Topical manganese peptide in the treatment of photodamaged skin

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Abstract

This study evaluated the effects of a manganese peptide complex in the treatment of various signs of cutaneous facial photodamage. Individuals used a facial serum formulation containing the manganese peptide complex Manganese Tripeptide-1 twice a day for up to 12 weeks. At the end of the treatment period, the individuals and a blinded investigator noted improvement in the appearance of several signs of cutaneous photodamage. Predominant among the parameters showing improvement were those associated with hyperpigmentation. In general, at the end of 12 weeks of treatment, photodamage ranking moved from moderate to mild. Treatment was well tolerated with no significant cutaneous inflammation induced by the manganese peptide complex.

Key words: Photodamage, topical agents, manganese, Manganese Tripeptide-1

Introduction

Copper peptide complexes such as Copper Tripeptide-1 have been used successfully for a number of years to combat the appearance of photoaging skin (1–3). These compounds are complexes of the transition metal copper with the peptide glycyl-L-histidyl-L-lysine. Another transition metal, manganese, is also an essential nutrient involved in bone, amino acid, cholesterol, carbohydrate metabolism, and antioxidant protection.

Superoxide dismutase is one of the most important defenses against oxidative damage in the body. Manganese-superoxide dismutase is important in the defense against UV-induced photoaging. In epidermal cells, treatment with UV-B increases the activity of manganese-superoxide dismutase through the action of the inflammatory mediators interleukin 1 (IL-1) and TNF-α (4,5). In a similar manner, irradiation with the UV-A wavelengths also increases the level of manganese-superoxide dismutase (6,7). Supplementation of cultured cells with manganese protects cells against UV-A toxicity (8). These studies, and others, suggest that manganese might be useful in the treatment of photoaging in a similar manner as is seen with copper peptide complexes. To this end, Manganese Tripeptide-1, a manganese glycyl-L-histidyl-L-lysine complex, has been formulated.

Preliminary in vitro screening assays (9) show that Manganese Tripeptide-1 inhibits the formation of melanin pigments in cultured B16 melanocytes in a non-toxic manner. These observations led to the current study evaluating the effects of a topical serum formulation containing Manganese Tripeptide-1 on the appearance of cutaneous photoaging.

Methods

Study population

The study consisted of 15 female participants aged 40–70 years with moderate photodamage and hyperpigmentation of the face with a severity rating score of 2–3 on a 5-point scale. All individuals were required to discontinue topical and systemic retinoids, alpha and beta hydroxy acids, and other topical skin care products. Four weeks prior to study initiation all participants were required to discontinue direct facial sun exposure. They were excluded if they had a history of reactions to skin care products or were undergoing concurrent topical and/or systemic drug therapy for skin disorders.
Study design

This was an open label study to determine the effects of a manganese peptide complex containing serum (Manganese Tripeptide-1, INCI nomenclature; Procyte Corporation, Redmond, WA, USA) on the facial skin of individuals with moderate signs of photodamage and hyperpigmentation. The test material consisted of a manganese peptide complex (glycyl-histidyl-lysine manganese) formulated in a non-irritating facial serum base. The product was applied to the face and neck twice a day for up to 12 weeks.

Participants were instructed to wash their face and neck using their current pre-study skin care regimen, provided that all products had already been used for at least 30 days with no irritation or dryness. They were also permitted to use their standard cosmetics and/or other make-up on all days except study evaluation days. New cosmetic products were not allowed to be introduced during the course of the study. A SPF 30 sunscreen was provided to all participants. Informed consent was obtained from all study participants. The test material was applied approximately 15 minutes after cleansing and drying the face in the morning and the evening.

Evaluations

The clinical signs of photodamage and hyperpigmentation were rated by the clinical evaluator on a scale of 0–4 as follows: 0 = none; 1 = minimal; 2 = mild; 3 = moderate; 4 = severe.

The clinical signs were evaluated pre-study, and at weeks 1, 4, 8, and 12.

