

# A randomized, single-blinded trial of a tripeptide/hexapeptide healing regimen following laser resurfacing of the face

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## Summary

**Background:** A topical healing system containing a combination of active ingredients including a tripeptide and hexapeptide (TriHex Technology™) has been found to stimulate ne elastogenesis and neocollagenesis.

**Objective:** Evaluate the use of the tripeptide/hexapeptide topical system following fractionated CO<sub>2</sub> laser resurfacing compared to a bland ointment and cream.

**Patients/Methods:** In this single-blinded, randomized study, 15 female subjects aged 45-70 years underwent laser resurfacing of the face. Subjects were randomized to use of the tripeptide/hexapeptide system (n=10) or a bland dimethicone-based ointment and petrolatum-based cream (n=5) from 3 weeks pre- until 12 weeks post-procedure. A blinded investigator graded erythema, edema, crusting, exudation, and healing on postprocedure days 1, 3, 4, 7, 28, and 84. A photodamage/wrinkle scale was completed on days 28 and 84. Subjects performed symptomatology grading on days 1 through 14 and completed self-assessments at days 28 and 84.

**Results:** Data from 14 subjects were analyzed. Blinded-investigator-rated healing was better for the tripeptide/hexapeptide system, reaching statistical significance at day 7. The tripeptide/hexapeptide group demonstrated less erythema and exudation during the first postprocedure week, reaching significance at day 3. On days 1 through 14, subjects using the tripeptide/hexapeptide system reported less tenderness and burning/stinging, also reaching significance on day 3. At day 84, subjects using the tripeptide/hexapeptide system reported higher satisfaction and were more likely to recommend the treatment to others.

**Conclusion:** Postresurfacing use of a tripeptide/hexapeptide system proved effective and well-tolerated. Subject satisfaction was greater among those using this system, which may indicate an improved patient experience following laser resurfacing.

## KEYWORDS

esthetic medicine, laser treatments, topical therapy, wound healing

## 1 | INTRODUCTION

Intrinsic and extrinsic aging results in the accumulation of collagen and elastin protein fragments within the dermal extracellular matrix (ECM). Healthy young skin is able to utilize proteolytic mechanisms to repair this damage, prevent accumulation of protein fragments, and blunt the effects of photoaging.<sup>1</sup> However, as skin ages, these

compensatory mechanisms begin to fail and extrinsic methods of skin rejuvenation such as laser resurfacing become more important for improving the appearance of skin rhytides, texture, and pigmentation. Although modern fractional ablative CO<sub>2</sub> lasers have decreased healing time and cause less pain, erythema, and dyspigmentation than traditional fully ablative lasers, the recovery time required after laser resurfacing remains a primary patient concern.

A healing system containing a tripeptide and hexapeptide (TriHex Technology™, Alastin Procedure Enhancement Invasive System, ALASTIN Skincare, Inc., Carlsbad, CA, USA) is a kit that includes a cleanser, a healing gel, occlusive ointment, moisturizing cream, and sunscreen. This system utilizes an innovative peptide technology designed to promote ECM remodeling before and after procedures, improving skin responsiveness to treatment and minimizing postprocedure adverse effects. The gel and cream incorporate the tripeptide and hexapeptide to stimulate the production of tropoelastin and procollagen resulting in neoelastogenesis and neocollagenesis.<sup>2</sup> The tripeptide/hexapeptide system also exhibits antioxidant properties to decrease inflammation and irritation to promote an accelerated epidermal healing process.<sup>3</sup> The tripeptide/hexapeptide healing system may, therefore, shorten the downtime and decrease symptoms following laser resurfacing of the face, thereby improving patient experience. The ability of the healing system to stimulate neocollagenesis and elastogenesis may further act to improve overall skin quality and augment the results of laser resurfacing.<sup>4,5</sup>

The primary objective of this study was to evaluate the efficacy of this new tripeptide/hexapeptide topical healing system in accelerating wound healing and improving skin quality following our laser resurfacing regimen which includes the use of an intense pulsed light (IPL) and/or pulsed dye laser (PDL) with 755-nm quality-switched (QS) alexandrite, followed by 10 600-nm fractionated carbon dioxide (CO<sub>2</sub>) laser resurfacing of the face compared to our practice's standard of care which consists of a bland dimethicone-based ointment (Vaniply™, Pharmaceutical Specialties, Inc., Rochester, MN, USA) for 10 days postprocedure followed by a petrolatum-based cream (Vanicream™, Pharmaceutical Specialties, Inc., Rochester, MN, USA). Secondary objectives included examination of safety and subject improvement, satisfaction, and experience.

