

Growth Factors: harnessing healing power, from restoration to rejuvenation

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Abstract— Since the Nobel Prize-winning discovery of nerve growth factor (NGF) and epidermal growth factor (EGF) in 1986, scientists and physicians alike have sought to understand and apply the physiological benefits of growth factors. In both tissue remodeling and systemic restoration, strides have been made in this regard. While the activity of growth factors and other elements of the cell secretome in response to acute wound damage are becoming increasingly well known, it remains a novelty to many that similar principles of repair can be employed for the sake of cosmeceutical rejuvenation. Within this domain, topical serums containing an intricate balance of growth factors, cytokines and other peptides have proven effective in reversing the signs of extrinsic aging. Perhaps the most effective of these serums include those engineered and patented (U.S. Pat. 8,518,819) by AQ Skin Solutions.

Index Terms— Growth Factors (GF), aging skin, skin rejuvenation, wound healing

1 INTRODUCTION

Multiple steps have been made in order to arrive at the formulation of a cell-free therapeutic for skin rejuvenation. First and foremost, before the technology could be applied to aesthetics, an affirmation of the efficacy of specific fibroblast cell-conditioned media as opposed to stem cells themselves was wanting.) Repeatedly, it was found that application of such media, containing the host of molecules—growth factors and cytokines, most notably—secreted from fibroblast cells, proved as effective in wound healing as a transplantation of such stem cells (1) These results are consistent with the reports of Chimenti et al., which indicate the preeminence of paracrine activity for cell therapies (2,3). This being the case, the benefits provided by cell-free therapy make it preferable over mere transplantation. While transplanted stem cells can be limited by variability in survival, localization, and differentiation, the application of fibroblast conditioned media exerts its regenerative force independent of any such limitations (2); after all, it is the secretome which is responsible for stimulating recruitment of endogenous cells, which include free roaming stem and progenitor cells, that activate the healing pathway and promote building of the extracellular matrix, regardless of the presence of original cells at the site. Furthermore, the topical applicability of growth factor serums (4) presents a practical advantage.

Beyond the clinical application of growth factors for wound healing, the efficacy of such treatments for skin rejuvenation has been affirmed in multiple studies (5). Considering that conventional rejuvenating therapies such as lasers and certain topicals operate by creating a mild wound of sorts, and thus effecting

the natural wound healing response, it is unsurprising that an application of serums or conditioned media containing growth factors would help accelerate the regenerative process when used as a supplement (6). What is striking, however, is the efficacy of topical growth factor serums in the absence of any flagrant skin barrier insult. Despite the fact that the stratum corneum is generally impenetrable to most molecules greater than 500Da, these growth factors and cytokines (on the order of 15,000Da) seem to provide an exception, as penetration is evident; while a handful of explanations have been proposed, the mechanism allowing this penetration is as yet unknown. Interestingly, there is enough biochemical correspondence between the effects of skin aging and those of wound formation to invite one to inquire as to the potential correspondences in recovery from such insults (4). While photo aging or oxidative damage may cause a decrease in fibroblast number and function within the dermis leading to degeneration of collagen sufficient for visible aging, such subtle, continuous, insults to the cells' health may fall below detection of the metaphorical radar of the inflammatory response, a prerequisite for eventual re-epithelialization (4). This being the case, it would follow that the use of topical growth factors would assist in rejuvenation; it would be as if the age damage were a sort of wound which, while requiring the same therapy for healing as a gaping sore, was unable to be treated without an external indication that such a process were in order; in the case of growth factor application, the subsequent activation and proliferation of fibroblasts would serve to alert the senescent cells to their pseudo-wounded state, thus allowing the body's own healing potential to be unleashed and used for rejuvenation. Surely,

this would account for the significant regeneration expressed in individuals treated with topical growth factors for wrinkles, discoloration, roughness, and other unsightly cosmetic concerns, though further experimentation is required in order to grasp the underlying pathway. Nevertheless, in proper concentration and ratio, growth factors have been shown to drastically improve the health of the skin (4).

As the body works synergistically and systematically, so too must an approach to rejuvenation, seeking to harness the innate power of its healing pathways, be engineered with similarly synergistic principles in mind. For this reason, a patented proprietary mixture of cytokines and human growth factors has proven exceptional in delivering the desired rejuvenation across the board (U.S. Pat. 8,518,879).

2 PROCEDURE

2.1 Subjects Chosen for the study

Males and females between 30 to 78 years of age of good general health not nursing or pregnant with demonstrable fine or deep wrinkles in the face, including around both eyes, at least barely visible dark areas, and at least slightly coarse and grainy lower eyelids.

