IFSCC 35TH CONGRESS
FRANCE_CANNES 15-18 SEPT 25
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IFSCC 2025 full paper (IFSCC2025-1260)

Evaluation of a Peptide-Protein Complex for ECM Improvement and Anti-Aging Effects

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1. Introduction

Skin aging is characterized by a gradual loss of both structural and functional integrity in the extracellular matrix (ECM), leading to visible signs such as reduced skin elasticity, the formation of wrinkles, and a loss of facial contours. The ECM, a complex network of proteins and polysaccharides, provides essential structural support to the skin. Collagen and elastin, two key ECM components, are critical in maintaining skin firmness, strength, and resilience. With aging, the production of collagen and elastin significantly decreases, while their degradation accelerates, particularly under the influence of environmental factors like ultraviolet (UV) radiation. This imbalance results in the weakening of dermal structures, contributing to skin sagging, the formation of wrinkles, and compromised skin barrier function. Over time, these structural impairments culminate in dermal atrophy and a diminished ability to retain moisture, further exacerbating the signs of aging.

The degradation of collagen, in particular, is one of the primary contributors to the visible signs of aging. As collagen fibers lose their tensile strength and become fragmented, the skin’s ability to resist stretching and retain its shape is reduced. Additionally, the synthesis of collagen is impaired with age, leading to a decreased amount of this vital protein. Similarly, elastin, responsible for skin’s elasticity and its ability to "bounce back," also undergoes structural degradation, further impairing skin resilience. These changes in the ECM are further aggravated by photoaging, a process in which UV radiation accelerates the breakdown of collagen and elastin fibers, making the skin more prone to wrinkling and sagging.

In contrast to traditional single-component anti-aging strategies, the Peptide-Protein Complex (PPC) evaluated in this study represents an innovative approach by integrating multiple functional peptides and ECM proteins. This synergistic combination aims to simultaneously stimulate fibroblast activity, enhance ECM synthesis, and provide antioxidant as well as anti-glycation protection. Such a multi-targeted formulation offers a comprehensive strategy for ECM repair and dermal rejuvenation, particularly effective for photo-damaged skin. This complex consists of a combination of peptides that can effectively stimulate fibroblasts, the primary cells responsible for collagen production, thereby increasing the synthesis of collagen and improving overall ECM quality.

The PPC also incorporates a synergistic blend of elastin, type III collagen, and fibronectin, which work together to further enhance ECM integrity. Elastin and type III collagen are key components that contribute to the skin's elasticity and strength, while fibronectin plays a critical role in ECM remodeling and cell adhesion. The combined action of these components helps to restore the structural foundation of the skin, improving its firmness and resilience.

Additionally, the inclusion of decarboxylated carnosine, known for its powerful antioxidant and anti-glycation effects, adds further benefit to the PPC. Glycation, a process in which excess sugar molecules bind to proteins, can lead to the formation of advanced glycation end products (AGEs), which impair the structure and function of ECM proteins. By mitigating this process, decarboxylated carnosine helps to maintain the quality of collagen and elastin, preventing their premature degradation and ensuring that the skin retains its youthful appearance. Overall, this Peptide-Protein Complex offers a multifaceted approach to combat skin aging, improving ECM integrity and providing clinically relevant anti-aging effects.

2. Materials and Methods

Peptide-Protein Complex (PPC):

The Peptide-Protein Complex (PPC) consists of three peptides: Acetyl Hexapeptide-8, Hexapeptide-11, and Acetyl Tetrapeptide-9, in combination with decarboxylated carnosine hydrochloride. These components were selected for their synergistic effects in promoting extracellular matrix (ECM) synthesis, enhancing fibroblast function, and providing protection against structural damage, thereby contributing to the restoration of skin integrity and rejuvenation.

Immunohistochemical Analysis:

To assess the effects of PPC on skin rejuvenation, immunohistochemistry was performed to quantify changes in collagen and elastin fibers in ex vivo skin tissue. Skin samples were irradiated with a combination of UVA and UVB radiation to simulate photoaging. The levels of various collagen types (I, III, IV, V, VI, VII, XVII, XVIII) and elastin fibers were measured. Immunofluorescence microscopy, in combination with multiphoton microscopy, was employed to evaluate the structural changes in collagen and elastin content. Primary antibodies targeting specific collagen types and elastin were applied to tissue sections, followed by incubation with secondary antibodies and detection using chromogenic substrates. The intensity and distribution of the staining were quantified to evaluate PPC's effects on skin firming, wrinkle reduction, and its ability to promote ECM synthesis and protect against photoaging-induced structural damage. This analysis provided insights into the rejuvenating effects of PPC, supporting its potential in the development of anti-aging skincare formulations.

