

An Open Label Clinical Trial of a Peptide Treatment Serum and Supporting Regimen Designed to Improve the Appearance of Aging Facial Skin

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ABSTRACT

A 14-week single-center clinical usage study was conducted to test the efficacy of a peptide treatment serum and supporting skincare regimen in 29 women with mild to moderately photodamaged facial skin. The peptide treatment serum contained gamma-aminobutyric acid (GABA) and various peptides with neurotransmitter inhibiting and cell signaling properties. It was hypothesized that the peptide treatment serum would ameliorate eye and facial expression lines including crow's feet and forehead lines. The efficacy of the supporting skincare regimen was also evaluated. An expert investigator examined the subjects at rest and at maximum smile. Additionally, the subjects completed self-assessment questionnaires. At week 14, the expert investigator found a statistically significant improvement in facial lines, facial wrinkles, eye lines, and eye wrinkles at rest when compared to baseline results. The expert investigator also found statistically significant improvement at week 14 in facial lines, eye lines, and eye wrinkles when compared to baseline results at maximum smile. In addition, there was continued highly statistically significant improvement in smoothness, softness, firmness, radiance, luminosity, and overall appearance at rest when compared to baseline results at the 14-week time point. The test regimen was well perceived by the subjects for efficacy and product attributes. The products were well tolerated with no adverse events.

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INTRODUCTION

Facial skin ages over time, showing signs such as fine lines and wrinkles, increased visual and tactile roughness, reduction in firmness and radiance of the skin, and an increase in redness and hyperpigmentation.[1,2] Collagen breaks down and a decrease in the amount of water held in the epidermis leads to fine lines and wrinkles.[3] Additionally, repeated facial expressions made over time cause persistent wrinkles in the same pattern as the expression line that is formed.[4]

Peptides are a family of ingredients thought to ameliorate aging skin. Peptides are comprised of amino acids and are used in the body to signal between cells and influence the up- and down-regulation of numerous cellular functions. They have been shown to play an important role in cell signaling, collagen synthesis, and inhibition of neurotransmitter release for reduced muscle contraction.[5]

A multi-ingredient peptide-based treatment serum has been designed to improve the signs of facial aging especially due to expression lines such as crow's feet and forehead lines. Effective ingredients include gamma aminobutyric acid (GABA) and 7 different peptides including acetyl hexapeptide-8, acetyl octapeptide-3, dipeptide diaminobutyroyl benzylamide diacetate (DDBD), trifluoroacetyl tripeptide-2, and palmitoyl tetrapeptide-7. GABA is the primary inhibitory neurotransmitter naturally occurring in the central nervous system and has also been associated with skin barrier homeostasis.[6,7] Topical application of peptides, especially those with a fatty acid group attached, have been shown to reduce the signs of aging in facial skin including minimizing fine lines and wrinkles and increasing firmness.[8-10] There are several different neurotransmitter inhibiting peptides that are commercially available and these peptides work to reduce fine lines and wrinkles associated with facial expressions caused by underlying facial muscles. The most popular neurotransmitter inhibiting peptide is acetyl hexapeptide-8, which works through inhibition of the formation of the SNARE protein complex and thus inhibits acetylcholine release.[11] Reduction in the depth of wrinkles with topical application of acetyl hexapeptide-8 was shown in two previous studies.[12,13] Acetyl octapeptide-3 is similar to a sequence found in the SNAP-25 protein and regulates neuronal exocytosis to inhibit neurotransmitter release.[14] DDBD is a tripeptide-like compound similar to Waglerin-1, a protein found in the venom of the Temple viper, which blocks neuromuscular contraction.[15] DDBD inhibits acetylcholine activity at the neuromuscular synapsis and has an enhanced muscle relaxation activity profile.[16] Trifluoroacetyl tripeptide-2 has a lifting effect, reducing skin slackness and sagging. It boosts the production of collagen and inhibits matrix metalloproteinases.[17] Palmitoyl tetrapeptide-7 restores communication balance in aging skin specifically by inhibiting proinflammatory interleukin-6 and interleukin-8.[18]

The peptide treatment serum containing these ingredients with known topical benefits should produce a statistically significant anti-aging result, especially with expression lines, in this single-center clinical usage study. Additionally, the supporting skincare regimen of a gentle facial cleansing lotion, eye moisturizer, a daily moisturizer SPF 50, and a night cream should also produce an overall anti-aging effect.

