

A multi-center, double-blind, split-face placebo-controlled study to evaluate the effects of filtrate of the Secretion of the *Cryptomphalus Aspersa* (SCA) on photoaged skin – **WHITE PAPER**

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This multi-center, double-blind, split-face, placebo-controlled study evaluated the safety and efficacy of a proprietary anti-photoaging topical product containing the secretion of the snail *Cryptomphalus aspersa* compared to a vehicle placebo. Investigator and patient evaluations were performed after twelve weeks of twice-daily application. Results showed a statistically significant improvement in the appearance of crow's feet on the active ingredient side when compared to the vehicle side. There was also some indication of efficacy for improving the appearance of minor facial wrinkling as well as textural abnormalities. Subjective patient evaluations also showed benefit.

Introduction

Growth factors (GFs) are chemical messengers that regulate specific cellular activities such as cell proliferation, chemotaxis, and formation of the extracellular matrix.[Babu] They may be derived from a variety of sources including humans, animals, and microbes as well as yeast and plants.[Bonin-Debs] Topical growth factors have emerged as a therapeutic modality readily harnessed for aesthetic and medical uses. As our understanding of the mechanisms of action behind these powerful GF compounds increases, so does our ability to fully apply the benefits associated with these mechanisms in the clinical setting.

While there is documentation that growth factors derived from human sources (HGFs) provide some benefit in wound healing and repair of photodamage, there are also concerns of potential deleterious side effects.[Liu, Lazar-Molnar, Draelos] Increased angiogenesis secondary to excessive vascular endothelial growth factor (VEGF) exposure may be a fundamental step in the transition of benign tumors to a malignant state. Furthermore, various melanomas have been shown to carry receptors for growth factors such as VEGF.

Because of these concerns, scientists have long considered non-human sources for GFs. One successfully-yoked *animal* derived GF, the secretion of the snail *Cryptomphalus aspersa* (SCA), was discovered by Abad Iglesias, M.D. This biologically active glycosaminoglycan secretion is generated by the snail during times of stress. The secretion is composed of a combination of contributions from the snail's mucous, salivary as well as proteic glands. SCA stimulates biochemical, structural and functional processes and can regenerate damaged structures of the animal's skin in less than 48 hours. Figure 1 reveals SCA-related anatomy.

SCA has since been processed into a topical product with anti-photoaging effects (Tensage, Biopelle, Inc, Ferndale, MI). Through a patented process, snails are stimulated and their secretions are collected. These secretions are then filtered for purity and tested for consistency. Of note, snails are not harmed during this process.

Results of an initial, pilot, non-randomized, open-label study using SCA for the treatment of cutaneous photoaging [Tribo-Boixareu, et al, 2009] were promising. Sallowiness decreased by 50% within the first 30 days of SCA use and by more than 75% by day 90. Significant ($p < 0.05$) reduction was noted in fine lines, deep wrinkles, as well as elasticity; dryness and roughness resolved in all patients by day 90 as well. Improvement in collagen was reflected in a softening of coarse lines and wrinkles as well as a global improvement/reduction of wrinkles, and improvement in skin texture. Outcomes suggested increases in hyaluronic acid content. Improved skin tone and elasticity suggested beneficial effects of SCA on elastin fibers. Biopsy results showed a reduction of solar elastosis through improved elastin quality following 90 days of SCA application, a result which is significant in itself. Investigators concluded that twice daily

application of SCA would yield continued improvement in all parameters assessed during the study, and that these results served as adequate preliminary evidence supporting the benefits of regular use.

Patients and Methods

In response to these findings and subsequent conclusions, an investigation was designed using a similar protocol. Subjects (n=26, all women between 35-65 years old, Fitzpatrick skin types II & III) presenting with facial photoaging, including demonstrable wrinkling of periocular and perioral skin, were enrolled in the study (13 subjects at each of our two study sites). Exclusion criteria included unwillingness to avoid excessive sunlight or wear protective clothing and sunscreen, unwillingness to forego any other topical dermatological or drug therapy (including corticosteroids) on the face, as well as use of AHAs, BHAs, retinoids, or Vitamins C or D containing topicals within 30 days prior to as well as throughout the course of the study.

The washout periods adhered to by subjects in this study included the following: six months free from dermabrasion, deep chemical peels, ablative laser treatments, neurotoxin or filler injections, and cosmetic surgery; three months free from non-ablative laser, light (including IPL) or radiofrequency treatments; and one month free from microdermabrasion as well as light and medium depth chemical peels.

Each subject's treatment regimen included daily morning application of cleanser followed by randomized, double-blind, split-face application of SCA 8% cream (vehicle/placebo and active). Sunscreen was applied as well. The nighttime regimen included cleanser as well as randomized, double-blind, split-face application of SCA 40% serum (vehicle/placebo and active). This regimen was maintained for 12 weeks.

In addition to subjective patient evaluations of facial skin and adverse events, investigator assessments were conducted at baseline (day 0) as well as at weeks 8 and 12. Additional investigator assessments were performed at week 14, two weeks after discontinuation of product use. Evaluations included digital imaging, silicone molding, and 3D imaging. Independent evaluations were performed by David Goldberg, M.D., Vivian Bucay, M.D., and Michael Gold, M.D.