Restoration of ECM Structure in Photo-Damaged Skin:

This study's primary aim was to establish an ex vivo skin damage model using UV radiation (UVR) and assess the firming and anti-wrinkle effects of PPC. Skin tissue was irradiated with UVA and UVB to induce photoaging. Biological tissues naturally contain fluorescent substances such as NAD(P)H, porphyrins, melanin, AGEs, and elastin, which emit stable fluorescence signals when excited by specific wavelengths of light. Elastin fibers, a major source of spontaneous fluorescence, were detected through two-photon excited fluorescence (TPEF), while collagen fibers, with their highly crystalline, non-centrosymmetric triple-helix structure, produced strong second harmonic generation (SHG) signals. The fluorescence intensity and distribution of these signals were analyzed to evaluate the effects of PPC on collagen and elastin content, enabling the assessment of its firming and anti-wrinkle efficacy.

Clinical Efficacy Study:

A clinical study was conducted with 30 healthy Chinese female participants aged 25 to 65 years. Inclusion criteria included healthy females with sensitive skin (confirmed by a lactic acid prick test), visible nasolabial folds, marionette lines, and tear troughs (severity $\geq$ 2), dry or combination dry skin, facial skin laxity, dull skin, and redness. Participants had to be able to use the test product, complete questionnaires, and cooperate with study procedures. Exclusion criteria included individuals with a history of skin diseases (e.g., atopic dermatitis, psoriasis, severe acne), current skin conditions (e.g., folliculitis, birthmarks, moles), pregnancy, breastfeeding, or menopause, as well as those intolerant to retinol or involved in other clinical trials recently.

Participants applied a PPC-containing cream to their face twice daily for four weeks. Skin assessments were performed at baseline and after four weeks using VISIA imaging and 3D skin analysis to measure changes in skin elasticity, wrinkle depth, and facial contours.

3. Results

Effects of PPC on Collagen and Elastin Synthesis:

Compared to the control group, treatment with the Peptide-Protein Complex (PPC) significantly increased the levels of Collagen IV, Collagen VII, and Collagen XVII in ex vivo skin tissue, with increases of 92.06%, 69.57%, and 33.33%, respectively. These results indicate that PPC effectively promotes the synthesis of key ECM components, contributing to enhanced skin firmness and reduced wrinkle formation. Furthermore, Collagen I, Collagen III, Collagen V, Collagen VI, and Collagen XVIII levels were significantly elevated with improvements of 93.94%, 126.09%, 125.00%, 54.17%, and 60.71%, respectively, highlighting PPC's ability to enhance the synthesis of various collagen types, further supporting its anti-aging properties(Figure 1a, 1b)..

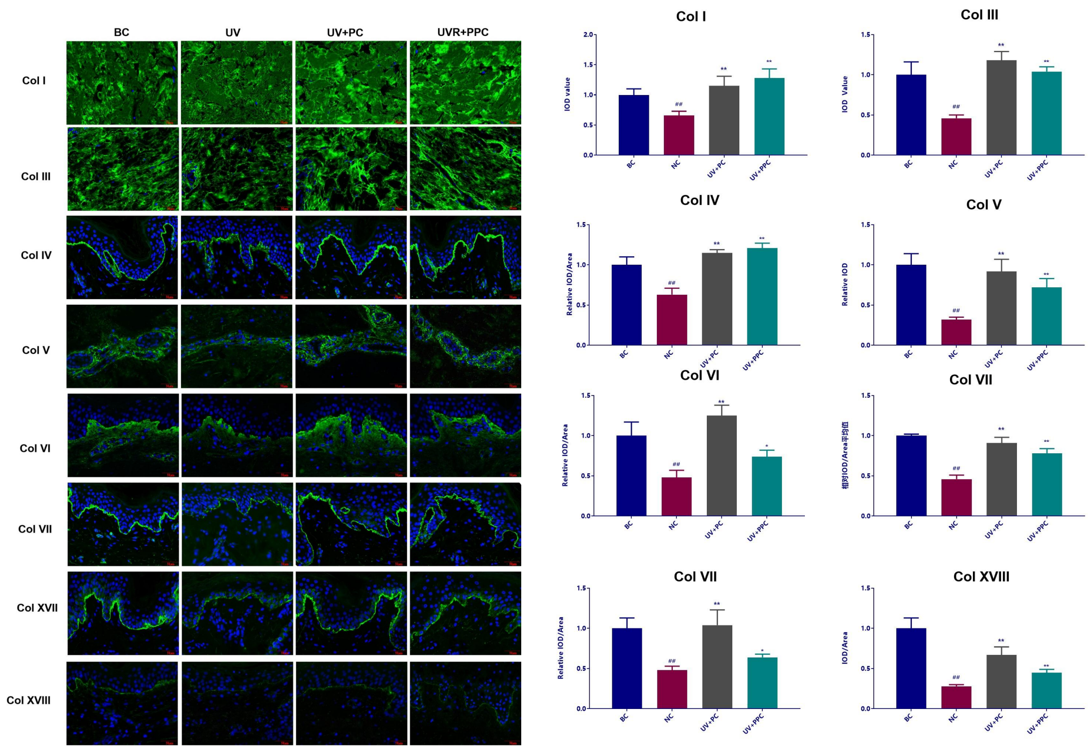
Multiphoton Microscopy Results:

Using multiphoton microscopy, PPC treatment resulted in a significant increase in collagen fiber content compared to the control group, with an improvement of 305.41%. Elastin fiber content also increased by 137.78%, confirming the efficacy of PPC in promoting the synthesis of both collagen and elastin fibers, which are critical components responsible for skin elasticity and firmness (Figure2).

Clinical Efficacy Study:

In the first week, skin elasticity (R2) increased significantly by 8.66% ($p<0.001$), while skin firmness (R0) decreased by 9.93% ($p<0.001$). By the second week, skin elasticity further improved by 9.50% ($p<0.001$), and skin firmness showed a further decrease of 10.29% ($p<0.001$). By the fourth week, skin elasticity increased by 19.03% ($p<0.001$), and skin firmness decreased by 26.81% ($p<0.001$). At week 8, elasticity improvement reached 28.42% ($p<0.001$), and firmness decreased by 48.30% ($p<0.001$). Jawline contour showed significant improvement throughout the study. The jawline arc angle decreased by 0.53% in the second week ($p=0.013$), by 0.82% in the fourth week ($p=0.009$), and by 1.46% in the eighth week ($p<0.001$), indicating a noticeable improvement in the jawline's definition.

In terms of wrinkle length and depth, in the first week, tear trough wrinkle length significantly decreased by 6.45% ($p=0.003$), but there were no significant changes in other wrinkles such as nasolabial folds, marionette lines, and tear trough depth ($p>0.05$). By week 2, nasolabial fold length, marionette line depth, and tear trough length significantly decreased by 12.42%, 4.60%, and 8.41%, respectively ($p<0.05$). In the fourth week, significant reductions were observed in all wrinkles, including nasolabial fold length (17.22%), depth (2.60%), marionette line length (9.72%), depth (6.34%), tear trough length (13.08%), and depth (2.65%) ($p<0.05$). By week 8, reductions continued across all wrinkles, with nasolabial fold length (23.22%), depth (5.93%), marionette line length (14.22%), depth (5.73%), tear trough length (22.63%), and depth (6.62%) showing significant improvements (p<0.001). For volume reduction, cheek sagging volume decreased significantly by 5.96% at week 2 (p<0.001), by 7.61% at week 4 (p<0.001), and by 9.58% at week 8 (p<0.001). Jawline sagging volume showed reductions of 7.88% at week 2 (p<0.001), 8.11% at week 4 (p=0.002), and 11.63% at week 8 (p<0.001), indicating significant improvement in skin contour and tightness(Figure3)..



(**a**) (**b**)

Figure 1. Multiphoton imaging and quantitative analysis of collagen subtypes in ex vivo skin tissues. (a) Representative multiphoton images of collagen types I, III, IV, V, VI, VII, and XVIII in each group: baseline control (BC), UV-irradiated (UV), UV plus vehicle cream (UV+PC), and UV plus peptide-protein complex cream (UV+PPC). (b) Quantification of fluorescence intensity for each collagen subtype, showing the effects of PPC treatment on collagen synthesis after UV exposure. Values are mean ± SD. p < 0.05, p < 0.01 vs. UV group.

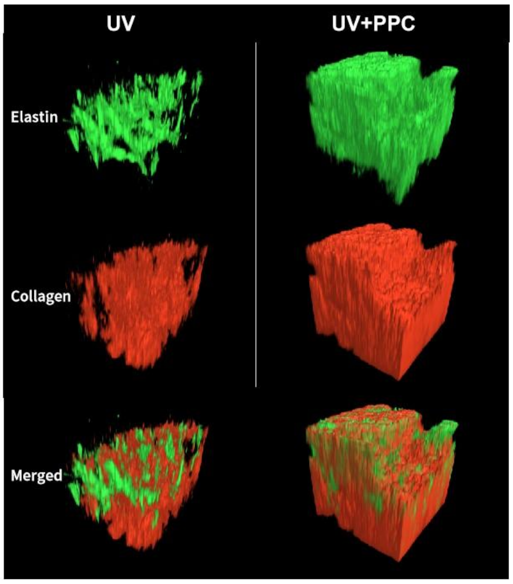


Figure 2. Multiphoton microscopy images showing the effects of UV radiation (UV) and PPC treatment on elastin and collagen fibers. The UV panel shows the distribution of elastin (green) and collagen (red) after UV exposure, while the UV+PPC panel demonstrates enhanced collagen and elastin content following PPC treatment. The Merged image illustrates the combined increase in both collagen and elastin, reflecting improved extracellular matrix (ECM) integrity after PPC treatment.