2.2 Subjects that were not included

Subjects with any active or any history of skin disease affecting the face area or under the eyes were not included. In addition, subjects were asked to stop their current regime of using any products that may enhance skin condition and aid in reduction of wrinkles. Make-up and sunscreens were permitted. Subjects, who have undergone cosmetic surgery affecting facial skin within 6 months, were also excluded from the study.

2.3 Treatment regimen

AQ Active Serum and AQ Eye Serum (AQ Skin Solutions, Inc., Mission Viejo, CA) containing the patented proprietary mixture of cytokine and growth factors were applied in mornings and evenings to the facial skin, including the peri-orbital skin area over a period of six weeks (42 days). Subjects were asked to document each application of AQ Active and Eye Serums.

2.4 Evaluation at baseline and after 6 weeks

Subjects were evaluated by:

Clinical assessment:

- Clinical photography under standardized conditions.
- Where available, the VISIA-CR imaging system (Canfield Scientific, Inc., Fairfield, NJ) was used
- Clinical assessment of skin quality, including

Table 1: Clinical scores for quality of skin

Clinical evaluation	Scores
Texture	1-10
Wrinkles	1-10
Fine-lines	1-10
firmness	1-10

1= no improvement (lowest possible score)

2-9= different degrees of improvement

10= great improvement (highest possible score)

the peri-orbital skin using 1- to 10-point visual scoring system given in Table 1

3 RESULTS

The present study demonstrated that AQ Active Serum and AQ Eye serum (AQ Skin Solutions, Inc., Mission Viejo, CA), containing a proprietary mixture of human growth factors and cytokines combined with antioxidant factors is safe and efficacious for facial skin rejuvenation in cases of mild to moderate skin aging. The serum's efficacy, excellent tolerability, including the delicate periorbital skin area, and ease of use and pleasant sensory properties of the product explain why a large majority (98%) would continue regular use of AQ Active Serum.

Eighty-one subjects were enrolled in this study. Of this number of subjects enrolled, seventy-nine subjects averaged 52 ± 9 years of age (between 30 to 78 years) completed the study. Two subjects dropped out of the study for product unrelated reasons. Results were tabulated using scores generated by the clinical evaluations (**Figure 1**) and subject questionnaire (**Figure 2**). All results showed a statistical significant of $p= 0.05$. All subjects (100%) reported to have

tolerated the skin serum well. All subjects (100%) liked the way the skin serum felt, while 98% would continue its regular use after the six weeks study period. Improvement is shown as difference between the averaged score before (baseline) and the averaged score after treatment expressed in percentages of the averaged baseline score and includes all seventy-nine subjects completing the study.

In conjunction with this study, a comparison study was performed, comparing AQ Active Serum to other products of similar properties or claim similar properties. This study will serve two purposes, to show how effective AQ Active Serum compared to other products in the market and secondly, be used as a negative control for the study in addition to using a placebo (Figure 3). In addition, subjects were asked to evaluate the AQ Active Serum in terms of quantity per bottle, quality of serum, fragrance, re-order and overall satisfaction (Figure 4).

FIGURE 1

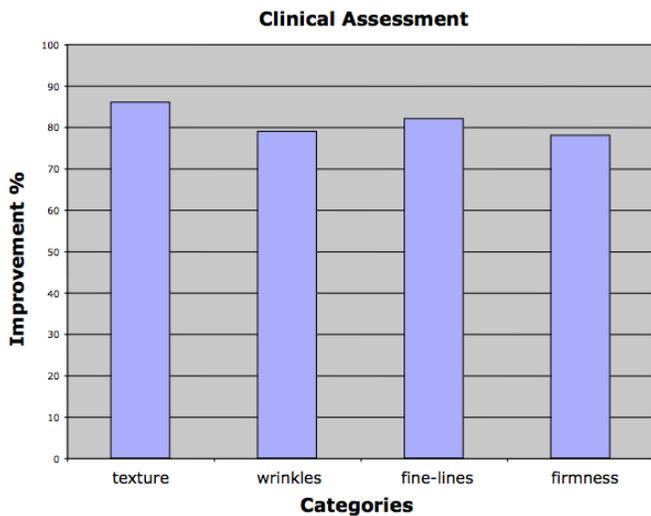
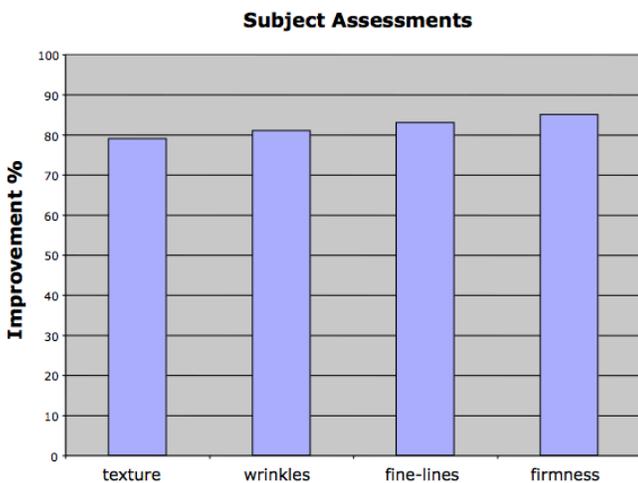


