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Impact of targeting collagen diversity on skin aging signs: a pilot study

Abstract

Introduction: Skin aging is marked by a decline in proteostasis, significantly impacting collagen, the skin's major structural protein. The human skin collagenome comprises 16 types with diverse roles, classified into four families: junctional, initiator, pillar, and bonding. Preserving this collagen biodiversity is crucial for addressing skin aging. This clinical exploratory study assessed the anti-aging activity of a serum containing *Grifola frondosa* fruiting body extract 0.5%, Rhamnose 5%, and different peptides at 3% (Palmitoyl Tripeptide-1 and Palmitoyl Tetrapeptide-7).

Methodology: Fifty-three women (mean age: 62.1 years) applied a novel serum twice daily for 12 weeks after a 30-day washout period. Efficacy was assessed through clinical scoring, self-assessment questionnaires, and collagen density measurements.

Results: The serum significantly improved all assessed skin aging signs after 12 weeks, with improvements in fine lines, plumpness, and radiance appearing as early as after 2 weeks. Fine lines, plumpness, radiance, wrinkles and sagging were reduced by 32.7%, 16.1%, 15.0%, 13% and 7.5% respectively after 12 weeks, alongside a 2.4% increase in collagen density. All observed effects were statistically significant and clinically relevant.

Conclusion: This study demonstrated the efficacy of a novel serum in improving signs of aging, including a physiologically relevant increase in collagen density despite the short treatment duration. The observed improvements in skin structure reflected in enhanced plumpness and reduced ptosis, likely contribute to the observed reductions in fine lines, wrinkles, and improved skin radiance. These findings support the importance of targeting collagen for anti-aging benefits and encourage further research into the serum's mechanism of action on skin collagen stimulation.

Keywords: skin aging, collagens, *Grifola frondosa,* serum, face, neck

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Introduction

A hallmark of aging is the decline in proteostasis, which significantly impacts collagen, the most abundant protein family in human skin (comprising 70-80% of its dry weight).[1] The collagen family comprises many different types of collagen. In adult human skin, the collagenome consists of 16 collagens identified at the protein level. These collagens have diverse roles, and while some are less abundant, they all contribute to the collagen network and overall skin structure.[2–3] To date, these collagens are classified in different subfamilies based on their role in the extracellular matrix comprising Fibril Associated Collagen with Interrupted Triple helix (FACIT), microfilaments and anchoring collagens.[3] Conversely, some collagens, such as collagen VI, XI cannot be classified.

Skin aging is characterized by a well-documented decline in both collagen density and the qualitative integrity of collagen fibers.[4–5] Effectively addressing skin aging issues requires preserving this collagen biodiversity in order to restore collagen homeostasis and as a result the skin structure and function and targeting all four collagen families is crucial for restoring skin structure.

We created a new skin specific collagen classification system considering both their role in network formation and their location within the skin. Moreover, a clinical exploratory study assessed the anti-aging activity of a serum containing *Grifola frondosa* fruiting body extract 0.5%, Rhamnose 5%, and different peptides at 3% (Palmitoyl Tripeptide-1 and Palmitoyl Tetrapeptide-7). All ingredients stimulate different collagen families (data not shown).

Methods

Collagen classification

As identified by Theocharidis et al., the human skin collagenome comprises 16 collagens expressed at the protein level in adult human skin.[2] Based on the work of Schulz et al, 4 families were defined to classify the different types of collagen, considering their location in the skin, their role in the skin's structure, and/or their role in organizing the collagen network.[3] The ECM is composed of different collagen structures, including fibrils made up of collagens I, III, and V; FACIT collagens that decorate the surface of fibrils (e.g., Collagens XII and XIV); microfilaments of collagen (e.g., collagen VI); and, finally, anchoring collagens like collagen VII.

Exploratory clinical study

A 12-week open-label single group study was conducted in 53 women aged between 40 and 70 years with mild to moderate wrinkles, fine lines, lower face ptosis, and imperfections in radiance and plumpness. Following a 30-day washout period maintaining their usual moisturizer containing no anti-aging ingredients, participants applied the serum twice daily to the face and neck, followed by their moisturizer. Efficacy of the serum was assessed through clinical scoring by an expert grader (0-9 scale for wrinkles, fine lines, ptosis, radiance, and plumpness), self-assessment questionnaires, SIAscope® (Laboratoire Cosderma, France) measurements of collagen density and spontaneous safety feedback (data not presented). The mean age

of participants was 62.1 years (range: 41-70), and the study included diverse phototypes and skin types.