OBJECTIVE

This single-center study was conducted to evaluate the tolerability and efficacy of a peptide treatment serum and supporting skincare regimen in improving the appearance of aging eye and facial skin, with a focus on expression lines in the crow's feet and forehead area.

MATERIALS AND METHODS

A regimen of facial skincare products was developed that included a gentle facial cleansing lotion, a peptide treatment serum, an eye moisturizer, a daily moisturizer SPF 50, and a night cream. The gentle facial cleansing lotion, which was mild and non-foaming, was developed for all skin types. The daily moisturizer SPF 50 consisted of a lotion containing UVA and UVB sunscreens as well as anti-aging technology including peptides, antioxidants, and standardized botanical extracts. The eye moisturizer was a basic moisturizing cream with no anti-aging ingredients included. The night cream consisted of a moisturizer with various anti-aging ingredients including peptides, antioxidants, and standardized botanical extracts. The peptide treatment serum consisted of GABA and 7 different peptides that worked via different pathways to reduce the appearance of fine lines and wrinkles caused by repeated facial expressions including acetyl hexapeptide-8, acetyl octapeptide-3, DDBD, trifluoroacetyl tripeptide-2, and palmitoyl tetrapeptide-7.

A 14-week single-site monadic study was completed by 29 female subjects in the age range of 35-60 years. Qualified subjects exhibited mild to moderate photoaging (Fitzpatrick skin types I-IV). The demographic information is shown in Figure 1. Subjects were asked to use the product twice daily as instructed. Subjects went through a wash out period for 2 weeks following study enrollment by using the study gentle facial cleansing lotion, daily moisturizer SPF 50 (avoiding the eyes), and eye cream in the morning followed by use of the gentle cleansing lotion, eye moisturizer, and night cream in the evening. The peptide treatment serum was added at week 2 with morning and evening application from the lower eyelids up to the forehead, but not the upper eyelid. Subjects used the peptide treatment serum for a total of 12 weeks and the remainder of the skincare products for a total of 14 weeks.

Areas important for the peptide treatment serum application were the crow's feet area, the glabellar line, and the forehead lines. The eye moisturizer was applied on top of the anti-aging peptide treatment serum around the eyes.

FIGURE 1. Demographic information. Demographics of enrolled subjects (per-protocol population).

Demographic Information

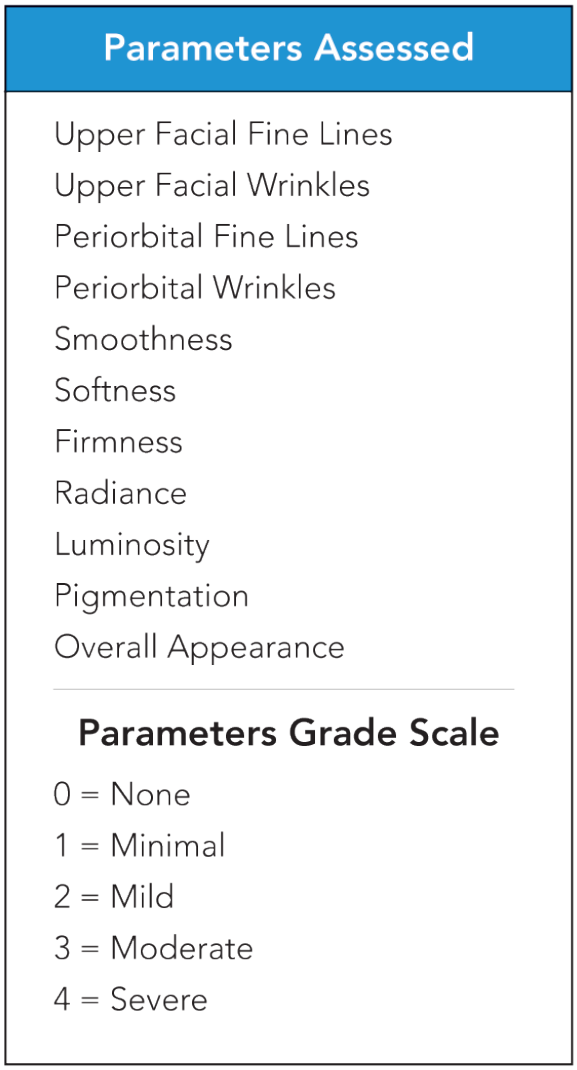
Demographics of Enrolled Subjects (Per-Protocol Population)