## 2 | MATERIALS AND METHODS

### 2.1 | Study design

This was an investigator-blinded, randomized clinical study comparing the tripeptide/hexapeptide topical healing system to a bland ointment and petrolatum-based cream after laser resurfacing. All subjects underwent treatment with an IPL and/or PDL for erythema, as well as a QS alexandrite laser to individual lentigines, immediately followed by a fractionated CO<sub>2</sub> laser resurfacing to the entire face (Fraxel; Solta Medical Inc., Hayward, CA, USA) plus or minus the 2940-nm erbium laser (Sciton Profile Contour Tunable Resurfacing Laser [TRL], Sciton, Inc., Palo Alto, CA, USA) periocularly. Subjects were assessed on postprocedure days 1, 3, 4, 7, 28, and 84.

This study was performed in accordance with the principles of the Declaration of Helsinki and was approved by an independent Institutional Review Board prior to initiation.

### 2.2 | Materials

The tripeptide/hexapeptide topical healing system included a gel containing the TriHex technology (Regenerating Skin Nectar™ with

TriHex Technology™), a healing ointment (Soothe+Protect Recovery Balm, ALASTIN Skincare, Inc.), a moisturizer containing the TriHex technology (Ultra Nourishing Moisturizer with TriHex Technology™), sunscreen (Alastin Broad Spectrum SPF 30+), and a gentle cleanser (Alastin Gentle Cleanser). The standard-of-care regimen consisted of a dimethicone-based ointment (Vaniply™), a petrolatum-based cream (Vanicream™), SPF 30+ sunscreen (Alastin Broad Spectrum SPF 30+), and a gentle cleanser (CeraVe® Foaming Facial Cleanser, Valeant Pharmaceuticals North America, Bridgewater, NJ, USA).

The tripeptide/hexapeptide gel used in this study contains cyclopentasiloxane, dimethicone cross-polymer, pentaerythrityl tetra-isostearate, heptyl undecylenate, glycin soja (soybean) oil, panthenyl triacetate, palmitoyl hexapeptide-12, palmitoyl tripeptide-1, naringenin, Arnica montana extract, Eunaliella salina extract, disteardimonium hectorite, tocopherol, squalane, caprylic/capric triglyceride, stearammonium hectorite, and propylene carbonate. The ointment contains petrolatum, microcrystalline wax, Physalis angulata extract, caprylic/capric triglyceride, Butyrospermum parkii (shea butter) extract, bisabolol, and tocopherol. The tripeptide/hexapeptide moisturizer contains Water/Aqua/Eau, Caprylic/Capric Triglyceride, Caprylyl Methicone, Glycerin, Cetearyl Alcohol, Dimethicone, Glyceryl Oleate Citrate, Glyceryl Stearate, Potassium Olivoyl Hydrolyzed Oat Protein, Palmitoyl Tripeptide-1, Palmitoyl Hexapeptide-12, Helianthus Annuus (Sunflower) Extract, Avena Sativa (Oat) Kernel Extract, Tremella Fuciformis Sporocarp Extract, Oryza Sativa (Rice) Bran Extract, Rosmarinus Officinalis (Rosemary) Leaf Extract, Phospholipids, Betaine Bisabolol, Linoleic Acid, Tocopherol, Glyceryl Oleate, Caprylyl Glycol, Glycine Soja (Soybean) Sterols, Disodium EDTA, Polyacrylate-13, Polyisobutene, Polysorbate 20, Caprylhydroxamic Acid, Ethylhexylglycerin, Phenoxyethanol.

