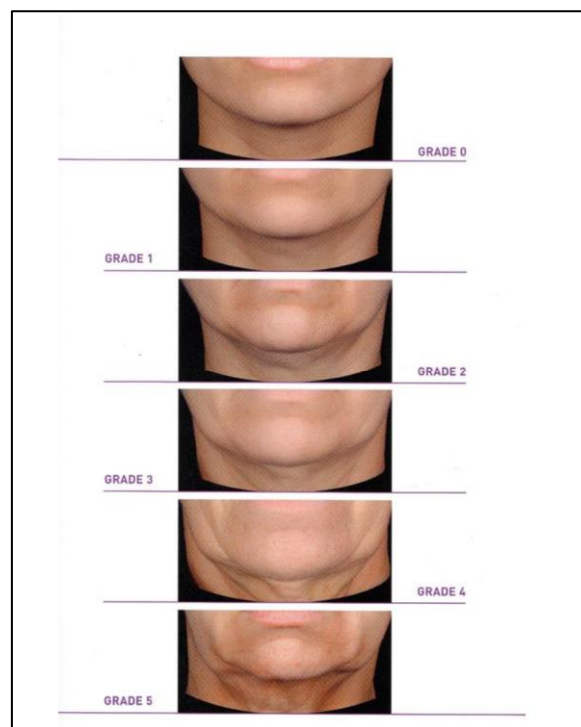
Only panelists presenting with facial sagging scores greater than 3 on the Bazin and Doublet scale were enrolled [5]. The oval face improvement parameter was assessed on the jawline through macrophotographs taken with Visioface® 1000 D (Courage+Khazaka electronic GmbH, Germany) and subsequent analyses using an image analysis software (ImageJ), to determine the area of the neck/submandibular triangle (Figure 1). The measurements were

done before (D0), after 14 (D14), 28 (D28) and 56 (D56) consecutive days of products' twice-daily application,

Visual clinical grading of facial sagging is performed by an expert using a recognized visual scoring scale (Figure 2)



**Figure 1:** Photo and Image analysis of jawline and under the chin area allowing the measurement of facial sagging area parameter (yellow area).



**Figure 2:** Clinical grading used to assess facial sagging. Jawline volume deficiency scale according to Bazin, Roland and Doublet, Eric, Skin Aging Atlas, Volume 1: Caucasian Type. Med'Com (2007) [5].

In addition, to validate that the results of oval shape improvement are not due to a loss of weight effect, we recorded the Body Mass index (BMI) at each time point of the study (baseline, D14, D28 and D56).

Then, to provide, illustrative pictures of the oval face improvement and neck area, we used 3D image illustrations (Lifeviz Mini).

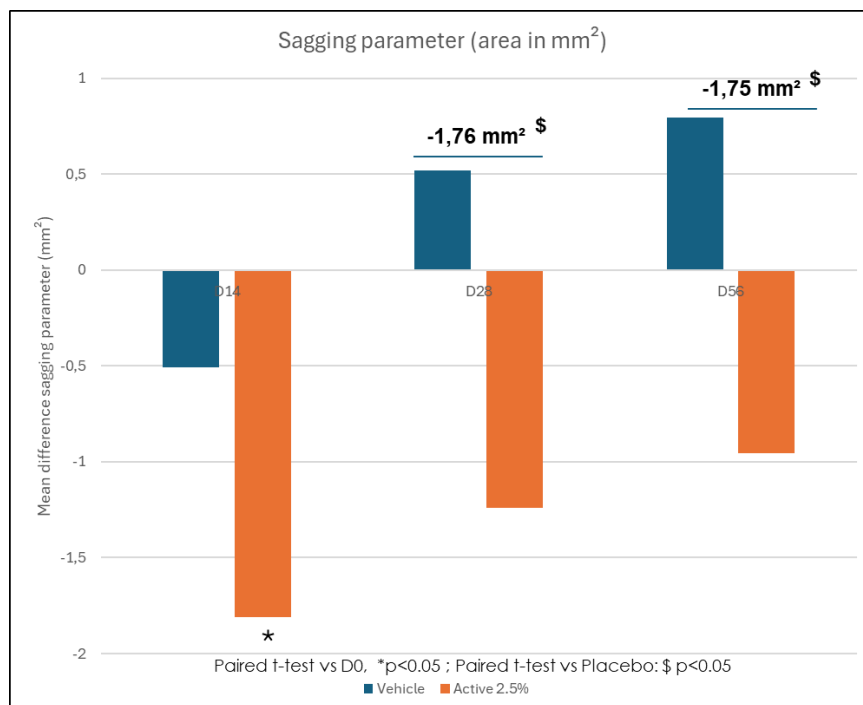
The biomechanical properties of the skin were determined by the measurement of skin stiffness parameter with EasyStiff® device (Biomeca, france) along the cheek of both hemifaces [6]. Because the neck area is difficult to measure using devices like the Cutometer® or Easys-tiff®, efficacy in this region was assessed using 3D imaging.