	All Subjects
N	29
Age (Years)	
Mean	47
Standard Deviation	6.6
Minimum	35
Median	48.5
Maximum	60
	N (%)
Sex	
Female	29 (100)
Ethnicity/Race	
Caucasian	29 (100)

Assessments consisted of investigator evaluations, subject evaluations, and photographs of the face with eyes open at relaxation and with maximum smile at each time point. Subjects were seen at baseline, week 2, week 6, week 10, and week 14.

Both the investigator and the subjects assessed the study parameters listed in Figure 2 below with the face at rest. The investigator assessed the face at maximum smile at each time point for facial lines, facial wrinkles, eye lines, and eye wrinkles. The parameters were assessed using the grading scale shown in Figure 2. In addition, the overall face was assessed for the following tolerability parameters: erythema, desquamation, stinging, burning, and itching. Subjects also assessed the aesthetic characteristics of the serum and the remainder of the products on a 0-4-point scale with a grade of 0 being strongly agree with the aesthetic characteristic description and a grade of 4 being strongly disagree. High quality jpeg photographs

FIGURE 2. Parameters Assessed.



Half point assessments were allowed.

were taken of the complete front face at rest and at maximum smile with eyes open. Subjects were placed in a Canfield 3-point head mount with Canfield designed Nikon camera and flash system. Subjects were given a diary at the baseline visit to record their twice daily application and for compliance checks. At each study visit, the amount of study product remaining was checked along with the diary entries, and the unused product was weighed for compliance purposes.

A two-tailed Mann Whitney t-test was used to analyze the nonparametric data sets with significance set at $P<0.05$. A longitudinal analysis was performed in the monadic study with each time point compared with baseline where study products were initiated except for the peptide treatment serum. Concerning the peptide treatment serum, baseline is considered to be the 2 week time point when this product application was initiated after the washout period.

RESULTS

Clinical Grading of Efficacy Parameters: Expert Investigator Evaluation at Rest

By week 2, the regimen had produced a highly statistically significant improvement in skin smoothness and softness ($P<0.001$) when compared to baseline results. The peptide treatment serum was added for morning and evening application at week 2 and applied from the lower eyelids up to the forehead, but not the upper eyelid. At week 6, a highly statistically significant improvement in smoothness and softness ($P<0.001$) continued, with additional statistically significant improvement in firmness and radiance $P<0.001$), luminosity ($P=0.003$), and overall appearance ($P<0.001$) when compared to baseline results.

Improvement continued throughout the study period. At week 10, there was a highly statistically significant ($P<0.001$) improvement in smoothness, softness, firmness, radiance, luminosity, and overall appearance when compared to baseline results; there was also a significant improvement in eye lines ($P=0.003$) and eye wrinkles ($P=0.007$) compared to baseline results. At week 14, there was significant improvement in facial lines ($P=0.006$), facial wrinkles ($P=0.018$), eye lines ($P<0.001$), and eye wrinkles ($P=0.001$) when compared to baseline results. In addition, there was continued highly statistically significant improvement ($P<0.001$) in smoothness, softness, firmness, radiance, luminosity, and overall appearance when compared to baseline results (Table 1).

Clinical Grading of Efficacy Parameters: Expert Investigator Evaluation at Maximum Smile

At week 6, there was a significant improvement in eye lines ($P=0.025$) compared to baseline results when smiling. This improvement continued into week 10 where there was significant improvement in facial lines ($P=0.043$), eye lines ($P=0.005$), and eye wrinkles ($P=0.014$) when compared to baseline results. Continued improvement was seen at week 14 in facial lines ($P=0.018$), eye lines ($P<0.001$), and eye wrinkles ($P=0.006$) when compared to baseline results (Table 2).