The bland ointment used in this study contains dimethicone 1%, C30-45 alkyl methicone, C30-45 olefin, hydrogenated polydecene, microcrystalline wax, polyethylene, and silica dimethyl silylate, while the moisturizer contains purified water, white petrolatum, propylene glycol, cetearyl alcohol, sorbitol solution, cetareth-20, simethicone, glyceryl monostearate, polyethylene glycol monostearate, sorbic acid, and BHT.

### 2.3 | Subjects

Fifteen healthy female subjects aged 45-70 years with Fitzpatrick skin types I-III and moderate to severe photodamage were enrolled in the study. All subjects provided written informed consent, as well as photographic release. Subjects were not compensated for their participation.

Exclusion criteria included treatment with any energy device to the face within 6 months, tanning within 7 days or expectation of tanning, dermabrasion or chemical peel within 3 months, use of systemic retinoids within the past year, pregnancy or lactation, and a history of hypertrophic scarring or keloids. Subjects must not have used systemic steroids or topical tretinoin within 3 months. Subjects must also not have had any topical products containing alpha-hydroxy acids, salicylic acid, and vitamins C or E (including derivatives thereof) on the face within 14 days prior to the study period.

## 2.4 | Intervention

Beginning 3 weeks prior to the laser procedure, subjects randomized to the tripeptide/hexapeptide arm washed their faces twice daily with the gentle cleanser followed by twice daily application of the tripeptide/hexapeptide gel, tripeptide/hexapeptide moisturizer, and SPF 30+ sunscreen. The group randomized to the practice's "standard of care" washed their faces twice daily with the gentle cleanser followed by twice daily application of the petrolatum-based moisturizer and SPF 30+ sunscreen.

Immediately prior to laser treatment, topical anesthesia (23% lidocaine/7% tetracaine ointment) was applied for 30 minutes. Intravenous conscious sedation and local nerve blocks were performed as needed. Subjects then underwent treatment with the IPL and/or PDL with QS alexandrite laser, followed by fractionated CO<sub>2</sub> laser resurfacing to the full face. Following the procedure, the randomized topical product was applied to the face by a nonblinded study coordinator with sterile gloves.

On postprocedure days 1 through 10, subjects were instructed to perform vinegar soaks every 2 hours while awake as long as exudate was present. Those randomized to the tripeptide/hexapeptide arm used the tripeptide/hexapeptide gel and ointment after each soak. The standard-of-care group used a dimethicone-based ointment every 2 hours after each soak. At day 10, subjects discontinued the use of the ointment in each arm. The group randomized to the tripeptide/hexapeptide arm washed their faces twice a day with the gentle cleanser followed by twice daily application of the tripeptide/hexapeptide gel, tripeptide/hexapeptide moisturizer, and SPF 30+ sunscreen. The group randomized to the practice's standard of care washed their face twice a day with the gentle cleanser followed by twice daily petrolatum-based moisturizer and SPF 30+ sunscreen.

## 2.5 | Assessment

Subjects were evaluated in the office on postprocedure days 1, 3, 4, 7, 28, and 84. The Canfield 3D Vectra photography system (Canfield Scientific Inc., Fairfield, NJ, USA) was utilized at all visits. The Canfield VISIA photography system was utilized at the screening and final visit on day 84.

At each postprocedure visit, a blinded investigator graded the percentage of surface area healed and rated erythema, edema, crusting, and exudation on a 5-point scale (none [0] to severe [4]). An overall healing grading (poor [0] to excellent [4]) and a 5-point rating comparing the current healing experience to the investigator's past experiences with postresurfacing healing were also completed at each visit. A photodamage/wrinkle score was given on postprocedure days 28 and 84 using a standardized 10-point scale with fine lines, coarse lines, abnormal pigmentation, and global assessment rated from absent (0) to severe (9).

On postprocedure days 1 through 14, subjects completed a take-home diary that documented their own assessment of the erythema, swelling, crusting/flaking, bruising, itching, tenderness, and burning/stinging they experienced on a standard 10-point scale.