Results

Collagen classification

Figure 1 shows these four collagen families. Junctional collagens (IV, VII, XIII, XV, XVII, and XVIII) can be found at the dermal-epidermal junction or within the epidermis, anchoring the epidermis and dermis or providing structural support within the epidermis itself. Initiator collagens (V and XI) are located within the core of collagen fibers, regulating fiber diameter and mechanical properties. Pillar collagens (I and III) are the most prevalent collagens and form the fiber skeleton. They are crucial for the dermal architecture. Bonding collagens (VI, XII, XIV, XVI, XIX, and XXII) connect fibers to each other or to other components of the extracellular matrix (ECM).

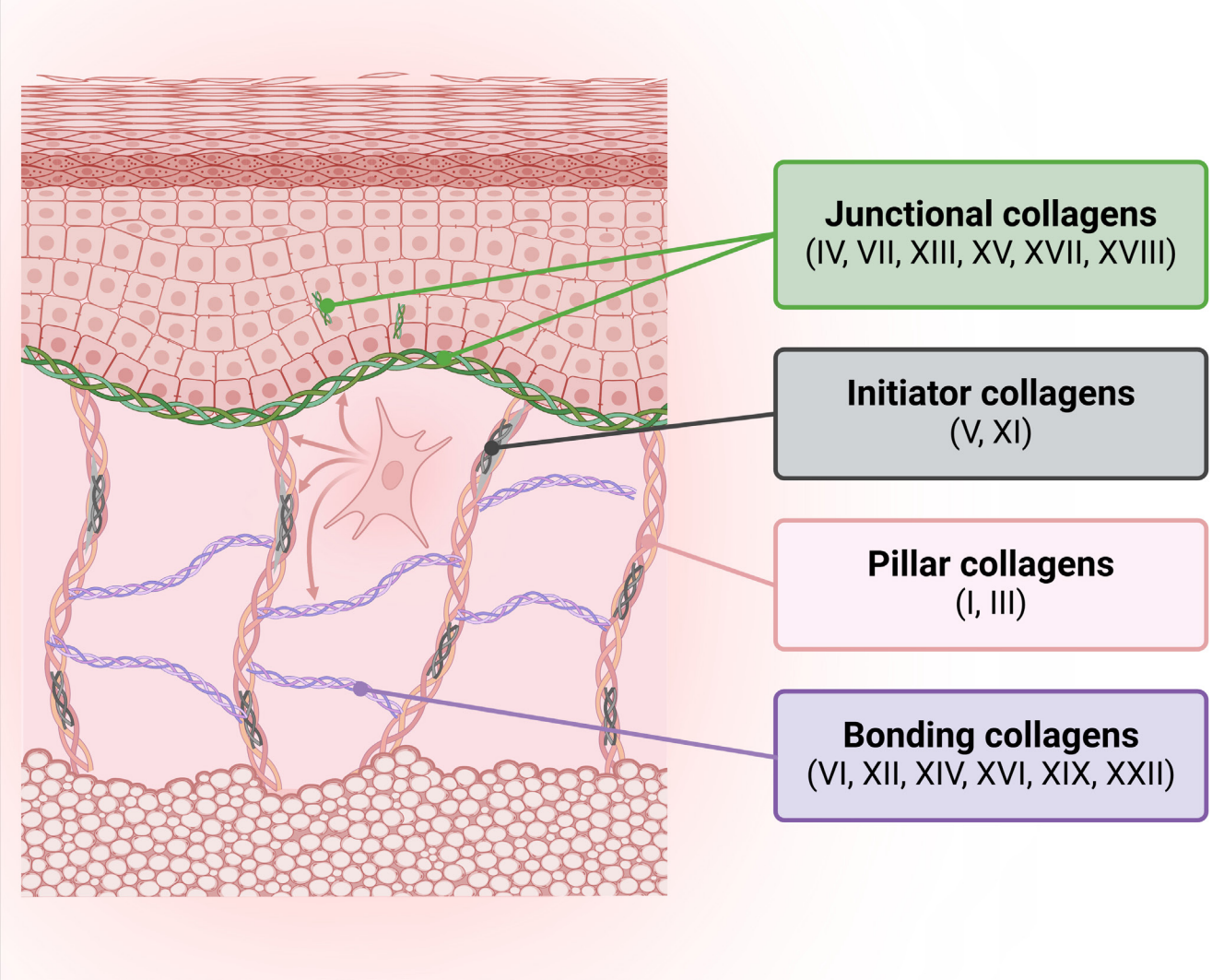

Figure 1 A proposed classification of the 16 skin collagens based on their role in network formation or their location within the skin.

Exploratory clinical study

The mean age of participants was 62.2±6.5 years (range: 41-70 years). Phototype type I accounted for 13.5%; type II for 32.7%; type III for 15.4%; Type IV for 17.3%; Type V for 