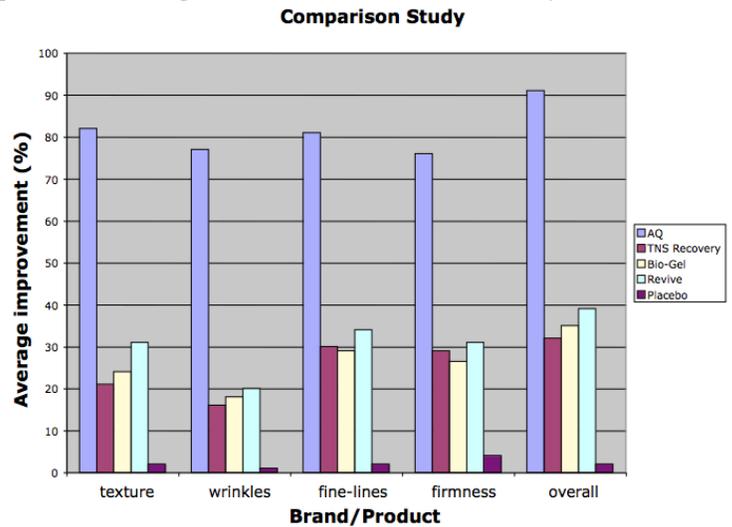
FIGURE 2



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FIGURE 3

The cosmetic benefits of this well balance combination of growth factor serum is evident in the case study example shown in figure 5 which shows rapid visible improvement of fine line around the eye and periorbital region. In addition, facial rejuvenation



and healing has also been observed in a case study of one subject with chronic acne demonstrated in figure 6 over a course of 6 weeks with use of growth factor serums of the AQ Recovery and AQ Active Serum (AQ Skin Solutions, Inc., Mission Viejo, CA) in combination with micro-needling. In terms of clinical benefits, the topical application of growth factor serum to a skin wound improves the healing time and leads to the closure to even a non-healing wound as shown in Figure 7.

FIGURE 4

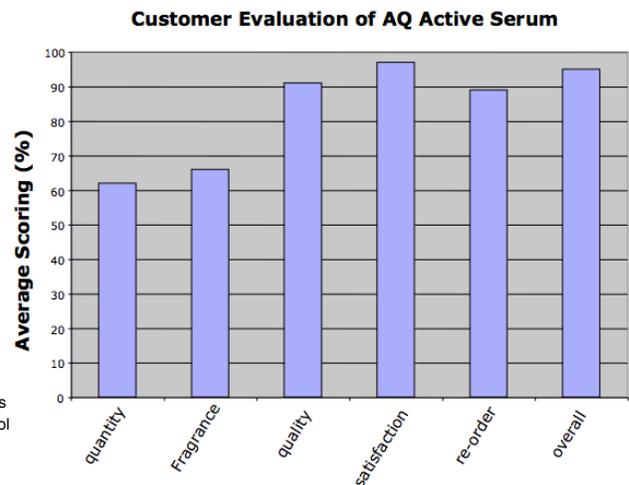


FIGURE 5



FIGURE 6



FIGURE 7



4 CONCLUSION

This study, with regular topical application of the

growth factor serum helps to restore and rejuvenate facial skin from fine lines to skin texture. Observed clinical improvement over the length of the study for all measures and data were collected. The results from the application of the growth factor serum shown in Figure 1 and 2 of the clinical and subject assessments indicates that a physiological balance combination of growth factors and cytokines with selected antioxidants produces an overall dermal resurfacing and regeneration of either aging or damaged skin.

Growth factors and cytokines have in past research shown to improve healing times in skin wounds by promoting the activation and proliferation of fibroblasts cells and also production and distribution of collagen and elastin. It is through these and the regulation of essential cellular activities that are most likely to account for the observed improvements in skin wrinkles, fine line, texture, and appearance.

Overall, the human skin is remarkable. As the body's largest organ, its role in homeostasis is imperative, and its corresponding potential for healing and regeneration is impressive. As the mysteries behind the pertinent mechanisms are investigated and understood, such breakthroughs in regenerative medicine as the use of growth factor-induced therapy will continue to change the face of vitality and health.

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