Subjects completed a 5-point self-assessment scale (none [0] to severe [4]) of wrinkle severity on days 28 and 84. Subject-assessed Global Aesthetic Improvement Score (GAIS) and satisfaction were also assessed at days 28 and 84. Any adverse events were noted at each follow-up visit.

## 2.6 | Statistical analysis

Data from 14 subjects were analyzed; one subject was excluded from analysis after the data were deemed outliers. Statistical analyses were conducted on an intent-to-treat basis. Continuous data were summarized with descriptive statistics such as percentages, means, ranges and standard deviation, while frequencies were calculated for categorical variables. Statistical tests were performed using one-tailed t-tests. A *P*-value of .05 or less was considered significant.

## 3 | RESULTS

### 3.1 | Subjects

Of the 15 subjects enrolled into the study, 10 were randomized to the tripeptide/hexapeptide system and five to the standard of care, consisting of the dimethicone-based ointment and petrolatum-based moisturizer. The average age of the subjects was 56 years (range, 45-68 years). There were no significant differences between the baseline characteristics of the two treatment groups in the following parameters: age, photodamage, and subject wrinkle self-assessment (Table 1).

### 3.2 | Healing

Investigator-rated healing was superior for the tripeptide/hexapeptide system at each follow-up visit, reaching statistical significance at day 7 (*P*=.01; Figure 1). The tripeptide/hexapeptide group demonstrated less erythema and exudation during the first postprocedure week, reaching statistical significance at day 3 (*P*=.02 and .01, respectively). On days 1 through 14, subjects using the tripeptide/hexapeptide system reported less tenderness and burning/stinging, also reaching significance on day 3 (*P*=.02 and .03, respectively; Figure 2). Subjects using the tripeptide/hexapeptide system also reported less bruising than those using standard of care on postprocedure days 3-14, reaching significance on day 13 (*P*=.03).

There were no significant differences between the tripeptide/hexapeptide system and standard-of-care groups in crusting and edema as rated by investigators. The percentage healing was similar between the two groups at each time point. Subjects reported no statistical difference in redness, swelling, crusting/flaking, and itching.

### 3.3 | Skin quality

Subject self-assessment of skin quality was performed at days 28 and 84 using the GAIS, in which subjects were asked the degree to

which they agree with a series of statements (scored from “disagree strongly” [−2] to “agree strongly” [2]). Subjects in the tripeptide/hexapeptide group were significantly more likely to agree with the following statements on day 28: the product “improved the evenness of my skin tone” ( $P=.03$ ) and “made my skin look brighter and more healthy” ( $P=.03$ ). At day 84, subjects in the tripeptide/hexapeptide group were significantly more likely to agree with: “made my skin look more youthful” ( $P=.01$ ), “I would continue using this regimen” ( $P=.03$ ), and “I would recommend this treatment to others” ( $P=.03$ ). At both days 28 and 84, tripeptide/hexapeptide system users were significantly more likely to state the product “made me feel more confident in the way my skin looks” ( $P=.08$  and  $.02$ , respectively). There was no difference between the treatment

groups in subject wrinkle self-evaluation at days 28 or 84 ( $P=.74$  and  $0.82$ , respectively).

An analysis of investigator assessments of photodamage/wrinkling at days 28 and 84 did not demonstrate a difference between treatment groups in fine lines, coarse lines, abnormal pigmentation, or global photodamage. However, investigator-rated fine wrinkling in the tripeptide/hexapeptide group compared to standard of care trended toward greater improvement at day 28 ( $P=.06$ ).