Aesthetic Attributes of Products Other Than Serum: Subject Assessment at Week 14

The subjects were asked to rank several attributes of the products other than the peptide treatment serum at week 14 on a numeric scale (0=strongly agree, 1=agree, 2=neutral, 3=disagree, and 4=strongly disagree). The subjects agreed that the product smell (mean=0.55), texture (mean=0.52), and ease of application (mean=0.59) were excellent. They also strongly agreed that the product did not cause irritation (mean=0.34), and that they would purchase the product (mean=0.69).

TABLE 1.

Change from Baseline Statistics for Clinical Grading of Efficacy Parameters (Expert Investigator Evaluation at Rest)

Change From Baseline Statistics for Clinical Grading of Efficacy Parameters (Expert Investigator Evaluation at Rest)		
Parameter and Time Point	**Average % Improvement of Subjects**	**P Value***
Facial Lines		
Week 10	-8	.074
Week 14	-18	**.006**
Facial Wrinkles		
Week 10	-8	.155
Week 14	-18	**.018**
Eye Lines		
Week 10	-19	**.003**
Week 14	-30	**<.001**
Eye Wrinkles		
Week 10	-19	**.007**
Week 14	-27	**.001**
Smoothness		
Week 10	-82	**<.001**
Week 14	-89	**<.001**
Softness		
Week 10	-82	**<.001**
Week 14	-95	**<.001**
Firmess		
Week 10	-60	**<.001**
Week 14	-78	**<.001**
Radiance		
Week 10	-50	**<.001**
Week 14	-64	**<.001**
Luminosity		
Week 10	-43	**<.001**
Week 14	-56	**<.001**
Pigmentation		
Week 10	4	.725
Week 14	-1	.870
Overall Appearance		
Week 10	-36	**<.001**
Week 14	-45	**<.001**

*Bolded p values indicate statistical significance

The only negative recurring comment was that the treatment regimen had too many products and was too time-consuming. This comment was expected with enrollment of a broad range of female consumers with varying skincare routines.

Efficacy of Products Other Than Serum: Subject Assessment at Week 14

The subjects were asked to assess the appearance of their skin for the products they used, other than the peptide treatment serum, at week 14 using the same scoring system noted above. They agreed that they had better skin texture (mean=0.90), more radiance (mean=1.17), more even skin tone (mean=1.34), less skin discoloration (mean=1.31), less redness (mean=1.34), less noticeable fine lines (mean=1.10), less noticeable wrinkles (mean=1.31), healthier-looking skin (mean=0.90), younger, firmer skin (mean=1.31), more moisturized skin (mean=0.62), and overall improved appearance (mean=0.86) when compared to baseline results.

Aesthetic Attributes of Serum: Subject Assessment at Week 14

The subjects were asked to assess the aesthetic attributes of only the peptide treatment serum at week 14 using the same numeric scale. The subjects agreed that the product absorbed well (mean=1.38) and that the smell (mean=1.00), texture (mean=0.66), and ease of application (mean=0.86) were excellent. They agreed that the product did not cause irritation (mean=0.62) and that they would purchase the product (mean=0.93).

Efficacy of Serum: Subject Assessment at Week 14 Eye Area

The subjects were asked to examine only the area around the eyes at 14 weeks and assess the peptide treatment serum using the numeric scale. They agreed that they had better skin texture (mean=1.07), more radiance (mean=1.14), improved fine lines (mean=1.21), improved wrinkles (mean=1.34), healthier-looking skin (mean=1.10), younger, firmer skin (mean=1.48), more moisturized skin (mean=0.83), and overall improved appearance (mean=1.07) around the eyes when compared to baseline results.

TABLE 2.