The clinical evaluator also rated the signs and symptoms of cutaneous irritation on a similar scale of 0–4. The symptoms rated were: 1 = erythema; 2 = scaling/peeling; 3 = edema; 4 = comedones; 5 = papules/pustules; 6 = clinical appearance of tightness/dryness.

Participants were also given a self-assessment questionnaire to fill out at the above evaluation times. Questions related to the improvement in the signs of photoaging and hyperpigmentation. Additional questionnaire responses related to product aesthetics and tolerance.

The questionnaire consisted of questions on the following:

1. overall skin improvement
2. reduction of superficial fine lines and wrinkles
3. reduction in the number of ‘age/brown spots’
4. improvement in skin clarity
5. improvement in skin texture
6. relief of skin dryness
7. reduction in blotchy discolorations
8. improvement in skin elasticity
9. improvement in skin radiance
10. reduction in appearance of pores
11. the attainment of skin that looks and feels healthier
12. lightening/brightening of skin.

Participants were to note if they: agree strongly; agree somewhat; neither agree/nor disagree; disagree somewhat; disagree strongly.

Statistical analysis

Evaluation of the data from individuals that completed the protocol was conducted by comparison of the baseline evaluation data with the data from the individual evaluation days by the appropriate non-parametric test procedure. A 0.05 one-tailed significance level was employed in all analyses.

A chi-square analysis was done on each questionnaire statement comparing the frequency of individuals who selected the top two responses (combined) versus those who selected the bottom two responses (combined). Neutral responses were not examined in these analyses.

Results

A total of 15 individuals were enrolled in the study; 14 completed the 12-week treatment protocol. One participant was dropped from the study due to non-compliance. The pre-study entrance photodamage evaluations are shown in Table I. The rankings for surface roughness, sallowness, mottled hyperpigmentation, lentigines, and fine rhytids were all in the mild to moderate range. In general, telangiectasia were not present and are not evaluated in the study.

The manganese tripeptide serum was well tolerated as evidenced by the ratings of both the clinical evaluator and the participants in a self-evaluation questionnaire. Only one of the 14 participants experienced mild erythema and there was only one instance of tightness and drying associated with the treatment. Examination of the subject self-assessment questionnaires demonstrated good tolerance of the manganese tripeptide treatment. At the termination of the treatments, 100% of the participants rated the product as non-irritating and good for everyday use. Only one out of the 14 rated the product as ‘pore clogging’.

Table I. Pre-treatment photodamage evaluations.

<table>
<thead>
<tr>
<th>Photoaging sign</th>
<th>Mean ranking ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surface roughness/dryness</td>
<td>2.50 ± 0.52</td>
</tr>
<tr>
<td>Sallowness</td>
<td>2.50 ± 0.52</td>
</tr>
<tr>
<td>Mottled hyperpigmentation</td>
<td>3.07 ± 0.27</td>
</tr>
<tr>
<td>Lentigines</td>
<td>2.79 ± 0.80</td>
</tr>
<tr>
<td>Fine rhytids</td>
<td>2.92 ± 0.62</td>
</tr>
<tr>
<td>Telangiectasia</td>
<td>0.14 ± 0.53</td>
</tr>
</tbody>
</table>

0 = none, 1 = minimal, 2 = mild, 3 = moderate, 4 = severe.
The blinded clinical evaluator rated the signs of photodamage and hyperpigmentation at pre-study and weeks 1, 4, 8 and 12. A number of the parameters showed significant (\(p < 0.05\)) improvement, generally moving from the moderate to mild ranking. Predominant among the photodamage parameters showing improvement were those associated with pigmentation.

Treatment with the manganese peptide complex produced a significant improvement in the appearance of mottled hyperpigmentation, sallowness, lentigines and surface roughness/dryness as rated by the clinical evaluator. Figure 1 and Table II shows the average rankings for these parameters at week 12 compared with the pre-study evaluation. In general, improvements were noted at the week-8 evaluation with continued improvement at week 12. There was no significant effect on the appearance of fine lines (Table III).