### 3.4 | Investigator and subject satisfaction

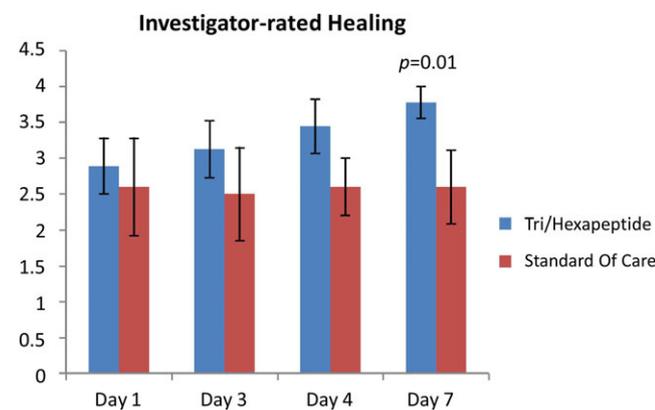
Subject satisfaction trended toward greater improvement in the tripeptide/hexapeptide group over standard of care at day 28 ( $P=.07$ ) and ultimately reached significance at day 84 ( $P=.03$ ; Figure 3). Similarly, investigators consistently rated the tripeptide/hexapeptide healing as compared to previous experience superior to that of standard of care at each follow-up time point, reaching significance at day 7 ( $P=.02$ ; Figure 4).

### 3.5 | Safety

No significant adverse events were reported. Signs and symptoms of allergic and irritant contact dermatitis were not noted in either treatment group.

**TABLE 1** Baseline characteristics (n=15)

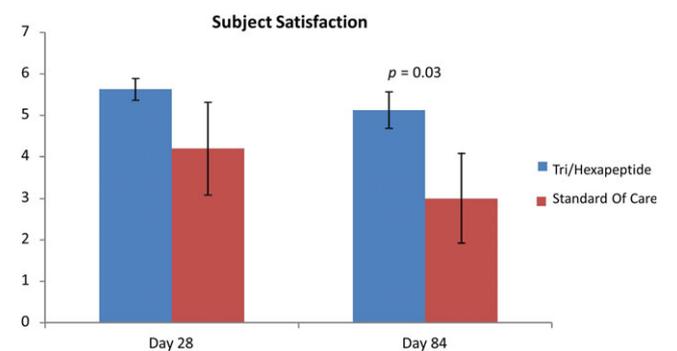
	Tri-/Hexapeptide system (n=10)	Dimethicone-based ointment/ petrolatum-based cream (n=5)
Age (years)	58.4±7.4	51.2±2.6
Photodamage		
Fine lines/wrinkling	7±1.4	6±1.9
Coarse lines/wrinkling	6.4±1.6	5.2±1.6
Abnormal pigmentation	5.7±2.5	5.4±1.1
Global assessment	6.5±1.7	6.4±1.3
Subject self-assessment	3±0.5	2.8±0.4



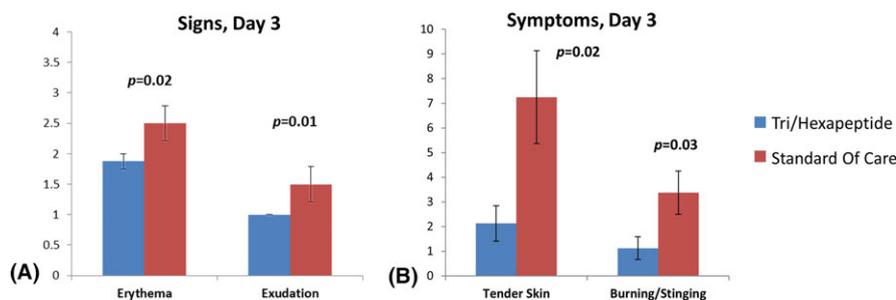
**FIGURE 1** Investigator-rated healing (graded from poor [0] to excellent [4]) was better for the tripeptide/hexapeptide group at every follow-up visit, reaching significance at day 7

## 4 | DISCUSSION

A healthy extracellular matrix is critical to wound healing and maintenance of youthful skin. Aging and chronic photodamage induce the

