

ORIGINAL CONTRIBUTION

Tripeptide/Hexapeptide Topical in Esthetics: Evidence behind the Skincare Formulation

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ABSTRACT

The skincare market, which is projected to be worth over \$180 billion by 2024, has experienced a recent rise in formulations utilizing peptides. These products have been marketed to consumers as offering many esthetic benefits. We review the literature for a tripeptide and hexapeptide formulation that has been shown to offer improved healing and clinical outcomes in conjunction with resurfacing and cryolipolysis, as well as demonstrating benefit for cutaneous rejuvenation. (*SKINmed*. 2021;19:116–119)

The extracellular matrix (ECM) is an important structural component of the skin that is heavily involved in both cutaneous aging and wound repair. Changes to the ECM can contribute to factors related to aging. This includes a decreased ability to remove collagen fragments secondary to non-enzymatic cross-linkages between collagen and elastin, reactive oxygen species, and neutrophil elastase damage.¹ There are also conformational changes to fibroblast structure caused by fewer focal adhesion points between fibroblasts and collagen that render fibroblasts less active.

Particular tripeptides and hexapeptides are matrikines, which are ECM protein fragments that have several effects on the ECM. These promote the clearance of unwanted protein fragments by increasing matrix metalloproteinase (MMP) production, reducing oxidative stress, reducing the MMP-1 destruction of normal collagen fragments, promoting optimal function of fibroblasts, and improving function of the proteasome system to remove damaged protein fragments.² These changes can prepare the ECM for neocollagenesis and improved healing.

While the skincare market has seen a recent rise in peptide formulations, it is not uncommon for products to be marketed to consumers with exaggerated claims. Few peptide-based skincare products have scientific studies supporting them that are made readily available. Products utilizing a novel tripeptide/hexapeptide (TriHex Technology; Alastin Skincare, Carlsbad, CA) formulation have evidence demonstrating their

clinical utility. Here, we review and evaluate the current available literature.

RESURFACING AND TIGHTENING

Topical formulations containing TriHex Technology have been studied in conjunction with laser and radiofrequency (RF) microneedling treatments. The purpose of these procedures is to create microtrauma and thermal denaturation to the skin in order to promote new collagen and elastin formation; however, these procedures have variable downtime and side effects, such as temporary erythema, edema, and roughness. By preparing the ECM for optimal wound healing, these formulations have been shown to reduce downtime and improve overall outcomes from these procedures.

A recent study compared a topical regimen containing TriHex Technology to a basic topical regimen for reducing the side effects and improving the results of non-ablative thulium-doped resurfacing of the face and neck.³ In this split-face randomized controlled trial, 10 subjects were instructed to use either regimen on half of the face and décolleté twice daily for 2 weeks prior to laser treatment. Participants then continued the split-face regimen for another 2 weeks following the procedure. Results were evaluated by blinded investigators on days 2, 4, and 14. By day 4 post-procedure, blinded investigators rated improvements in texture and Global Skin Quality as significantly higher for the TriHex regimen. Additionally, patients reported subjective improvements

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in the look and feel of their skin. These results continued to be statistically significant at day 14. This study demonstrates that TriHex Technology can improve healing after laser resurfacing.

Another study evaluated the use of a TriHex-containing regimen to a basic “standard of care” regimen as an adjunct to ablative fractional laser resurfacing.⁴ In this randomized study, 15 women were instructed to use either skincare regimen twice daily for 3 weeks prior to laser treatment. For 10 days following fractionated CO₂ laser treatment, participants were instructed to do vinegar soaks every 2 hours when awake if exudate was present and to apply either the TriHex-containing product or the dimethicone-based ointment. After day 10, patients resumed the pre-procedural protocol for skin care. Within the first 1 and 2 weeks following treatment, the TriHex-treated participants demonstrated less erythema and exudation, and less tenderness and burning/stinging, respectively. Each of these reached significance on day 3. Blinded investigator healing assessments at day 7 showed significantly improved healing in the TriHex arm. On days 28 and 84 post-treatment, this group also reported significantly greater improvements in skin tone, youthfulness, brightness, and overall confidence in the appearance of their skin; however, subject and blinded investigator assessments did not report a statistically significant difference in the appearance of fine lines and wrinkles on days 28 or 84 between the regimens. Overall, the TriHex-treated group enjoyed greater satisfaction, reduced duration of side effects, and improved early healing, which could reduce the immediate healing downtime for patients.