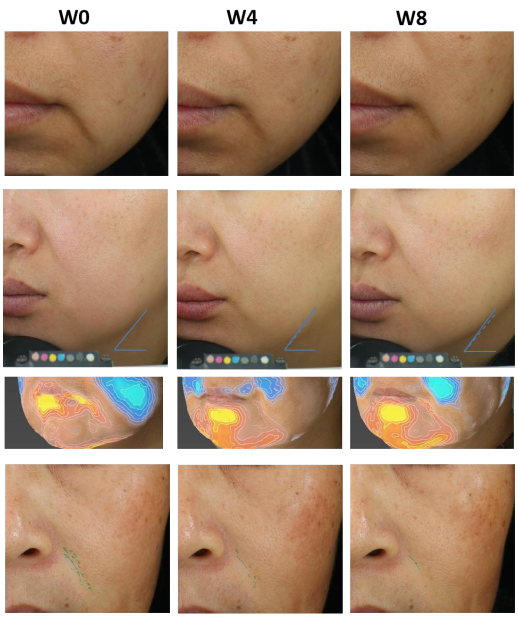


Figure 3. Facial improvements over 8 weeks are shown, highlighting enhanced jawline firmness, reduced cheek and jawline sagging, and overall skin tightening, with visible improvements in facial contours and skin resilience.

4. Discussion

The results of this study demonstrate the significant potential of the Peptide-Protein Complex (PPC) in promoting skin rejuvenation, improving both skin elasticity and firmness, and reducing wrinkles and sagging over an 8-week period. The significant increase in skin elasticity (R2) and the corresponding decrease in skin firmness (R0) indicate that the PPC-containing cream effectively enhances skin structure and tone. These observed improvements in elasticity and reductions in skin sagging are crucial markers of anti-aging efficacy, likely associated with increased collagen synthesis and improved skin resilience.

The multiphoton microscopy results from the ex vivo skin tissue treatment confirm that PPC stimulates the synthesis of collagen and elastin fibers, which are vital for maintaining skin elasticity and firmness. The substantial increase in collagen fiber content (305.41%) and elastin fiber content (137.78%) in ex vivo tissues suggests that PPC can stimulate fibroblast activity and enhance extracellular matrix (ECM) integrity. This structural change is likely responsible for the observed improvements in skin appearance, such as reductions in wrinkle length and depth in the clinical study.

In the clinical study, where participants applied the PPC-containing cream, the ability of PPC to reduce facial wrinkles—especially nasolabial folds, marionette lines, and tear troughs—was observed at multiple time points. Notably, significant reductions in wrinkle length and depth were observed by week 8, with reductions as high as 23.22% for nasolabial folds ($p<0.001$), confirming that the PPC-based formulation provides an effective solution for visible signs of skin aging. These results suggest that PPC's peptide-based formulation can stimulate ECM repair and regeneration, helping to counteract photoaging and skin laxity.

The jawline contour improvement observed in this study, marked by a significant reduction in the jawline arc angle (1.46%, $p<0.001$) over 8 weeks, further supports the efficacy of the PPC cream in restoring facial structure. The reduction in sagging volume in the cheeks (9.58%) and jawline (11.63%) further emphasizes its potential for combating skin laxity and improving facial contours. These findings suggest that PPC could play a significant role in non-invasive facial rejuvenation therapies, contributing to an overall improved facial appearance.

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5. Conclusion

The findings from this study indicate that the Peptide-Protein Complex (PPC), delivered through a topical cream, offers promising anti-aging benefits by significantly enhancing skin elasticity, firmness, and texture. The PPC's ability to increase collagen and elastin synthesis, reduce wrinkle depth and length, and improve facial contours demonstrates its potential as an effective ingredient in skincare formulations. Notably, the significant reduction in facial sagging and wrinkles, particularly in the nasolabial folds, marionette lines, and tear troughs, highlights its capacity to rejuvenate aging skin.

Given the positive outcomes observed in both ex vivo and clinical settings, the PPC-containing cream appears to be an effective approach for improving the structural integrity of the skin, reducing visible signs of aging, and enhancing facial contours. These results support the development of PPC-based skincare products aimed at providing both immediate and long-term anti-aging effects. Further studies with larger, more diverse populations are needed to confirm these findings and fully assess the long-term benefits of PPC in various skin types and conditions.