Results and Discussion

All enrolled subjects completed the study; data analysis is now complete. Assessments from independent evaluators showed a significant improvement of active side versus placebo side and are summarized in Table 1. Silicone impression data analysis showed a slight improvement for fine lines ($p < 0.10$) and a moderate improvement for wrinkles ($p < 0.05$). Vehicle-active differential is moderate, but overall improvement is significant. Significant differences were noted between sites; the importance/relevance of these site-specific differences is uncertain.

Investigator Analysis

Silicone impressions showed obvious improvement. For coarse crow's feet lines, 77% of subjects improved overall. Differences in improvement with respect to a decrease in the number of lines when the active side was compared to the placebo side were consistent and significant ($p < .05$). Improvement was noted on the active side with respect to overall luminance as well as to decreases in the breadth and depth of wrinkles ($p < .10$), while the placebo side showed no improvement. For minor wrinkles, 50% of subjects demonstrated a global improvement, with a 10% greater overall improvement of the active side compared to that of the placebo side. Reduction in the number as well as the length of fine lines was greater on the placebo side; this likely reflects the effect that simple moisturization has on fine lines and minor wrinkles. Figure 2 shows before and after photographs of silicone impressions taken from areas of minor wrinkles. Overall wrinkle reduction in terms of number of wrinkles as determined by investigator analysis is shown in Figure 3. The results of patient evaluations are delineated in Table 2.

Conclusion

On both the active as well as the vehicle side, patients showed significant overall improvement in wrinkling and photodamage after daily application of SCA active as well as vehicle/placebo preparations. Results showed statistically significant improvement of crow's feet on the active ingredient (SCA) side, with some indication of efficacy for minor wrinkling and textural improvements as well. Patient satisfaction ratings were high, with 83% of subjects noting that they would recommend the product to others. Tables and Figures

Table 1. Percentage Improvement of Periorcular and Perioral Areas at Weeks 8, 12, and 14*

	Week 8		Week 12		Week 14	
	Periorcular	Perioral	Periorcular	Perioral	Periorcular	Perioral
Active	56	45	53	45	48	39
Placebo	15	8	14	8	9	4

* Approximated percentage improvement from baseline averaged between the three independent evaluators.

Table 2. Results of Subjective Patient Evaluations*

Improvement Category	Evaluation at	
	Week 8	Week 12
Lines	39	52
Elasticity	30	48
Texture	52	52
Hydration	52	57
Overall Appearance	47	44
Would Recommend	83	83

*Expressed as percentage improvement from baseline.

Figure 1. The anatomy of the snail *Cryptomphalus aspersa* (SCA)

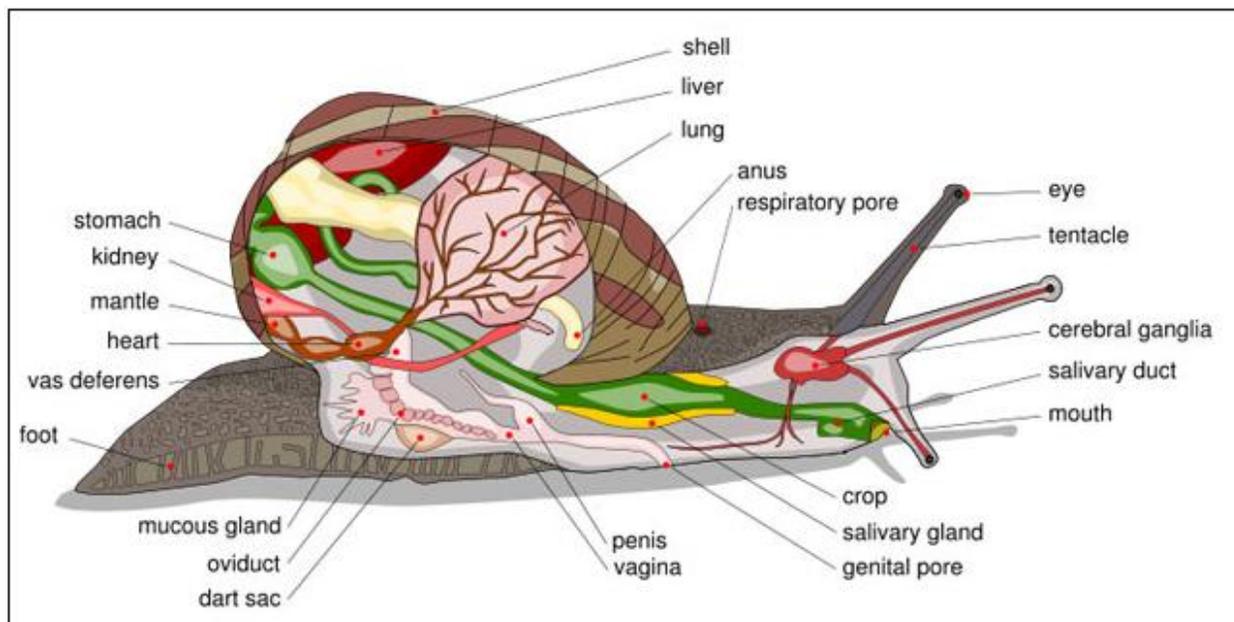


Figure 4. Caucasian female at baseline (left) and 12 weeks (right). Right side of the face is active. Photos courtesy of Mitchel P.Goldman, M.D.



Figure 5. Active Side Caucasian female at baseline (left) and 12 weeks (right). Photos courtesy of Mitchel P.Goldman, M.D.



Figure 6. Caucasian female at baseline (left) and 12 weeks (right). Left side of the face is active. Photos courtesy of Joel L. Cohen, M.D.



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