Change from Baseline Statistics for Clinical Grading of Efficacy Parameters (Expert Investigator Evaluation at Maximum Smile)

Change From Baseline Statistics for Clinical Grading of Efficacy Parameters (Expert Investigator Evaluation at Maximum Smile)		
Parameter and Time Point	**Average % Improvement of Subjects**	**P Value***
Facial Lines		
Week 10	-10	**.043**
Week 14	-15	**.018**
Facial Wrinkles		
Week 10	-9	.148
Week 14	-13	.070
Eye Lines		
Week 10	-22	**.005**
Week 14	-25	**<.001**
Eye Wrinkles		
Week 10	-19	**.014**
Week 14	-21	**.006**

*Bolded p values indicate statistical significance

Efficacy of Serum: Subject Assessment at Week 14 Lower Eyelids to Hairline

The subjects were asked to examine only the lower eyelids to the hairline at 14 weeks and assess the peptide treatment serum using the numeric scale. They agreed they had better skin texture (mean=0.97), more radiance (mean=1.10), improved fine lines (mean=1.03), improved wrinkles (mean=1.31), improved crow's feet wrinkles (mean=1.24), improved undereye wrinkles (mean=1.28), healthier-looking skin (mean=0.93), younger, firmer skin (mean=1.52), more moisturized skin (mean=0.86), and overall improved appearance (mean=1.10) on the skin from the lower eyelids to the hairline when compared to baseline results.

Clinical Grading Efficacy Parameters: Subject Assessment at Rest

A marked improvement was noted by the subjects at week 10. There was significant improvement in facial lines (P=0.049), facial wrinkles (P=0.030), eye wrinkles (P=0.020), smoothness (P=0.023), softness (P=0.004), firmness (P=0.001), radiance (P=0.001), luminosity (P<0.001), pigmentation (P=0.028), and overall appearance (P<0.001) when compared to baseline results.

At week 14, there was statistically significant improvement in facial lines (P=0.002), facial wrinkles (P=0.013), eye lines (P=0.002), wrinkles (P=0.043), smoothness (P=0.003), softness (P=0.003), firmness (P=0.001), radiance (P<0.001), luminosity (P<0.001), and overall appearance (P<0.001) when compared to baseline results (Table 3).

Concerning tolerability attributes, the panelists noted a statistically significant increase in erythema (P=0.025) and desquamation (P=0.018) at week 2 when compared to baseline results. The subjects returned at week 6, and the desquamation was no longer statistically significant, although the increased erythema remained significant (P=0.022). The subjects continued to note that erythema remained significant (P=0.038) at week 10 when compared to baseline results but this cleared at week 14.

TABLE 3.

Change from Baseline Statistics for Clinical Grading of Efficacy Parameters at Rest (Subject Evaluation at Rest)

Change From Baseline Statistics for Clinical Grading of Efficacy Parameters at Rest
(Subject Evaluation at Rest)

Parameter and Time Point	Average % Improvement of Subjects	P Value*
Facial Lines		
Week 10	-17	**.049**
Week 14	-27	**.002**
Facial Wrinkles		
Week 10	-17	**.030**
Week 14	-22	**.013**
Eye Lines		
Week 10	-32	.052
Week 14	-40	**.002**
Eye Wrinkles		
Week 10	-20	**.020**
Week 14	-18	**.043**
Smoothness		
Week 10	-22	**.023**
Week 14	-31	**.003**
Softness		
Week 10	-28	**.004**
Week 14	-33	**.003**
Firmess		
Week 10	-32	**.001**
Week 14	-33	**.001**
Radiance		
Week 10	-32	**.001**
Week 14	-38	**<.001**
Luminosity		
Week 10	-35	**<.001**
Week 14	-40	**<.001**
Pigmentation		
Week 10	-28	**.028**
Week 14	-22	.660
Overall Appearance		
Week 10	-28	**<.001**
Week 14	-44	**<.001**

*Bolded p values indicate statistical significance

Safety/Tolerability

The facial peptide-based regimen was well tolerated by the panelists with no statistically significant increase in erythema, desquamation, stinging, burning, or itching noted by the expert investigator when compared to baseline results at any time point. The subjects noted a statistically significant increase in desquamation and erythema at week 2 compared to baseline results. The increase in desquamation was resolved and was no longer significant after week 2. The erythema persisted to week 10 but was resolved and was no longer statistically significant at week 14 when compared to baseline results. The increase in desquamation and erythema perceived by the subjects was not perceived by the investigator. In addition, the subjects agreed that the peptide treatment serum (mean=0.62 on a 0-4-point scale) and the other products (mean= 0.34 on a 0-4-point scale) did not cause irritation when compared to baseline results. Also, concerning the efficacy of the products other than the peptide treatment serum, the subjects agreed that they had less redness (mean=1.34 on a 0-4-point scale) at week 14 compared to baseline results. Lastly, no adverse events were observed or reported during the study period.