The results of the subject self-assessment questionnaires were in close agreement with the ranking of the clinical evaluator. Several of the questions related to the appearance of hyperpigmentation. Up to 70% of the participants noted that the appearance

![Figure 1. Pre-treatment and 12-week post-treatment blinded investigator evaluations of photodamage.](image)

![Figure 2. Pre-treatment and 12-week post-treatment subject evaluations of photodamage.](image)
of lentigines and blotchy discolorations was reduced, that treatment lightened and brightened the skin, and skin radiance was improved (Figures 2–4).

As with the clinical evaluator rankings, the predominant improvements were in parameters associated with hyperpigmentation.

Although the overall response in terms of the resolution of the appearance of photoaging was ranked by the blinded evaluator as moderate for 42% of the participants, almost 80% of the participants rated their skin as looking and feeling healthier in the self assessments.

**Discussion**

The results of this study demonstrate that twice-daily treatment with a peptide manganese complex, Manganese Tripeptide-1 or glycyl-histidyl-lysine manganese, produces improvement in the appearance of facial photoaging. Both the blinded observer and participants noted the greatest degree of improvement in hyperpigmentation associated with photoaging.

As described above, a number of photoaging parameters, as evaluated by the blinded observer, showed statistically significant (p < 0.05) improvement; rankings generally moving from moderate to mild. Predominant among the photodamage parameters showing improvement were those associated with various aspects of pigmentation, including sallowness, mottled hyperpigmentation, and the appearance of lentigines. Corresponding questions on the subject self-assessment questionnaires related to the reduction of the appearance of ‘age spots’ and blotchy discolorations, and increase in skin radiance and brightness showed similar improvement. The effects of the Manganese Tripeptide-1 on other aspects of photaged facial skin, such as fine lines and wrinkles, was limited.

A variety of copper peptide complexes have been used successfully to combat the appearance of aging skin (1–3). Those compounds are complexes of the transition metal copper with the peptide glycyl-histidyl-lysine. In a similar manner, the Manganese Tripeptide-1 is a complex of another transition metal, manganese, with the

**Table II. Twelve-week post-treatment photodamage evaluations.**

<table>
<thead>
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<th>Mean ranking ± SD</th>
</tr>
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<tbody>
<tr>
<td>Surface roughness/dryness</td>
<td>1.43 ± 0.65</td>
</tr>
<tr>
<td>Sallowness</td>
<td>1.43 ± 0.65</td>
</tr>
<tr>
<td>Mottled hyperpigmentation</td>
<td>2.21 ± 0.70</td>
</tr>
<tr>
<td>Actinic lentigines</td>
<td>1.93 ± 0.62</td>
</tr>
<tr>
<td>Fine wrinkles</td>
<td>2.71 ± 0.83</td>
</tr>
<tr>
<td>Telangiectasia</td>
<td>0.14 ± 0.53</td>
</tr>
</tbody>
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0=none, 1=minimal, 2=mild, 3=moderate, 4=severe.

**Table III. Comparison of pre- and 12 weeks post-treatment photodamage evaluations.**

<table>
<thead>
<tr>
<th>Photoaging sign</th>
<th>Pre-treatment</th>
<th>12 weeks post-treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surface roughness/dryness</td>
<td>2.50 ± 0.52</td>
<td>1.43 ± 0.65</td>
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peptide glycyl-histidyl-lysine. While the actions of the copper complexes are mainly centered on decreasing the appearance of fine lines and wrinkles, those of the manganese complex would seem to be better targeted at lessening the appearance of hyperpigmentation associated with photoaging.

Although this was a limited study in terms of the number of participants and the duration of treatment, the results suggest that Manganese Tripeptide-1, a new manganese peptide complex, has the potential to be an important addition to the treatment regimen used for hyperpigmentation associated with photoaging.

References