13.5% and type VI for 7.7% of the subjects. A total of 46.2% had a combination skin type, 13.5% had dry, 28.8 normal and 11.5 oily skin and the study included different photo- and skin types.

After 12 weeks of treatment, clinical expert scoring revealed improvement of all assessed signs of aging. Improvements in fine lines, plumpness, and radiance were observed as early as 2 weeks (-15.5%, -7.6%, and -8.9%, respectively), reaching -32.7%, -16.1%, and -15.0%, respectively, after 12 weeks. A reduction in wrinkles was first observed after 6 weeks (-9.7%), with a gradual improvement continuing throughout the study, culminating in a -13.0% reduction after 12 weeks. A positive effect on sagging was observed at 8 weeks (-7.1%), with a final improvement of -7.5% at the end of the treatment period. All observed effects (Figure 2A) were statistically significant and clinically relevant. The SIAscope® analysis revealed a 2.4% increase in collagen fiber density at the end of treatment (Figure 2B).

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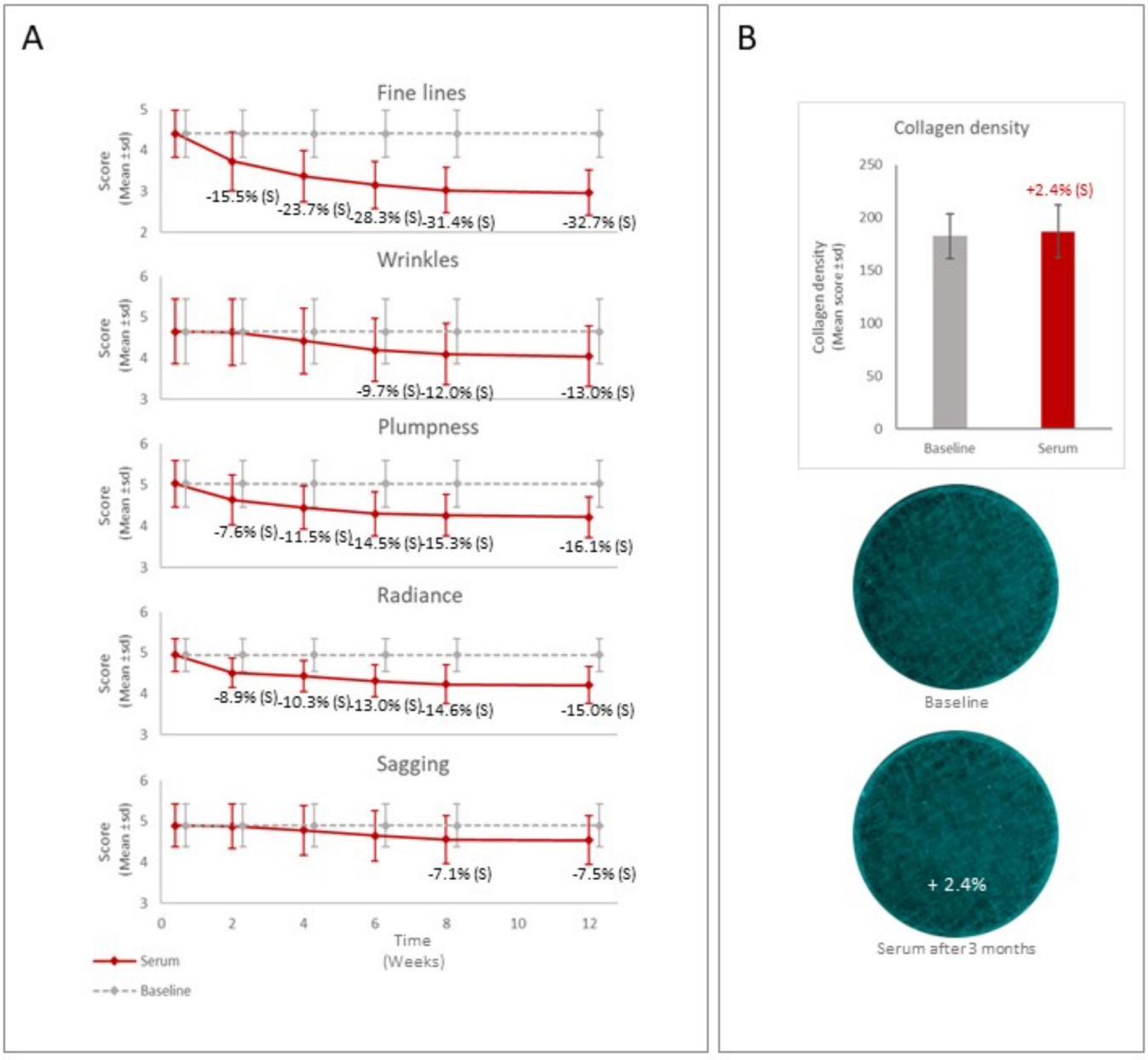