Compliance

No compliance issues were noted during the study either by diary or product weight.

DISCUSSION

Overall, the results of this single-center study indicate that the use of this peptide treatment serum and supporting regimen was effective in improving signs of facial skin aging, especially expression lines such as crow's feet and forehead lines, when compared to baseline results and used over the course of 14 weeks by women with mild to moderate photoaging. There was a statistically significant difference in skin appearance from the lower eyelids to the hairline after 12 weeks of peptide treatment serum application as assessed by both the investigator and by the subjects when compared to baseline results. Of special interest are the investigator's results of eye lines and eye wrinkles both at rest and at maximum smile when compared to baseline results. The investigator found a statistically significant reduction in these parameters. The investigator's findings are supported by the before and after photos of the subjects with 2 examples illustrated in Figures 3 and 4. Both the peptide treatment serum and eye cream were applied to this area, however, because the eye cream was for moisturizing purposes only and contained no anti-aging ingredients, it is believed that these results can be entirely attributed to the efficacy of the peptide serum. This evidence supports the hypothesis that combining various neurotransmitter inhibiting and cell signaling peptides, such as acetyl hexapeptide-8 and DDBD, with known topical benefits, into a treatment product will reduce the signs of aging caused by repeated facial expressions. In addition to the results in the eye area, there was a significant difference in skin appearance over the entire face after 12 weeks of application of the peptide treatment serum and 14 weeks of the supporting regimen when compared to baseline results as assessed by the investigator. A number of attributes significantly improved over the course of the study, both at rest and maximum smile when compared to baseline results. Lastly, subjects rated the regimen as effective and aesthetically pleasing and noted that they would purchase the product. The product regimen took 8 weeks to produce visual results in the subjects' opinion, but these positive results continued once obtained.

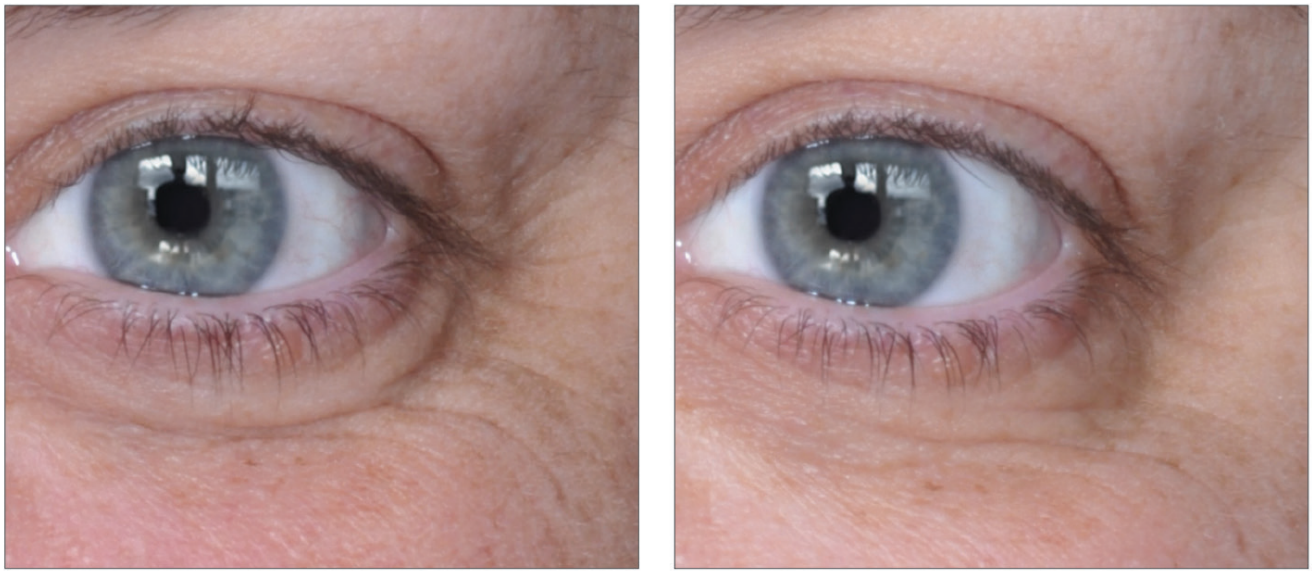
Worsening of erythema and desquamation was reported by subjects at 2 weeks, but this resolved by the end of the study and was not supported by the investigator's findings. No adverse events were reported.