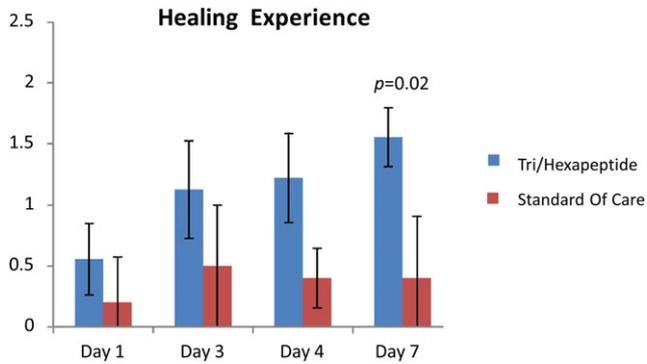


**FIGURE 3** Subject satisfaction was higher in the tripeptide/hexapeptide group at days 28 and 84



**FIGURE 2** (A) Erythema and exudation were less in the tripeptide/hexapeptide group during the first postprocedure week, reaching significance at day 3. (B) Subject-reported tenderness and burning/stinging were less in the first 2 postprocedure weeks, reaching significance on day 3

fragmentation of collagen, elastin, and proteoglycans, leading to aggregation of proteins and impairment of the dermal ECM and its healing mechanisms. Models of chronic wound healing suggest the importance of wound and skin bed preparation, or clearance of these



**FIGURE 4** Investigator-rated healing as compared to prior experience with healing after resurfacing procedures. Blinded investigators rated the tripeptide/hexapeptide group as having a better healing experience at each time point, reaching significance at day 7

aggregates, to any therapeutic procedure. The tripeptide/hexapeptide healing system is a preconditioning and postprocedure series of topicals containing potent peptides, lipids, and botanicals that aid in clearing and modulating the ECM, transforming it to a pro-regenerative environment from one of inflammation. This shift ultimately promotes neocollagenesis and elastin production. Thus, the tripeptide/hexapeptide healing system utilizes TriHex Technology™ to optimize ECM function both before and after rejuvenation procedures to speed healing and maximize outcomes.

The findings of this study are the first to demonstrate that this system may improve healing and patient symptomatology in the first postprocedure week. Although healing was only statistically significantly better in the tripeptide/hexapeptide group on day 7, the blinded investigators rated healing as better in the tripeptide/hexapeptide subjects at every follow-up time point (Figures 5 and 6). This improved healing is further reflected in lower rates of erythema, exudation, tenderness, and burning/stinging during the first postprocedure week among those using the tripeptide/hexapeptide system.

This novel postprocedure healing system may also improve the quality of skin after resurfacing procedures, as evidenced by



**FIGURE 5** Subject in the tripeptide/hexapeptide group (A) preprocedure and at (B) postprocedure day 1, (C) postprocedure day 4 and (D) postprocedure day 7



**FIGURE 6** Subject in the standard-of-care group (A) preprocedure and at (B) postprocedure day 1, (C) postprocedure day 4 and (D) postprocedure day 7

subjects' statements that the products made their skin look youthful, brighter, and healthier. There was also a trend toward significant improvement in investigator-rated fine wrinkling at day 28. A larger study would delineate these influences on skin quality more clearly.

The bland dimethicone-based ointment utilized in this study is considered standard of care after fractional ablative procedures in our practice because it does not contain dyes, lanolin, masking fragrances, petrolatum, parabens, formaldehyde, and other preservatives and therefore is unlikely to produce irritant and allergic contact dermatitis when applied to fragile resurfaced skin. Even when compared to this bland ointment, the tripeptide/hexapeptide healing system was remarkably well-tolerated and appears safe for use after resurfacing.

The tripeptide/hexapeptide system is more cosmetically appealing than the ointments commonly used after resurfacing procedures. Cosmetically elegant topicals often improve patient compliance, which may shorten postresurfacing healing times. Enhancing patient satisfaction also leads to return visits and repeat procedures.

Limitations of the study include the small study size. A larger study using double-blinded randomization would allow for confirmation of these findings.

## 5 | CONCLUSION

In this study, the tripeptide/hexapeptide system was a safe postprocedure topical regimen that improved healing after facial resurfacing.

Application of this system may produce improved skin quality and patient experience following laser resurfacing of the face.

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