Data were analyzed using paired statistical methods, as each subject served as her own control in this split-face design. Comparisons between the treated and placebo sides were performed using paired t-tests or Wilcoxon signed-rank tests, depending on data distribution. A p-value < 0.05 was considered statistically significant. All analyses were conducted using standard statistical software.

### 3. Results

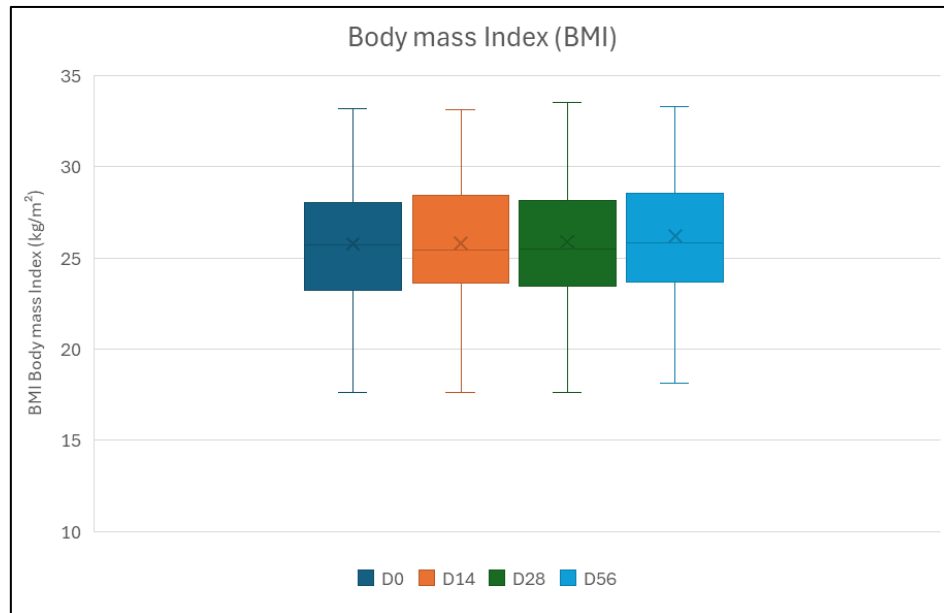
#### 3.1 Improvement of facial sagging

In the figure 3, we can observe that the active ingredient demonstrates a marked effect as early as day 14, with its efficacy reaching a plateau by day 28, as no further improvement is observed at day 56. In contrast, the changes observed in the vehicle group over time are not statistically significant.



**Figure 3:** Facial sagging area parameter variation at D14, D28 and D56 (yellow area). Statistical analysis was performed using a paired *t*-test. (n=33 panelists)

As facial sagging can be influenced by weight loss, BMI was monitored throughout the study. which BMI showed no significant changes over time (Figure 4), confirming that changes in facial sagging could be linked to the treatments.



**Figure 4:** Evaluation of BMI stability across study time points. (n=33 panelists)

As shown in Figure 5, 3D surface modeling of the lower face demonstrates a noticeable reshaping effect following treatment with the Active 2.5% formulation compared to the Vehicle. The overlay masks (grey: baseline; white: post-treatment) clearly illustrate the reduction in surface area, particularly along the jawline, supporting the efficacy of the miniprotein in improving facial contours.