Figure 2 Clinical efficacy of the tested serum on the improvement of aging signs in female healthy volunters.

(A) Effects on wrinkles, fine lines, plumpness, sagging, and radiance were assessed by expert scoring using 10-point scales. **(B)** Collagen density was measured using the SIAscope®.

Discussion

During aging, a loss of proteostasis, a hallmark of aging, occurs. Collagen, the most abundant protein family in skin by mass, is significantly affected by this phenomenon, resulting in age-related decline in density and structural integrity.[4–5] The human skin collagenome comprises 16 collagen types we propose to classify into the 4 following families: junctional, pillar, initiator, and bonding. All are impacted by aging. Both collagen I and III, the major fibril-forming collagens, decrease with age,[6] disrupting the organization and structure of the collagen network. Additionally, during skin aging the structure and composition of the dermal-epidermal junction (DEJ) is altered due to a decrease in key components like collagen IV and VII;[7] both are junctional collagens. While age-related changes in other collagen types are not fully elucidated, preserving skin collagen biodiversity is crucial for restoring collagen homeostasis and, consequently, skin structure and function. To provide preliminary evidence supporting this hypothesis, we conducted a clinical study to evaluate the anti-aging efficacy of a serum containing three active ingredients (*Grifola frondosa* fruiting body extract, Rhamnose, and peptides (Palmitoyl Tripeptide-1 and Palmitoyl Tetrapeptide-7) which stimulate the expression of various collagen types.[8–10] This study demonstrated a clear improvement in signs of aging, including a 2.4% increase in collagen density. While this increase may be modest, it

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is physiologically relevant considering the average annual collagen loss during adulthood of approximately 1%[11] and the short treatment duration.

The study has 2 major limitations. The protocol did not plan for biopsies to confirm histological changes and we did not make any photos at baseline and at the end of the study which would have allowed to visually appreciate changes. Moreover, we were not able to directly link these results to skin collagen biodiversity. However, we demonstrated that the tested serum significantly stimulates the overall collagen production confirmed through improved skin aging signs. Concomitantly with the increase in collagen density, improvements in ptosis and plumpness scores were observed, suggesting enhanced skin mechanical properties. This structural improvement likely contributes to the observed improvements in skin appearance, as reflected in the fine lines, wrinkles, and radiance scores.

Conclusion

The present exploratory results support the importance of collagen in reducing skin aging signs and support the value of the tested triple combination. The present results encourage to continue research to better characterize the mechanism of action of the tested active ingredients and provide further evidence of their efficacy in stimulating skin collagen.

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Conflict of interests

The authors declare there is no conflict of interest.

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