Hybrid lasers combine ablative and non-ablative modalities to provide resurfacing, while minimizing the risks and side effects attributed to fully ablative laser treatments. A study evaluated a TriHex gel when combined with hybrid laser treatment.⁵ In this split-face trial, five patients were randomly assigned to apply either a TriHex gel or generic cream to each side of the face twice daily for 2 weeks pre-procedure. Patients were instructed to continue applying the gel to the assigned side for 7 days post-procedure. Physician blinded assessment showed that the side treated with the TriHex gel had decreased redness and roughness in the week following the procedure. Patient satisfaction was greater for this side as well.

TriHex Technology has also been studied as an adjunct to RF microneedling.⁶ In a recent study, 10 participants were instructed to use a TriHex topical twice daily for 2 weeks prior to and 1 week following RF microneedling of the neck. After 1 week post-treatment, subjects were instructed to switch products to another TriHex-containing product designed specifically for the neck twice daily for the remainder of the observation period. Subject and investigator assessments were completed at 3, 7, 30, and 90 days. Investigator ratings at 90 days were significant for improved tone, visual smoothness, texture, blotchiness, and overall appearance in all subjects. Subjects also reported a brief duration of tolerable side effects, including post-procedural burning and tingling. In our own practice, we have also found TriHex Technology to improve the clinical results and post-procedural downtime associated with RF microneedling treatments (Figures 1 and 2).

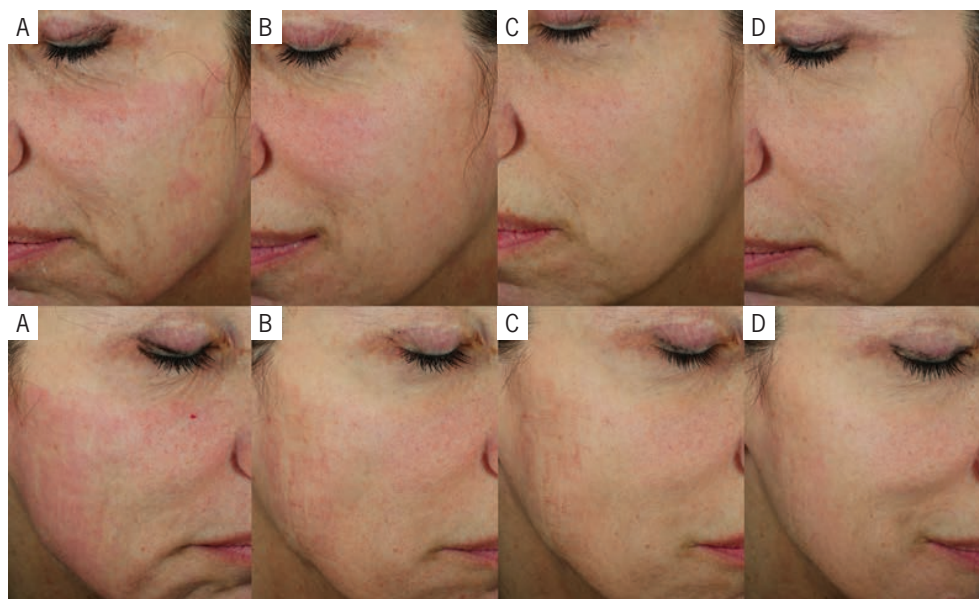


Figure 1. Female subject following radiofrequency microneedling at (A) immediate post, (B) 2 days post, (C) 5 days post, and (D) 7 days post treatment, with use of Alastin Regenerating Skin Nectar (top) demonstrating improved and hastened recovery with less track marking, erythema, and dyspigmentation compared to control (bottom). Courtesy of Jordan V Wang, MD, MBE, MBA and Roy Geronemus, MD.