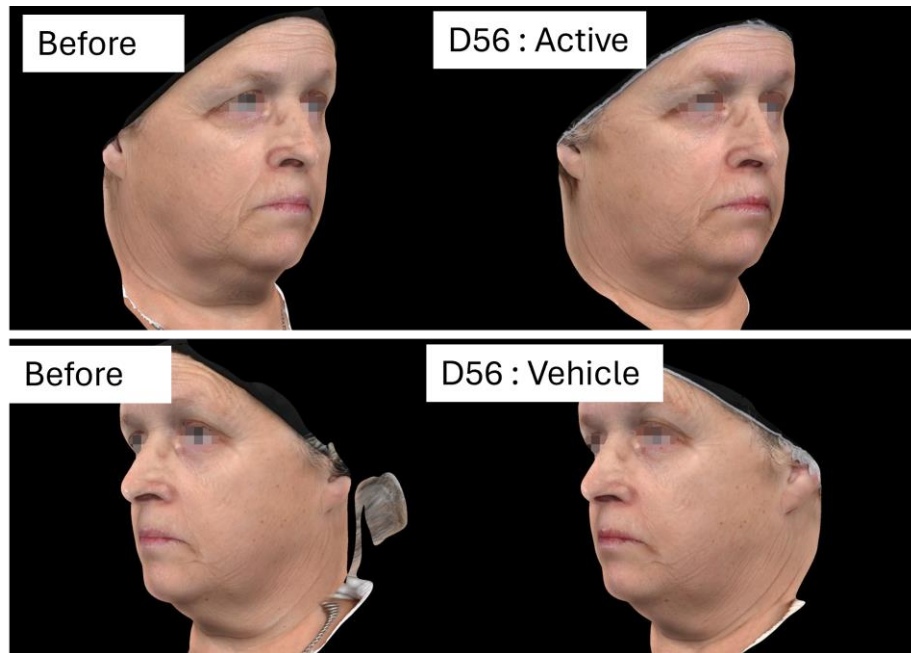
**Figure 5 :** Oval face surface modelling after treatment with Active 2.5% versus Vehicle. Representative images and 3D reconstructions done with Lifevize Mini device illustrating the reduction of the lower face area following application of Active 2.5% compared to Vehicle. Grey and white overlay masks illustrate the facial contours before and after treatment, respectively, highlighting a visible reshaping effect, particularly in the jawline area.

Clinical grading of jawline volume deficiency showed that after two months of miniprotein application, the percentage of hemifaces with no increase in the assigned score was higher in the active group compared to the placebo (85% vs 75%). Additionally, the percentage of hemifaces that maintained their baseline score was greater in the active group (39% vs 31%). These findings confirm the miniprotein's efficacy in counteracting age-related facial changes.

### 3.2 Representative Case: Improvement of Neck and Lower Face Area in a 61-Year-Old Subject

In the area treated with Active 2.5% (top row), a clear improvement was observed in the neck and jawline region after 56 days of application in a 61-year-old subject. The skin appeared smoother and firmer, with a noticeable reduction in sagging beneath the chin and along the mandibular contour. Conversely, the vehicle-treated side (bottom row) showed persistent skin laxity and folds, with no significant improvement in the neck profile or jawline definition over time.