A limitation of this study includes the lack of a control product.

CONCLUSION

A 14-week single-center clinical usage study was conducted to test a facial peptide treatment serum and supporting regimen in 29 women with mild to moderately photodamaged skin. At week 14, an expert investigator found statistically significant improvement in facial lines, facial wrinkles, eye lines, and eye wrinkles at rest when compared to baseline results. In addition, there was continued highly statistically significant improvement in smoothness, softness, firmness, radiance, luminosity, and overall appearance at rest when compared to baseline results. The expert investigator also found statistically significant improvement at week 14 in facial lines, eye lines, and eye wrinkles when compared to baseline results at maximum smile. The test regimen was well-perceived by the subjects for efficacy

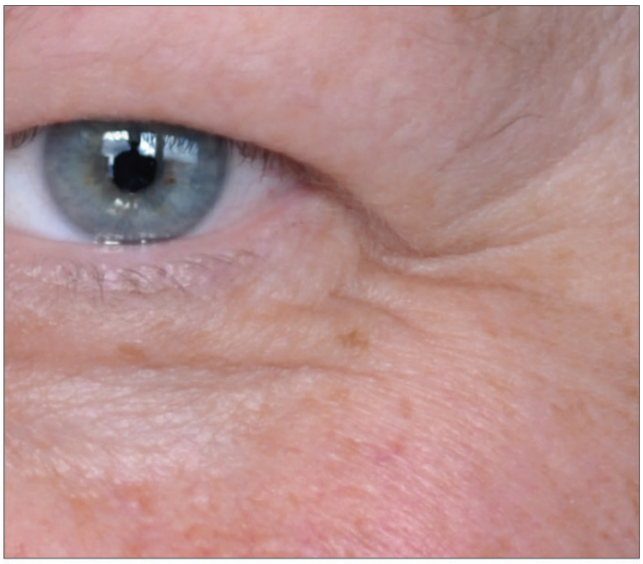
FIGURE 3. After 2-week washout period (left). After 8 weeks of peptide treatment serum use (right).



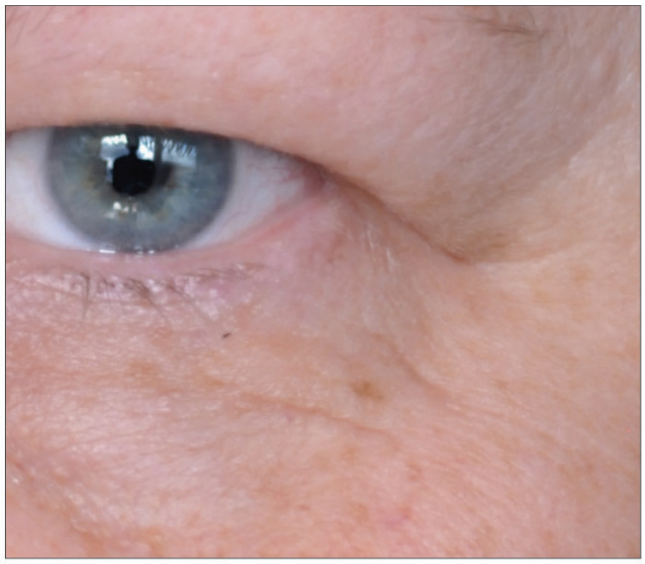
After 2 week washout period

After 8 weeks of peptide treatment serum use

FIGURE 4. After 2-week washout period (left). After 8 weeks of peptide treatment serum use (right).



After 2 week washout period



After 12 weeks of peptide treatment serum use

and product attributes. The products were well tolerated with no adverse events. These results provide medical professionals with information that may benefit patients seeking treatment for expression line wrinkles and photodamaged facial skin.

DISCLOSURES

The study was 100% sponsored by Revision Skincare. Dr. Draelos has no conflicts of interest to declare. Tatiana Kononov and Theresa Fox are employees of Revision Skincare.

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