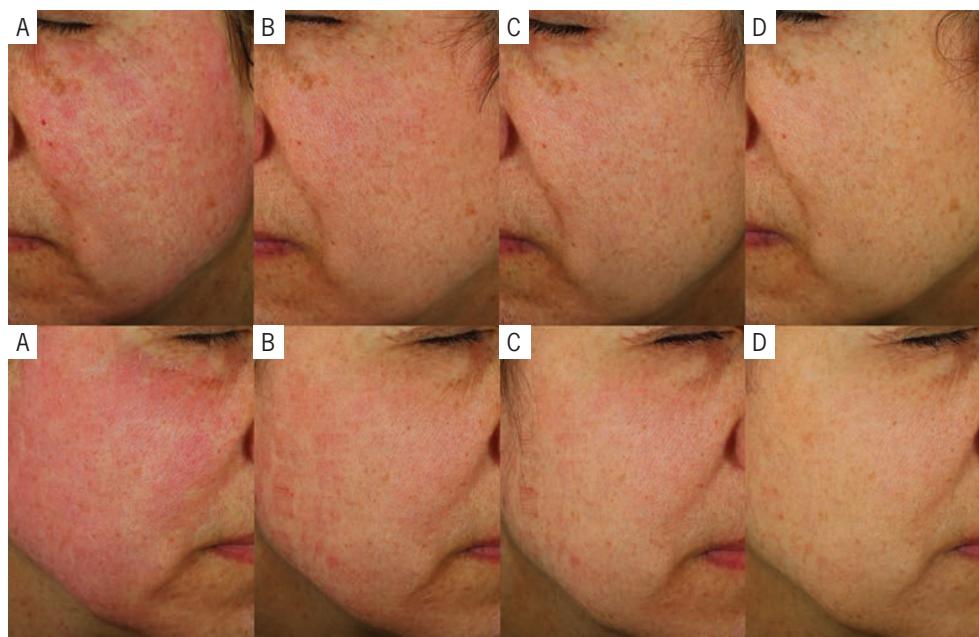


Figure 2. Female subject following radiofrequency microneedling at (A) immediate post, (B) 2 days post, (C) 4 days post, and (D) 7 days post treatment, with use of Alastin Regenerating Skin Nectar (top) demonstrating improved and hastened recovery with less track marking, erythema, and dyspigmentation compared to control (bottom). Courtesy of Jordan V Wang, MD, MBE, MBA and Roy Geronemus, MD.

CRYOLIPOLYSIS

While the exact mechanisms behind cryolipolysis are still being investigated, it is thought to be due to cold-induced programmed cell death, crystallization, and ischemic necrosis.⁷ Regardless of the mechanism, once the adipocyte is damaged, there is a release of triglycerides, which triggers local inflammation and tumor necrosis factor (TNF)-alpha induced activation of macrophages. These macrophages are subsequently responsible for clearing the lipid particles; however, these particles can be large and difficult to phagocytose, with clearance occurring over the course of several months.⁸ Three months is typically the time frame when patients can expect the majority of fat loss, but effects have been shown to continue further out.⁹ Topical applications are able to have an effect on subcutaneous fat through absorption to the base of hair follicles, which can allow for communication with the subcutaneous fat.⁷ Matrikines may have a role in clearing these lipid particles from the ECM to allow for enhanced cryolipolysis treatments.

A double-blind randomized controlled trial compared a topical TriHex preparation to a bland emollient in combination with cryolipolysis.¹⁰ In this study, 11 patients received cryolipolysis to both arms and were assigned to use either the TriHex topical or bland emollient twice daily to each arm for 24 weeks post-procedure. Results were evaluated by blinded investigator and

computer software. Both methods of evaluation demonstrated significantly increased fat reduction on the TriHex-treated arm. The most significant effects were seen at week 8, which showed fat reduction of the TriHex-treated arm that was equivalent to that of the emollient-treated side at 12 weeks. These results suggest that TriHex Technology has utility in cryolipolysis procedures.

TOPICAL REJUVENATION

TriHex topical formulations have also been studied as standalone treatment for rejuvenation. In a recent study, a TriHex-containing facial regimen was evaluated for its ability to improve mild to moderate wrinkles and skin sagging of the face in 22 women.¹¹ The facial regimen was utilized for 12 weeks. By week 12, clinical evaluation showed significant improvements in fine lines, skin sagging, radiance, firmness, and plumpness in all parameters studied. 3D imaging technology also confirmed the significant reduction in length, width, and depth of wrinkles. A skin biopsy was taken from five subjects on weeks 8 and 12. Results at week 12 showed improvements in solar elastosis, corneocyte layer strength/function, neocollagenesis, and epidermal thickening. For four of the samples, there was an increase in elastin fibers.

Another study evaluated the use of a TriHex-containing eye cream for periocular skin rejuvenation in 10 subjects.¹² The

topical was applied twice daily for 12 weeks. Results were evaluated at 1, 2, and 3 months by a facial plastic surgeon and subject questionnaire. There were significant improvements in lines/crow's feet (41% reduction), under eye hollowing (29% reduction), and dark circles (39% reduction) seen over the course of the study. All subjects noted improved appearance of the periocular skin.

CONCLUSIONS

Topical skincare treatments containing peptides have demonstrated diverse utility in the world of esthetics. When used alone or in combination with cosmetic procedures, current clinical and histologic studies show that TriHex Technology has demonstrated efficacy. While additional larger studies are still needed, this is a step in the right direction for an industry characterized by marketing claims that often outpace our current understanding. In the skincare market, which is projected to be worth over \$180 billion by 2024, it is important for manufacturers to have readily available studies. Consumer education should remain a cornerstone in the field.

DISCLOSURE

Nazanin Saedi is a consultant for Alastin Skincare. The authors have no other relevant conflicts of interest to declare.

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VINTAGE LABEL

CAUTION: Avoid habitual use. Do not use in case of acute abdominal pain, nausea and vomiting which may be indicative of appendicitis.