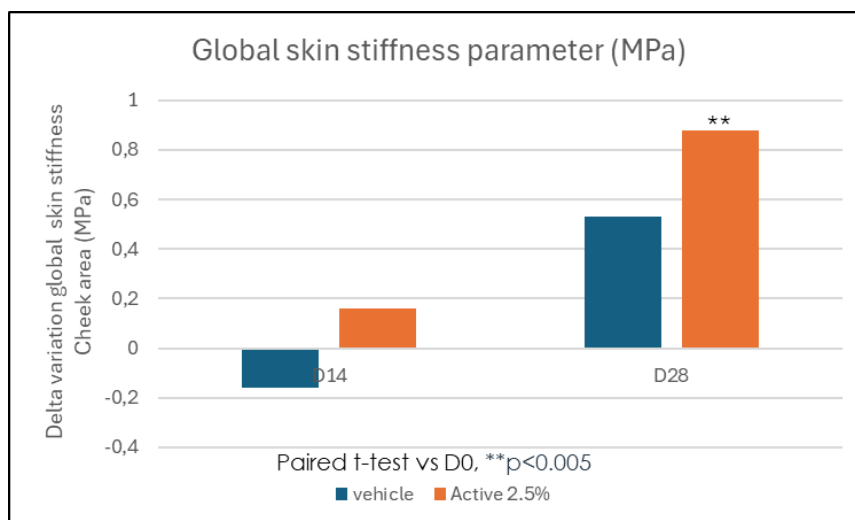
These 3D visualizations, captured using the LifeViz® Mini system, support the efficacy of the active in improving facial and neck firmness, particularly in aged skin.



**Figure 6:** 3D imaging of the lower face and neck in a 61-year-old subject before and after 56 days of treatment. Side views acquired with the LifeViz® Mini system, comparing the effects of Active 2.5% (top) and Vehicle (bottom). The active-treated side exhibits visible improvements in skin firmness, reduced sagging and improved neck area. The vehicle-treated side shows no noticeable changes.

### 3.3. Improvement of skin facial biomechanical properties

In the figure 7, the results show that the skin stiffness in the cheek area is significantly increased after 28 days of treatment with the active ingredient, whereas no changes were observed in the vehicle-treated group.





**Figure 7:** Variation in skin stiffness in the cheek area after 14 and 28 days of treatment.

The results are expressed as the difference of the mean skin stiffness values measured using the EasyStiff device on the cheek at Day 14 and Day 28 following application of Active 2.5% and Vehicle. A significant increase in stiffness is observed with the active at Day 28, while no notable change is detected in the vehicle-treated group. Statistical analysis was performed using a paired *t*-test. (n=33 panelists).

#### 4. Discussion

Facial contour, particularly the definition of the lower face and neck, plays a crucial role in the perception of beauty and youthfulness in women. With age, structural changes such as loss of firmness, skin sagging, and reduced tissue support lead to a less defined jawline and the appearance of a heavier lower face. These modifications are often among the earliest and most visible signs of aging, directly impacting self-perceived attractiveness and prompting cosmetic intervention.

In this study, we evaluated the efficacy of a topical cosmetic active ingredient, a miniprotein with rejuvenative properties, applied in a randomized split-face design, focusing on its ability to improve the oval of the face and neck region. A combination of quantitative surface analyses, clinical grading, skin stiffness measurements, and 3D photographic imaging allowed for a comprehensive and multi-dimensional assessment of efficacy. Our results demonstrate that the active ingredient significantly improved the firmness and contour of the lower face and neck after 56 days of application. 3D imaging revealed a visible reshaping effect in the jawline region and lower face. These effects were absent in the vehicle-treated area, further supporting the specific efficacy of the active ingredient. Notably, the increased skin stiffness observed in the cheek area at Day 28 is consistent with the visual and structural improvements in the lower face, suggesting enhanced dermal support as a key mechanism.

Importantly, this study also highlights the relevance of targeted and active cosmetic treatments for refining facial contours. By enhancing firmness and redefining the facial oval and neck contour, the active contributes to a more harmonious and youthful appearance—an essential aspect of perceived female beauty.

#### 5. Conclusion

This study demonstrates the clinical efficacy of a cosmetic miniprotein active ingredient with rejuvenative properties in improving the contour and firmness of the lower face and neck in women. Through a combination of clinical grading, instrumental measurements, and 3D imaging, we observed significant improvements in skin stiffness and facial reshaping on the active-treated side, particularly in the jawline and lower face areas. By restoring firmness and redefining the oval of the face and neck, the active contributes to a more youthful and aesthetically pleasing appearance an essential component of perceived beauty. These findings support the use of targeted topical formulations as effective, non-invasive strategies to address visible signs of aging and enhance facial harmony.

## References

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